The International Workshop on the History of Chemistry 2015
Tokyo (IWHC 2015 Tokyo)

TRANSFORMATION OF CHEMISTRY

FROM THE 1920S TO THE 1960S

PROCEEDINGS

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Cover illustration: Cherry Blossom on the Tokyo Institute of Technology
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Preface

About fifty historians and chemists participated in the International Workshop on the History of Chemistry (IWHC 2015 Tokyo) held at the Tokyo Institute of Technology between March 2 and 4, 2015.

The main theme of this workshop was the transformation of chemistry from the 1920s to the 1960s. Chemistry underwent many changes during these years: We saw the development of biochemistry, the emergence of polymer, quantum, and computational chemistry, and the so-called Instrumental Revolution. New methods, theories, and technologies opened up new fields in the chemical sciences. Chemistry expanded its scope by interacting with other sciences such as physics, biology, medicine, and mathematics. The chemical industry grew in importance and supported national and international economies. Production of plastics, synthetic fibers and rubber, fertilizers, drugs, and numerous chemicals shifted from coal to petroleum. The environmental problems caused by synthetic materials tarnished the public image of chemistry as well. Chemistry was also greatly influenced by World War II and the Cold War, when it served military and security purposes.

In Japan, too, this period saw remarkable developments in chemistry. The first generation of Japanese chemists began conducting research in the early 20th century. To compete with Western chemists, Japanese chemists adopted a research strategy using techniques developed in Europe to study the structural components of Japan's local natural products, such as *urushi* lacquer, *ai* (indigo), green tea, and rice. Japanese researchers also chemically studied the products of indigenous industries, such as *sake*, soy sauce, *miso,* and ceramics. After half a century, however, the accomplishments of, for example, the seven Japanese Nobel laureates in chemistry did not appear fundamentally different than those of their Western counterparts. Clearly, a transformation in chemical research in Japan occurred between the 1920s and the 1960s. Was this change simply due to the globalization of Western chemistry or also due to how chemistry in Japan was institutionalized? Does this change have to do with any peculiarity of Japanese chemistry?

The aim of this workshop was to stimulate discussion of the transformation of chemistry in Japan and in the world during this period. This conference brought together scholars investigating the history of chemistry in the 20th century from different perspectives. The three-day workshop included three keynote lectures and eight sessions with twenty-three papers. The keynote speakers consisted of these distinguished historians of chemistry: Jeffery Johnson and Mary Jo Nye from the United States, and Ernst Homburg from the Netherlands. Each presentation was followed by lively discussions. The IWHC 2015 Tokyo was a fruitful and successful international conference on the history of modern chemistry. We are delighted here to make the proceedings open to the public.

Yasu Furukawa

Chair, Program Committee, IWHC 2015 Tokyo

Nihon University

Acknowledgements

From Bio-organic Chemistry to Molecular and Synthetic Biology: Fulfilling Emil Fischer's Dream

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Introduction

The following paper is intended to provide a broad context for many of the subsequent papers of the workshop. I will do this by reflecting on a century of development in one area of the discipline of chemistry, with a particular focus on what I am calling "Emil Fischer's dream." In 1915 Fischer envisioned a central aspect of the transformation of chemistry in the twentieth century, the development of an interdisciplinary approach to the chemistry of life that would not only result in greater insight into the nature of life, but ultimately allow human beings to change the nature of life itself.

A century later, I believe we can agree that Fischer's dream is being fulfilled, and as I will argue, the critical developments that have made this possible occurred precisely during the period of the workshop's primary focus, the 1920s-1960s. I will assess developments in this period, including the loss of German leadership to other nations and the increasingly significant role of Japanese chemists, within the broader context of the development of synthetic-chemical and biochemical technologies applied to the study of living nature during the 20th century as a whole. I would like to divide the era from 1915 to 2005 into three principal generations, the first of which was a generation of crisis bracketed by world wars. Key transitions to new generations occurred around 1945 at the end of the Second World War, and in the mid-1970s, with the advent of modern biotechnology and genetic engineering. It is surely not a coincidence that each of these transition periods was followed by a flood of crucial innovations in the chemistry of biology and natural products, as well as physical methods and instrumentation. Space will not permit more than some selected references to developments since the 1970s, including the most recent wave of innovation in the current generation beginning around 2005, which is characterized by the emergence of the new discipline of synthetic biology. I will conclude by mentioning some interesting developments related to this new discipline in our host institution, the Tokyo Institute of Technology.

Emil Fischer's dream

Emil Fischer (1852-1919) was of course the second Nobel Prizewinner in Chemistry (1902), leading organic chemist of his day and a pioneer of the synthetic chemistry of natural products, director of the largest chemical institute in Germany, and by 1915 Vice President and most influential scientist in the leadership of the young Kaiser Wilhelm Society for the Advancement of the Sciences, today's Max Planck Society. The Society was creating a series of research institutes, with emphasis on the physical and biological borders of chemistry –

which reflected Fischer's own goals of promoting interdisciplinary collaboration outside the increasingly conservative German universities and academies.[1]

What was Fischer's dream? It was a vision he expressed both publicly and privately, especially in a lecture presented about one hundred years ago at the beginning of the second year of the Great War, which had devastated scientific life in Europe. Looking beyond the war and indeed beyond his own lifetime, he envisioned the fruits of collaboration between organic chemistry and biology in creating a discipline he called "synthetic-chemical biology."[2] What did Fischer envision by the phrase "synthetic-chemical biology"? Essentially it was the chemical understanding and control of living matter. Fischer's lecture and his other correspondence at the time effectively present a research program for the new discipline, which I would like to briefly summarize here.

- First: to understand the individual cell "not only as a machine that constructs and repairs itself, but also as a chemical laboratory of the most amazing kind," and its chemical interactions with other cells in an organism through the metabolic processes of life.[3]

- Second: to understand the origins, composition, function, and changes undergone by various chemical substances in these processes, in order to duplicate and where possible to improve upon the already highly efficient processes of intra-cellular synthesis.[4] Thus while a plant could produce carbohydrates from carbon dioxide in a matter of minutes and with almost 100% yield using the energy from sunlight, a chemist could only achieve "minute yields" by synthesizing those same carbohydrates in a chemical laboratory – which Fischer knew all too well, as his work in this field had led to his Nobel Prize.

- Third: to focus especially on the role of enzymes in achieving amazingly high yields in biosynthesis and fermentation processes, "with a view toward their artificial preparation or replacement."[5] In other words, synthetic enzymes and chemically modified microorganisms would be the key to controlled biosynthesis on an industrial scale of carbohydrates and proteins for food and other purposes, as well as products such as ammonia (by duplicating bacterial nitrogen fixation).[6]

- Finally: the total synthesis of the nucleic acids, and the introduction of artificial nucleic acids into cell nuclei, in order to "gain a radical chemical influence on the development of the organism" by altering "the chemical building material of the cell," so as "in a sense to trick (*betrügen*) it."[7] On the assumption that the mutations postulated by Hugo de Vries' theory of discontinuous evolution were related to

[1] Jeffrey Allan Johnson, *The Kaiser's Chemists: Science and Modernization in Imperial Germany*, Chapel Hill, N. C.: University of North Carolina Press, 1990, chs. 1-2; Robert E. Kohler, *From Medical Chemistry to Biochemistry: The Making of a Biomedical Discipline*, Cambridge, UK: Cambridge Univ. Press, 1982, ch. 1.

[2] H. Emil Fischer, "Die Kaiser-Wilhelm-Institute und der Zusammenhang von organischer Chemie und Biologie" (presented 28 October 1915), in *Untersuchungen aus verschiedenen Gebieten*, ed. Max Bergmann, Berlin: Julius Springer, 1924, 797-809, on 808.

[3] Fischer (note 2), 798.

[4] Fischer (note 2), 799.

[5] Fischer (note 2), 805-806.

[6] Fischer (note 2), 804-805; for wartime efforts of the Germans along these lines cf. Robert Bud, "Molecular biology and the long-term history of biotechnology," in *Private Science: Biotechnology and the Rise of the Molecular Sciences,* ed. Arnold Thackray, Philadelphia: University of Pennsylvania Press, 1998, 3-19, on 7; Robert Bud, *The Uses of Life: A History of Biotechnology*. Cambridge, UK: Cambridge Univ. Press 1993, 45; Luitgard Marschall, *Im Schatten der chemischen Synthese: industrielle Biotechnologie in Deutschland (1900-1970)*, Frankfurt a.M.: Campus, 2000, 70-75.

[7] Fischer (note 2), 808.

chemical changes in the cell nucleus, Fischer intended to begin with experiments on "lower life forms," and he only half-jokingly called this "my lusting for creation."[8]

"And thus I see," he concluded, "half in a dream, the emergence of a synthetic-chemical biology that will transform the living world as fundamentally as chemistry, physics, and industry have done for so long with non-living nature."[9] Here then was Fischer's dream – to transform life itself, using chemical means to "trick" the cell into developing in an artificially-controlled way, or producing something other than it would "naturally" produce. It is a vision of a future whose realization we are currently witnessing, through what began as molecular biology and genetic engineering, but today encompasses much more diverse and precise methods in fields known as protein engineering, metabolic engineering, and synthetic biology. Note that none of these fields contains the word "chemical" in its name, yet I further submit that Fischer would have recognized them as the "synthetic-chemical biology" whose emergence he predicted in 1915.

In regard to this I would like to mention one other project Fischer had at that time: to synthesize a "giant" organic molecule and make it visible under an ultramicroscope (then the most powerful imaging device) by incorporating a "strongly fluorescent" compound. Fischer's target would have a molecular weight of 8,000.[10] That might hardly seem "giant" by today's standards, but it was twice the size of the largest "record molecule" he (let alone anyone else) had yet attained by total synthesis.[11] And that might have been enough to satisfy Fischer's doubts about the even larger molecular weights, up to 16,000 or more, that others had published for proteins. Sadly, his research was interrupted by the Great War that killed millions across Europe, including two of Fischer's three sons. Never in robust health, Fischer exhausted himself as a scientific and technical advisor in the service of his country's war effort. His death in 1919 left to future generations the dream of synthesizing giant fluorescent molecules, creating synthetic enzymes for artificial biosynthesis, and inducing mutations through artificial nucleic acids.

Fulfilling Fischer's dream – or not: the work of later generations
1) The crisis generation, 1915-1945

The era of the first generation following Fischer's 1915 speech, the three decades until the end of the Second World War in 1945, can best be described as an era of crisis. A crisis is by definition a period of transition, but also a period of danger in which "normal" development becomes difficult if not impossible. This was certainly the case for Germany, but also even for countries like the United States, which was spared the worst impact of the world wars. The recognition gained by chemists as a result of the First World War, the "chemists' war," was at best a mixed blessing, because the association of chemistry with poison gas cast a stigma on the discipline, from which arguably its reputation has never fully recovered. In the 1920s the German economy itself never fully recovered from a hyperinflation followed by a

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8   Fischer to Adolf von Baeyer, 4 Aug. 1913, in Outgoing Letters, Box 4, Emil Fischer Papers, Bancroft Library, UC Berkeley, CA. As early as 1907 Fischer had, in a humorous speech to his students, envisioned a future chemist synthesizing artificial life, including a homunculus that could replace their professor. See "Festrede gesprochen bei dem Ausflug des chemischen Instituts ... am 20. Juli 1907," in Folder "Addresses 1906-1910," Carton 4, Emil Fischer Papers, cited in Joachim Schummer, *Das Gotteshandwerk: Die künstliche Herstellung vom Leben im Labor*, Berlin: Suhrkamp, 2011, 76, 219-220.

9   Fischer (note 2), 808; cf. Horst Remane, *Emil Fischer*, Leipzig: B. G. Teubner, 1984, 63; Ute Deichmann, "Crystals, Colloids, or Molecules: Early Controversies about the Origin of Life and Synthetic Life," *Perspectives in Biology and Medicine* **55/4** (2012): 521–42, on 531.

10   Fischer to Carl Duisberg, 27 June 1914, in Outgoing Letters, Box 4, Fischer Papers (note 8).

11   Kurt Hoesch, *Emil Fischer: sein Leben und sein Werk*, Berlin: Verlag Chemie, 1921, 475.

drastic stabilization of the currency in the aftermath of the First World War, which reinforced an attitude of austerity in the minds of German financial experts that has continued to the present day. The resulting limits on funding for science including chemistry became worse in the wake of the Great Depression beginning in 1929, and the renewed expansion of the discipline in the late 1930s came in the context of a National Socialist regime with a policy of rearmament and economic autarky. This ideological attitude also fostered an autarkic intellectual tendency among scholars and scientists, which seriously hampered the free exchange of ideas particularly with scholars of the "wrong" ethnicity, religion, or political outlook.[12] Similar tendencies occurred in other nations, including the Soviet Union and arguably also to some extent Japan during the wartime period 1937-1945. But the outcome was most detrimental to chemistry in Germany; as the discipline's ostensible world leaders, the Germans had the most to lose.

Consider the factors in this period that affected German chemists in Fischer's area, the structure and synthesis of biological molecules:

First, the problem of leadership: Fischer's death in 1919 robbed the University of Berlin and the Kaiser Wilhelm Society of his scientific leadership in the postwar crisis period. One possible successor, Richard Willstätter, was widely recognized as the leader of the next generation of German organic chemists. But Willstätter, who had left the Kaiser Wilhelm Society to succeed Adolf Baeyer in Munich in 1915, refused to come back to Berlin. The best-known of the Society's chemists, Willstätter's friend Fritz Haber, famous or infamous as the scientific leader of German chemical warfare, encountered highly influential opposition within the dye industry because he was a physical chemist and not deemed capable of contributing effectively to organic chemistry.[13] Little did his opponents realize that in the new era, organic and biological chemistry would increasingly depend upon physical methods and instruments, beginning with x-ray crystallography.

Willstätter in the early 1920s continued to be the most respected German organic chemist. But he developed a theory of enzymes as "small reactive molecules adsorbed on colloidal carriers" rather than proteins. Clearly uneasy with his results (which may have been due to impure samples), and at the same time depressed by the rising tide of anti-Semitism affecting his university (Munich was then the major center of Nazism), in 1924 he resigned his professorship with an open protest against his faculty's inability to ignore ethnic considerations in making appointments. He never again took a position or set foot in a laboratory (until late in 1938, when he realized that he would have to leave Munich to escape a concentration camp or worse, he remained in his home in the city and worked through an assistant, communicating by telephone).[14] By the late 1920s, however, the research of the American biochemists James B. Sumner at Cornell and John H. Northrop at the Rockefeller

[12] There is now a very large literature on the impact of National Socialism on German science. Some useful general historiographical considerations are in Margit Szöllösi-Janze, "National Socialism and the Sciences: Reflections, Conclusions and Historical Perspectives," in *Science in the Third Reich* ed. Margit Szöllösi-Janze, Oxford, UK: Berg, 2001, 1-35; for chemistry and biochemistry see the works of Ute Deichmann, esp. *Flüchten, Mitmachen, Vergessen: Chemiker und Biochemiker im Nationalsozialismus*. Weinheim: Wiley-VCH, 2001, and most recently Helmut Maier, *Chemiker im "Dritten Reich". Die Deutsche Chemische Gesellschaft und der Verein Deutscher Chemiker im NS-Herrschaftsapparat*, Weinheim: Wiley-VCH, 2015.
[13] Margit Szöllösi-Janze, *Fritz Haber 1868–1934: Eine Biographie*, Munich: C. H. Beck, 1998, 438-447.
[14] Richard Willstätter, *From my Life: The Memoirs of Richard Willstätter*, trans. Lilli Hornig from the 2d German ed. (Weinheim, 1958), New York: W. A. Benjamin, 1965, 360-367, 428-431; Freddy Litten, *Der Rücktritt Richard Willstätters 1924/25 und seine Hintergründe: ein Münchener Universitätsskandal?* München: Institut für Geschichte der Naturwissenschaften, 1999.

Institute demonstrated that enzymes were proteins.[15] This won them shares of the Nobel Prize in 1946, while undermining the authority both of Willstätter and, by extension, German structural biochemistry.

Fischer's closest associate in his final synthetic projects, Max Bergmann, had been unable to get a university position and in 1921 became director of the newly established Kaiser Wilhelm Institute for Leather Research in Dresden, where he investigated the chemistry of skin and continued the synthetic peptide and protein research begun in Berlin. This led to a major achievement in 1932 with the carbobenzoxy method developed by Bergmann and his associate Leonidas Zervas. This was the first effective means of synthesizing longer chains of peptides and integrating amino acids that were not susceptible to Fischer's earlier methods.[16] Bergmann also mentored a young American postdoc, Vincent du Vigneaud, who would later make a name for himself in protein synthesis.[17] But in 1933, the advent of the National Socialist regime forced Bergmann as a "non-Aryan" out of his position, so that he and Zervas (who was Greek) emigrated to the United States, where they continued their research in the Rockefeller Institute, enhancing its status as one of the major American biochemical research centers.

<u>Second, funding limitations:</u> As the postwar inflation had initially worsened in 1920, several institutions had been established to develop alternative sources of funding. Among these were the *Notgemeinschaft* (Emergency Association for German Science, later known as the *Deutsche Forschungsgemeinschaft* or German Research Foundation) co-founded by Fritz Haber with mainly federal government support, as well as the chemical industry's funding groups organized by Carl Duisberg of the Bayer Corporation. For the support of chemistry by the *Notgemeinschaft* in particular, an unexpected supplementary source came from Japan through the philanthropy of Hajime Hoshi, founder and president of the Hoshi Pharmaceutical Company (specializing in vaccines, alkaloids, and other natural products) and also founder of a pharmaceutical school that eventually became Hoshi University. Along with a larger endowment for German science in general, after meeting Haber in Berlin in the fall of 1922 Hoshi offered supplementary support for the physical sciences in 1922-25 in the amount of 2,000 yen or $1,000 per month, for which Haber organized the Japan Committee chaired by himself with Richard Willstätter as the vice chair, and several other top chemists and physicists along with government officials as members. This committee directed around a hundred grants to critical projects in a non-bureaucratic manner over two years, including Carl Neuberg's biochemical studies of sugar fermentation at the Kaiser Wilhelm Institute for Experimental Therapy.[18] Unfortunately the devastating Tokyo earthquake of Sept. 1, 1923, severely affected Hoshi's company and reduced his ability to extend his support, so that from 1924 the Japan Committee's more modest grants had to be matched by German government or industry funds. After 1925 the committee became inactive.

Haber and Willstätter sought to revive the Japan Committee in 1928, making an appeal to the German federal government by using a classic declinist argument: that German leadership in chemistry was threatened from abroad, particularly in the interdisciplinary fields on the borders with physics and biology. Funding was particularly vital in these fields, because on both sides of the discipline the growing significance of instrumentation and physical approaches – ultracentrifuges, x-ray apparatus, etc. – meant that cutting-edge research was increasingly expensive. By that time the declinist argument was becoming highly popular

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[15] Joseph S. Fruton, *Proteins, Enzymes, Genes: The Interplay of Chemistry and Biology*, New Haven, Conn.: Yale University Press, 1999, 208.

[16] Fruton (note 15), 189.

[17] Deichmann (note 12), 258.

[18] Szöllösi-Janze (note 13), 363-364.

among German chemists, so that it was beginning to seem more than a rhetorical device. Despite promising beginnings before the war, and the establishment of some Kaiser Wilhelm Institutes related to biochemistry, the field was encountering institutional difficulties in the universities.[19] Even in the relatively prosperous years of the mid-1920s, academic institutes appeared to be underfunded, and the major German chemical associations had submitted memoranda to the government in the hopes of obtaining greater support. In regard to biochemistry, Haber and Willstätter asserted that Gemany had already lost its leadership to the "Anglo-Saxon lands," and that due to inadequate funds and a lack of qualified students, German laboratories saw themselves "mostly excluded from significant areas of biochemistry."[20]

Support for this view even came from abroad; in 1926 the British biochemist F. Gowland Hopkins had pointed out that "modern Germany provides but little institutional freedom" for biochemistry, warning that it would be "difficult to see how she can continue to lead along the path she has trod almost alone."[21] Haber and Willstätter therefore requested an additional 200,000 to 250,000 marks per year over the next five years to support strategic grants for physical and biochemistry. But such funds would not be forthcoming in the face of an imminent economic collapse that led to drastic austerity policies in Germany. By 1931 the new Kaiser Wilhelm Institute for Cell Physiology, under Emil Fischer's former associate Otto H. Warburg, had to receive its major support not from within Germany at all, but rather from the American Rockefeller Foundation.[22]

<u>Impact of National Socialism:</u> It is well-known that large numbers of Jewish or "non-Aryan" scientists (including both Willstätter and Haber as well as Bergmann) could no longer work in Germany after 1933. Chemistry and especially biochemistry were among the disciplines worst-hit by National Socialism, with more than one hundred dismissals, nearly one-quarter of those in academic positions in German institutions (or Austrian and Czech institutions in 1938).[23] One of the rare exceptions to this ban was Otto H. Warburg, who was allowed to continue to direct his Kaiser Wilhelm Institute and was able to keep up a high level of biochemical research (seeking a cure for cancer). But as Deichmann has shown, National Socialism tended to quash scientific debate and mute criticism of senior researchers, so that some of the leading "Aryan" researchers, including Emil Abderhalden and Adolf Butenandt (who avoided contact with Warburg), continued to advocate incorrect views with little opposition during this period. This further undermined the prestige and quality of biochemistry in Germany by 1945, with negative effects extending into the postwar era.[24]

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[19] Kohler (note 1), ch. 1.

[20] Fritz Haber and Richard Willstätter, "Denkschrift betreffend die Erneuerung des Japan-Ausschusses der Notgemeinschaft der Deutschen Wissenschaft," submitted to the President of the Notgemeinschaft, Friedrich Schmidt-Ott (signed Willstätter, Munich, Feb. 2, Haber, Berlin-Dahlem, Feb. 9, 1928). In: Geheimes Staatsarchiv Preußischer Kulturbesitz, Berlin-Dahlem, Rep 92 (Friedrich Schmidt-Ott), Nr. 43: 11-19, on 14.

[21] Cited in Fruton (note 15), 57.

[22] Fruton (note 15), 44. Cf. also Kristie Macrakis, *Surviving the Swastika: Scientific Research in Nazi Germany*, Oxford and New York: Oxford University Press, 1993, 63-64.

[23] Deichmann (note 12), 106-107.

[24] On Butenandt's uncritical support for the problematic and in part possibly fraudulent results of his friends Fritz Kögl and Emil Abderhalden in the field of cancer-related proteins and enzymes, see Ute Deichmann, "Proteinforschung an Kaiser-Wilhelm-Instituten 1930-1950 im internationalen Vergleich," *Ergebnisse: Vorabdrucke aus dem Forschungsprogramm "Geschichte der Kaiser-Wilhelm-Gesellschaft im Nationalsozialismus,"* 21 (Berlin: Max-Planck-Gesellschaft zur Förderung der Wissenschaften, 2004), 28-36; on Abderhalden see Ute Deichmann, "'I Detest his Way of Working'. Leonor Michaelis (1875-1949), Emil Abderhalden (1877-1950) and Jewish and non-Jewish Biochemists in Germany," in *Jews and Sciences in German Contexts: Case Studies from the 19th and 20th Centuries*, ed. Ulrich Charpa and Ute Deichmann, Tübingen: Mohr-Siebeck, 2007, 101-126.

<u>The innovative role of x-ray crystallography, and its limits:</u> It is of course true that a great deal of effort in German research centers during the 1920s went into the development of x-ray crystallography for structural analysis. This is a crucial innovation and one whose potential value for elucidating complex organic structures Emil Fischer was apparently unaware of in 1915. It is also remarkable that the first scientists to subject organic materials (natural fibers such as silk and wool) to x-ray crystallographic analysis, as early as 1913, were two young Japanese researchers at the University of Tokyo, the physics graduate students Shoji Nishikawa and S. Ono. The war prevented this from being followed up in Europe until the 1920s, though Nishikawa did influence American researchers during a visit to Cornell in 1916-19.[25]

X-ray crystallography showed that in the new generation, crucial advances would come not merely from the interaction of organic chemistry with biology (as Fischer had expected), but also and even more decisively from the collaboration of physical chemistry and physical instrumentation with biology. One can cite, for example, the work of the Kaiser Wilhelm Institute for Fibers Research in Berlin-Dahlem led by Rudolf Herzog, with several brilliant young scientists including Max Bergmann (before he moved to Dresden), Michael Polanyi, Hermann Mark and others.[26] It is worth noting that both Polanyi and Mark, as well as many of their young KWI colleagues, had come to Dahlem to escape from the chaos of the disintegrating Austro-Hungarian Empire and its successor states. In the revolutionary spirit of the immediate postwar era, these rebellious outsiders brought fresh ideas, creativity, and a willingness to defy established authorities, which led to dramatic improvements in the apparatus and methodologies, which were now being applied systematically to organic structures for the first time.[27] Organic chemists themselves, however, tended not to use this method, in part because it required sophisticated mathematical analysis; as one German physical chemist put it as late as 1938, "with a mixture of fear and repugnance, most chemists seek to avoid everything mathematical."[28]

But the main orientation of x-ray crystallography in the German and other European contexts at this time was related to the textile industry, especially cellulose fibers, and also inorganic crystals or metals rather than biologically significant molecules such as proteins or nucleic acids. The lack of attention to biologically active molecules applied not only to Hermann Staudinger and his macromolecular theory, whose origins have been well described by our colleague Yasu Furukawa, but also to Staudinger's main rivals after 1926, K. H. Meyer and Hermann Mark, whose theory of "polymers" (chiefly applying to cellulose, rubber and plastics) arose from collaborative research at the I.G. Farben works in Ludwigshafen (the once and future BASF corporation). During the 1920s, however, most organic chemists, even

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[25] André Authier, *Early Days of X-ray Crystallography*, Oxford: Oxford Univ. Press, 2013, 136-137, 260. Note: this paper uses the Western style for Japanese names, with surnames following given names.

[26] Mary Jo Nye, *Michael Polanyi and His Generation: Origins of the Social Construction of Science*, Chicago: The University of Chicago Press, 2011; Jeremiah James et al., *One Hundred Years at the Intersection of Chemistry and Physics: the Fritz Haber Institute of the Max Planck Society, 1911-2011*, Berlin: De Gruyter, 2011; Ulrich Marsch, *Zwischen Wissenschaft und Wirtschaft: Industrieforschung in Deutschland und Grossbritannien 1880-1936*, Paderborn: Schöningh, 2000, 431-463 (for funding and organization of the fiber research institute).

[27] Michael Polanyi, "My Time with X-rays and Crystals," in Paul Peter Ewald, ed. *Fifty Years of X-ray Diffraction: Dedicated to the International Union of Crystallography on the Occasion of the Commemoration Meeting in Munich, July 1962*. Utrecht: Published for the International Union of Crystallography by A. Oosthoek's Uitgeversmij, 1962, 629-636 (http://www.iucr.org/publ/50yearsofxraydiffraction/full-text, accessed 2/24/2015).

[28] Cited in Jeffrey Allan Johnson, "The Case of the Missing German Quantum Chemists: On Molecular Models, Mobilization, and the Paradoxes of Modernizing Chemistry in Nazi Germany," *Historical Studies in the Natural Sciences*, **43/4** (2013): 391–452, on 440.

those dealing with organic products such as vitamins, continued to emphasize relatively small molecules; in Germany, many physical chemists such as Wolfgang Ostwald also advocated a colloidal aggregate theory.[29] Interestingly enough, it has been argued that the Staudinger vs. Meyer-Mark vs. colloidal aggregate controversies were largely irrelevant to protein chemists at the time, because most were already persuaded in effect that proteins were macromolecules, even before The Svedberg's ultracentrifuge provided more conclusive evidence against colloidal aggregates from 1926. The main issue was the details of protein structure.[30]

The structural question for proteins came to be a central focus of the work of the British physical scientist William T. Astbury, who from 1926 began to examine natural fibers including hair and wool. Like many of the Germans, he too benefited from a productive relationship with the local textile industry in Leeds. During this period, Leeds was a particularly fertile location for physical organic chemistry, as C. K. Ingold was also there (1924-30) before returning to University College London. Astbury's studies of natural fiber proteins in the 1930s, with a focus on keratin as a component of wool, led to proposals for two distinct structures, an α-form (coiled) and a β-form (stretched). These later inspired Linus Pauling and Robert Corey's protein structures after 1945. Nevertheless Astbury did not initially check his crystallography-based model against an organic-chemical, space-filling molecular model, so that in the late 1930s other scientists pointed out various weaknesses in the structural details of his model. Astbury was primarily a physicist and crystallographer, not an organic or biochemist, so that here again, despite his interest in the newly emerging interdisciplinary field of "molecular biology," his results were limited by a lack of full interdisciplinary collaboration. Similarly, with his pioneering examination of nucleic acids he did not seek to combine the crystallographic analysis with molecular model-building.[31]

2) The Cold War generation, 1945-1975: unlocking the secrets of life

The post-1945 generation began under the sign of global reconstruction following the most destructive war in history, but the process of postwar recovery was further complicated by the political division of the world with the advent of the Cold War between the contending superpowers, the USA and the Soviet Union. Historians are still investigating the details of how the aftermath of the Second World War may have affected the recovery of scientific activity, and of work in chemistry in particular, but it does appear that the victorious American and British scientific establishments emerged from the war with great prestige and public support. The opposite was true in Germany, not least because of the association of the chemical industry with National Socialist mass murder in Auschwitz. Along with other factors including the postwar division of the country and the removal of technical experts by both Soviets and Americans, as well as the reluctance of most interwar political emigrants to return to postwar Germany, this confirmed the loss of scientific leadership that the Germans had feared in the interwar era. Thus it was perhaps not coincidental that in the first postwar decade, the most significant developments in the chemistry of the proteins and nucleic acids occurred in the USA and Britain. In Japan, the situation was somewhat different. My impression is that in response to the American occupation and enforced demilitarization of the country, along with the war-related economic devastation and ensuing food shortages, the chemistry and industry of natural products appeared as a logical and desirable focus for many

[29] Authier (note 25), 261; Yasu Furukawa, *Inventing Polymer Science: Staudinger, Carothers, and the Emergence of Macromolecular Chemistry*, Philadelphia, Penn.: University of Pennsylvania Press, 1998; Claus Priesner, *H. Staudinger, H. Mark and K. H. Meyer: Thesen zur Größe und Struktur der Makromoleküle*, Weinheim: Verlag Chemie, 1980.

[30] Charles Tanford and Jacqueline Reynolds, *Nature's Robots: A History of Proteins*. Oxford: Oxford Univ. Press, 2001, 51-52, 59-60.

[31] Robert C. Olby, *The Path to the Double Helix*, Seattle: University of Washington Press, 1974, 63-70.

talented young Japanese scientists in the postwar era. Reviving and expanding trends already begun before the war, in the 1950s and 1960s a significant and productive academic-industrial symbiosis developed in pharmaceuticals and natural products such as vitamins, amino acids, and peptides. As I will mention later, and as some of the papers in our workshop discuss, the result would be a series of innovations by Japanese scientists, some of which would ultimately lead to Nobel Prizes and other awards.

First, however, let me discuss some of the best-known innovations by Anglo-American scientists in the post-1945 generation. Linus Pauling's alpha-helix model of protein structure is of course famous, and Mary Jo Nye's paper discusses Pauling's influence and his work leading up to this, so I need say little here.[32] I will point out that Pauling benefited from an interdisciplinary approach including the use of structural ideas derived from quantum theory and x-ray crystallography as well as physical model-building, in this case going far beyond the interwar protein scientists such as Astbury. One of the more advanced versions of the alpha-helix model employs space-filling molecular models of a type first developed in the 1930s by a German (and National Socialist) physicist, H. A. Stuart, who had apparently in part been inspired by Pauling's earlier work employing quantum ideas to elucidate molecular structures. But the use of the models by German organic chemists was quite limited.[33]

Given a new model of protein structure, an organic chemist would want to confirm it by synthesis. A crucial breakthrough came in 1953, which everyone knows was the year of the double-helix model of DNA. Only specialists are aware of the total synthesis of oxytocin by Vincent du Vigneaud, which was nevertheless so significant that he became the sole winner of the Chemistry Nobel Prize in near record time – only two years later – in 1955. What was the significance of this achievement? It was the first synthesis of a polypeptide hormone, following the Bergmann-Zervas carbobenzoxy process developed a generation earlier. But although that process was effective and came "universally" into use among peptide chemists after this success, it was also "difficult and time consuming," which inspired young chemists to develop newer, faster and more productive methods of peptide and protein synthesis.[34] Here I will mention two of these new methods.

In 1959 Robert Bruce Merrifield at the Rockefeller Institute had the idea for one of these new methods, the "solid phase peptide synthesis." This he described in a sole-authored paper in the *Journal of the American Chemical Society* in 1963, which became one of the most often cited in the journal's history.[35] He and a colleague went on to effect the first synthesis of the enzyme Ribonuclease A in 1969. Ultimately Merrifield's new, highly influential method brought him the honor of a sole Nobel Prize in Chemistry in 1984. A crucial feature of Merrifield's process was that, as he put it in his Nobel Lecture, it could be "mechanized and automated," a goal he had already announced in his 1963 paper. Thus for the first time, it would be possible to commercially mass-produce peptides using various types of machines,

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[32] Mary Jo Nye, "A Career at the Center: Linus Pauling and the Transformation of Chemical Science in the Twentieth Century," in the present volume.

[33] Johnson (note 28), 401-412; H.-J. Schneider (personal communication by courtesy of Stephen J. Weininger), 2015.

[34] Robert Bruce Merrifield, "Solid Phase Synthesis" (Nobel lecture, 8 December 1984), in: *Chemistry, 1981-1990*, ed. Tore Frängsmyr and B. G. Malmström (Singapore: World Scientific, 1992); series: Nobel Lectures, Including Presentation Speeches and Laureates' Biographies, 149-174, on 149.

[35] R. B. Merrifield, "Solid Phase Peptide Synthesis. I. The Synthesis of a Tetrapeptide," *Journal of the American Chemical Society* **85** (1963): 2149–2154.

developed in several different countries.[36] This foreshadowed many later devices used in genetic engineering and modern biotechnology.

During the same period in Japan, the biochemist Shumpei Sakakibara was just beginning his research career at Osaka University in the early 1950s. His first project was to attempt to replicate du Vigneaud's 1953 synthesis. Although he was only partially successful, it was a starting point for his further research leading to the development of a methodology for the solution synthesis of proteins, which may be considered an alternative to the Merrifield solid-phase process.[37] As is well-known to Japanese historians of chemistry, Sakakibara became head of the Peptide Center of the Osaka Institute for Protein Research, which had been founded in 1959 under the later president of Osaka University, Shiro Akabori. The Peptide Center synthesized a long series of biologically active peptides, the first to be produced in Japan and an important stimulus to the expansion of Japanese peptide and protein research. Ultimately Sakakibara became head of the Protein Research Foundation (PRF), which took over responsibility for peptide production from the Osaka Institute when the demand became too great.[38] The PRF came to be supported by a dozen or so of the leading Japanese chemical, pharmaceutical, and natural-products firms, some of which date to the era before the First World War. Hence it may be considered an exemplary model of a successful academic-industrial symbiosis in the Japanese context.[39] As a student of the original German version of this symbiosis established in the dye industry during the late nineteenth century, I suspect that a comparative study of the German and Japanese cases would be of great interest.

Returning to the Anglo-American context of biological chemistry in the postwar era, I note that the history of the double helix model of 1953 is so well-known that a brief mention will suffice here. As with Pauling's alpha helix, the model produced by James D. Watson and Francis Crick is a product of modern structural organic chemistry, and it exemplifies the interdisciplinary nature of the new "molecular biology." It was, of course, based on the work of a physical chemist and x-ray crystallographer, Rosalind Franklin, who produced the famous image of the B-form of DNA from which the biologist Watson and the physicist Crick deduced (without acknowledgment) much of the details of the structure, with the help of advanced mathematics in the form of Fourier analysis. Moreover, the organic chemist Jerry Donohue provided crucial assistance to them in working out the structural details of the base-pairings, the idea for which derived from the work of the biochemist Erwin Chargaff.[40]

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[36] Merrifield (note 34), 156; Merrifield (note 34), 2149; cf. Robert Bruce Merrifield, *Life during a Golden Age of Peptide Chemistry: The Concept and Development of Solid-Phase Peptide Synthesis.* Washington, DC: American Chemical Society, 1993.

[37] Shumpei Sakakibara, "Fifty years of my Protein Synthesis," in *Frontiers of Peptide Science*: *Proceedings of the Fifteenth American Peptide Symposium June 14–19, 1997, Nashville, Tennessee, U.S.A.,* ed. James P. Tam and Pravin T. P. Kaumaya, Dordrecht, NL: Kluwer, 1999, 1-10, on 1-2.

[38] Terutoshi Kimura, "Message from Chairman of the Board" (Protein Research Foundation: https://www.prf.or.jp/aisatsu-e.html, accessed 2/18/2015; Fruton (note 15), 78.

[39] Firms listed with links to their websites and corporate histories at: https://www.prf.or.jp/sanjo-e.html, accessed 2/18/2015.

[40] For this well-known but controversial episode of modern science, see various accounts including Fruton (note 15), 392-454; Horace Freeland Judson, *The Eighth Day of Creation: Makers of the Revolution in Biology*, New York: Simon and Schuster, 1979; Erwin Chargaff, *Heraclitean Fire: Sketches from a Life Before Nature*, New York: Rockefeller University Press, 1978; Olby (note 31); James D. Watson, *The Double Helix: A Personal Account of the Discovery of the Structure of DNA*, ed. Gunther S. Stent, New York: Norton, 1980 (Norton Critical Edition of *The Double Helix,* orig. publ. New York: Atheneum, 1968); Brenda Maddox, *Rosalind Franklin: The Dark Lady of DNA*, New York: HarperCollins, 2002; Maurice Wilkins, *The Third Man of the Double Helix: Memoirs of a Life in Science*, Oxford, UK: Oxford University Press, 2003.

While Watson and Crick's double helix continues to be celebrated in the popular press, I would prefer to emphasize a far less popularly known pioneering achievement in DNA chemistry, yet one that stands more directly in Emil Fischer's tradition. This was the Nobel Prize-winning work of the American biochemist Arthur Kornberg (1918-2007) who, beginning in 1955, isolated the first DNA polymerase enzyme, the enzyme that played a central role in the actual construction of DNA. With it he could test the Watson-Crick model of the double helix. This required a difficult process of purification of the enzyme, without which the DNA it produced would have serious defects and remain inert.[41] In 1967 Kornberg finally achieved Fischer's elusive goal of synthesizing biologically active DNA from its components, by using the polymerase to build a single strand of Phi X 174 viral DNA. He thereby became the subject of global headlines about "life created in the test tube." Although Kornberg noted that producing a strand of viral DNA was hardly the same as creating an artificial organism, nevertheless he later recalled that he felt like an observer of the first nuclear detonation in 1945; both were equally revolutionary events.[42] He had demonstrated the biological activity of the synthetic DNA by infecting the E. coli bacterium, which was already well on its way to becoming a favored vehicle for genetic experimentation. Kornberg's thinking and language, as cited in 1969, was remarkably similar to Fischer's, a half-century earlier, when he had spoken about using artificial nucleic acid to "trick" an organism: "If we know how to use this enzyme [polymerase] to copy this particular virus then we can copy other viruses, and . . . we can modify their structure by putting in alternative or *fraudulent* building blocks to create new forms of the virus. We can then use the synthetic virus to infect cells and produce altered responses. . . . We can look forward to the correction of genetic defects." In other words, Kornberg was looking toward gene therapy with the help of what was now being called "genetic engineering," which would spark a biotech boom in the next generation.[43]

3) The millennial generation, 1975-2005: from molecular biology to synthetic biology

Space does not permit a full discussion of the emergence of genetic engineering, protein engineering, and metabolic engineering as exemplars of the new academic-industrial symbiosis in the post-1970s generation, but I would like to mention research on Green Fluorescent Protein (GFP) and its analogues. Osamu Shimomura's work on GFP is discussed in this workshop by my esteemed colleague Masanori Kaji.[44] Shimomura was of course honored by the 2008 Nobel Prize in Chemistry, along with two younger Americans, Martin Chalfie and Roger Tsien. These three men represent the transition from the post-1945 to the post-1970s generation. Chalfie and Tsien in particular reflect how scientific work on the chemistry of life became both far more collective and far more interdisciplinary than in the pre-1970s generations.[45] Their work on fluorescent proteins made these into ubiquitous and variegated tools of synthetic biology. Like the 19th century "rainbow makers" of the synthetic dye industry who produced thousands of artificial colors, today's rainbow makers, epitomized by Tsien and his colleagues, have created a "fluorescent protein paintbox."[46] And recalling

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[41] Arthur Kornberg, "The Biologic Synthesis of Deoxyribonucleic Acid" (Nobel Lecture, December 11, 1959), in: Nobel Foundation (Stockholm), *Nobel Lectures, Physiology or Medicine 1942-1962*, Elsevier Publishing Company, Amsterdam, 1964, 665-680, on 670.

[42] Arthur Kornberg, "Never a Dull Enzyme," *Annual Reviews of Biochemistry* **58** (1989):1-31, on 14.

[43] Cited in Fred Warshofsky, *The Control of Life*, New York: Viking Press, 1969 (Series: The 21st Century), 35-36 (emphasis added).

[44] Masanori Kaji, "The Transformation of Organic Chemistry in Japan," in the present volume.

[45] Roger Y. Tsien, "Constructing and Exploiting the Fluorescent Protein Paintbox" (Nobel lecture December 8, 2008), in: *Les Prix Nobel. The Nobel Prizes 2008*, ed. Karl Grandin, Stockholm: Nobel Foundation, 2009, 186-214.

[46] Tsien (note 45), Fig. 12; cf. Anthony S. Travis, *The Rainbow Makers: The Origins of the Synthetic Dyestuffs Industry in Western Europe*. Bethlehem: Lehigh University Press, 1993.

Emil Fischer's effort to create a visible fluorescent molecule by total synthesis, it is worth noting that in 1998 Shumpei Sakakibara and his team, using a version of the solution-synthesis technique they had first described in 1981, reported the total chemical synthesis of the precursor molecule of natural green fluorescent protein and its conversion to GFP.[47]

4) The contemporary generation: fulfilling Fischer's dream?

I would like to conclude by briefly touching on the new generation that has begun to emerge in the 21st century, particularly in regard to the still forming and developing interdisciplinary discipline known as "synthetic biology."[48] The practitioners in this discipline whom I have recently interviewed look forward to the engineering of living systems in a systematic way, going well beyond the older "genetic engineering," which from their perspective is not "engineering" at all because it cannot mas-produce in a standard way with predictable results. Going even beyond Fischer's dream of a "synthetic-chemical biology," today's practitioners come from an amazing range of professional and disciplinary backgrounds including electrical engineering and artificial intelligence, each with a somewhat different goal or even definition of the discipline. Part of it clearly fulfills Fischer's dream: the total synthesis of artificial chromosomes, a difficult project but with a few promising recent achievements such as the creation of "synIII," an artificial but functional yeast chromosome.[49] Yet at the opposite end of the spectrum is a project promoted by some of its advocates such as Drew Endy and Tom Knight, which has captured the attention of young people on a global scale through the International Genetically Engineered Machine (iGEM) competition. In this, teams of undergraduates are given so-called "BioBricks" – a "set of standard and reliable engineering mechanisms" for use in the "assembly of genetic components into larger systems" – to carry out synthetic biology projects.[50]

But I hardly need to describe this here, because Tokyo Tech has been one of the most successful institutions in the iGEM competition in recent years. Its Information Processing team can boast of winning the world iGEM competition in its division for the past three years in a row, a feat equaled by no other university in the world.[51] I am pleased to have had the opportunity while at the Tokyo Institute of Technology to speak with some of those involved in this work, which strikes me as something which the German chemists of the nineteenth century would have applauded: for had not the great Justus Liebig demonstrated that the best way to learn chemistry and to promote chemical creativity was through doing chemistry in a laboratory? So I salute my colleagues of Tokyo Tech, and its bright, hardworking, and ingenious students. Perhaps one among them will be a Nobel Prizewinner in future years, and

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[47] Yuji Nishiuchi et al., "Chemical Synthesis of the Precursor Molecule of the *Aequorea* Green Fluorescent Protein, Subsequent Folding, and Development of Fluorescence," *Proceedings of the National Academy of Sciences of the United States of America* **95.23** (1998): 13549–13554; T. Kimura et al., "Strategy for the Synthesis of Large Peptides: An Application to the Total Synthesis of Human Parathyroid Hormone [hPTH(1–84)]," *Biopolymers* **20** (1981): 1823-1832; Shimpei Sakakibara, "Chemical Synthesis of Proteins in Solution," *Biopolymers* **51/4** (1999): 279–296.

[48] Luis Campos, "Outsiders and In-Laws: Drew Endy and the Case of Synthetic Biology," in *Outsider Scientists: Routes to Innovation in Biology*, ed. Oren Harman and Michael Dietrich, Chicago: University of Chicago Press, 2013, 331-348.

[49] Narayana Annaluru et al. (80 co-authors), "Total Synthesis of a Functional Designer Eukaryotic Chromosome," *Science* **344/6179** (4 April 2014): 55-58.

[50] Luis Campos, "The Biobrick™ Road," *Biosocieties* **7.2** (June 2012): 115-139; quotation from Tom Knight, *Idempotent Vector Design for Standard Assembly of Biobricks*, Cambridge, Mass.: MIT Artificial Intelligence Lab / Synthetic Biology Working Group, 2003, 2 (http://hdl.handle.net/1721.1/21168, accessed 2/20/2015).

[51] Tokyo Institute of Technology, "Tokyo Tech Students Win at iGEM Three Years in a Row," *Tokyo Tech News* (January 21, 2015) (http://www.titech.ac.jp/english/news/2015/029586.html, accessed 2/18/2015).

for this reason they deserve to be placed in the company of Emil Fischer, Linus Pauling, and Osamu Shimomura.

Postscript

While the preceding paper has generally taken a positive perspective on the work on chemists, biochemists, and synthetic biologists since Emil Fischer, it should not be forgotten that Fischer's idea of gaining "a radical chemical influence on the development of the organism"[52] may raise fundamental problems for many observers, including scientists, when the organism in question is human. A recent publication by Chinese scientists has indeed presented serious ethical and practical questions about the appropriateness of seeking, for the first time in world history, to "edit" the human genome at the zygote stage during the process of in vitro fertilization, using currently available techniques. The goal was to produce permanent modifications to a single gene (with no unintended changes to others), which would also be capable of being transmitted to descendants. Unfortunately, as the Chinese acknowledged, the experiments were essentially failures and produced numerous unintended, damaging modifications of the genomes of the 85 embryos used (which would not have been viable in any case).[53] One of the authors claimed that both *Nature* and *Science* refused to publish their paper; if so, it would not be surprising, as both journals have publicly warned against this type of human experimentation.[54] It is also not surprising that online comments on news reports of these experiments used phrases like "mad scientists, "Frankenstein," and "Brave New World," using these iconic cultural images to express a deep distrust of human genetic experimentation.[55] To these commenters, perhaps Emil Fischer's dream would seem more a nightmare. Hence the larger project, of which my present paper is a part, will discuss not only the scientific and technical developments, but also explore the fundamental cultural issues raised by the emergence of technologies of artificial life.

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[52] Fischer (note 2), 808 (cited above, note 7).

[53] Puping Liang et al., "CRISPR/Cas9-mediated Gene Editing in Human Tripronuclear Zygotes" *Protein & Cell* (18 April 2015), DOI 10.1007/s13238-015-0153-5 (open access; accessed 4/30/2015), print publ. **6/5** (May 2015): 363-372.

[54] David Cyranoski and Sara Reardon, "Chinese Scientists Genetically Modify Human Embryos," *Nature / News* (22 April 2015) (http://www.nature.com/news/chinese-scientists-genetically-modify-human-embryos-1.17378#/b1 (accessed 4/30/2015)).

[55] Examples: comments by "Bandylion," "KB," W. Wolfe, and William LeGro on the article of Gina Kolata, "Chinese Scientists Edit Genes of Human Embryos, Raising Concerns," *New York Times* (23 April 2015) (http://www.nytimes.com/2015/04/24/health/chinese-scientists-edit-genes-of-human-embryos-raising-concerns.html?_r=0, accessed 4/24/2015); comment by Dr. Upinder Fotadar on the Cyranoski & Reardon article (note 53).

The Transformation of Organic Chemistry in Japan: From Majima Riko to the Third International Symposium on the Chemistry of Natural Products

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Introduction: The Period from 1930 to 1960 as a Turning Point of Chemistry in Japan

Majima Riko (1874–1962), one of the first organic research chemists of Japan[1], is widely known especially for his study of urushiol, the main component of Japanese lacquer tree sap. His research strategy involved studying the structure of the components of Japan's local natural products using newly developed methods from Europe to catch up to and compete with chemists in more advanced countries in the West[2]. Majima's approach became the primary research method employed by research organic chemists in Japan until the 1950s.

After Fukui Ken-ichi received the Nobel Prize in chemistry in Japan in 1981, six Japanese chemists went on to receive the same award. Most of these scientists discovered and developed new methods or theories from the 1950s to the 1970s.

This paper considers the Third IUPAC Symposium on the Chemistry of Natural Products in Kyoto in 1964, two years after Majima's death, as indication of the transformation of organic chemistry in Japan. By analyzing the circumstances behind this symposium, the topics presented in the symposium, and its consequences in the 1960s, this paper will elucidate the major factors that influenced the transformation of organic chemistry research in Japan.

1. Majima's Research Strategy: Research on the Structure of Urushiol

Majima was born in Kyoto in 1874, the eldest son of an affluent medical doctor. His generation was the first to study within a completely modern educational system established after the Meiji Restoration in 1868. Majima entered the chemistry department of the Imperial University in Tokyo in 1896. Soon after his graduation in 1899, he remained in the department as a research assistant and a graduate student under the supervision of Professor Sakurai Joji (1858–1939), one of the first Japanese professors of the department. Sakurai gave him complete freedom to choose research topics, but provided no real advice as to what area he should focus on. Moreover, while Sakurai studied physical chemistry, Majima's interests focused on organic chemistry. Because of the lack of an advisor to guide his research in organic chemistry, Majima studied the works of well-known German organic chemists that had been published in German journals and were available in his department[3]. When he began

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[1] In this paper, the author follows the Japanese custom with regard to personal names of historical figures: the family name is provided first, followed by the given name. Here, *Majima* is the family name and *Riko* is the given name. Japanese contemporary authors' names, including the author of this paper, follow the western custom, i.e., the given name is provided first. To learn more about Majima, see Masanori Kaji, "The Role of Riko Majima in the Formation of the Research Tradition of Organic Chemistry in Japan (in Japanese)," *Kagakushi-Kenkyu (The Journal of the Japanese Society for the History of Chemistry)* **38** (2011): 173-185.

[2] Majima Riko, "Waga Shogai no Kaiko (1)[Reminiscence of My Life (1)] (in Japanese)," *Kagaku no ryoiki*, **8** (1): 1-11 (1954), p.6.

[3] Monthly reading seminars of articles of western scholarly journals, called "Zasshikai," began in 1890 at the

to conduct research in organic chemistry, he decided to study local natural products to compete with chemists in the West and first studied the structure of urushiol, the main component of Japanese lacquer tree sap. The lacquer tree is an important indigenous commercial source of natural lacquer. Studies on lacquer tree components began in 1882 in Japan, with the main component being named urushiol by Miyama Kisaburo (1873–?) in 1906[4]. Majima asked Miyama to allow him to study the structure of urushiol; Miyama himself studies its application for lacquer.

In 1903, Majima was promoted to associate professor, and the Ministry of Education sent him to Europe for further study in 1907. During his Europe until 1911 he conducted research in Kiel under Carl Dietrich Harries (1866–1923) and in Zurich under Richard Willstätter (1872–1942). While in Europe, besides research on topics provided by his European supervisors, Majima continued to study urushiol using advanced methods available in the laboratory, including Harries' vacuum distillation and ozonolysis[5] and Willstätter's hydrogenation of alkenes by platinum catalysis[6].

Majima returned to Japan in January 1911 and became a professor of organic chemistry at Tohoku Imperial University, a newly established imperial university in Sendai, northern Japan, in March. After establishing his laboratory, he restarted his research on the structure of urushiol using newly introduced advanced instruments and methods from Europe. Within six years, he succeeded in elucidating the structure of urushiol as a catechol (*o*-dihydrobenzene) derivative.

Majima's approach to urushiol research and his study of local natural products using newly developed European methods was adopted as a major research method in Japan until the 1950s. Many of his students followed this line of research.

2. Research Tradition of Natural Products Chemistry in Japan after Majima and Its Consequences (I): Nozoe Tetsuo and Hinokitiol[7]

Nozoe Tetsuo was one of Majima's students at Tohoku Imperial University, and his research path showed how Majima's research line was developed by his students. Nozoe was born in Sendai in 1902. He entered the chemistry department of the science faculty at Tohoku Imperial University in 1923. During his tenure at the university, Majima became Nozoe's mentor and played a decisive role in his career.

After his graduation in March 1926, Nozoe stayed on as Majima's assistant but left Sendai for Formosa (now Taiwan) at the end of June 1926 to become a researcher at the Monopoly Bureau in Taipei, the capital of Formosa, a move he made under Majima's strong recommendation. Nozoe was a candidate professor at a newly planned imperial university in Formosa. In 1928, Taihoku Imperial University (Taihoku is the Japanese name for Taipei) was established, and young Nozoe was appointed as an associate professor the following year. Taihoku Imperial University was the second Japanese imperial university to be established

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chemistry department of the Imperial University. See *Tokyo Daigaku Rigakubu Kagaku-kyoshitsu no Ayumi* [in Japanese, The History of the Chemistry Department of the Science Faculty of the University of Tokyo], Tokyo: Kokusai Bunken Insatsu Sha, 2007, p.58 and the site: http://www.zasshikai.jp/html/2setsuritsu.html.

[4] Majima Riko, "Urushi seibun kenkyu no kaiko [in Japanese, Reminiscence on the studies of the Japanese lacquer components]" in *Majima Riko Sensei Iko to Tsuioku* [Majima Riko, his posthumous manuscripts and Reminiscence], Tokyo: Tokyo Kagaku Dojin, 1970, pp.63-102, p.64. This article was first published in 1945.

[5] Fischer, Emil und Carl Harries, "Ueber Vacuumdistillation," *Ber. Dtsch. Chem. Ges.* **35** (1902): 2158-2163; Harries, Carl, "Ueber die Einwirkung des Ozones auf organische Verbingungen," *Liebigs Ann. Chem.* **343** (2-3) (1905): 311-344.

[6] Willstätter, Richard, "Über Reduktion mit Platin und Wasserstoff beigewöhnlicher Temperatur. I," *Ber. Dtsch. Chem. Ges.* **41** (1) (1908): 1475-1480.

[7] Kaji, Masanori "Nozoe Tetsuo's Chemical Research at Taihoku Imperial University in Taiwan and Its Colonial Context," *Historia Scientiarum*, vol. 18-2 (2008): 132-139.

among its colonies after Keijo Imperial University in Keijo (now Seoul), which was founded in 1925. Nozoe's main research interests lay in the study of natural products, especially those found in Formosa, following his mentor's approach.

Nozoe's well-known work in Formosa concerned the chemical components of *taiwanhinoki*, a native conifer growing in high mountainous areas. Nozoe determined a new compound, hinokitiol, from the components of this species and reported it for the first time in 1936 in a special issue of *Bulletin of the Chemical Society of Japan* to celebrate Professor Majima's sixtieth birthday[8].

By studying hinokitiol's structure, Nozoe determined that the compound may be a new type of aromatics stabilized by resonance involving intramolecular hydrogen bonds after reading Linus Pauling's *The Nature of the Chemical Bond* (1939). While hinokitiol was later proven to exist not as a resonance hybrid but as a pair of tautomers that interconvert through intramolecular hydrogen bonds, Nozoe's idea was the first step in establishing new research on nonbenzenoid aromatics.

After World War II, Formosa was returned to the Republic of China and Taihoku Imperial University was renamed National Taiwan University. While most Japanese citizens left Taiwan for Japan, Nozoe stayed on in the country and worked as a chemistry professor at National Taiwan University under the orders of the Chinese government, who needed specialists to advance their academic agenda.

Since Nozoe regarded hinokitiol as a compound with a novel aromatic structure, he examined various substitution reactions, including halogenation, nitration, and azo coupling. He managed to return to Japan at the end of May 1948, with his alma mater, Tohoku University offering him a teaching position. The results of his group's research on hinokitiol at National Taiwan University were published in 1950–1952 in Japanese journals, especially in *Proceedings of the Japan Academy* in English.

When the symposium "Tropolone and Allied Compounds" was organized by the Chemical Society of London in November 1950, Nozoe's work on hinokitiol was mentioned as a pioneering contribution to tropolone chemistry, thereby helping Nozoe's research gain recognition in the West. Nozoe was able to publish his work on hinokitiol and its derivatives in *Nature* in 1951 thanks to J.W. Cook, the chairman of the symposium[9].

Nozoe's work, which began with research on natural products in Taiwan and became developed fully in Japan in the 1950s and the 60s, introduced a new field of organic chemistry, i.e., the chemistry of non-benzenoid aromatic comppounds. His work was well appreciated in Japan and Nozoe received the Order of Culture, the highest honor for contributing researchers and artists in 1958 at a relatively young age of 58. Nozoe's work is an excellent example of how Majima's students developed his line of research. Majima's research school demonstrated the level of organic chemistry research in Japan that had been reached by the 1950s.

3. Research Tradition of Natural Products Chemistry in Japan after Majima and Its Consequences (II): Shimomura Osamu and the Chemistry of Marine Natural Products

Shimomura Osamu, a Japanese biochemist who won the Nobel prize for chemistry in 2008, studied the chemistry of marine natural products by essentially following Majima's approach[10]. Shimomura's work is an example of how local approaches may transform into universal methods[11].

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[8] Nozoe, Tetsuo, "Über die Farbstoffe in Holzteile des "Hinoki" Baumes. I. Hinokitin und Hinokitiol." *Bull. Chem. Soc. Japan*, 11 (1936): 295-298.
[9] Nozoe, Tetsuo, "Substitution Products of Tropolone and Allied Compounds," *Nature* 167 (1951): 1055-1057.
[10] To learn more about his biography and work, see (1) Osamu Shimomura - Biographical" <http://www.nobelprize.org/nobel_prizes/chemistry/laureates/2008/shimomura-bio.html>; and (2) "Discovery of

Shimomura Osamu was born on August 27, 1928 in Kyoto prefecture. After graduating from the pharmaceutical special division, attached to Nagasaki School of Medicine, in 1951, he became an assistant in the analytical chemistry laboratory for students of Nagasaki University, into which Nagasaki School of Medicine was incorporated in 1949.

In 1955, he obtained a one-year leave of absence with pay to study in the organic chemistry laboratory of Hirata Yoshimasa (1915–2000) in Nagoya University, the last imperial university with prominence in research. During his stay at the university, he was asked by Prof. Hirata to purify and crystallize luciferin, an unstable light-emitting compound obtained from the sea-firefly; which no one had been able to do until then. After 10 months of hard work, Shimomura finally succeeded in crystallizing the compound and was invited to stay in the laboratory for another year to study its structure[12]. Shimomura's research attracted the attention of Dr. Frank Johnson of Princeton University, who later invited Shimomura to work in his laboratory.

At the end of August 1960, Shimomura left Japan for the United States with a Fulbright travel grant. Every summer beginning from 1961 until 1978, he and Dr. Johnson evaluated bioluminescent substances in luminous jellyfish found in Friday Harbor at San Juan Island, Washington State. As early as the fall of 1961, Shimomura had succeeded in extracting several few milligrams of purified protein aequorin, the first example of photoproteins ever discovered[13]. His work also uncovered trace amounts of another protein exhibiting bright green fluorescence; this protein was later named "green fluorescent protein (GFP)" by other researchers. Shimomura elucidated the structure of GFP in 1979 when he had obtained an adequate amount of GFP as a by-product of an 18-year study on aequorin[14]. GFP has become indispensable in molecular biological studies because it contains a fluorescent chromophore within its peptide chain and can be expressed in living bodies. Shimomura, along with other researchers, was awarded the Nobel prize for the discovery of GFP and development of its use as a tagging tool in bioscience.

4. The International Symposium on the Chemistry of Natural Products in Kyoto, 1964

The Third IUPAC Symposium on the Chemistry of Natural Products was held in Kyoto on April 12–18, 1964, two years after Majima's death[15]. This symposium was the first international conference on organic chemistry in Japan[16]. A total of 1,454 chemists consisting

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Green Fluorescent Protein, GFP," Nobel Lecture, December 8, 2008.
<http://www.nobelprize.org/nobel_prizes/chemistry/laureates/2008/shimomura_lecture.pdf>

[11] To learn more about problems of "places" in scientific activity, see David N. Livingstone, *Putting science in its place: geographies of scientific knowledge* (Science・Culture), University of Chicago Press, 2003.

[12] Shimomura, Osamu, Goto, Toshio and Hirata Yoshimasa, "Crystallin Cypridina luciferin," *Bull. Chem. Soc. Japan* 30 (1957): 929-933; Shimomura, Osamu, "Umi-Hotaru Luciferin no Kyozo [in Japanese, Structure of Cypridina luciferin] II," *Nihon kagaku zassi* (*J. Chem. Soc. Japan. Pure Chem. Section*) 81 (1960): 179-182.

[13] Shimomura, Osamu, Johnson, Frank H., Saiga, Y., "Extraction, purification and properties of aequorin, a bioluminescent protein from the luminous hydromedusan, Aequorea," *J. Cell Comp. Physiol.* 59 (1962): 223-239.

[14] Shimomura, Osamu, "Structure of the chromophore of Aequorea green fluorescent protein," *FEBS* [the Federation of European Biochemical Societies] *Lett.* 104 (1979): 220-222.

[15] To learn more about this symposium, see (1) Nihon Gakujutsu Kaigi [Science Council of Japan] Kokusai Tennenbutsu Kagaku Kaigi Soshiki Iinkai [the organizing committee of the International Symposium on the Chemistry of Natural Products], ed., *Kokusai Tennenbutsu Kagaku Kaigi* [in Japanese, the International Symposium on the Chemistry of Natural Products], Tokyo: Tokyo Kagaku Dojin, 1965; and (2) International Union of Pure and Applied Chemistry. Organic Chemistry Division and The Science Council of Japan, *Special lectures presented at the 3rd International Symposium on the Chemistry of Natural Products, held in Kyoto, Japan, 12-18 April, 1964*, London: Butterworths, 1964.

[16] Tsuda Kyosuke, "Interview: Yakugaku no ima to mukashi Tuda Kyosuke sensei ni kiku [in Japanese, Present and Past of Pharmacy: Interview with Professor Kyosuke Tsuda]," Faurmashia (Pharmaceutical Society of Japan) 29(12) (1993): 1351–1354, p.1353.

of 1,212 Japanese and 242 foreign scholars participated in the conference, and 223 presentations, including 11 special lectures, were given. Many Japanese participants considered this conference to be a success and a major turning point in the history of organic chemistry in the country[17].

In this symposium, presentations on the structure of tetrodotoxin, the poisonous compound of puffer fish, were given by four groups, two from Japan and two from the US. Tsuda Kyosuke (1907–1999) and associates at the University of Tokyo, Hirata Yoshimasa and associates at Nagoya University, and R. B. Woodward (1917–1979) of Harvard University presented recent independent results on the structure of tetrodotoxin; the findings of these groups were identical with one another. H. S. Mosher and associates at Stanford University proved that the structure of tarichatoxin, the poison extracted from the eggs of various species of Western American newts, is identical to that of tetrodotoxin. All of these groups employed instrumental analysis, including infrared, ultraviolet, nuclear magnetic resonance, and mass spectroscopy, as well as X-ray diffractometry.

While puffer fish and other species of its family are found in tropical and semi-tropical seas all over the world, they are prized as delicacies only in Japan and China because they are highly toxic when eaten. Tahara Yoshizumi (1855–1935), a Japanese pharmacologist, first isolated the poison from puffer fish and named it tetrodotoxin in 1907[18]. After a long pause in research on this component, Tsuda and his associates began to study tetrodotoxin in 1950. After two years, this group successfully crystallized the poison by following an improved crystallization method. Woodward did not discuss why he began to study the structure of tetrodotoxin; I suppose that he and his group only began work on it to show off their superb techniques after Woodward was invited in Japan as a keynote speaker in a special lecture on natural products chemistry. In the acknowledgement section at the end of his paper, Woodward gave special thanks to researchers in Loma Linda University in South California, who extracted pure tetrodotoxin from several tons of puffer fish entrails for Woodward's work[19].

These events in the International Symposium in Kyoto show the limitations of Majima's approach as a method to compete with those of top-level researchers overseas. One of Tsuda's co-workers later wrote about his group's work on tetrodotoxin and confessed that they first believed that one should only compete with colleagues in Japan because of the alleged unavailability of the poison and the difficulty of its crystallization. However, while only a limited number of people eat puffer fish, the fish itself lives in wide areas of tropical sea. Moreover, advances in instrumental analysis provided little "first-mover advantage" to scholars who had begun their research earlier; for top-level researchers, such as Woodward, these advances did not make any difference in their work.

5. Transformation of Organic Chemistry in Japan

Due to Instrumentation, Majima's approach was not valid anymore for competition with Western colleagues, like Woodward. However, the Japanese became well prepared to compete on an equal footing with their Western counterparts without taking advantage of local advantage by the end of the 1950s.

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[17] See, for example, note 15 (1), p.iii; Ikegawa Nobuo et al., eds. *Yakugaku to tomoni Rokuju-go nen: Tsuda Kyosuke Sensei 85 sai kinen bunshu* [65 years with pharmacy: Collection of essays to commemorate the 85th birthday of Professor Tsuda Kyosuke], Tokyo: Hirokawa Shoten, 1992, pp.23, 30–31, 45, 230–233.

[18] Tahara Yoshizumi, "Fugu doku kenkyu hokoku [Studies on the poison of puffer fish]," *Tokyo Kagaku Kaishi* (1909): 121–173.

[19] R. B. Woodward, "The Structure of Tetrodotoxin," *Pure Appl. Chem.* 9 (1964): 49–74, p.74.

Majima's approach gave "first-mover advantage" to Japanese chemists during the period between 1906, when Majima thought out his research strategy and attempted to apply it to urushiol, and 1950, when Tsuda started to study tetrodotoxin.

The Nuclear Fission Table in the Deutsches Museum: A Special Piece of Science History on the Eve of World War II

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The Deutsches Museum in Munich is one of the largest science and technology museums in the world. At 50,000 square meters, we show masterpieces from such diverse disciplines such as chemistry, physics, aircraft, marine, biotechnology or glass technology.

Since the beginning of the museum, there was an exhibition about chemistry. The chemical collection has a long tradition. Dye samples, laboratory equipment, and many other objects - about 10,000 in total - make up our collection.

One of the most famous objects is the table displaying the original equipment used by the researchers who discovered nuclear fission of uranium atoms in 1938: Otto Hahn, Lise Meitner and Fritz Straßmann.[1]

The discovery of nuclear fission

Since the 1890s, the scientific community had formed an increasingly accurate idea of the atom. After the first investigations of radioactive substances by, for example, Becquerel discovering the peculiar radiation emitted by uranium compounds, the Curies discovering the element radium and creating the term "Radioactivitity", Ernest Rutherford explaining correctly the nature of α-, β-rays, he and his coworker Frederick Soddy noticed in 1902 that by radioactive decay chemical elements change into each other. In 1913, Niels Bohr established his atomic model, postulating a positive nucleus with negative electron shells. In 1919, the first man-made change of elements took place, again by Rutherford: By bombarding nitrogen atoms with helium nuclei, he obtained oxygen atoms and a positively charged particle which, a short while later, he identified as the proton.[2] As a result, several research groups attempted to obtain element changes by bombarding atomic nuclei with protons. In this case, however, the repulsion of the positive particles and the positive nucleus always was an obstacle.

It was not until the discovery of the neutron by James Chadwick in 1932 that a new possibility was opened: This nucleon should be able to penetrate the nucleus without electrostatic repulsion.[3] At that point, the atom had become anything but indivisible. Bohr

1. S. Rehn, Kultur und Technik 3/2013, p. 18-25
2. For milestones in Rutherford's scientific life, see:
http://www.nobelprize.org/nobel_prizes/chemistry/laureates/1908/rutherford-bio.html
3. J. Chadwick, Nature *129*, 1932, S. 312; J. Chadwick, Proc. Roy. Soc. A. *136*, 1932, p. 692-708

spoke of a possible "explosion" [4] or "breaking" [5] of atomic nuclei. He formulated the theory that the nucleus behaves similar to a large water drop.

Enrico Fermi then irradiated a variety of elements with neutrons. By neutron capture and subsequent β-decay, he was hoping to obtain elements with an atomic number increased by one compared to the starting materials. In the case of uranium, at the time believed to be the heaviest chemical element, this transformation would lead to an artificial element. A transuranic element should arise.[6]

Lise Meitner thought these results so fascinating that in 1934 she persuaded Otto Hahn to join forces again in trying to bombard heavy nuclei, including uranium and thorium, with neutrons, in order to obtain transuranic elements.[7] The two scientists had known each other since 1907.[8] In the late 1930ies, Hahn led the Department of Radiochemistry and was director of the Kaiser Wilhelm Institute for Chemistry in Berlin. Lise Meitner directed the Radio-Physical Department.

The collaboration of the physicist and the chemist must have been extremely fruitful and affected by great friendship. Hahn described it in 1963 as "stroke of luck" to have met Lise Meitner.[9] Together with the chemist Fritz Straßmann, they conducted the following experiments: A sample of purified uranium was brought into a paraffin block and put next to a neutron source of beryllium and radium. After different exposure times, the uranium sample was removed and chemically analyzed. After dissolving it in hydrochloric acid, a compound similar to the suspected product was added. By doing so, the team expected that this added compound and the reaction product should precipitate together from the solution. Excessive uranium remained in the solution. Subsequently, the filtrates were dried and the filter papers were glued into the cylindrical hollow of a lead block. Home-made Geiger-Muller counters were set onto the filter papers. The counter tube consisted of an aluminum cylinder filled with a special argon gas mixture with a wire in the center. Strong batteries put the wire under voltage. The negative β-particles emitted from the radioactive sample were accelerated toward the wire and caused a cascade of ionizations and an electrical pulse. This pulse was amplified and displayed by a mechanical counter. Plotting the counts against time yielded the radioactive decay rates of the reaction products.

Indeed, the team found reaction products emitting β-particles and concluded that transuranic elements were formed. They assumed that nuclei with atomic numbers 93-96 were formed and found that their chemical properties met the expectations. Since they found new radioactive compounds which could be precipitated with platinum salts they took this as prove for the chemical similarity of the elements. Despite the probably long series of β-decay, which was never observed before, the finding of new chemical elements was published and not doubted by anyone.[10] But why do we today read eka-osmium, eka-rhenium, eka-iridium and eka-platinum in these publications? To answer this question, we have to have a look at

4. N. Bohr, Nature *137*, 1936, p. 344-348

5. N. Bohr, Science *86*, 1937, p. 161-165

6. E. Fermi, Nature *133*, 1934, p. 757; E. Fermi, *ibid.*, p. 898-899

7. Lise Meitner: Wege und Irrwege zur Kernenergie (1963). In: L. Meitner, D. Hahn (Ed.), Erinnerungen an Otto Hahn. Hirzel Verlag Stuttgart, 2005, p. 69 – 73

8. F. Krafft, Otto Hahn und die Kernchemie, Museumsverein für Technik und Arbeit, Mannheim, 1991, p. 14 - 15

9. Otto Hahn – 25 Jahre Atomzeitalter. Television movie produced by the North German Television Network NDR, 1963. In German, Hahn uses the term "Glückszufall", which is a mixture of the words "luck" and "chance". Deutsches Museum archive, AV-F 0026 & 1743. (All translations of original German quotes by S. Rehn-Taube.)

10. a) L. Meitner, O. Hahn, F. Straßmann, Z. f. Physik *106*, 1937, p. 249 - 270; b) O. Hahn, L. Meitner, F. Straßmann, Chem. Ber. *70*, 1937, p. 1374-1392

the periodic table of the time: Despite the knowledge of the Lanthaoids, the scientists believed that the chemical elements following uranium had to be heavier homologes of the *transition metals*. Since the Berlin groud found new radioactive compounds which could be precipitated with platinum salts they took this as prove for the chemical similarity of the elements.

In the year 1937, Irène Joliot-Curie and her colleague Paul Savitch in Paris conducted similar experiments and found a product with a half-life of 3.5 hours. The group gave various explanations for the chemical nature of this nucleus, claiming to have found lighter elements as well as transuranic elements.[11]

Hahn and his team were very clear about the fact that they weren't the only ones working on this particular topic.

It was the summer of 1938. At this exciting point of their work, Lise Meitner had to flee from Germany. After the "Anschluss" of Austria by Germany, she was threatened with persecution by the Nazis as an Austrian Jew. With the help of Otto Hahn and other colleagues, she left Germany on July 13th, 1938 for the Netherlands and eventually Sweden. Her scientific celebrity status did not protect her in any way: She could only cross the German border because she was fortunate enough to not be controlled by the SS guards on the train. The flight must have left a great break in the Berlin team. Otto Hahn wrote later: "I'll never forget the 13th of July 1938".[12] "Hähnchen" and "Lieschen", as they called themselves according to legend, remained in intensive contact by correspondence nonetheless.

In Berlin the team focused on the chemical analysis of the irradiation product. The results seemed to indicate radium as product.[13] This could be the result of two consecutive α-decays of uranium. Two consecutive α-decays had never been observed before, and many experts were skeptical.

To identify radium chemically, Hahn and Straßmann first added barium chloride to the uranium solution and hoped to precipitate a radium barium mixture. The precipitate was filtered and dissolved again. From this solution the team tried to separate barium and radium by fractional crystallization. The solution was heated and first treated with acid, until a small portion crystallized. This precipitate was filtered off. The solution formed a second precipitate which was also filtered off. Subsequently, a third fraction was crystallized. Since radium salts are usually less soluble than barium salts, the former should be enriched in the first fraction and the latter in the last fraction. The radioactive decay of all fractions was analyzed. Since different nuclei were assumed to be present, each fraction should emit their specific radioactive activity. However, Hahn and Straßmann discovered that there were no differences in the activities of the fractions. Apparently, a chemical separation had not taken place.

To verify this, the team also conducted the fractional crystallization with radium salts. It seemed possible that radium in such small quantities behaved in a peculiar and unexpected way. And afterwards, the famous indicator experiment should bring final clarity: Hahn and Straßmann irradiated the uranium sample, mixed it with a radium sample of known radioactive activity and conducted the fractional crystallization with this mixture.[14] And all these series of experiments showed that all the differences in the activity of the separate fractions were only due to the "honest" (quote: O. Hahn [9]), *i.e.* the added radium. The artificial radium showed constant activity through all fractions. Thus, it was a nucleus

11. a) I. Curie, P. Savitch, J. Phys. Radium *7*, 1937, p. 385 - 387; b) I. Curie, P. Savitch, C. R. *206*, 1938, p. 906 - 908; c) I. Curie, P. Savitch, J. Phys. Radium *9*, 1938, p. 355 - 359
12. O. Hahn, Mein Leben. Bruckmann, München,1968, p. 150
13. O. Hahn, F. Straßmann, Naturwissenschaften *46*, 1938, p. 755 - 756
14. A very detailed description of the experiments is given in: F. Krafft, Im Schatten der Sensation. Leben und Wirken von Fritz Straßmann. Verl. Chemie, Weinheim 1981, p. 212 and following pages.

inseparable from barium. The product of the irradiation experiments had to be barium. These results left Hahn and Straßmann clueless. They had no explanation how irradiation of uranium could lead to barium, a much lighter element.

In a letter written on December 19th, 1938 Otto Hahn asked Lise Meitner for an explanation, because he knew that "[uranium] cannot burst into barium". "The more we think about it, the more we come to this terrible conclusion: Our radium isotopes do not behave like radium, but like barium. [...] If you could suggest anything, it would still be like a result of the three of us!" [15]

His point of view that Lise Meitner was still part of the team led to this wish that the results would still be a work of the whole team. Meitner was skeptical and asked very critically whether all other possibilities had been ruled out.[16] She spent Christmas of 1938 with her nephew, physicist Otto Frisch, in Kungälv, Sweden. According to legend, the pair spent hours of walking in the snow and they developed a revolutionary interpretation of the experiments. According to Bohr's liquid drop model, the uranium nucleus started to move after penetration by a neutron.[17] Afterwards appeared constriction and finally separation into two roughly equal-sized fragments, which were each much smaller than the uranium nucleus itself. Thus, an explanation for the light nucleus barium was found. The fragments flew apart with high kinetic energy. Otto Robert Frisch had the honor of giving the new process its name: *nuclear disintegration* and later *nuclear fission*. On New Year's Day, 1939, Lise Meitner told Otto Hahn in a letter that "perhaps it is energetically possible that such a heavy nucleus bursts into pieces." [18]

Today, one can only try to sympathize with Meitner's feelings, which oscillated between frustration and excitement. Her entire life had been turned upside down, apparently she had missed the most important discovery, and this discovery also questioned her own work about the transuranic elements. Hahn and Meitner also corresponded about their feelings in their letters. Hahn wrote: "How beautiful and exciting it would be if we could have done this work together like before." From Meitner's reply he could read the fear that her participation in the discovery could not be adequately approved. And Hahn replied immediately: "It shocked me to see you so depressed." [19]

On January 6th, 1939, the results of Hahn and Straßmann were published. The interpretation culminated in the famous phrase: "As chemists, we should actually call the new nuclei not radium but barium." [20] And the next major publication by Hahn and Straßmann followed February 10th, 1939. [21] The authors reported with absolute certainty that all the previously suspected radium isotopes were in truth barium isotopes. Hahn and Straßmann apparently tried to show that there was indeed a group of three that had obtained the results. The previous publications of the trio and Lise Meitner's name were mentioned several times. Hahn and Straßmann mentioned the transuranic elements: "We are still certain, that the transuranic

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15. Letter quoted in: a) J. Lemmerich, Die Geschichte der Entdeckung der Kernspaltung. Catalogue of the exhibition by the Deutsches Museum and the Hahn-Meitner-Institute of the Technical University, Berlin, 1989, p. 166 - 170; b) W. Gerlach: Otto Hahn, Ein Forscherleben in unserer Zeit. Deutsches Museum Abhandlungen & Berichte, *37*, 1969, p. 52 - 53
16. J. Lemmerich (note 15a), p. 171
17. A modern essay about the finding of nuclear fission and the liquid-drop model is found in: H. J. Krappe, K. Pomorski, „Theory of Nuclear Fission". Springer Verlag Berlin, Heidelberg, 2012
18. Letter quoted in: J. Lemmerich (Ed.), Gedächtnisausstellung zum 100. Geburtstag von Albert Einstein, Otto Hahn, Max von Laue, Lise Meitner 1.3. – 12.4. 1979. Catalogue of the exhibition held in the Staatsbibliothek Preußischer Kulturbesitz, Berlin. Berlin, 1979, p. 122
19. Letters quoted in: J. Lemmerich (note 15a) p. 171, 177
20. O. Hahn, F. Straßmann, Naturwiss. *27*, 1939, p. 11 - 15
21. O. Hahn, F. Straßmann, Naturwiss. *27*, 1939, p. 89 - 95

elements remain." The second fission product was stated to be a noble gas, either krypton or xenon. The publication concluded with the statement that the finding of the new irradiation products was "only possible by the experience we have gained in the earlier, systematic experiments on the transuranic elements, carried out in association with L. Meitner."

Meitner and Frisch published their conclusions in *Nature* in February 1939. [22] They predicted the other fission product correctly: subtracting the atomic number barium (56) from uranium (95) led to krypton (36). This work also explicitly stressed the existence of transuranic elements. In subsequent publications, Frisch and Meitner already provided calculations of the enormous amount of energy released during the reaction and found experimental proof for the fission fragments.[23, 24]

After those publications, various groups all over the world instantly began to repeat, confirm and continue the experiments. Frédéric Joliot-Curie realized that the fission reaction led to the emersion of free neutrons. These could lead to the subsequent fission of further uranium atoms and a self-maintaining chain reaction was thinkable.[25] Soon the whole world was interested in nuclear fission. Frisch and Bohr explained the energy released during the reaction with Einstein's equation $E = mc^2$. [26] The fragments of the nuclear fission reaction combined had a smaller mass than the uranium core. The equivalent of this mass difference was released as free energy.

The different isotopes of uranium have been extensively studied. As early as 1939, Niels Bohr recognized that the fission process only occurs in the rare uranium isotope ^{235}U.[27] In the following year, the American group led by McMillan and Abelson published confirmation that, by irradiation of uranium-238, a transuranic element could be produced. However, this element had different chemical properties than the assumed eka-rhenium. In the article, it is somewhat uncertainly stated that the results, in particular the chemical similarity to uranium, would suggest that there could be a second series of rare earths subsequent to uranium.[28] Thus, the path was clear for the periodic system we know today: Below the lanthanide series follows a series of elements later called actinides. Hahn and Straßmann confirmed and supplemented the results. They provisionally named the new element group "Uranides".[29]

Otto Hahn later said that because they did not recognize the uranium isotope with the half-life of 23 minutes as a precursor of the chemical element neptunium, they missed a Nobel Prize.[30] Later [31] McMillan and others also found the heaviest natural element, plutonium, with an atomic number of 94. It emerged from the bombardment of uranium atoms with deuterium nuclei.[32]

The transuranic elements 93 and 94 were later called neptunium and plutonium in the order of the planets Uranus, Neptune, and Pluto.[33] Plutonium is considered the heaviest naturally

22. L. Meitner, O. R. Frisch, Nature *143*, 1939, p. 239 - 240
23. O. R. Frisch, Nature *143*, 1939, p. 276
24. L. Meitner, O. R. Frisch, Nature *143*, 1939, p. 471 - 472
25. H. v. Halban, F. Joliot, L. Kowarski, Nature *143*, 1939, p. 470 - 471
26. N. Bohr, J. A. Wheeler, Phys. Rev. *56*, 1939, p. 426-450
27. N. Bohr, Phys. Rev. *55*, 1939, p. 418 - 419
28. E. McMillan, P. H. Abelson, Phys. Rev. *57*, 1940, p. 1185 - 1186
29. F. Straßmann, O. Hahn, Naturwissenschaften *30*, 1942, p. 256 - 260
30. O. Hahn (Note 12), p. 167
31. The results were not published until 1946. In the publications it was mentioned that the corresponding experiments took place in 1941.
32. a) G. T. Seaborg, E. M. McMillan, J. W. Kennedy, A. C. Wahl, Phys. Rev. *69*, 1946, p. 366 - 367; b) G. T. Seaborg, A. C. Wahl, J. W. Kennedy, Phys. Rev. *69*, 1946, p. 367; c) J. W. Kennedy, A. C. Wahl, Phys. Rev. *69*, 1946, p. 367 - 368; d) J. W. Kennedy, G. T. Seaborg, E. Segrè, A. C. Wahl, Phys. Rev. *70*, 1946, p. 555 - 556
33. Uranium was discovered in 1789 and named after the recently discovered planet Uranus.

occurring element. It was found in trace amounts in natural uranium ore. The naturally occurring transuranic elements are just like the ones in the laboratory created via neutron capture by uranium-238 atoms.

All other transuranic elements were produced during the following period in nuclear reactors, in part in such large quantities that they found their own technical application. One example is americium, an artificial element with the atomic number 95, which used to be in use in smoke detectors. Other transuranic elements were later detected after collisions in particle accelerators. Those elements produced as individual atoms fell apart after a few seconds.

During World War II, Otto Hahn was a member of the "Uranium Association," a group of scientists who were supposed to work on the technical use of nuclear fission in Germany. But the next generation of radio chemists and physicists had already taken over. During his captivity in England, Otto Hahn learned of the nuclear explosions in Japan by the Americans and of the fact that he had been awarded the Nobel Prize for Chemistry in 1944. Later, Otto Hahn referred to the use of nuclear fission for military purposes as a "mess" [34] that he wanted no part of. He initiated actions against the military use of nuclear power, such as the Mainau Declaration in 1955 or the Göttingen Declaration in 1957.

To receive his Nobel Prize, Hahn had to wait until the ceremony of 1946. He met with Lise Meitner, who expressed her displeasure at having been sent to Sweden by Hahn.[35] Hahn took this for a certain disappointment that he alone was awarded the prize. In fact, awarding the prize to Otto Hahn alone probably remains one of the most debated decisions of the Nobel committee until today. Hahn and Meitner were both nominated several times. Meitner wrote to a friend, "Hahn surely earned the Nobel Prize in Chemistry, there is really no doubt. But I believe that Frisch and I have contributed something essential to the investigation of the uranium fission process – how it is explained, and that it is connected with such a large energy release, Hahn was not aware."[36] Lise Meitner obviously addressed problems directly and spoke clearly about them.

In his Nobel Lecture on December 13th, 1946, Hahn explained the work of the team Hahn, Meitner, and Straßmann in great detail.[37] Being a Nobel Laureate, Otto Hahn later led the Kaiser-Wilhelm-Gesellschaft and its successor, the Max-Planck-Gesellschaft, whose presidency he held until 1960.

But the developments that occurred in other fields after the discovery of nuclear fission have certainly had a much greater impact on humanity. The enormous energy release of the fission process soon led the scientific community to think about the possibilities of a power reactor or an explosive bomb, in the beginning cautiously called "machine". The first nuclear reactor in the world was built by Enrico Fermi in Chicago in 1942. The first atomic bomb was developed in the *Manhattan Project*. With an incredible amount of money and manpower, the Americans pushed their nuclear program. Today, we see it as the beginning of a new era when the first atomic bomb was detonated on July[16th], 1945 in the New Mexico desert. This development is still especially real to the people in Japan since the Japanese people were victims of the two terrible atomic bombings on Hiroshima and Nagasaki on August[6th] and August[8th], 1945. From today's perspective, one might assume that the images of the destroyed

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34. Radio interview with Otto Hahn (1967), Deutsches Museum archive, AV-T 0457
35. O. Hahn (Note 12), p. 206
36. L. Meitner to Mrs. B. Aminoff, 20.11.1945, letter quoted in: J. Lemmerich, Dahlemer Archivgespräche, *6,* 2000, p. 158 – 167
37. O. Hahn (Note 12), p. 247 and following pages

cities would have caused those responsible to rethink, but no: The nuclear arms race was just beginning. To this day, the earth has been shaken by 2053 nuclear explosions.[38]

The artifact: The "Otto-Hahn-table"

In 1952, the director of the Max Planck Institute for Chemistry in Mainz got in touch with the Deutsches Museum to discuss the existing equipment by Otto Hahn. Parts of the original equipment that had been moved after the war from Berlin via the small city of Tailfingen to Mainz, had been arranged there on a table and presented to the public. Neither the museum nor any of the parties involved ever cast doubt on the authenticity of the devices. A description of the exhibit by Fritz Straßmann in 1974 was pragmatic: The table would certainly be one of the then usual work tables from Berlin, but the devices "not entirely the same."[39] "But never mind," Straßmann said, pointing out that some parts "had to be replaced" already during the experiments. One can try to imagine how big the probability is that all the batteries, amplifier tubes and wires survived World War II and at least three moves across Germany after being in Meitner's, Hahn's, and Straßmann's hands.

Once the table and the apparatus were erected in the museum, they waited for a text to explain their meaning. It was planned that a marble tablet should bear the following text:

OTTO HAHN

discovered in 1938, together with Fritz Straßmann, the fission of uranium by neutrons, thus creating the basis for the technical realization of atomic energy.

Otto Hahn was specifically asked by the general director Jonathan Zenneck about his opinion of this synopsis. In his reply dated April 8th, 1953 Hahn was unenthusiastic about the plans of the Museum:

"As much as I am delighted about the attention [...] I'm a little depressed about the presentation that is apparently intended. It seems to me somewhat exaggerated to construct a special niche with a marble table, because if the fission of uranium has been found in aftermath to be very important, neither Mr. Straßmann nor I had any share in this development." In his letter, he goes on to mention Lise Meitner and again asks for his name not to be "mentioned with a special appearance".[40]

This letter clearly contradicts the image that has sometimes been drawn of Otto Hahn that he had spoken too rarely about the share of his colleagues in the discovery, particularly Lise Meitner's share. The mere mentioning of the two colleagues in this letter should have demonstrated to Zenneck that the display as "Otto Hahn table" was wrong. Zenneck and his successors, however, did not change anything for several decades and the name "Otto-Hahn table" stuck.

And this is how the visitors found the artifact: It was called "workbench" but displayed devices which were never used together on one table. The paraffin block and the neutron sources (which were displayed as reproductions) were used in an irradiation room, while the chemical analysis was undertaken in the chemical laboratory of Straßmann. The measurement of the radioactive activities was conducted in the measuring room. The pairwise arrangement

38. http://www.ctbto.org
39. Quote by F. Straßmann in: F. Krafft (note 14), p. 227
40. Hahn to Zenneck, 8.4.1953, Archive of the Max-Planck-Gesellschaft, Abt. III, Rep. 14, Nr. 5287, Bl. 14

of the counters on the table had no scientific grounding, but gave the whole thing a wonderful symmetry. Interestingly, Hahn always talked about three counters that were available (and thus limited the number of possible parallel experiments).[41] That the measurements would have been impossible if set so closely to the neutron source was never mentioned in one of the museum texts.[42]

Otto Hahn was in the museum in 1963 on the occasion of the 25th anniversary of the discovery. He gave a television interview in which he told the entire story in great detail.[9] Hahn emphasizes the contributions and the great teamwork between himself, Meitner and Straßmann. A still image from the movie is now regarded as the moment Hahn arranges the devices for the museum himself, a legend that is just as wrong as it is persistent.

Only in 1989, on the occasion of a major exhibition, a balanced and correct presentation of Meitner's and Straßmann's contributions was finally shown in the museum.[43]

In 1998, the table was lent to the branch musem in Bonn. When lifting the paraffin block, the museum professionals found a trace of historical uranium powder. They locked the paraffin block with a tight fitting glass hood. Since that time, repeated measurements have shown that this museum artifact does not radiate anymore. Since December 2012, the table has been on display in the permanent exhibition.

The majority of visitors connect the object to the development of nuclear power and all its consequences, rather than to the various stories around the discovery of nuclear fission. In the museum, the table became an icon of the history of science, an art object whose aura is fueled not only by its history, but also by its altar-like arrangement.

41. Hahn to Meitner (21.12.1938), letter quoted in: J. Lemmerich (note 15a), p. 171
42. The author thanks Jost Lemmerich for this special note. Personal message (16.4.2013)
43. R. L. Sime, Phys. Perspect, *12,* 2010, p. 190 - 218

Preserving the History of Modern Chemistry

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Introduction

Today I want to provide a broad overview of the issues that concern how we can preserve the history of chemistry and chemical engineering starting in the late 20th and 21st centuries. I don't have time to go into great detail as this is a complex subject, but I hope I can begin a discussion on the matter. I expect that many of these issues are not new to you, but it is rare to discuss them all together as a distinct problem set, so I hope you find this to be a useful exercise. I believe this topic to be of particular interest to us at the Chemical Heritage Foundation (CHF) because we should take the lead and set the example of how to collect the history of science and technology among collecting institutions.

Today I hope to cover many of the issues involved in collecting, preserving, and making accessible to historians a variety of materials: (1) archives, (2) printed materials, (3) physical locations and material culture, (4) digital materials, and (5) oral histories.

Archival materials

For the most part, the greatest resources for the historian of modern chemistry are archival collections. They are the grist of the historian's mill and critical for the historical record. These records have historically been primarily in paper format, though as we know, archival collections can have practically anything in them. They have often been collected by individuals who have gathered whatever they had and placed them in folders, boxes, and even paper bags. They will have letters, memos, offprints, photographs, conference programs, menus, postcards, memorabilia, and anything else they felt the need to keep.

Archival collections can be that of individuals, companies, and other organizations. Each group has different and very specific issues that archivists need to deal with. Personal papers reflect the life of an individual and perhaps others in their family. Some people keep their correspondence and other materials in a very diligent fashion (often the case with engineers) while others pile stuff in drawers and boxes in the order in which it was obtained (often the case with scientists). There is a personal nature to this material and individuals are often unclear about the need to keep and share this others. And scientists are occasionally unclear as to why anyone would want to read their personal correspondence; many think their published record should be sufficient and that more personal materials are irrelevant to their scientific achievements. This is where education is so very important; archivists have to find ways to connect with people and their families throughout their careers and to help them understand why we need to know as much about them to preserve the historical record. Historians must also do their best to make people realize how their stories will be told; it might be a difficult challenge but it could be very worthwhile. There should also be some clarity on whose papers we should collect. Should it just be the prize-winners or are there valuable stories among the less notable stars of science and engineering. Undoubtedly all these stories should be preserved but practically this is not possible for all the archives to do. Most archival collecting policies will target high-profile scientists and engineers and others who worked on projects of great historical importance (like the Manhattan Project, for example). It is very likely that regular "line" academic scientists and engineers will not have their materials preserved. Basically, for someone to have their story preserved, they need to have a champion who will

let us know that this is a person who needs to have their archival legacy preserved. And even that does not ensure success.

The archival records of organizations like the American Chemical Society, the IUPAC, the Smithsonian, and others are also worth preserving as they have important information as to how science is organized and make community decisions. These organizations may not be too concerned with their history initially but they eventually develop some method of preserving founding documents and records of their meetings and decisions. It is important for these organizations to eventually partner with an archive (or create their own) to provide a resource for historians. IUPAC has partnered with CHF to preserve a great deal of their historical materials and these have proven to be one of the most heavily used archives at CHF. Even if these places create their own archives, it should be done in a manner that makes them open to all researchers. Fortunately, most national governments have created archives to preserve their history (in the USA the National Archives and Records Administration takes on this responsibility) but recent events show us that these are not supported to the extent that is really adequate. Budget shortfalls prevent proper processing and storage of these materials and make access difficult. There are promises to digitize much of these national archives but how quickly and effectively can this be done and how sustainable will these efforts be? Anything we can do to ensure that our government representatives know the value of archives is worthwhile, but with the many priorities that a national government has, it seems that archives does not make it very high on that list.

Perhaps highest on the list of archives that are in risk of being lost are the historical records of chemical companies. Companies maintain a records-management policy but that often means that most records are destroyed after a certain period of time. The reason that many historical materials of chemical companies exist is that some employees recognized the value of certain materials and hoarded them or plucked them out of the wastebaskets. Sometimes the company realizes the error of its ways and collects these materials in order to tell its history. The corporate records at CHF (Dow, Union Carbide, J.T. Baker Chemical, Hercules, Rohm & Haas, Spinco, Beckman, etc.) are often a result of retired employees contacting us when they can no longer keep the materials they have collected and asking if we want them (and yes, we do). And sometimes we then have to work with the corporate lawyers to ensure that there is no intellectual property in the material so that they will release the material to us. Fortunately, in general companies have proven to be very good to work with in these matters. But in order to ensure that future materials are not lost, we must be able to build relationships with these companies and constantly keep track of mergers & acquisitions in order to tell when materials might be available or at risk. If one company buys out another, they often do not desire to keep their former rival's materials around and we must be ready to scoop it up as the window of opportunity is very short.

For an institution like CHF, we have a very broad collecting policy and want archival records of every type. So often it can seem like our collecting is random when actually it is opportunistic. To offset this, it can be worthwhile to consider special programs to collect in depth in a very focused area. This seems like it is so obvious, but it requires a lot of things to fall into place in order to be successful. One successful program is a recent one done by the Huntington Library in southern California called the Aerospace History Project. Recognizing that the history of the aerospace industry in southern California was vast yet not found in the archival record, the Huntington joined with the University of Southern California to spend several years in scouring the Los Angeles area to collect whatever still existed on the topic. Because of the extent of the project—identifying potential sources, collecting them,

processing them, and mounting an exhibition and publication about the topic, it required substantial funding beyond that in the Huntington's normal budget. Funding was obtained from the National Science Foundation and the Northrop Grumman Foundation and the project was a great success. CHF did similar projects in its earlier history (polymer science project) and is currently working on the Beckman Legacy project which will hopefully help preserve the legacy of Arnold O. Beckman.

Even assuming that we can successfully collect much of the modern archival record in chemistry and related areas, this can only be done realistically if there are institutions with room to store and staff to process them. In 2010 CHF was at a critical time in its collecting history. A good portion of our building on Chestnut Street in Philadelphia was used to house our collections, but our archival storage was past full capacity. We were at 105% capacity with the excess being stored offsite at a repository in Delaware for a monthly fee. Fortunately, the institution prioritized archival storage as a priority and thanks to a local foundation we were able to convert an adjacent building into a modern archival storage facility, the John C. Haas Archive of Science and Business. It was opened in late 2013 and featured a state-of-the-art high-bay mobile shelving system dedicated to archival record boxes. But in the 15 months we have been using it we have reached 15% capacity. If we continue acquiring new archives at this rate, we can expect to fill the building by the year 2022. If we run out of room again, that could be a problem because few institutions are collecting broadly and deeply in science and technology; so continuing to give CHF the room it needs to collect archives will be important for future generations of historians!

Printed Materials

In the 21st century, collecting printed materials is a new and complex problem for libraries. With the continuing digitization of printed books and journals, the modern academic library is naturally moving to dispose of printed books (and the costs of needing to store them) and focus on providing access to information through digital means. This may be fine for academic libraries that are looking for more efficient and economical ways of providing access to information, but what about historical research libraries like the Othmer Library at CHF? These libraries provide a valuable niche by collecting printed materials by seeing them as historical artifacts, not simply containers of information. With the desire to provide artifacts for exhibition and/or high-resolution reproduction—not to mention our mission of preserving the world's chemical heritage—it makes sense for CHF to focus on collecting historical printed materials. Not all of them, of course, but then which ones? Certainly rare books (hand-printed books before 1850) are worth preserving despite the regular digitization of these titles. For modern post-1850 books, it becomes difficult to preserve everything due to the vast number of printed primary sources to be had. In this area CHF focuses on modern books that are not typically collected by other academic libraries. These consist of scarce titles (very few copies located in the OCLC database) and corporate and industry publications (particularly privately-printed corporate histories and trade journals). We also look to collect all editions of influential textbooks as these are valuable to study and to see how the canonical scientific and engineering information changes over time. For now, most sources of these works for CHF are academic libraries that are disposing of books and journals as well as corporate libraries that downsize or go out of business. But we occasionally find that the most interesting sources of obscure modern printed materials are collectors who have had the foresight to collect things that nobody else collected (for example, materials relating to the development of electronics, genetics, computers, and mass spectrometers). The more we can identify these collectors and work with them to give these materials to libraries when they no longer need them, the better off we will be.

A potential concern for the future of printed materials is the fact that they may become obsolete soon. The future of publishing is not in traditional print but in digital formats (e-books, online resources, etc.). The publishing paradigm is changing now and rather than libraries being able to buy books and have them permanently, they now have to license content from publishers and are not guaranteed of having access to digital publications should their license expire. The collectors of digital publications will not be libraries or individuals but more likely the publishers themselves. What should happen if these publishers go out of business? Fortunately, entities like JSTOR and the Hathi Trust have been developed to ensure long-term access to publications, but the sustainability of these efforts is hard to predict. Things in digital publishing are likely to evolve but for now there is some unease. And for those of us who like to exhibit physical books and articles that mark an important discovery, what do we do now that these will be described in digital publications? Do we exhibit a printout or perhaps do we display a digital display showing these works? Perhaps not a major issue but one that may perplex future history of science exhibitions.

Physical Locations and Material Culture
This may not be a tremendous problem in chemistry, but it has been in other areas of science and engineering, and with the recent Sites of Chemistry conferences, I thought I should include it. Early 20th century observatories like Mount Wilson and Lick Observatory are barely hanging on and may be forced to shut down. Some of the first linear accelerators are also at risk. Much of the United States' early industrial sites have disappeared due to the fact that they are not appreciated for their industrial aesthetic not to mention possible contamination. While we may appreciate that many of these sites may not survive or stay in their original condition, the Historic American Engineering Record (HAER) was established in 1969 by the National Park Service, the American Society of Civil Engineers and the Library of Congress to document historic sites and structures related to engineering and industry. This agreement was later ratified by four other engineering societies: the American Society of Mechanical Engineers, the Institute of Electrical and Electronic Engineers, the American Institute of Chemical Engineers, and the American Institute of Mining, Metallurgical and Petroleum Engineers. Appropriate subjects for documentation are individual sites or objects, such as a bridge, ship, or steel works; or larger systems, like railroads, canals, electronic generation and transmission networks, parkways and roads. HAER helps train people to document, photograph, and produce blueprints and engineering drawings for deposit in the Library of Congress to provide some historical record of engineering and industry. There are other international activities ongoing as well, such as Europa Nostra's Industrial and Engineering Heritage Committee, the European Route of Industrial Heritage, and the Chemical Heritage of Japan project.

The most notable sites of chemistry in the 20th century are chemical laboratories (both academic and industrial) and chemical industrial plants in general. These are very high-risk sites due to the critical need for space in universities and industries and to the difficulty in arguing for "historic" sites to be conserved at the expense of current research needs. If we can count on HAER to document industrial sites, we might want to look at how we can document the academic laboratories. What we tend to have are photographs of work in laboratories that find their way into archival collections but we should look at more systematic ways to document modern laboratories. The logical place to start in the US is with the American Chemical Society's National Historic Chemical Landmarks program. This program aims to celebrate seminal historic chemical activities by recognizing the site with a plaque, even if the site is no longer in existence or in its original form or location.

Unlike large physical sites that are hard to sustain, smaller historic artifacts are easier to preserve, but who is actively doing so? Robert Anderson posits that only CHF is collecting traditional chemical historic artifacts and our collection is predominately 20th-century in scope. But as we are now nearing capacity it will be difficult to be comprehensive in collecting the 20th century. Rather than a complete collection of every chemical science instrument, we have to focus at the present on artifacts that have an important historic story to tell. This has been a challenge for us, primarily because of staffing and space. We have depended on a Historic Instruments and Artifacts Committee to help advise us on what to collect, but it would benefit from expanding the group's topical expertise, and for CHF to be aggressive in collecting chemistry's material culture we need to find additional storage space like we did for our archives. And chances are that material will become available as smaller museums go out of business and as colleges and universities look to find homes for these instruments (assuming they don't just throw them away, as sometimes happens).

Additional material objects that can be collected relate to the products of chemistry, from Bakelite to silicon chips to nylon dresses and Pyrex glassware (if we confine ourselves to synthetic material). These are important items to collect as they exhibit the importance that industry has in developing and making items that we use every day and that we can't imagine being without, making for a strong connection in how science and engineering has an impact on modern society and culture. Because of the ubiquity of much of this type of material, we can afford to collect much of it as we develop a need for specific exhibition material.

Digital Materials
There is a growing amount of digital materials being produced, either as surrogates of physical objects or as born-digital objects (email, photographs, etc.). This material will only continue to grow as historians appreciate the value of having a critical mass of data available for remote research and digital humanities projects. For digital archivists that collect and create this data and make it available on the internet, this is a tremendous resource problem. In order to ensure that every unique digital object is described properly so that researchers can find them and use them efficiently there is a great deal of behind-the-scenes work in capturing images and texts, providing consistent descriptive metadata, establishing digital rights management, and developing user-friendly websites. This is a resource-intensive problem and requires large teams to succeed. All of this is on top of staff and resources to manage physical collections as well. While academic libraries can manage this by downsizing physical collections and repurposing staff for digital activities, smaller historical research libraries have to find new resources to have a digital presence. CHF has addressed this need by adding additional staff to the library in order to initiate a digital collections program. This allows us to address our digital activities appropriately by developing in-house expertise and establishing a robust digital infrastructure to support a long-term online digital collection. This Digital Library team will allow CHF to begin dealing with the often difficult issues of digitization and to take the lead in how to manage and preserve scientific and engineering history in digital form.

An important part of having an active digital collections program is being able to ensure the preservation of digital objects. This is still an issue that is being dealt with, but some things have become clear. Early in our digital lives, the big issue of preservation was how long the physical storage medium (CDs and DVDs) would last. As we have moved to electronic and cloud-based storage, that issue has faded from the scene. But this has been replaced by the issue of software volatility. Even if we preserve digital texts, images, and audio and video

files, the software in which it was produced has a relatively short-lived lifespan. As software formats change, archives will have to be prepared to migrate their data from one format to another at various intervals. Failure to do so regularly may lead to an eventual inability to read the data we have fought hard to preserve.

Another important digital preservation issue is that of websites. Much ephemeral material that used to be printed (corporate information, newsletters, conference programs, etc.) are now appearing only on the internet. This is rarely archived properly by the hosting institutions and so disappear from existence after a short time. While printed ephemera was often saved and eventually collected by libraries, who is saving digital ephemera? Visionaries like Brewster Kahle, founder of the Internet Archive, recognized this early on, but can we rely solely on this organization to preserve our internet history? Or should organizations like CHF actively preserve websites of places that fit their heritage mission? I would argue in favor of adding this activity to our mission but it would require some additional resources that may be hard to come by. Still, I think it worth pursuing.

Oral Histories

It is generally considered that the best way to capture recent historical information is through the creation of oral (or video) histories. This has been an excellent way to capture voices that might have been lost due to their subjects' relative anonymity, especially in documenting labor and social history. In history of science and technology, oral histories developed primarily as a way to learn more details about the lives of relatively prominent individuals such as Nobel Prize winners or other luminaries. Eventually historians began producing oral histories of more obscure subjects to try to preserve marginalized voices. One example was the American Institute of Physics' (AIP) Center for the History of Physics' history of big science project. Knowing that many physics projects were large-scale efforts of hundreds of people from different institutions, the Center selected a few projects to document as they happened by taking oral histories with scientists, technicians, graduate students, and others involved in the project, before their memories faded and everyone went their separate ways. The Smithsonian and Johns Hopkins did a similar project with the History of the Space Telescope. Since the AIP started their program in the 1960s they have perhaps the largest collection of oral history interviews, over 1,500. The Chemical Heritage Foundation was founded as the Center for the History of Chemistry in 1982 and its early activities were modeled on those of the AIP. As a result, CHF began conducting oral histories in the 1980s and has conducted some 425 up until now. Like the AIP, CHF's oral histories were focused on notable individuals but we began moving into modern oral history practice by focusing on collecting a broad sample of voices in a number of project areas such as atmospheric science, mass spectrometry, synthetic rubber, women in chemistry, and the chemical history of electronics. It seems clear that oral histories are, when used in conjunction with other historical evidence, an important resource for history of science and technology, and CHF will endeavor to be a leader in this area.

Conclusion

In conclusion, let me quickly go over some points I tried to address in this paper. I think that in order to be successful in preserving the history of modern chemistry, it is crucial that CHF take an active role and work with partners, if not take the lead, to:
- educate scientists and engineers in why they should preserve their personal papers
- partner with organizations to preserve their historical record
- let companies and their employees know that it is in their best interests to preserve their history

- effectively store the archival record of chemistry
- collect scarce printed materials
- find ways to document sites of chemistry
- continue to collect the material culture of chemistry
- find new and innovative ways to use and preserve our digital heritage
- continue to collect oral histories

I hope this was a useful starting point and I look forward to continued discussion and action going forward.

The Two International Congresses Held in Tokyo in the 1920s: The Rise of the First Generation of Japanese Scientists

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1. Introduction

This paper examines the significance for the state of science and engineering in Japan of two international congresses held in Tokyo in the 1920s: the Third Pan-Pacific Science Congress (PPSC) in 1926 and World Engineering Congress (WEC) in 1929. These two congresses were the first meetings that were not restricted to only one branch of science or engineering but embraced various fields. I will argue that these congresses promoted the rise of the first generation of Japanese scientists.

In my review of academic institutions and societies, I discovered much about the historical situation of science in Japan after the late 19th century. In this paper, I will first introduce some general information about these two congresses, and then I will compare them by discussing their characteristics and what they can tell us about the academic situation in Japan in the 1920s.

After the Meiji Restoration in 1868, the goal of Japanese modernizers was to emulate the Western powers, and Japan began to absorb Western knowledge about science and engineering. The Japanese government had made disadvantageous treaties with European nations in the late 1850s and early 1860s. New higher educational institutions, such as the old University of Tokyo and the Imperial College of Engineering, invited teachers from Europe and the US. Around 1882, Japanese scholars who had studied under foreigners became teachers in the same colleges in order to replace them. In this paper, I call these students the "first generation" of Japanese scientists, who included the chemist Jōji Sakurai (1858–1939) and the civil engineer Kōi Furuichi (1854–1934). Sakurai and Furuichi served as the leaders of PPSC and WEC, respectively.

Generally, international congresses in the 1920s were historically significant: they marked the beginning of academic activities in all international organizations, which had been suspended for more than four years during World War I.[1] The first groundbreaking conference was held in London in October 1918 under the auspices of the Royal Society. About 30 delegates from 10 countries gathered to participate in this conference, and Japan sent two delegates, the chemist Jōji Sakurai and the physicist Aikitsu Tanakadate (1856–1952). Subsequently, Sakurai began paying attention to the international relations among the circle of Japanese academics.

2. General Features of the Congresses

2-1 The Third Pan-Pacific Science Congress in 1926

The Pan-Pacific Science Congress (PPSC) is one of the oldest international meetings. The first PPSC meeting was held in Hawaii in 1920, and the second was held in Australia in 1923. The Pan-Pacific Congresses are still held today. The 22nd PPSC, the most recent congress,

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[1] Sakurai, Jōji, *Omoide no Kazukazu* (Tokyo: Kyuwakai, 1940), p. 286.

was held in 2011 in Kuala Lumpur, Malaysia. The next congress will be held in Taipei, Taiwan in 2016.

The PPSC has two purposes. One is "to initiate and promote cooperation in the study of scientific problems relating to the Pacific region, more particularly those affecting the prosperity and well-being of Pacific peoples." The other is "to strengthen the bonds of peace among Pacific peoples by means of promoting a feeling of brotherhood among the scientists and, through them, among the citizens in general of all the Pacific countries." [2] Approximately 1,000 participants have attended each congress. In 1929, the meeting in Tokyo was held under the auspices of the Japanese National Research Council. Around 1,000 Japanese and 200 foreign scientists gathered as delegates from 106 academic societies in 21 countries. Two years after this meeting, the National Research Council of Japan published the proceedings of this Congress in two volumes.[3] It consisted of 470 papers (including 210 papers by Japanese scientists), and was 2,600 pages in length.

History of Pacific Science Congress[4]

No. (Year)	Venue	No. of Countries	Total Participants (from Japan)
1 (1920)	Honolulu, Hawaii	9	101 (4)
2 (1923)	Sydney and Melbourne, Australia	-	1389 (10)
3 (1926)	**Tokyo, Japan**	21	ca.1200 (ca.1000)
4 (1929)	Java, Netherlands East Indies	-	578 (more than 50)
5 (1933)	Vancouver and Victoria, Canada	-	410 (-)
6 (1939)	Berkeley, USA	-	586 (-)
7 (1949)	Auckland and Christchurch, New Zealand	-	1012 (0)
8 (1953)	Quezon, Philippines	-	- (30)
9 (1957)	Bangkok, Thai	-	ca.1000 (30)
10 (1961)	Honolulu, Hawaii	-	2654 (149)
11 (1966)	Tokyo, Japan	68	6096 (3936)
22 (2011)	Kuala Lumpur, Malaysia	44	824 (-)

2-2. World Engineering Congress in 1929

The World Engineering Congress (WEC) in Tokyo was triggered by a telegram from the US four years prior to the meeting. Masao Kamo (1876–1960), who had served as president of the Japan Society of Mechanical Engineers, received a telegram from the American mechanical engineer, Elmer Sperry (1860–1930) asking if it would be possible to hold a congress in Japan in five years.[5]

Kamo probably felt that it would be too difficult for the Society of Mechanical Engineers to plan and manage the congress. Nevertheless, he brought this inquiry to the attention of the Society of Engineering. In 1922, three years before Kamo received the telegram, the Society of Engineering changed its status from an assembly of individual engineers to an administrative body of 12 engineering societies, including the Society of

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[2]   "The Third Pan-Pacific Science Congress," *Science*, **62**(1595) (1925): 73–74.

[3]   The National Research Council of Japan, ed., *Proceedings of the Third Pan-Pacific Science Congress, Tokyo, 1926*. Vol. I and II (Tokyo: National Research Council of Japan, 1928).

[4]   Masai, Yasuo, "Taiheiyo Chiiki no Tameno Taiheiyo Gakujutsu Kaigi," *Rissho Daigaku Bungaku-bu Ronso* [*The Jornal of the Faculty of Letters, Rissho University*], (82) (1985): 137–141; Hidaka, Kōji, "Kaiso-roku," *Tenki*, **24**(6) (1977): 299–316, p. 310.

[5]   World Engineering Congress, *The Report of World Engineering Congress* (Tokyo: WEC, 1931), p. 1.

Mechanical Engineers. The Society of Engineering asked the government if a budget for holding an international congress would be available in the near future. Thus, the congress began to take shape.

There were nine planning committees, and 765 members were involved in preparing for the congress. The budget they received from the government was 500,000 yen, which is 5 billion yen or 45 million US dollars in today's currency. Four years later, they successfully held the congress. Kōi Furuichi, who was president of the Society of Engineering, became the president of the WEC. The participants had to be members of their local engineering societies, through which the WEC accepted their participation in the congress. At total of 4,495 scholars were registered by the WEC. About 3,000 Japanese and 1,000 foreigners gathered in Tokyo in October 1929, which was roughly four times the number of participants at the PPSC. The WEC covered 12 fields in engineering, and 83 sectional meetings were held. The WEC collected 813 articles (371 from Japan, 442 from overseas). Two years after the congress, it published 39 volumes of proceedings, which ran to 16,000 pages.

3. Features

3-1 Differences

There were of course some differences between these two congresses, such as fields, sizes, and purposes. However, I would like to focus on one major difference: the continuation of these organizations. The PPSC still operates today, but the WEC held only the single, huge congress in Tokyo in 1929.

PPSC has continued for three reasons: First, the organizers intended from the beginning to establish a permanent organization. On the other hand, the organizers in the WEC focused only on the meeting in Tokyo. Second, in the PPSC, the topics were specified, and scientists from various fields participated in each session in order to enhance joint research projects. On the other hand, in the WEC, the fields of engineering were specified according to 12 branches, but the presenters were clustered in each session and were less conscious of collaborating with their audiences and vice versa. Third, the PPSC improved with each congress. On the other hand, because the WEC meeting was perfect, nobody thought that it could be improved, so it was the first and the last.

First, the leading members of the PPSC consciously established a permanent institution with a solid constitution. This action started in 1923 in Australia. The readers of the major journals, such as *Nature* and *Science*, had been notified repeatedly about the establishment of a permanent institution. For example, a final announcement to the readers and the academic world appeared in *Science* one month prior to the congress. The notice states, "One of the principal matters to be considered on this occasion will be the formation of a permanent or continuing organization for this series of congresses. Steps toward this were taken at the Second Pan-Pacific Science Congress, held in Sydney and Melbourne in 1923."[6] Sakurai intended to make the congress permanent at the meeting in Tokyo.

Second, the topics of the papers and discussions were clearly set by the PPSC. Moreover, scientists were encouraged to present papers that enhanced joint research. The organizing committee introduced several issues regarding the Pacific region and then selected 53 of the most significant. Participants gathered from various branches of the sciences to deal

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[6] "The Third Pan-Pacific Science Congress," *Science*, **64**(1655) (1926): 269–272, p. 271.

with each issue.[7] In his inaugural address at PPSC, Sakurai emphasized the features of the congress:

> It is with these views in mind that the Pan-Pacific Science Congress has been organised. Its primary object is to study the scientific problems of the Pacific by cooperative effort, and these problems do not concern one or two only, but many if not all branches of science. In this respect, the Pan-Pacific Science Congress differs from all other scientific congresses. Also because of the primary object of the Congress, which is not the direct advancement of knowledge in general, it is plainly evident that the activities of the Congress should be limited to sciences as applied to definite Pacific problems.[8]

However, in the WEC, even though the purpose of the congress was to include all branches of engineering, the participants did not understand the intention of the organizers because there were no academic communications among other divisions.

Third, all PPSCs have been developed separately. According to Sakurai, the first congress in Hawaii was a trial to see if it was feasible. When the next meeting was held in Australia, Hawaii was called the first congress. In 1923, Sakurai attended the second congress of the PPSC in Australia. He reported three areas that he felt could be improved in future congresses:

> (1) The purpose of the congress was vague; there were many papers dealing with various issues that were not related to the Pacific. I thought topics should be limited to issues related to the Pacific region. (2) The topics of many papers were too narrow to share and discuss with other participants at each session. I was disappointed at this situation. (3) There were 15 or 16 sessions simultaneously; it was deplorable that there were few opportunities for each scientist to meet other participants from different fields in each session. However, it was still natural to see some awkwardness because the second congress in Australia was actually the first official congress.[9]

Sakurai realized that such problems should be addressed to improve the following congress in Tokyo.

Compared to the organizing committee of the PPSCs, the committee of the WEC was too eager to prepare thoroughly for its success. The service of the WEC's organizing committee paradoxically resulted in its termination after just one meeting in Tokyo. The committee members were fully content with all activities, such as banquets and excursions, as well as the academic sessions. Moreover, no country volunteered to host the following congress. Even the Japanese organizers were satisfied with the success of the congress. Consequently, the WEC held only one congress because it was very well organized. After the meeting, academic activities were postponed because of the Japanese military activities that took place in the 1930s. The organizers did not discuss the continuity of the WEC, even though an idea was put forward after the meeting to make the WEC a permanent organization.

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[7]   Standing Committee of the Third Pan-Pacific Science Congress, ed., *The Second Circular for the Third Pan-Pacific Science Congress* (Tokyo: Office of the Third PPSC), pp. 4–5.

[8]   Sakurai (note 1), p. 290.

[9]   Sakurai (note 1), p. 42.

3-2. Common Features

The main purpose of both congresses, of course, was the international exchange of academic work. However, the first generation of Japanese scientists saw these congresses as a chance to enhance the prestige of Japan in the international academic world. The congresses had two distinct features. First, the Japanese leaders promoted the use of English in academic activities. Second, the leaders recognized that the congresses provided good opportunities to enhance the prestige of Japan in the world.

First, the Japanese participants had to use English at both congresses, which was promoted by the leaders, especially Sakurai. At that time, he repeatedly insisted that Japanese scientists should give their papers in English in order to gain the attention of Western scientists.[10] In the chemistry field, for example, the Tokyo Chemical Society (currently the Chemical Society of Japan) began publishing a journal in English in January 1926. In the same month, the Society of the Chemical Industry also began circulating abstracts of their papers in English.

Both PPSC and WEC succeeded in holding meetings in English. As I mentioned previously, about 1,000 Japanese scientists participated in the PPSC. In the proceedings published two years later, 210 papers of 470 papers were submitted by Japanese scientists. In the case of the WEC, 3,000 Japanese engineers gathered in Tokyo. The congress collected 813 papers of which 371 were by Japanese scientists. Most of these papers were written in English.

Second, the Japanese organizers tried to attract the attention of participants from foreign countries. Although neither Sakurai nor Furuichi were particularly successful academically in their lifetimes, they showed strong administrative ability in organizing these congresses. They made the most of their opportunities to enhance the prestige of Japan. Sakurai later recalled the time when he decided to hold an international congress in Tokyo. The delegate members to Hawaii in 1920 suggested that it would be possible to hold the third international congress six years after the one in Australia. Sakurai stated, "If we missed this opportunity to invite many foreign intellectuals, and give them correct recognition of Japan, I was not sure when we would have a next chance to do so. Then, I decided, in my mind, to manage the congress."[11] He reported the outcome of the meeting:

> We successfully held a congress without any problems, like a smooth mechanical clock. Not only did we fulfil our mission, but also we gave the participants from overseas full satisfaction intellectually and materially. As a result, the intellectuals deepened their understanding of our country. Then we promoted goodwill; it was a by-product of this academic meeting. However, I thought this might be more significant than our academic success. This is not our self-praise; many prominent figures from overseas praised the success of this congress, and they said it should be a model for international meetings.[12]

Toshikata Sano (1880–1956), who served as vice president of WEC and as president of Architectural Institute of Japan at that time, reported their motivation for holding WEC in Tokyo, and states:

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[10] Sakurai, Jōji, "Honpo Kagaku no Kokusaika" *Toyo Gakugei Zasshi* (520) (1926): 467–469; Sakurai, Jōji, "Dai 3kai Han-taiheiyō Gakujutsu-kaigi no Kekka ni tsuite no Kansō" *Toyo Gakugei Zasshi* (525) (1927): 1–4.

[11] Sakurai (note 1), p. 40.

[12] Sakurai (note 1), pp. 52–53.

If we welcome many prominent engineers from abroad [...], and let those specialists know traditional Japanese culture besides new industry, they would explain those facts to the people when they went back to their countries. It would be a meaningful occasion to introduce a correct image of Japan to the world; this is what we thought. Then we decided to hold the congress in Japan.[13]

Besides promoting academic exchange, the congress extended its hospitality to activities offering the enjoyment of food and cultural excursions. For example, the Japanese organizers of WEC planned 100 reception parties and banquets. One participant even joked that WEC stood for "We Eat Constantly!"[14] In addition, they prepared 52 excursions, including trips to Yokohama, Aichi, Kyoto, Osaka, and Kōbe for as long as one month after the congress ended.

The National Research Council published a book called *Scientific Japan*, which was made available to all congress participants. Sakurai proudly stated that

Current science in our country is not necessarily the result of the transplantation of western science; seismology, of course, was born and developed in our country. Mathematics and astronomy have been studied and developed since ancient times. To make these accomplishments clear and to let all participants know it, we published a book titled *Scientific Japan* and gave it to them.[15]

In addition to the several common features of these congresses, the WEC congress is historically significant in the development of the field of chemistry in Japan. The implementation of applied chemistry among Japanese scholars was introduced at the WEC congress. The historian of chemistry, Minoru Tanaka, analyzed the number of articles that had been published in the *Journal of the Tokyo Chemical Society* by 1900. He counted 58 articles that dealt with inorganic chemistry. Most articles were about pure chemistry, and only one article dealt with applied inorganic chemistry.[16] In 1898, the Society of the Chemical Industry was established because the academics in this field felt that they needed to work with the industrial sector. Furthermore, since 1924, the Society of the Chemical Industry has held workshops to encourage closer cooperation with chemical engineers. These efforts evolved from the WEC congress, at which 39 out of 71 papers in the division of the chemical industry were presented by Japanese scholars.

4. Discussion

These two congresses represent the final stages of the first generation of Japanese scientists and engineers.

In the early decades of the 20th century, Japan was a country trying to catch up with Western science and engineering. However, the international congresses held in the 1920s were historically significant, symbolic events that demonstrated to the outside world Japan's

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[13]   Sano, Toshikata, "Progress of the World Engineering Congress," *Kenchiku Zasshi* [*Journal of the Institute of Japanese Architects*], **44**(534) (1930): 1193–1204, p. 1194.
[14]   Nakamura, Gentoku, *Nihon Kogyo Kurabu 25 Nenshi, Jō* (Tokyo: Nihon Kogyo Kurabu, 1943), p. 652.
[15]   Sakurai (note 1), p. 52.
[16]   Tanaka, Minoru, *Nihon no Kagaku to Shibata Yūji* (Tokyo: Dainihon-tosho, 1975), p. 70.

rise in the field of science and engineering. In fact, the first generation of Japanese scientists succeeded in holding these major events in Japan. They successfully expanded the academic circle in Japan and raised the international status of Japan in the field of science and engineering. Among these forerunners, Sakurai proudly introduced to the world the rise of Japanese academics in the 60 years since the Meiji Restoration in 1868.[17] Hence, the 1920s was the decade when Japanese academics changed their international status from borrowers of ideas to self-sufficient, innovative researchers.

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[17]   Sakurai (note 1), pp. 124–135.

Jean Gérard, Secretary General and Driving Force of the International Chemical Conferences between the Wars

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The numerous positions that the chemical engineer Jean Gérard (1890-1956) occupied before the Second World War gave him power on a scale that led contemporaries to refer to him as a linchpin, or "cheville ouvrière" in the world of chemistry. His tenacity, far-sighted aims, and organizational skills were the foundation of his success. Here, I examine his activities as secretary general of IUPAC and his crucial role in the foundation of the International Office of Chemistry (IOC).

1. Jean Gérard and the Birth of IUPAC

The International Union of Pure and Applied chemistry (IUPAC) was established as an inter-allied association from which the Central Powers were excluded, in accordance with the decision taken by the Interallied Scientific Academies at meetings in London and Paris in 1918. At a further meeting in Brussels in July 1919, the International Association of Academies (IAA) was dissolved and immediately replaced by the International Research Council (IRC), working under an executive committee and with Britain's Arthur Schuster as secretary general.[1]

In chemistry, the French, notably the chemist Charles Moureu and the chemical engineer Jean Gérard, played a key role in formulating the statutes of the future Union. These were discussed at a meeting of the Allied chemists in London in July 1919 and then immediately submitted to the IRC in Brussels.[2] On 28 July, the transformation of the Interallied Confederation into the International Union was formally approved, with Moureu as its president and Gérard as secretary general.

The Union endorsed the core priorities of the old International Association of Chemical Societies (IACS) that had been created in Paris in 1911.[3] Of the IACS's aims, the Union took up again not only the reform of nomenclature but also documentation in all its aspects, notably the standardization of abstracts and journal titles, the provision of bibliographical tools, and the proper choice of languages. IUPAC's aims, however, went beyond those of the IACS, to embrace several activities that had previously been the responsibility of the pre-war international congresses of applied chemistry.[4]

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[1] Frank Greenaway, *Science International. A History of the International Council of Scientific Unions* (Cambridge: Cambridge University Press, 1996).

[2] See Danielle M.E. Fauque, "French chemists and the international reorganisation of chemistry after World War I", *Ambix*, **58** (2) (2011): 116–135. For the history of IUPAC, see Roger Fennell, *History of IUPAC, 1919-1987* (Oxford: Blackwell Science, 1994).

[3] Brigitte Van Tiggelen, and D. Fauque, "The Formation of the International Association of Chemical Societies", *Chemistry International*, **34** (1) (2012): 8–11.

[4] On the Congresses of applied chemistry, see Duncan Thorburn Burns & Hendrik Deelstra, "The origins and impact of the international congresses of applied chemistry, 1894-1912", *Microchim Acta*, **172** (2011): 277–283. D. Thorburn Burns & H. Deelstra, "Establishing a vital tradition: the series of international congresses of applied chemistry, 1894-1912", *Chemistry International*, **33** (4) (2011): 11–14.

2. Jean Gérard (1890-1956): the Making of a Manager

Jean Gérard was born in Nancy on 16 April 1890, the son of a tanner, Edmond Gérard, who was also a philanthropist.[5] He began his academic career, from 1911 to 1913, as a laboratory assistant in chemistry in the science faculty in Nancy, but then moved to the university's Institut chimique, where he worked as an assistant to Victor Grignard, winner of the Nobel Prize for Chemistry in 1912. Grignard respected Gérard for his skill as an analyst and in 1915 brought him to Paris to undertake war work on poison gases in his laboratory at the Sorbonne.[6]

Gérard's contacts with other laboratories engaged in war-related research led to a meeting with Camille Matignon, professor of chemistry at the Collège de France, who had risen to become one of France's leading chemists. As a prominent figure at chemical congresses before 1914 and someone whose interests embraced both pure and applied chemistry, Matignon had built up an extensive network of international contacts in the industrial as well as the academic world. He introduced the young Gérard (now 26) to his friend Paul Kestner, an industrialist from near Lille. Gérard and Kestner soon discovered a common interest in seeking to create the conditions that would allow chemists and industrialists to collaborate in the reconstruction of France after the war. To that end, in 1917, they established the Société de chimie industrielle (SCI), modelled on Britain's Society of Chemical Industry (BSCI), of which Kestner had long been an enthusiastic member.[7]

Founded during the war, the French SCI benefited in particular from the support of the Ministry of Trade and Industry, as part of its policy of strengthening the links between science and industry. The society's programme outlined three main aims: 1. The creation of a comprehensive chemical library; 2. The establishment of an information service for chemists and manufacturers; 3. The publication of a journal, *Chimie et Industrie*, that would serve as a source of information across the whole field of chemistry, pure and applied. The SCI, along with the BSCI, had encouraged the foundation of the new international union of chemistry, and both bodies were to be centrally involved in the preliminary discussions that led to the establishment of IUPAC in 1918 and early 1919.[8]

This new institutional context presented rich opportunities for Gérard, who saw it as a means of advancing a wider plan that he had been contemplating for some time. His plan was for the reorganization of chemical documentation in accordance with the universal classification prescribed by the International Institute of Bibliography (IIB) that had functioned under Paul Otlet in Brussels since 1895. An immediate measure was the installation of IUPAC in the premises of the SCI at 49 rue des Mathurins in Paris. The French Federation of Chemical Societies (FNAC), the national body that represented France in IUPAC, was also installed at the same address, with Gérard again much to the fore as FNAC's secretary general and Moureu as president. This move was to have decisive consequences both for chemistry and for Gérard's future career. The three bodies were to remain together, always under Gérard's watchful eye, until the Second World War.

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[5] D. Fauque, "Un ingénieur chimiste de Nancy et la chimie internationale dans l'entre-deux-guerres: Jean Gérard (1890-1956)", *Bull. ENSIC*, (174) (2009): 11.

[6] Roger Grignard, *Centenaire de la naissance de Victor Grignard* (Lyon: Audin, 1972), p. 74.

[7] For the history of the SCI, see Ulrike Fell, "Quelle liaison entre la science et l'industrie? La Société de chimie industrielle entre les deux guerres, 1917-1939", in U. Fell (ed.), *Chimie et industrie en Europe. L'apport des sociétés savantes industrielles du XIXe siècle à nos jours* (Paris: Éd. des Archives contemporaines, 2001), p. 69–95; U. Fell, *Disziplin, Profession und Nation. Die Ideologie der Chemie in Frankreich vom Zweiten Kaiserreich bis in die Zwisschenkriegszeit* (Leipzig: Leipziger Universitätsverlag, 2000). For the BSCI, see Robin Mackie and Gerrylynn K. Roberts, "Un secteur à part? Les chimistes industriels et la Society of Chemical Industry dans le contexte de la communauté chimique britannique", in Fell (ed.) (2001) (note 7), 127–147.

[8] See Fauque (note 2).

3. Jean Gérard: Secretary General

The IUPAC statutes of 1919 laid down that the Union's business should be conducted by a Council, with the support of a secretariat and a permanent office. By article 7, the Council was to devolve executive power to a bureau consisting of the president, four vice-presidents, and a secretary general. Members of the bureau were to be elected every three years by a majority vote, none of them, however, being eligible for immediate re-election, with the single exception of the secretary general, who could be re-elected any number of times and so could hold the post indefinitely.[9] Gérard made the most of this dispensation, which allowed him to remain as secretary general until 1944. His most demanding task was to keep the Union's commissions working, a responsibility that involved him in maintaining the flow of correspondence between the various officers, in particular with the president. The volume of paper-work that this entailed was immense.

Article 11 of the statutes also allowed for the creation of a consultative committee made up of delegates, representing the different areas of the chemical industry, who were to be available for consultation on « chemical questions ». This provision was never properly implemented, and it disappeared when the regulations were revised in 1928. But Gérard achieved the same end through the SCI's congresses of industrial chemistry, which he organized from 1921. These congresses quickly became international affairs at which senior figures from IUPAC were often present. Matters bearing on the chemical industry and related issues discussed within the Union would commonly be aired in meetings or congresses of the SCI as well. This was especially the case where questions of industrial property and liquid fuels were concerned.[10]

Another important element in IUPAC's structure was the International Conference of Chemistry (CIC), an event that brought together the Council and representatives of IUPAC's commissions. From 1921 until 1928 these conferences took place annually. Thereafter, under the revised statutes, they were held every two years, with the exception of 1932, when the conference was replaced with three meetings of the Council. CICs invariably lasted two or three days, usually beginning with a reception offered by the host nation, continuing with a programme of scientific lectures, visits to places of scientific, industrial, or touristic interest, and concluding with a conference banquet.

At any CIC the first meeting of the Council began with a report on the Council's activities since the last Conference. General reports on the work of the Union were always prepared by Gérard before being sent on to the president for comment and any amendment. No meeting passed without Gérard's being warmly thanked. This might have been a simple formality, but his correspondence with successive presidents points rather to a close, productive collaboration. While Gérard was flexible and responsive to the Council's views, he was also good at conveying his own wide-ranging vision of the future of the Union and its interactions with other international organizations. His involvement was relentless and it took many forms, often discreet but always efficient, notably in his determination to secure Germany's admission to the Union from 1925.[11]

Here, I shall mention just two areas that particularly concerned him: 1. The management of the commissions; 2. The foundation of the International Office of Chemistry.

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[9] Union internationale de chimie pure et appliquée, *Comptes-rendus de la n^e conférence internationale de la chimie* (Jean Gérard), 1920 à 1938, cited hereafter with an indication of the year and city as 'CR-CIC city year'. The proceedings were undated but invariably appeared a few months after the conference, under the imprint of the Union, and with Gérard's name as publisher. Here, CR-CIC Rome 1920: statutes, 58–59.

[10] D. Fauque, "Les congrès de chimie industrielle dans l'entre-deux-guerres: vitrine des relations entre l'industrie, la science et la politique", *L'Actualité chimique*, (380) (2012): 39–44.

[11] I addressed the German question, in particular the discussions of whether and when Germany should be allowed to join the Union, in my paper at the symposium. This material is being prepared for publication elsewhere.

4. Managing the Commissions

The first IUPAC conference, held in Rome in 1920, provided an opportunity of assessing the Union's achievements so far and presenting a programme of future activities. Provision was made for a number of specialized commissions, several of which had already existed before 1914.[12] The oldest commissions were those for the nomenclature of organic chemistry (1889),[13] analytical chemistry (1900), atomic weights (1902), and tables of constants (1909). Newer ones concerned industrial property and bibliographical documentation.

It was always arranged that commissions should meet during conferences. They were expected to submit their reports well in advance to Gérard, as IUPAC's secretary general, in time for them to be printed and distributed to the IUPAC delegates. But problems were soon evident, as Gérard explained at the 1924 conference in Copenhagen. A first requirement, which he advocated in the interests of efficiency, was that commissions should respond more promptly to the correspondence they received from the secretary general.[14] Secondly, Gérard identified the fact that commissions had no permanent president as a real weakness, one that he wanted to see rectified.

In response to Gérard's concerns, a list of the commissions' presidents for the next three years, agreed upon by correspondence, was submitted to the General Assembly for ratification at the Copenhagen conference. The problems, however, were not resolved. At the Washington conference in 1926, Ernst Cohen, as IUPAC president, laid out the shortcomings, in particular a structure that prevented the commissions from working effectively. As he insisted, experts in the commissions' various areas were frequently absent, so that the conclusions and recommendations coming from them lacked authority.[15] Advocating one possible remedy, Cohen quoted a letter from the British Federal Council (BFC) which requested that resolutions should be distributed in writing before each annual conference. The BFC saw this as a way of facilitating the work of the Bureau and providing a permanent record that might otherwise (as the BFC put it, rather brutally) lie forgotten on some library shelf.[16]

In his remarks at the Warsaw conference in 1927, Cohen returned to the question of the commissions. His assessment remained uncompromising: in his words, « The level of activity in certain commissions stands at absolute zero ».[17] In response to the contention of some members that the practical value of their contribution was negligible, Cohen argued that the Union should concentrate its efforts on projects that were both urgent and feasible: « Our science is too noble and life is too short for us to expect the ablest among us to undertake a type of work whose usefulness is in most cases dubious ».[18]

At the 1928 conference in The Hague Cohen, now at the end of his term as IUPAC president, was as uncompromising as ever: « You all know that the Union's methods of working have been seriously criticized in some circles ». That point, he said, had been recently conveyed in an article in the December 1927 issue of *Industrial and Engineering Chemistry*.[19] In the name of the British Federal Council, Sir William Pope intervened.[20] For him, the Union was in imminent danger. It had been conceived as the foundation for a true chemical congress, but now it was very far from that. Instead of the original plan for groups

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[12] Thorburn Burns & Deelstra (note 4).
[13] On the nomenclature of organic chemistry, see Pieter E. Verkade, *A history of the nomenclature of organic chemistry* (Dordrecht, Boston, Lancaster: D. Reidel Cʸ, 1985), a translation of a series of French texts originally published in *Bull. Soc. Chim. Fr.* (1966–1969). See E. Hepler-Smith in these proceedings.
[14] CR-CIC Copenhagen 1924: p. 27.
[15] CR-CIC Washington 1926: Cohen, 13 September, p. 10–11.
[16] Cohen (note15), 10.
[17] CR-CIC Warsaw 1927: Cohen, 5 September, p.10.
[18] Cohen (note 17), 11.
[19] CR-CIC The Hague 1928: Cohen, 18 July, p.14. "Editorial", *Ind. Eng. Chem*, **19** (12) (1927).
[20] CR-CIC The Hague 1927: Council meeting, 18 July, p. 21.

of experts that would present authoritative reports, what had emerged were commissions of very diverse character, some functioning irregularly, some not at all. Pope's view was that certain commissions should be laid down, while the others should be urged to do what was expected of them. There should be no substitute members: it was for the appointed permanent members to do the work. According to both Pope and Cohen, the statutes and regulations needed to be reviewed. Cohen's criticisms had their effect. In the course of the conference, new statutes and regulations were adopted.[21]

Two years later, in 1930, the Union changed its name to *Union internationale de chimie*.[22] Henceforth, a conference was to be held every two years (an annual conference not leaving enough time for adequate preparation). As the delegates agreed, the mounting of a congress had become an urgent necessity, the last congress of applied chemistry having taken place as long ago as 1912 in Washington. The Spanish proposal to receive the congress in Madrid in 1932 was accepted.

The 1930 conference took place in the course of the universal exhibition in Liège. During the previous winter, the members had voted by correspondence in favour of admitting Germany to the Union, and the German chemists were invited to the Conference. They duly attended and, with Fritz Haber as head of their delegation, were welcomed with applause.[23] Gérard had engaged in intense correspondence with IUPAC members, with a view to ensuring that Germany would be received cordially. It was also reported that Bulgaria had become a member in 1928 and that Hungary, Sweden, and the USSR had been invited.

The 1930s were to be beset with difficulties both for the Union and for Gérard's role in it. Most of the difficulties arose from the economic crisis of 1929 and its repercussions in the early 1930s in France and in Spain, where it proved impossible for either the congress or the annual conference to be held in 1932. The IRC was disbanded in 1931, replaced by the new organization ICSU. There were many instances of cooperation between ICSU and other international organizations, especially the International Institute for Intellectual Cooperation (IIIC) and the associated International Committee for Intellectual Cooperation (ICIC), on such questions as tables of constants, atomic weights, radioactive constants, and bibliography. The Union also developed its own relations with these bodies, which were not always easy. As I point out below, the closest contacts seem to have been with ICIC's sub-commission on bibliography.

Gérard was invariably a member of the delegations representing the Union in its exchanges with the IRC and later with ICSU. In these delegations he was always close to the president, sometimes acting in his place. And, it was he who wrote on the Union's behalf to the general secretaries of the International Union of Physics and the IIIC.

The last three conferences before the war were held in Lucerne in 1936 and in association with the congresses in Madrid (1934) and Rome (1938). In these years a number of new commissions were created, and a major change occurred when the headquarters of the SCI, the FNAC, and IUPAC were all transferred to the Maison de la Chimie, with Gérard as its head, in 1934.

5. The International Office of Chemistry

Since the end of the nineteenth century, the question of chemical documentation had been a constant concern among scientists. An important response was that of Paul Otlet at the IIB; his proposal was for a universal system of classification (CDU). In France, General Hippolyte Sébert applied this system in the Bureau Bibliographique de Paris (BBP), a Parisian

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[21] CR-CIC The Hague 1927: Council meeting, 21 July, p. 42; General Assembly, 21 July, p. 54; new statutes, 56-59; new regulations, 60–62.
[22] CR-CIC Liège 1930: Council meeting, 15 September, p.17.
[23] CR-CIC Liège 1930, (note 22), 18.

bibliographical office linked with the IIB. Gérard was familiar with the work of the BBP and may well have seen the BBP as a model for an International Office of Chemistry supported by IUPAC.

UPAC's Commission on Bibliography and Documentation was a body that particularly engaged Gérard's attention, because of its significant international ramifications. Its objectives included the establishment of agreed systems for bibliographical references and the presentation of abstracts, an international agreement on a programme of documentation, the compilation of an exhaustive corpus of chemical knowledge, and the preparation of a comprehensive bibliography, as reported on by Gérard and approved at the Rome conference of 1920.[24] The permanent office, what was to be called the « Office international de chimie », would be funded by financial contributions that had yet to be secured (art. 9 and 10).

Reports on the work of the Commission were submitted by I. F. Donker-Duyvis in 1922 (Lyon) and 1923 (Cambridge), then in 1924 (Copenhagen) by Matignon, in his capacity as the commission's president.[25] At this last meeting, it was decided that a special conference of government-appointed delegates and experts would be organized. Gérard and Donker-Duyvis were to be in charge of the planning, and the aim would be to agree on international conventions and in due course a fundamental restructuring of the provision for documentation.

A number of events outside IUPAC were at work in this sudden acceleration of interest. The League of Nations had finally approved the creation of the ICIC, with its headquarters in Paris and members appointed as distinguished representatives of their various fields rather than of the nations to which they belonged.[26] In Geneva in August 1922, the vice-president of the ICIC, Gilbert Murray, specified the Committee's three objectives: to resume exchanges between universities, to resurrect and promote international relations in science and scholarship, and to improve the quality of bibliographies, notably in the sciences. The sub-committee on bibliography (a special section of the ICIC) approached several international associations, asking them to turn their attention to provision in their various fields.

The objectives of the ICIC overlapped with those of a number of the international unions and even of the IRC. It was also a competitor with the International Union of Universities and, in bibliography, with Otlet's IIB in Brussels and the Dutch Institute of Documentation (IID), under Donker-Duyvis in The Hague.

In 1924, at the Copenhagen conference, it was announced that the Commission on Documentation had completed its preparatory work, and that the plan for an International Office of Chemistry had been discussed. It now remained for the plan to become reality. Predictably, Gérard emerged as a prominent figure at this next stage, organizing a series of specialized international meetings between 1924 and 1926 that must have served to clarify the terms of the future agreement.

The plan for the International Office of Chemistry (IOC) made a quest for support, both financial and political, essential. There was also the question whether the wider public could be won over. Gérard's answer was an international celebration that would impress the world! On the IUPAC Council he had the support of the president Ernst Cohen and the other members of the Commission on Documentation, including Jean Timmermans (from Belgium), the future IUPAC president Einar Biilman (Denmark), and Friedrich Fichter who was to host the IUPAC conference in Switzerland in 1936.

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[24] CR-CIC Rome 1920: 22 June, p.25; statutes (art. 3), 57; regulations, 62–63.

[25] CR-CIC Lyon 1922: Donker-Duyvis, "Rapport présenté au nom du Conseil national des Pays-Bas et de l'Institut néerlandais de documentation", 93–105. CR-CIC Cambridge 1923: Donker-Duyvis, "Rapport général présenté à la commission", 95–97. CR-CIC Copenhagen 1924: Matignon, "Rapport général", 58–61.

[26] See Jean-Jacques Renoliet, *L'Unesco oubliée. La Société des nations et la coopération intellectuelle (1919-1946)* (Paris: Publications de la Sorbonne, 1999).

From 1925, diplomatic moves were made on a variety of fronts. Gérard, predictably, was the prime mover. His tactic was to alert major figures in the university world, politics, and industry to the benefits that would flow from the celebration of the centenary of the birth of Marcelin Berthelot that he was intending to mount in Paris in 1927. A meticulously planned national and international subscription was to raise the funds for the construction, in Paris, of a Maison de la Chimie. Conceived as a truly international centre, the Maison de la Chimie was to house the Office, along with its various services, including a centre for documentation, congress facilities, and a vast international library.

The Berthelot celebration duly took place between 23 and 26 October 1927, immediately after the Congress of industrial chemistry, held in Paris from 16 to 22 October, both events being organized by Gérard. The official celebration involved ceremonies at locations associated with the life of the « great savant », ending at the Panthéon in the presence of the President of the Republic, ministers, and diplomatic delegations and other foreign representatives.[27] Finally, on 27 October, what had always been conceived as a major goal of the centenary was fulfilled in the form of a conference in the Ministry of Foreign Affairs to discuss the creation of the International Office of Chemistry. The outcome was an international convention specifying the functions of the Office and its eventual installation in the future Maison de la Chimie.[28]

Of the responsibilities of the Office, the only one to be given concrete form was the provision for chemical documentation. As chapter II of the 1920 regulations stipulated, such an office was to function as a formally constituted institution, a status that made it natural for the Union to have its headquarters in Paris and hence for Jean Gérard to exercise control over all the Union's different activities. Such a degree of centralization was unacceptable to some other IUPAC members, and in 1928, when the statutes were reviewed, it was decided that the location of the Union's headquarters would be voted on every four years. By now, all mention of a permanent Office had disappeared.

Seven years later, in 1934, the Maison de la Chimie was inaugurated in the rue St Dominique, an elegant street close to ministries and the Palais-Bourbon, the home of the National Assembly. With Gérard as the overall administrator, it housed the SCI, the SCF, the FNAC, and IUPAC. In a complex administrative structure, in which Gérard held the title of director general, the functions of the International Office of Chemistry, an administrative entity, overlapped to some extent with those of the SCI's Office of Documentation, which incorporated the associated technical services necessary for information management.[29]

The reports that Gérard submitted to the International Conferences of Chemistry in Madrid (1934), Lucerne (1936), and Rome (1938) convey the immense contribution of the Office to such cutting-edge technologies as photocopying, microphotography, and microfilming (done on 35mm film perforated on both sides and with a 24mm-wide image, as recommended by the Office in 1935).[30] The work of the Office also included consideration of the best practices in information management, the tasks of « documentalists », international indexes, and equipment, all of them matters that extended beyond the realm of chemical documentation alone.[31] This was a world of new, advancing techniques on which Gérard reported to successive IUPAC conferences. He also made a significant contribution to planning the

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[27] *Centenaire de Marcelin Berthelot, 1827-1927* (Paris: Imp. Vaugirard, 1929), p. 706: the subscriptions received to 28 December 1930 amounted to 24 895 242 francs.

[28] Charles Normand, "Création de l'Office international de chimie", *Chimie et Industrie*, **18** (5), (1927): 926–932.

[29] These included services for photography, microfilming, photocopying, the preparation of files on demand, a technical centre for testing, etc. Also a publishing company, the SOPRODOC (Société de productions documentaires) was managed by Gérard in the basement of the Maison de la Chimie.

[30] CR-CIC Lucerne 1936: Gérard, 64–75.

[31] CR-CIC Rome 1938: Gérard, 44–52.

World Congress on Universal Documentation in 1937 in Paris and then, in 1938, to the meeting of leading experts in documentation, said to have been « stimulated by the IOC », that took place in Rome during the congress of chemistry.[32]

It is hard to imagine that in the 1930s the Union would have been so committed to the cause of documentation had it not been for Gérard's powerful position, all mention of the Office having disappeared from the statutes and regulations since 1928. The Union's priorities were now turning quite markedly towards pure chemistry.

Eventually, heightened international tensions and then the war put an end to further development of the Office. The prospects of the Maison de la Chimie, too, changed. After the war, for a host of reasons, the Office was no longer up to its various tasks.

Conclusion

In 1940, Gérard made the crucial decision to support the Vichy Regime. He remained at the head of the institution to which he was most attached, the Maison de la Chimie. In 1944, following the Allied victory, he was obliged to resign as secretary general of IUPAC and administrator of the Maison de la Chimie. After an absence of four years, however, he returned to his post at the SCI, and by 1950 was organizing the exhibitions known as *Salons de chimie* held at the Palais des Congrès in Paris, near the Porte de Versailles. He was still involved in this work when he died on the eve of one of the salons in 1956.

Gérard's leadership qualities and the organizational efficiency that he brought to bear on a variety of national and international ventures were nothing less than astonishing. He had an immense capacity for work and was always ready to act, and almost invariably act successfully. He appeared as the model of a manager applying rational principles of work to the goal of collaborative intellectual endeavour; it was this that made him a driving force in everything he touched, a linchpin or "cheville ouvrière", as he was called in many reports.

It is true that in histories of the CNRS, a new organization that was to play a fundamental role in the political as well as the scientific life of the country from the 1930s, Gérard has been interpreted as a hostile force.[33] The fact remains, however, that the SCI owes him a profound and enduring debt. His foundation of the IOC was also important as a central element in what became, in 1932, the Union française des offices de documentation (UFOD), a body of which he was both founder and first president.[34] The UFOD built strong links with the IIIC, and in this context the IOC was widely regarded as an example to be followed in the establishment of offices of documentation everywhere.

Acknowledgments

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[32] CR-CIC Rome 1938: Gérard (note 32), 44.

[33] Denis Guthleben, *Histoire du CNRS de 1939 à nos jours. Une ambition nationale pour la science* (Paris: Armand Colin, 2009). Nicolas Chevassus-au-Louis, *Savants sous l'Occupation* (Paris: éd. Perrin, 2008): 135–141 (222).

[34] On the UFOD, see Sylvie Fayet-Scribe, *Histoire de la documentation en France. Culture, science et technologie de l'information, 1895-1937* (Paris: CNRS Éditions, 2000).

San-ichiro Mizushima and the Realignment of the International Relations of Japanese Chemistry

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Introduction

The period between the 1920s and the 1960s was transformative for both the history of chemistry in Japan and the history of chemistry worldwide. One key way to discuss the relationship between these two concurrent developments is to analyze how Japanese chemistry became connected to chemistry at large by focusing on the personal connections of key players, international congresses and organizations, and also on publications in this process. The question I hope to address here is how these three media together affected the realignment of the international relations of Japanese chemistry around the time of the Second World War.[1]

San-ichiro Mizushima (1899-1983) is an ideal key player on whom to focus.[2] A notable Japanese physical chemist of international standing, Mizushima pioneered studies in quantum chemistry and conformational analysis, and around 1940 coined the "gauche" form of rotational isomers, a conformation where two vicinal groups are separated by a 60 degree torsion angle. He had extensive personal connections with top chemists and physicists around the world. For example, a picture was taken at the old shogunal capital of Kamakura on February 23, 1955, while Linus Pauling (1901-1994) and his wife, Ava Helen (1903-1981), were visiting Japan for the first time.[3] It features the Paulings, the famous Great Buddha statue in Kamakura, and Mizushima who was their host during their Japan tour. This photograph suggests that he had strong connections with American scientists.

This was not the case at the beginning of Mizushima's career. After training in chemistry at Tokyo Imperial University, he went through an overseas study with Dutch physicist Peter Debye (1884-1966) at the University of Leipzig between 1929 and 1931. Mizushima immersed himself in the German scientific world right after completing his university studies, publishing papers in the prestigious physics German journal, the *Physikalische Zeitschrift*.[4]

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[1] For the history of internationalism in science, see, for example, Frank Greenaway, *Science International: A History of the International Council of Science Unions* (Cambridge: Cambridge University Press, 1996) and Geert J. Somsen, "A History of Universalism: Conceptions of the Internationality of Science from the enlightenment to the Cold War," *Minerva* 46 (2008): 361-379. For examples in chemistry, see Roger Fennell, *History of IUPAC, 1919-1987* (Blackwell Science, 1994), Danielle Fauque, "French chemists and the International Reorganisation of chemistry after World War I," *Ambix* 58 (2011): 116-135, and Yoshiyuki Kikuchi, "World War I, International Participation and Reorganisation of the Japanese Chemical Community," *Ambix* 58 (2011): 136-149.

[2] For an outline of Mizushima's life, work and their historical context in Japanese chemistry, see Yoshiyuki Kikuchi, "Mizushima, San-ichiro," in *New Dictionary of Scientific Biography*, ed. Noretta Koertge (8 vols, Farmington Hills, Mich.: Scribner's/Thomson Gale), vol. 5, 167-171.

[3] One can browse this picture on the webpage (http://scarc.library.oregonstate.edu/coll/pauling/calendar/1955/index-document.html, last accessed May 1, 2015). The Ava Helen and Linus Pauling Papers, Oregon State University Libraries Special Collections and Archives, Corvallis, Ore., USA. This source is hereinafter referred to as "the Pauling Papers."

[4] San-ichiro Mizushima, "Anomale Dispersion und Absorption elektrischer Wellen," *Physikalische Zeitschrift* 28 (1927): 418-421; and *idem*, "Streuung von Atomen," *Physikalische Zeitschrift* 32 (1931): 798-803

However, after the end of the Second World War, he quickly established himself as one of the leading scholars in conformational analysis especially influential in the United States. He was offered the prestigious G. F. Baker lectureship at Cornell University and the P.C. Reilly lectureship at the University of Notre Dame, both in 1951. Mizushima published an English monograph based on the content of these lectures, published by the New York-based Academic Press in 1954.[5]

Significantly, Japan was readmitted to the International Union of Pure and Applied Chemistry (IUPAC) in 1951. Mizushima was one of the few Japanese participants in the 1951 IUPAC meeting in New York. Four years later in 1955, he became a bureau member of the IUPAC and stayed in this office until 1967. Japan's increasing standing in the IUPAC thus seems to have been entwined with the evolution of Mizushima's international relations from predominantly German to American connections.

This narrative of realignment away from German connections to those American around the time of the Second World War is well-known among historians of science in Japan and possibly elsewhere in the world.[6] The key question here is *whether and how* these international functions and personal connections were related to each other. To answer to this question, I shall focus on the year 1951, when Mizushima made his first overseas trip after the outbreak of the Second World War. What factors made this trip possible? Did Mizushima's participation in the IUPAC international functions affect the evolution of his personal American connections, or was it the reverse? I shall first look at the respective roles of Pauling, Debye and others in Mizushima's 1951 trip to the United States. I will then address the question of why Mizushima was involved in the IUPAC's business. In conclusion, I will discuss the need to reconsider the very notion of being *international* vis-à-vis *transnational* in order to understand Mizushima's behavior in the post-Second World War world.

Pauling, Mizushima, and "a symposium"

In one of his first letters written after the end of the Second World War, in September 1950, Mizushima told Pauling:[7]

> I have been recently invited to participate in a symposium on "Bond Energies, Force Constants and Bond Distances" to be held in New York next September and to talk to the seminaries of some laboratories about the research works of our laboratory.
>
> On this occasion I should like to realize my dream of visiting your very excellent laboratory of structural chemistry, if you would kindly allow me to do so. I would be very grateful, if any member of your laboratory would discuss on our works on internal rotation or on our infra-red investigation of proteins, […]

To which Pauling replied that he looked forward to seeing Mizushima in the symposium, adding that "we have discussed your papers in the Journal of Chemical Physics and the

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[5] San-ichiro Mizushima, *Structure of Molecules and Internal Rotation* (New York: The Academic Press, 1954).
[6] See, for example, Shigeru Nakayama, Kunio Gotō, and Hitoshi Yoshioka, eds., *A Social History of Science and Technology in Contemporary Japan* (4 vols., Melbourne: Trans Pacific Press, 2001), Vol. I: The Occupation Period 1945-1952, pp. 249-260.
[7] Letter from Mizushima to Pauling, September 10, 1950, the Pauling Papers.

Journal of the American Chemical Society a good bit," and suggesting that Mizushima visit Pasadena after the symposium.[8]

These letters strongly suggest that the symposium they mentioned would be the primary trigger for Mizushima's visit to the United States in 1951. What was this symposium, and who organized it?

Debye and Mizushima's growing reputation in the postwar United States

The correspondence between Mizushima and his old teacher, Peter Debye tells us much more. Debye had immigrated to the United States and took up a professorship at Cornell University in 1940.[9] In a letter written a couple of weeks before, in August 1950, Mizushima told Debye:[10]

> About ten days ago I received a letter of invitation from Dr. Glockler of Iowa to a symposium on "Bond Energies, Force Constants, and Bond Distances" to be held at the time of the meeting celebrating the 75th birthday of the Am[erican] Chem[ical] Society. I am asking our government to send me to the meeting.

This excerpt shows that the symposium Mizushima mentioned to Pauling was part of the *American* Chemical Society meeting also in New York, and that its organizer was a person named Glockler. I shall return to Glockler's identity and his connection with Mizushima a bit later. Mizushima continues:

> This would be the best chance to realize my dream to see you again in your laboratory. Would you kindly help me to do so?
>
> As you know, Japan is economically in bad condition and our government will not allow me to visit your laboratory, unless I can convince it of the necessity of seeing you. The best way of convincing our government is to receive a letter of invitation from your laboratory in which you make me a request of reporting our works in your laboratory, […]

Debye accepted Mizushima's request by writing a letter of invitation for him to present at Cornell's Department of Chemistry, showing the importance of Debye's role in Mizushima's visit to Cornell.[11] It would have been natural for Debye to be desirous to see his old student again after years of separation due to the war. This patronage was therefore quite predictable.

Debye's patronage went far beyond that predictable level. In Mizushima's follow-up letter in November, he further asked Debye:[12]

> You know that the 12th International Congress of Pure and Applied Chemistry will be meeting in New York at the same time and I was told by our

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[8] Letter from Pauling to Mizushima, September 20, 1950, the Pauling Papers.

[9] Debye's career in the Third Reich and his subsequent immigration to the United States was a topic of recent controversies, especially in the Netherlands. See, for example, Martijn Eickhoff, *In the Name of Science: P. J. W. Debye and His Career in Nazi Germany* (Amsterdam: Aksant Academic Publishers, 2008) and Jurrie Reiding, "Peter Debye: Nazi Collaborator or Secret Opponent?" *Ambix* 57 (2010): 275-300.

[10] Letter from Mizushima to Debye, August 30, 1950. Box 21, Folder 5, Correspondence letter M., Archief prof.dr. P.J.W. Debye, (code 21.318A), Regionaal Historisch Centrum Limburg, Maastricht, the Netherlands. This source is hereinafter referred to as "the Debye-Mizushima Correspondence."

[11] Letter from Debye to Mizushima, October 20, 1950, the Debye-Mizushima Correspondence.

[12] Letter from Mizushima to Debye, November 14, 1950, the Debye-Mizushima Correspondence.

Government that it can give me the travelling fee more easily, if I can be invited also by the international congress.

I should be very grateful, if you would kindly write Dr. Harry L. Fisher, National Research Council, […] or any other suitable person and ask to invite me to a section or sections of the international congress suitable to me (e.g. Physical Chemistry, Structural Chemistry, Protein Chemistry, High Polymers).

The circumstance of Mizushima's trip in 1951 has become all but clear: 1) The symposium which triggered the whole event was part of the *American* Chemical Society meeting also in New York; 2) The symposium organizer was "Dr. Glockler of Iowa"; 3) Mizushima's G. F. Baker lectureship of Cornell University and his participation in the IUPAC business relied on Debye's patronage.   The question that remains is: Who was "Dr. Glockler of Iowa"?

The answer lies in Mizushima's first paper, published in 1941 in the *Journal of Chemical Physics,* "Molecular Configurations in Rotational Isomerism."[13]   This was the second of Mizushima's papers that carried the term "*gauche*" in which he and his coauthors claimed priority to the discovery of the *gauche* form against W. F. Edgell and George Glockler of Iowa State University, who had been performing similar research.[14]   So, Mizushima's invitation from Glockler to an American Chemical Society symposium likely signals the growing importance (if not acceptance) of Mizushima's work on rotational isomers among American physical chemists such as Glockler.

This sequence of events shows the crucial importance of Mizushima's 1941 paper, published in the *JCP* just before Japan entered the Second World War, leading to his rising reputation in the postwar United States.   How was it possible for Mizushima to publish it?   In short, it was the result of Debye's timely intervention.   In the first surviving letter to Debye dated January 18, 1950, Mizushima told his mentor:[15]

Since you kindly sent my first manuscript to the editorial board of the Journal of Chemical Physics, the same editorial board as well as that of the Journal of the American Chemical Society accepted many our manuscripts [sic] for publication.   I thank you very much.

It would not be surprising to learn that Debye viewed Mizushima as his old student and supported the development of Mizushima's international career.   What is interesting is the variety of forms in which Debye's patronage was bestowed upon Mizushima.

Mizushima and Japan's Readmission to the IUPAC

Thus far I emphasized the importance of Mizushima's personal connections to Debye.   I am not arguing, however, that his participations in in international conferences were not important.   Mizushima badly needed to get invited to the IUPAC meeting primarily because it would make it easier for him to get funding from the Japanese government.

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[13] San-ichiro Mizushima, Yonezo Morino, and Masatami Takeda, "Molecular Configurations in Rotational Isomeism," *Journal of Chemical Physics* 9 (1941): 826

[14] Walter F. Edgell and George Glockler, "Rotational Isomerism in the Alkyl Halides," *Journal of Chemical Physics* 9 (1941): 375-376.   Edgell and Glockler used the term "the C_2 form."   The first of Mizushima's papers carrying the term "the gauche form" is: Mizushima, Morino and Shizuo Nakamura, "Raman Effect and Dipole Moment in Relation to Free Rotation. XII. Raman Spectra of Ethylene Chlorhydrin, *n*-Propyl Chloride, and *n*-Butane in the Liquid and Solid States," *Scientific Papers of the Institute of Physical and Chemical Research* 12 (1940): 205-215; on p. 213.

[15] Letter from Mizushima to Debye, January 18, 1950, the Debye-Mizushima Correspondence.

To understand the context of its importance, we need to know that, first of all, Japan's poor economic situation just after the end of the Second World War heavily restricted scientists' travels abroad, as Mizushima explained to Debye. Japan became a member of the World Bank (WB) and the International Monetary Fund (IMF) in August 1952 and borrowed a total of US$863 million from the WB spread out as 31 loans between 1953 and 1966, mainly for financing foreign exchange expenditures.[16]

Also significant was the issue of the readmission of Japan *and* West Germany to the IUPAC, which was discussed as a whole between June and November 1950 by the IUPAC's Executive Committee. The committee decided that, because of certain oppositions from Israel, Poland and the Soviet Union, it would defer the question of readmissions until the IUPAC meeting in New York in 1951, though German as well as Japanese chemists would be allowed to participate in this meeting "as individuals,"[17] a typical Cold War solution.

The Japanese chemical community was well informed of this situation. Naoto Kameyama (1890-1963), a Japanese electrochemist and the president of the Science Council of Japan (Nihon Gakujutsu Kaigi or SCJ, which had officially represented Japan at international events since 1949) wrote in November 1950 to Harry L. Fisher (1885-1961), whom Mizushima mentioned in his November letter to Debye above. Fisher was an American organic chemist at the National Research Council in charge of organizing the IUPAC meeting in New York.

Kameyama expressed the SCJ's wish to send official delegates to the New York meeting, and Fisher replied by informing Kameyama of the IUPAC decision above and added that "[it] is our hope that Japan will be well represented at the Congress."[18] In short, the SCJ would need to secure a decent number of participants in the IUPAC meeting for this historic moment. West Germany and Japan were indeed officially readmitted to the IUPAC in the New York meeting in 1951.[19] Mizushima's participation in the IUPAC meeting was thus beneficial to both himself and to the SCJ, and, again, Debye made it possible.

Conclusion: International or transnational?[20]

To put Mizushima's behavior into a more extensive historical context, it would be useful to compare his with those of his academic "grandfather," Joji Sakurai (1858-1939), who also

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[16] Yoshiaki Abe, "Japan and the World Bank, 1951–1966: Japan as a Borrower," *Journal of Asia-Pacific Studies* (Waseda University), No. 17 (October 2011): 217-244.

[17] Letter from R. Delaby (IUPAC Secretary General) to J. Timmermans (President, Belgian National Committee of Chemistry), November 4, 1950. Folder October-December 1950, Box II.8 Bureau Correspondence 1950-1951, International Union of Pure and Applied Chemistry (IUPAC) Archive, Othmer Library of Chemical History, Chemical Heritage Foundation, Philadelphia, Penn., USA. This source is hereinafter referred to as "the IUPAC Papers."

[18] Letter from Naoto Kameyama to Harry L. Fisher, November 30, 1950; and the letter from Fisher to Kameyama, December 7. 1950. Folder: Correspondence re readmission of West Germany and Japan into IUPAC, Box XIX.A1 Conference, NYC, 1951. the IUPAC Papers. See also the letter from Delaby to Fisher, December 16, 1950, confirming Fisher that his reply to Kameyama was perfectly in line with the position of the IUPAC. Folder October-December 1950, Box II.8 Bureau Correspondence 1950-1951, the IUPAC Papers. Delaby added that Yuji Shibata (1882-1980), member of the Japan Academy and senior Japanese chemist who spoke French, visited him in Paris, and he explained about the IUPAC's position to Shibata who, according to Delaby, "seemed satisfied with the position of the Union."

[19] Fennell (note 1), p. 100.

[20] Discussion in this section was inspired by the conversation with Susan Lindee, Betty Smocovitis, and Kenji Ito during the SOKENDAI "Science and Society" Workshop (No. 2) on "The Cold War and Science" (December 13 and 14, 2014), Hayama, Japan, in which I participated as a discussant.

had numerous international connections and was a vice-president of the IUPAC twice, 1923-1925 and 1928-1930.[21]

For Sakurai, the most important issue was how the Japanese chemical community could and should be represented at international conferences. His answer was to establish a National Research Council of Japan (Gakujutsu Kenkyū Kaigi, the predecessor of the SCJ), thereby creating a system in which the Chemistry Division of the National Research Council of Japan, not any of the chemical societies in Japan, represents a national chemical community. In short, being *international*, or the act of representing a nation, was crucial and primary to Sakurai's international activities.

This role of representing a nation seems to have mattered less in Mizushima's international activities after the Second World War. He rather casually used international functions for his own purposes, to fund his trips to attend whatever conferences he preferred or to take up visiting lectureships. It is in this sense, using his casual attitude towards being international, that we can discuss Mizushima's *transnationality,* his going beyond national frameworks.

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[21] Kikuchi (note 1), pp. 146-147.

Female Scientists Whom Nobuo Yamada Encountered：Early Years of Radio Chemistry and the Radium Institute

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Introduction

"Recently, I've been attending Professor Curie's lecture once a week. She seems quite smart, though aged." [1] Nobuo Yamada (1898–1927), a 27-year-old chemist, wrote this in 1923 to his wife in Tokyo, soon after going to Paris to study. He was the first Japanese scientist to join the Radium Institute and receive the guidance of Marie Curie (1867–1934). He jointly conducted research with Irène Curie (Mme Joliot, 1897–1956), Marie's eldest daughter, and published five articles on this collaborative research. Yamada was one of the few Japanese scientists working in the early field of radio chemistry, and his experience was even more unique, as he was the first Japanese male scientist to have a female teacher and female colleagues. Unfortunately, since Yamada died young due to radiation injury, the above-mentioned letter is the only description that he provided of his teacher.[2]

Shocked by the news of Yamada's death just two years after his return to Japan, Marie and Irène, respectively, wrote condolatory letters to Yamada's supervisor and his wife. The Curie Museum in Paris houses copies of those letters. These were the first such letters sent to Japanese recipients by female scientists, as opposed to the wives or daughters of male scientists. Yet Marie and Irène Curie were not the only female scientists that Yamada met in Paris. In the 1920s, the Radium Institute employed many female scientists, including Catherine Chamié (1888–1950), Sonia Słobodkine (Mme Cotelle, 1896–1945).

This paper discusses women of the Radium Institute, with a focus on the period when Yamada was in Paris (1923–1925). In the world, it was the only institute where male and female scientists, who came from various countries, working together under a female leader. The fame of Marie Curie—the first two time Nobel Prize winner (1903 in physics; 1911 in chemistry)—attracted disciples from across the world and stimulated a dramatic increase in the number of women conducting scientific research, especially in radio chemistry. In fact, the fields of atomic science, besides astronomy and crystallography, had a higher ratio of female scientists' involvement. Moreover, as Marie Curie's two Nobel Prizes indicate, this field enabled chemists and physicists to work together closely.

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[1] Post card of Nobuo Yamada, dated November ? 1923. By courtesy of Mr. Mitsuo Yamada.

[2] On Nobuo Yamada, see Keiko Kawashima, "Deux savants japonais et la famille Curie, Nobuo Yamada et Toshiko Yuasa," *Actualité chimique*, mai 2012, n.363 (2012): 51-55.

How did the female disciples work in Marie Curie's laboratory? And what did Marie's existence and role mean for those female scientists? This paper analyses these points from the gender perspective.

1. Curie's First Laboratory and the Radium Institute

From the time when she opened her first laboratory in 1906 to her death in 1934, Marie accepted more than 40 female researchers. This period can be divided into three segments. The first one was the period of the two-room laboratory (from 1906 to June 1914). The second (from July 1914 to November 1918) and third (from December 1918 to May 1934) ones, are during and after World War I.

Even before Pierre and Marie Curie won the Nobel Prize in 1903, their studies into radioactivity attracted the world's attention, but the French government would not give them an independent laboratory. It becomes almost a myth that the couple discovered radium in "a dilapidated shed."[3] After receiving the Nobel Prize, Pierre became a professor at the Sorbonne in 1904, but the post did not give him a new laboratory. Only in 1906, just before his death, Pierre was given the narrow two-room laboratory.[4]

Radium, the element they discovered, was expected to have medical and industrial applications. Yet it was not until 1909 that the government implemented a plan to build the Radium Institute. The Institute, consisting of a medical department and basic research department, opened in July 1914. So, the first period started after Pierre's death in 1906, when Marie succeeded his post as a teacher at the Sorbonne, and started accepting researchers in the two-room laboratory.

Fig.1 Marie Curie in the Radium Institute (about 1923) Musée Curie (coll. ACJC)

When Henri Becquerel discovered the radioactivity of uranium in 1896, radiation was a complete mystery. But α, β and γ-rays were distinguished before World War I. It became clear that radioactivity research meant probing the atom.

Research should be further developed when the new building opened in 1914, but soon after that, World War I broke out. Up until the end of the war in 1918, the Radium

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[3] Eve Curie, translated by Vincent Sheean, *Madame Curie* (London & Toronto: William Heinemann Ltd., 1938), p. 165.

[4] For the definition of "Curie laboratory", see Natalie Pigeard-Micault, "The Curie's Labo and its Women (1906-1934)," *Annals of Science*, 70-1 (2013): 71-100, pp. 2-3: J.L. Davis, "The Research School of Marie Curie in the Paris Faculty, 1907-14," *Annals of Science*, 52 (1995): 321-355, p. 324.

Institute did something unusual. Since the men were off fighting the war, it became a female-centred institution.

However, the war did not completely stop the radioactivity research. In Berlin, Lise Meitner (1878–1968) and Otto Hahn (1879–1968), who later became Irène's rivals, discovered a new radioactive element, protoactinium, in 1917. Moreover, although the announcement was made after the war, Ernest Rutherford (1871–1937), Marie's friend, confirmed that bombarding the nucleus of a nitrogen atom with an α-ray would result in an oxygen nucleus and hydrogen nucleus (proton).

The third period, from the end of the war to 1934, was the most prosperous time for the Radium Institute during Marie's lifetime. Especially in the 1920s, when Yamada was there, France enjoyed favorable business conditions, called *les années folles*, when people from around the world, visited France. Such trends led to the development of the Institute. In addition to aid from the Carnegie Foundation that had been given before the war, Marie gained substantial funds from wealthy supporters and many business enterprises, and she made the Institute the world's centre of radioactivity research.[5]

The great breakthrough of this period was James Chadwick's (1891–1974) discovery of the neutron in 1932, revealing the major components of the atom. As seen in Rutherford's above-mentioned experiment, the scientists were beyond searching to define radiation or the atom, and were introducing the idea of changing the atom. Irène and Frédéric Joliot-Curie's (1900-1958) discovery of artificial radioactivity was also an attempt at achieving the transmutation of the atom. Though nuclear fission had yet to be discovered, the neutron became a new tool for creating additional artificial substances.

2. Curie's First Laboratory (1906–1914) and distinctive features of Marie's female disciples

What did Marie do before 1906? When her husband was alive, she was a physics teacher at Sèvres Higher Normal School for Women since 1900. After Pierre became a professor of the Sorbonne, she held the additional post of *chef de travaux*, laboratory chief of her husband's lab. She was the only woman working in this laboratory at the time.

Now, let's discuss the students of Sèvres, though they were not members of Curie Laboratory. Even after moving to the Sorbonne, Marie arranged for the students of Sèvres to attend her lecture. Among them, her most notable student was Eugénie Feytis (Mme Cotton, 1881-1967), who became a scientist and a famous educator. Later, she became the principal of Sèvres and struggled to realize gender equality in education, especially promoting science education for women. She was also awarded the *Légion d'honneur*.

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[5] As for the development of the Radium Institute and the Curie Institute, see Curie Museum's site:
http://musee.curie.fr/media/files/04_De%20l'institut%20du%20radium%20%C3%A0%20l'institut%20curie.pdf

In the first period—even when Marie Curie had the two-room laboratory—there were always young, female researchers in the laboratory. By what standard did Marie accept these researchers? The pattern was basically as follows. She would accept a person if he or she had an adequate recommendation letter and his or her research theme fit with the work being carried out in her laboratory. Later, ceasing to work hard would mean the discontinuation of one's acceptance.[6] No gender discrimination occurred; Marie judged men and women by the same standard. In fact, this was an amazing

Fig.2 Marie and Irène Curie, and Students of Sèvres. Eugénie Feytis is on the extreme right. (1903) Musée Curie (coll. ACJC)

standard. As Meitner's case reveals, discrimination against women was common at the time.[7] The idea of not distinguishing between the sexes itself was exceptionally rare. So, the news of the establishment of a laboratory led by a woman was a boon to female researchers globally, especially those who wanted to work in radioactivity.

What did those women, or men, come to Curie to do? Most of them were there to gain a PhD or a DES, the qualification for a PhD. Indeed, Yamada earned a Doctorate of Science from Tokyo Imperial University with dissertations he wrote in Paris. The Institute also had many people intending to pursue what would now be called a postdoctoral fellowship. Thus, staying there for about a year, often for only a few months, was common. Such researchers usually remained there on scholarships and paid registration fees to a university and the Institute. Thus, Irène and Marguerite Perey (1909–1975), paid by the Institute and worked there for a long time to make great discoveries, were exceptions. Therefore, many of the young researchers were disciples of Marie as well as Rutherford and/or Stephan Meyer (1872-1949).

For example, Harriet Brooks (Mme Pitcher, 1876–1933) from Canada, the first female researcher at Curie Laboratory, was also Rutherford's disciple, of whom he was proud. Brooks was the first researcher in the world to observe the phenomenon of radioactive recoil. As Rutherford stated, her "work on radioactivity has been of great importance in the analysis of radioactive transformations and next to Marie Curie."[8] There were also many women

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[6] Suzan Quinn, *Marie Curie* (New York: Simon & Schuster, 1995), pp. 402-403.

[7] However, this standard does not explain why Marie denied Lise Meitner the opportunity to work at the Radium Institute. Meitner was an exception; it is true that the Radium Institute was easy to enroll in, but there was a rigorous selection of people after acceptance. On Lise Meitner, see Ruth Lewin Sime, *Lise Meitner: A Life in Physics* (California: Univ. of California Press, 1996).

[8] On Harriet Brooks, see Marelene F. Rayner-Canham & Goeffrey W. Rayner-Canham,

working in Rutherford's laboratory. Rutherford and Marie recommended their disciples to each other according to their specialties. Marie accepted many foreigners. Having been a poor, foreign student herself, she was kind to foreign student. Among her female disciples, more than half were foreigners.[9]

At that time, besides Brooks, other female researchers included Ellen Gleditsch (1879–1968) from Norway, Eva Julia Ramstedt (1879–1974) from Sweden and May Sybil Leslie (Mme Hamilton-Burr, 1887-1937) from England. The trio went on to become great friends.

Gleditsch studied chemistry at the University of Oslo and worked in Curie Laboratory for five years, beginning in 1907. In the lab, she learned fractional crystallization, a difficult technique, and also started measuring the half-life of radium. She returned to Oslo once, and then went to Yale University where she established the half-life of radium as 1,686 years (now adjusted to 1,620 years). She also played a major role in confirming the existence of isotopes. Gleditsch became the second female professor in Norway. She also joined Oslo's Academy of Science. She had been eager to support female scientists; for example, she recommended her two female disciples to the Radium Institute, and she treasured her bond with Marie and other ex-colleagues in Paris for the rest of her life.

Ramstedt worked in Curie Laboratory for one year, from 1910. After returning to Sweden, she became a professor at Stockholm University. While she was president of Sweden Women's High School Committee, she also contributed toward improving women's education internationally.

Leslie belonged to Curie Laboratory for one year, from 1909. She worked on the molecular weight of thorium's emanation and decomposed thorium compounds, about which she published articles. After returning to England, she continued her research in Rutherford's laboratory and also researched emanation from actinium. Later, she found a job in another university's chemistry laboratory in England. During World War I, she worked in the manufacturing of explosives. She continued in her career by taking up various teaching jobs and conducting research until just before her death.

As for people with unique careers, there was Jadwiga Szmidt (Mme Tshernyshev, 1889-1940) from Poland. She belonged to Curie Laboratory for one year, from 1910, and later continued her research under Rutherford in England. Her research focused on comparing α-rays from various sources of radiation and the α-ray absorption ratio difference between various gases. After she married Tshernyshev, a physicist, she worked on the research and development of oscillograph technology for television in Russia. However, the couple

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Harriet Brooks, Pioneer Nuclear Scientist (Montreal & Kingston, London, Buffalo: McGill-Queen's University Press, 1992).

[9] The basic information of the research school of Marie Curie and her female disciples, such as name, nationality and years of birth and death, are based on Pigeard-Micault, (note 4); *Les femmes du laboratoire de Marie Curie* (Paris: Editions Glyphe, 2013). For the period before the WWI, Davis' article (note 4) is also helpful.

mysteriously died in 1940.

Margaret von Wangell (Mme Andronikov, 1876-1932), Russian aristocrat, was forced to flee to Germany during the Russian Revolution. She belonged to Curie Laboratory from 1911 to 1912, and her specialty was thorium. However, later, she turned to the field of agriculture (research on seeds and/or fertilizer). As a nutrition botanist, she became the first female university professor in Germany in 1923. As for the first female professor, there was Irén Götz (Mme Dienes, 1889-1941) in Hungary.

Many of these women joined the Federation of University Women and played active roles in it. This evidences the increase in the number of women who entered, and graduated from universities, and went on to secure relatively good positions in society.

3. The opening of the Radium Institute and World War I (1914–1918)

The Radium Institute with dedicated buildings, which Marie had long awaited, opened in July 1914. But in August, World War I broke out. When the men were sent to the battlefields throughout Europe, it stimulated the social progress of the women. The importance of female researchers also increased at the Institute. Yet as women were engaging in war back-up activities, basic research hardly progressed.

As mentioned previously, Marie organized troops of medical X-ray cars active on the front lines. Many ordinary women were trained at the Institute and worked as X-ray technicians.[10] Researchers including Irène, Suzanne Veil (1886–1956), Marthe Klein (Mme Weiss, 1885–1953) and Madeleine Monin (Mme Molinier, 1898–1976) taught many women the photographic technique of X-ray, and also played an active role in the battlefields. Monin acquired her nursing license after marriage. She received a medal from the Red Cross.

The exceptional research conducted during the war concerned the measurement of radioactive substances against the international radium standard. The Radium Institute had a measurement department. It functioned efficiently during the war, and Irène and Klein developed various measurement methods.

The four women at that time, including Irène, who became an official member in March 1918, were all French. The war influence can be clearly seen in this absence of foreigners.

4. Development of the Radium Institute (1918–1934)

France was victorious in the war, but it lost many human resources. Many women who had made social advancements during the war, and the following generation, continued to work. Women's university enrolment also increased. In fact, in the Sorbonne, almost 30 per

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[10] As for the Radium Institute during the WWI, see Anaïs Massinot & Natalie Pigeard-Micault, *Marie Curie et la grande guerre* (Paris: Edition Glyphe, 2014).

cent of the students enrolled in the faculty of science were female. Therefore, scientist became a career option for women. By this time, most of the women at the Radium Institute had already earned a PhD. This tendency was especially pronounced among the foreigners, among whom 40 per cent had PhDs. Moreover, the total number of researchers at the Institute increased. When Pierre died, there were only seven men and Marie in his laboratory, but when Yamada was there in the 1920s, there were almost 40 researchers in Marie's laboratory, about 10 of whom were female.
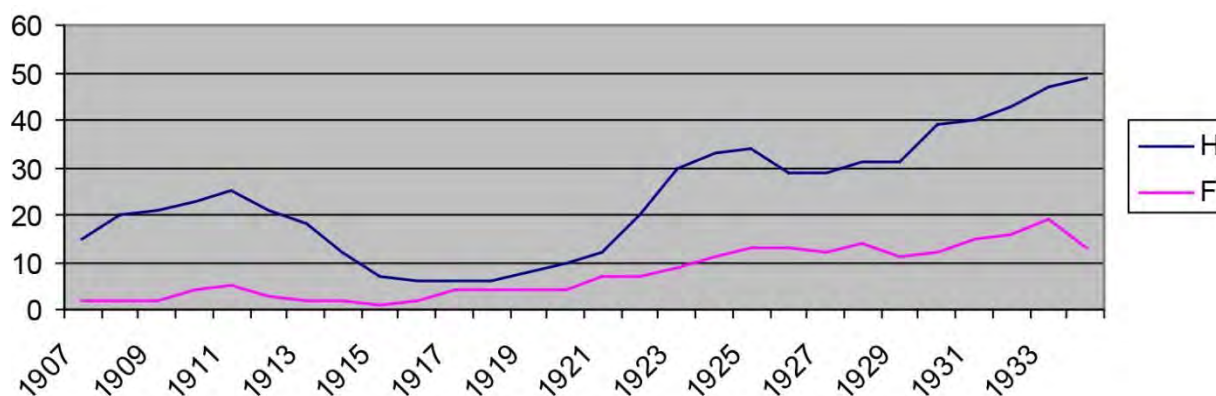
Fig 3. Evolution by sex of person in the Curie laboratory (1906 – 1934) in Natalie Pigeard-Micault, "The Curie's Lab and it's Women (1906-1934), Le laboratoire Curie et ses femmes (1906-1934)," *Annales of Science*, Vol.70, No.1: 71-100, p.80.

The Institute also gained economic strength. Paris brilliantly flourished as a city of sciences and arts. Though Marie criticized the atmosphere of Paris, saying, "Our society, in which reigns an eager desire for rich and luxury, does not understand the value of science,"[11] this economic boom largely contributed to the Institute's development by facilitating the acquisition of research funds and/or scholarships.

It was during this period that Missy Melony, an American journalist, mobilized a women's group to collect funds to invite Marie to the United States. Thanks to the one gram of radium donated on their first visit to the United States (1921), the Institute gained a strong radioactive source. American women also seemed to be encouraged by Curie's visit. In 1920, the year before her first trip to the United States, only 41 women had been granted PhDs in science. But in 1932, three years after her second visit in 1929, there were 138.[12]

Yet 1929 was also the year of the world economic crisis. As the number of unemployed men increased, public opinion became conservative, and the social advancement of women was regarded as an "invasion." Consequently, women's enrolment in university started to decline gradually. And the world plunged into World War II.

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[11] Marie Curie, translated by Charlotte and Vernon Kellog, *Pierre Curie* (New York: Macmillan, 1923), p. 145.
[12] Quinn (note 6), p.396-397.

During the brilliant era between the two world wars, Marie had the largest number of disciples, and she accepted more than 30 women to the Institute. The most brilliant female member after World War I was Irène. While she was a university student, she became already her mother's right hand. In the 1920s, Irène was preparing a doctorate, and she jointly conducted research with Yamada and analyzed the α-ray of polonium from various angles. Later, she married Frédéric Joliot, who had been accepted as Marie's assistant when Yamada was there. The couple conducted a joint study and discovered artificial radioactivity in 1934, for which they were awarded the Nobel Prize for chemistry the following year. This made Irène the second woman to win the Nobel Prize in a scientific field.[13]

Someone in France who was a match for Irène would be Marguerite Perey, who discovered francium, a new radioactive element. Perey, after graduating from a school for female technician workers, joined the Radium Institute as Marie Curie's assistant. That is, she did not initially intend to become a scientist, but Marie recognized her talents. After Marie's death, thanks to the recommendation of André Debierne, the second director of the Institute, Perey enrolled in university in 1936, ultimately receiving her PhD in 1946. Similar to Marie, who named polonium after her country of origin, Perey named the new element after her homeland. This achievement earned her the *Légion d'honneur* award, and she was made the head of the Department of Nuclear Chemistry at the Institute of Nuclear Research of Strasbourg. In 1962, she became the first female corresponding member of the Paris Academy of Science—an organisation which rejected Marie Curie as its member 50 years earlier because she was a woman.[14]

Among the foreigners, Marietta Blau (1894–1970), born in the Austro-Hungarian Empire, was nominated for the Nobel Prize many times. She was highly evaluated by Erwin Shlödinger (1887–1961) and received the award bearing his name. Blau was the first scientist to use nuclear emulsion to search for neutrons. Using this method, she confirmed the decay of the atomic nucleus caused by cosmic rays.[15]

Alicja Dorabialska (1897–1975), Marie's Polish junior, specialized in calculating the energy released by nuclear reactions and measured the heat from polonium with Irène. She became the first female professor at Ukraine University. Many of Curie's disciples, especially foreigners, became the first female professors, heads of research centres or members of academies after they returned to their home countries. Antonia Elisabeth Korvezee (1899–1978), a Dutch, was the first female professor at Delft University of Technology. Branca Edmée Marques (Mme Torres, 1899–1986) was also the first female university professor in Portugal.

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[13] On Irène Joliot-Curie, see Louis-Pascal Jaquemond, *Irène Joliot-Curie* (Paris: Odile Jacob, 2014).

[14] The first woman who became an official member of Paris Academy of Sciences was Yvonne Choquet-Bruhat (the physics department in 1979). As for the chemistry department, Odile Eisenstein became the first female member in 2013.

[15] On Marietta Blau, see Brigitte Stronhmaier & Robert Rosner, English Edition Ed. By Paul F. Dvorak, *Marietta Blau* (Riverside, California: Ariadne Press, 2013).

Fig.4 In the Radium Institute (1930)
Musée Curie (coll. ACJC)

As for someone with a unique background, there was Catherine Chamié, who was born in the Russian Empire to an exiled Lebanese father and a Russian mother. She escaped to Paris during the Russian Revolution and later became naturalized in France. She worked in the measurement department of the Radium Institute and later became director of the department. In addition to creating various radioactive sources and providing them to other researchers, she wrote more than 40 articles.

This was also the period during which the problem of radiation injury increased slightly. In 1925, Margaret Carlough, an American factory worker who painted dials with radium-mixed fluorescent paint, sued U.S. Radium Corporation for causing health hazards. During the lawsuit, the responsible investigators concluded that the dial painters' deaths were due to radiation. However, this news did not spread immediately throughout the world to raise people's awareness about the risk of radioactivity.[16]

Yet, among these female disciples, there were wide individual differences in presenting symptoms. Monin, who was much exposed to X-rays during World War I, and Erzsébet (Elisabeth) Róna (1890–1981), who was involved in the Manhattan Project, lived long lives. Incidentally, the average lifespan of the female disciples was about 70 years; therefore, we cannot say that they died young. Considering that more than half of these women were born in the nineteenth century, it is difficult to judge the harm of the radioactive rays on the basis of their lifespans.[17]

Furthermore, World War II had a huge impact on both the male and female disciples. Quite a few disciples, because they were Jews, were forced to go into exile to escape Nazi persecution. On Einstein's recommendation, Blau left Vienna for Mexico, and then moved to the United States. She returned to Vienna in 1960 and died there. The person who witnessed the most dramatic scene was Róna, born in the Austro-Hungarian Empire. At the Radium Institute, she learned from Irène how to create a strong source of polonium. Later, in 1933, she was awarded the Haitinger Prize from the Vienna Academy of Science for creating radioisotopes through neutron irradiation. However, she immigrated to the United States in

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[16] On the industrial health problem of radioactivity before WWII, see Claudia Clark, *Radium Girls* (Chapel Hill & London: Univ. of North California Press, 1997).

[17] Needless to say, there were several researchers died of radiation injury. On this question, see Anne Fellinger, "Women radio-chemists facing radioactive risks in France," *The Global and the Local: The History of Science and the Cultural Integration of Europe, Proceedings of the 2nd ICESHS* (Cracow, Poland, September 6-9, 2006), ed. by M. Kokowski: 534-539; "Femmes, risqué et radioactivité en France," *La Découverte/ Travail, genre et sociétés*, n.23 (2010): 147-165.

1941 and, like other exiled Jewish scientists, was asked by the U.S. government to back up the war. Róna is said to have been the only female scientist who participated in the Manhattan Project.

This war largely changed the meaning of science. Marie herself died without knowing about the damage that the atomic bombs caused, but many of her disciples were forced to face this reality. The most famous activity regarding war and science was the appeal for the peaceful use of atomic energy by Irène and Frédéric. Apart from them, the activities of Gleditsch and Feytis-Cotton were remarkable. They were deeply involved in anti-Nazi activities during the war and continued the peace movement activities after the war. Specifically, Feytis-Cotton became the vice chairman of the World Peace Council, and received the Stalin Peace Prize in 1951.

While guiding her female disciples, Marie Curie worked actively as a researcher until the end of her life. What did Marie leave to her disciples of the same gender?

Conclusion

"What great model and what encouragement for other women did Marie Curie give!" said Feytis-Cotton.[18] She and her classmates witnessed Marie Curie's oral defense for her PhD, and she was impressed by the attitude of "their teacher," who delivered a dignified speech in front of distinguished scientists. Further, she confirmed that Marie's role for her female students was one of "model and encouragement."

This person, who was a great role model and source of encouragement for women, had other factors that attracted people's attention, such as being the first female Nobel Prize winner or "a tragic widow." Thus, Marie Curie's presence dimmed other female scientists. Besides having many able and talented female disciples, Marie's other aspects as a leader and her female disciples' achievements are not well-known.

Moreover, it is truly unfortunate that some people tried to erase the imprints of these female scientists, as in the case of Brooks. Brooks' negative view on the role of women[19] in nuclear science is completely wrong. There is no doubt about the contributions of women, such as Gleditsch, Perey and Blau, to this field. On top of that, Brooks herself was a person of great achievement, having discovered the recoil of a radioactive atom. The fact is, as mentioned previously, many of Marie's female disciples followed their teacher and became role models for junior female scientists. Those who did not become scientists also inherited Marie's spirit in their own careers, such as in teaching and nursing.

Marelene and Geoffrey Rayner-Canham, who co-wrote Brooks' biography, said that a case like that of Brooks, who abandoned research after marriage and became a full-time housewife, was a typical gender problem.[20] This may be true among women as a whole, but

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[18] Eugénie Cotton, *Les Curies* (Paris: Seghers, 1963), p. 48.
[19] Rayner-Canham (note 8), p. 88.
[20] Regarding this question, see Rayner-Canham, (note 8); *A Devotion to Their Science,*

not among Marie's disciples. Besides seven people whose lives after they left the Radium Institute are unknown due to a lack of documents, the number of people who abandoned research to fulfil a "woman's role", such as marriage, child-bearing or nursing, was only 4 out of 37. In other words, the majority of those disciples continued to work using their scientific skills, whether as scientists, nurses or teachers. Further, most of them, besides being career women, worked toward achieving world peace and/or improving women's social status. Brooks herself, who became a "bourgeois wife," conducted activities for women with various organizations, including the Canadian Federation of University Women.

From the gender perspective, Marie Curie's contribution as an active scientist as well as in leading the radioactivity research, merits special attention. As the first female researchers who had the world-renowned female scientist as their teacher, Marie's female disciples could think of their own potential for becoming teachers of both male and female students. It was impossible for male scientists, such as Rutherford, to do this, no matter how faithfully they might have guided their female disciples. Gender is undeniably the most important point with respect to a role model.

For example, when Irène was single, a journalist asked her if being a scientist was a difficult occupation for a woman. She asserted, "I believe that the scientific aptitudes of men and women are exactly the same." And as for housework, she answered promptly that we should abandon it "on the condition that it is accepted as an additional burden."[21] Furthermore, Mme Tonnerat, Marie's student at the Sorbonne, purposely used the words "male scientists and female scientists" at the commemorative lecture for the fiftieth anniversary of Marie's first class at the university.[22] Irène and Tonnerat had a firm belief that scientific research is for both sexes. We can consider that behind this confirmation was the fact that they knew Marie Curie personally and had colleagues of the same gender.

Lastly, I would like to mention a Japanese female scientist for whom Marie Curie was a spiritual mentor. Toshiko Yuasa (1909-1980) conducted her research in France during World War II. Yuasa, who had been an associate professor at Tokyo Higher Normal School for Women, was the first Japanese woman to receive the French government's scholarship in science. She studied under Frédéric Joliot-Curie and had a close friendship with Irène. In 1943, she obtained a doctorate in science in France. She was forced to return to Japan in 1945, but went back to France after the war, and finally became a researcher at the National Center for Scientific Research. She then spent the rest of her life in Paris.

Even after she became a permanent resident of France, Yuasa continued to encourage her juniors in Japan. After her death, her old school (Now Ochanomizu University)

Pionner Women of Radioactivity (Montreal et. al.: McGill University Press, 1997).
[21] Robert Reid, *Marie Curie* (New York: The New American Library, 1974), p. 247.
[22] M.A. Tonnelat, "Discours de Mme T.A. Tonnerat, Professeur de Physique Mathématique à la Sorbonne," *Cinquantenaire du premier cours de Marie Curie à la Sorbonne* (Paris: A. Coueslant, 1957): 38-39, p. 38.

established a scholarship in her name for female scientists in 2002.[23] We can say that this is part of the heritage passed down from Marie Curie's laboratory, from a female scientist to her juniors.

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[23] On Toshiko Yuasa, see *Catalog of Toshiko Yuasa's (1909–1980) Archives* (Tokyo: Institute for Gender Studies, Ochanomizu University, 2009): Kawashima (note 2).

Changing Names and Naming Change: Transformations in the "International Machinery" of Chemical Information

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"It all began, we are told" mused Austin Patterson, meaning the business of attaching names to things, "when Adam named the animals; his descendants have extended the practice to everything, including chemicals." In this sense, chemical names were no different from any others. However, in his 1951 column in the newsmagazine of the American Chemical Society, Patterson wanted to discuss what *was* distinctive about chemical names – especially the systematic chemical names that many of his colleagues found so vexing. As Patterson put it, "Why trouble about rules for naming?"[1]

Chemical science and industry have long depended on their information technologies. Chemistry – particularly organic chemistry – was and is a science of the archive, in which an exhaustive search through the discipline's accumulated achievements is often prerequisite to making new knowledge, and new knowledge duly joins the mass from which it came.[2] This process involves chemical names (or, more generally, identifiers), the technological systems in which chemical information is ordered and made accessible by means of these names, and the institutions that build and maintain these information systems. Only by examining the interconnections among systems of chemical nomenclature, chemical reference media, and chemical institutions can we historicize Patterson's question and begin to assemble an historical answer.[3]

Writing for an audience made up mostly of chemists working in industry, Patterson offered a more mundane response: "Inferior names and lack of good indexing systems are exceedingly expensive." What made a good nomenclature system – and thus a potential boon to chemical science and industry – was simple: each chemical compound should have a unique name that unambiguously indicated the network of atoms and bonds that made it up, as expressed by the compound's structural formula (*Fig. 1*). This vision of a one-to-one correspondence between chemical name, chemical diagram, and chemical substance was forged at the 1892 Geneva Nomenclature Congress.[4] Actually establishing such a system on an international basis proved elusive. Even in 1951, Patterson cautioned his readers to hope for no more from an upcoming international symposium on chemical nomenclature than that "some decisions will become definitive, some will be tentative, and some matters will merely be discussed without decision. That's the way the international machinery works."[5]

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[1] Austin M. Patterson, *Words About Words: A Collection of Nomenclature Columns* (Washington: American Chemical Society, 1957), 1.
[2] Lorraine Daston, "The Sciences of the Archive," *Osiris* 27 (2012): 156–87.
[3] There is an emerging historiography addressing the practices, technologies, and social order of scientific compilation and other topics sometimes loosely referred to under the heading of "Big Data." Chemical compilation at the turn of the 20th century has a pivotal place in this history about which we so far know too little. However, see Evan Hepler-Smith, "Nominally Rational: Systematic Nomenclature and the Structure of Organic Chemistry, 1889-1940" (Ph.D. Diss., Princeton University, forthcoming 2016).
[4] Evan Hepler-Smith, "'Just as the Structural Formula Does': Names, Diagrams, and the Structure of Organic Chemistry at the 1892 Geneva Nomenclature Congress," *Ambix* 62 (2015): 1–28.
[5] Patterson, *Words About Words*, 4.
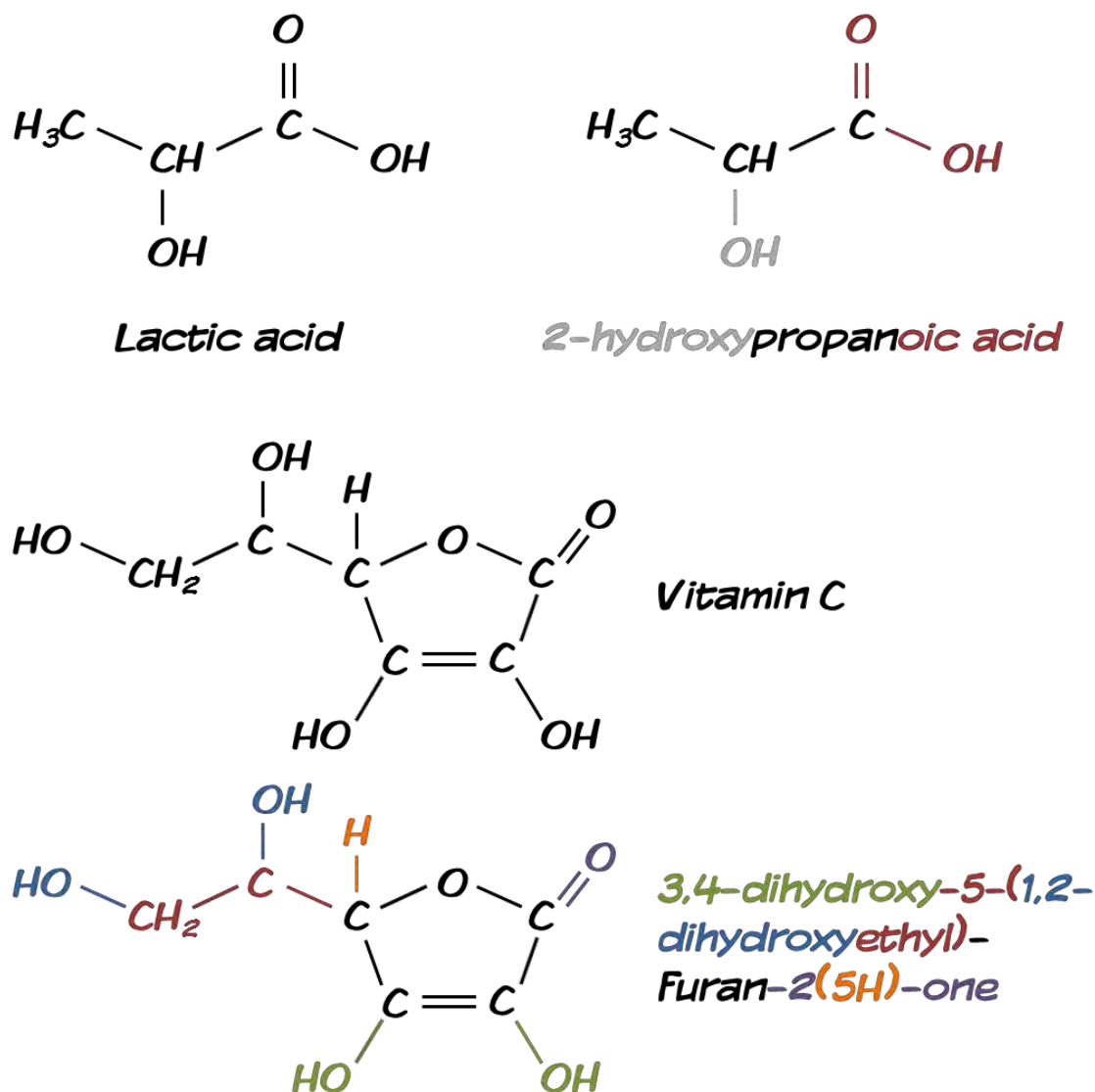
Figure 1. The correspondence between systematic names and structural formulas, per current IUPAC nomenclature guidelines.

The ideal of the unique, unambiguous representation of a chemical structure played a central role in the development of the "international machinery" of chemical information from the 1920s through the 1960s.[6] During the 1920s, an international nomenclature commission broke with this ideal in order to establish rules that would support rather than interfere with the compilation of print reference works. After World War II, chemists working in associational and industrial settings sought to realize it in a form of notation adapted to the medium of punched cards. During the 1960s, a collaborative effort to bring computers to bear on the management of chemical information generated a new way of identifying a compound and describing its structure using two different forms of representation, brought together in the computer.

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[6] For a detailed technical account of the history of organic chemical nomenclature during this period, see Pieter Eduard Verkade, *A History of the Nomenclature of Organic Chemistry*, trans. S. G. Davies (Boston: Reidel, 1985).

I. Name • Print • Union

In the wake of the First World War, the International Union of Pure and Applied Chemistry (IUPAC) took up the reform of organic chemical nomenclature as part of its standardizing mission. However, the editors of chemical reference works had gotten there first. Such publications as the American abstract journal *Chemical Abstracts* and the magisterial German compilation *Beilsteins Handbuch* gathered vast amounts of chemical data and literature references under the headings of the tens of thousands of chemical compounds to which they referred. In order to facilitate both the use of these works and the unending process of compiling them, editors developed their own elaborate rules for naming and ordering chemical compounds. Each of these schemes drew upon elements of the Geneva nomenclature, but they adapted and expanded the narrow Geneva rules in different ways. Editors could little afford to tinker with nomenclature or organization once their works began to be published. Furthermore, the editors of the all-important German reference works would surely spurn any guidelines issued by IUPAC, which, like other postwar scientific unions organized by representatives of the victorious Entente, banned Germany and the other former Central Powers from membership.[7]

The recent appearance of the collective index to *Chemical Abstracts* and the first volumes of the fourth edition of *Beilstein* therefore circumscribed IUPAC's ambitions for its own nomenclature rules. The Union's working group on organic nomenclature, led by Dutch chemist Arnold Holleman, shifted its focus to guiding chemical nomenclature in general in a "more rational direction, which had been the goal of the Geneva Congress."[8] The various systems of nomenclature and organization adopted in reference works *liberated* the IUPAC reformers from the pressure of codifying unique, unambiguous names, allowing them instead to develop rules that they hoped would be more broadly useful and acceptable.

For example, several group members advocated ordering the prefixes of each chemical name according to a hierarchy of chemical precedence; Patterson, the group's American member, favored ordering them alphabetically. Instead of putting its work on hold until the dispute could be resolved, Holleman's group opted simply to permit either approach. Similarly, the group accepted some inconsistency in the expression of structural features in exchange for making individual names shorter and easier to read.[9]

In the opinion of Victor Grignard, the working group had abused its freedom. To Grignard, a 1912 Nobel laureate and the French member of the IUPAC commission to which Holleman reported, the recommendations amounted to an abrogation of the logic of the Geneva nomenclature. He referred to the group's tolerance for alternatives and inconsistencies as "Anglo-Saxon illogic" that threatened to "destroy the fine order established by the Geneva Congress."[10]

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[7] Daniel J. Kevles, "'Into Hostile Political Camps': The Reorganization of International Science in World War I," *Isis* 62 (1971): 47–60; Brigitte Schroeder-Gudehus, *Les Scientifiques et la Paix: La Communauté Scientifique Internationale au Cours des Années 20* (Montréal: Presses de l'Université de Montréal, 1978); Michael D. Gordin, *Scientific Babel* (Chicago: Chicago University Press, 2015), 159–85.

[8] IUPAC *Comptes-Rendus* 3 (1923): 83.

[9] A.-F. Holleman et al., *Rapport du Comité de Travail de Réforme de la Nomenclature de Chimie Organique* (Paris: IUPAC, 1927), 4.

[10] Grignard to Gérard, 20 May 1928, IUPAC Archive, Chemical Heritage Foundation, Box 52; Victor Grignard, *Remarques au Rapport du Comité de Travail* (Paris: IUPAC, 1927), 5.
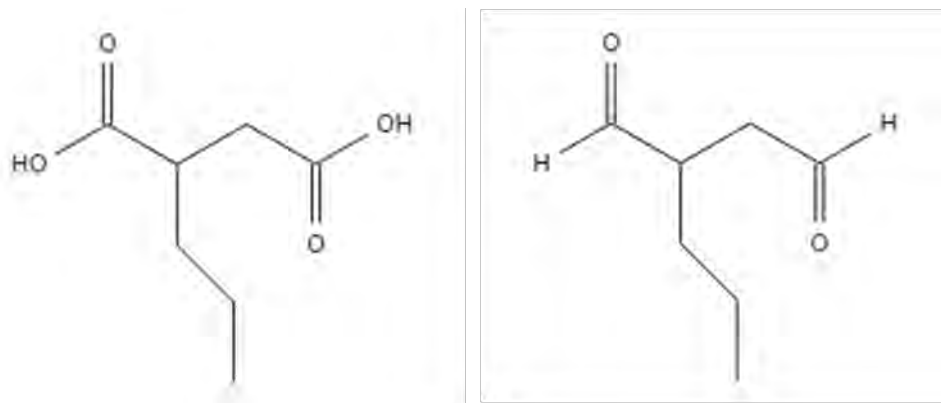
Geneva: 3-methyl-1,3[1]-hexanedioic acid   *Geneva*:   3-methyl-1,3[1]-hexanedial

WG: 1,2-pentanedicarboxylic acid   *WG*:   propylbutanedial
             propylsuccinic acid   propylsuccinaldehyde

Grignard: 2-propylbutanedioic acid   *Grignard*: 2-propylbutanedial

Figure 2. Naming a diacid and its corresponding dialdehyde according to the Geneva rules, the rules proposed by Holleman's working group in 1927, and Grignard's alternative to their "Anglo-Saxon illogic." The Geneva rules assign systematic names to each compound using a consistent logic. These names are cumbersome, but they express the structural relationship between the two compounds unambiguously. The working group's names are easier to read, but they are not unique and do not capture the structural similarity of the compounds as precisely. Grignard sought to clarify the Geneva names without making such compromises.

At the IUPAC annual meetings in 1927 and 1928, Grignard staved off a vote to affirm the working group's report and even rallied his fellow commission members against certain of its provisions. Between the meetings, he published his criticisms for consideration by the chemical general public. Grignard considered the active participation of chemists all over the world a necessary part of this process. "It is indispensable," Grignard wrote, "if the new nomenclature is not to remain a dead letter, like the old, that it be able to rely on the authority of the greatest possible number of scientists who will make a tacit commitment to teach it and to enforce it locally."[11]

For Holleman, the success of the IUPAC nomenclature effort rested not on the approval of the chemical public but of the editors of chemical reference works. From the beginning, he had worked with Patterson to ensure that the staff of *Chemical Abstracts* knew of the working group's plans. The delay in the approval of the working group's rules due to Grignard's machinations opened up an opportunity to secure the approval of another set of editors, when Union leaders began to negotiate terms for Germany's return to the fold of international chemistry. The worldwide prominence of *Beilstein* and other German reference works made nomenclature an important bargaining chip in the effort to convince Germany to join the Union that had snubbed it for a decade.

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[11] Victor Grignard, "Quelques Remarques à propos du Projet de Réforme de la Nomenclature de Chimie Organique," *Bulletin de la Société Chimique de France* 45 (1929): 983.

Holleman met with the editors of *Beilstein* and the other major reference works published by the Deutsche Chemische Gesellschaft in Berlin in May 1930. The Germans editors wanted to make absolutely certain that the IUPAC rules were not promulgated as an official nomenclature that might interfere with their editorial work. In exchange for the support of these editors, Holleman agreed to exempt their publications explicitly from the IUPAC nomenclature rules. Three months later, Germany joined IUPAC, *Beilstein* editor-in-chief Bernhard Prager joined the organic nomenclature commission, and the Union finally approved the working group's recommendations. [12] The new preface to the rules stated unequivocally, "This report is not intended to interfere with the editing of *Beilstein* or of *Chemical Abstracts*, publications which have followed for many years their own systems of nomenclature."[13]

The exemption of these reference works was not a sign of the independence of IUPAC nomenclature rules and the print technology and institutional configuration of chemical reference works, but a sign of how deeply the latter shaped the making of the former. Grignard himself recognized this. He gave up his campaign against the rules, having realized that, as he put it a few years later, Holleman's group "found itself in the presence of nearly insurmountable difficulties, because of methods of nomenclature already in use in the major references such as *Chemical Abstracts* and the *Chemisches Zentralblatt* and in the fourth edition of *Beilstein*. ... The new reform arrived twenty or thirty years too late."[14] The IUPAC nomenclature commission codified a set of rules and a method of rule-making that *protected* the institutions of chemical information and the reference works that they compiled against nomenclature rules that might have interfered with the making or use of their works.

II. Cipher • Card • Publisher/Firm

Shortly after the end of the Second World War, the British chemist G. Malcolm Dyson repeated the observation that Grignard had made a decade earlier: "by the time of the [1930] Liège report, such wide differences had been set up between British, American and Continental usage that any hope of reconciling them fully had vanished."[15] The relentless accumulation of chemical compounds and publications, along with the disorder brought on by war, especially in Germany, had slowed the compilation process.

To salvage the ideal of precise correspondence between name and structural formula, Dyson turned away from nomenclature to a parallel genre of chemical notation. For reasons of both economy and epistemology, chemists often condensed graphical structural formulas into text-only formulas, using punctuation conventions rather than diagrams to represent patterns of connection among atoms.[16] For any but the simplest compounds, these linear formulas were lengthy, ambiguous, or both, and they could be written in nearly as many ways as a structural formula could be drawn. Dyson, in contrast, looked beyond the limited vocabulary of chemical symbols, subscript numbers, and parentheses, mining the rest of the keyboard to

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[12] Verkade, *A History*, 146.

[13] Austin M. Patterson, "Definitive Report of the Commission on the Reform of the Nomenclature of Organic Chemistry," *Journal of the American Chemical Society* 55 (1933): 3906–07.

[14] Victor Grignard, *Traité de Chimie Organique* (Paris: Masson, 1935), 1075.

[15] G. Malcolm Dyson, *A New Notation and Enumeration System for Organic Compounds* (London: Longmans, Green, 1947), 2.

[16] There was ample precedent stretching back to the early nineteenth century for the use of text-based formulas as "paper tools" for experimenting with models of chemical constitution and classification. See Ursula Klein, *Experiments, Models, Paper Tools: Cultures of Organic Chemistry in the Nineteenth Century* (Stanford: Stanford University Press, 2003).

develop a system of unique, compact text-based representations of structural formulas. Dyson called his linear formulas "ciphers."[17]

Much of the advantage that Dyson attributed to his ciphers related to their use in a medium of information technology that was just beginning to be applied to ordering chemical compounds.[18] "Using the cipher," Dyson explained, "both the structure of the compound and the key to its literature references can be recorded on a punched card; such cards can be manipulated by automatic machines."[19] The capacity of the cipher to unlock punched cards as a resource for chemical editors was the key to how they would clear the backlog in indexing.[20]

Dyson brought his work on ciphering to institutions that could establish and use it as an international standard to aid in the compilation of chemical reference works. Soon after publishing his first detailed account of his rules for ciphering in 1947, Dyson took up the presidency of a new IUPAC Commission on Codification, Ciphering, and Punched Card Techniques.[21] After about a decade of study, the commission adopted a modified version of Dyson's cipher as an official IUPAC standard.[22] Around the same time, in the late 1950s, Dyson took a position as research director for Chemical Abstracts Service (CAS), the American Chemical Society division responsible for publishing *Chemical Abstracts*.[23] In this position, he trumpeted the particular advantages of his notation for index-makers: his ciphers grouped structurally-related compounds together, could serve as a basis for generating systematic names, and had official IUPAC approval.[24]

As in the case of chemical nomenclature, different ciphers seemed preferable in different circumstances. The most broadly-adopted alternative to Dyson's cipher was a notation designed by the American chemist William J. Wiswesser. Wiswesser Line Notation (WLN), as it became known, achieved much wider use among American chemical firms than Dyson's cipher ever did. Users cited several reasons for preferring it over Dyson's IUPAC-approved notation. WLN was simpler: on average, it required fewer symbols, leaving a greater proportion of a punched card available for coding other sorts of information. Many chemists also found it easier to learn and to read.[25] Perhaps most importantly for the American firms that took it up, WLN notation could be handled by standard IBM machines – machines that many of these firms likely already leased.[26] The Dyson-IUPAC system, in contrast, required customized equipment.[27]

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[17] Dyson, *A New Notation*, 4.

[18] On the history of punched card data-processing systems, see James W. Cortada, *Before the Computer: IBM, NCR, Burroughs, and Remington Rand and the Industry They Created, 1865-1956* (Princeton: Princeton University Press, 1993).

[19] Dyson, *A New Notation*, 7.

[20] Ibid.

[21] Verkade, *A History*, 204–05.

[22] National Research Council, *Survey of Chemical Notation Systems* (Washington: National Academies, 1964), iii.

[23] Dale B. Baker, interview by Robert V. Williams and Leo B. Slater at Columbus, Ohio, 9 June 1997 (Philadelphia: Chemical Heritage Foundation, Oral History Transcript # 0160), 15 (cited hereafter as "Baker oral history").

[24] National Research Council, *Chemical Notation Systems*, 47.

[25] Simplicity, of course, could be subjective; Dyson claimed that his cipher was "easier to use." Ibid.

[26] Ibid., 46-47.

[27] Ibid., 29.
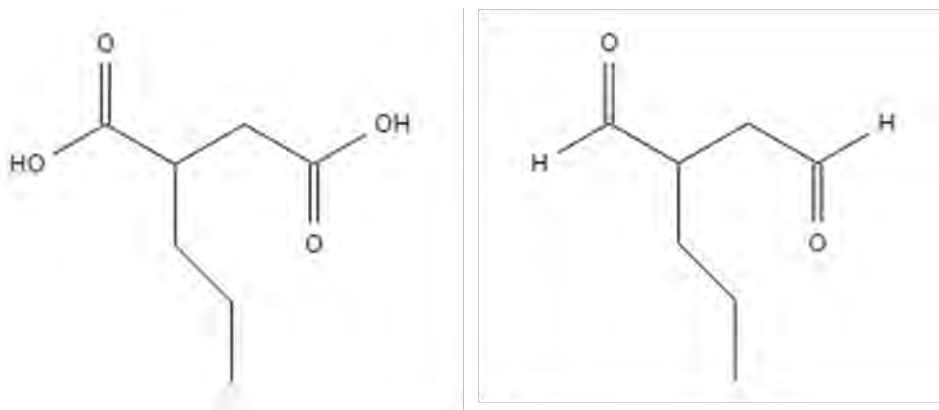
Condensed formula (one of many):
$CO_2HCH(CH_2CH_2CH_3)CH_2CO_2H$

Dyson: C6 . 3C . 1, 7X

Wiswesser: QVY3.1VQ

Condensed formula (one of many):
$COHCH(CH_2CH_2CH_3)CH_2COH$

Dyson: C6 . 3C . 1, 7EQ

Wiswesser: O:2Y3.1:O

Figure 3. Line formulas: Condensed formulas, Dyson's IUPAC-sanctioned notation, and Wiswesser's WLN.

The spread of the Dyson and WLN ciphers during the 1950s showed both the power and limits of this means of "starting afresh." There was still no *unique* unique identifier; different ciphers were deemed preferable by chemists with different priorities working in different institutional settings. A 1961 study found that manual searches of printed lists of ciphers were significantly faster and more reliable than searches conducted using punched cards and automatic equipment.[28] Institutions, modes of representation, and material media were linked, not chained, to each other.

III. Table + Number • Computer • Publisher + Firm + Government

During the 1960s, both private firms and organizations like CAS turned to digital media and computer systems to automate the process of compiling and accessing information about chemical compounds. The promise of computers came with a high price tag, both in equipment costs and in the distinctive formats of information and forms of expertise needed to take advantage of their capacity to automate intellectual labor. CAS capitalized on an alignment of projects and institutional interests with federal funding agencies and the chemical firm Du Pont to support Dyson's computerization plans.

These plans relied equally on yet another system for the unique, unambiguous representation of chemical structures. Unlike systematic names and ciphers, this system had two parts: the connection table and the Registry Number. Since the Geneva Congress, the ideal of a system of unique, unambiguous representations of chemical structure had been undone by the competing pressures of effectively identifying a chemical compound and precisely classifying it according to its chemical structure. The connection table and the Registry Number achieved this end by separating these two functions into two separate forms of representation, linked within (and only within) the computer system in which they were generated.

Beginning around 1960, the chemical firm Du Pont embarked upon a project to consolidate the diverse information-management activities of its divisions in a centralized computer-based

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[28] Ibid., 67.

system.[29] To bring computers to bear upon the problem of organizing information about chemical structures, Du Pont engineers Donald Gluck and Leslie Rasmussen developed a method for representing the structural formula of a molecule in digital form, which they called the connection table. The connection table was formed in two steps. First, a worker took a compound's structural formula, numbered each of its atoms, and used these numbers to fill out a sheet indicating the chemical identity of each atom and the bonds connecting them. The resulting list of atoms and bonds was transferred to a punched card. The punched card was input into the computer, and a specially-designed algorithm checked the input data for errors and transformed the connection table into a compressed form for more efficient storage and search.[30]

At the same time, CAS was engaged in transferring its rapidly diversifying operations to computers, under the leadership of Dyson, Director Dale Baker, and Assistant Director Fred Tate.[31] To support the automation plans, Baker secured grants from the NSF, Defense Department, and NIH.[32] In 1962, Du Pont executives decided to collaborate with CAS as well, assigning Gluck and another engineer to help adapt the connection table for use by CAS.[33]

As an unambiguous expression of a structural formula, the connection table identified a chemical compound. However, it was not itself to be used as an identifier, but as a means of generating a more convenient one, which Dyson christened a "registry number."[34] The connection table provided a means of verifying whether a compound was already in the database; the registry number, in contrast, did the work of identification in the system.[35] Registry numbers tied chemical identity to structural formulas without constantly relying on information about structural formulas to indicate chemical identity.
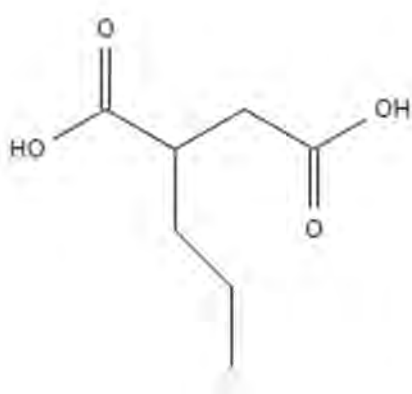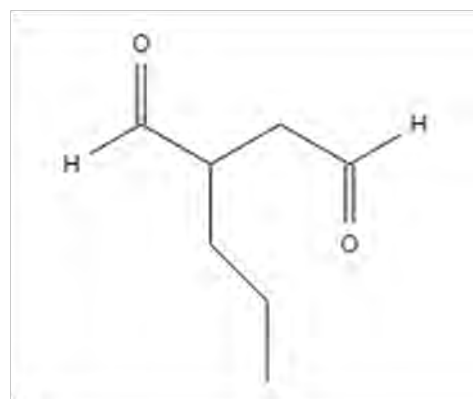
618-57-5   105409-75-4

Figure 4. CAS Registry Numbers.

[29] Florence Kvalnes, "The History of Managing Technical Information at DuPont," in Mary Ellen Bowden et al., eds., *Proceedings of the 1998 Conference on the History and Heritage of Science Information Systems* (Medford, NJ: Information Today, 1999), 107–14.

[30] D. J. Gluck, "A Chemical Structure Storage and Search System Developed at Du Pont," *Journal of Chemical Documentation* 5 (1965): 43–51.

[31] Baker oral history, 36–37.

[32] Ibid., 26, 55.

[33] "CAS and Du Pont to Collaborate," *Chemical & Engineering News* 42 (1964): 66.

[34] H. L. Morgan, "The Generation of a Unique Machine Description for Chemical Structures," *Journal of Chemical Documentation* 5 (1965): 107.

[35] G. Malcolm Dyson, "Current Research at Chemical Abstracts," *Journal of Chemical Documentation* 1 (1961): 25.

Furthermore, the Registry Number was a *unique* unique identifier, because its meaning was tied to the CAS computer system. Since 2000, members of several organizations have collaborated on the development of a new cipher called InChI and an (open) algorithm for mapping that notation to a unique and arbitrary string of digits, in the style of the Registry Number. InChI is now being developed under the umbrella of the reorganized IUPAC Division of Chemical Nomenclature and Structure Representation. The international machinery runs on.

KEYNOTE LECTURE

A Career at the Center: Linus Pauling and the Transformation of Chemical Science in the Twentieth Century

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In my talk today, I want to focus on Linus Pauling in order to analyze some of the principal transformations in chemical science during the twentieth century. Pauling lived throughout most of that century, from 1901 to 1994, and chemistry was the center of his life. His career was spent mostly at an American institution that was an outpost when Pauling first went there in 1922, but the California Institute of Technology became a major player in chemical science by the height of Pauling's career at mid-twentieth century. Pauling moved from one cutting edge in chemistry to another, always on the lookout for something new, but never abandoning his earlier areas of research, whether X-ray crystallography, statistical mechanics and quantum mechanics, electron diffraction, thermodynamic studies of molecules, the chemistry of life and molecular biology, immunology, structural studies of metals and of intermetallic compounds, or studies of disease in relation to genetic abnormalities and diet.

At the meeting of the International Conference in the History of Chemistry in Uppsala in August 2013, I included Pauling as one of three case studies for an analysis of patterns of collaboration and co-authorship in 20th century chemistry. One of my points in that paper was not only to highlight differences in styles of scientific leadership, by personality and institution, but also to focus attention on the increase in collaborative chemical work during the course of the twentieth century. In 1800 only about 2% of all published scientific papers were co-authored, a figure that increased to 7% in 1900.[1] In chemical science, co-authorship was more frequent than in other fields. Around 20% of chemistry papers were co-authored in 1900, increasing to 80% in the early 1960s and into the high 90s percentile by the end of the twentieth century.[2] This exponential increase in collaboration and co-authorship is one of the striking transformations in twentieth-century science.

The increase in co-authorship occurred partly because of the introduction of a broad range of increasingly specialized instruments that required expertise that a laboratory director might not personally possess even if wanting to make use of a new technique. University laboratory facilities became larger, with a greater division of labor, in order to support a steadily increasing clientele in undergraduate, graduate, and postgraduate education and research. In addition, more rapid means of transportation made possible an expansion in international exchange and collaboration across the Atlantic and Pacific thoroughfares. Yet, the main driver

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[1] Donald de B. Beaver and Richard Rosen, "Studies in Scientific Collaboration: Part II. Scientific Co-Authorship, Research Productivity and Visibility in the French Scientific Elite, 1799-1830," *Scientometrics*, 1, #2 (1979): 133-149, on 134.

[2] Derek J. deSolla Price, *Little Science, Big Science* (New York: Columbia University Press, 1963), 86-91; and Beverly L. Clarke, "Multiple Authorship Trends in Scientific Papers," *Science*, new series, 143, #3608 (21 February 1964): 822-824.

for change was innovation in physical instrumentation, a point persuasively argued in his 2006 book on post-1950 chemistry by Carsten Reinhardt.[3]

In an article on very recent laboratory science, the sociologist Edward J. Hackett emphasizes two kinds of skills required of the successful laboratory director. One is the craft skill of bench manipulation, working with one's hands and achieving knowledge that is "experiential, embodied, or etched in the senses." The laboratory leader's main skill, however, according to Hackett, is design of research strategy and tactics, requiring the "articulation work" of "managing people, ordering supplies, remaining in touch with collaborators, competitors, and funding agencies."[4] Hackett finds that the laboratory director often gradually withdraws personally from craftwork, and this withdrawal may be essential for a group to "progress" by adopting new techniques and instrumentation that the laboratory head may never have mastered in practice.[5]

In this paper I focus on the instruments and techniques that Pauling gradually introduced for his researches and his researchers at Caltech from 1922 to 1963, in the period when co-authorship increased from around 30% to 80% of all published chemistry papers. The expansive range of Pauling's research agenda and the growth at Caltech required new strategies for organizing workers into collaborative research groups, a theme that Jeremiah James has explored in his study of what he calls Pauling's program for "naturalizing the chemical bond" from 1927 to 1942.[6] In keeping with Hackett's generalizations, we will see in what follows that Pauling did not himself master all the craft skills of instruments that were necessary to solve problems, but he did master knowledge of how new techniques could be useful and how to interpret their results. That was his genius. Let us turn now to some of the transformations in Pauling's research agenda and in twentieth century chemistry, more generally.

The 1920s and 1930s: The Craftsmanship of X-Ray Crystallography and Quantum Chemistry

When Linus Pauling first came to Pasadena in 1922, he had majored in chemical engineering at Oregon Agricultural College. He was inspired as an undergraduate by his reading of Irving Langmuir's and G. N. Lewis's recently published articles on the electron theory of the valence bond. At Caltech Pauling studied classical thermodynamics, statistical mechanics, kinetic theory, and elements of the new quantum theory as taught by Richard Chace Tolman, Arthur Noyes, Robert Millikan, and visiting European scientists. He scoured the CRC Chemical Handbook for details and values of physical properties in molecules, such as diamagnetism and paramagnetism, and he tabulated and compared interatomic distances in crystals published by William and Lawrence Bragg.[7] Part of Pauling's later success was the result of his astonishing memory for data and his relentless search for order and meaning in numbers, much like Dmitri Mendeleev in the nineteenth century.

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[3] Carsten Reinhardt, *Shifting and Rearranging: Physical Methods and the Transformation of Modern Chemistry* (Sagamore Beach, MA: Science History Publications, 2006).
[4] Edward J. Hackett, "Essential Tensions: Identity, Control, and Risk in Research," *Social Studies of Science*, 35, #5 (October 2005): 787-826, on 796.
[5] Hackett (note 4), 797-799.
[6] Jeremiah Lewis James, "Naturalizing the Chemical Bond: Discipline and Creativity in the Pauling Program, 1927-1942" (Harvard University Ph.D. dissertation, 2007).
[7] Sources for the History of Quantum Physics, Interview with Dr. Linus Pauling by John L. Heilbron, Pasadena, 27 March 1964. Online at: http://www.aip.org/history/ohilist/3448.html (accessed 23 January 2015).

At Caltech in 1922, Arthur Noyes assigned Pauling to work in the new field of X-ray crystallography. Pauling learned the craft under young Roscoe Dickinson who about that time made the first crystal structure determination of an organic compound with his student Albert Raymond.[8] Dickinson had begun using photographic plates, rather than the Bragg technique of ionization effects, to register X-ray reflections, and Pauling learned Dickinson's methods.

One procedure in the photographic method (the rotational "spectral" method) directed X-rays onto the crystal under investigation and also onto a reference crystal, with the two crystals mounted one above the other on a holder that oscillated or rotated about an axis in the plane of the crystal faces. The rays that were reflected from both crystals hit a photographic plate placed perpendicularly to the incident beam. This technique gave the size of the smallest possible size of the crystal's unit cube. Then, a second process (the Laue method) was used, as developed originally at Cornell by Ralph W. Wyckoff and the Japanese scientist Shoji Nishikawa.[9] A thin section of a crystal was ground into powder and fixed on a rod, or, alternatively, a thin crystal was mounted in a holder, and photographs were made with an X-ray beam traversing the crystal.[10]

Calculations to determine the crystal and molecular structure used the wavelength of incident radiation, the spacing of planes in the atomic lattice, and the angle between the incident ray and the scattering planes. The hundreds or thousands of spots appearing on a photographic plate, after an exposure time of four to twenty-four hours, had to be assigned to particular planes in the crystal. Calculations were made of angles of reflection of the X-rays from the crystal planes, using data from the rotation photographs which specified the smallest possible size of the unit cell and its multiples. Measurements of density and molecular weight also had to be made, along with the initial growing or purification of the crystal. Finally, the nineteenth-century theory of 230 possible space groups was applied to find arrangements of atoms compatible with observed crystal symmetry and with the other data, resulting in a decision on the best fit. In the early years, Pauling learned to do all these tasks himself.[11]

It is hardly surprising, given the many steps in a crystal structure analysis, that most of Pauling's crystal structure papers were co-authored. His earliest student research notebooks include data and calculated results in the handwriting of his wife Ava Helen, who spent time with him at the laboratory when he was a student. By the late 1920s detailed entries for X-ray data calculations and, then, quantum mechanical calculations can be found in the handwriting of Pauling's student and later assistant Sidney Weinbaum. Pauling's notebooks indicate that Pauling persisted in doing hands-on work in X-ray diffraction into the mid-1930s (now with film rather than plates).[12]

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[8] See James (note 6), 261-262.

[9] Linus Pauling, "Fifty Years of Physical Chemistry in the California Institute of Technology," *Annual Reviews of Physical Chemistry*, 16 (1965): 1-15, on 27.

[10] Linus Pauling, "Early Work on X-Ray Diffraction in the California Institute of Technology," in *Fifty Years of X-Ray Diffraction*, ed. P.P. Ewald (Utrecht: Oosthoek's Uitgeversmaatschappij, 1962): 623-628; and Pauling, "X-ray Crystallography in the California Institute of Technology," in *Crystallography in North America,* eds. Dan McLachlan, Jr. and Jenny P. Glusker (New York: American Crystallographic Association, 1983): 27-30.

[11] Pauling, "Early Work" (note 10), 625-626; Roscoe G. Dickinson and Linus Pauling, "The Crystal Structure of Molybdenite," *Journal of the American Chemical Society*, 45 (1923): 1466-1471, on 1466.

[12] Pauling Research Notebook #3 (1923-1925), OSU Special Collections Box 3R, pp. 37-38; Notebook #6 (begins August 9, 1929), no numbered pages, Special Collections Pauling RNB6; Notebook #8 (1931-1936), Box 8R, letter tucked in between pp. 138-139, dated 27 September 1935 from LP to Lynn (Hoard). Weinbaum co-authored two crystal structure papers with Pauling.

Pauling had completed his Ph.D. on crystal structure work in 1925. He then embarked for eighteen months in Europe, where he thoroughly learned quantum mechanics in Munich, Copenhagen, and Zurich just at the time that the quantum wave interpretation of the stability of the hydrogen bond was first developed. After returning to a new faculty position at Caltech in 1927, Pauling began to sketch out a theoretical treatment of the chemical bonds in methane, which, as a chemist, he considered to be the most crucial molecule after hydrogen. By developing the notion of mixed or "changed quantization" (later called hybridization) of electron energy levels, Pauling (and independently, John Slater at Harvard University) demonstrated that electron wave functions project out in characteristic directions, thus explaining mathematically the distribution in space of atoms in molecules such as methane. Pauling next explained the aromatic structure of benzene and other conjugated molecules as an effect of the quantum mechanical exchange phenomenon.

Nineteenth-century chemists had pioneered the notion of chemical valence, with lines representing bonds, but they had not been able to explain how the bond works. They also had proposed three-dimensional geometries of molecules on the basis of chemical isomerism and substitution patterns, but without a firm explanatory basis. The atomic orbital theory of chemical bonding, developed by Walther Heitler, Fritz London, Slater and Pauling, complemented by the rival molecular orbital theory developed by Friedrich Hund, Robert Mulliken and Erich Hückel, transformed and motivated researches in theoretical chemical science for the rest of the twentieth century.

1930s and 1940s: Expanding Strategies and Technologies

In 1930 Pauling visited Munich, where he met Herman Mark in his laboratory in Ludwigshafen and discovered Mark's electron diffraction apparatus for studying the structure of gas molecules.[13] With Mark's encouragement, Pauling took sketches of Mark's apparatus back to Pasadena and asked his graduate student Lawrence O. Brockway to build the apparatus with help from Pauling's faculty colleague Richard Badger, whose research field was molecular spectroscopy.[14]

Brockway and Pauling's first co-authored paper on electron diffraction in 1932 reported on the atomic configuration and interatomic distances in three inorganic molecules using photographic results calculated according to equations based in the work of Peter Debye and Nevil Mott. In this technique, a well-defined beam of electrons traveling with uniform velocity intersects a jet of gas, and the scattered electrons are recorded on photographic film set at right angles to the direction of the initial beam. Comparison is made of measured curves (rings) on a photograph with theoretical intensity curves that have been calculated for different models corresponding to different relative positions of the atoms.[15]

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[13] "I was overwhelmed by the possibilities of this new technique," Pauling later wrote, because "for some time I had been looking for a diffraction method of determining the structure of molecules without having at the same time to determine the sometimes very complicated way in which the molecules are arranged relative to one another in a crystal." Pauling, "Fifty Years" (note 9), 10-11.

[14] Pauling, "Fifty Years" (note 9), 7, 11. On electron diffraction, see Mari Yamaguchi, "Pursuit of Accurate Measurements: Gas Electron Diffraction from the 1930s to the 1960s," paper delived at the 2015 International Workshop on the History of Chemistry, Tokyo, 2-4 March 2015.

[15] L. O. Brockway and Linus Pauling, "The Determination of the Structures of the Hexafluorides of Sulfur, Selenium and Tellurium by the Electron Diffraction Method," *Proceedings of the National Academy of Sciences*, 19, #1 (January 1933): 68-73, quotation on 69.

Brockway became head of Pauling's group assigned to electron diffraction studies. For the next seven years after completing his Ph.D., Brockway continued in this role, until another new Caltech Ph.D., Verner Schomaker, took it over when Brockway left for England and the University of Michigan.[16] From about 1917 to the mid-1960s the Gates and Crellin Labs at Caltech published about 400 papers on the structure of some 400 crystals, complemented after 1930 by electron diffraction determinations of the structure of some 225 molecules.[17] Jeremiah James writes that Pauling never sought personally to master the craftsmanship of the electron diffraction apparatus, unlike X-ray diffraction. Thus Pauling's role became an example of what Hackett calls articulation, rather than craftsmanship, in laboratory leadership.[18]

By the mid-1930s, Pauling was head of Caltech's Division of Chemistry and Chemical Engineering. He supervised twice as many graduate students and postdocs as other faculty colleagues in two large, multi-story and adjoining laboratory buildings.[19] As Jeremiah James discusses in his 2007 dissertation, Pauling introduced divisions of labor and forms of collaboration previously foreign to Caltech.[20] His broad interests and program of chemical researches required collaborators who were experts in different areas and who came and went from far and wide, as Pnina Abir-Am has discussed in a study of what she calls "Pauling's Boys."[21]

James Holmes Sturdivant became one of Caltech's paid Research Fellows after he took his Caltech Ph.D. He helped, and then took over, what previously had been Pauling's craft work of making X-ray diffraction photos, indexing diffraction patterns, and analyzing simple structures. Eventually Sturdivant ran the X-ray laboratory and expanding instrument shop.[22] For mathematical assistance, Pauling turned to graduate students such as the postdoctoral fellow George Willard Wheland (who has been studied by Buhm Soon Park), and the graduate students Jacob (Jack) Sherman and E. Bright Wilson, Jr.[23] Each became co-author as well as assistant. Wilson, for example, later a star at MIT, co-authored with Pauling the

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[16] James, (note 6), 281, 283. On Badger, see "Richard M. Badger, 1896-1974," *Engineering and Science*, 38 (December 1974-January 1975): 24. At http://calteches.library.caltech.edu/357/1/badger.pdf (accessed 23 January 2015); and Oliver R. Wulf, "Richard Mclean Badger 1896-1974," *National Academy of Sciences Biographical Memoir* (Washington DC: NAS, 1987): 1-20. [Mclean is the correct spelling.]

[17] Pauling, "Fifty Years" (note 9), 7, 11.

[18] James (note 6), 250.

[19] James, (note 6), 71-78; and Thomas Hager, *Force of Nature: The Life of Linus Pauling* (New York: Simon and Schuster, 1995), 170, 203. Pauling recruited personnel from his undergraduates, graduate students, postdocs, and other institutions, with the advantage of being able to appoint short-term, but renewable, experienced researchers as Research Fellows, some of whom eventually became Caltech faculty members or, mostly, took positions elsewhere. For the numbers, see *Bulletin of the California Institute of Technology. Catalogue for 1934* (Pasadena: The Institute, December 1933), 45.

[20] James (note 6), 249.

[21] See: Pnina G. Abir-Am at https://paulingblog.wordpress.com/2012/11/21/dr-pnina-abir-am-resident-scholar/ (accessed 23 January 2015) and Pnina G. Abir-Am, "Pauling's 'Boys' and the Mystery of DNA Structure: On Mentorship in Structural Chemistry and Molecular Biology," paper delived at the 2015 International Workshop on the History of Chemistry, Tokyo, 2-4 March 2015.

[22] James (note 6), 66, 279; and Pauling, "Fifty Years" (note 9), 7. Sturdivant became Assistant Professor at Caltech in 1938 and studied crystal structures until well after the Second World War, although his focus on inorganic structures was increasingly distant from Pauling's interests. See James (note 6), 280.

[23] Buhm Soon Park, "Chemical Translators: Pauling, Wheland and Their Strategies for Teaching the Theory of Resonance," *British Journal for the History of Science*, 32 (1999): 21-46.

1935 textbook *Introduction to Quantum Mechanics with Applications to Chemistry*. [24] Pauling's longest-term mathematical collaborator was Sidney Weinbaum, who worked regularly with Pauling from the late 1920s until 1943, spending months at a time with desktop electric calculators carrying out calculations in X-ray and electron-diffraction analysis, as well as quantum mechanics. [25] Weinbaum later assisted with calculations for the work that became Pauling's papers of 1950 and 1951 with Robert Corey and Herman Branson on the spiral or helix structure of polypeptide chains. [26]

Transformations in instrumentation soon changed mathematical calculation. When Weinbaum and Pauling first were working together, they were using pencil and paper, slide rules, published trigonometric tables, and adding machines. For X-ray studies of molecular structure it was necessary to evaluate one, two, or three-dimensional Fourier series. In the 1930s the series were evaluated by use of an adding machine and the Beever-Lipson cardboard strips in which each strip represents a sine or cosine function for one value of wavelength and one value of frequency. A strip corresponding to each term of the series was taken from a file, and the strips were then arranged to permit the convenient addition of terms for constant x coordinate. For electron diffraction, similarly designed strips were the Sherman-Cross strips. [27]

As Pauling later described in *The Journal of Chemical Physics*, the process of calculation was slow and required the constant attention of the operator putting numbers into the adding machine and recording the results. The wrong strips might be drawn or errors made in summing them. Tabulated functions were not sufficiently precise. By the early 1940s, however, there was a breakthrough that transformed twentieth century chemical science everywhere. It was the appearance of the punched card automated computer.

Wartime computer development hastened the access to such machines in the sciences. In using this new technique, Pauling again was an articulator and strategist, not a craftsman, for the work at Caltech. In the early 1940s, Verner Schomaker had started putting data from the Beevers-Lipson strips onto cards using sixteen 4-place fields on one card each and wiring a tabulating machine to get the sixteen different totals. [28] In doing this, Schomaker worked with Edward W. Hughes, who arrived at Caltech from Cornell in 1938 and had introduced the

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[24] James, (note 6), 261, 278-279; Pauling, "Fifty Years" (note 9), 11. The textbook is Linus Pauling and E. Bright Wilson, Jr., *Introduction to Quantum Mechanics, with Applications to Chemistry* (New York: McGraw-Hill, 1935).

[25] Weinbaum later described his thesis as the first application of quantum mechanics to molecular problems. From oral history interview of Sidney Weinbaum by Mary Terrall, 15, 20, and 25 August 1985, Pasadena, in Mary Terrall, "Sidney Weinbaum: Politics at Mid-Century," *Engineering and Science,* Fall 1991: 30-38, on 33.

[26] See Ted Goertzel and Ben Goertzel, *Linus Pauling: A Life in Science and Politics* (New York: Basic Books, 1995), 95-98, quoting from Pauling's letter to Branson.

[27] For one dimension,

$$f(x) = \sum_{h=0}^{\infty} (A_h \cos 2\pi hx + B_h \sin 2\pi hx)$$

where x = distance of a point in the x direction along a lattice and h = a component of the Miller index h,k,l for the position of a lattice plane. In the 1930s the series were evaluated by use of an adding machine and the Beever-Lipson Strips, which were cardboard strips on which are printed values of **A cos 2πhx** and **B sin 2πhx**, with **A = +/- 1, 2, 3, 4 . . . 100**, **h = 0, 1, 2, 3, ..., 20**, and **x = 0 to ¼**, **Δx = 1/60**. Each strip represents a sine or cosine function for one value of the wavelength and one value of frequency.

[28] California Institute of Technology Oral History Project. Interview with Verner Schomaker by Shirley K. Cohen. Pasadena, Caltech Archives, 1998. 4 session, 2 Feb, 4 Feb, 8 Feb, 10 Feb 1993: 79 pages, on pp. 33-34.

technique of the method of least squares for handling data in crystallography.[29] Around 1945 International Business Machines Corporation made one of their new automated punched-card machines available to Pauling.[30]

In a 1946 article in the *Journal of Chemical Physics*, co-authored with Schomaker and P. A. Shaffer, Pauling and his collaborators could hardly contain enthusiasm in the article's description of the cards, brushes, roller, synchronized card feed, plugboard, electrical circuit, etc. of the IBM machine. They reported that a structure problem could be solved in "only a few hours, as compared to one or two days with use of an adding machine, and . . . the accuracy of the work is assured."[31]

Hughes remarked later in 1979 on the differences that new machines made for X-ray crystallography in research centers across the globe, first computers and then the automated diffractometer that was invented in 1963. Instead of estimating visually perhaps 5,000 spots on photographic film, a diffractometer could automatically work away night and day measuring and counting photons from crystals. One round of refinement of a structure based in over a hundred observations and eighteen unknowns used to take 24 hours, but after computers it took one minute.[32]

1930 to 1950s: Larger Molecules and Instruments of Biological Chemistry

As is well known, Pauling's interests turned to larger and larger molecules as research funds from the Rockefeller Foundation and other agencies were redirected in the mid-1930s away from physical chemistry toward medically relevant studies of biological molecules. Pauling continued studies of inorganic structures, ionic crystals, minerals, metals, and alloys, with funding from industry and other sources, but his priorities shifted, his collaborations broadened into new fields, and his level of funding increased.[33] In 1946 Pauling submitted a 74-page proposal to the Rockefeller Foundation and to the National Foundation for Infantile Paralysis, co-authored with the Caltech geneticists George W. Beadle and Alfred H. Sturtevant, requesting $6 million to be expended over 15-20 years. The focus of the cooperative research aimed at what they called the great fundamental problems of biology and medicine: the structure and nature of proteins, nucleic acids and other constituents of living matter, the structure of the gene and mechanisms of inheritance, cell division and growth, the molecular and structural basis of the physiological activity of chemical substances, and the structure and properties of antibodies, enzymes, viruses, and bacteria.[34] All this was to be

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[29] In the method of least squares, the best fit to data that overdetermines the system is obtained by minimizing the sum of residuals, where a residual is the difference between an observed value and the fitted value provided by a model.

[30] P.A. Shaffer, Jr., Verner Schomaker, and Linus Pauling, "The Use of Punched Cards in Molecular Structure Determinations. I. Crystal Structure Calculations," *Journal of Chemical Physics*, 14, #11 (November 1946): 648-658, on 647-649. P.A. Shaffer, Jr., Verner Schomaker, and Linus Pauling, "The Use of Punched Cards in Molecular Structure Determinations. II. Electron Diffraction Calculations," *Journal of Chemical Physics*, 14, #1 (November 1946): 659-664.

[31] Schaffer, Schomaker, and Pauling, "Use of Punched Cards. I" (note 30), 658.

[32] Caltech Oral History. Edward W. Hughes. Caltech Archives, 1984. Interview by Graham Berry, Pasadena, 20 November 1979: 35 pp. on pp. 16-17. For the diffractometer, "H. Cole, Y. Okaya, and F. W. Chambers, "Computer-Controlled Diffractometer," *Review of Scientific Instruments*, 34, #8 (August 1963): 872-876.

[33] Caltech Archives, 1.020.4 Meetings, Correspondence, etc. C&CE, 1945-1949. 2-page typescript of meeting of professorial staff of the Division of C&CE, 13 December 1945.

[34] Caltech Archives. 1.020.1. CIT Materials re Div. C&CE 1946-1956. G. W. Beadle, Linus Pauling, and A. H. Sturtevant, "A Proposed Program of Research on the Fundamental Problems of Biology and Medicine by the

accomplished by collaboration of chemical, physical, and biological methodologies in what they called chemical biology.[35]

Biologically significant compounds like urea, oxamide, and oxamic acid were among the compounds that Pauling and his associates investigated in the 1930s from the standpoints of thermodynamics, bond configurations, and resonance structure in the amide group. The nucleic acid bases guanine and purine were among the compounds for which Sherman and Pauling calculated resonance energy in 1933. Pauling's visit to Herman Mark's Ludwigshafen laboratory, near Mannheim, in 1930 had familiarized Pauling with Mark's ideas on the structure of proteins, which Mark and Kurt Meyer described in 1932 as large molecules composed of long and flexible polypeptide chains, a history described by Yasu Furukawa in his book on macromolecular science.[36] Pauling himself turned to the structures of proteins in 1932, including hemoglobin and other molecules of medical interest.

In 1934 Pauling borrowed a large water-cooled magnet from the astronomer George Ellery Hale's private laboratory, so that E. Bright Wilson might do an experimental part in his doctoral thesis by investigating the magnetic properties of nitroso-compounds, a problem corresponding to Pauling's interest in the three-electron-bond theory of the triplet normal state of the oxygen molecule.[37] Wanting to better understand the interaction between oxygen molecules and hemoglobin, Pauling directed his postdoctoral fellow Charles Coryell to study the difference in magnetic properties of different hemoglobin derivatives, thus beginning Pauling's laboratory collaborations on proteins and biological chemistry.[38]

Pauling was encouraged by Rockefeller Institute immunologist Karl Landsteiner to think about possible structural relationships between molecules of antibodies and antigens in serological reactions, since antibodies and most antigens are proteins. Pauling arranged for Landsteiner's young colleague Alfred Mirsky to come to Caltech from the Rockefeller Institute. They published a paper in 1936 on the structure and shape of the polypeptide chain in protein, suggesting that the chain is coiled in a specific shape stabilized largely by hydrogen bonds. The next year Robert B. Corey came to Caltech from the Rockefeller Institute and joined Pauling's project.

In 1940 Pauling proposed that polypeptide chains might fold and wind around the exterior of a foreign antigen structure, creating an antibody that is complementary in structure to the invading antigen, similar to a lock-and-key (a metaphor used by the German protein chemist Emil Fischer in 1894 for an enzyme and its substrate). As Bruno Strasser puts it, Pauling's was an "instructive" theory in which the antigen directs the folding of a peptide chain into a complementary structure.[39] In the long run, this template theory turned out to be wrong, but it inspired a great deal of work by other scientists as they followed up on Pauling's research.

Division of Biology and the Division of Chemistry and Chemical Engineering of the California Institute of Technology. 1946. 74-page typescript, 1-3.

[35] California Institute of Technology Archives, Division of Chemistry. Box 1.Letter, dated October 28, 1945 from G. W. Beadle at Stanford to LP.

[36] Yasu Furukawa, *Inventing Polymer Science: Staudinger, Carothers, and the Emergence of Macromolecular Chemistry* (Philadelphia: University of Pennsylvania Press, 1998).

[37] Pauling, "Fifty Years" (note 9), 11.

[38] Pauling, "Fifty Years" (note 9), 12; Pauling, "Fifty Years of Progress in Structural Chemistry and Molecular Biology," in *Daedalus*, Vol. 99, #4, *The Making of Modern Science: Biographical Studies*, Fall, 1970: 988-1014, p. 1002.

[39] Bruno Strasser, "A World in One Dimension: Linus Pauling, Francis Crick, and the Central Dogma of Molecular Biology," *History and Philosophy of the Life Sciences*, 28 (2006): 491-512, on 497.

The early template theory was given initial experimental support in the work of Harvey Itano, a second-generation Japanese-American who received his medical degree in 1945 from the St. Louis School of Medicine after having been briefly interred along with thousands of other West-Coast Japanese American families in the winter of 1942. After Itano entered Caltech as a graduate student in the fall of 1946 to study for a Ph.D. in chemistry and physics, Pauling directed him to study molecular differences between normal hemoglobin and hemoglobin in the blood of individuals afflicted with sickle-cell anemia. After failing to get results using absorption spectra or magnetic techniques, Itano began studying the hemoglobins using moving boundary electrophoresis, which makes use of the movement of particles through fluid in an electric field.[40]

Electrophoresis was another new technique and kind of instrumentation. The machine had been invented in 1937 by Arne Tiselius in Uppsala and was available in the 1940s only if constructed in a laboratory. Pauling's Rockefeller Foundation money included funds for such construction. Stanley M. Swingle, a general chemistry instructor at Caltech, had an idea for an improved design using mirrors rather than lenses in the optical system (as well as a kinematic mechanical design and a current regulating power supply). He relied on Sturdivant for advice on the mechanical design and on George G. Wright, who was working in the group on antibodies, for cooperation in the initial installation and operation of the apparatus. The instrument makers Alex Logatcheff and William Schuelke made sure that the design worked, and A. L. Wahrhaftig designed the power supply. Swingle and Wahrhaftig were part of the team that worked on punched cards for automated computer diffraction calculations.[41]

Itano and another postdoctoral fellow, Seymour Jonathan Singer, later like Itano an eminent cell biologist at the University of California at San Diego, used the Caltech machine to find that sickle-cell hemoglobin has more positive charge on its surface than does normal hemoglobin. Pauling proposed that this extra charge on the surface led to hemoglobin molecules sticking together, twisting the red blood cells out of shape from flat discs into sickles and clogging small blood vessels in the body. Pauling coined the term "molecular disease" in their co-authored paper, which became Pauling's third most cited paper.[42]

During the war years, Pauling worked at Caltech on military-related projects, and at war's end he continued wartime research on the synthesis of artificial antibodies, working with immunologists Dan Campbell and David Pressmann.[43] Among the members of this research

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[40] Tiselius received the 1948 Nobel Prize in chemistry for his work on the separation of colloids through electrophoresis.

[41] Stanley M. Swingle, "An Electrophoresis Apparatus Using Parabolic Mirrors," *Review of Scientific Instruments*, 18, #2 (1947): 128-132; and Stanley M. Swingle, "Improved Electrophoresis Cell and Cell Holder," *Science*, new series, 105, #2732 (9 May 1947): 501-502.

[42] Russell F. Doolittle, "Harvey A. Itano. 1920-2010," *Biographical Memoirs of the National Academy of Sciences*, 2014: 1-25; Letter from Linus Pauling to Stanley Swingle, 2 March 1948, Correspondence ID corr378.2-lp-swingle-19480302; and Letter from Linus Pauling to Robert B. Corey, 3 March 1948, Correspondence 67.5 LP to Corey, OSU Special Collections.

[43] These included the invention with colleagues of an oxygen meter for monitoring the air in submarines. This instrument made use of the magnetic susceptibility of oxygen and consisted of a small glass dumbbell with attached mirror suspended on a stretched fused-silica fiber in an inhomogeneous magnetic field produced by a small permanent magnet. He arranged its production with Arnold Beckman, who had left teaching chemistry at Caltech to establish a scientific instruments business. Linus Pauling, Reuben E. Wood, and J. H. Sturdivant, "An Instrument for Determining the Partial Pressure of Oxygen in a Gas,"*Journal of the American Chemical Society*, 68 (May 1946): 795-798. Pauling also directed wartime research projects at Caltech on rocket propellants and

group were two undergraduate students, Miyoshi or "Mike" Ikawa and Carol Kazuo Ikeda, who prepared compounds used in the experiments. Pauling was determined to help the two Nisei students avoid internment in 1942, following their Caltech graduation in 1941. In this, Pauling succeeded. Ikawa, known by his undergraduate classmates for his phenomenal grades, early bedtime hours, and membership in the Fleming House wrestling team, entered the University of Wisconsin graduate program, where he became a co-discoverer with his mentor Karl Paul Link of warfarin, or Coumadin, before eventually joining the biochemistry department at the University of New Hampshire.[44] Ikeda became one of 104 Nisei students enrolled at the University of Nebraska between 1942 and 1945, where he finished his doctorate and became a research chemist for Dupont Chemicals.[45]

1950s: Proteins, DNA, and Technologies of Molecular Models

Pauling's government and Rockefeller Foundation-sponsored research during the war years kept him focused on hemoglobin, immunology, and proteins along with other projects. A striking characteristic in Pauling's work in these years was his straddling two different communities of molecular researchers, one relying on immunological and biochemical techniques and another applying physical methods to the study of large molecules of biological interest.[46] Protein research had become an expanding research area by the 1930s, with British X-ray crystallographers such as J. D. Bernal, Dorothy Hodgkin, and William Astbury among its pioneers.

While visiting Oxford in 1948, where he cemented a friendship with Hodgkin, Pauling started building protein models by using paper, ruler, and pencil. After his return to Caltech, his collaboration with Corey and visiting physicist Herman Branson resulted in the single-coiled alpha-helix model, which broke with the usual assumption that the helix should have an integral number of residues per turn. Pauling also demonstrated the triple helix structure of collagen, in which two identical chains entwine with an additional chain that differs slightly in its chemical composition. As has often been recounted, the triple helix made an unfortunate reappearance in Pauling and Corey's proposed structure for deoxyribonucleic acid (DNA), the molecule that some biologists were beginning to think played a major role in genetics. James Watson and Francis Crick's double helix structure, published in spring 1953, from Lawrence Bragg's Cavendish Laboratory, instead won the day, relying on Rosalind Franklin's photographs of hydrated DNA and on chemical insights and model-building techniques gleaned from Pauling's own work.

This DNA research brings to the fore one of Pauling's most powerful instruments in chemical research: the material model of the chemical molecule. Pauling's method of modeling

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explosives powders, and he headed a team for the synthesis of artificial plasmas that enlisted the expertise of the immunology expert Dan Campbell.

[44] See "The 'T'", *California Institute of Technology Yearbook*, 1941, pp. 33 and 34. Online: http://caltechcampuspubs.library.caltech.edu/2260/1/1941.pdf (accessed 23 January 2015); and "Ikawa, One of Inventors of Warfarin, Dies at 87," *The Capital Times* (Madison, Wisconsin), 27 May 2006, Metro Section, p. B3.

[45] Obituaries, *Caltech News*, 30, #1 (Winter 1996), p. 18. Online: http://caltechcampuspubs.library.caltech.edu/2120/1/1996_30_1.pdf (accessed 23 January 2015).
Also, "Nisei Collection at the University of Nebraska." Online: http://unlhistory.unl.edu/exhibits/show/nisei/nisei-experience-at-unl/list-of-nisei-students (accessed 23 January 2015).

[46] On the two communities, see Angela N. H. Creager and Gregory J. Morgan, "After the Double Helix: Rosalind Franklin's Research on Tobacco Mosaic Virus," *Isis*, 99, #2 (June 2008): 239-272, on 262-262.

structures employed not only paper and pencil, but also wooden and then plastic models including new and precise "space-filling" models. These models transformed chemical research and education in the late twentieth century.

Space-filling models first were designed in Germany by H. A. Stuart in 1934, and they began to be marketed in 1939 by the Fisher Scientific Company using a redesign by University of Wisconsin chemist Joseph Hirschfelder. Pauling found these commercial models inexact for his purposes. Instead, he directed the Caltech instrument shop, managed by Sturdivant, to make two types of model kits that Corey and Pauling described in an article in 1953 in *The Review of Scientific Instruments*.

One set was made of hard wood to the scale 1 inch = 1 Angstrom, with dimensions tied to experimental Van der Waals radii, bond radii, and bond angles. Atoms, such as carbon, hydrogen, oxygen, and nitrogen, were joined together by means of short pieces of 5/16 inch steel rod, which fit into steel bushings imbedded in the atoms. The bushings were locked on the rod in any desired position for fixing the relative orientation of atoms around a bond. Different valences for a single atom were modeled into different atom spheres, and the dimensions for the bonding of N-H with O for amino acids and peptides were incorporated into a model of the hydrogen-bonding atom. Data from X-ray crystallography, electron diffraction, and quantum mechanical mathematical modeling refined measurements and structures. This kind of model was intended to study probable molecular configuration, including steric hindrance, and intermolecular packing, and the models could be substituted for mathematical calculation.[47] In contrast, the second kind of model had parts cast on a smaller scale from colored, rubber-like vinyl plastic with easy alteration of molecular configuration. Hydrogen bonds were simulated by embedding magnets in the hydrogen and oxygen atoms. Corey and Pauling cautioned that these smaller-scale models were useful for qualitative studies only and could not be substituted for large-scale models in quantitatively precise work.[48]

Technicians at Caltech continued to make space-filling models in the laboratory shop through the 1950s. Caltech provided selected scientists elsewhere with blueprints, conforming to designs from visual drawings by Roger Hayward and data provided by Pauling, Verner Schomaker and Sturdivant.[49] Barbara Low, a former student of Dorothy Hodgkin's and visitor at Caltech who joined the physical chemistry laboratory at Harvard, bought a kit in 1951 for $880. In the spring of 1959, Alexander Rich, a former Pauling protégé now at MIT, learned that his order would likely be the last one to be supplied to outside institutions.[50]   By

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[47] Robert B. Corey and Linus Pauling, "Molecular Models of Amino Acids, Peptides, and Proteins," *The Review of Scientific Instruments*, 24, #8 (August 1953): 621-627.

[48] Ina Heuman, "Linus Pauling, Roger Hayward und der Wert von Sichtbarmachungen," *Berichte zur Wissenschaftsgeschichte*, 32 (2013): 313-333, on Hayward. Richard Marsh, "Robert Brainard Corey. 1897-1971. A Biographical Memoir," *Biographical Memoirs. National Academy of Sciences* (Washington DC: National Academies Press, 1997): 49-68, on 62.

[49] Eric Francoeur, "The Forgotten Tool: The Design and Use of Molecular Models," *Social Studies of Science*, 27, No. 1 (Feb., 1997): 7-40, on 23-24; and Jeremiah James, "Modeling the Scale of Atoms and Bonds: The Origins of Space-Filling Parameters," in *Objects of Chemical Inquiry*, eds. Ursula Klein and Carsten Reinhardt (Sagamore Beach, MA: Science History Publications, 2014): 281-320, esp. 308-310. See Ewart Thomas, "Molecules Tailored to Order," *Popular Mechanics*, Aparil 1952: 149-153, 250, 254.

[50] The kit included 100 carbon (tetrahedral), 25 carbon (ethylene double bond), 25 carbon (carboxyl), 200 hydrogen, 30 hydrogen (H-bond), 70 oxygen (single bond), 30 oxygen (double bond), 30 nitrogen (trigonal), 12 nitrogen (tetrahedral), 12 phosphorus (tetrahedral), 8 purine nucleus, 6 pyrimidine nucleus, 10 benzene rings, 30 peptide amide group (planar OCN), 12 sulfur, 20 nitrogen radius adapters, 500 stud connectors, 50 orienting pins. Labor $510, Material (150), Overhead (220). Cal Tech Archives. The Papers of Robert Brainard Corey.

the 1960s, commercially available kits made their way into laboratories and classrooms following a five-year development program that involved Caltech and other scientists, federal agencies, and scientific societies.[51]

Conclusion

Pauling received the Nobel Prize in Chemistry in 1954. Following his trip to Stockholm, he and Ava Helen Pauling visited Israel, India, Thailand, and Japan, arriving in Japan in February 1955. They were appalled to learn that the crew of the *Lucky Dragon* still was under observation following the US explosion of thermonuclear devices over Bikini Atoll the previous spring. Pauling entered a long-running scientific debate over the biological effects of chronic, low-level radiation from atmospheric nuclear tests, and he organized scientists worldwide to press for a ban on atmospheric nuclear testing. After criticism by colleagues of his (1962) Nobel Peace Award in 1963, he resigned from Caltech and founded his own research institution in 1974 after appointments at the University of California at Santa Barbara and at San Diego, and then at Stanford University. His collaborations continued, although with fewer numbers of publications and fewer coworkers, in researches on the evolutionary molecular clock and on the health effects of Vitamin C.[52]

During his Caltech period from 1922 to 1963, Pauling published a total of 370 scientific publications. He had 106 different co-authors on 175 co-authored papers, and 23 individuals

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1.11. Carbon copies of Letter from Corey to Dr. Barbara Low at Laboratory of Physical Chemistry, Harvard, 19 November 1951; carbon copy of Letter from G. A. Green, Caltech Vice-President for Business Affairs to Professor Herbert Jehle, Physics Department, University of Nebraska, 10 January 1958 , with cc to Corey; carbon copy of letter from Corey to Dr. Alexander Rich, Dept. Biology, MIT, 1 May 1959. Jack Dunitz, a former collaborator of both Pauling's and Hodgkin's, wrote Corey in late 1958 from the ETH in Zurich that none of the commercially-available atomic models were as good as the ones from Caltech. Letter to Corey from Jack Dunitz at Laboratorium für organische Chemie, Eidg. Technische Hochschule, Zurich, 17 November 1958.

[51] Caltech Archives. The Papers of Robert Brainard Corey. 1.11. Correspondence between Walter L. Koltun, Program Director, Molecular Biology Section, NSF and Robert Corey at Caltech, 11 March 1965, 16 March 1965, for the naming of the Koltun-Corey-Pauling models in a recommendation by Koltun, 9 March 1965, to Robert A. Harte at the American Society of Biological Chemists, etc., chair of the Atomic Models Committee meeting in San Francisco. Also see Francoeur (note 49), and Mary Jo Nye, "Paper Tools and Molecular Architecture in the Chemistry of Linus Pauling,"in *Tools and Modes of Representation in the Laboratory Sciences*, ed. Ursula Klein, *Boston Studies in the Philosophy of Science* (Dordrecht: Kluwer, 2001): 117-132.

[52] One of Pauling's collaborators at the Linus Pauling Institute was Roy Teranishi, a Japanese-American researcher, who was already well known in the field of food and flavor chemistry and worked with the USDA in the Bay area. The Japanese-American researcher, Koichi Miyashita, later assisted with metabolic and Vitamin C studies in the 1970s. For example, Linus Pauling, Arthur B. Robinson, Roy Teranishi, and Paul Cary, "Quantitative Analysis of Urine Vapor and Breath by Gas-Liquid Partition Chromatography," *Proceedings of the National Academy of Sciences*, 68, #10 (October 1971): s2374-2376; "Dedication to Dr. Roy Teranishi, 1922-2000," *Journal of Agricultural and Food Chemistry*, 49, #2 (February 2001): 535. On Miyashita, letter from Stephen Lawson to Mary Jo Nye, 13 October 2014. The Vitamin C research received a great deal of public and professional attention, including interest in Pauling's research from several Japanese researchers with whom Pauling talked or corresponded. One coauthored paper appeared in 1983 with Fukumi Morishige: "Eiji Kimoto, Hidehiko Tanaka, Junichiro Gyotoku, Fukumi Morishige, and Linus Pauling, "Enhancement of Antitumor Activity of Ascorbate against Ehrlich Ascites Tmuor Cells by the Copper:Glycylglycylhistidine Complex," *Cancer Research*, 43 (February 1983): 828-828. Akira Murata of Saga University visited the Pauling Institute during 1977-1978 while collaborating on vitamin C and immunology with George Feigen at Stanford. Morishige did clinical trials at Fukuoka Torikai Hospital. Naoyuki Ohtsu, one of their colleagues, spent time briefly at the Pauling Institute in the early 1980s, according to Stephen Lawson, in letter to Mary Jo Nye, 13 October 2014.

co-authored three or more publications with Pauling.[53] Many hundreds of chemists in diverse specialties, and especially in physical techniques and modeling applied to structural chemistry, learned or extended their expertise under his leadership at Caltech. Pauling's success, like that of so many eminent leaders of large laboratories in twentieth-century chemical sciences, was based in skills of consummate "craftsmanship" achieved at an early age and in skills at a later stage in his career that Hackett calls "articulation." Pauling's research precipitated and reflected achievements and transformations in chemical sciences of the twentieth century. To this work, Pauling consistently applied the vocabulary of "discovery" and "progress" as well as "puzzle" and "surprise" when he described transformations in twentieth-century chemistry. He did not use the more radical language of "revolution."[54]

Pauling had his faults, to be sure. His open-mindedness did not always extend to chemical theories that he viewed as contrary to his own way of seeing things. His resistance to molecular orbital theory is one case in point. He was highly competitive, protective of his personal claims to discovery, and sometimes ungenerous in giving credit to coworkers. In conclusion, however, I want to emphasize that it was not possible for one person, no matter how intelligent and creative, no matter how hard-working and disciplined, to achieve the range of results associated with Pauling's name. His discoveries and innovations may appear at first glance to be the achievement of a single individual, relying of course on other chemists' work with which he became familiar, but his accomplishments were collaborative and collective. This fact is the result of a very real transformation in laboratory organization and allocation of expertise.   Pauling is exemplary of the eminent chemist whose career made use of the skills both of craftsmanship and articulation, while demonstrating ingenious creativity, mastery of current chemical knowledge, and a passion for leadership in the vanguard of chemical practices.

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[53] Pauling's most frequent co-authors were Robert B. Corey (33 papers on the structure of proteins and nucleic acids in the 1950s), David Pressmann and Dan H. Campbell (18 and 10 papers mostly on serology and antibodies in the 1940s), Lawrence O. Brockway (10 papers on electron-diffraction studies of structure in the 1930s), Jacob (Jack) Henry Sherman (7 papers on quantum mechanics and chemical structure in the 1930s) and Richard (Dick) Marsh (7 papers on chemical structure). For a complete list of Linus Pauling's papers, see Chris Petersen and Cliff Mead, eds. *The Pauling Catalogue*, 6 volumes (Corvallis: Oregon State University Valley Library Special Collections, 2006), Volume 1, 106-152.

[54] For example, see Pauling, "Fifty Years of Progress" (note 38); Linus Pauling, "Chemical Achievement and Hope for the Future," *American Scientist*, 36, #1 (1948): 50-58; or Pauling and Wilson, *Introduction to Quantum Mechanics* (note 24), where "discovery" appears (n35, n44, n59, n217, n323, n399), but where there are no claims of radical transformation or revolution.

A Child of Many Fathers: The Question of Credit for the Discovery of Thiamine, 1884-1936

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Credit for scientific discoveries can be a contentious affair. Not only do the success and failures of individual careers rest on such, but so can matters of national prestige. One of the less-substantial properties of science has to do with the prestige that adheres to credit for uncovering knowledge that is deemed revolutionary. Such prestige is intangible and unquantifiable, and yet seems to possess a great deal of importance, as demonstrated by the recognition given to those researchers fortunate enough to uncover these wonders, and the awards they are given for such. This acclaim many times also expands to encompass the scientists' country of origin, confirming or heralding its status as a technically and scientifically advanced nation.

For thiamine, or vitamin B_1, because the process of uncovering its secrets was so convoluted and lengthy, fraught with laboratory errors and mis-drawn conclusions, many scientists became involved in reaching a more perfect understanding of its properties and structure, each making his own contribution to the totality of its knowledge. Despite this, and depending upon who is asked, only two of them are generally recognized popularly, and when they are, as the sole discoverer of vitamin B_1: Casimir Funk and Suzuki Umetarō (鈴木梅太郎). But to acknowledge either of these researchers as the discoverer of thiamine would be a mistake. True credit rests elsewhere.

At the turn of the twentieth century, orthodox nutritional theory only recognized proteins, carbohydrates and fats, in addition to salt and water, as necessary for a healthy diet. However, the proliferation of a variety of diseases, including scurvy, beriberi, and pellagra, led to the realization that other nutritional factors were also involved. Vitamin theory states that certain foodstuffs contain trace compounds that are not protein, carbohydrate, or fat in character, but still are essential for proper health, and indeed, life.

Vitamin B_1, also known as thiamine, is essential for the proper metabolic health of most vertebrates and some microorganisms. It is a water-soluble vitamin, and in animals is concentrated in the liver, heart, kidneys, and skeletal muscle. Thiamine is important to the body's oxidation processes, particularly those concerned with the metabolism of carbohydrates and fats. It additionally is vital to the proper health and functioning of the cardiovascular, digestive, and nervous systems, and to appetite and growth.

In humans, its deficiency results in beriberi, the onset of which manifests itself as fatigue and drastic weight loss, followed by nervous disorders and atrophy of the muscles, especially in the legs.[1,2] Paralysis and severe pulmonary edema may occur, and death, usually from heart failure, is the result if the condition progresses. As little as 0.6 milligrams of thiamine per day is enough to deter symptoms of beriberi in an average human. Although the disease had been known in China as long ago as 2600 BCE, beriberi reached crisis

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[1]   Williams, et al., *The Biochemistry of B Vitamins*, New York, Reinhold, 1950, 400-401.
[2]   The term "beriberi" originated in Sri Lanka, from *beri*, the Singhalese word for weakness.

proportions during the nineteenth century due to the impact of certain changes on the eating habits of humans. Processed and preserved foods, which often had removed from them undesirable parts of vegetable and animal products, also could have essential nutrients removed coincidentally.[3]

Investigations into the nature of beriberi were misled initially by its geographical distribution and the sometimes unpredictable conditions under which it occurred. It seemed to concentrate itself in the then non-industrialized regions of the world and was originally thought to be an infection brought about by unsanitary living conditions. The disease was particularly a problem in Asia, where some estimates of resulting deaths reach into the hundreds of thousands. Perhaps for this reason, it was the Japanese who led inquiries into this disorder, which they refer to as *kakke* (脚気).

In the 1880s, Takaki Kanehiro (高木兼寛), the Director-General of the Imperial Navy's Medical Department, made the connection between beriberi and diet. He discovered that up to forty percent of the Japanese Navy was afflicted with *kakke* and instituted various reforms, including less rice, more bread and milk, and improved hygiene in sailors' living quarters. The incidence of *kakke* plummeted from almost two thousand cases in 1879 to zero in 1887, but Takaki attributed improvement solely to an increase in exercise and dietary protein, and a decrease in carbohydrates and fats.[4]

Further inquiries provided limited insight until 1896, when Christiaan Eijkman, a Dutch physician practicing in Java, published a paper that described a beriberi-like disease that the chickens kept by his hospital contracted when fed polished rice.[5] He found that feeding the chickens rice bran, or the husks of polished rice, was curative for the disorder. However, he mistakenly concluded that the chickens metabolized the white rice's starch into a neurotoxin which subsequently was neutralized by some chemical in the pericarp of the rice.[6] Although Eijkman's suppositions were wrong, the news that a physical disorder similar to beriberi could be duplicated in a non-human species created a great deal of excitement among those who would study the ailment in humans.

In 1908, at the urging of the Imperial army, the Japanese government established a commission to deal with the high incidence of beriberi among soldiers and people who had immigrated to the cities from the countryside. Due to his success in dealing with a mulberry blight in 1899 and to his studies under Emil Fischer, Suzuki was among those appointed to investigate.[7] So began his studies on the nutritional value of rice, leading to his discovery of a substance which was neither protein, fat, carbohydrate, nor mineral, the dietary absence of which leads to beriberi and the death by wasting of the patient. For two years, Suzuki's research group, but primarily the Professor and Shimamura Torai (島村虎猪), worked

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[3]   Leslie J. Harris, *Vitamins and Vitamin Deficiencies* (London: Churchill, 1938), 4.

[4]   Ibid., 53.

[5]   Which is to say, rice that has had its pericarp, also known as its bran or husk, removed. The distinction is that between "white" and "brown" rice. The ailment of the chickens is known as "polyneuritis gallinarum." Eijkmann shared the Nobel Prize for Medicine or Physiology in 1929 with Sir Frederick G. Hopkins of England for their work with vitamins.

[6]   A 1930 journal article reiterating this was written by Yutaka Teruuchi of Keio University. Suzuki wrote a refutation, showing that the toxin theory was not dying an easy death. Umetaro Suzuki, Toshikazu Sahashi, Tsune Ariyama, Nobuzo Nakamura, Nabetaro Hashimoto, and Toshiichi Kasai, "On the So-called Polished Rice Intoxication," *Scientific Papers of the Institute of Physical and Chemical Research 9(3)* (March 1930), 26-27.

[7]   Fujioka Nobukatsu, *Kyōkasho ga Oshienai Rekishi 3*, Tokyo: Jiyūshugi Shikan Kenkyūkai, 2005, 198.

"without taking even a day's break."[8] In 1910, Suzuki isolated a substance from rice bran which he said possessed anti-beriberi properties. He named it "aberic acid."

On December 13, 1910, at 6 o'clock in the evening, Suzuki presented his paper on aberic acid before the Chemical Society of Tokyo at Tokyo Imperial University's Main Lecture Hall. It subsequently was published in the January 1911 issue of the *Journal of the Chemical Society, Tokio*.[9] On January 7, 1911, he filed his application with the Japanese patent office concerning his method of extracting aberic acid (patent no. 20785), and on July 21, 1911, did the same for a second method (patent no. 21314).[10]

In Japan, the initial reception to Suzuki's paper was cool. His fellow chemists refused to comment on his findings, while the reaction of medical doctors was less ambiguous, bordering on outright hostility.[11] The Imperial army previously had convened a panel of the most prominent physicians in Japan to investigate the prevention of and cure for beriberi, and these worthies were convinced that beriberi was an infectious disease. So when Suzuki was able to definitively assert that he had discovered a factor that would cure beriberi in one hundred percent of cases, the outcry from this faction was profound.[12] "He plagiarized his data," and "he debased scholarship" were among the criticisms heard.[13] This group included one whose reported response was pungent, "I hear Suzuki says rice bran is effective against beriberi. This is idiocy. He can believe what he likes, but if rice bran cures beriberi, then drinking urine will too."[14]

Although Suzuki scrupulously avoids identifying this person, Imperial Army Medical Chief Mori Ōgai (森鴎外, born Mori Rintarō 森林太郎) was a possible source for this damning statement.[15] He was a staunch proponent of the belief that beriberi was a bacteria-caused infectious disease, and refused to modify the diet of the Imperial Army by the addition of barley during the Russo-Japanese War, unnecessarily leading to a quarter-million cases, including roughly 27,000 fatalities.[16] Mori would remain adamantly opposed to a nutritional basis to the disorder and the curative properties of aberic acid/oryzanine until his death in 1922. In fact, out of all the chemists and medical doctors in Japan, the only word of support, albeit distinctly lukewarm, came from Ikeda Kikunae of Tokyo Imperial University's chemistry department. According to Suzuki, he said, "This accomplishment, if true, is

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[8] *Kenkyū no Kaiko*, 6. The beriberi research group also included Suzuki's former academic advisor Kozai Yoshinao and Andō Hirotarō (安藤廣太郎). Suzuki, Umetarō, "Chemical Studies of Vitamin-B in Japan," *Scientific Papers of the Institute for Physical and Chemical Research*, 4(63), 1926, 295.

[9] *Journal of the Chemical Society, Tokio 32 (Meiji 44) (1911), 4-17*

[10] The first patent, no. 20785, was approved on October 19, 1911, while the second, patent no. 21314, gained the same status on December 21, 1911. Suzuki soon changed the name from "aberic acid" to "oryzanine" (sometimes "oryzanin"), naming it after the source of his discovery, the rice plant *oryza sativa*.

[11] *Gekidōki no Rikagakukenkyūjo: Ningenfūkei: Suzuki Umetarō to Yabuta Teijirō*, Tokyo: Kyōritsu Shuppan, 1987, 9.

[12] *Suzuki Umetarō Sensei-Den*, 9

[13] Dōke Tatsumasa in Tsuneishi Keiichi, ed., *Nihon Kagakusha-den*. Tokyo: Shogakukan, 1996, 145.

[14] Suzuki, *Kenkyū no Kaiko*, 10. Also, Yuasa Mitsutomo, *Kagaku-shi*, Tokyo: Tōyō Keizai Shinpō-sha, 1961, 214. This person, who Suzuki identifies only as "some scholar" would later confront Suzuki and call his oryzanin research "a lie" to his face. Suzuki, *Ibid.*, 11. In point of fact, however, the statement is a correct one since, like all water-soluble vitamins, excess thiamine is excreted via the urine.

[15] There is also evidence that the source of the "urine" remark was Aoyama Tanemichi (青山胤通), the dean of Tokyo University's faculty of medicine and Mori's main academic ally in the nutrition/contagion controversy. However, according to Alexander Bay, the target of his wrath was not Suzuki, but Tsuzuki Jinnosuke, an army medical doctor. Alexander Bay, "Beriberi, Military Medicine, and Medical Authority in Prewar Japan," *Japan Review*, 2008, **20**:130.

[16] Alexander Bay, *Beriberi in Modern Japan*, University of Rochester Press, 2012, 53.

extremely interesting."[17] In the face of a preponderance of criticism, a chastised Suzuki retreated to his lab to confirm his results.[18]

Suzuki had, unwittingly or not, stepped into a dispute over the cause of beriberi that had raged between the Imperial Navy medical department on one hand, and Imperial Army and Tokyo University physicians on the other, since the 1880s. The Navy, because of Takaki Kanehiro's studies, adhered to a nutritional cause, while the Army and the Tokyo Imperial University faculty of medicine had staked their reputations on a bacterial origin. Supporting the bacterial faction's assertion was Mori's experiments on the nutritional value of white rice which seemingly ruled out a dietary basis to the disease. He concluded that an as-yet undiscovered bacilli must be responsible. This thesis gained most of its weight from the institutional authority of its proponents. Further, Mori was very heavily invested in this hypothesis, if for no other reason than admitting that he made an error would be tantamount to accepting culpability for the deaths of thousands of Japanese soldiers.[19]

Suzuki guessed that the widespread criticism of his findings was because he was "neither a medical doctor nor a pharmacist."[20] This seems disingenuous, however, given both his position at Tokyo University, and the fact that his detractors went so far as to involve the newspapers in lambasting him. Although Suzuki could not have been unaware of the feud between the contagion and nutrition factions in the beriberi debate, he still must have been puzzled at the stubborn resistance to his theory which persisted even after he published a number of studies that seemed to conclusively demonstrate that beriberi was a nutritional deficiency disorder rather than a bacterial one, including one involving 20 orphans, aged five to seven, all afflicted with *kakke*, all conclusively cured with oryzanine.[21]

Suzuki probably would have continued his *kakke* experiments, which could perhaps have eventually won over domestic support for publicizing his case internationally, but the advent of World War I superseded his efforts. Prior to the summer of 1914, most of Japan's technical supplies and scientific knowledge came from Germany, as was the case with most of the industrialized world of the time. However, as Japan was an ally of England and the Entente, this source was no longer available. The coming of the First World War, therefore, while an initial blow to Japan's scientific and industrial communities due to the shortages in raw and finished materials that it caused, also created the opportunity to expand production in cheap consumer goods, chemicals, and pharmaceuticals. So it was in 1915 that Suzuki was ordered to cease his beriberi research and devote his energies to the synthesis of Salvarsan,[22]

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[17] *Kenkyū no Kaiko*, 8.

[18] *Suzuki Umetarō Sensei-Den*, 9. The account of the *kakke* controversy, Suzuki's side of it at any rate, also has appeared in comic form. Although typically (for the genre) overly dramatic, it is, broadly speaking, true to events, even as it wonders why Suzuki did not receive a Nobel Prize. The *manga* version of Suzuki's nemesis is never identified explicitly, and while he does make the "urine" comment, albeit at the Chemical Society conference, his image resembles neither Mori Ōgai nor Aoyama Tanemichi. Itō Tomoyoshi and Morita Shingo, *Eikō-naki Tensai-tachi v.4*, Tokyo: Shūeisha, 1997.

[19] Bay, 126. For a more detailed account of the nutrition/contagion debate, see Alexander R. Bay, "Beriberi, Military Medicine, and Medical Authority in Prewar Japan," *Japan Review*, (2008), v20, 111-156.

[20] *Kenkyū no Kaiko*, 11. It also could be that the Mori/Aoyama faction saw his assertions as a betrayal, given that Suzuki was both alumnus and faculty at Tokyo Imperial University. Moreover, there may have been some anger at Suzuki for "interfering" in a medical matter that was none of his affair, despite his appointment to the commission. See Bay, Ibid., for examples of this concerning Japan's domestic beriberi debate, and Bartholomew, Ibid., for those in Japan's general scientific community.

[21] Suzuki Umetarō, Araki Bunsuke, and Sasaki Sei, "Shōni no Eiyō ni oyobosu Oryzanin no Kōkō ni tsukete," *Tokyo Kagakukai-shi*, 36 (1915), 1153-1171.

[22] Also known as arsephenamine, it was discovered by Paul Ehrlich and Hata Sahachirō (秦 佐八郎) in 1910. It was the first drug capable of effectively treating syphilis.

one of the pharmaceuticals previously supplied by Germany, which he did until he was tapped to head a laboratory upon the founding of Riken two years later.

The controversy between whether *kakke* was a dietary malady or infectious disease would not be laid to rest in Japan until Shimazono Junjirō (島薗順次郎) definitively established the connection between beriberi and a deficiency in thiamine, thereby finally silencing Suzuki's critics. Shimazono also worked out preventive dietary measures and received the Japan Academy Prize in 1926.

On August 1, 1911, Suzuki's aberic acid abstract appeared in *Zentralblatt für Biochemie und Biophysik*, a periodical that served as a clearinghouse for research in medicine and the life sciences. Written by someone identified as "Teruuchi, Tokio," it described Suzuki's methodology in great detail, down to specific concentrations of reagents, and the sequence of the various procedures.[23] This did not look to be a unique occurrence for *Zentralblatt*, but seems unnecessary, given that brevity is supposedly one of the conventions involved in writing journal abstracts.

In the December 22, 1911 issue of the *Journal of Physiology,* Casimir Funk, a researcher at the Lister Institute in London, published a paper entitled "The Preparation from Yeast and Certain Foodstuffs of the Substance the Deficiency of Which in Diet Occasions Polyneuritis in Birds." [24] The following May, the abstract of Funk's article made its appearance in the publication, *Chemical Abstracts*, an English-language equivalent of *Zentralblatt.* The abstract of Suzuki's *Zentralblatt* article, although it preceded Funk's paper by almost a year, for some reason or other did not make its own appearance until October 1912. Biochemist Donald Dexter van Slyke, who wrote the abstract to Suzuki's article with the translated title "Oryzanine, a Component of Rice Bran and its Physiological Significance," seemed to be compelled to conclude it with: "The results of the authors constitute a confirmation and enlargement on the discovery of Casimir Funk *of which they were unaware* (emphasis added)."[25]

This sort of editorializing does not appear to have been very common in a publication that was ostensibly a collection of purely scientific abstracts, and indeed, seems a little unreasonable. One might have thought that van Slyke might have been more forgiving of a scientist's lack of awareness given that *Chemical Abstracts* cited literally tens of thousands of scientific journal articles each year. Most especially since van Slyke himself seems to have been similarly unaware of the original citation on Suzuki's oryzanine research from *the Journal of the Tokyo Chemical Society* that *Chemical Abstracts* had published in an earlier edition.[26]

So, despite the fact that his oryzanine article essentially was cited twice in *Chemical Abstracts*, only in Japan is Suzuki accorded credit for discovery of the anti-beriberi factor. Casimir Funk, with varying degrees of indignation, is, even now, derided in Japan as a plagiarist and opportunist. Sekine Hidesaburō (関根秀三郎), an agricultural chemistry professor at Tokyo University remarked,

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[23] Probably Teruuchi Yutaka (照内豊), a Medical Chemist of the Meiji to early Showa eras.
[24] Casimir Funk, "The Preparation from Yeast and Certain Foodstuffs of the Substance the Deficiency of Which in Diet Occasions Polyneuritis in Birds," *Journal of Physiology 43(5), 75-82.*
[25] D.D. Van Slyke, *Chemical Abstracts* 6(3) October-December 1912, 2774-5.
[26] I.K. Phelps, *Chemical Abstracts* 6(1) January-April 1912, 251.

"Funk used the same procedure as Suzuki, and produced the same substance (oryzanine) … Suzuki introduced the abstract of his results in German in August of 1911 and Funk presented his report in December of that year – from August to December is four months … Funk should have read Suzuki's research result in *Zentralblatt für Biochemie und Biophysik* – at the time, it was a fairly prominent journal and medical doctors, physiologists, and biochemists had to at least browse it, no matter who they were."[27]

It is indisputable that, as a scientist educated prior to World War I, Funk should at least have been passingly familiar with German, and since he was schooled in Switzerland and Germany, most assuredly was quite fluent in that language, and should have been aware of Suzuki's abstract in *Zentralblatt*.[28] After all, Funk's own abstracts were published therein. Notably, in an article carried in the November 1911 edition of the British medical journal *The Lancet*, three months after Suzuki in *Zentralblatt* and one month before Funk's "groundbreaking" article in the *Journal of Physiology*, the authors Funk and Evelyn Cooper announced that the "precise nature of [an anti-beriberi substance] is being at present investigated by one of us (C.F.)."[29] Although this paper does not disclose the precise form that the investigation was taking, and whether it involved laboratory experimentation or a rigorous search of published materials, it also reveals that it was Dr. Charles James Martin, FRS, and Director of the Lister Institute from 1903 to 1930, who apparently suggested that Funk direct his attention to beriberi in the first place.[30] At any rate, if the procedure for extracting the anti-beriberi substance did not originate with Funk, at the very least, academic integrity obliged him to cite his source or face charges of plagiarism.

Nonetheless, the popularity of Funk's invented term, "vitamine," presumably what elision had made of "vital amine," took off.[31] But his motive for inventing the term may not have been of a strictly scientific nature. He said,

"… I must admit that when I chose the name, "vitamine," I was well aware that these substances might later prove not to be of an amine nature. However, it was *necessary* for me to choose a name that would sound well and serve as a catchword, since I had already at that time no doubt about the importance and the *future popularity of the new field*" (emphases added).[32]

Perhaps this statement may be construed to indicate his intention to link his name to a revolutionary new area of study, and that he may have been searching for a project with which he could elevate himself to prominence, at least within the scientific community. Whether this

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27 Sekine Hidesaburō, in *Suzuki Umetarō Sensei-den*, p.146. Sekine also was a professor of agricultural chemistry at Tokyo University. He felt that Suzuki should have been awarded a Nobel for his work on vitamins, and felt the same about Takamine Jōkichi and his adrenaline research. *Ibid.*, 142.
28 Fred Jueneman, "Scientists Who Were Shafted," *R & D 39(3),* S1 (2).
29 Cooper and Funk, 1367.
30 Ibid., 1267.
31 Incidentally, the term "thiamine," also known as vitamin B_1 comes from the joining of "sulfur-bearing" or "thio-" and "amine."
32 Funk, *Vitamines*, 36.

is so or not, it must have been quite a disappointment to Funk when he was not awarded the Nobel Prize for their work on vitamin theory. Suzuki must similarly have been disappointed not to have been so honored, if also a touch vindicated to share that non-status with his "rival," Funk.

My criteria for "discovery" of thiamine is admittedly narrow, but I think proper. I define it as being the first to identify the correct molecular formula, as agreed upon by current convention. If another compound were under consideration, it might be necessary to amend the definition to include "identify the correct molecular structure." However, the first scientist to do so was also the first with the correct molecular formula, so for vitamin B_1, molecular formula alone is sufficient.

So as to the proposition, who should receive credit for the discovery of vitamin B_1, should it be Takaki Kanehiro? His work positing that beriberi was due to a dietary deficiency and his subsequent clinical studies was an indispensable step toward illumination of this matter, but his hypothesis that it was a lack of dietary protein that caused beriberi was erroneous. His contribution to resolving the question of dietary deficiency disease in general, and beriberi in particular, is akin to that of James Lind and scurvy, although a number of successful treatments for that disorder had been discovered, forgotten, then re-discovered over the centuries.

Then should it be Suzuki? The truth is, there is one very large problem with Suzuki's oryzanine research and according him credit for the discovery of vitamin B_1. When he broke oryzanine into its constituents, he produced choline, glucose, nicotinic acid, an organic acid he dubbed "alpha," with the formula $C_{10}H_7NO_4$, and a "beta" acid with $C_{18}H_{16}N_2O_2$.[33] The accepted chemical formula for thiamine is $C_{12}H_{17}N_4OS$. While it is possible that Suzuki's method of extraction fractured the vitamin B_1 molecule, if this indeed were the case, one would expect the chemical formula "sum" of the two acids to equal that of thiamine. Not only does it not do this, but the sulfur atom is conspicuously missing from Suzuki's results.[34]

But there also are problems with Funk's results. Despite what Sekine Hidesaburō said, Funk's compound was not the same as Suzuki's. Referencing the chemical formula he published for his "vitamine," $C_{17}H_{20}N_2O_4$, the identity of the molecule is not clear. The closest candidate is nicotine salicylate, $C_{17}H_{20}N_2O_3$, which is not a chemical that occurs naturally, and as with Suzuki's results, the essential sulfur atom also is missing.[35,36] So, despite entries in numerous Japanese popular writings, biographical dictionaries and encyclopedias, Suzuki did not correctly identify the pertinent molecule. However, neither did Funk, who to this day, also despite entries in numerous popular writings, biographical dictionaries, encyclopedias and online databases, is accorded the credit for first discovering vitamin B_1 (and sometimes A, C, and E) when in fact he is only the second one to *incorrectly* identify it.

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[33] One chemical that shares the same formula with Suzuki's alpha acid is xanthurenic acid, a chemical that is excreted by pyridoxine-deficient animals after being fed tryptophan. If albino rats are fed nothing but fibrin, this chemical will be in their urine. The beta acid most resembles 1-xylyl-azo-2-naphthol, a coloring agent banned by the US Food and Drug Administration. Of course with such large molecules, there are a number of isomers possible which have structure and properties in wide variance to each other. But the ones proposed by myself are the only possibilities listed by the Merck index, or those that come closest.

[34] Suzuki, "Chemical Studies of Vitamin-B in Japan," 296.

[35] It is used to treat nicotine withdrawal, and as an insecticide.

[36] Barend Coenraad Petrus Jansen and Willem Frederik Donath, "On the Isolation of Antiberiberi Vitamin". *Koninklijke Nederlandse Akademie van Wetenschappen* 29 (1926), 1390.

Then what of the two researchers who received a Nobel for their work with vitamins? According to the Nobel Committee that awarded them the 1929 Prize in Physiology or Medicine Christiaan Eijkman was being honored "for his discovery of the antineuritic vitamin" and Sir Frederick Gowland Hopkins "for his discovery of the growth-stimulating vitamins." However, neither did any such thing. Eijkman believed beriberi was caused by a toxin in white rice that was neutralized by some compound found in its pericarp. He never delved deeper into the subject than stating that it was brown rice or its husks that, when fed to chickens, prevented them from developing beriberi-like symptoms.

Likewise, Frederick Gowland Hopkins was at Cambridge University in 1906 when he declared that there were "minimal qualitative [dietetic] factors," which he also referred to as "accessory food factors," that are essential if an animal is to thrive.[37] But if theorizing the existence of unspecified dietetic factors constitutes "discovery of vitamins," then Cornelis Adrianus Pekelharing has a stronger claim to Hopkins' half of the prize. In 1905 he proposed that:

> There is still an unknown substance in milk, which, even in very small quantities, is of paramount importance to nutrition. If this substance is absent, the organism loses the power properly to assimilate the well-known principal parts of food, the appetite is lost and with apparent abundance the animals die of want. Undoubtedly this substance not only occurs in milk but in all sorts of foodstuffs, both of vegetable and animal origin.[38]

Of course, Pekelharing passed away in 1922, thereby making him ineligible for a 1929 Nobel Prize. Although it seems strange to award someone an internationally prestigious medal because he was the second person to make the supposition, the person who proposed it first being dead, Hopkins was nevertheless so honored, even if his "accessory food factors" did not prove as popular a "catchphrase" with the scientific and general public as did "vitamins."

In spite of scientific squabbling and the handing out of medals, research on the anti-neuretic vitamin continued, fortunately, as it turned out. In 1926, Barend Coenraad Petrus Jansen (1884-1962) and Willem Frederik Donath (1889-1957) reported that they had crystallized a thiamine molecule, which they dubbed "aneurine." The ability to crystallize a substance is an indicator that researchers have isolated a pure sample. Unfortunately, the chemical formula they had so elucidated ($C_6H_{10}NO_2$) still lacked a sulfur atom.[39] The next step was to develop a procedure to synthesize vitamin B_1, but their omission stymied attempts in this endeavor, and furthermore, cast doubt on their findings.

Finally, in 1934, Robert Runnels Williams (1886-1965) managed to determine the correct molecular formula from a crystallized sample, and two years later, while working for the Merck chemical company, developed a procedure to produce thiamine in the laboratory. Now a pure version of the cure for beriberi was available, rather than the extracts that had heretofore been the only pharmaceutical alternative to a healthy diet. [40] The synthesized version being curative for beriberi conclusively demonstrated that the correct formula had at

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[37] *Ibid.*, 10.

[38] Leslie J. Harris, *Vitamins and Vitamin Deficiencies*, London: Churchill, 1938, 14.

[39] C. Eijkman, "Experiments with Jansen and Donath's Antiberberi-vitamin," *Proceedings of the Royal Academy of Amsterdam v.30* (1927), 375-382.

[40] R.R. Williams and J.K. Cline, "Synthesis of Vitamin B1," *Journal of the American Chemical Society 58(8)* (August 1936), 1504-1505.

last been determined. Therefore, it is Robert Runnels Williams who should receive final acclaim for discovery of thiamine, since it was he who, not only isolated it in pure form, but also elucidated its structure accurately. Additionally, he was the first to synthesize it, definitively putting a cap on any further dispute as to its molecular formula.

Although Suzuki felt that he had been robbed of rightful acknowledgment for his discovery, unlike many of his supporters even up until the present day, he knew he did not deserve credit for having discovered thiamine. However, in 1926 he wrote, "So I believe, that, my experiments . . . apart from their significance in the genesis of the (sic) beriberi, established the first firm foundation of the Vitamin theory of to-day (sic)."[41] For while he did not correctly chemically identify any one particular vitamin, what he did was even more significant. He took the study of these essential macromolecules from the realm of nutrition, to that of chemistry; to the molecular level.

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[41] Umetarō Suzuki, "Chemical Studies of Vitamin-B in Japan," *Scientific Papers of the Institute of Physical and Chemical Research*, 4 (63) (1926), 297.

"Pauling's Boys" and DNA Structure: Collaborative Failure in the Transition from Structural Chemistry to Molecular Biology

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Introduction: Pauling's failed DNA structure as a historiographical challenge

In February 1953, Linus Pauling, (1901-1994) a most accomplished and versatile structural chemist[1] who contributed, often decisively, to solving the structure of over 200 inorganic and organic compounds; author of best-selling textbooks, most notably the influential *Nature of the Chemical Bond: An Introduction to Modern Structural Chemistry* which ran into several editions since its publication in 1939; Chairman of the Department of Chemistry and Chemical Engineering at Caltech; (1937-1958) one of youngest members of the US National Academy of Science at his election in 1931; and soon to become a Nobel Laureate[2], published a profoundly flawed model of DNA structure.[3]   Pauling's model was disproved only two months later, in April 1953, when seven scientists from two labs sponsored by the British government's Medical Research Council (hereafter MRC) in London and Cambridge-UK, published three back-to-back papers supporting a totally different structure for DNA, a structure which would become famously known as the DNA double helix, or just the "double helix",[4] because it revolved around two intertwined helical strands of paired polynucleotides.

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[1] For a dozen or so fields of chemistry to which Pauling contributed, by himself as well as by training students turned leading scientists, see Alexander Rich and Norman Davidson, eds. *Structural Chemistry and Molecular Biology,* (volume honoring Pauling's 65th birthday, San Francisco: Freeman, 1968) Each section includes 4-10 chapters written by over 100 former associates. Pauling's 90th birthday was marked by a volume in which the contributors were Nobel Laureates, see Ahmed H. Zewail, ed. *Linus Pauling. The Chemical Bond: Structure of Dynamics.* (Boston, Academic Press, 1992) For the range of Pauling's contributions, both scientific and public, see Paulingblog*, https://**paulingblog**.wordpress.com/ m*aintained by the Oregon State University Libraries, Special Collections & Archives Research Center. (hereafter SCARC)

[2] For the Nobel Foundation's justification of the 1954 Prize in chemistry to Linus Pauling and for the Laureate's Nobel Lecture see http.//nobelprize/1954/chemistry. For Pauling's nominations as a potential laureate prior to 1954 see the archives of the Nobel Foundation, Swedish Academy of Sciences, Stockholm. For the nomination background of the Nobel Prizes in chemistry in the 1940s and 1950s which explains in part why Pauling received his Nobel in 1954 see Robert Marc Friedman, *The Politics of Excellence, Behind the Nobel Prize in Science, (New York: Times Books, 2001)*

[3] Linus *Pauling* and Robert B. Corey*, "A Proposed Structure For The Nucleic Acids", *Proc Natl Acad Sci U S A. 1953* Feb; 39(2): 84–97. See also Linus Pauling, "Fifty Years of Physical Chemistry in the California Institute of Technology", *Annual Review of Physical Chemistry, 16* (1965) 1-15; DOI: 10.1146/annurev.pc.16.100165.000245

[4] See the section "A molecular structure for deoxyribonucleic acid", Nature, April 25 (1953) 731-740; it includes a paper by Rosalind Franklin & Raymond Gosling, a paper by James Watson & Francis Crick, and a paper by Maurice Wilkins, William Seeds, and Robert Wilson. For the confusion over the conceptual and historical relationships between these papers as a result of their publication order (which placed the Cambridge lab paper by Watson & Crick ahead of the two papers from King's College, London, as well as a result of asymmetric references of these papers to each other, especially between the first and third papers, see Aaron Klug, *Journal of Molecular Biology, 335*, (2004) 3-26; Pnina G. Abir-Am, "DNA at 50: Institutional and Biographical Perspectives", *Minerva, 51* (2004), 167-193; idem, "Photo 51 – A Recent Addition to History-of-Science-Inspired Theatre", *History of Science Society Newsletter*, July 2012, 30-35; idem, "Setting the Record Straight: Review of *My Sister Rosalind Franklin, Une Vie a Raconter, and Genesis of the Salk Institute", Endeavour* (2015) http://dx.doi.org/10.1016/j.endeavour.2014.10.011; idem, *DNA at 50: History, Memory, and Politics in Scientific Discovery,* forthcoming. See also Robert Olby, *The Path to the Double Helix,* Section V. (London: Macmillan, 1974; New York: Dover, 1994) which was however written prior to the opening

By contrast, Pauling's structure revolved around three helical strands, though the wrong number of strands was only the <u>first</u>, most obvious and best known of several flaws and differences between what would emerge as the correct structure of DNA and a symbol of the new field of molecular biology, and Pauling's largely forgotten "blunder". A <u>second</u> key difference pertained to the location of the phosphate backbone in the center of the macromolecular assembly in the structure proposed by Pauling, as opposed to being at its periphery as discovered by Rosalind Franklin, and adopted by Crick and Watson in their second effort at a DNA model.[5]

A <u>third</u> difference pertained to the uncharged nature of the DNA structure proposed by Pauling, even though under physiological conditions DNA is a negatively charged acid. (DNA stands for deoxyribonucleic acid) The charges in Pauling's structure were balanced, as in a salt, largely, though not entirely, because he vastly underestimated the water content of the macromolecular assembly, being primarily concerned with the structural-chemical challenge presented by DNA, as if such a challenge could be considered apart from DNA's biological environment.[6]

A <u>fourth</u> difference between Pauling's proposed structure and the one proposed by the teams from the two British labs pertained to stereochemical feasibility and stability, or the requirement that certain distances obtain between different atoms in a molecule. Pauling's proposed structure was overly "crowded", i.e. it did not satisfy the minimal Van der Waals distances between various atoms, especially the larger phosphate ones. This aspect was particularly baffling since Pauling was a world expert in stereochemistry. His proposed structure for DNA thus amounted to no less than disregarding the key role of stereochemistry, which he himself had done so much to establish, for the sole purpose of securing priority in the topic of DNA structure, a topic which evidently had been and remained profoundly unfamiliar to him despite a five week "blitz" of a focused effort.

Last but not least, the <u>fifth</u> flaw was that Pauling's structure had no functional implications even though it was by then increasingly accepted that DNA was most closely involved in heredity.[7] This feature was also rather odd especially since Pauling discussed the type of structures that might be suitable to carry out the function of genetic duplication five

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of the archives of the above DNA co-author protagonists, and hence offers a limited understanding of this confusion.

[5] Prior to becoming "acquainted" with Franklin's decisive work, in the fall of 1951, Crick and Watson built a failed DNA model which, much as Pauling late in 1952, put the phosphate backbone in the middle of the molecule. See Olby, Klug, and Abir-Am. (note 4)

[6] This approach reflected Pauling's philosophy of chemistry's supremacy over biology, or as he put it while offering guideline to his post-doc Alexander Rich, "Do the chemistry first, and look for biological ramifications, if any, later" in Rich, "Linus Pauling's approach to biomolecular structure" in John T. Edsall, *Selected Topics in the History of Biochemistry and Molecular Biology*, (Boston, MA.: American Academy of Arts and Sciences, 1973), 71-77.

[7] Alfred D. Hershey, and Martha Chase, Independent functions of viral protein and nucleic acid in growth of bacteriophage. *The Journal of General Physiology*, 36 (1952) 39–56; this paper was discussed at the International Congress of Biochemistry held in Paris in the summer of 1952, which Pauling attended. However, Pauling spent his time in Paris as a political hero, who prevailed over the US State Department's decision to revoke his passport as a result of international pressure. Pauling did not attend Congresses of Biochemistry but was specifically invited to the 1952 Congress so as to provide him with a good reason to travel outside the US.

years earlier,[8] while specifically highlighting the role of complementary molecular templates of the sort proposed for the DNA double helix by others in 1953.[9]

Yet, during the late 1940s and early 1950s when the interest in DNA grew steadily worldwide, not only did Pauling not gravitate toward DNA but on several occasions he missed distinct opportunities for a closer encounter.[10] His failed effort at solving the structure of DNA late in 1952 and early in 1953 thus cannot be understood without a detailed clarification of those missed earlier opportunities which eventually converged into a five dimensional, colossal failure.

The historical background of Pauling's belated move toward DNA

Linus Pauling's failed attempt to solve the structure of DNA has long baffled scientists, historians of science, and others interested in great scientists and the making or missing of great discoveries. The Center for Research Integrity has even established a blog in which over 60 scientists have debated whether Pauling's DNA paper should be retracted, given the fact that it has remained incorrect on all five key counts for more than half a century.[11]

This paper departs from previous attempts to justify Pauling's failure with DNA by invoking his own busy life in both science and politics, a life which has already received considerable attention from biographers and historians.[12] This paper accepts that Pauling's many responsibilities in science management at that time, such as serving as department chairman, supervising twice the average number of graduate students per adviser in his

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[8] Linus Pauling, "Molecular Architecture and the Processes of Life", Sir Jesse Boot Foundation Lecture at the University of Nottingham, May 28, 1948. The author thanks Mathew Meselson for a copy. Pauling's lecture in 1948 is also discussed in Olby. (note 7) and Crick. (note 9)

[9] For the role of Pauling's ideas on complementary molecular templates in stimulating Crick's outlook on DNA structure and its duplication function see Francis Crick, "Linus Pauling's contributions to molecular biology" in Zewail, ed. (note 1), p. 33-44.

[10] See below pp. 10-11; for greater detail see Abir-Am. (note 4)

[11] http://retractionwatch.com/2012/06/27/should-linus-paulings-erroneous-1953-model-of-dna-be-retracted/. For the stance of Paulingblog, a website dedicated to disseminating research on Linus and Ava Helen Pauling's life and work, which is maintained by the Special Collections and Archive Research Center (hereafter SCARC) at Oregon State University in Corvallis, the home of the Paulings' Personal Papers as well as of the Linus Pauling Research Institute, see https://paulingblog.wordpress.com/2009/04/28/the-pauling-corey-structure-of-dna/. This site attributes Pauling's failure to "insufficient data and an overloaded research schedule": "As a result of insufficient data and an overloaded research schedule, Pauling's structure turned out to be incorrect. However, it is interesting to see the ways in which one of the world's leading scientists went wrong with his approach to the structure of this hugely-important molecule", ibid, first paragraph. The PaulingBlog concludes in a way common among scientists: "For Pauling, this event was a single failure in a sea of successes. In fact, the very next year, he would win the Nobel Prize in Chemistry – the first of his two Nobel Prizes. Despite his embarrassing mistakes, Pauling was to remain in good standing with the scientific community", ibid. As recent as August 2012 when the author interviewed former Pauling associates Ken and Lise Hedberg at Oregon State University in Corvallis, they refrained from attempting to clarify Pauling's approach to DNA on the ground that Pauling was successful so many times (having solved over 200 structures with his many collaborators) that his isolated failure with DNA was of no consequence.

[12] Ramesh Krishnamurthy et al (eds.) "The Life and Work of Linus Pauling (1901-1994) : A Discourse on the Art of Biography", video and transcripts of a symposium held 2/28-3/2/1995, http://scarc.library.oregonstate.edu/events/1995paulingconference/index.html; Goertzel, Ted and Ben Goertzel (1995). *Linus Pauling: A Life in Science and Politics* . New York: Basic Books, Thomas Hager, *Force of Nature: The Life of Linus Pauling.* (New York: Simon & Schuster, 1995) Mary Jo Nye, "Pauling, Linus Carl (1901-1994) *New Dictionary of Scientific Biography*, ed. Noretta Koertge, (New York: Scribner's Sons, 2007) Vol. VI, pp. 36-44; John W. Servos, Physical che*mistry from Ostwald to Pauling: The Making of a Science in America*, Princeton, N.J. : Princeton University Press, 1990; Mina Carson, *Ava Helen Pauling: Partner, Activist, Visionary*, Corvallis, OR: Oregon State University Press, 2013; Pnina G. Abir-Am, "Nobelesse Oblige: Lives of Molecular Biologists*", ISIS, 82* (1991) 326-343. (which includes an essay review of the 1989 Pauling biography by Anthony Serafini)

department, updating best-selling textbooks, and being constantly in demand for talks, both professional and lay, greatly constrained the span of his attention for any topic, including DNA. Pauling's growing involvement in Cold War politics[13] also took a toll.

For example, Pauling's passport difficulties at the time[14], stemming from his political activism in causes perceived by the US State Department to be sympathetic to Communism during the McCarthy era,[15] were invoked to justify his failure with DNA in terms of his being prevented to travel to a major conference in London in May 1952. Presumably, once there, Pauling would have seen the DNA X-ray work done at King's College; and presumably he would have solved the structure of DNA once he would have been able to glance[16] at the sharpest X-ray photo obtained by Rosalind Franklin and Raymond Gosling, now widely known via books, plays and films as Photo 51.[17]

Pauling's own belated assessment that he took his time and his chance with DNA because he felt entitled to do so since in his opinion no one else could have solved it,[18] though very telling of Pauling's excessively confident state of mind, it also remains as a rather limited and misleading explanation, some sort of "wishful thinking", since Pauling continued to ignore critical work pertinent to DNA structure which had been accomplished in several

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[13] Goertzel and Goertzel; (note 12) Hager; (note 12) Carson. (note 12)

[14] See for example the Editor's note to Linus Pauling's chapter "Fifty Years of Structural Chemistry", in Stephen Graubard (ed.) *Intellectuals and Change*, summer issue of *Daedalus* on *The Making of Modern Science: Biographical Studies* (Boston: American Academy of Arts and Sciences, 1972) p. 787; see also Hager, (note 13) and https://paulingblog.wordpress.com/2011/03/30/pauling-obtains-his-fbi-file/

[15] Though Pauling was involved in many hearings as a result of his political activism, the passport issue stemmed from his carelessness in becoming listed as an officer of an organization viewed as a communist front by the State Department. Even though he was too busy to be so active, Pauling's sense of self importance and his admiration for politically involved scientists such as his friendly rival in the pursuit of protein structure,   J.D. Bernal, who served at the time as Vice-President of the Association of Scientific Workers, led him to accept his listing as more than a regular member; he did not know that the latter category was not subject to passport revocation. Indeed, his passport was reinstated after he resigned from his otherwise empty of content position as an unusually busy officer.

[16] This assumption reflects a belief that Pauling's experience with proteins two years earlier will repeat itself with DNA, a belief which informed Pauling who may have shared it with others. Obviously, it is impossible to know what might have happened had Pauling been able to travel to UK in April & May 1952. He was eventually allowed to travel to both UK and other countries in July and August 1952, but that travel made no difference in preventing Pauling from embarking on his failed approach to DNA structure in December 1952. The author posed this very question to Pauling at a special session of the History of Science Society at its annual meeting in Seattle, WA. in 1990, a session attended by hundreds of HSS members and organized by former Caltech archivist Judy Goodstein. By then Pauling took the view that he planned to eventually tackle DNA but saw no rush in so doing. This reply sheds light on why he did nothing on DNA during 1951 and 1952, but does not clarify why he published after five weeks of work only.
This excuse revolving around the incorrect assumption that a mere glance at the best diffraction photo would have been sufficient to deduce the structure appears to have been further influenced by James Watson's account, *The Double Helix, A Personal Account of the Discovery of the Structure of DNA,* (New York: Atheneum, 1968) which remains the most widely disseminated account despite its author's various retractions, as well as a growing awareness that such an account remains not only partial but very misleading. Though that account mentions Pauling's failed attempt as a reason Crick and Watson were allowed to have a second try on DNA structure, it does not contain any information, let alone insights, into Pauling's take on DNA. For the social and historical context of Watson's account see Abir-Am (note 4) On why the DNA X-ray data was necessary but not sufficient to deduce the structure see Klug. (note 4)

[17] Abir-Am. (note 4) Lynn O. Elkin, "Rosalind Franklin and DNA", *Physics Today, 23* (2003), 42-48.

[18] "In 12/1988, Linus was the keynote speaker at the UCLA winter school on molecular evolution… As we were leaving the lecture…he suddenly asked my wife and me in his uniquely direct way if we ever wondered "why he hadn't solved the structure of DNA" …He said that one day his wife asked his question. It had made him think and he replied something to the effect of "I don't know, I guess that I always thought that the DNA structure was mine to solve, and therefore I didn't pursue it aggressively enough". Quoted in James Lake, "Why Pauling did not solve the structure of DNA?", *Nature*, 2001, 558.

major labs in both US and UK in the late 1940s.[19] He did so because much as other scientists who came of scientific age before WW2, Pauling retained a fixation on the pre-WW2 macromolecule of utmost interest, the proteins.[20]

Furthermore, as the first "winner", in 1951, of a long raging international debate on protein structure, when Pauling's discovery of the alpha-helix as a major structural principle of protein structure was published; Pauling had a huge vested interest in disseminating his major success with the alpha-helix.[21] He further saw the alpha-helix as a triumph validating not only 15 years of effort against the best structural minds at the time, but also his "indirect" approach of prioritizing structural chemistry over X-ray crystallography.[22]

Collaborative failure as the root cause of Pauling's strategy toward DNA

Under these circumstances, to which one must add the then rising political activism on the part of both Paulings,[23] due to intensification of the Cold War in the international arena with the outbreak of the Korean war in 1951, Pauling persisted in overlooking the dramatic changes in DNA research in the late 1940s and early 1950s. What remains to be addressed is why Pauling did not delegate the challenge posed by DNA structure to some of his many research associates who abounded in his lab, department, institution, and beyond.

Even more so, since other, equally busy, department chairs who had a structural interest in biomolecules, did invariably deploy such research associates in addressing the new challenge of DNA structure. Indeed, all the seven co-authors of the three back-to-back DNA structure papers published in April 1953, papers which demolished Pauling's then only two months old proposed structure, were research associates to whom the DNA challenge was delegated by their lab directors and/or department chairs.[24]

This paper thus regards Pauling's failure with DNA as an "interactive failure" or an issue of failed collaboration between him, an accomplished, senior and powerful scientist and his gifted, junior, research associates during a period of transition from structural chemistry to molecular biology.[25] Such a transition was triggered after WW2 by new solutions of biomolecular structures, most notably those of proteins and DNA. Since the complex

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[19] Abir-Am. (note 4) Recent research suggests that Pauling's deliberate ignoring of most DNA labs was also influenced by a fair amount of social prejudice which he held against major DNA scientists who were women and "racial refugees"; as well as prejudice against disciplines he considered to be beneath chemistry, most notably biochemistry, and biology at large, Abir-Am, ibid.

[20] P. Srinivasan, Joseph Fruton, and John T. Edsall, eds. *The Origins of Biochemistry, A Retrospect on* Proteins. (New York City: New York Academy of Science Press, 1979) Abir-Am, "Toward a Historical Ethnography of Science: The 50th Anniversary of the First Protein X-ray Photo", *Social Epistemology, 7,* 1992. (special issue in December devoted to this topic)

[21] Linus Pauling and Robert B. Corey, "Atomic Coordinates and Structure Factors for Two Helical Configurations of Polypeptide Chains", *PNAS, 37*, (May 1951) 235-240. The travel to London in April 1952 which Pauling was prevented from taking due to the revocation of his passport, was meant to present Pauling's discovery of the alpha-helix to other protein workers, many of whom were based in UK. When eventually he reached Europe and UK in July and August 1952, Pauling still spent the bulk of his time on proselytizing for the alpha-helix. For details see Abir-Am. (note 4)

[22] For debates on the "direct" versus the "indirect" approaches to protein structure see J. Desmond Bernal, "Linus Pauling's Pattern of Work in Molecular Biology" in Rich and Davidson, (note 1) 345-356. Bernal championed the "direct" approach but despite their methodological divergences, Bernal and Pauling remained friendly since both shared a rival who anticipated both in proposing the first theory of protein structure. Abir-Am. (note 4 and note 20)

[23] Carson; (note 13) Goertzel and Goertzel; (note 13) Hager. (note 13)

[24] Five of them, organized in two teams, one team led by Rosalind Franklin and another team led by Maurice Wilkins, belonged to the Biophysics Lab and Sub-department chaired by John T. Randall (later Sir John) at King's College, London. The other two, Crick and Watson, belonged to the Molecular Structure of Biological Systems Lab, housed in the Physics Laboratory at the University of Cambridge, and directed by Sir W. Lawrence Bragg. Abir-Am (notes 4, 20)

[25] On this transition see Rich and Davidson. (note 1)

structures of such macromolecules required a wide range of instrumentation, as well as transdisciplinary team efforts, the locus of success or failure can no longer be sought in the conduct of a single individual, however accomplished, but must be pursued in connection with the rise, duration, management, and eventual dissolution of such teams.[26]

Furthermore, since Pauling's institution, California Institute of Technology (hereafter Caltech) did not accept women until the mid- and late-1950s,[27] the relevant social structure of a team or teams around Pauling in the early 1950s revolved by necessity around "Pauling's boys", i.e. a contingent of former students turned research associates who served as an easily available reservoir of labor, strategic information on scientific advances and other scientists, and specialized expertise.[28]

The question thus persists as to how "Pauling's boys" were deployed to meet the DNA challenge, as well as whether their eventual limited deployment stemmed from the fact that both Pauling and his "boys" remained captive of outdated forms of hierarchical social organization and asymmetric power relations. As a result, the paper argues, both sides were precluded from engaging in a more egalitarian collaborative effort and credit sharing, of the sort that would have been required for scaling the transdisciplinary frontier of molecular biology, or a frontier which built upon but extended well beyond Pauling's brand of structural chemistry.[29]

Pauling's rapport with his "boys" can be best understood in comparative terms, i.e. in light of similar relationships between lab directors and their respective research associates in other DNA labs. Though such a systematic comparison is beyond the scope of this paper, it is useful to remember that the more limited aim here, i.e. to clarify not only why Pauling and his many gifted "boys" failed but why they failed so badly, or why they were not even close to solving the structure of DNA, remains informed by the author's parallel study of pertinent "boys" in other DNA labs.

The question thus persists as to why, if Pauling himself has remained fixated on the pre-WW2 problem of protein structure[30], further remaining slow to seize upon the shift in the

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[26] On this issue with special reference to three major chemists and their respective collaborators and co-authors, including Pauling, see Mary Jo Nye, "Mine, Thine and Ours: Collaboration and Co-authorship in Material Culture of the mid-20th Century Chemical Laboratory", *Ambix, 61,* August 2014, 211-235; Joseph S. Fruton, Contrasts in scientific style: Emil Fischer and Franz Hofmeister, Their research schools and their theories of protein structure", *Proceedings of the American Philosophical Society 129* (1985) 313-370.

[27] For the story of a woman physicist whose gender identity was hidden by her post-doctoral adviser, the noted physicist Thomas Lauritzen, at Caltech, see Fay Ajzenberg Selove, *A Matter of Choice, Life of a Woman in Physics*. (New Brunswick/NJ: Rutgers University Press, 1994) Undergraduate women students were accepted in the 1970s only, as a result of affirmative action legislation in 1972.

[28] Mathew Meselson, "We were all Pauling's boys", in his oral history, Cold Spring Harbor: Cold Spring Harbor Laboratory Library & Archive, 2007; also as speaker on "The origins of the Meselson-Stahl experiment" at Caltech" in a session on "DNA at 60: New sources, new methods, new perspectives" organized by Pnina G. Abir-Am at the annual meeting of the History of Science Society in Boston, November 22, 2013, http://50.87.139.59/wp-content/uploads/2014/04/Apr2014-Newsletter.pdf.

[29] For details of the argument that the transdisciplinary nature of molecular biology required a restructuring of the Comptean, positivist, hierarchical and reductionist relationships between biology and the exact sciences see the theoretical, second part of Pnina G. Abir-Am, "The Biotheoretical Gathering, Transdisciplinary Authority and the Legitimation of a New Discourse in Molecular Biology: New Perspectives in the Historical Sociology of Science", *History of Science*, 25 (March 1987), 1-70.

[30] For the international dimensions of this problem prior to WW2 see Srinivasan, Fruton, and Edsall, eds. (note 20) Abir-Am 1992; for evidence in favor of the argument that Pauling's ongoing fixation upon protein structure was justified by the unenthusiastic British response of Pauling's discovery of the Alpha-helix at the famous May 1, 1952 meeting in London, as well as afterwards, see Edward Hughes, Oral History by Caltech Archives. Hughes, one of Pauling's longest serving "boys" to whom Pauling delegated the reading of his paper at the London conference once it became clear that he won't be able to attend, recalled that in Pauling's absence, all the protein worker attendees overtly expressed doubts; Ibid.

biological frontier from proteins to nucleic acids,[31] his "boys" who as members of a younger generation were not so fixated, still proved so useless in his quest for DNA structure? After all, the seven DNA scientists who co-authored the DNA structure papers which disproved Pauling's were also someone else's scientific "boys".

For example, one of those scientists, Maurice Wilkins who called himself "the third man of the double helix",[32] was a former Randall student turned long term protégé and heir[33] whose eventual place in the DNA story hinges on his role as a dual "boy" serving two masters, Randall's in London and W.L. Bragg in Cambridge.[34] Equally crucial was the "boys" status of JD Watson (1928-) & F. Crick (1916-2004) known at the time (and in science policy quarters until the late 1960s)[35] as "Bragg's boys", so as to signal their being part and parcel of the agenda of their Lab director, W. L. Bragg. (1890-1971) Holder of the most prestigious Chair of science in the British Empire, the Cavendish Chair at the University of Cambridge,[36] which he held between 1938-1954, Bragg continued to refer to these two as his "boys" into the late 1960s, when DNA structure became widely known as a major discovery, and his "boys" had become household names.

The only one among the seven authors of the simultaneously published three DNA papers in April 1953 who declined the "privilege" of being the "boy", or the "gal", of a lab director was Rosalind Franklin who left Randall's lab, relocating to Bernal's a mile away, where she was able to find the independence she so cherished. However, declining a "boy" status at a time the publication of the three DNA papers was being negotiated between the lab directors (i.e. the above mentioned J.T. Randall and W.L. Bragg) was not without consequence. The lab directors gave priority to their respective boys, as that was the only way to credit themselves at a time the work of "boys" was habitually attributed to their lab directors. As a result of this "boy effect", for half a century or roughly until 2003, neither Pauling nor other lab directors, let alone their beneficiary "boys", admitted to or revealed Rosalind Franklin's key role.

Who were Pauling's boys and why did they prove unable to prevent his DNA blunder?

Pauling's "boys" (Figure 1) were part of Pauling's accumulation of major symbolic and material assets prior to his involvement with DNA. He established key signposts in the post-WW2 biomedical frontier by putting together a team which discovered in 1949 that sickle cell anemia was a molecular disease[37]. Another team of his discovered in 1951 that the alpha-helix was a major principle of protein structure.[38]

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[31] For this shift see Abir-Am, "The Molecular Revolution in 20th Century Biology: The Impact of Three post-War Phases" in John Krige & Dominique Pestre, eds. *Science in the 20th Century,* (London, Harwood, 1997) 495-520.

[32] Maurice Wilkins, *The Third Man of the Double Helix, The Autobiography of Maurice* Wilkins. (Oxford: Oxford University Press, 2003)

[33] On Randall see Wilkins; (note 33) Abir-Am. (note 4)

[34] For details on Wilkins' concern with the succession of Randall's position as Director of the Biophysics Unit see Wilkins, note 32.

[35] Abir-Am. (note 4)

[36] Graham Hunter*, Light is a messenger; The Life and Science of William Lawrence* Bragg. (Oxford: Oxford University Press, 2004)

[37] Pauling, Linus; Harvey A. Itano; S. J. Singer; Ibert C. Wells (1949-11-01). "Sickle Cell Anemia, a Molecular Disease". *Science 110* (2865) (1949) 543–548.

[38] Linus Pauling, Robert B. Corey, and Howard R. Branson, " The Structure of Proteins, Two Hydrogen-Bonded Helical Configurations of the Polypeptide Chain", *Proceedings of the National Academy of Science, USA, 37,* (1951) April, 205-211.

Under these conditions, the category of Pauling's "boys" grew to include students,[39] post-docs, junior faculty, domestic and foreign visitors. Most often arrived on personal fellowships but were able to stay on grace to Pauling's many grants and contracts. Pauling's "boys" were often scientists who were impressed by his scientific prowess and calculated that the advantages of working in his company (access to his drive, many ideas, some of which turned out to be wrong but more often they were right, lab resources, his scientific influence and contacts, opportunity to delegate for Pauling when he was too busy, the institutional prestige of Caltech, and the life style and climate of Southern California) outweighed the disadvantages of working and living in the shadow of a giant, while having to "stand by" so as to "serve" on Pauling's many projects. (thus making it more difficult to establish one's own independent line of work)

Above all, the "boys" had to consent to a skewed distribution of scientific credit since Pauling believed that he should put his name first on any project that he had initiated.[40] Some Pauling "boys" were former graduate students, who remained in research positions in Pauling's Department for years[41]; others were former Pauling Ph.Ds who became faculty in the Chemistry Department chaired by Pauling[42]; or in other institutions[43] and provided occasional input, both solicited and unsolicited. Others were foreign visitors to Pauling's lab, e.g. Jack Dunitz who came for several years (1948-51; 1953-54) from Dorothy Hodgkin's (1910-1994) lab at Oxford, a Pauling friend and comparable colleague.[44] Dunitz suggested to Pauling to use the term "helix" rather than "spiral" as more appropriate for its three-dimensional reference.[45]

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[39] The students were mostly graduate but an occasional brilliant undergraduate such as Mathew Meselson, Pauling's last student, and the would-be "Mozart of molecular biology" was also included. Pauling handpicked him as a graduate student but also delayed his involvement with the Meselson-Stahl experiment which proved the semi-conservative mode of DNA duplication, see Pnina G. Abir-Am, "Mathew Meselson", "Franklin Stahl" and the "Meselson-Stahl experiment", *Electronic Encyclopedia of Life Sciences, eLS*, published May 2014. Meselson remained at Caltech for all the 1950s, mostly in research positions, while transferring from the Division of Chemistry from which he graduated in 1956 to that of Biology, until he left in 1961 for the Department of Biology at Harvard.

[40] On Pauling's attitude to sharing scientific credit see Nye. (note 29)

[41] For example, Ken Hedberg stayed for 8 years (1948-1956) until he left for a position at Oregon State University in Corvallis, eventually becoming its Chairman. Hedberg & Pauling shared a cultural affinity due to their origins in the State of Oregon. Ken Hedberg and his scientist wife Lise were friends of the Paulings and became instrumental in the transfer of their Personal Papers to OSU. Ken Hedberg, Oral History at OSU-SCARC; Ken Hedberg and Lise Hedberg, (separate) conversations with the author in their respective offices at OSU, August 21 and 24, 2012.

[42] E.g. Verner Shomaker, a 1938 Pauling Ph.D. who was full professor by the early 1950s and was considered to be the only one whom Pauling consulted frequently.

[43] E.g. David Harker, a 1936 Ph.D. who became director of a large scale, also in the $1 million range, project on protein structure at the Brooklyn Polytechnic Institute in New York, in 1950; or David Shoemaker, a Pauling Ph.D. in 1948 who became an assistant professor at MIT.

[44] For comparisons between Pauling and Dorothy Hodgkin see *Newsletter* of the *American Crystallographical Association,* joint memorial issue, 1994; Nye. (note 29)

[45] Jack Dunitz, "Linus Carl Pauling, 1901-1993", Biographical Memories of Members of the National Academy of Science/ USA, Washington D.C., National Academies Press, 1997, 221-261. Dunitz, Professor Emeritus of Chemical Crystallography at ETH-Zurich, left Pauling's lab twice, in 1951 and 1954, because he sought to return to his native UK. Despite several offers in the US, Dunitz returned to the Royal Institution, London, in 1956 after two years with Alex Rich, another Pauling "boy" at NIH. Dunitz was more theoretically minded than most other associates of Pauling so one can only wonder whether Pauling's effort with DNA might have fared better had Dunitz not left for UK in 1951. Though he returned on February 1, 1953, at Pauling's specific invitation to work on DNA monomers, by the time he arrived the DNA episode was over. Pauling, To Whom it may concern, December 3, 1952 (terms of J. Dunitz's appointment as research fellow: "…He will, under this appointment, carry on research on the structure of nucleoside, nucleotide, and related substances"), Pauling Folder, Jack Dunitz Personal Papers, OSU-SCARC.

In addition to their specialized skills, the relevance of Pauling's "boys" was also determined by their geographical distribution. During the key period of 1951-1953, Dunitz was away at Oxford, Edward Hughes, who served as a jack of all trades, running a wide variety of errands for Pauling including reading his paper at conferences when Pauling could not travel, and teaching sections, was away at Leeds for the year 1951-1952; and Jerry Donohoe was away in Cambridge/UK for 1952-1953. Hence, the only "boy" whom Pauling could recruit for his sudden interest in DNA was Alexander Rich[46], an MD who arrived in 1949 at the suggestion of his Harvard tutor John T. Edsall.[47] (1902-2002) Edsall shared Pauling's interest in protein structure, spent a sabbatical in Pauling's lab in 1941, remained friends with Pauling and some of his associates, and played a role in the US reception of Pauling's alpha-helix.[48]

Though Rich (who later became a central figure in molecular biology, having discovered Z-DNA, among other key discoveries in both DNA and RNA) stayed with Pauling as a post-doc for five years, (1949-1954) he was prone to be called anytime into service as a military physician, especially during the Korean War in the early 1950s. Possibly for this reason, i.e. that Rich might not be able to continue in the field of X-ray diffraction, Pauling decided not to train him in experimental crystallography, instructing Dunitz to limit Rich's participation to observing, and assisting with interpreting the X-ray photos.[49]

It is thus strange that after he had limited Rich's training, despite the fact that an X-ray crystallographic expert such as Dunitz overlapped with Rich for two years, (1949-1951) Pauling sent Rich a memo in December 1952 (when Dunitz was still in Oxford) to take better X-ray photos of DNA than those available in literature which dated to 1947 and 1939.[50]

Given the fact that it took Rosalind Franklin, a particularly gifted physical chemist with much longer research experience than Rich, (a former medical student with only three research years and little if any experimental experience with X-ray diffraction) 18 months to get Photo 51; (the sharpest in a long series which eventually led to the interpretation of DNA structure as a double helix) Pauling's cavalier memo to an inexperienced Rich in December 1952 suggests that Pauling not only underestimated the critical role of mastering the X-ray technique for obtaining fully interpretable photos but further missed the key role of collaboration between a boy and a lab director in addressing the challenge of DNA structure.

Pauling's lack of interest in investing in X-ray studies of DNA, whether at Caltech or elsewhere, is also evident from his correspondence with two of his "boys" located at other US institutions. David Shoemaker, (1923-1997) who completed his Ph.D. with Pauling in 1948 and moved to MIT, had a student who wrote to Pauling early in 1952 that he wanted to work with him on DNA. Though Pauling admitted that he had funds for such research, he did

[46] Rich and Davidson, eds. (note 1) Rich passed away on 4-28-2015, as this paper was being finalized, see https://newsoffice.mit.edu/2015/obituary-alexander-rich-dies-90-0428, downloaded 4/40/2015.

[47] Howard K. Schachman & Cyril M. Kay, "John Tileston Edsall, 1902-2002", Biographical Memories of Members of the National Academy of Science/ USA, Washington D.C., National Academies Press, 2010, 3-21.

[48] Abir-Am, "J.T. Edsall (1902-2002) biochemist and moral leader of post-WW2 American bioscience". (work-in-progress, 2012-present)

[49] Pauling to Dunitz, (cc to Robert B. Corey) January 30, 1950: (Jack Dunitz Personal Papers, Pauling folder, OSU-SCARC) "…not worthwhile to train AR (Alex Rich) in experimental technique of X-ray diffraction since he is not planning to continue in this field". Pauling was further concerned that X-ray equipment might be misused or damaged, because they are planning to do "so much X-ray work during the coming year".

[50] W.T. Astbury "X-Ray Studies of Nucleic Acids." 1947, Symposia Soc. Exp. Biol. 1: 66–76.   Astbury, W. T., & Bell, F. O. (1939). X-ray data on the structure of natural fibres and other bodies of high molecular weight. Tabulae Biologicae, 17, 90–112.

not respond in a timely fashion, so the MIT student, upon completing his Ph.D. with Shoemaker, took a teaching job in a small college.[51]

David Harker[52], (1906-1991) a 1936 Ph.D. of Pauling and since 1950 the director of a large scale project in protein structure at Brooklyn Polytechnic Institute in New York, hosted in 1953 two foreign visiting post-docs intimately involved with DNA research, Vittorio Luzzati of Paris and Francis Crick of Cambridge/UK.[53] Though Crick arrived in the second half of 1953, or only after he completed his Ph.D. thesis, as well as co-authoring several papers on DNA structure; Luzzati arrived in December 1952 and told Harker that his former colleague in Paris, Rosalind Franklin, by then at King's College, London, where she continued to consult with Luzzati, worked out a 3-dimensional contour map of DNA and was willing to collaborate with Pauling on its interpretation. Harker passed this critical information to Pauling but to his surprise, Pauling was in no rush to meet with Franklin.

Pauling still hoped for a repetition of his experience with the alpha-helix, when an experimental piece of data which delayed his publication of the alpha-helix for two years, turned out to be irrelevant because it was not due to the basic structure of the protein but to supercoiling. Pauling published only when industrial or artificial fibers of polypeptides were shown to lack that feature of supercoiling.[54]

Pauling continued to avoid a meeting with Franklin during the critical months of February and March 1953, at a time he was planning a trip to Europe with a stop over in England to see his second son Peter, a first year research student at Cambridge, UK, in Bragg's lab where he was befriended by his boys, Crick, Watson, and Wilkins. Instructing Peter on how to organize his visit in England, Pauling again gave low priority to a potential meeting with Franklin.[55]

The question persists as to whether Harker (or Shoemaker beforehand) could have pressed Pauling to meet with Franklin sooner, or to start the work on DNA sooner. Harker already knew what may happen in such a case. When he sided with another woman scientist who contested Pauling's opinion, Dorothy Wrinch, (1894-1976) on the key issue of protein structure in the late 1930s,[56] Harker was threatened by Pauling in no uncertain terms.

By the time Pauling arrived in England, in the first week of April 1953, the double helix model had already stood up at Cambridge, where Pauling had to admit, before WL Bragg and his various boys, a coterie of rivals who prided themselves at beating him at his own game; as well as at the prestigious Solvay meeting in Brussels in mid-April 1953, to which he travelled in WL Bragg's company, that Bragg's "boys" were right and he, Pauling,

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[51] Correspondence of Pauling and David Shoemaker, David and Clara Shoemaker Personal Papers, OSU-SCARC, Folder "L. Pauling".

[52] Herbert A. Hauptman, "David A. Harker, 1906-1991", *Biographical Memoires of Members of the US National Academy of Science, 74* (Washington D.C.: The National Academies Press, 1998) 1-19; http://www.nap.edu/catalog/6201/biographical-memoirs-v74

[53] Vittorio Luzzati, *Une Vie a Raconter*, Paris, Editions HB Temoignage, 2011; Abir-Am 2015, (an essay review of Luzzati's autobiography jointly with other books including one on Rosalind Franklin) note 4.

[54] Pauling and Crick solved the problem of supercoiling in the fall of 1952; on this episode see Hager, (note 6) chapter 15; Olby, (note 4) Abir-Am. (note 4)

[55] This sordid episode of Pauling avoiding a meeting with Franklin, the only person who could have saved him from major embarrassment, is analysed in detail in Abir-Am (note 4) Peter Pauling did not know Franklin but heard his friends complaining about her lack of interest to cooperate with them even though they had nothing to offer, so he informed his father that Franklin was seen as difficult. Pauling seemed reluctant to contact Franklin because he did not meet her earlier, so she remained an unknown quality with whom he did not know how to deal.

[56] Abir-Am. (note 10)

was wrong.[57] Still, it took Pauling longer to digest such news, since at a meeting at Caltech in May 1953 he was still championing his own model as if the outcome was still undecided.

Even in September 1953, when he had to modify the program of an international meeting he had long planned at Caltech to celebrate his success with the alpha helix as the long sought solution to the structure of proteins, so as to add a session on DNA, Pauling still devoted the bulk of the meeting to protein structure. The transition from structural chemistry to molecular biology was not quite the one he had envisaged, as DNA was not about to remain very long in the shadow of proteins. Pauling's "vision" fell short of sustaining the molecular revolution in biology which had DNA at its center.[58] Jack Dunitz observed that chemistry was about "mental discipline, adventure, and aesthetic experience"[59]; yet, neither attribute quite captured Pauling's wishful thinking that biology in general, and DNA in particular, were merely derivative, or just an afterthought for a very busy structural chemist.

Though Pauling's prioritizing of proteins and politics over DNA in the period 1951-1953 suggests why he was nowhere near a solution of DNA structure, his inability to treat his own "boys" as potential partners also played a role in the ultimate irony of Pauling's not only being beaten by a top rival's "boys", but being beaten with help from Pauling's own "boys". During the "finale" of the DNA saga, between January and April 1953, Pauling's "boy" Jerry Donohoe[60] (1920-1985) shared an office with Bragg's boys at the Cavendish, while Pauling's biological boy, the scientifically inclined second son Peter, had also been there as a first year research student since the fall of 1952, also in WL Bragg's lab.

These two were sent there in part because Pauling hoped they would enable him to keep an eye on his competition, but they were handicapped not only by the clever strategy of Bragg's boys but also by the fact that Pauling would not deploy his "boys" as equal partners. Since Pauling greatly appreciated the shock value of surprise, that is to say a bad and shocking surprise for his rivals, he concealed his purpose from his own "boys".

Pauling cherished the alpha-helix not only because of its scientific value but also because at the same time it exposed the scientific nakedness of his rivals; all their prior models of protein structure were demolished by the alpha-helix in one masterful stroke. Little did Pauling know that he will share that experience of being similarly exposed in less than two years. Perhaps, it was a matter of some consolation that he did not invest as much time in DNA (five weeks) as his rivals, WL Bragg and his various boys, had invested in proteins. (over a decade)

So, what went wrong with Pauling's boys and their encounter with DNA?

Long accustomed to accept Pauling's supreme power as lab director, department chairman", and public figure, the "boys" lost (if they ever had) the ability to argue with him. Though some "boys" voiced objections (e.g. Verner Shomaker, a full professor regarded as brilliant but one who did not publish much and could not match Pauling's standing) Pauling ignored them since in the aftermath of recent big successes, especially the alpha helix, he was no longer seeking or listening to advice. Pauling kept the boys in the dark re: his interest in DNA since he sought to shock rivals and "boys" alike with his latest trick. So, what could Pauling's "boys" have done?

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[57] Linus Pauling to Ava-Helen Pauling, April 1953, in Ava-Helen & Linus Pauling Personal Papers, SCARC-OSU.

[58] Abir-Am. (note 31)

[59] Jack Dunitz to E.G. Cox, April 18, 1951 while quoting Cyril Hinshelwood's Centenary address to the Chemical Society in UK as published in its journal in 1947, p. 1271; Jack Dunitz Personal Papers, OSU-SCARC, Folder, C-misc.

[60] Mark Ladd and Sidney Kettle. "In memoriam: Professor Jerry Donohue". *Journal of Chemical Crystallography* **15** (4) (1985) 303.

On the issue of improving Pauling's timetable, i.e. of starting earlier to work on DNA, rather than the last five weeks of 1952, which turned out to be both "too late and too little" even for a master structurist who tackled the structures of 225 compounds; none of the "boys" surrounding Pauling knew of his tacit interest in DNA. Even Shoemaker and Harker who could mediate between Pauling and their own acquaintances who had an interest in DNA were careful not to try to influence Pauling's priorities. Corey and Shomaker had no interest in DNA, Rich and Peter Pauling was too inexperienced, while Donohue, ended up helping Pauling's rivals.

On the issue of collecting better X-ray data, Pauling could have suggested that Rich, the only post-doc with a biological background, be trained by Dunitz as soon as Pauling learned of the existence of high quality DNA X-ray photos at King's Collge, London. Even if Dunitz had no interest in either proteins or DNA he could have trained Rich. But again, Pauling did not suggest that Dunitz train anyone in X-ray crystallography of biological compounds, further limiting the training Dunitz was asked to give to Rich.

As to collaboration in DNA model building, Pauling left it in the hands of Robert Corey, his sole co-author of the DNA structure paper, who however had no interest in DNA. Corey was also afflicted with health issues due to his work on explosives during WW2, but Pauling did not provide him with help other than students he supervised directly, and who again were not taught to develop an interest in DNA. Though Corey was shown by Franklin her great X-ray photos in mid-1952, he apparently did not pay attention since at that time Pauling was still fighting his old battles with protein structure.

As to the issue of help with calculations, though Pauling habitually used help from old timer colleagues such as Stephen Weinbaum, he left the DNA calculations to Corey who had no interest in DNA. Even Shomaker criticized the strereochemical features of their proposed DNA structure Pauling did not listen since he remained confident that he could fiddle with the stereochemical parameters.

On the issue of delegating responsibility for presenting Pauling's papers at major conferences, again Pauling relied on close associates such as Corey and Hughes but neither (they presented the alpha-helix paper in Pauling's absence at the May 1952 critical conference in London) could offer a suitable substitute for Pauling's impressive lecturing style, rhetorical abilities, and show business tenor of his public talks. As a result, Hughes noted that the attendees came out missing the importance of the alpha-helix.[61]

On the issue of collecting information on Pauling's rivals while visiting their labs, neither Donohue, an advanced "boy" and expert in hydrogen-bonding, nor Peter Pauling, an inexperienced first year graduate student socializing with leading scientists because of the latter's interest in his father, were technically or mentally capable of such a demanding task, especially since Pauling did not sufficiently guide them as to what to specifically collect,[62] further overwhelming them with frequent demands for general information of all sorts.

As to the issue of betraying Pauling by passing information on him to his rivals, both Donohoe and Peter Pauling ended up sending faulty information to Pauling on his rivals, intentionally or otherwise, to some extent because Pauling offered nothing in return. Pauling's, and their own belief in Pauling's omnipotence may have obscured from them the fact that they were actually serving Pauling's rivals.[63]

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[61] Hughes, Oral history. (note 35)

[62] Abir-Am. (note 4)

[63] Both Donohoe and Peter Pauling remained obsessed for the rest of their lives with their inability to reveal what they witnessed at a time they were forced to pass information from and to Pauling as well as from and to his rivals. For details on their role see Abir-Am. (note 4)

Conclusions

Pauling and his boys were nowhere close to solving DNA structure, despite the many assets at their disposal. Key scientific (a-d) and personal character issues played a key role in malpositioning them as a collaborative endeavour addressing the challenge of DNA structure.

a) Pauling's ongoing obsession with protein structure issues even after the alpha-helix was published and became a peak of his achievements, led him to focus on consolidating his gain rather than opening new frontiers. The "boys" were deployed to enhance old victories rather than seek new ones.

b) Pauling's relationship with the Division of Biology at Caltech remained shallow, merely social, (Ken Hedberg , Jack Dunitz, others' testimony) or a scheme to get big money. This meant that Pauling missed the rising interest in DNA among biologists, because his Caltech Biology main contacts whom he helped hire (George Beadle, the Chairman and Max Delbruck, the bacterial virus geneticist) also failed to do so, because they long aligned with Pauling's own preference for proteins.

c) Pauling's refusal to meet with Rosalind Franklin at the informed advice of his mature "boy" David Harker suggests gender bias, as befits someone whose entire scientific career was spent in an institution which denied women the right to an engineering and scientific education. Long accustomed to pliant "boys", Pauling could not see that his only salvation (i.e. rescuing him from a terrible DNA model which would taint his reputation, despite various efforts to "cover up" the sheer magnitude of his blunder) might come from a "gal", or just a colleague of the other gender.

d) Pauling's failure to follow up on Erwin Chargaff's discoveries of the base-ratios in DNA in the period between 1947-53, reflects a combination of scientific bias against biochemistry as presumably a lesser discipline than structural chemistry. But it also reflects Pauling's cultural and racial bias against émigré biochemists, whose cultivated demeanor he could not match thus leaving himself indifferent to their plight as Central, Eastern and Western European refugees from the totalitarian onslaught of European fascism. Having ignored Chargaff's base-ratios, Pauling had no chance to come close to a solution of DNA structure, even if he had overcome his gender bias so as to deal with Rosalind Franklin, as an equal.

e) Pauling's habit of taking advantage of others, or of engaging in unilateral transactions always beneficial to himself but not to other parties, (as with Randall, Todd, among others) a habit stemming from his déclassé background and need to struggle to support his widow mother and siblings, precluded collaborations on an equal footing with others, whether lab directors and research associates who had pursued DNA earlier; or even his own "boys".

Since Linus Pauling has long been a scientist hero, having won two (sole) Nobel Prizes, scientists, historians of science, biographers, commemorating colleagues, and other authors chose to focus on his many achievements, often dismissing his failure with DNA as an aberration of no consequence. By contrast, this paper has argued that Pauling's failure with DNA is uniquely instructive for better understanding not only his lack of proximity to an eventual solution of DNA structure, but also his role as leader of many teams, yet a leader so steeped in bias against other scientific disciplines, as well as in social prejudice on all counts of race, class, gender, and their intersectionality that he entirely missed the transition from structural chemistry into molecular biology, a transition which was to largely revolve around the ramifications of DNA structure.
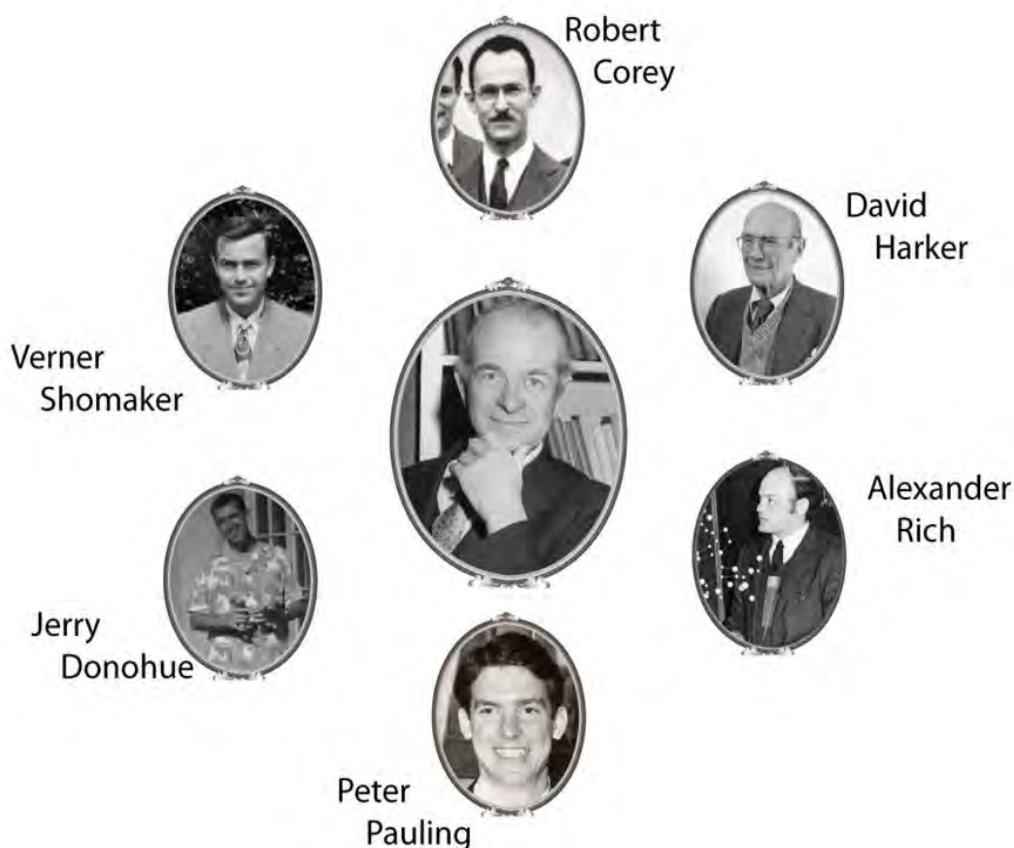
Figure 1: "Pauling's boys" most related to his quest for DNA structure, by Christy Turner, Special Collections & Archives Research Center, Oregon State University Library

Acknowledgements

Structure of the NMR Revolution

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Introduction

Was there an nmr revolution in chemistry, and what did it consist of? This paper will answer the first question in the affirmative. The second question is more interesting. I shall contend that, notwithstanding conventional wisdom, the nmr revolution did not add just one more analytical technique to the existing ones (UV-visible and vibrational spectroscopies, mass spectrometry) feeding run-of-the-mill, paradigmatic chemistry. Nmr caused a revolution from altogether different quarters. It ushered in many a discovery in chemistry. It opened up new avenues of research.[1] Yet more importantly, it changed the thinking of chemists.

The title of this piece borrows deliberately from the title of Thomas S.Kuhn's classic.

Periodization

I choose to focus on the period 1960-1975. The first date is that of the first nmr conference — known thereafter as ENC —, it is also when the first commercial spectrometers became available, devoted to proton nmr. The second date coincides with the heyday of carbon-13 nmr. It happened a couple of years after Paul Lauterbur introduced what he had named «zeugmatography», afterwards renamed imaging (MRI). [2]

My own involvement in nmr [3] was contemporary with its entry into chemistry. During the summer of 1960, I acquainted myself with a spectrometer in Grenoble, a 40 MHz wideband solid state machine. Applied to structural work on zeolites, it was a prized possession in the group of physicist Michel Soutif.

During the 1960-61 winter, I served an apprenticeship in high-resolution nmr at Imperial College in London, in Derek Barton's group, under the distant supervision of Lloyd M. Jackman and the more direct supervision of J. W. Lown.

In 1961-1962, jointly with Alain Gaudemer, I worked in Pierre Grivet's laboratory in Orsay on a Varian HR-60 spectrometer. I chose to analyze strongly-coupled three-spin systems [4] in diterpene molecules. For which I wrote Fortran software that ran on the university's IBM 650 mainframe computer. During that time, Alain and I attended the lectures on nuclear magnetism by Professor Anatole Abragam, at Collège de France.

In 1962-63, I served a post-doctoral stay in Paul Schleyer's group at Princeton University.

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1. A section of my article "On the self-image of chemists, 1950-2000," *Hyle*, **2006**, *12*(1), 99-130, dealt already with the nmr revolution in chemistry. Accordingly, I shall strive not to repeat it here, only to complement it by tackling issues absent from that paper, due to space restrictions.

2. Dawson, M. Joan. *Paul Lauterbur and the Invention of MRI*. Cambridge, MA: MIT Press, 2013.

3. Appearances to the contrary, this is not a personal memoir. The genre it belongs to is that of *ego-histoire*. As Pierre Nora wrote when defining it, "It serves to clarify, in historical mode the link between the history that was made and the history that made you."

4. Castellano, Salvatore, and John S. Waugh. "Strong Coupling in Nuclear Resonance Spectra. IV. Exact Analysis of Three-Spin Spectra." *J. Chem. Phys.* 34 (1961): 295-309.

The department had just acquired a Varian A-60 spectrometer. We outfitted it with a CAT device, for higher sensitivity. [5] I applied it to carbon-13 satellites of proton resonances. Which enabled me to discover the dependance of the coupling constants between ethylenic protons upon ring size, [6] which I reported at the 4th ENC (then known as OCEANS) in Pittsburgh in 1963. I was responsible also for a comprehensive analysis of spin-spin couplings within norbornene molecules. [7]

My doctoral dissertation in 1964 took coupling constants as its topic. Back in Princeton as an assistant professor from 1966 to 1970, I led a research group doing organic chemical projects, with a strong emphasis on nmr as our tool of study.

At that time I was called by the University of Liège in Belgium to a full professorship, I published, together with Peter Stang, a textbook on *Organic Spectroscopy*, heavily slanted towards nmr. [8] By 1975, the closing date for the period I have chosen to emphasize here, with my group in Liège we were pioneering sodium-23 nmr, with applications ranging from inorganic chemistry to biophysics. [9] The advent of Fourier transform nmr came with a major switch in supplier of spectrometers. The German Bruker bumped the Californian Varian from the first rank. This advent, with much easier access to a whole bunch of nuclei, [10] opened the gates for a flourishing of organometallic chemistry — a major subdiscipline that came into being, predominantly because of nmr. But this is outside my self-imposed periodization.

Carsten Reinhardt has provided useful accounts of the history of applications of nmr to chemistry. [11,12] There is an abundance of historical accounts of the beginnings of nmr. Most emanate from physicists. [13] The vast majority deal with methodological advances their authors pioneered.

The present paper strives to sketch out the influence of nmr upon chemistry and why it turned out to be profound.

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5. I have already published my recollection of the CAT story : Laszlo, Pierre. "Letting the Cat out of the Bag." *Journal of Magnetic Resonance* 94, no. 1 (1991): 214-18.

6. Laszlo, Pierre, and Paul von R. Schleyer. "Ring Size Effect on *cis*-Olefinic Coupling Constants of Cycloalkenes. Use of ¹³C Patterns " *J. Am. Chem. Soc.,* 85, no. 13 (1963): 2017-18.

7. Laszlo, Pierre, and Paul von R. Schleyer. "Analysis of the Nuclear Magnetic Resonance Spectra of Norbornene Derivatives. ." *J. Am. Chem. Soc.* 86 (1964): 1171-79.

8. Laszlo, Pierre, and Peter J. Stang. *Organic Spectroscopy. Principles and Applications.* . Edited by Stuart A. Rice, *Harper's Chemistry Series*. New York: Harper & Row, 1971.

9. Laszlo, Pierre. " Sodium-23 Nuclear Magnetic Resonance Spectroscopy." *Angewandte Chemie International Edition in English,* **17**, no. 4 (1978): 254-66.

10. Laszlo, Pierre, ed. *Nmr of Newly Accessible Nuclei.* 2 vols. Volume 1 *: Chemical and Biochemical Applications.*; Volume 2: *Chemically and Biochemically Important Elements*. New York: Academic Press, 1983.

11. Reinhardt, Carsten. "Chemistry in a Physical Mode: Molecular Spectroscopy and the Emergence of NMR." *Annals of Science* 61, no. 1 (2004): 1-32; "A Lead User of Instruments in Science: John D. Roberts and the Adaptation of Nuclear Magnetic Resonance to Organic Chemistry, 1955-1975." *Isis* 97 (2006): 205-36; *Shifting and Rearranging – Physical Methods and the Transformation of Modern Chemistry*. Sagamore Beach, MA: Science History Publications, 2006.

12. He has sensibly focused on contributions by a few outstanding individuals. In this area, as in others, historians ought to cover the early scouting of a new field by a few — a handful usually — daring explorers, and not to delve on the later Gold Rush by 'me-too' exploiters.

13. Some examples are Brey, Wallace S. *Magnetic Resonance in Perspective: Highlights of a Quarter Century*. New York: Academic Press, 1996; Shoolery, J. N. "Nmr Spectroscopy at the Beginnings." *Analytical Chemistry* 65, no. 17 (1993): 731A-41A ; Slichter, Charles P. "The Golden Anniversary of Nuclear Magnetic Resonance Nmr: Fifty Years of Surprises." *Proceedings of the American Philosophical Society* 142, no. 4 (1998): 533-56 ; Waugh, John S. "Nmr Spectroscopy in Solids. A Historical Perspective." *Analytical Chemistry* 65, no. 17 (1993): 725A-729A.

Context

The historical context for nmr bursting upon chemistry was the end of the Fifties-beginning of the Sixties, in the aftermath of WWII and recourse of the military to radar. A key element of this context was conversion of physicists to peacetime physics. Advances in electronics vastly helped, the transistor was invented in 1947. The location was the United States, first and foremost. It was at that time and by far the dominant economic power in the world.

From the combination of Vannevar Bush's report to the President, "Science the Endless Frontier," and the Sputnik launch in 1957, American research universities were undergoing unprecedented growth, with generous allocation of federal funding. Some of these grants were allocated to the purchase of mainframe computers. At Princeton, I thus had access during the Sixties to an IBM 7040, housed in the Engineering Department building.

Industrial laboratories, during this 1960-1975 period, led by Bell Telephone Laboratories, did not lag behind academic laboratories in the excellence of fundamental scientific studies. [14] In particular, Varian Associates, in Palo Alto, California, had recruited an outstanding team of physicists working on nmr applications : Weston A. Anderson, Richard R. Ernst, Ray Freeman, Jim Hyde, Martin Packard, and Harry Weaver. [15] To cite only a single other industrial laboratory, DuPont de Nemours then had William D. Phillips, [16] D. R. Eaton, Earl Muetterties doing brilliant pioneering work on chemical applications of nmr.

Lastly, this context included two outstanding books. One was a magnificent exposition by Anatole Abragam of the principles of nuclear magnetism, published in 1961. [17] The other, nicknamed The Bible from a pun on the senior author's name, was by John A. Pople, William G. Schneider and Harold J. Bernstein, with a timely publication in 1959. [18]

Just another analytical technique?

According to this widespread thesis, applications of nmr to chemistry did not differ in kind from earlier devised techniques. Mi Gyung Kim conveys this viewpoint in a nutshell in a recent article :

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14. Could the interaction between industrial scientists and academic scientists, over nmr, during the Sixties, be described as a galisonian trading zone ? In spite of the lone but shining example of Varian Associates, it was much more a case of all those scientists sharing in the goals and values of pure science. Bell Labs provided the beacon around which other industrial and government laboratories set themselves : Argonne - IBM - JPL - DuPont - NIH - Xerox - Syntex, to name but a few. A joint zone rather than a trading zone. Which is substantiated by individuals — Fred W. McLafferty, Earl Muetterties, George Olah, Ed Wasserman — shuttling between the two spheres.

15. An industrial scientist, James N. Shoolery, played a major role in providing nmr to chemists in a form they could assimilate. After joining Varian Associates in 1952, he became that company's chief scientist-propagandist for nmr. He was responsible for publication of catalogs of spectra, for organization of workshops educating chemists in the basics of nmr and, arguably most important, for providing them with the user-friendly A-60 spectrometer. See his paper «NMR spectroscopy in the beginning,» *Anal. Chem.*, **1993**, *65* (17), 731A–741A.

16. Ferguson, R. C. "William D. Phillips and Nuclear Magnetic Resonance Spectroscopy at Dupont." In *Encyclopedia of Nuclear Magnetic Resonance*, edited by D. M. Grant and R. K. Harris, 309-13. Chichester: Wiley, 1996.

17. Abragam, Anatole. *The Principles of Nuclear Magnetism.* Oxford, UK: Clarendon Press, 1961.

18. Pople, J. A., W. G. Schneider, and H. J. Bernstein. *High Resolution Nuclear Magnetic Resonance.* New York: McGraw-Hill, 1959. See the perceptive assessment by Roberts, John D. "Pople, Schneider, and Bernstein - a Truly Seminal Treatise of NMR." *Can.J.Chem.* 83 (2005): 1626-28.

«A sudden advancement in chemical practice is more often caused by a radical innovation in analytic method than by a new theory. One can also make a similar argument about the introduction of NMR as a method of identifying organic compounds.» [19]

This is not an isolated view, to the contrary it reflects a consensus. If we look at the overall picture, at the ordinary, routine uses of nmr by run-of-the-mill chemists, nmr appears indeed as just another analytical tool.

Its introduction, during the late Fifties and early Sixties, made it into a sister technique to, basically, infrared spectroscopy (IR) and mass spectrometry (MS). All three were applied to determination of molecular structure.

The methodology of nmr as a molecular spectroscopy of that type was indeed analytical, there is no doubt about it. Chemists identified groups of atoms from the positions of characteristic absorptions. Nmr improved upon both IR and MS because it provided information on interactions between hydrogens on neighboring atoms: one could follow this coupling pattern, in simple linear logic, and establish gradually the connectivity matrix for the whole molecule studied.

In other applications, that typically monitored chemical transformations in real time, seeing intermediates appear and then disappear, looking at the progressive build-up of reaction products, nmr was also just another analytical tool.

Is that all ? Is such an assessment sufficient to describe the input of nmr to chemical science ? Absolutely not.

In order to make my point, allow me first to jump forward in time by a couple of decades, to the time when the Nobel prizewinner and Swiss physicist Richard R. Ernst was able to rest from his pioneering contributions to nmr methodology and to turn his remarkable abilities to mainstream nmr-in-chemistry studies. [20]

A New World

A small group of signpost publications [21] by Richard R. Ernst will serve us as a guide into the New Territories, opened up by the nmr revolution. After he had done most of the R&D

19. Kim, Mi Gyung. "Stabilizing Chemical Reality: The Analytic-Synthetic Ideal of Chemical Species." *Hyle* 20 (2014): 117-39.

20. Ernst, Richard R. "Recent Development in Nmr Methodology for the Study of Molecular Structure and Dynamics." *Pure & Appl. Chern.* 66, no. 8 (1994): 1583-86.

21. *Signpost* publications deserve special attention from historians of science. They reveal, at a particular time and place, a trend, not only worthy of study, but deserving particular attention. It may be an origin or a closure, but other types also present themselves.

New departures belong in this category. Typically, an overachiever feels a need to display his mastery with a topic in another field than his major discovery. An example is Svante Arrhenius's announcement of CO_2-induced climate warming in 1896, quite a few years after his ionic theory (1884).

Another, more recent example, also from a Nobel prizewinner in chemistry, is Richard R. Ernst's work on the antamanide antibiotic, ca. 1990, a number of years after he had completed most of his work on 2D nmr, centered around 1976. His publications on antamanide are notesworthy for being totally outside the norm of Richard R. Ernst earlier output, in which he provided new tools to the toolbox of nmr spectroscopists. When he started publishing these antamanide papers, he knew not only that he had been nominated for a Nobel prize, that it was only a matter of time before he was awarded one. What then do these antamanide papers signal ? That Ernst could have been, had he wished, a member of the club too, with work typical of organic chemists doubling up as nmr spectroscopists. These signpost papers are precious because, as the minor masterpiece they represent, they also pinpoints the areas of study that the NMR Revolution had opened up.

work on 2D nmr that secured him a Nobel prize, he turned to other directions.

He interested himself in antibiotics, of the cyclic peptide family. After a false start with lasalocid, he latched on to antamanide, as his molecule of choice. He devoted several papers to an nmr study of this cyclic decapeptide.

There are basically two interpretations of what might be termed, by analogy to an artist's *oeuvre*, Ernst's Last Period. These two readings of the evidence are complementary rather than mutually exclusive. It can be seen as a return to the fold, as joining the mainstream of nmr in chemistry. It can be seen also as exploratory, a pioneering move to explore novel productive uses of nmr.

I submit that this late work by Richard Ernst in and by itself defines what the nmr revolution in chemistry consisted of : a focus on the brand-new molecular reality of stereochemistry and intramolecular dynamics, viz. internal motions within molecules that interconvert various conformations, i.e., instantaneous arrangements of their atoms.

Ernst's antamanide work thus studied the backbone of that molecule. He showed that it fluctuated between different states. He and his group identified two pairs, syn and anti, of hydrogen bond exchanging systems, located at residues [1]Val and [6]Phe. [22] He went on to study the motion of the phenylalanine sidechains. [23]

New Territories Found by Nmr

As Richard Ernst's work on antamanide illustrates, a cardinal virtue of nmr was its ability to characterize a molecule, not only by its structure, i.e., the precise arrangement of its atoms in space, but also by its dynamics. Nmr gave to chemists the tools to anchor a molecule in both space and time.

Given the novelty of conformational analysis at the turn of the 1960s, ring inversions became an early application of nmr for their full, accurate characterization. [24] As a keynote episode, I would single out the bond shift of the ethylenic bonds in cyclo-octatetraene : as this eight-membered ring undergoes inversion, it goes through a planar transition state which, more than incidentally, is anti-aromatic. [25,26]

Fluxional molecules were such a major new territory opened by nmr. A key episode, in nmr impacting chemistry, was the bullvalene story, originating in 1961 and developing from 1963

22. Blackledge, M. J., R. Brüschweiler, C. Griesinger, J. M. Schmidt, P. Xu, and R. R. Ernst. "Conformational Backbone Dynamics of the Cyclic Decapeptide Antamanide. Application of a New Multiconformational Search Algorithm Based on Nmr Data." *Biochemistry* 32, no. 41 (1993): 10960-74.

23. Bremi, Tobias, Matthias Ernst, and Richard R. Ernst. "Side-Chain Motion with Two Degrees of Freedom in Peptides. An Nmr Study of Phenylalanine Side Chains in Antamanide." *J. Phys. Chem.* 98, no. 37 (1994): 9322-34.

24. Frank Anet played a major role in that part of the story. See : Anet, F. A. L., and J. S. Hartman. "Ring Inversion in Cycloöctane." *J. Am. Chem. Soc.* 85, no. 8 (1963): 1204-05; Anet, F. A. L. "Ring Inversion in Cycloheptatriene. ." *J. Am. Chem. Soc.* 86, no. 3 (1964): 458-60; Anet, F. A. L., A. J. R. Bourn, and Y. S. Lin. "Ring Inversion and Bond Shift in Cyclooctatetraene Derivatives." *J. Am. Chem. Soc.* 86, no. 17 (1964): 3576-77; Anet, F. A. L., Gwendolyn. Chmurny, and Jostein. Krane. "Ring Inversion in Cyclohexanone." *J. Am. Chem. Soc.* 95, no. 13 (1973): 4423-24; Anet, F. A. L., and M. Z. Haq. "Ring Inversion in Cyclohexene." *J. Am. Chem. Soc.,* 87, no. 14 (1965): 3147-50.

25. Anet, F. A. L., A. J. R. Bourn, and Y. S. Lin. "Ring Inversion and Bond Shift in Cyclooctatetraene Derivatives." *J. Am. Chem. Soc.* 86, no. 17 (1964): 3576-77.

26. Since I mentioned Frank Anet, an Australian by birth, I should add that, if the US was the birthplace of nmr in chemistry, a number of immigrants, some only temporary, had a major impact: Richard R. Ernst from Switzerland, Ray Freeman and John A. Pople from England, Gerhard Closs from Germany, others too.

on. Its importance stems from nmr having been crucial, first to establishing the molecular structure unambiguously, second and most importantly to enable measurement of the rate of internal rearrangement.

Bullvalene is a $C_{10}H_{10}$ hydrocarbon. It was designed by William von Eggers Doering (1917-2011). Bullvalene undergoes multiple Cope rearrangements, [27] each of which returns the molecule to itself — a so-called degenerate rearrangement. However, this is a permutational exchange process, interchanging the four different carbon types. Bullvalene, when it started being studied, was the prototypical fluxional molecule, i.e., an entity uniquely suited to determination by nmr of its dynamics.

Doering had a junior colleague at Yale, Martin Saunders (1931-   ) who did the nmr work on bullvalene. In addition, he wrote the software that accounted for the nmr lineshape as a function of temperature, thus enabling extraction of the rate constant. [28]

Nmr was the tool of choice to measure the kinetics of other degenerate rearrangements. A whole class is that of pentacoordinate molecules, of which phosphorus pentafluoride PF_5 is the prototype. During the very early years of nmr, an interesting discrepancy showed between the vibrational spectrum, consistent with the geometry of a trigonal bipyramid, and the temperature-dependent fluorine-19 nmr spectrum. [29] The explanation, termed pseudorotation, [30] following the Berry mechanism, [31] is interchange between the two axial fluorines and two of the equatorial ones, the remaining equatorial fluorine serving as the pivot in this exchange.

I can find no better example than CIDNP for a new chapter of chemistry having been opened by nmr. The acronym stands for chemically-induced nuclear polarization. What it translates into is a means to monitor free-radicals in the nascent state, as a chemical reaction is run directly in the nmr tube. [32] The most frequent situation, as first explained by Gerhard Closs, is the radical-pair mechanism. Kaptein has pioneeered application of the photo-CIDNP

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27. More than 1,200,000 structures interconvert!

28. Saunders, Martin. "Measurement of the Rate of Rearrangement of Bullvalene." *Tetrahedron Letters* 4, no. 25 (1963): 1699-702.

29. Gutowsky, H. S., D. W. McCall, and C. P. Slichter. "Nuclear Magnetic Resonance Multiplets in Liquids." *J. Chem. Phys.* 21 (1953): 279-92.

30. I single out, among the authors who made a major contribution to nmr studies of this phenomenon, Paul Lauterbur, Earl L. Muetterties, Fausto Ramirez and George Whitesides : Lauterbur, Paul C., and Fausto Ramirez. "Pseudorotation in Trigonal-Bipyramidal Molecules. ." *J. Am. Chem. Soc.* 90, no. 24 (1968): 6722-26; Muetterties, E. L., W. Mahler, and R. Schmutzler. "Stereochemistry of Phosphorus(V) Fluorides ." *Inorg. Chem.* 2, no. 3 (1963): 613-18; Muetterties, Earl L., and R. A. Schunn. "Pentaco-Ordination." *Quarterly Reviews* 20 (1966): 245-99; Ramirez, Fausto. "Oxyphosphoranes. ." *Acc. Chem. Res.,* 1, no. 6 (1968): 168-74 ; Whitesides, George M., and H. Lee Mitchell. "Pseudorotation in Tetrafluorodimethylaminophosphorane." *J. Am. Chem. Soc.* 91, no. 19 (1969): 5384-86.

31. Berry, R. S. "Correlation of Rates of Intramolecular Tunneling Processes, with Application to Some Group V Compounds." *J. Chem. Physics* 32 (1960): 933-38

32. Closs, G. L., and M. S. Czeropski. "Amendment of the Cidnp Phase Rules. Radical Pairs Leading to Triplet States. ." *J. Am. Chem. Soc.* 99, no. 18 (1977): 6127-28; Closs, G. L., and C. E. Doubleday. "Determination of the Average Singlet-Triplet Splitting in Biradicals by Measurement of the Magnetic Field Dependence of CIDNP [Chemically Induced Dynamic Nuclear Polarization];   ." *J. Am. Chem. Soc.* 95, no. 8 (1973): 2735-36; Closs, G. L., and R. J. Miller. "Photoreduction and Photodecarboxylation of Pyruvic Acid. Applications of CIDNP to Mechanistic Photochemistry." *J. Am. Chem. Soc.* 100, no. 11 (1978): 3483-94; Closs, Gerhard L., Robert J. Miller, and O. David Redwine. "Time-Resolved CIDNP: Applications to Radical and Biradical Chemistry." *Acc. Chem. Res.,* 18, no. 7 (1985): 196-202; Closs, Gerhard L., and Donald R. Paulson. "Application of the Radical-Pair Theory of Chemically Induced Dynamic Nuclear Spin Polarization (CIDNP) Aldehydes and Ketones." *J. Am. Chem. Soc.* 92, no. 24 (1970): 7229-31.

experiment to proteins. [33]

Grand unification: bridges to molecular biology

A key aspect of the nmr revolution was exploration and establishment of the tight connexion between molecules of organic chemistry and those of molecular biology, proteins and nucleic acids especially. Small biomolecules, for instance the cyclic peptide ionophores (such as antamanide), bridged what had been earlier perceived as a gap, as a difference in kind — rather than just in size.

I have just mentioned CIDNP, a methodology that bridged chemistry and biochemistry, whether of proteins or nucleic acids. I will illustrate this point with another three examples.

The first is the co-called magnetic nonequivalence. Nmr spectroscopists taught their colleagues in organic chemistry that pairs of nuclei, or groups, could be diastereotopic, enantiotopic or homotopic. This characteristic hinged on molecular symmetry. For instance, a chiral molecule could have only diastereotopic protons. [34] Of course, biochemists had made such distinctions much earlier, but they had not penetrated at all the field of organic chemistry. Nmr spectra thus helped to bring closer together the two disciplines.

A second link between organic and biochemistry came about from the ability of nmr to measure rate constants for extremely fast processes, of the type exemplified by some of the side chains in antamanide, as studied by Ernst and his coworkers. Measurement of relaxation times gives access to processes in the timescale of nanoseconds to picoseconds. [35] This proved crucial in the study of the molecular dynamics of proteins, and therefore in the understanding of the binding of small drug molecules to their receptors, for instance.

My third exhibit is measurement of the nuclear Overhauser effect. Rather shortly after Frank Anet showed its operation in some crowded organic molecules which had been synthesized by Saul Winstein, [36] it became a very important tool in the nmr determination of protein structure. [37]

Other key features of the NMR Revolution.

Chemists taught themselves how to read a spectrum, i.e., to attach meanings to features such as resonance frequency, line intensity, lineshape, relaxation time, etc. Those meanings amounted to an abundance of information about molecular characteristics such as the connectivity of atoms, their spatial nearest neighbors, electronic distribution, internal motions such as rotations of groups of atoms, ring inversions, pyramidal inversions of atoms such as nitrogen or phosphorus, tumbling times for the molecule as a whole, etc. The complete understanding of a molecule nmr allowed for and invited was truly revolutionary.

33. Kaptein, Robert. "The Early Days of CIDNP." In *Encyclopedia of Nmr*, vol. 1, edited by David M. Grant and Robin K. Harris, 418-20. Chichester: Wiley, 1996.

34. Mislow, Kurt, and Morton Raban. "Stereoisomeric Relationships of Groups in Molecules." In *Topics in Stereochemistry*, edited by Norman L. Allinger and Ernest L. Eliel, 1-38. New York: Wiley, 1967.

35. Laszlo, Pierre. "Fast Kinetics Studied by Nmr." *Progress in NMR Spectroscopy* 13 (1979): 257-70.

36. Anet, Frank A. L., and A. J. R. Bourn. "Nuclear Magnetic Resonance Spectral Assignments from Nuclear Overhauser Effects. " *J. Am. Chem. Soc.,* 87, no. 22 (1965): 5250-51.

37. see for instance Thomas, P D, V J Basus, and T L James. "Protein Solution Structure Determination Using Distances from Two-Dimensional Nuclear Overhauser Effect Experiments: Effect of Approximations on the Accuracy of Derived Structures.." *PNAS* 88, no. 4 (1991): 1237-41.

Thus, nmr spectra provided representations of molecules in three-dimensional space, known as stereochemistry. As a fortuitous coincidence, the advent of nmr in chemistry was contemporary with conformational analysis, also synonymous with stereochemistry.

A key feature, rather unique to nmr in self-evident simplicity, was equivalence between atoms and groups of atoms in pairs, triads, etc., that specified the type of symmetry inherent in a molecule. [34]

Chemists, whether of the organic, inorganic, organometallic or biochemical subdivision, could thus partake of what can only be termed "molecular intimacy:" a familiarity with details of molecular structure and dynamics at the microscopic scale, that of nanometers.

The nmr revolution brought about social consequences too. Since nmr illustrates quantum mechanics with impressive accuracy, chemists had to teach themselves a modicum of quantum physics. To put it another way, quantum chemistry, from being a marginal subdiscipline reserved to a tiny number of specialists, became integrated into mainstream chemistry.

Introduction in 1961 of the Varian A-60 nmr spectrometer made it possible for non-specialists to use the machine themselves. This hands-on policy ensured that graduate students could run their own spectra and, in so doing, watch molecules at play. Which led to many a discovery. It antedated and probably influenced the general move from mainframe to personal computers.

Discussion

The word «revolution» was part of my title. Is it accurate, or just a wild exaggeration? To examine this implicit claim, in order to either justify or refute it, will be my final point.

First, the contrarian view : the term «revolution» is poorly chosen and inadequate. During the Sixties and Seventies, chemistry did not undergo an upheaval, a refoundation comparable to, say, the revolution wrought by Lavoisier in the 1780s; nor anything like the advent of quantum mechanics in physics during the 1920s. I know that this feeling, if collective, is no proof. But another couple of arguments bolster it. The first is that chemistry was already a mature science in mid-twentieth century. Hence, pretending that it then underwent a revolution would be oxymoronic and preposterous. In any case, as the second additional argument, we are still too close to the event to be able to evaluate it.

How then should we describe the effects nmr had on chemistry? Can it qualify as a revolution, in the sense Thomas Kuhn gave memorably to this notion? If so, if indeed a mutation had occurred, what were the two paradigms, the ancient and the newer one that replaced it? The mere mention of this question suffices, one does not readily have an answer, the kuhnian description does not seem to be applicable to the event, or group of events I am discussing.

Granted that the kuhnian description does not seem to apply, how then should historians view the impact of nmr on chemistry? What jumps to mind is a contribution by Derek de Solla Price to science historiography. In his view, invention of new scientific instruments was the engine of change. Nmr thus belongs with the telescope and the microscope. Its sway over chemistry might compare with X-ray diffraction or mass spectrometry. While this view is held by many, it does not satisfy me. There was definitely more to nmr than an instrumental innovation, however powerful.

Before I state my answer to the question, allow me to mention some of the evidence one has to contend with. Maybe first, the significant number of Nobel prizes awarded because of nmr.

[38] As already mentioned in connexion to Richard Ernst's work on antamanide, nmr accelerated the ongoing unification of chemistry and biology. Nmr of proteins became a logical extension of nmr of organic molecules. Antamanide, a decapeptide, marked an intermediate point, in between the small molecules of organic chemistry and biological macromolecules.

Another piece of evidence, from a different quarter, from my intuition since there is no room here for supporting data, at least at this time, is the slow reorganization of chemistry as a university discipline. The advent of nmr, intriguingly, coincided with the wane of analytical chemistry as a powerful subdiscipline; and, as already mentioned, with the infusion of quantum chemistry instead.

Since I bring to bear, in a sociological light, departments and institutes of chemistry, a related observation is the close relationship between the power structure within a department and control over the nmr spectrometer(s). This is another point worthy of more research, for whose corroboration at this stage I can only state personal experience.

Let me not forget the obvious, how quickly nmr became a standard tool for chemists. The most important aspect though is not material, nor technological, it has to do with perception : nmr brought about molecular intimacy. Such a result was the epitome of rationality.

Going from the nmr to the underlying molecular structure is an entirely logical construct, the molecule itself identifies to an edifice obeying the laws of logic. A new mental set-up for knowledge build-up came to the fore. I submit, as a prime example of the new mentality nmr brought about, retrosynthetic analysis : E. J. Corey was not only one of the leading synthetic organic chemists, his thought processes were influenced by nmr — of which he had indeed an in-depth understanding. [39]

Accordingly, the advent of nmr, if it influenced chemistry in numerous ways, above all advanced knowledge by algorithmic reasoning, pushing aside traditional trial-and-error. Chemists, henceforth, would achieve their goals by design rather than haphazardly.

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38. The following scientists owed their award to nmr, to a small or a major degree: E. J. Corey, Donald J. Cram, Richard R. Ernst, Martin Karplus, Paul Lauterbur, Jean-Marie Lehn,, George Olah, John A. Pople, Kurt A. Wüthrich. By itself, their sheer number is highly significant.

39. Musher, J. I., and E. J. Corey. "Virtual Long-Range Spin-Spin Couplings in Nmr : The Linear 3-Spin System and Qualitative Implications of Higher Systems." *Tetrahedron,* 18, no. 6 (1962): 791-809.

The Pursuit of Accurate Measurements:
Gas Electron Diffraction from the 1930s to the 1960s

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Introduction

Most scientific instruments and experimental methods have been improved continually since their invention. Such improved methods sometimes change scientific practices and usually enable more accurate measurements that replace existing data with new ones. In his book, *An Introduction to Scientific Research*, the American chemist, E. Bright Wilson wrote the following about measurements at higher accuracy.

> Sometimes measurements at higher accuracy bring to light new and unforeseen discrepancies of fundamental importance. An example of this is the Lamb-Retherford measurements of hyperfine structure of hydrogen spectrum, which showed that the Dirac theory needed modification.[1]

This example showed the interrelationship between the theory and the measurement. The question this raises is: if there are discrepancies between the results of two measurement methods, does this render one of them obsolete or changed? To answer this question, I look to the case of the determination of molecular structures in the gas phase. Gas-phase molecules are less influenced by the environment than in the solid and liquid phase, and gas molecular structural studies have thus provided much fundamental information about molecular structures. In the 1960s, the methods for investigating gas molecules were gas electron diffraction and spectroscopy. In this paper, I trace the history of gas electron diffraction, which was considerably improved in the late 1940s.

The Development and Improvement of the Gas Electron Diffraction

Gas electron diffraction, GED, is a method of determining molecular structures of gases by measuring the internuclear distances and valence angles of molecules by electron diffraction.[2] Herman Mark and Raimund Wierl published a paper on the structure of molecules, such as cyclopentane and tetrachloroethene with GED in 1930.[3] In the same year, Linus Pauling visited Mark and learned about GED, and subsequently wanted to utilize GED for his research. Pauling acquired the design of the apparatus from Mark, who was not going to continue his GED research any longer.[4] After Pauling's return to the US, one of his students, Lawrence

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[1] E. Bright Wilson, *An Introduction to Scientific Research*, Dover edition (New York: Dover Publications, 1990, original work published in 1952), p. 59.

[2] In the late 1920s, Peter Debye started to study gas molecules using X-ray diffraction. It took more than ten hours to achieve exposure with X-ray. On the other hand, it took a few seconds with an electron beam because the scattering power of electron is much larger than X-ray's. In the mid-1930s, X-ray diffraction studies on free molecules were abandoned.

[3] Herman Mark and Raimund Wierl, "Die Ermittlung von Molekülstrukturen durch Beugung von Elekronen an einem Dampfstrahl," *Zeitschrift für Electrochemie*, 36 (1930): 675-676.

[4] Linus Pauling, "Fifty Years of Physical Chemistry in the California Institute of Technology," *Annual Review of Physical Chemistry*, 16 (1965): 1-15. Mark invited Odd Hassel to show his GED apparatus in 1930. Hassel started GED in Norway and his group became one of the leading GED research groups before the war.

Brockway constructed an apparatus and this was used to start GED research at Caltech, making Brockway a pioneer in studies of GED. Pauling regarded one of the results of their GED work as empirical evidence of the existence of resonance among several valence-bond structures in 1933.[5]

After the invention of GED, researchers employed what was called the 'visual method', wherein the diffraction intensities on imaging plate were measured using their own eyes. The maximum and minimum intensities were so faint that they could not be measured mechanically, but human eyes were (are) sensitive enough to detect the relative intensity. This procedure is a form of artisanal work wherein trained eyes measure intensity. The GED researchers achieved several successes in structural chemistry by using the visual method.[6] For example, Verner Schomaker and Glauber at Caltech demonstrated the failure of the first Born approximation.[7] As Pauling mentioned in his paper in 1939, Schomaker had an especial skill in measuring electron diffraction photographs.[8]

One of Schomaker's co-workers, however, complained, "But Verner, you can see the rings so much better than I can."[9] Schomaker refuted, "Mostly not so! I just tried harder and got further behind,"[10] This argument demonstrates the subjectivity of GED research. Even if Schomaker worked harder, as did the naturalists in the Enlightenment, with 'meticulous patience and manual delicacy',[11] how could the accuracy of the result be verified or how did the GED researchers decide which molecular structure was the correct one? In reality, the members of Schomaker's group said that the result was always right if it was measured with the well-trained eyes.[12] In most cases, GED results were compared with the results of X-ray diffraction of solid molecular structure because, in general, differences of structure between solid and gas are slight, and were in good agreement. Unfortunately, soon afterward, some of the earlier molecular structures obtained by the visual method proved unreliable or definitely wrong,[13] and this led to a deep-rooted mistrust of GED.

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[5] Lawrence O. Brockway and Linus Pauling, "The electron-diffraction investigation of the structure of molecules of methylazide and carbonsuboxide," *Proceedings of the National Academy of Sciences*, 19 (1933): 860-867.

[6] Kozo Kuchitsu, "Gas Electron Diffraction," in ed. Peter Goodman, *Fifty Years of Electron Diffraction*, (Dordrecht, Holland; Boston: D. Reidel, 1981), pp. 356-377, p. 359.

[7] Verner Schomaker and Roy Glauber, "The Born Approximation in Electron Diffraction," *Nature*, 170 (1952): 290-291.; Roy Glauber and Verner Schomaker, "The Theory of Electron Diffraction," *Physical Review*, 89 (1953): 667-671.

[8] Linus Pauling, H.D. Springall, and K.J. Palmer, "The Electron Diffraction Investigation of Methylacetylene, Dimethylacetylene, Dimethyldiacetylene, Methyl Cynaide, Diacetylene, and Cyanogen," *Journal of American Chemical Society*, 61 (1939): 927-937.

[9] Verner Schomaker and Kenneth Hedberg, "Gas Electron Diffraction: Continuation at Cal Tech and Oregon State," in ed. Peter Goodman, *Fifty Years of Electron Diffraction*, (Dordrecht, Holland; Boston: D. Reidel, 1981), pp. 208-221.

[10] Schomaker & Hedberg (note 9), 211.

[11] Lorraine Daston, "Attention and the Values of Nature in the Enlightenment," in eds. Lorraine Daston and Fernando Vidal, *The Moral Authority of Nature* (Chicago and London: The University of Chicago Press, 2003), pp. 100-126, p. 115. I thank Dr. Buhm Soon Park for this information.

[12] Masao Kimura, "Kitai Denshisen Kaisetsu to Karuforunia Kodai (The Gas Electron Diffraction and Caltech)," *Kagaku to Kogyo*, 12 (1959): 628-633. (in Japanese), p. 630. (the author's translation) Kimura's report of this visit to the GED group at Caltech describes how Schomaker conducted GED experiment. When Schomaker left Caltech in 1958 the GED research at Caltech was terminated.

[13] Wheatley pointed out that there were two main reasons for the errors. The first was the ignorance of hydrogen atoms for determining molecular structures because the scattering from them was small, and the effect could be submerged in the scattering due to heavier atoms. The second was that the number of diffraction rings were insufficient to investigate structures of gas molecules and it sometimes led to completely incorrect models of molecular structures. (Peter J. Wheatley, *The Determination of Molecular Structure*, 2nd ed. (New York: Dover Publications, 1981, original work published 1968), p. 86.

In the late 1940s, several GED researchers in Norway and the US developed the sector method independently. By using a rotation sector above the imaging plate during recording the diffraction pattern, the sector method made it possible to mechanically measure the intensity on the imaging plate with a micro-photometer. The sector method became widely used from around 1950, and it gave credibility to GED as this mechanical method was more objective and accurate than the artisanal visual method.[14]

Above all, the importance of the improved measurement method was brought to light by Isabella Karle and Jerome Karle at the Naval Research Institute in the US. In 1949 they demonstrated the ability of GED measurement to evaluate vibrations between pairs of atoms in a molecule by the sector method.[15] It broadened the range of application for GED in structural chemistry.

What Kinds of Problems Were Caused by the Different Method? - The Discrepancies and the Mistrust

After World War II, a promising method achieved status as one of the most powerful techniques with high accuracy to investigate molecular structures. It was microwave spectroscopy. The GED researchers compared the results provided by spectroscopy and GED of molecular structures at 0.001Å-digit accuracy. However, they found that there were the discrepancies between them.[16]

There were two different reactions from GED people to the discrepancies. One was negative, the other positive. Brockway, the pioneer of GED, was typical of those who reacted negatively. The discrepancies made him pessimistic about the future of this method. For example, at an international conference in 1961, he expressed concern that "[n]o standard procedure can be applied in an automatic fashion with a guaranteed precision."[17] On the other hand, Yonezo Morino's attitude was positive. He believed that the discrepancies could be explained by taking into account the fact that a molecule is a dynamical system and also pointed out, especially, that the GED researchers believed that all researchers who engaged the molecular structure determination investigated the same dimension of a molecule.[18]

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[14] Even after the sector method became available, Schomaker clung to the visual method. Pauling suggested that they should introduce the sector method and Schomaker finally agreed and introduced it. (Schomaker (note 9))

[15] Isabella Lugoski Karle and Jerome Karle, "Internal Motion and Molecular Structure Studies by Electron Diffraction," *Journal of Chemical Physics*, 17 (1949): 1052-1058. Concerning this paper, Yonezo Morino pointed out that the formula by Peter Debye which Karle and Karle introduced for the discussion on the thermal motion, should be corrected. (Yonezo Morino, "On the Mean Amplitudes of Thermal Vibrations in CO_2 Molecule," *Journal of Chemical Physics*, 18 (1950): 395.) This case shows that the measurement at higher accuracy revealed the discrepancy between theory and experiments.

[16] James has pointed out that comparisons of results from different techniques could provide a basis for extrapolation. (Jeremiah James, "Modelling the Scale of Atoms and Bonds: The Origins of Space-filling Parameters," in eds., Ursala Klein and Carsten Reinhardt, *Objects of Chemical Inquiry*, (USA: Science History Publications, 2014), pp. 281-320.)

[17] Lawrence O. Brockway, "Recent Problems in Diffraction by Gases," in *Proceedings of the International Conference on Magnetism and Crystallography, Kyoto, 25-30 September, 1961*, pp. 1-3.

[18] Yonezo Morino, "Jitsurei wo Toshite 'Seimitsu Sokutei wo Kangaeru (Examining the Precise Measurement through the Examples), *Kagaku Sosetsu* 10 (1976): 40-48. (in Japanese) I think that there were the directional differences between the GED researchers, Brockway and Morino. Brockway often asserted the precision of GED measurement. On the other hand, Morino wanted accurate measurement. In 1963, Churchill Eisenhart defined the difference between precision and accuracy: precision has to do with closeness of results to each other and accuracy has to with closeness to the truth. (Churchill Eisenhart, "Realistic Evaluation of the Precision and Accuracy of Instrument Calibration Systems," *Journal of Research of the National Bureau of*

Practically, GED involves looking at the thermal distribution of vibrational states, whereas microwave spectroscopy looks at a molecule in a specific vibrational state. In other words, the gas electron diffractionists and the microwave spectroscopists were looking at different states. The words 'molecular structure' meant different things to different people. [19] Some diffractionists and spectroscopists mentioned this difference in their papers by the middle of the 1960s.[20]

Morino was one of the researchers who noticed the difference. Moreover, Morino had introduced microwave spectroscopy for investigating molecular structures along with GED in the late 1950s. He had a background in spectroscopy for determining molecular structures. He had started Raman spectroscopy with San-ichiro Mizushima when he was a graduate student, although he had been attracted to GED at the time.[21] It seems natural that he took such an interdisciplinary approach because of his background. He thought, "if the two methods were properly combined, we might gain more advanced knowledge of molecular structure."[22] Pursuing accurate measurement with not only on measuring technique was one of his strategies to better understand the true nature of molecules.[23] In Morino's phrase, he aimed at "unified molecular structure." [24] This was a scientific approach to the problem of the discrepancies, which would be later tackled by James Boggs and his colleague with the social and organizational method of using symposia, which Peter Galison has called a 'Trading Zone'.[25]

Morino and his students at the University of Tokyo performed GED research and utilized the spectroscopic method, combining the results from different techniques for determining the accurate molecular structure. When they proposed an internuclear distance parameter in 1962, Morino and his students noted:

Standards- c. Engineering and Instrumentation, 670 (1963): 161-187.) This definition is important when thinking about the difference between Brockway's and Morino's research-programs.

[19] Wheatley (note 13), i.

[20] The spectroscopists, Herschbach and Laurie, noted that most of the discrepancy arises from the inherent difference in the nature of the experimentally determined quantities. Dudley R. Herschbach and Victor W. Laurie, "Influence of Vibrations on Molecular Structure Determinations. I. General Formulation of Vibration—Rotation Interactions," *Journal of Chemical Physics*, 37 (1962): 1668-1686. The comparison between the results from spectroscopy and diffraction also fascinated the theoretical chemists. Charles Coulson expressed an interest in why spectroscopy and diffraction provided different value of the bond lengths. And, he believed that it would be very useful to obtain electron diffraction data on diatomic molecules for comparison with existing spectroscopic data. (Charles A. Coulson, "Comments on paper by B.P. Stoicheff," in the Epistelogue (Paper Symposium) on the Effect of Environment on the Properties of Carbon Bonds, *Tetrahedron*, 17 (1962): 254-255.) Understanding the origin of the discrepancies was not an experimental interest but also a theoretical one. In the early 1960s, there were several theories explaining the variation in C-C bond lengths, such as resonance, conjugation, hybridization, and non-bonded interaction.

[21] Mizushima's group, including Morino, performed GED work before World War II with the surface scientist Shigeto Yamaguchi at the Institute of Physical and Chemical Research, who had an electron-diffraction camera. Morino started his own GED work with help from the electron diffractionist, Ryoji Uyeda at Nagoya University after he left Mizushima group. Since Seishi Kikuchi observed the electron diffraction pattern from a thin crystal of mica in 1928, electron diffraction research became one of the strongest research areas before the war in Japan. I thank Dr. Jeremiah James for his question on this point.

[22] Yonezo Morino, "Fifty years in Tokyo, Nagoya, and Tokyo," in ed. Peter Goodman, *Fifty Years of Electron Diffraction*, (Dordrecht, Holland; Boston: D. Reidel, 1981), pp. 136-143, p. 141.

[23] One of his achievements was the Bastiansen-Morino shrinkage effect in 1960, where the vibrational motion of the atoms in a molecule have an effect on the structure. Morino explained the molecular structure, which Otto Bastiansen in Norway measured with GED, by means of calculation based on the spectroscopic data.

[24] Morino (note 22), 141.

[25] Peter Galison, *Image and Logic: A Material Culture of Microphysics* (Chicago and London: The University of Chicago Press, 1997)

it is not our intention to cause a confusion by introducing new distance parameters, but it seems to be of practical importance to get a reasonable way of correlating diffraction and spectroscopic parameters with each other of reading the equilibrium distance r_e based on these experimental quantities.[26]

This statement is a sort of defense against the criticism from other researchers. Indeed, most of those in the GED community had reacted unfavorably. For example, at an international conference in 1961, Brockway said that electron diffractioners would not conform to other disciplines.[27] And at the Congress of the International Union of Crystallography in 1963, Jerome Karle criticized Morino's idea saying that the result of spectroscopy should not be used if one wanted to determine molecular parameters from the GED experiment.[28] Morino needed more time and a change in situation to achieve acceptance of his idea in the field.[29]

The discrepancies threw into sharp relief the mistrust between the practitioners of the two methods. There had been mistrust between the two tribes, although both were struggling to give detailed and accurate information on molecular structures. Of this situation, James Boggs, the American chemist, wrote, "we were very concerned…to be frank, [about] the scorn with which each regards the other."[30]

What brought such distrust between them? A GED researcher said, for example, that spectroscopists showed no clear understanding of the extent to which that accuracy disappears by the time it is related to a molecular geometry parameter.[31] Also, Boggs said that he was told that [a diffractionist] "should never trust a microwave spectroscopist."[32] In return, Wilson, a microwaver, was "very skeptical at the time about the reliability of electron diffraction as a structural research tool,"[33] even after the development of the sector method.

Moreover, there was little social interaction between the two tribes. By the middle of 1960s, GED researchers usually attended chemistry meetings and were interested in structural information and theory. On the other hand, microwavers mostly attended physics meetings and were interested in the absolute values of molecular structure.[34] It should be mentioned that the GED community was very small and there were ten or fewer GED groups in the world in the late 1950s.[35] Spectroscopists had been having large meetings on spectroscopy,

[26] Yonezo Morino, Kozo Kuchitsu, and Takeshi Oka, "Internuclear Distance Parameters," *Journal of Chemical Physics*, 36 (1962): 1108-1109, p. 1109.

[27] Brockway (note 17), 2.

[28] Yonezo Morino, "Roma Kaigi ni Okeru Kitai Denshisen Kaisetsu ni Kansuru Hokoku (The report of the Conference on Gas Electron Diffraction at the Rome Conference), *Nihon Kessyo Gakkaishi*, 6 (1964): 31-33. (in Japanese)

[29] One of Morino's students, Kozo Kuchitsu pursued the idea of combining the analysis of GED and spectroscopic data and established the methods. The history of the process is also interesting, but needs more investigation.

[30] James E. Boggs, "History of the Austin Symposium," https://sites.smu.edu/dedman/austinsymposium/history.html, accessed June 30, 2014.

[31] James E. Boggs, "The integration of structure determination by computation, electron diffraction and microwave spectroscopy," *Journal of Molecular Structure*, 97 (1983): 1-16, pp. 1-2.

[32] Boggs (note 31), 2. Following this description, he continues, "[m]y own observation told me that you should never trust a result coming from electron diffraction either."

[33] Roberts L. Kuczkowski, "Lawrence S. Bartell: biographical notes," *Journal of Molecular Structure*, 485-486 (1999): xi-xxvii.

[34] Boggs (note 31), 3.; Leslie E. Sutton (ed.), *Tables of Interatomic Distances and Configuration in Molecules and Ions (Supplement 1956-1959)* Special Publication No.18 (London: The Chemical Society 1965), p. 6.

[35] Kozo Kuchitsu, "Kitai Denshisen Kaisetsu (Gas Electron Diffraction)", *Kagaku no Ryouiki*, 11 (1957): 52-76, p. 53. (in Japanese)

but the GED people had been having symposia and usually attended crystallography meetings or electron diffraction meetings.[36]

The GED researchers attended several meetings that were related to their interest, molecular structures. Occasionally, there were some cases where GED and microwave researchers met – or rather, attacked – each other. One of these few occasions was the Ohio State University International Symposium on Molecular Structure and Spectroscopy.[37] At the meeting in 1963, the participants witnessed a heated argument between Larry Bartell, a diffractionist, and Bright Wilson, a microwaver.[38] Around that time there were people who were very concerned about the situation.

Mediating a Settlement- A Symposium for Two Tribes

Boggs and his colleague, Harold Hanson, a GED researcher, at Texas University were the people concerned about the situation. Boggs was one of Brockway's students, but, interestingly, he did not earn his PhD degree for GED research. The two researchers thought that the lack of communication between the practitioners of the two methods caused difficulties for molecular structure studies.[39] They devised a social and organizational method to "force them to listen to each other"[40] and invited leading researchers from the two areas, who were mainly in the US.

The confrontation site was the 1966 Austin Symposium on Gas Molecular Structure, which was a session of the American Crystallographic Association Annual Meeting.[41] This was expected a one-off highly focused meeting. The topic of the symposium was accurate measurement of the molecular structures.

At the meeting, the participants shared problems and ideas about the determination of gas-phase molecules. For example, 'accurate bond length' was one of the topics at the meeting. Cecil C. Costain, who was a spectroscopist, started his talk by saying, "Those who were at the banquet last night will appreciate the fact that one can no longer discuss the accuracy of bond length without putting his money on the table."[42] This witty remark depicted the situation well.

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[36] The GED researchers tried to create an opportunity in the early 1960s to have a meeting with spectroscopists in order to discuss molecular structures. In 1963 during the Congress of the International Union of Crystallography in Rome, the GED people discussed the possibility of a joint symposium with spectroscopists, especially microwavers, on the determination of accurate molecular structure (Morino (note 28). It was supposed to be held at the European Congress on Molecular Spectroscopy in Copenhagen in 1963, but I have not yet been able to find any evidence that this symposium was actually held.

[37] By the 1970s, the organizers of the Ohio State University meeting decided not to include crystallography and gas electron diffraction because the symposium became larger and crystallographers and diffractionists began to attend other meetings. (Brenda P. Winnewisser, "An Array of Scarlet and Grey Booklets: 65 Years of the Symposium on Molecular Spectroscopy," *Journal of Molecular Spectroscopy*, 269 (2011): 2-11, p. 3.)

[38] These witness reports came from Kuczkowski's article (Kuczkowski (note 33)) and personal correspondence with John Muenter, dated August 28, 2014.

[39] Boggs (note 30)

[40] Boggs (note 30)

[41] The organizers arranged the symposium at the crystallography meeting because Hanson was a diffractionist and Boggs was a theoretical chemist, and the crystallography meetings might be one of their sphere of activities. I thank Dr. Mary Jo Nye for her question on this point.

[42] Cecil C. Costain, "Further Comments on the Accuracy of r_s substitution structures," in Proceedings of the Symposium on Machine Interpretations of Patterson Functions and Alternative Direct Approaches and the Austin Symposium on Gas Phase Molecular Structure at Austin, Texas, Feb. 28-March 2, 1966. *Transactions of the American Crystallographic Association*, 2 (1966): 157-164, p. 157.

Costain thereafter expressed his belief in the necessity of the collaboration between two areas, saying "I think ethyl fluoride is one example of a molecule for which we should ask for help and collaboration from the electron diffraction people."[43] In the discussion part of his presentation, several researchers from the both camps suggested that they should cooperate to determine accurate bond length.[44]

The meeting was a great success and Boggs and Hanson decided to continue the symposium biennially. The second symposium was held in 1968. The speakers at the symposium came from the US, Europe and Japan. Six invited speakers, including Morino, were from each tribe and there were two group discussions between both sides to discuss unsolved problems and think about the future of structural chemistry. They admitted the limitations of their own methods and the complementary relationship between the results from the two measurement methods for studies on gas molecule structure.

Conclusion

I have traced the history of gas electron diffraction to answer the question, if there are discrepancies between the results of two measurement methods, does this render one of them obsolete or changed? Improved GED with higher accuracy revealed the discrepancies in the results of GED and microwave spectroscopy. For example, Morino explained the origin of the discrepancies and combined the results from the two methods to pursue accurate molecular structure. However, his approach seemed a long shot at the time, and exposed the mistrust between two instrumental communities. Meanwhile Boggs and his colleague offered the binding site, or 'Trading Zone', of the Austin Symposium. In that zone, the researchers from the two disciplines exchanged ideas and shared information about their research on gas molecular structure. As a first step, the participants admitted that the information provided by both methods was a mutually complementary and that they shared a common goal – that of understanding molecular structure.

This case shows that, although the discrepancies in the results of the two different measurement methods revealed the biased attitudes on the both sides, neither method needed to be modified or corrected because of the discrepancies. Rather, the discrepancies triggered the collaboration between the two method people, and such collaboration eventually resulted in advancing knowledge about the target.

Acknowledgement

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[43] Costain (note 42), 160.
[44] Costain (note 42), 161-164.

Development of Vibrational Spectroscopy of Polyatomic Molecules in the 1930s and Its Implication for the Emergence of "Molecular Science"

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Introduction

When we look back the history of chemistry from 20s to 60s, application of the physical methods have made the most significant impact on the daily activity of chemists. The changes occurred in both of the experimental and theoretical aspects: Various physical instruments commonly equipped in chemical laboratories such as pH meters and chromatographs and more expensive spectrometers and diffractometers installed in department buildings replaced the laborious protocols of qualitative chemical analysis with quantitative data they provide automatically. These data can be now interpreted, thanks to the development of quantum chemistry and its implementation as computer programs, in terms of molecular structure. However, the very nature of chemistry as practice to transform matter into useful products seems to be unchanged, while the forefront of the research has nowadays shifted from homogeneous chemical compounds to heterogeneous nanomaterials.

On the other hand, physics as pursuit to unravel hidden law of nature have been changing in its forefront. In the beginning of the twentieth century atoms and molecules were the hottest target of research, which eventually led to emergence of quantum theory for microscopic entities. Soon it was successfully applied to explain the homopolar bonding of hydrogen molecule and Dirac gave his famous statement in 1929[2] and forefront of physics has moved to subatomic phenomena or solid-state physics. However, it was in 1930s after his statement that molecular structure of polyatomic molecules has begun to be understood based on quantum chemistry and molecular spectroscopy. This development would not be achieved without persistent contribution of certain number of physicists and chemists and their activity and achievement seems to be "neither physics nor chemistry".

Such ambivalent situation of this practice already has been recognized by one of the leading scientists. In 1965, at the symposium dedicated to Mulliken, he gave a lecture "Molecular Scientists and Molecular Science: Some Reminiscence". After describing his experimental study of isotope separation before starting molecular spectroscopy, he said:[3]

"Since then I have become neither a proper experimentalist nor a proper theorist, but a middleman between experiment and theory --- and between chemistry and physics."

He did not mention the term "molecular science" and simply described his experience through people he met around 1930, as if it is self evident that they were the molecular scientists and their activity was the molecular science.

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[1] This work was performed based solely on my personal interest and no relationship with the research activity in my affiliation.

[2] P. A. M. Dirac, Proc. *R. Soc. Lond. A* **123**, 714 (1929).

[3] R. S. Mulliken, *J.Chem. Phys*. **43**, S2 (1965). It should be noted that the title of his autobiography is "*The Life of a Scientist*", neither physicist nor chemist.

Actually the term "Molecular Science" was first widely recognized a few years before his lecture, when it appeared in the title of the book edited by von Hippel.[4] However, it was one of the three volumes on his dielectric materials research and seems different from what Mulliken meant with the same term. Rather it was closely related to the term in 1961 by Japanese scientists for a new research project "molecular science - physicochemical study of molecules" funded by the Grant-in-Aid for Scientific Research, as this project would not be realized without strong promotion by Nagakura who studied in Chicago in 1950s.[5] This activity has materialized Institute for Molecular Science in 1975 and Japan Society for Molecular Science in 2006. Such developments of molecular science in Japan is quite unique and its development would provide a clue to understand Japan's modern history of chemistry. However, before tackling this issue I would like to go back to 1930s when the studies on the molecular structure came into shape.

Among various branches in experimental studies related to the molecular science, vibrational spectroscopy has been particularly important as the vibrational frequencies and selection rules can be correlated with molecular structure and symmetry through mechanistic molecular models. Although there are several important previous studies on the history of vibrational spectroscopy, they mainly describe the development of the infrared spectra of diatomic molecules until around 1930,[6] or application of the infrared spectroscopy for chemical analysis after 1930[7]. Actually we can learn about the development of vibrational spectroscopy in 1930s from a review article[8] and even from a textbook[9] as the framework of the analysis of the vibrational spectra were established in this period. However, they are mainly the studies of small molecules by the scientists in the United States and it is difficult to know situation of the other countries only from these resources. Of particular important in connection with the emergence of the molecular science is Germany, as young promising Japanese scientists studied there and learned from German textbooks in 1930s.[10] In this presentation I tried to follow the development of vibrational spectroscopy of polyatomic molecules in Germany in 1930s.

Vibrational spectroscopy of polyatomic molecules before 1930

In 1905 Coblenz published a compilation of measured infrared absorption spectra of a large number of organic compounds.[11] He employed a radiometer, a mirror spectrometer and a rock salt or a quartz prism and recorded absorbance point by point and manually plotted the spectra. He found that isomeric compounds show markedly different spectra and certain atomic groups such as the methyl group show their characteristic absorption bands at certain

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[4] A. von Hippel, Ed., *Molecular Science and Molecular Engineering*, The Technology Press, Cambridge,   and John Wiley & Sons, New York (1959).

[5] *IMS Letters*, **58**, 8 (2008). (In Japanese: Prehistory of Institute for Molecular Science by Prof. Nagakura.)

[6] J. C. D. Brand, *Lines of Light : the sources of dispersive spectroscopy, 1900-1930,* Gordon and Breach (1995); C. Fujisaki, *Kagakushi Kenkyu*, **22**, 73 (1983) (in Japanese).

[7] Y. M. Rabkin, *Isis*, **78**, 31 (1987).

[8] D. M. Dennison, *Rev. Mod. Phys.* **12**, 175 (1940).

[9] E. Bright Wilson, Jr., J.C. Decius, P.C. Cross, *Molecular Vibrations: The Theory of Infrared and Raman Vibrational Spectra*, McGraw-Hill, New York, 1955.

[10] San-ichiro Mizushima and Juro Horiuti are the most famous cases of the physical chemists studied in Germany in 1930s.

[11] W. W. Coblenz, *Investigations of infrared spectra. Part I. Absorption spectra; Part II. Emission spectra.* Publication No. 35, Carnegie Institution of Washington (1905).

wavelengths. The results indicated that the infrared spectroscopy can provide information on molecular structure and has a potential as a tool for identification of chemical compounds.

At almost the same time Drude attributed dispersion frequencies to intrinsic vibrational frequencies of atoms and molecules, which are proportional to the ratio of the charge and the mass.[12] Thus the dispersion in the infrared region was due to intrinsic vibration of positively charged atoms in a molecule, whereas electrons are responsible for the dispersion in the ultraviolet region.

The first attempt to assign infrared absorption bands of a polyatomic molecule by calculating its vibrational frequencies was made by Bjerrum in 1914.[13] He treated carbon dioxide having a bent shape with two equivalent carbon-oxygen bonds and calculated normal vibrations by assuming the system as point masses connected with attractive force between atoms and obtained possible geometries by adjusting the bond angle and force constants to reproduce measured vibrational frequencies. He derived a bent structure by fitting the calculated values to the frequencies of the three absorption bands. Although this was turned to be wrong as one of the absorption bands was actually a combination band, the proposed procedure still works within the framework of the quantum mechanics until today.

In 1925 Dennison applied the same procedure to the analysis of the IR spectra of methane with a tetrahedral model.[14] By assuming spherical distribution of electrons around the carbon and the four hydrogen atoms, the potential energy of the molecule can be described as a function of the displacements of each of the hydrogen relative to the carbon and the mutual displacements of the hydrogen atoms. The system with nine internal degrees of freedom has only four normal modes, two of them were triply degenerate non-symmetric CH stretching (v_3) and bending (v_4) modes. The normal frequencies calculated by adjusting the force constants in the potential energy function were in fairly good agreement with the fundamental vibrational frequencies, although the bands assigned to the totally symmetric modes were later found to be combination bands.

This work was motivated by the infrared spectra of methane measured by Cooley of the same physics laboratory of University of Michigan[15]. By using a high-resolution grating spectrometer the bands at 7.7 μ (v_4) and 3.31μ (v_3) were resolved into rotational lines. However, the line spacing of 9.77 cm^{-1} near the center of the v_4 band was almost twice of that of the v_3 band (5.41cm^{-1}). This seemed puzzling as the line spacing is inversely proportional to the moment of inertia and the three principal values of the spherically symmetric methane molecule should be equal.

The most straightforward solution of this inconsistency is to lower the molecular symmetry to have two different rotational constants. Pyramidal carbon atom has already been proposed from an X-ray crystallographic study of pentaerythritol $C(CH_2OH)_4$.[16] Guillemin calculated pyramidal structure of methane to have two principal values of the moment of inertia derived from the rotational fine structure of the v_3 and v_4 bands.[17] His discussion was based on the ionic molecular model and he noted that the carbon ion should be polarizable to stabilize the pyramidal structure relative to the tetrahedral structure, which minimizes electrostatic repulsion of hydrogen ions. Henri reviewed these papers on the pyramidal structures of the

[12] P. Drude, *Ann. Physik* **14**, 677 (1904).

[13] N. Bjerrum, *Verhandl. Deut. Physik-Ges.* **16**, 737 (1914).

[14] D. M. Dennison, *Astrophys. J.* **62**, 84 (1925).

[15] J. P. Cooley, *Astrophys. J.* **62**, 73 (1925).

[16] H. Mark, K. Weissenberg, *Z. Physik* **17**, 301 (1923).

[17] V. Guillemin, Jr. *Ann. Physik* **81**, 173 (1926).

tetravalent carbon compounds and argued that the conformation of the tetravalent carbon atom is dependent on the nature of the atoms or atomic groups connecting to it.[18] However, Richardson mentioned this problem in his introduction in the Faraday Society in 1929 in favor of tetrahedral structure by citing the work by Dennison.[19] In X-ray crystallography Nitta argued for the tetrahedral carbon in pentaerythritol[20] and there seems no strong argument for pyramidal tetravalent carbon after around 1930. These arguments are just before the advent of the quantum chemistry and explanation of the tetrahedral carbon with orbital hybridization. However, they seemed to have certain influence on the chemists' attitude towards application of the physical methods.

The most significant event in the development of the vibrational spectroscopy is definitely the discovery of the Raman effect in 1928.[21] The Raman spectra of any type of substances (liquid, solid, gas) were obtained by use of a very simple setup, which showed bands of the scattered light whose shifts represent natural vibrational frequencies. The effect was discovered almost at the same time by several groups but Pringsheim named it as the Raman effect.[22] Vast number of papers on the Raman effect of various substances appeared and Raman received Nobel Prize in Physics in 1930. Eventually it was recognized that the selection rule of the natural vibrations of the Raman active modes are different from infrared active modes and its explanation based on molecular polarizability and its symmetry was given by Placzek.[23]

Research Activity in Germany in early 1930s

Mulliken's reminiscence is an illustration of not only his close relationship with many friends but at the same time their scientific activities in Germany around 1930. During his visits he also had chances to attend scientific meetings but interestingly he did not attend the meeting of Faraday Society on "Molecular spectra and molecular structure" held in 1929 at Bristol.[24] This meeting is famous in the history of quantum chemistry for discussion on notation of the molecular spectra but the discussion on the electronic spectra and electronic structure was only one part of the meeting and there were other two parts on the Raman effect and the infrared spectra. Scientists from different countries contributed to the discussion.

Next year during his visit to Europe he gave a presentation at the 35th general meeting of the Bunsen Gesellschaft in the next year at Heidelberg.[25] Following lectures were given for the main theme "Spectroscopy and molecular structure".[26]

J. Franck, "Determination of thermochemical quantities from spectroscopic data"
R. Mecke, "Experimental results and goals of the band research"
F. Hund, "Methods of interpretation and prediction of molecular spectra"
W. Weizel, "Structure and spectra of molecules H_2 and He_2"
R. S. Mulliken, "Electronic state und chemical bond in diatomic molecules"
O. Stelling, "Correlation between chemical constitution and K X-ray absorption spectra"
P. Debye, "Interferometric determination of structure of single molecule"

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[18]   V. Henri, *Chem.Rev.* **4**, 189 (1927).
[19]   R. Richardson, *Trans. Faraday Soc.* **25**, 899 (1929).
[20]   I. Nitta, *Bull. Chem. Soc. Jpn.* **1**, 62 (1927).
[21]   C. V. Raman, K. S. Krishnan, *Nature* **121**, 501 (1928).
[22]   P. Pringsheim, *Naturwiss.* **16**, 597 (1928); P. Pringsheim, B. Rosen, *Z. Physik* **50**, 741 (1928).
[23]   G. Placzek, *Z. Physik* **70**, 84 (1931).
[24]   *Trans. Faraday Soc.* **25**, 611 (1929).
[25]   *Z. Elektrochem.* **36**, 581 (1930).
[26]   Titles of the session and presentations were tentatively translated into English by the present author.

M. Czerny, "Infrared spectroscopy"

A. Smekal, "The Raman effect and its interpretation for the spectroscopy of molecular structure"

R. Ladenburg, "Allowed and forbidden quantum transitions"

C. Ramsauer, "Cross section and molecular structure"

W. Heitler, "On quantum theory of homopolar bonding"

E. Hückel, "On quantum theory of the double bond and their stereochemical behavior"

In contrast to the Faraday Society meeting there were few foreign scientists. However, the list of the lectures clearly shows activity of German scientists on experimental and theoretical issues on molecular spectra and molecular structure. Mulliken was the only scientist from the United States in the list, and his friendship with Hund is well known as two founders of molecular orbital theory and they met in Leipzig where Hund was full professor of theoretical physics from 1929. Heisenberg already became full professor of theoretical physics in 1927 and in the same year Debye moved from Zurich as full professor of experimental physics. They attracted young scientists from all over the world and Leipzig was emerging as a new center of quantum physics. Heisenberg himself had once worked on problems on polyatomic molecules when he was in Göttingen but he seemed to have lost interest on molecular problem. However, his students and visiting scientists like Teller, Placzek, Tisza, Fujioka worked on molecular spectra.

Debye was already an eminent professor in experimental physics when he moved to Leipzig and many young scientists came to his laboratory including Hückel and Mizushima. He organized a series of "Leipzig lecture" from 1928 and they were soon published as monographs.[27] The lecture in 1931 published as an English translation "The Structure of Molecules" included following contributions:[28]

K. L. Wolf, "Problems of free rotation about single and double carbon bonds"

R. Mecke, "Experimental results obtained from band spectroscopy of polyatomic molecules"

F. Rasetti, "The Raman effect and the structure of molecules and crystals"

G. Placzek, "The Raman effect and molecular structure"

H. Sponer, "Band spectra and dissociation"

V. Henri, "The experimental basis of the theory of predissociation of molecules"

R. de L. Kronig, "On predissociation"

G. Herzberg, "Valency and the electronic structure of molecules"

After 1933 many scientists had to leave Germany, including Franck, Sponer and Herzberg among the above-mentioned Bunsen society and the Leipzig lecture on molecular structure. However, many other contributors remained in Germany and continued working on the molecular spectra and structure. In 1934, following lectures were given at the 39th general meeting of the Bunsen Gesellschaft on the theme "Mission of the physico-chemical research in organic chemistry."[29]

E. Hertel, "Physico-chemical problems in organic chemistry"

H. Mark, "About the spatial image of organic molecules and molecular aggregates"

K. F. Bonhoeffer, "Photochemistry of simple organic compounds"

K. W. F. Kohlrausch, "Raman spectrum and organic chemistry"

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[27] Titles of the lecture series were *Quantentheorie and chemie* (1928), *Dipolmoment und chemische Struktur* (1929), *Elektroneninterferenzen* (1930), *Molekülstruktur* (1931) and *Magnetismus* (1933).

[28] P. Debye Ed. (authorized translation by W. M. Deans) *The Structure of Molecules*, Blackie and Sons, Glasgow (1932).

[29] *Z. Elektrochem.* **40**, 405 (1934).

R. Mecke, "Spectroscopic structure determination of simple hydrocarbons and their derivatives"

Although the number of the lectures decreased from four years ago, and Hückel did not accept invitation,[30] their contents indicate significant development of the methods and accumulation of the quantitative data on molecular structure. Mark summarized methods for determination of the molecular structure (X-ray and electron diffraction, permanent electric moment, polarization, vibrational spectra (infrared and Raman), specific heat) with their objects and available data in one table and compared their relative merits in another table.[31] Long lists of typical bond lengths and valence bond angles followed in the paper, which included large number of data obtained by electron diffraction. The paper by Kohlrausch summarized his long series of papers on the Raman effect since 1929 showing alteration of the Raman spectra along homologous substitution in certain types of molecules.[32] He wrote, although it is the first step of the detailed analysis, "The molecular spectrum is additively assembled from the spectra of the individual groups belonged to the molecule." As described also in the approach by Mecke on the infrared spectra, studies on the molecular structure by German scientists in this period made progress towards understanding of more complex molecules, rather than more detailed and complete analysis of simple molecules.

Teller and Placzek

Contributions of Teller and Placzek are particularly important for theoretical development of vibrational spectroscopy. Teller was born in Budapest and came to Germany to study chemistry in Karlsruhe.[33] During this period he had chances to attend lectures on quantum theory by Mark from I. G. Farben and he determined to change his subject to physics. He first moved to Munich in 1928 but soon moved again to Leipzig. Heisenberg told him to study application of group theory on quantum mechanics by Wigner. Teller calculated excited states of hydrogen molecule ion for his dissertation and after completing this work he became an assistant of Heisenberg. In autumn of 1930 he studied the problem of the rotational constants of methane and methyl halides with his Hungarian friend Tisza. He knew about this problem while he was in Karlsruhe from Mecke's work. Teller believed that the tetrahedral carbon should be retained in the solution of this problem. They found that an angular momentum arising from superposition of two degenerate vibrations perpendicular to the symmetry axis couples with molecular rotation to alter the moment of inertia.[34] Thus the riddle of the two different rotational constants of methane was solved and the tetrahedral carbon model was credited with another experimental evidence.

Placzek was born in Brno and studied physics in Wien.[35] Then he moved to Utrecht as a postdoc of Kramers who was famous for his dispersion theory and began to study the Raman effect. He derived the selection rule of the Raman lines and pointed out that molecular vibrations which affect polarizability are Raman active. This selection rule is different from the infrared spectra and in highly symmetric molecules they are mutually exclusive.

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[30] A. Karachaios (transated by A. M. Hentschel) *Erich Hückel (1896-1980): from physics to quantum chemistry (Boston studiesin the philosophy of science, vol. 283)*, Springer (2010).

[31] H. Mark*, Z. Elektrochem.* **40**, 413 (1934).

[32] K. W. F. Kohlrausch, *Z. Elektrochem.* **40**, 429 (1934).

[33] E. Teller, J. Shoolery, "*Memoirs: A Twentieth-Century Journey in Science and Politics*", Basic Books (2001).

[34] E. Teller, L. Tisza, *Z. Physik* **73**, 581 (1931).

[35] J. Fischer, http://cerncourier.com/cws/article/cern/29415 (Last accessed May 4, 2015).

In 1930 Teller moved Göttingen as an assistant of Eucken and collaborated with Franck and Herzberg on electronic spectra of polyatomic molecules.[36] Placzek also moved from Leipzig to Göttingen and they worked together on the theory of rotational line intensity of the Raman spectra. While this collaboration yielded a beautiful result, Teller recalls their relationship:[37]

"I began my collaboration with Placzek with enthusiasm, but as it turned out, our joint effort was one of the few times I did not enjoy a friendship with a collaborator. Placzek treated me to a large dose of derision, most of it trivial; for instance, he called me "Herr Molekular-Inspektor". The inference was that such a pursuit was a lower-class activity. As far as I was concerned, what happened in physics between 1920 and 1933 was so magnificent that it was a privilege to work even on minor details, and I thought it perfectly grand to be recognized even in an unglamorous field. I had made that decision in all consciousness, and I was content to remain Herr Molekular Inspektor."

Before completion of their collaborative work Placzek left to Fermi's group in Rome and worked on the Raman spectra of gases.[38] He wrote a monograph on the Raman effect in *Handbuch der Radiologie* which was published after he moved to Copenhagen and this became a standard textbook.[39] Teller also moved to Copenhagen when he had to leave Germany. Both of them finally settled in the United States and their wartime efforts are already well known. While after publishing the monograph Placzek changed subject to other scattering phenomena such as neutron, Teller continued working for a while on molecular spectra as still well known by the effects with his name (Herzberg-, Renner-, Jahn-Teller) and the review article on electronic spectra with Sponer as a good collaborator.[40]

Mecke

The most active scientist in vibrational spectroscopy during this period in Germany was definitely Mecke.[41] After having studied the band spectra of diatomic molecules he started to measure electronic spectra of polyatomic molecules in late 1920s, which were found to be too complicated for detailed analysis. Then he shifted the target to measure overtone and combination vibrational bands of simple polyatomic molecules by using the newly developed plates for infrared photography. Although absorption coefficients of the overtone and combination bands were much weaker than those of the fundamental bands, photographic detection was more sensitive than the bolometers for infrared detection and it could deserve the merit of the larger spectrograph for higher resolution.

The first report appeared in the general discussion of The Faraday Society in 1929.[42] He showed the spectrum of ammonia which corresponds to the third overtone of the NH stretching mode observed at 3 micron. Due to higher resolution he could determine the moment of inertia of ammonia as a symmetric top and consequently determined its pyramidal equilibrium geometry. Combination bands were assigned based on their position and the shape. Comparison was made for vibrational frequencies and bond lengths of a series of simple hydrides (CH_4, NH_3, H_2O, HF) with their corresponding diatomic hydrides (CH, NH,

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[36] G. Placzek, E. Teller, *Z. Physik* **81**, 209 (1932).

[37] Teller and Shoolery (note 33).

[38] E. Amaldi, G. Placzek, *Z. Physik* **81**, 259 (1932).

[39] G. Placzek, *Rayleigh-Streuung und Raman-Effekt (Handbuch der Radiologie; Bd. 6, T. 2 (2. Aufl.)),* Akademische Verlagsgesellschaft (1934).

[40] H. Sponer, E. Teller, *Rev. Mod. Phys.* **13**, 75 (1941).

[41] W. Lüttke, G. A. A. Nonnenmacher, *J. Mol. Struct.* **347**, 1 (1995).

[42] R. Mecke, R. M. Badger, *Trans. Faraday Soc.* **25**, 936 (1929).

OH, HF). This indicates that he already tried to interpret natural frequencies of polyatomic molecules from experimental data of diatomic molecules which he was very familiar.

The most successful results were obtained for acetylene as three papers in 1930.[43] Although acetylene contains four atoms it is a highly symmetric rod like molecule and it was possible to determine its moment of inertia. By assuming the same CH bond length as that of CH, the length of the CC triple bond was determined. Rotational lines showed intensity alteration of approximately 3:1 and this was due to nuclear spin states of two hydrogen having S=1/2. After consolidating a linear symmetric structure of acetylene, he showed in the third paper that the natural frequencies of linear tri- and tetraatomic molecules could be interpreted as n-1 stretching modes and n-2 doubly degenerate deformation modes. This distinction of the valence and the deformation vibrations was extended to the case of ethylene to successfully assign its natural frequencies.

In his presentation in the Leipzig Lecture in 1931 he calculated binding constants of polyatomic molecules by assigning the observed vibrational frequency to a certain bond of the molecule.[44] In this treatment he assumed that the potential function is quadratic to the bond displacement and angle deformation with force constants k and b, respectively, and the vibrational frequencies are expressed as functions of these force constants as well as bond lengths. Actually k was estimated to be ten times larger than b and by expanding the vibrational frequency as a power series of b/k the frequencies of the stretching and the bending modes can be approximately obtained with k and b only, respectively. Calculated binding constants along a series of molecules were surprisingly constant, indicating that they may be retained even in more complicated compounds. Then he derived figures of atomic displacements in vibrational modes of polyatomic molecules up to five atoms (tetrahedron) and assigned measured natural frequencies of some representative molecules of each type.

In 1932 he further extended the concept of the separation of valence and deformation vibrations in a series of papers.[45] He added the Coulombic interaction terms between bond dipoles to the potential function of the elastic terms and estimated their constants from measured vibrational frequencies of simple polyatomic molecules up to six atoms. For example, in the case of triatomic molecules such interaction was found to be much smaller than the elastic term in the case of linear molecules like CO_2, whereas the dipolar interaction had stabilization effect in the case of hydrides like H_2O and their magnitude was fairly large.

Although he made great success in the detailed analysis of rovibrational spectra of simple polyatomic molecules in the gas phase, the method is limited to small molecules as the rotational lines are not resolved even in the overtone and combination bands for larger molecules and completely absent in the liquid phase. However it was possible to discuss the position and shape of these near-infrared bands and he focused on the overtone bands of the CH stretching modes to study the effect of the neighboring group or resonance effect on their position and intensity, which are expected to be enhanced in the overtone compared to the fundamental bands.[46] The overtone bands of CH stretching mode were largely altered by the bond order (single, double or triple) of the carbon atom on which the CH unit is attached. Intensity of the CH overtone band of halogen-substituted alkanes was approximately proportional to the number of hydrogen atoms but the changes in the band position and their shape were did not allow simple interpretation. He developed his theory of interacting local valence vibrations for perturbative calculation of anharmonic vibrational frequencies and

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[43] K. Hedfed, R. Mecke, *Z. Physik* **64**, 151; W. H. J. Childs, R. Mecke, **64**, 162; R. Mecke, **64**, 173 (1930).

[44] Mecke (note 28).

[45] R. Mecke, *Z. Phys. Chem.* **B16**, 409; 421; **B17**, 1 (1932).

[46] R. Mecke, *Angew. Chem.* **48**, 320 (1935).

absorption intensity of the overtone bands and estimated bond dipole from the observed band intensity.[47] He also developed a general scheme for polyatomic molecules containing the same atomic groups such as hydrocarbons by second order perturbation theory and derived equations of coupling constants.[48] However, its practical application seems to be unpublished. Anyway, they were developed mostly within the harmonic approximation and did not go into treatment of vibration-rotation interaction or other higher order interactions as developed by theorists in the United States.

Conclusion

In this study I tried to describe the development of vibrational spectroscopy in Germany in 1930s. Although it is less known than the development in the United States, German scientists were active in this field in early 30s and their achievements were characterised by their efforts towards systematic understanding of the more complex organic molecules. Following studies are expected to clarify the relevance of these characteristics to the emergence of molecular science in Japan in 1930s as represented by the research by Mizushima and his coworkers on the rotational isomerism.

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[47] R. Mecke, *Z. Physik* **99**, 217 (1935).

[48] R. Mecke, *Z. Physik* **104**, 291 (1936).

From Fuel Chemistry to Quantum Chemistry: Kenichi Fukui and the Rise of the Kyoto School[1]

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Kenichi Fukui (1918–1998) was the first Japanese Nobel laureate in chemistry. He received the 1981 Nobel Prize for his frontier orbital theory, which clarified the mechanism and course of chemical reactions in terms of quantum mechanics. Roald Hoffmann who developed the principle of the conservation of orbital symmetry or the so-called "Woodward-Hoffmann rule" shared the award. Their joint award was the third Nobel Prize in the field of quantum chemistry, following the award received by Linus Pauling (1954) and Robert Mulliken (1966).

The frontier orbital theory is considered by many chemists to be one of the most important conceptual advances in the 1950s in the field of chemical sciences.[2] Despite its historical significance, the literature on the history of quantum chemistry has long been silent about Fukui and his work. Kostas Gavrogru and Anna Simões' recent book, *Neither Physics Nor Chemistry: A History of Quantum Chemistry* (2012)*,* deals with the history of quantum chemistry from the 1920s to the 1970s, but contains no mention of Fukui at all.[3] Today, I would like to talk about Fukui and his quantum chemistry from one perspective, namely, the rise of pure science in an applied academic setting.

When Fukui was awarded the Nobel Prize, there was some confusion about his professional identity among Western media and the people in the scientific realm. *Chemical and Engineering News* erroneously described him as a physics professor of Kyoto University.[4] In addition, the secretary of the Royal Swedish Academy asked whether Fukui was a student of Hideki Yukawa (1907–1981), Japan's first Nobel laureate in physics.[5] Yukawa was a physics professor in Kyoto University, but Fukui was not his disciple.

The confusion seems to have sprung due to the gap between affiliation and accomplishment. Throughout his long career, Fukui belonged to the Faculty of Engineering in Kyoto University, and not the Faculty of Science, which had both the chemistry department and the physics department. He was a professor in the Department of Fuel Chemistry. With this background, why was Fukui able to pursue pure science like quantum chemistry in such a strongly applied academic setting? How could he have established a world-renowned research school of theoretical chemistry there?

James Barthoromew has provided one answer to these questions.[6] In his paper,

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[1] Some aspects of this paper have been discussed in Yasu Furukawa, "Nenryo-kagaku kara ryoshi-kagaku e: Fukui Kenichi to Kyoto gakuha no mohitotu no tenkai (From Fuel Chemistry to Quantum Chemistry: Kenichi Fukui and a New Development of the Kyoto School)," *Kagakushi*, vol.41 (2014): 181–233.

[2] *E.g.*, Scott A. Davis, "Kenichi Fukui, 1981," in Frank N. Magill, ed., *The Nobel Prize Winners*, vol.3: *Chemistry* (Pasadena, CA: Salem Press, 1990), pp. 1061–1067, on p.1063.

[3] Kostas Gavrogru and Ana Simões, *Neither Physics nor Chemistry: A History of Quantum Chemistry* (Cambridge, Massachusetts: The MIT Press, 2012). E. Thomas Strom and Angela K. Wilson, eds., *Pioneers of Quantum Chemistry* (Washington, D.C.: American Chemical Society, 2013) mentions Fukui's name only once.

[4] "Five Win Nobels for Chemistry, Physics," *Chemical and Engineering News*, vol.59, no.43 (1981): 6–7, on p. 6.

[5] *Fukui Kenichi hakase kinenn gyouji kiroku-shu* (Record of the Dr. Keniichi Fukui Memorial Ceremony) (Kyoto University, 1998), p.7.

[6] James Bartholomew, "Perspectives on Science and Technology in Japan: The Career of Fukui Ken'ichi," *Historia Scientiarum*, Vol.4 (1994): 47–54.

"Perspectives on Science and Technology in Japan: The Career of Fukui Ken'ichi," he relates the case of Fukui to Japan's unique historical experience with modern science and technology. In the West, the tendency to stress the distinctions between science and technology has been very strong. By contrast, from the Meiji Restoration period in 1868 onward, the Japanese have adopted Western science and technology as one unified field of research, without considering the difference between the two cognitive domains.

This way of thinking has affected Japan's institutional systems. For example, the University of Tokyo, founded in 1877, taught several engineering specialties, together with physics, mathematics, and chemistry in a single unit prior to the establishment of separate faculties in 1885. Fukui's institution, Kyoto University, was founded in 1897. It, too, made do with a single Faculty of Science and Engineering during its formative years. In 1913, the original faculty was made into two separate faculties: the Faculty of Science and the Faculty of Engineering. In Japan's universities, the Engineering Faculty often received more funds than the Science Faculty. As Bartholomew states, "Fukui was materially better off in the Faculty of Engineering than he might have been in the Faculty of Science."[7] Given this background, it is not surprising that a pure scientist like Fukui emerged from Japan's Engineering Faculty.

However, if this thesis stands good, the same could also be said about the engineering faculties in Japan's other universities (including Tokyo, Tohoku, Kyushu, Hokkaido, Osaka, and Nagoya). In reality, the case of Fukui is exceptional. The University of Tokyo, for example, produced a few talented quantum chemists before World War II. They were either from the Department of Physics (*e.g.*, Masao Kotani) or the Department of Chemistry (*e.g.*, San-ichiro Mizushima) in the Faculty of Science. Chemists of Tokyo's large Department of Applied Chemistry in the Faculty of Engineering were probably materially better off than those of the Department of Chemistry in the Faculty of Science. However, no quantum chemists had come from the Department of Applied Chemistry.

To answer the above questions, then, it is essential to look into Fukui's own talent and career as well as the peculiar environment in which he pursued quantum chemistry.

The Making of a Domestic Quantum Chemist

Unlike earlier generations of Japanese scientists, Fukui had no opportunities to study abroad, as his student days and early career in chemistry concurred with the wartime. He later labeled himself as a purely domestic scholar.[8]

Fukui was born in 1918 in Nara, a province nearby Kyoto. As a high school student, Fukui's interest turned to mathematics and physics. He favored mathematics, because of its logical rigor and simplicity. By contrast, he disliked chemistry as it appeared to him as too empirical, nonmathematical, and far from theoretical. He thought of enrolling in the Faculty of Science at Kyoto Imperial University (renamed Kyoto University in 1947) and to major in physics. However, when it was time for him to enter the university in 1938, he applied and was accepted to the Department of Industrial Chemistry in Kyoto's Engineering Faculty instead. This department dealt with very practical subjects, like fibers, rubber, coal, petroleum, and plastics. His decision was based on advice he had received from Gen-itsu

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[7] *Ibid.*, p. 52.
[8] Kenichi Fukui, "Wastashi no rirekisho (My Curriculum Vitae)," *Watashi no rirekisho: kagaku no kyudosha* (My Curriculum Vitae: Seekers of Science)(Tokyo: Nikkei shinbun-sha, 2007), 119−226, on p.171. On Fukui, see also Kenichi Fukui, *Gakumon no sozo* (Creation of Scholarship), (Tokyo: Kosei shuppan-sha, 1984);Tokio Yamabe, ed., *Kagaku to watashi* (Chemistry and I) (Kyoto: Kagaku dojin, 1982); Teijiro Yonezawa and Chikayoshi Nagata, eds., *Noberu-sho no shuhen: Fukui Kenichi hakase to Kyoto daigaku no jiyu na gakufu* (The Surroundings of Nobel Prize: Dr. Kenichi Fukui and the Liberal Academic Style of Kyoto University), (Kyoto: Kagaku-dojin, 1999); and James B. Bartholomew, "Fukui, Ken'ichi," *New Dictionary of Scientific Biography*, ed. by Noretta Koertge, vol. 3 (Detroit: Thomson Gale, 2007), pp. 85–89.

Kita (1883–1952), a distant relative and lifelong mentor who impressed him greatly. Fukui sensed Kita's insight that chemistry would become based more and more on physics and mathematics. His insight about the future of chemistry proved correct.

Kita had built up a tradition that stressed the importance of basic research in applied chemistry in the Faculty of Engineering at Kyoto Imperial University.[9] He graduated from the Department of Applied Chemistry in Tokyo Imperial University in 1906. Right after his graduation, he served there as an associate professor for nine years. However, due to a conflict with his boss and his discontent with the department's practically-oriented teaching program, he left Tokyo for Kyoto in 1916. He maintained a sense of rivalry against Tokyo Imperial University. At Kyoto Imperial University's newly created Department of Industrial Chemistry, Kita realized his educational ideal, which stressed pure chemistry as the basis for applied chemistry.

During Fukui's undergraduate days, students of industrial chemistry were required to take courses in basic chemistry such as organic chemistry, inorganic chemistry, and physical chemistry in the Department of Chemistry of the Faculty of Science. The applied chemistry building was located next to the pure chemistry building. This geographical setting helped promote exchange between the two departments. This setting was in contrast with the setting at Tokyo Imperial University where the department of pure chemistry and the department of applied chemistry were separated both geographically and institutionally.

Aware of Fukui's distinct talent for mathematics, Kita further encouraged the undergraduate to learn fundamental science beyond chemistry. Fukui chose to study physics and to focus on quantum mechanics as a newly emerging fundamental science during that time. At that period, quantum mechanics was not taught even in the physics department. Fukui enjoyed teaching himself the subject by reading Erwin Schrödinger's famous papers in *Annalen der Physik*[10] as well as books such *as Handbuch der Physik* from the library of the Physics Department. He also read *Einführung in die Quantenchemie*, one of the earliest textbooks on quantum chemistry written by the exiled German scientist, Hans Hellmann[11]. Now, Fukui was convinced that quantum mechanics was a powerful means of mathematizing and theorizing chemistry. He also believed that it could be used in diminishing the empirical traits of chemistry. Fukui later recalled that the liberal atmosphere in Kyoto had a profound influence on his ideas.[12]

Fukui worked on his senior thesis under the guidance of Haruo Shingu (1913–1988), a young associate professor. The experimental study assigned to Fukui was the synthesis of isooctane which was used for raising the octane number of aircraft fuel. This experience aroused his interest in the chemical reaction of paraffinic hydrocarbons.

During this time, Fukui encountered Shingu's Japanese translation of Erick Hückel's famous lecture on the significance of the new quantum theory for chemistry.[13] The translation was published in a faculty bulletin. Hückle had delivered that lecture at the National Meeting of German Chemists which was held in Münich in 1936. In this lecture,

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[9] Yasu Furukawa, "Kita Genitsu to Kyoto gakuha no keisei (Genitsu Kita and Kyoto School's Formation)," *Kagakushi*, vol.35 (2010): 1–17.

[10] E. Schrödinger, "Quantiesierung als Eigenwertproblem (Erste Mitteilung)," *Annalen der Physik*, ser.4, 79 (1926): 361–376; *idem*., "Quantiesierung als Eigenwertproblem (Zweite Mitteilung)," *ibid*., 4, 79 (1926): 489–527; *idem*., "Quantiesierung als Eigenwertproblem (Dritte Mitteilung: Störungstheorie, mit Anwendung auf den Starkeffekt der Balmerlinien)," *ibid*., 4, 80 (1926): 437–490; *idem*., "Quantiesierung als Eigenwertproblem (Vierte Mitteilung)," *ibid*., 4, 81 (1926): 109–139.

[11] Hans Hellmann, *Einführing in die Quantenchemie* (Leipzig und Wien: Deuticke, 1937).

[12] "Science and Technology in Japan," *New Scientist*, 21 March 1985, 30–35, on p. 31.

[13] E. Hückel, "Shin ryoshi rikigaku no kagaku ni taisusru imi," trans. By Haruo Shingu, *Kagaku Hyoron*, Vol.3, No.3 (1938) : 115–121 ; Erich Hückel, "Die Bedeutung der neuen Quantentheorie für die Chemie," *Zeitschrift für die Chemie*, Bd.42, Nr.9 (1936): 657–662.

Hückel stated that there was a big gap between theoretical physicists and organic chemists. He said that the former should know more about actual chemistry, while the latter should learn more about new quantum mechanics. He also said that each group should apply then their specialized knowledge in their field. In all likelihood, Fukui was encouraged by this lecture. He wished to bridge the gap between theoretical physicists and organic chemists as an applied chemist.

In 1939, during Fukui's sophomore year, the Department of Fuel Chemistry was created as an expansion of the Department of Industrial Chemistry. At this time, Kita, who became its first chair, directed a large national project of synthetic fuel based on the Fischer-Tropsch method. As a graduate student, Fukui studied under Shinjiro Kodama (1906–1996), another loyal protégé of Kita, in the Department of Fuel Chemistry. Kodama had studied at the Kaiser Wilhelm Institute for Physical Chemistry and Electrochemistry in Berlin in the early 1930s. There, he was influenced by Michel Polanyi who asked him to learn the quantum theory to be able to conduct chemical research.[14] Back in Kyoto, Kodama proposed that Kita hire a physicist who would teach mathematics and quantum mechanics to applied chemistry students. Consequently, the theoretical physicist Gentaro Araki (1902-1980) was employed as a fulltime professor in the applied chemistry section of the Engineering Faculty, an appointment that surprised Japan's chemical community. Kita and Kodama thus created a unique environment that would encourage Fukui's research in quantum chemistry.

The Frontier Orbital Theory

Thanks to Kita and Kodama's arrangements, Fukui was exempted from the military draft during the war. Instead, he was allocated to engage in the Army Fuel Laboratory in Tokyo. There, he joined wartime research on the synthesis of gasoline additives from butanol (made by the fermentation of sugar), which aroused his deep interest in the reaction of olefinic hydrocarbon compounds. Aside from laboratory work, he was fortunate to spare ample time reading English and German books on quantum physics in the laboratory's well-equipped library.

In 1945, shortly before the end of the war, Fukui became an associate professor of fuel chemistry in Kyoto. One characteristic of the Japanese national university system was the *koza* system. *Koza* is a teaching and research unit consisting of a fixed hierarchy of one full professor, one associate professor, and one or two assistants. The inflexibility of the system sometimes caused problems, but the professor there at the time encouraged Fukui to work on his own research. As Fukui recalled, "Being allowed to be independent and pursue my own work at an early age was a major reason I could become what I am."[15] In 1951, while he was in his early thirties, he was promoted to full professor. Now, he has gained more administrative power.

While teaching applied subjects such as fuel engineering and industrial physical chemistry, he focused his investigative efforts on his long-cherished study: the quantum-mechanical understanding of the chemical reactions of hydrocarbon compounds. His interest in reactions was in contrast to Mizushima's group of theoretical chemistry at Tokyo University where the molecular structure was the main focus of research.[16]

Shingu helped Fukui to recognize the limits of the then dominant electronic theory of organic reactions, the theory developed by the English chemists Robert Robinson and Christopher Ingold. Fukui chose familiar aromatic hydrocarbons as the first object of his

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[14] Shinjiro Kodama, *Kenkyu kaihatsu eno michi* (The Path to Research and Development) (Tokyo: Tokyo kagaku dojin, 1978).

[15] "Science and Technology in Japan" (note 12), p.31.

[16] Mizushima's students at Tokyo's Department of Chemistry included Yonezo Morino and Saburo Nagakura.

investigation. The reactivity of naphthalene, for example, could not be sufficiently explained by the Robinson-Ingold electronic theory. The electrophilic substitution in the naphthalene molecule （like the nitration） predominantly yields α-substituted-derivatives. The reason behind this phenomenon was not clear.

Like other quantum chemists, Fukui considered the electron to be the critical entity in chemical reactions. He adopted the molecular orbital approach developed by Hückle and others. However, he "tried to attack this problem in a way that was at that time slightly unusual."[17] Fukui assumed that the molecular orbital with the highest energy level should play a crucial role in chemical reactions. Using the molecular orbital method, he manually calculated the electron density of the naphthalene molecule and found that the density was largest at the position of α where a chemical reaction took place. With the help of his graduate student Teijiro Yonezawa (1923-2008), he proceeded to calculate by using a mecahnical calculator the density of more complex hydrocarbons such as anthracene, pyrene, and perylene one by one. They found that his initial assumption perfectly coincided with empirical data. He recalled that to his surprise, no one else had ever conceived of such a simple mechanism.[18]

In 1952 Fukui began publishing a series of papers on the frontier orbital theory of reactions in the *Journal of Chemical Physics*.[19] There, he went on to propose that the highest occupied molecular orbital (HOMO) of one reactant and the lowest unoccupied molecular orbital (LUMO) of the other play a dominant role in chemical reactions. These two particular orbitals were referred to as frontier orbitals. He argued that the progress of a reaction depends on the geometries and relative energies of the HOMO and the LUMO frontier orbitals. During the 1950s and early 1960s, Fukui and his coworkers continued to refine and extend his theory.

Initially, the frontier orbital theory was either ignored or attacked. Its highly mathematical expressions were beyond the comprehension of many organic chemists of the time. To those who had been working in the forefront of quantum chemistry, Fukui was totally a stranger. His theory received critical comments from theoretical chemists, such as Harry Greenwood, the Pullmans, and Raymond Daudel, who, by and large, regarded the theory as too simplistic and extravagant.[20] In due course, however, Fukui's theory was supported by Robert Mulliken's work on the charge transfer theory and most importantly by the appearance of Woodward and Hoffmann's paper on the conservation of orbital symmetry in 1965.[21] I will not go into detail about what followed, as these will be discussed by other speakers including Professors Buhm Soon Park and Noboru Hirota.

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[17] Kenichi Fukui, "The Role of Frontier Orbitals in Chemical Reactions," Nobel Lecture, December 8, 1981, p.10. http://www.nobelprize.org/nobel_prizes/chemistry/laureates/1981/fukui-lecture.pdf

[18] Kosaku Kamio, "Fukui Kenichi sensei no omoide (My Memories of Professor Kenichi Fukui)," http://www.gijuturyoku.com/doc/doc11.html.

[19] Kenichi Fukui, Teijiro Yonezawa, and Haruo Shingu, "A Molecular Orbital Theory of Reactivity in Aromatic Hydrocarbons," *Journal of Chemical Physics*, 20 (1952):722–725; Kenichi Fukui, Teijiro Yonezawa, Chikayoshi Nagata, and Haruo Shingu, "Molecular Orbital Theory of Orientation in Aromatic, Heteroaromatic, and Other Conjugated Molecules," *Journal of Chemical Physics*, 22 (1954): 1433–1442.

[20] H. H. Greenwood, "Molecular Orbital Theory of Reactivity in Aromatic Hydrocarbons," *Journal Chemical Physics,* 20 (1952): 1653; *idem*., "Some Comments on the Frontier Orbital Theory of the Reactions of Conjugated Molecules," *ibid*., 23 (1955): 756–757; Kenichi Fukui, "A Simple Quantum-Theoretical Interpretation of the Chemical Reactivity of Organic Compounds," in P.-O. Löwdin, B. Pullman eds., *Molecular Orbitals in Chemistry, Physics, and Biology* (New York: Academic Press, 1964), pp. 513–537.

[21] Robert S. Mulliken, "Molecular Compounds and their Spectra. II," *Journal of the American Chemical Society*, 74(1952): 811–824; *idem*., "Molecular Compounds and Their Spectra. III. The Interaction of Electron Donors and Acceptors," *Journal of Physical Chemistry,* 56 (1952): 801–822; R.B. Woodward and Roald Hoffmann, "Stereochemistry of Electrocyclic Reactions," *Journal of the American Chemical Society*, 87 (1965): 395–397.

Maintaining Theoretical Chemistry in an Applied Setting

Kita died in 1952, and Kodama left Kyoto for Sumitomo Chemical Company in 1957. Now, Fukui was in a position to continue the academic tradition of his department. In 1966, the Department of Fuel Chemistry was renamed the Department of *sekiyu kagaku* which literally means petroleum chemistry. However, at Shingu's strong suggestion, the official English name was translated into the "Department of Hydrocarbon Chemistry." In the Faculty of Engineering, Fukui was tactful enough to maintain his circle of quantum chemistry in his *koza*. He managed a laboratory where his associate professor and assistants worked on conventional experimental studies on fuel-related practical subjects, such as catalysis, polymerization, and organic syntheses, while a select group of theoretical chemists focused on the expansion of his frontier orbital theory. That is to say that his *koza* consisted of two sections: experimental section and theoretical section.

Fukui, together with his coworkers, published 466 papers. Of these, about 60 % stemmed from the theoretical section, while the rest stemmed from the experimental section.[22] The experimental section filed nearly 200 patents with Fukui's name as one of the applicants. Through the experimental section, Fukui kept a good connection with industrial firms such as Sumitomo, which provided his *koza* with financial support. The study of the experimental section had nothing to do with quantum chemistry. Fukui needed the experimental section not to support or verify his frontier orbital theory, but to keep his theoretical section alive in a practical academic setting. That was a pragmatic way of *koza* management. He also encouraged his students to work first at the experimental section before entering the theoretical section, because he believed that theoretical chemists should have actual chemical experiences. As a number of quantum chemists and computational chemists emerged from the theoretical section, the Fukui school of theoretical chemistry flourished in Kyoto's Engineering Faculty.

Conclusions

In Fukui, we see the inquisitive mind of an experimental chemist, the intuitive faculty of a theoretician and mathematician, and the pragmatic mindset of an engineer. As Roald Hoffmann put it, "The building of a career in an applied setting was, I believe, crucial—it sensitized Fukui to problems of real chemical reactivity. In this he had an advantage over his 'purer' theoretician colleagues."[23] Fukui recalled that had he been a physicist in a physics department, he could not have done such a prize-winning work in quantum chemistry.[24] He acquainted himself with real chemical problems more than any theoretical physicists. Unlike many other applied chemists, he was well versed in mathematics and theoretical physics. Reciprocal intellectual stimuli between theoretical physics and chemical practices profoundly enhanced his scientific creativity.

Fukui succeeded in quantum chemistry because he stayed not in the Faculty of Science but in a strongly applied setting in the Engineering Faculty. Perhaps, Fukui was indeed materially better off in the Engineering Faculty than he might have been in the Science Faculty. Had he stayed at the Engineering Faculty in Tokyo University or somewhere else, he could not have done what he did at Kyoto. It was the unique tradition created by Kita and Kodama that nurtured him as a successful quantum chemist. How useful quantum chemistry was for fuel chemistry was not material to Fukui and his followers. Taking over that unique tradition, Kenichi Fukui skillfully founded a research school of quantum chemistry in Kyoto's Engineering Faculty in the 1960s.

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[22] Taken from SciFinder.

[23] Roald Hoffmann, "Obituary: Kenichi Fukui (1918–98)," *Nature*, 391 (19 February 1998): 750.

[24] Fukui, *Gakumon no sozo* (note 8), p. 114.

Physical Methods in the Twentieth Century
Between Disciplines and Cultures

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Introduction

This paper aims at contributing to the history of a type of science that focuses on the development and dissemination of research methods.[1] Although, as I will argue, the 'making of methods' is a crucial and widespread activity in twentieth-century science, it is not well represented in its historiography.[2] Similarly to research technologists,[3] 'method makers' are invisible because they represent hybrid, or interstitial, careers, respectively activities. Moreover, we may be blinded by one of the myths of science, according to which it is the solution of problems that counts as the true, and sometimes only, activity of scientists. The development of methods is, thus, just an intermediate step in the process of scientific research. By and large, these intermediate steps are forgotten, or suppressed, in both scientific and historiographical accounts.

In mid-twentieth century, I will argue, a novel socio-epistemic field of scientists focusing on the development of research methods came into existence, connecting instrument manufacturers, academic disciplines and professions, and governmental science funding agencies. Three relationships are best suited to characterize the socio-epistemic field of the 'method makers.' First, their relations inside academic disciplines and research fields. The basis for this is the research practice, most notably the influence of high-tech instrumentation on experiments and data management. Second, the academic-industrial partnership, most importantly that of academic scientists with industrial instrument manufacturers. Third, the impact of science funding, and the special relations of method makers with the relevant agencies. In historiographical and sociological research, these three layers, or strands, are largely disconnected. For the first, it is the new experimentalism and laboratory studies; for the second studies of the so-called science-based industry; for the third work about policy and governance. Some notions, such as triple helix, mode 2 and technoscience, are designed to connect these layers. The historian and sociologist of science, Terry Shinn, attempts to connect them as well with his notion of a transversal regime. According to Shinn, recent science is characterized by a plurality of contexts of applications, connected through the transfer of research technologies.[4] However, the ways how research technologies are transferred are in need of further elucidation. Thus, my paper will aim to identify and to characterize a socio-epistemic structure that allows us to better understand these transfers and their working modes.

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[1] This paper is based on Carsten Reinhardt, "Forschungstechnologien im 20. Jahrhundert. Transfer und Transformationen," in: Klaus Hentschel, ed., *Zur Geschichte von Forschungstechnologien. Generizität – Interstitialität – Transfer*, Diepholz: GNT-Verlag 2012, pp. 277-307.

[2] But see Patricia Nevers, Raimund Hasse, Rainer Hohlfeld, Walther Zimmerli, "Mediating Between Plant Science and Plant Breeding: The Role of Research Technology," in: Bernward Joerges, Terry Shinn, eds., *Instrumentation Between Science, State and Industry*, Dordrecht: Kluwer Academic Publishers 2001, pp. 97-118.

[3] Terry Shinn, "The Triple Helix and New Production of Knowledge: Prepackaged Thinking on Science and Technology," *Social Studies of Science* 32/4 (2002), 599-614.

[4] Terry Shinn, "New Sources of Radical Innovation. Research Technologies, Transversality, and Distributed Learning in a Post-industrial Order," in Jerald Hage, Marius Meeus, eds., *Innovation, Science, and Institutional Change*, Oxford: Oxford University Press 2006, pp. 313-333; Terry Shinn, Pascal Ragouet, *Controverses sur la science. Pour une sociologie transversaliste de l'activité scientifique*, Paris 2005.

Still today, the development of methods is marginalized in science. An example is the editorial of a new journal, *Nature Methods*, in 2004. Titled "Methods for Methods' Sake", the editorial laments the neglect of the coverage of methods development in 'regular' journals.[5] However, and in stark contrast to this neglect, the impact of methods development on science is huge: 'method makers' work with and on all kinds of research instrumentation, ranging from big science to table-top instruments. They interact with a multitude of groups of scientists (their 'clientele') in different disciplines, and they have close cooperations with industrial instrument manufacturers. Many of their activities rest on the standardization and commercialization of research instrumentation that can be used by large groups of scientists in academia, government, and industry.

To scrutinize the field of method makers, I use Pierre Bourdieu's concepts of habitus and field.[6] Each (scientific) field generates social structures, and these are governed by the distribution of symbolic capital. The command over research methods, and the ruling over their accurate and justified use, is one of the possibilities for scientific actors to change the rules of the game for the acquisition of symbolic capital. (There are others, of course, as well.) Thus, method makers have a unique access to power in a scientific field, and can be easily regarded as subversive by the establishment.[7] Access to research methods can lead directly to scientific reputation. With regard to Bourdieu's phrase that the clients of scientists are their competitors as well (because the use of scientific knowledge is in the further development of it), we note an interesting exception: method makers are only indirectly the competitors of their clients, because they work for the use and dissemination of their methods and they intrude into problem solving only insofar as this is needed to prove the usefulness and impact of the method in question. The users (clients), moreover, have an interest in receiving ready-to-use, routine research methods and welcome an occasional intrusion with regard to high-end problem solving. This may be regarded as a win-win situation. In consequence, we will need to ask if the method makers generate their own scientific-technical field, and to what extent they are able to establish their autonomy with regard to their users. Moreover, we may ask if this represents an 'internal periphery,' as the constitutive industrial and governmental relations, which are normally seen as exogenous, now play an endogenous role, as they are included in the field.

1. Methods of isolation, identification, and interpretation

In order to establish my case, I wish to address a conglomerate of research technologies that increasingly gained momentum in the twentieth century. Many mid-size instruments used in physics, biology, chemistry, medicine and engineering can be differentiated into methods of isolation, identification, and interpretation. The first class, or family, of instruments serves the separation and purification of materials. Noteworthy are the chromatographic techniques, but also electrophoresis and the ultracentrifuge. Next come the detecting techniques, most notably the spectroscopies. Of course, isolation normally entails identification, and spectroscopy works without isolation in many cases. But often these two classes are not competing, but coupled and work in tandem. The third class is that of interpretation, and I refer to the

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[5] "Methods for Methods' Sake," Editorial, *Nature Methods* 1 (2004), 1.

[6] Pierre Bourdieu, *Vom Gebrauch der Wissenschaft. Für eine klinische Soziologie des wissenschaftlichen Feldes*, Konstanz: UVK Universitätsverlag 1998; Carsten Reinhardt: "Habitus, Hierarchien und Methoden. 'Feine Unterschiede' zwischen Physik und Chemie," *N.T.M.* 19 (2011), 125-146.

[7] Carsten Reinhardt, "Zentrale einer Wissenschaft. Methoden, Hierarchie und die Organisation der chemischen Institute," in Rüdiger vom Bruch, Heinz-Elmar Tenorth, eds., *Geschichte der Universität Unter den Linden 1810-2010. Biographie einer Institution, Praxis ihrer Disziplinen*, volume 5, *Transformation der Wissensordnung. Verwissenschaftlichung der Gesellschaft und Verstaatlichung der Wissenschaft*, Berlin: Akademie Verlag 2010, pp. 575-603.

computer, and algorithms. Most visibly this is the case with the applications of artificial intelligence,[8] but there are many more cases. Access to all of these functions is of crucial importance for any researcher, and often these methods establish a large part of the identity in a discipline.[9] On the epistemic level, changes in the three classes, or families, of research methods contributed to the expansion, and partial transformation, of structural thinking in the relevant scientific disciplines during the twentieth century. The 'mental model' of thinking in molecular structures [10] expanded into biology, physics, and later into nanotechnology, materials science and others. Alongside with this epistemic development, the emergence of a new type of scientist, that of a method-based expert, or specialist, can be traced. The following model of method-based expertise will explain, to a certain extent, how method makers could connect academic science, industrial manufacturing, and governmental policy.

2. Method-based expertise

'Normally,' scientists search for methods that can be used to solve problems, which are in turn established by theories or applications. Method makers, in contrast, search for problems that are ready to be solved with their newest method at hand. My hypothesis, in a nutshell, is that in mid-twentieth century a division of labor between these two intertwined parts of scientific practice took place. Specialists for the development and use of instruments, and the related development of suitable methods complemented problem-solving researchers. I have analyzed their relation with the model of expertise,[11] and would like to add here that Bourdieu's field model enables us to understand the possibilities for respective gains in symbolic capital, for both sides at the same time.

It would be expected that the introduction of a whole new set of experimental methods for isolation, identification and interpretation into so many disciplines and sub-disciplines would have resulted in an overthrowing of traditional hierarchies inside disciplines. However, the novel methods did not completely change the power structures in the scientific field, though they crucially influenced its course and structure, and they institutionalized new relationships between scientists. An often-used term for the relevant interactions is scientific cooperation,[12] and we see here that in the 1960s, the cooperation between method makers and their clients was institutionalized. An important case is that of the *facilities* or *special research resources* of the U.S. National Institutes of Health (NIH).[13] In 1977, 52 centers were in use in the U.S., with a range from computers to spectroscopies and imaging technologies. NIH introduced the categories of service, training, cooperation, and core research to characterize the functions of the centers. This enabled the scientists in charge of these special research resources (almost always placed at major research universities) to establish their specialty while at the same time influencing, and catering for, a scientific field. At the same time, most chemistry departments at universities expanded their analytical laboratories into

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[8] Carsten Reinhardt, *Shifting and Rearranging. Physical Methods and the Transformation of Modern Chemistry*, Sagamore Beach, Mass.: Science History Publications 2006, chapter 5.

[9] Mary-Jo Nye, *From Chemical Philosophy to Theoretical Chemistry. Dynamics of Matter and Dynamics of Disciplines, 1800-1950,* Berkeley: University of California Press 1994.

[10] Thomas Steinhauser, *Zukunftsmaschinen in der Chemie. Kernmagnetische Resonanz bis 1980,* Frankfurt am Main: Lang Verlag 2012.

[11] Carsten Reinhardt, "Expertise in Methods, Methods of Expertise," in Martin Carrier, Alfred Nordmann, eds., *Science in the Context of Application* (Boston Studies in the Philosophy of Science 274), Dordrecht: Springer 2011, pp. 143-159.

[12] Jane Maienschein, "Why Collaborate?" *Journal of the History of Biology* 26 (1993), 167-183; Ivan Chompalov, Joel Genuth, Wesley Shrum, "The Organization of Scientific Collaborations," *Research Policy* 31 (2002), 749–767.

[13] Carsten Reinhardt, "Wissenstransfer durch Zentrenbildung. Physikalische Methoden in der Chemie und den Biowissenschaften," *Berichte zur Wissenschaftsgeschichte* 29 (2006), 224-242.

service laboratories in charge of acquiring, maintaining, and developing an ever-growing array of instruments and techniques.[14]

For saving resources, instruments were often shared, and this cost-saving argument played a large role in the establishment, and maintenance, of regional and national centers. At the same time, however, some of the new methods were performing so well, and so efficiently, that their capacity exceeded the abilities of a single small research group to come up with interesting problems. Thus, the (technical) performance in data acquisition and interpretation contributed to driving the establishment of centers, and it led to more and more collaborative (research) projects. At the same time, the sharing of the instrument was closely connected to teaching, and training.

For all concerned, centers of various sizes constituted a win-win situation. Method makers (scientists) gained access to relevant communities of users/clients in scientific disciplines. Instrument manufacturers generated a market for their instruments. Science funding agencies could point to driving scientific progress while at the same time having economic impact and acting with cost-efficiency in mind. For the clientele of scientists in academia and industry, this arrangement constituted the right distance to the development of novel methods. Interestingly, we can observe an analogous development in medicine at the same time. As Stuart Blume has analyzed, radiologists formed a similar community standing between the clinic and the medical device manufacturers. In this case, the different size of the industry (multinationals), and the different economics involved led Blume to coin the phrase of the *medical-industrial complex*.[15] In both cases, the question of governing modes requires attention.

3. Research or innovation? The regulation of research methods

In January 1957, members of the *Divisional Committee of Mathematical, Physical and Engineering Sciences* of the National Science Foundation (NSF) opined that the new research technologies challenged the established means of science funding:

 "Effective as it is, the research grants program is able to supply only the most modest of the scientists' needs for research equipment. Much can still be done with test tubes, slide rule, paper and pencil, but there is now convincing evidence that great scientific discoveries are to be expected through the development and use of the expensive new tools of scientific research. The necessary funds to provide such equipment are not now available."[16]

But money alone wasn't the problem. The question was the distribution of funds. The tools of big science, such as particle accelerators, research ships and observatories, required special programs, just because of their sheer size and cost. "Research apparatus for infrared, ultraviolet, Raman, mass, and nuclear magnetic resonance spectra and for many other uses," however, was a category that normally had been integrated into research projects and their funding. To find a solution of this bottleneck was an urgent task: "Practically all areas of the

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[14] Pierre Laszlo, "Tools, Instruments and Concepts. The Influence of the Second Chemical Revolution," in Peter J. T. Morris, ed., *From Classical to Modern Chemistry*, Cambridge: Royal Society of Chemistry 2002, pp. 171-187.

[15] Stuart S. Blume, *Insight and Industry. On the Dynamics of Technological Change in Medicine*, Cambridge, Mass.: MIT Press 1992; Carsten Timmermann, Julie Anderson, eds., *Devices and Designs. Medical Technologies in Historical Perspective*, Houndmills: Palgrave Macmillan 2006; Stefan Timmermans, Marc Berg, "The Practice of Medical Technology," *Sociology of Health and Illness* 25 (2003), 97-114.

[16] National Science Foundation (NSF), MPE Divisional Committee, Chairman Thomas K. Sherwood to Bronk and Waterman, 21 January 1957. National Archives Record Administration (NARA), RG 307, Office of the Director, General Records, 1949-63, 1960-61, Box 48, folder Division of M, P, and ES.

physical and biological sciences are characterized today by an accelerating development of instrumental techniques permitting types of measurements and precisions which were not known a few decades ago. (...) As the pace of scientific advancement quickens, the amount and quality of research that is performed in some areas is limited by the sheer expense of such instruments."[17]

For chemistry, NSF in 1957 established a program to specifically support "research instruments."[18] In the 1960s, it had a percentage of between 5 and 20% of all chemistry-related research projects funded by the National Science Foundation.[19] But the difference between research and equipment was never solved completely, and academic chemists had to lobby for the special role that instruments now played for their daily laboratory routine.[20] The situation was similar in the bio-medical field, when scientists claimed the establishment of instrument centers and the introduction of a "biological engineer" degree. Paul E. Klopsteg, a staff member of the National Science Foundation, in the so-called Klopsteg-Report of 1956 called for a union of physics and biology, already in education.[21] In a similar way argued members of the Biophysics and Biophysical Chemistry Study Section of the National Institutes of Health (NIH), founded in 1955. The early roots of the above-mentioned special research resources can be traced back to this period. However, until the mid 1960s the rich supply with funding through governmental agencies allowed a smoothing over the structural deficits. The economic crisis of the late 1960s then led to a cutting-back especially with regard to equipment. For example, the proportion of instruments budgets in the total funding amount of NSF and NIH decreased from 12% to 6% between 1966 and 1971.[22]

This crisis of the late 1960s threatened the supremacy of science, American style. The physicist Philip H. Abelson, president of the Carnegie Institution and editor of *Science*, wrote in 1971:

"To a large extent, American leadership in science has been based on the widespread availability of excellent instrumentation. (...) Current trends indicate that, in the future, leadership in science will be even more contingent on pioneering the use of new and increasingly powerful equipment. American scientists are fortunate in having the support of an innovative instrumentation industry that has been a by-product of federal support of research. The grants system placed considerable sums of money at the disposal of a large number of investigators who were a good market for effective apparatus."[23]

The biochemist Philip Handler, president of the National Academy of Sciences, was of the same opinion:

"Similarly, the commercial development of the electrostatic accelerator, the mass

[17] *Federal Financial Support of Physical Facilities and Major Equipment for the Conduct of Scientific Research. A Report to the Bureau of Budget*, Washington D.C: National Science Foundation, June 1957, p. 42.

[18] Jeffrey K. Stine, "Scientific Instrumentation as an Element of US Science Policy: National Science Foundation Support of Chemistry Instrumentation," in Robert Bud, Susan E. Cozzens, eds., *Invisible Connections. Instruments, Institutions, and Science*, Bellingham: SPIE Optical Engineering Press 1992, pp. 238-263, here pp. 241-242.

[19] Stine (note 18) and Appendix A of Roberts to Haworth, 13. August 1963, NARA, RG 307, NSF Office of the Director subject Files, MPS Chemistry folder, 307-75-051, box 3; NSF annual reports 1965, 66, 67, 72, 73.

[20] Stine (note 18).

[21] National Research Council, Biology Council, *Instrumentation in Bio-medical Research. Report of a Survey by Paul E. Klopsteg*, Washington D.C., 1956 (National Academy of Sciences, National Research Council Publication 472).

[22] Jeffrey K. Stine, Gregory A. Good, "Government Funding of Scientific Instrumentation. A Review of U.S. Policy Debates Since World War II," *Science, Technology and Human Values* 11 (1986), 34-46, here p. 42.

[23] Philip H. Abelson, "The Role of Scientific Instrumentation," *Science* 174 (1971), no. 4014, Editorial.

spectrometer, the nuclear-resonance spectrometer, the electron microscope, high-pressure equipment, and hundreds of other instruments, initially handmade with great travail by laboratory scientists, has permitted researchers to concentrate on the scientific questions rather than on merely reproducing research technologies already pioneered by others. The rapid commercialization of laboratory techniques and instruments has generated a new style of research in which the United States has been in the lead. It has been made possible by the quality and scale of United States research activity, the magnitude of Federal development programs, and the entrepreneurship of our industry."[24]

Here we recognize the triad of the involved institutions: Governmental science funding led to a boom in the instruments manufacturing industry, and on this the success of the scientists depended. [25] We can find this intertwinement also at the level of specific research technologies. In 1980, C.V. Shank of Bell Laboratories, one of the inventors of a dye laser applied in high-speed spectroscopy, wrote:

"It is apparent that with the freedom to develop a new dye laser instrument capable of generating very short pulses, we have been able to influence a broad range of scientific endeavors. (...) Many of the techniques which we have developed have become or are becoming commercial products. The field of the investigation of picosecond phenomena was one that began in the early 60s with a great deal of excitement and enthusiasm but interest began to wane because of the difficulty in making measurements with primitive equipment. We now see this area of picosecond phenomena beginning to show a great deal of growth with the availability of commercial equipment."[26]

Thus, method makers construed their own scientific-technical fields, using the commercial impact of their instruments. In a sense, method-makers relied two-fold on governmental research funding: First, they needed funds to develop their methods, and the related instruments. Second, they depended on the availability of resources for their scientists-clients to buy the necessary instrumentation. These resources had a substantial size. In 1982, the number of instruments at US universities in the range of 10,000 $ to 1,000,000 $ per piece was estimated to be 25,000 in the physical sciences, the computer sciences and engineering—totaling one billion US$. Chemistry had a share of 25 %, physics (without big science) 22%, engineering 33%. Approx. 50% of the instruments were older than five years, 30% older than 10. 57% of cost was paid by federal agencies, with the National Science Foundation and the Department of Defense being the biggest spenders.[27]

Since the mid 1970s, when it became clear that budget cuts would lead to an erosion of US research capabilities, scientists and members of governmental agencies attempted to stem the tide. At a meeting in March 1976, scientists asked the National Academy of Sciences

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[24] Philip Handler, *The Physical Sciences. Report of the National Science Board Submitted to the Congress*, Washington D.C.: Government Printing Office 1970, p. 24.

[25] Carsten Reinhardt, Thomas Steinhauser, "Formierung einer wissenschaftlich-technischen Gemeinschaft. NMR-Spektroskopie in der Bundesrepublik Deutschland," *N.T.M.* 16 (2008), 73-101; Steinhauser (note 10).

[26] Charles V. Shank, "The History of Subpicosecond Optical Spectroscopy," in Association of American Universities, *The Scientific Instrumentation Needs of Research Universities. A Report to the National Science Foundation*, Washington D.C., June 1980, Appendix 1, pp. 30-31, here p. 31.

[27] Kenneth Burgdorf, Kristine White, *Academic Research Equipment in the Physical and Computer Sciences and Engineering. An Analysis of Findings from Phase I of the National Survey of Academic Research Instruments and Instrumentation Needs*, Rockville: Westat Research Inc. 1984, pp. 20, 23, 28.

to lead a study addressing "the general problem of major instrumentation for chemistry and biology"[28] and in July 1976 two of the involved scientists summarized the sitiation as follows:

"One of the most important problems facing research in chemistry and biology today is the escalating sophistication, size, and associated costs of major instrumentation. (...) The performance level of these instruments is often orders of magnitude ahead of their previous state-of-the-art counterparts, and they offer unusual opportunities for major breakthroughs in many areas of research. Effective usage of some of this sophisticated instrumentation, and efficient use of instrumentation dollars may require new institutional mechanisms (i.e. cooperative efforts and facilities) for research."[29]

The speed of innovation of instrumentation, to a large degree accelerated by the very same scientists involved in the study, led to an increase in spending needs. But rarely the situation was described as bluntly as by a representative of the department of energy in 1982: "The instrumentation problem is somewhat like the balance between food supply and population in primitive societies. If a tribal group, living at the margin of survivabilty, discovers a means by which it can increase its food supply, then it begins to overpopulate and gradually finds itself once again living at the margin."[30]

The scientists argued that the leading international ranking of US science was based to a large extent on previous investments in instrumentation.[31] The pleas based on this argument were twofold: "The first is that funds and opportunities have to be provided for the invention and development of new instruments. (...) The second point is that state of the art instrumentation has to be made accessible to research scientists who need to use it. And, considering the state of tight funding, this requires that instrumentation be shared."[32] Thus, for two reasons, instrument-sharing became the miracle cure for the problems of the 1970s and early 1980s: Fewer means, and an improved channeling of access worked hand in hand, and the latter worked for the benefit of the method makers.[33] In 1984, a third of the instruments in the Physical Sciences were shared, in computer science 82%.[34]

Thus, it became clear to those involved that access to instrumentation, and especially the capability of instrument and methods innovation, constituted an instrument of science policy. In 1981, the Biotechnology Resource Program of NIH held two workshops on the technical support of the life sciences. The 65 delegates from science, industry and government postulated a linear model of problem solving, which showed a convergence of the identification of problems and the development of new technologies leading to the distribution of methods and their availability. For the panel, the problematic issue was the lack in the development of risky technologies, caused by the shortfall of physicists and

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[28] John D. Roberts et al. to Philip Handler, 15 March 1976, Oleg Jardetzky Papers, Ad hoc Committee, folder "Notes."

[29] John D. Roberts, Richard N. Zare, Appendix 3, 1. July 1976, "Report on Ad hoc Panel on Cooperative Efforts and Facilities for Research in Chemistry and Biological Chemistry," 23 October 1976, National Academy of Sciences. Oleg Jardetzky Papers, Ad hoc Committee, folder "Notes."

[30] Alvin Trivelpiece, in National Research Council, Office for Physical Sciences, *Revitalizing Laboratory Instrumentation. The Report of a Workshop of the Ad hoc Working Group on Scientific Instrumentation, March 12-13, 1982,* Washington D.C.: National Academy Press, 1982, 17-19, here p. 17.

[31] Elkan R. Blout, D.M. Grant, O. Jardetzky, W.D. Phillips, K.R. Porter, "Instrumentation Funding," *Science* 202 (1978), no. 4366, Editorial.

[32] Statement Oleg Jardetzky, Subcomittee on Science, Research and Technology of the Committee on Science and Technology, U.S. House of Representatives, protocol, p. 403, 26. February 1979. Oleg Jardetzky Papers, folder "Ad hoc Committee, Congressional Testimony."

[33] Charles C. Coulter, "Research Instrument Sharing," *Science* 201 (1978), 415-420.

[34] Burgdorf, White (note 27), p. 36, fig.15.

engineers in commissions, and especially the lack of recognition of instrument and methods development as being part of science. Thus, they proposed "the interpretation of 'research' be classified and made explicit to include technologic innovation and discovery."[35] The duration and size of projects should be flexible, and the production of prototypes should be included. At the same time, the interaction of universities and industry should be strengthened.

The actors had a much larger market in mind than just universities and governmental research institutions. By far the largest share was held by industry, in both research and manufacturing.[36] Often, the development of novel instrumentation was driven by companies, especially in the petrochemical industry, and this gave rise to important spin offs of instrument manufacturing companies.[37] The global market (the largest 22 nations, with the exclusion of the USA) in 1971 had a size of approx. 3.7 billion US$.[38] For Germany alone the size was estimated to be more than one billion, with a prognosis of 1.5 billion in 1975.[39]

Medical technology had an even larger size: "The industry that manufactures medical devices in the United States has grown (...) from less than $1 billion in 1958 (...) to more than $17 billion in 1983. Even after adjustment for inflation, industry sales increased sixfold during that period."[40] Here, as well, similar mechanisms of research funding and regulation of innovation were in place as a report of the Office of Technology Assessment from 1984 demonstrates:

"A recent analysis of NIH, NSF, and Department of Energy grants and contracts active as of May 1983 revealed that almost $50 million was related to diagnostic imaging. This medical imaging R&D was scattered throughout the institutes and agencies and covered a wide assortment of subjects including not only development or refinement of new imaging devices, but the use of imaging techniques to enhance understanding of disease processes. A high proportion of these grants went to academic and other nonprofit institutions, and therefore supplemented the R&D on medical imaging conducted by industry. NIH funding in the medical imaging area has, in retrospect, had important impacts on the later development of commercial imaging devices."[41]

Thus, innovation of both scientific and medical instruments showed a similar pattern. Funded by governmental agencies, the instrument industry supplied science with the necessary tools. At the same time, method makers enjoyed a key position as they were in charge for growing the market size. However, this led to problems in the funding of universities, as they could not keep pace with the speed of innovation.

Eric von Hippel's model of 'user-dominated innovation' describes the academic partners of instrument manufacturers as users.[42] However, these users were not passive, but actively engaged and stood in a symbiotic relationship with industry. Out of self-interest,

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[35] Richard J. Johns, Ernest D. Cravalho, "Final Draft. Workshops on Technology in Support of Biomedical Research," 5. November 1981, p. 5. Oleg Jardetzky Papers, folder "Workshops on Technology in Support of Biomedical Research."

[36] Frost & Sullivan, Inc., *The Analytical Instruments Market*, New York 1972.

[37] Davis Baird, "Encapsulating Knowledge: The Direct Reading Spectrometer," *Foundations of Chemistry* 2 (2000), 5-46; Yakov M. Rabkin, "Technological Innovation in Science. The Adoption of Infrared Spectroscopy by Chemists," *Isis* 78 (1987), 31-54.

[38] U.S. Department of Commerce, *Global Market Survey. Industrial and Scientific Instruments*, Washington D.C.: U.S. Government Printing Office 1972.

[39] U.S. Department of Commerce (note 38) p. 7.

[40] Office of Technology Assessment, *Federal Policies and the Medical Device Industry,* Washington, D. C.: U.S. Congress, Office of Technology Assessment, October 1984 (OTA-H-230), p. 3.

[41] Office of Technology Assessment (note 40), p. 80.

[42] Eric von Hippel, *The Sources of Innovation*, New York: Oxford University Press 1995.

method makers relied on innovation of instruments, in order to grow their scientific capital in form of reputation. The scale and scope of such relationships has been described with the example of a symbiotic competition between the industrial scientist James Shoolery and the academic scientist John D. Roberts, featuring the example of NMR methods and physical organic chemistry.[43] In the biomedical field, Rosenberg, Gelijns and Dawkins emphasize the importance of the cooperation between the industrial instrument manufacturers (with their expertise in electrical engineering) and the clinicians (thus, not the researchers). In this case, the users are a crucial part of innovation, at least in the stage of (clinical) development. At the same time, the authors distinguish the role of NIH in the field of medical technology from such techniques that involve chemical, biological and medical know-how, especially in the pharmaceutical field.[44]

The US style of scientific research, as diagnosed by Abelson and Handler, relied in large parts on the commercial development of research instruments. This was the basis for the method makers' strategy to distribute their methods as widely as possible. At the same time, it changed the definition of research projects in such a way that it included the innovation of instrumentation and the development of methods. The use of instruments outside the academy, for example in industrial and environmental applications, had some beneficial effects, because it decreased the dependance on one sphere of application only. On the other hand, science depended on the commercialization of its main research tools.

4. Methods of Research—a Conclusion

The transformation of research technologies in the middle of the twentieth century was the cradle for a novel type of scientist, with the major goal of development and dissemination of research methods. The support came from governmental science funding agencies and a well performing instrument industry. In the resulting triangle of science, industry and government, method makers had a central, but also precarious, role. Central for their long-term survival was their standing inside the scientific field, as with access to novel methods scientists obtained the means to gain reputation. However, method makers had the potential to threaten established power positions in a discipline. In the end, a middle path was taken, that led to the containment of the new methods in centers, but ensured change and innovation. As a result of this centralization and institutional separation, the transfer of methods through service, training, and cooperation channeled the further development of methods. As experts, the method makers could forward their research, but not completely rule disciplinary trends. The more new methods became routine in certain disciplines, the more urgent it became for method makers to expand their reach. Innovation processes and expert roles of method makers were thus dynamically intertwined. The autonomy of method makers was rooted in their ability to cater for many different clientele groups. Their alliances with instrument manufacturers and funding agencies stabilized their strong standing further. Because many methods were used not just in science but also in industry and government, the circle of science-industry-government relations closed.

Largely originating in World War II, this advantageous constellation developed further in the immediate postwar period. The focus on mid-size and table-top instruments of isolation, identification, and interpretation allows us to trace the transformations in the 1950s and 1960s. The chromatographical and spectroscopical methods, including the data management by computers, entered into the centers of practice of almost all established research directions, and they were constitutive for novel directions as well.

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[43] Carsten Reinhardt, "A Lead User of Instruments in Science. John D. Roberts and the Adaptation of Nuclear Magnetic Resonance to Organic Chemistry, 1955-1975," *Isis* 97 (2006), 205-236.

[44] Nathan Rosenberg, Annetine C. Gelijns, Holly Dawkins, *Sources of Medical Technology. Universities and Industry*, Washington D.C.: National Academy Press 1995.

The Small-Scale Ammonia Production of China in the Time of Mao Zedong

Mine Takeshi

Japan

1. Introductiion

It is said that the fear for the supply shortage of raw materials of explosives forced engineers to invent the technology to synthesize ammonia from the air. Computers, radars etc. were developed during the wartime. We can say that the war develops the technical progress generally speaking. In the early time of People's Republic of China, however, the reversal phenomenon was observed. It appears that technical progress turned reversely backward to the pre-war initial level due to the fear of the war with USA and USSR. Namely China sought and pursued small scale production under the Chairman Mao Ze Dong's self-reliance policy. The ammonia production was the typical case of such small-scale production.

2. Ammonia Production in China

1) Middle scale productiion

The first ammonia plant with 50,000 t/y production capacity was constructed in Dalian by Japan in 1935. Besides Fan Xudong and Hou Debang of Yongli Company of PR China constructed the ammonia plant with 33,000 t/y production capacity in Nanjing in 1937 under the aid of the government of PR China. Dalian ammonia plant process was Uhde of Germany and Nanjing plant process is NEC of the United States. Both of them were one of the most advanced process among the pre-war ammonia technologies.

In 1949 the new government of China was formed The economy of the new China was recovered to the prewar level in 1952 and the ammonia plants in Dalian and Nanjing were reconstructed and re-started production. During the First 5-Year (1953-57) Plan additionally 3 more ammonia plants were constructed in Jilin, Lanzhou and Taiyuan with 50,000t/y production capacity each under the technical and financial aid of USSR.

Thus the newly born China succeeded in getting the technology to construct and operate the middle-scale, namely 50,000t/y, ammonia plants, through the reconstruction of the old plants and the construction of new plants. Then China constructed 15 middle-scale ammonia plants additionally by 1965 without depending on foreign companies. As a result ammonia production in China at that time were mostly from middle scale plants, covering 88% of national production in 1965.

Table1 shows ammonia production by plant capacity scale during 1952-1983. In 1952, 97% of national production in China was from middle scale plants. In 1957, the year Chinese economy was very active due to the First 5 Year Plan, 100% of ammonia production was from middle scale plants. The share of the production from middle scale pants,however, decreased afterwards throughout 1960's, 19707s and 1980's as the Table1 shows. The share in 1983 was only 22%, despite the share of 100% in 1957.

Table1 Ammonia production capacity by scale										Total
年	Large scale			Middle scale			Small scale			
	No. of plants	Production		No. of plants	Production		No. of plants	Production		
		1000t	%		1000t	%		1000t	%	1000t
1952				2	37	97	1	1	3	38
1957				3	153	100				153
1962				8	455	94	45	28	6	483
1965				22	1,301	88		185	12	1,484
1970				30	1,445	59	300	1,000	41	2,445
1973				38	2,155	45	961	2,589	55	4,744
1974				42	2,074	44	1,078	2,651	56	4,725
1975				45	2,533	42	1,199	3,544	58	6,077
1976	4	170	3	47	2,334	38	1,319	3,681	59	6,185
1977	5	1,245	14	49	2,579	30	1,450	4,880	56	8,704
1978	8	2,061	17	53	3,190	27	1,533	6,584	56	11,835
1979	10	2,706	20	54	3,518	26	1,539	7,257	54	13,481
1980	13	3,127	21	56	3,655	24	1,439	8,194	55	14,975
1981	13	3,359	23	56	3,667	25	1,357	7,808	52	14,833
1982	13	3,448	22	56	3,637	24	1,279	8,378	54	15,464
1983	13	3,631	21	56	3,683	22	1,244	9,457	57	16,771

Remark:Large scale is imported technology, Middle scale is 10,000-50,000 t/y, Small scale is less than 10,000 t/y.
Source:DANDAI ZHONGGUO DE HUAXUE GONGYE, 1986, Appendix Table 5.

2) Small scale production

On the one hand China developed the small scale, namely 800 t/y, ammonia plant in1958 in Dalian. The world famous chemist Hou Debang was the leader of the newly developed small scale plant. Furthermore 2,000 t/y plant was developed in Shanghai. But the development of the ammonia production from small scale plants was moderate until 1965.

Ammonia production from the small scale plants began to increase from 1965. 12% of the national production was from small scale plants this year. After the second half of 1960's a number of small-scale ammonia plants were constructed in the rural area of China under the self-sufficient strategy. In 1970 the number of small scale plants increased to 300 and 41% of national production was from small scale plants. The number of small scale plants continued to increase during 1970's to more than 1,500, resulting the share near 60% of the total national production.

The small scale production was peculiar to China in the time of Mao Zedong. In other words Mao Ze Dong, facing the conainment strategy by USA and USSR, began to consider that USA and/or USSR will attack and invade into China. China feared that the concentration of production will cause a serious damage on the Chinese economy in case USA and /or USSR attack China.

Thus, under the Chairman Mao's leadership, China walked the way of the geographically dispersed small scale production structure. Despite the ability of constructing the middle scale ammonia plants, China newly developed the technology of small scale ammonia plants, namely 800 t/y or 2,000t/y. More than 1,500 small-scaled ammonia plants were constructed in the rural area of all over China during end 1960's and early 1970's, the period when Chairman Mao was seriouly afraiding USA's attack on China.

3) Large scale production

The meeting of Mao Zedong and Nixon in 1972 changed drastically the fundamental relation between China and USA. In 1973 China contracted importation of 13 large-scale ammonia plants with 330,000 t/y capacity and urea plants with 500-600,000 t/y capacity with the companies of USA, Japan and Europe.

We can see the situation in Table 1. The first large-scale ammonia/urea plant started production in 1976 in Sichuan Province and afterwards large-scale fertilizer plant started production one after another. The share of the large scale plants has increased to over 20% in the early 1980's.

4) The reversal development of the ammonia production technology in China

We have obserbed that the ammonia production in China developed from the middle scale plant to the small scale plant and then from the small scale plant to the lagre scale plant. Namely, China shifted from the middle-scale to the small-scale, resulting 55% of national ammonia production from the small-scale plants in 1973, though only 6% in 1962.

The main stream of the world ammonia industry in 1960's is toward the large-scale plants with 330,000 t/y capacity. For example, the first ammonia plant capacity in pre-war Japan was 5 t/d, namely 1,650 t/y, according to the monument in Shimonoseki City. Ammonia plant capacity of the company (Toyo Koatsu Industries) was then increased to 8,910 t/y in Omuta City and then to 66,500 t/y in Sunagawa City during WW II. Japan's development model is from small scale to middle scale and from middle scale to large scale: 1,650 t/y→ 8,910 t/y → 66,500 t/y→ 330,000 t/y. China's development model is from middle-scale to small-scale: 50,000 t/y → 800t/y (or 2,000 t/y) → 330,000 t/y.

The reversal movement to the pre-war initial technology in China was caused by the Mao Ze Dong's self-reliance policy. Under the self-reliance policy China denied the division of labor and aimed to construct the self-sufficient economy in each rural area. The denial of the division of labor prevented the technical progress development and ammonia production technology reversed to the pre-war small-scale level.

3. Nitrogen fertilizer production in China

1) Variety of nitorgen fertiliers

Ammonia is the raw material of the nitrogen fertilizers, and the major nitrogen fertilizer which Chinese farmers used in the prewar China was ammonium sulphate. In the prewar China ammonium sulphate was the only nitrogen fertilizer domestically produced. Ammonium nitrate was newly introduced during the first 5-year plan by USSR. Ammonium chloride was produced as the by-product of soda ash production. Besides, the technology of urea was developed and a new urea plant with 40,000 t/y capacity was constructed in 1965 in Wujing as the symbol of the self-reliance technology[1].

2) Ammonium bicarbonate (AB) as the fertilizer

When the first small-scale ammonia of 800 t/y capacity was constructed in Dalian in 1958, most of the ammonia produced was used as the liquid fertilizer by adding water to ammonia. Soon later China developed the technology to use ammonia from the small-scale

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[1] According to the compaany brochure the production capacity was designed as follows: ammonia 50,000 t/y, sulpharic acid 80,000 t/y, ammonium sulphate 100,000 t/y, urea 40,000 t/y.

plant as the raw material for the production of AB (ammonium bicarbonate: NH_4HCO_3) which was utilized as the fertilizer. Under the supervision of worldwide famous chemist Hou Debang the model plant of 8000 t/y AB and 2,000 t/y ammonia plant was developed in Shanghai. AB with only 17.5% nitrogen content is not an effective fertilizer since it is easy to deteriorate during storage and transportation.

Although AB is not an efficient fertilizer AB plant is easy to construct and operate. Besides the cost of AB is very cheap. The geographically dispersed small-scale production reduced the loss during transportation and storage and covered the defects of AB. The raw material of AB is coal which can be obtained easily all over the nation. As a result China constructed more than 1,500 AB plants all over the rural areas supplying the fertilizer to the poor farmers. Construction of small-scale ammonia and AB increased dramatically during the latter half of 1960's when Chairman Mao feared the possible war with USA and USSR. The more than 50% of nitrogen fertilizer after 1970 was from small-scale ammonia, though near 100% from middle-scale ammonia during 1950's. China is the only nation in the world which utilized AB as the fertilizer.

Table 2 shows the small scale nitrogen fertilizer production in China. The small scale nitrogen fertilizer production started in 1958 in Dalian, using 800 t/y ammonia as the raw material for AB. Then AB plant was improved in Shanghai and the model plant developed in Shanghai spread throughout the nation. Thus AB became the major nitrogen fertilizer. AB production increased rapidly after the second half of 196o's when the war between China and USA might break out. In 1968 AB share in the total national nitrogen production reached 50%. Since that time the share of AB continued to be more than 50% until 1992.

|	Small scale ammonia		Small scale N fertilizer		Small scale urea		AB	
	production	share	production	share	production	share	production	share
	1000t	%	1000t	%	1000t	%	1000t	%
1958	1.1	0.5	o.7	0.5			4.1	0.5
1959	1.3	0.4	0.9	0.6			5.3	0.6
1960	2.7	0.6	2.1	1.1			12.4	1.1
1961	15.5	5.1	10.4	6.0			61.2	6.0
1962	28.1	5.8	19.4	5.7			114.1	5.7
1963	46.7	7.3	32.6	7.1			191.8	7.1
1964	87.2	9.4	60.3	8.9			354.7	8.9
1965	183.5	12.4	126.8	12.2			745.9	12.2
1966	405.8	19.1	281.4	19.3			1,655.3	19.3
1967	403.1	26.5	279.3	27.5			1,642.9	27.5
1968	370.4	35.4	341.9	50.0			2,011.2	50.0
1969	578.3	35.9	364.1	35.6			2,141.8	35.6
1970	1,000.4	40.9	764.9	50.2			4,473.1	50.2
1971	1,349.3	43.5	967.8	50.8			5,659.6	50.8
1972	1,971.4	49.8	1,377.0	53.9			8,052.6	53.9
1973	2,589.3	54.6	1,798.9	60.0			10,508.2	60.0
1974	2,451.3	54.2	1,656.8	58.6			9,688.9	58.6
1975	3,544.2	58.3	2,321.3	62.6			13,574.9	62.6
1976	3,681.0	59.5	2,421.9	63.5			14,163.2	63.5
1977	4,879.9	56.1	3,212.7	58.2			18,787.7	58.3
1978	6,484.5	54.8	4,348.9	57.5			25,432.2	57.5
1979	7,257.0	53.8	4,809.8	54.5			28,127.5	54.5
1980	8,193.5	54.7	5,528.5	55.3			32,330.4	55.3
1981	7,807.9	52.6	5,258.6	53.4			30,752.0	53.4
1982	8,378.5	54.2	5,461.4	53.4			31,938.0	53.4
1983	9,457.2	56.4	6,401.1	57.7			37,433.3	57.7
1984	10,525.9	57.3	7,121.2	58.3			41,644.4	58.3
1985	8,202.5	50.0	6,061.8	53.0			35,449.1	53.0
1986	8,343.3	50.3	6,103.5	52.7	193.3	0.8	34,562.6	51.9
1987	10,637.2	54.9	7,617.0	56.8	211.5	0.7	43,307.0	56.0
1988	11,292.0	57.1	7,894.1	55.6	245.7	0.8	44,727.5	54.8
1989	11,615.3	56.1	8,143.4	56.1	323.8	1.0	45,728.7	55.1
1990	11,950.6	56.1	8,398.0	56.4	312.0	1.0	47,286.5	55.4
1991	12,389.6	56.3	8,430.2	55.8	916.1	2.8	43,942.1	53.0
1992	13,033.4	56.7	7,484.8	56.7	1,230.4	4.3	36,575.4	52.4
1993	12,300.0	55.7	6,921.0	54.5	1,537.7	5.6	31,481.3	42.4
1994	13,836.5	56.7	7,107.1	56.0	2,140.6	7.8	29,043.9	48.2
1995	15,187.0	54.9	9,850.5	53.1	3,569.4	8.8	36,731.6	44.2
1996	18,251.0	59.6	11,962.5	57.6	5,311.3	11.8	38,895.9	45.9
1997	17,038.0	56.7	11,421.0	53.2	6,767.0	29.4	48,872.0	38.7
1998	17,311.0	54.3	11,541.0	52.6	7,540.0	29.4	47,486.0	36.8
1999	18,730.0	54.3	12,649.0	52.6	9,870.0	33.6	47,560.0	34.0
2000	19,373.0	57.6	11,436.0	51.9	11,575.0	38.0	37,023.0	26.4
2001	19,189.0	56.3	12,162.0	56.0	12,848.0	40.8	33,626.0	23.0
2002	22,321.0	60.5	14,686.0	59.1	15,100.0	44.0	38,391.0	25.5
2003	23,838.0	62.9	14,967.0	61.3	16,812.0	47.2	35,692.0	23.7
2004	26,575.0	62.9	16,721.0	61.0	18,617.0	47.6	38,955.0	22.3
2005	30,562.7	66.0	18,484.8	63.3	20,982.6	50.6	39,756.5	21.2
2006	33,614.0	68.1	21,301.0	66.1	25,011.0	54.6	37,919.0	19.1
2007	35,698.0	69.2	23,215.0	67.7	28,981.0	58.1	32,750.0	15.0
2008								13
2009								12
2010								11
2011								10
2012								
2013								
2014								
2015								6.5

Remark: Small scale nitrogen fertilizer production is in terms of nitrogen 100%.
Source: *Zhongguo Xiao Danfei Gongye Dashiji 1958–2008*, 2008 and internet information on AB.

Table2 Small Scale Nitrogen Fertilizer Production in China

3) Significance of AB as the nitrogen fertilizer

AB played an important role contributing poor farmers in the days of Mao Zedong. AB continued to play an important role even in the days of the reform and open-up policy. Figure 1 illustrates such kind of the situation. In 1978 the share of AB is 48% and the share of urea is 23% in the national total nitrogen fertilizers. AB production and share still increased afterwards and the share reached 60% in 1988. After 1989 the share of AB began to decrease slightly but the share in1996 is still near to 50%. On the other hand the share of urea increased consistently and the share in 1997 reached 50%, exceeding the share of AB 41%.

In the latter half of 1990's AB share decreased rapidly. After 2000 there is no data concerning AB in *China Chemical Industry Yearbook*. It is quite hard at present to get consistent information data on AB. It is said that AB share is planed to be 6.5% in 2015 in the 12th 5-Year Pan.

Figure 1 The share of urea and ammonium bicarbonate
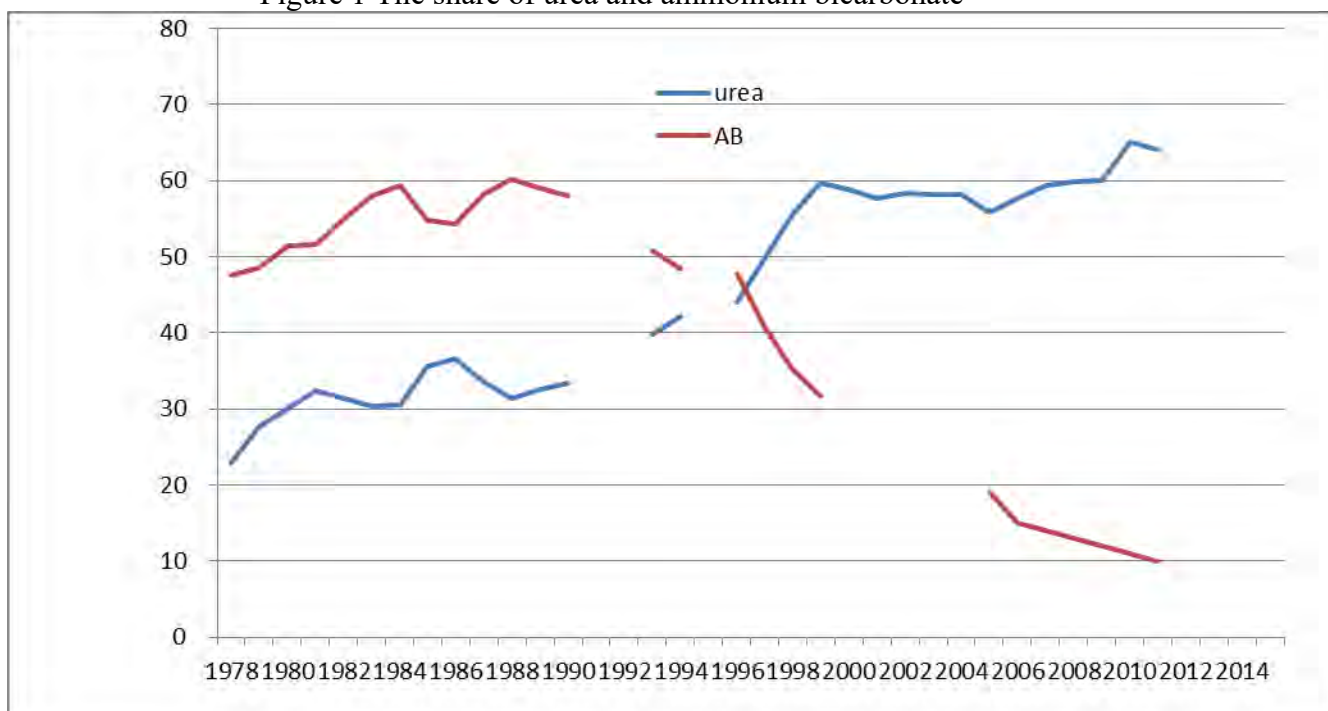
It is noteworthy that Shanghai Research Institute of Chemical Industry developed the technology to convert AB plant into urea plant in mid 1980's. We can see the situation in Table 2. 193,300 tons of urea were produced in 1986 in such from AB converted urea plants, namely small scale urea plant. The model plant capacity developed by Shanghai Research Institute of Chemical Industry is 40,000 t/y. Therefore more than several AB plants seemed to be converted into small scale urea plants and started production in this year. The production of small scale urea plants increased year by year. Near 30million tons of urea was produced in 2007, counting 58.1% of the national urea production.

4. Implication

1) Reversal development of technology

China's technology level turned back to the pre-war primitive level due to the denial of the division of labor and self-sufficient economy. Namely, because of the containment by USA and USSR, Mao Zedong selected the self-reliance policy, and China walked the way of self-sufficient economy. The people's commune was the base of the self-sufficient economy. The people's commune denied the division of labor which brought about the technology

development of capitalism. We can say that China's ammonia production technology developed reversely to the pre-war level due to the fear of the war with USA and USSR.

2) AB as the appropriate technology
AB (Ammonia Bicarbonate) was the so-called 'appropriate technology' at the time of Mao Zedong. AB is easy to deteriorate during storage and transportation but easy to construct and operate, and the price is very cheap. Construction of plants in rural area reduced the loss during storage and transportation. Production of ammonium sulfate, the most standard nitrogen fertilizer at the early time of Mao Zedong, consumes a lot of sulfuric acid which consumes a lot of sulphur, a scarce resource in China. Production of urea needs stainless steel whose supply was limited in the time of Mao Zedong.

3) Starting year of China's open-up policy
The small scale production was the widespread industrial structure in the time of Mao Zedong. From the viewpoint of production technology development, China's reform and open-up policy appears to have started in 1972. Because soon after the meeting of Mao Zedong and Nixon in 1972 China decided the import of 13 large-scale ammonia/urea plants from USA, Japan and Europe. Since that time China began to seek the same large-scale production technology as western countries. People say that reform and open-up policy started in 1978. It appears from the viewpoint of the production technology, however, that China started open-up policy in 1972, rather than in 1978.

'Ideal' Gases: Anaesthetics in the Heart of the Twentieth Century

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1.   Introduction

By 1920 only three gaseous anaesthetics were widely used – nitrous oxide, diethyl ether (ether) and chloroform. The toxicity of chloroform was acknowledged, nitrous oxide did not induce deep anaesthesia, and ether was extremely inflammable, so in the 1920s there were good reasons to search for new anaesthetics. While my concern is with gaseous anaesthetics, I recognise that there were parallel developments in two related fields, that of topical or local anaesthetics, typified by the natural product cocaine and a host of synthetic substances, and injectable anaesthetics starting with opiates, then barbiturates and leading to modern materials such as propofol (2,6-diisopropylphenol).

2.   Theories of anaesthetic action

Hans Meyer[1] noted that the anaesthetic substances were soluble in both fatty and aqueous media, proposed a general theory of anaesthesia based on the partition or distribution coefficient as a critical determinant. Meyer enunciated the following three principles that underpinned his theory:

- all chemically inert substances that are soluble in fats and fatty materials will produce narcosis;
- the line of action is in the nerve cells;
- the comparative strengths of substances depend on their solubility in fatty material and in water, that is, on the distribution coefficient.

Charles Overton arrived at the same idea independently.   Some years after completing his PhD research on cell permeability studies, Overton first presented his theory of narcosis in a lecture to the Society for Natural History in Zurich in October 1898, in a paper published the following year[2] and in his book[3] which included a full exposition.   Although his contribution to the theory of narcosis was recognised in the term 'Meyer-Overton theory', the details were not widely accessed although some excerpts of his work (and Meyer's) were published in translation in 1963.[4]   A full translation of Overton's book, commissioned by the US Environmental Protection Agency, and accompanied by remarks by modern authors was published in 1991.[5]

According to the Meyer-Overton theory the anaesthetic substances interacted in reversible ways with fatty membranes and thus mediated their effects on consciousness. Since it was not possible to predict the distribution coefficients of potential anaesthetic substances, the

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[1] H. Meyer, 'Zur Theorie der Alkoholnarkose. Erste Mitteilung. 'Welche Eigenschaft der Anästhetica bedingt ihre narkotische Wirkung?', *Naunyn-Schmiederbergs Archiv für experimentelle Pathologie und Pharmakologie* (1889), **42** (2-4), 108-118.
[2] E. Overton, title, *Viertlejahrsschrift der Naturforschenden Geselleschaft in Zurich* (1899), **44**, 88-135.
[3] C.E. Overton, *Studien über die Narkose zugleich ein Beitrag zur allgemeinen Pharmakologie* (Gustav Fischer, Jena, Switzerland, 1901).
[4] B. Holmstedt and G. Liljestrand, *Readings in Pharmacology* (Pergamon Press, Oxford, 1963), pp. 147-154.
[5] R.L. Lipnick, ed., *Studies of Narcosis* (Springer, Netherlands, 1991).

Meyer-Overton theory was not helpful in guiding researchers to structures of organic molecules that might deserve further investigation. Winterstein[6] provided a detailed critique of the theory, showing that the relationship did not hold when a broader range of chemically inert substances was tested, and other researchers also concluded that the Meyer-Overton theory was 'not entirely satisfactory' but was the best available and had gained widespread acceptance.[7] Addressing the apparent inconsistency, Henderson and Brown postulated three types of anaesthetic action: '(a) due to changes in the anesthetic in the body; (b) due to secondary effects produced in metabolism; (c) inherent in the anesthetic.' In their view only the last of these might be correlated with physical parameters, while the others could account for toxicity but the lack of predictive value remained a serious obstacle to the search for new anaesthetics. Nicholas Franks at Imperial College, London, discovered that binding by anaesthetic agents to soluble proteins, and consequent competitive antagonism, was likely to be the true mechanism of anaesthetic action.[8] Reviewing the progress that followed his initial discoveries, Franks[9] observed that although there were many exceptions the Meyer-Overton theory survived because it had 'beguiling simplicity' and was not inconsistent with developing ideas of the lipid bilayer nature of nerve membranes.

3. Hydrocarbons leading to cyclopropane

Ethylene and acetylene had been investigated in the late nineteenth century and found to be effective anaesthetics but they did not become established in the repertoire of the anaesthetist until the 1920s.[10] The use of acetylene ($CH{\equiv}CH$) became more common, mainly in Germany, after Hermann Wieland,[11] in Freiburg, reported extensively on its use and it was marketed as Narcylen. Wieland was led to experiment with acetylene by noting the facility with which nitrous oxide dissolved in blood and could therefore be transported to sites of (unspecified) action. 'The proof of this hypothesis', he wrote, 'was shown by the experiments with other gases such as acetylene that dissolved even more easily in water'.[12] Note was taken by the anaesthetists in other jurisdictions[13] but acetylene was mainly used in Germany. Wieland had generated acetylene from the reaction of calcium carbide and water, purifying it before use in anesthesia. Since acetylene had industrial uses in lighting and welding it was available

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[6] H. Winterstein, *Die Narkose in ihrer Bedeutung für die allgemeine Physiologie* (Springer, Berlin, 1919), pp. 203-228.

[7] V.E. Henderson and W.E. Brown, 'The theory of anesthesia and the problem of toxicity', *Journal of Pharmacology and Experimental Therapeutics* (1926), **29**(1), 269-278.

[8] N.P. Franks and W.R. Lieb, 'Do general anaesthetics act by competitive binding to specific receptors?', *Nature* (1984), **310**, 599-601. This is now the accepted mechanism and several specific receptors have been identified. C.J. Weir, 'The molecular mechanisms of general anaesthesis; dissecting the $GABA_A$ receptor', *Continuing Education in Anesthesia, Critical Care & Pain* (2006), **6**(2), 49-53.

[9] N.P. Franks, 'Molecular targets underlying general anaesthesia', *British Journal of Pharmacology* (2006), **147**, S72-S81.

[10] F. Shipway, 'Acetylene, ethylene and propylene', *Lancet* (1925), **205**, 1126-1130.

[11] H. Wieland, 'Über den Wirkungsmechanismus betäubender Gase, des Stickoxyduls und des Azetylens', *Naunyn-Schmiederbergs Archiv für experimentelle Pathologie und Pharmakologie* (1922), **92**, 96-152.

[12] My translation, from C.J. Gauss and H. Wieland, 'Ein neues Betäubungsverfahren', *Klinische Wochenschrift* (1923), **2**(3), 113-158.

[13] T. Brand, 'Narcylen (acetylene gas) anesthesia', *Norsk Magazin for Lagevidenskaben*, August 1924, abstracted by T. Batrud, *Current Researches in Anesthesia and Analgesia* (1925), **4**(1-6), 128. T. Brand, 'Acetylene-oxygen anesthesia in gastric surgery', *Current Researches in Anesthesia and Analgesia* (1926), **5**, 329-331. C.H.S. Horwitz, 'A new general anaesthetic', *Lancet* (1923) (1), 619. Anonymous, 'New anesthetics: ethylene and acetylene', *Journal of the American Medical Association* (1923), **80**(19), 1383-1384.

commercially but that material had to be cleansed of small quantities of acetone with which it was stored under pressure.[14]

V.E. Henderson at the University of Toronto was drawn into work on anaesthetics by W. Eason Brown, an anaesthesiologist at Toronto General Hospital, who had joined the department of Pharmacology in 1922 and by George Lucas, a young chemist he hired to pursue the work. They wrote about their experience with ethylene as an anaesthetic and related their findings to those of other researchers.[15] Their intention was to increase the efficiency of nitrous oxide for general anaesthesia by adding other substances to it, but their reasons for choosing ethylene were not explicit. In the event, they found ethylene to be more potent than nitrous oxide, producing rapid and effective anaesthesia in animals and humans when administered in mixtures containing 10-15% oxygen. They generated ethylene by pyrolysis of ethanol vapour over aluminium oxide at 350° but later used cylinders supplied by a manufacturer. Although Brown and Henderson published further work on ethylene[16] they ceded the research field to others and ethylene, on grounds of odour and flammability, never became a major anaesthetic.

Instead they turned to propylene, which they found possessed anaesthetic properties, as did methane, although only at higher concentrations.[17] Brown suggested that higher hydrocarbons might be better anaesthetics but this does not seem to have been followed up, and there was more to learn about C_3 hydrocarbons. Cyclopropane was found to be a good anaesthetic.[18] Researchers were unable to conduct a partition experiment with it, but instead they determined separately the solubilities of cyclopropane in water and olive oil, which were in ratio 1:64.4 and that compared favourably with ethylene 13.2, ether 2.5 and acetylene 2.1.

As a result of further work by Ralph M. Waters of the University of Wisconsin,[19] cyclopropane was introduced to practice from 1933 in the United States and Australia, but not in Britain. A number of deaths of patients under anaesthesia in Toronto hospitals at about that time made doctors unwilling to experiment with cyclopropane,[20] which Exhibited toxic effects when it was used in high doses. In addition, the constant danger of explosion in the operating theatre made doctors cautious about its use. The explosion risk, shared by other inflammable agents like diethyl ether and acetylene, was heightened when electrocautery was introduced into surgery in the late 1920s and when electronic monitoring devices later became common.

4.   Rare gases

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[14] For safety reasons compressed acetylene is dissolved in acetone (later dimethylformamide) which is absorbed on a porous medium. E. Almqvist, *History of Industrial Gases* (Springer, Boston, 2003), pp. 242-243.

[15] W.E. Brown and V.E. Henderson, 'On ethylene as an anaesthetic', *Archives internationales de pharmadynamie et de thérapie* (1923), **28**, 257-264.

[16] W.E. Brown and V.E. Henderson, 'Experiments with anaesthetic gases', *Journal of Pharmacology and Experimental Therapeutics* (1926), **27**, 1-8.

[17] W.E. Brown, 'Experiments with anesthetic gases propylene, methane, dimethyl ether', *Journal of Pharmacology and Experimental Therapeutics* (1924), **23**(5), 487-496.

[18] D. Gavrus, 'Envisioning cyclopropane: scientific product or medical technology?', *Scientia Canadensis* (2010), **33** (1), 3-28.

[19] R.M. Waters, 'Cyclopropane anesthesia', *Journal of the American Medical Association* (1934), **103**(13), 975-983.

[20] G.H.W. Lucas, 'The discovery of cyclopropane', *Current Researches in Anesthesia and Analgesia* (1961), **40**(1), 15-27.

Experience with deep-sea divers and other humans working under increased pressures of nitrogen gas showed that nitrogen has narcotic (= anaesthetic) effects, and this led to the investigation of other chemically inert gases. The noble – at that time regarded as inert – gases from Group 8 of the periodic table naturally attracted attention, although it was known that helium had only a very small narcotic effect.[21] The solubility of the gases in water increased with increasing atomic weight and so it seemed likely that higher members of the group might have interesting properties.

Argon, twice as soluble in water and in fat as nitrogen, was found to have approximately twice the narcotic effect.[22] Referring to the Meyer-Overton hypothesis that the fat-water solubility ratio is an important determinant of anaesthetic effects, Lawrence *et al.*[23] brought together the relevant data for solutions in water or corn oil or olive oil (Table 1) and confirmed that mixtures of oxygen and xenon (but not krypton) produced physiological effects when animals were exposed to recirculating gas mixtures with removal of carbon dioxide by soda-lime.

Table 1. Solubility ratios for chemically inert gases
(n/a indicates data unavailable)

Inert gas	Oil/water solubility ratio	
	22°C	37°C
Nitrogen	3.5-4.2	4.7-5.2
Helium	n/a	1.7
Neon	n/a	n/a
Argon	4.0	5.3
Krypton	7.5	9.6
Xenon	14.5	20.0
Radon	110	125

Krypton and xenon were investigated further in the early 1950s, the former having 'no significant narcotic properties' while xenon was about as effective as ethylene,[24] and 'although it may not by virtue of its cost of manufacture prove to be a satisfactory agent commercially, it may materially assist in solving one of the important theoretical problems of anesthesia'. The main use of xenon as an anaesthetic seems to have been in Russia, where it was also used in training athletes for low-oxygen conditions until this practice was banned by the World AntiDoping Agency in June 2014.

An interesting outcome of the discovery of the anaesthetic action of xenon was Linus Pauling's interest in the phenomenon and his decision to look more broadly at other anaesthetic molecules because 'their chemical properties are such that it is impossible to believe that they produce narcosis by taking part in chemical reactions involving the formation and breaking of ordinary chemical bonds.' Because many substances fitted the Meyer-Overton criterion of fat-water partition without exhibiting anaesthetic action, he sought

[21] H.J. Taylor, 'The use of helium in diving', *Chemical Society Lecture, 4th June, 1953*.

[22] A.R. Behnke and O.D. Yarborough, 'Respiratory resistance, oil water solubility and mental effect of argon compared with helium and nitrogen', *American Journal of Physiology* (1939), **126**, 409-415.

[23] J.H. Lawrence, W.F. Loomis, C.A. Tobias and F.H. Turpin, 'Preliminary observations on the narcotic effect of xenon with a review of values for solubilities of gases in water and oils', *Journal of Physiology* (1946), **105**, 197-204.

[24] S.C. Cullen and E.G. Gross, 'The anesthetic properties of xenon in animals and human beings with additional observations of krypton', *Science* (1951), **113**, 580-582.

a more specific physical mechanism and proposed that this might involve 'hydrate crystals of the clathrate type'.[25] A similar theory was put forward, at about the same time, by Stanley Miller.[26] Unsuccessful experiments undertaken in Pauling's laboratory with brine shrimp and goldfish, and the consideration that such clathrates could form only under conditions that were far from physiological, meant that the theory gained little purchase and had almost no predictive value, although Pauling himself never entirely relinquished the idea.[27]

5. Elaborating the Ether Structure

The structure of one of the oldest anaesthetics, diethyl ether was the starting point for the exploration of anaesthetic properties of a range of aliphatic ethers that began in the 1920s. The American anaesthesiologist Chauncey Leake[28] noted that 'there has not yet been a systematic effort to determine whether or not there is any relation between chemical constitution and physiological action … of a relatively large series of related compounds'. His proposal was to bring together the structural elements of two known anaesthetics, diethyl ether and ethylene, and so to test divinyl ether (CH_2=CH-O-CH=CH_2) and some related compounds. This approach, he claimed, 'involves the climax of the scientific method – the ability to predict in a reasonable manner that a certain proposition will be true on the basis of observed phenomena and a workable theory'. He also noted the general tendency for higher members of a homologous series to exhibit greater toxicity, which directed attention to small molecules as those most likely to have useful properties.

Leake mentioned oil-water partition coefficients of the ethers he investigated and noted that 'if the partition coefficient may be taken as an index of anesthetic efficiency, then, divinyl ether meets our expectations'. From this we might conclude that he was aware of the Meyer-Overton theory but regarded it as providing a check on experimental results but not something with predictive value. Although divinyl ether was an effective anaesthetic it was degraded by exposure to light and air. This problem was partly overcome by addition of a small amount of ethanol as a stabilizer, and the product achieved commercial success for a few years under the name 'Vinethene' which was used in dental and other minor surgery and obstetric cases.[29]

Thinking along the same lines as Leake, John C. Krantz at the University of Maryland felt that ethyl vinyl ether 'represented more completely a cross between the two anesthetic molecules than does divinyl ether' and accordingly investigated its properties.[30] Before then, however, he had introduced another 'hybrid' molecule, combining the ether link with the structure of a recently introduced hydrocarbon anaesthetic, cyclopropane. The research group investigated cyclopropyl alkyl ethers[31] and then alkenyl ethers[32] which were found to be more

[25] L. Pauling, 'A Molecular Theory of General Anesthesia', *Science*, 1961, **134**, 15-21.

[26] S.I. Miller, 'A Theory of Gaseous Anesthetics', *Proceedings of the National Academy of Sciences of the United States*, 1961, **47**, 1515-1524.

[27] B. Marinacci, ed., *Linus Pauling in His Own Words* (Simon & Schuster, New York, c. 1995), pp. 225-228.

[28] C.D. Leake and M-Y Chen, 'A preliminary note on the anesthetic properties of certain unsaturated ethers', *Current Researches in Anesthesia and Analgesia* (1931), **10**(1), 1-2.

[29] F.M. Marvin, 'Clinical use of Vinethene', *Current Researches in Anesthesia and Analgesia* (1935), **14**, 257-262. L.F. Anderson, 'Newer anesthetic agents', *American Journal of Nursing* (1937), **37**(3), 276-280.

[30] J.C. Krantz Jr., C.J. Carr, R.D. Musser and M.J. Sauerwald, 'Anesthesia. XXVIII. The anesthetic action of ethyl vinyl ether', *Journal of Pharmacology and Experimental Therapeutics* (1947), **90**, 88-94.

[31] J.C. Krantz Jr., C.J. Carr, S.E. Forman and W.E. Evans Jr., 'Anesthesia. I. The anesthetic action of cyclopropyl methyl ether', *Journal of Pharmacology and Experimental Therapeutics* (1940), **69**, 207-220. J.C. Krantz Jr., C.J. Carr, S.E. Forman, E.E. Evans Jr. and H. Wollenweber, 'Anesthesia. IV. The anesthetic action of cyclopropyl ethyl ether', *Journal of Pharmacology and Experimental Therapeutics* (1940), **72**, 233-244.

effective than diethyl ether. Difficulties were experienced in measuring the oil-water partition coefficient directly by equilibrating the distribution between the two phases, and new methods were introduced but there was poor agreement between data obtained by the Leake and Krantz groups, not that it seemed to matter since effect anaesthetic agents had been discovered by more traditional approached of structure variation.

6.   Halogenated hydrocarbons after chloroform

Ethyl chloride,[33] trichloroethylene[34] and mixtures containing methyl chloride and ethyl bromide[35] were investigated for their anaesthetic properties. All were toxic to some degree, but trichloroethylene especially so since it was converted to highly toxic dichloroacetylene (Cl-C≡C-Cl) when exposed to soda lime in the recirculating system.[36] All four chlorinated methanes were found to possess anaesthetic activity. Of these, dichloromethane (methylene chloride, CH_2Cl_2) was the most favoured but a later review made a strong case that the real anaesthetic material was a chloroform present as an impurity.[37] Pure dichloromethane was later found to have the disadvantage that in the body it was converted to carbon monoxide which reduced the oxygen-carrying capacity of the blood.

7.   Fluorinated substances as anaesthetic gases

The development of organo-fluorine chemistry in the 1930s offered new opportunities for development of analogues of know anaesthetics, but none of dichlorofluoromethane ($CHCl_2F$) and chlorodifluoromethane ($CHClF_2$)[38] decafluorobutane and decafluorocyclopentane[39] were suitable and more extensive studies showed that while a number of small fluorine-containing molecules exhibited some degree of anaesthetic activity they also had pronounced toxicity.[40]

In Britain, Imperial Chemical Industries (ICI) had prepared many fluorine compounds and investigated possible uses for them as refrigerants, foam-forming agents and aerosols and it

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[32] J.C. Krantz Jr., C.J. Carr, S.E. Forman and H. Wollenweber, 'Anesthesia. VI. The anesthetic action of cyclopropyl vinyl ether', *Journal of Pharmacology and Experimental Therapeutics* (1942), **75**, 30-38. J.C. Krantz Jr., C.J. Carr, A.G. Horney and W.E. Evans, 'Anesthesia. IX. The anesthetic action of isopropenyl vinyl ether', *Journal of Pharmacology and Experimental Therapeutics* (1943), **79**, 179-185.

[33] M.J.P. Flourens, 'Note touchant l'action de l'ether sur les centres nerveux', *Comptes rendus hebdomadaire des Séances de l'Academie des Science* (1847), **24**, 340-344.

[34] K.B. Lehmann, V. Behr, L. Quadflieg, M. Franz, G. Herrmann, A.H. Knoblauch, K. Gundermann and H. Würth 'Experimentelle studien über den einfluss technisch und hygienisch wichtiger gase und düampfe auf organismus XVI-XXIII' *Archiv für Hygiene* (1911), **74**, 1-60.

[35] G.B. Rolland and F. Robinson, 'Somnoforme', *Journal of the British Dental Association* (1902), 23, 321-333.

[36] Recirculating systems only became common when cyclopropane was introduced but thereafter they were commonly employed with all anaesthetics. Production of toxic products by interaction anaesthetic gases with strong bases in the recirculating system was observed with trichloroethylene and also with sevoflurane, a fluoroether that was introduced later in the twentieth century. The use of less aggressive bases to remove carbon dioxide made these systems compatible with trichloroethylene and other gases.

[37] W.S. Sykes, *Essays on the First Hundred Years of Anaesthesia* (Churchill Livingstone, Edinburgh, 1982), Vol 3, pp. 153-167.

[38] H.S. Booth and E.M. Bixby, 'Fluorine derivatives of chloroform', *Industrial and Engineering Chemistry, Industrial Edition* (1932), **24**, 637-641.

[39] H.C. Struck and E.B. Plattner, 'A study of the pharmacological properties of certain saturated fluorocarbons', *Journal of Pharmacology and Experimental Therapeutics* (1940), **68**, 217-219.

[40] B.H. Robbins, 'Preliminary studies of anesthetic activity of fluorinated hydrocarbons', *Journal of Pharmacology and Experimental Therapeutics* (1946), **86**, 197-204. G. Lu, J.S.L. Ling and J.C. Krantz Jr., 'Anesthesia. XLI. The anesthetic properties of certain fluorinated hydrocarbons and ethers', *Anesthesiology* (1953), **14**, 466-472.

was recognized that the properties that made fluorocarbons valuable in these applications might also make them suitable as anaesthetics. Seeking a theoretical rationale for anaesthetic action, the research leader linked anaesthetic efficiency to chemical potential[41] but active research had to wait until after World War 2. 1,1,1-Trifluoro-2-bromo-2-chloroethane (CF$_3$-CHBrCl, Fluothane, Halothane), sometimes called the 'first designer anaesthetic' was synthesized in 1953.[42] A range of fluorinated compounds was synthesized by Dow Chemical Company in the late 1950s and submitted for testing at Abbott Laboratories, leading to the discovery of 1,1,1,2-Tetrafluoro-2-bromoethane (CF$_3$CHBrF, Teflurane). It had a solubility ratio of several hundred and differed from Halothane only by substitution of F for Cl.[43] While Halothane took a dominant place in the market, Teflurane was marketed for a time but was found to cause cardiac irregularities and its use was abandoned.

The interest in fluorine-containing moieties converged with that for aliphatic ethers when trifluoroethyl vinyl ether was investigated and found to be to a potent anaesthetic.[44] Several values of the oil/water solubility ratio, in the range 91-100, suggested that according to the Meyer-Overton theory it should be more potent but in fact its potency was similar to that of diethyl ether. It was marketed under the trade names Fluoromar and Fluroxene and was widely used until competition with other fluoro-ethers and Halothane restricted its use.[45] Research at Dow Chemical Company, referred to above, also produced a large number of fluorinated substances, among which was one judged to be suitable for clinical use (Methoxyflurane, CH$_3$-O-CF$_2$-CHCl$_2$) and it was market successfully from 1960. Research to identify other fluoro-ethers with useful anaesthetic properties continued. Ross C. Terrell of Ohio Medical synthesized over 700 compounds in a search for the 'ideal anesthetic' that commenced in 1960, eventually discovering Enflurane, Isoflurane and Desflurane,[46] while Sevoflurane came from researchers at Travenol Laboratories (Table 2).[47]

Table 2. Fluoro-ether anaesthetics

Anaesthetic name	Chemical structure	Introduction
Enflurane	CHF$_2$-O-CF$_2$-CHClF	1973
Isoflurane	CHF$_2$-O-CHCl-CF$_3$	1981
Desflurane	CHF$_2$-O-CHF-CF$_3$	1992
Sevoflurane	CH$_2$F-O-CH(CF$_3$)$_2$	1994

[41] J. Ferguson, 'The Use of Chemical Potentials as Indices of Toxicity', *Proceedings of the Royal Society B* (1939), **127**, 387-404.

[42] C.W. Suckling and J. Raventos, 'A new halohydrocarbon and methods of making the same', British Patent 767,779, 1957. C.W. Suckling, 'Some chemical and physical factors in the development of fluothane', *British Journal of Anaesthesia* (1957), **29**, 466-472.

[43] A. van Poznak, 'Methoxyflurane and Teflurane', in *Modern Inhalation Anesthetics*, ed. M. B. Chenoweth (Springer, Berlin Heidelberg, 1972), pp. 77-92.

[44] J.C. Krantz, Jr., C.J. Carr, G. Lu and F.K. Bell, 'Anesthesia. XL. The anesthetic action of trifluoroethyl vinyl ether', *Journal of Pharmacology and Experimental Therapeutics* (1954), **108**, 488-495. M.S. Sadove, R.C. Balogot and H.W. Linde, 'Trifluoroethylvinyl ether (Fluoromar®). I. Preliminary clinical and laboratory study', *Anesthesiology* (1956), **17** (4), 591-600. J.W. Dundee, H.W. Linde and R.D. Dripps, 'Observations of trifluorovinyl ether', *Anesthesiology* (1957), **18**, 66-72.

[45] L.E. Morris, 'Fluroxene', in *Modern Inhalation Anesthetics*, ed. M. B. Chenoweth (Springer, Berlin Heidelberg, 1972), pp. 93-102.

[46] W. Burns and E. Eger, 'Ross C. Terrell, PhD, an anesthetic pioneer', *Anesthesia & Analgesia* (2011), 113**(2)**, 387-389.

[47] M.D. Larsen, 'History of anesthetic practice', in R.D. Miller, ed., *Miller's Anesthesia* (Churchill Livingstone, Elsevier, Amsterdam, 2010), 7th edition, 3-42.

All the fluoro-ether anaesthetics, as well as Halothane, can be responsible for some degree of liver damage and as a result their uses are carefully controlled.

8.   Concluding remarks

Meyer and Overton's theory was widely referred to but did not provide a sure path to the development of new anaesthetic gases[48] and although researchers in the 1920s and 1930s measured partition coefficients and solubility ratios they were only paying lip-service to theory. Forman[49] has argued that the various lipid hypotheses, did not meet Popper's criterion that a scientific hypothesis should be falsifiable. Nonetheless, researchers proceeded to ring the changes in molecules and test them in animals against a number of criteria. And although it is three decades since it emerged,[50] neither has the receptor binding mode of action facilitated the discovery of new anaesthetics. Perhaps the fluorinated ethers now in use can be regarded as the long-sought 'ideal gases' for inducing the sleep that takes us away from the realm of pain and facilitates surgery of many kinds.

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[48] M. Perouansky, 'The quest for a unified model of anesthetic action: a century in Claude Bernard's shadow', *Anesthesiology* (2012), **117**(3), 465-474.
[49] S.A. Forman, 'A paradigm shift from biophysical to neurobiological: the fading influence of Claude Bernard's ideas about general anesthesia', *Anesthesiology* (2012), **118**(4), 984-985.
[50] C. Grasshoff, U. Rudolph and B. Antkowiak, 'Molecular and systemic mechanisms of general anaesthesia: the 'multi-site and multiple mechanisms' concept', *Current Opinions in Anaesthesiology* (2005), **18** (4), 386-391.

Perfume at the Forefront of Macrocyclic Compound Research: From Switzerland to Du Pont

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A set of corporate publicity photographs from 1937 depicts several stages in the making and testing of perfumes, including one tableau of a perfume laboratory with a man and a woman sniffing smelling strips, and another depicting the "director of the perfume laboratories".[1] These photographs were not taken for a perfume house or an essential oil supplier; neither do they depict the workings of a firm in Grasse or Paris. These are instead portraying one line of business of the venerable giant of the American chemical industry, E.I. du Pont de Nemours & Company. From the 1930s into the postwar period, Du Pont manufactured and sold synthetic scents and aroma chemicals. While these chemicals were never important either in terms of output or revenue, their production by Du Pont is significant. One of these scents, a synthetic musk, was a direct product of Du Pont's famed Experimental Research Station, 'Purity Hall', an output of the research of Wallace Carothers and his group. In this paper I will argue that the study of perfume was a driver for research in organic chemistry in the twentieth century, particularly in investigations of macrocyclic compounds. This was possible because of the strong financial support given by the fragrance industry, which was willing to invest in expensive processes. After situating this claim in historiography, I will focus in particular on the scent of musk and its synthesis, tracing the research of Nobel Prize chemist Leopold Ruzicka as well as the continuation of his work by Wallace Carothers and his group.

Reflecting on the development of modern perfumery, Ruzicka asserted that "right from the earliest days of scientific chemistry up to the present time perfumes have substantially contributed to the development of organic chemistry as regards methods, systematic classification, and theory".[2] Such a statement seems astonishing considering how little attention has been given to perfumery in the study of academic and industrial chemical research. How did a Nobel Laureate come to make this claim? Did perfume indeed have an effect on the research questions of organic chemistry and if so, how?

In the historiography on the chemical industry, perfumery is given limited attention.[3] Insofar as it has been studied, it has been a story of the rise of synthetic chemistry in the late

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[1] From the Aromatics-synthetic perfumes folder, Box 4, DuPont Company Product Information photographs (Accession 1972.341), Hagley Museum and Library, Wilmington, DE 19807.

[2] *Firmenich and Co: Successors to Chuit Naef and Co*, Geneva, 1895-1945. 1945. (Geneva: Firmenich). 38.

[3] For example it receives sparing mention in the general histories of Ihde, Aaron J, 1964, *The development of modern chemistry*, New York: Harper and Row, and Aftalion, Fred, 1991, *A History of the International Chemical Industry*, Otto Theodor Benfey, translator, Philadelphia: University of Pennsylvania Press, no attention in histories of firms which produced aroma chemicals such as Du Pont in Hounshell, David and John Smith, 1988, *Science and Corporate Strategy: Du Pont R&D 1902-1980*, Cambridge: Cambridge University Press, and no attention in more recent volumes on the European chemical industry such as Lesch, John E., ed, 2000, *The German Chemical Industry in the Twentieth Century*, Dordrecht: Kluwer.

nineteenth century. [4] Subsequent research into chemical products has received less consideration as though the twentieth-century development and use of these materials was an inexorable advancement given the breakthrough of the 1880s. This account is both invention-centric and does not seriously assess the perfume industry as part of the twentieth-century organic chemical industry and obscures its global connections. [5] The story of Carothers' work on scents is most thoroughly described in a couple of pages in Matthew Hermes' biography of Carothers. [6] Hermes, a professor of organic chemistry, clearly related the highlights of the Carothers group research, and noted that it was an extension of Ruzicka's findings, but treated this work as a small amusing episode in Carothers' career and did not further discuss Du Pont's perfume business or Ruzicka, nor make claims about the role of perfume in organic chemistry research. Hounshell and Smith also very briefly noted that Du Pont sold one of Carothers' synthetic compounds as a perfume ingredient but did not mention Ruzicka's work as foundational. [7] Similarly, Ruzicka's work on fragrances has only been examined in his biography, by the historian Gerhard Oberkofler, and mentioned in short biographies written by chemists working in the perfume industry, the most important of which is the Royal Society biographical memoir written by Ruzicka's former students and colleagues Vladimir Prelog and Oskar Jeger. [8] These two works do give due attention to Ruzicka's collaboration with the perfume industry and I will be reliant on them for my analysis of Ruzicka's work; however they do not discuss the continuation of his work by Du Pont. Additionally, I will be supplementing my discussion of Ruzicka's research with primary material from oral interviews and scientific publications.

Perfume in industrial research: Switzerland

One reason for the importance of perfumes to organic chemistry is that perfumes were complex substances, but ones it was very well worthwhile making synthetically if possible. They were expensive and rare. [9] For example, musk was a subject of dedicated study among academically-trained chemists from the 1880s; natural musk is one of the most expensive materials used in perfumery. While one was not reliant on chance to obtain it, as for ambergris, it did involve the hunting of musk deer for their fragrant pouches in Tibet, China, Assam, Nepal and Russia. 30-50 deer were sacrificed for a kilogram of musk. [10] The first suitable synthetic musk substitute however was a chance product, a result of Albert Baur's

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[4] Recent historiography of cosmetics and perfumery has focused on the nineteenth century and the French case, without deeply engaging with the history of chemistry. For example, see: Briot. Eugénie. 2008. *La chimie des élégances : La parfumerie parisienne au XIXe siècle, naissance d'une industrie du luxe*. (Conservatoire National des Arts et Métiers, Centre d'Histoire des Techniques et de l'Environnement).

[5] This claim builds on Geoffrey Jones' work (Jones, Geoffrey. 2010. *Beauty Imagined: A History of the Global Beauty Industry*. [Oxford: Oxford University Press]).

[6] Hermes, Matthew E. 1996. *Enough for one lifetime: Wallace Carothers, inventor of Nylon*. (Washington, D.C.: American Chemical Society and the Chemical Heritage Foundation).

[7] Hounshell and Smith (note 3): 243.

[8] Oberkofler, Gerhard. 2001. *Leopold Ruzicka, 1887-1976: schweizer Chemiker und Humanist aus Altösterreich*. (Innsbruck: Studien Verlag).
Prelog, Vladimir and Jeger, Oskar. 1980. Leopold Ruzicka. 13 September 1887-26 September 1976. *Biographical Memoirs of Fellows of the Royal Society*, **26**: 411-501.

[9] In this a parallel can be drawn with natural, expensive dyes and the history of synthetic dyes.

[10] Kraft, Philip. 2005. Aroma Chemicals IV: Musks: 143. In: *Chemistry and Technology of Flavors and Fragrances*. David Rowe, ed. (Oxford: Blackwell): 143-168.

experiments with explosives in 1888. In 1906 it was a chemist in Leipzig at the fragrance company Schimmel (a firm which invested extensively in the creation of an industrial centre for perfume materials research) who isolated the main compound for musk's odour, a macrocyclic compound.[11] Heinrich Walbaum also identified the compound as a ketone, named it muscone and derived its empirical formula.[12] Civetone, a musk odour compound from the civet cat, was also identified as a ketone and isolated in 1915 by E. Sack.

It was with Chuit and Naef that Ruzicka would continue the research of Heinrich Walbaum. Chuit and Naef, with whom Ruzicka would remain involved throughout his career, was founded by a businessman, Martin Naef, and a chemist, Philippe Chuit, in 1898. Chuit studied chemistry with Carl Graebe in Geneva and Henri Brunner in Lausanne and worked for Sandoz in Basel; thus he was firmly inscribed in the Swiss chemical industry.[13]

Industry was not Ruzicka's first choice.[14] He had completed his doctorate in 1910 at the Technische Hochschule in Karlsruhe under Hermann Staudinger, and afterwards worked as Staudinger's assistant in Zurich when the former was appointed Professor and Chair of the Department of Chemistry at the ETH (Eidgenössische Technische Hochschule/Swiss Federal Institute of Technology) in 1912.[15] Staudinger was awarded a Nobel Prize in chemistry in 1953 for his demonstration of the existence of polymers, large molecules composed of repeating subunits, and subsequent work.[16] In was in his postdoctoral work with Staudinger from 1911-1916 that Ruzicka embarked upon the field of study which would become his lifetime career, natural product chemistry and terpenes.[17] Staudinger and Ruzicka isolated and determined the structure of pyrethrins, insecticidal compounds found in certain species of daisy, including one of Dalmatian origin, such as *Chrysanthemum cinerariifolium, Tanacetum cinerariifolium* and *Chrysanthemum coccineum*. The pyrethrins are of a class of compounds called terpenoids, multicyclic chemicals similar to terpenes. Extracted pyrethrins and the synthetic analogues, pyrethroids, continue to be important insecticides. Ruzicka's first independent work continued the focus on natural terpenes, which would be foundational for his later work in the perfume industry as a number of fragrant compounds are terpenes. He performed the synthesis of a fragrant ketone called fenchone, a component of fennel oil and some leaf oils. He completed a synthesis of linalool in 1919 and of α-pinene in 1921.

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[11] These macrocyclic molecules should be distinguished from polycyclics; macrocyclic substances are composed of one large many-membered ring, while polycyclic molecules are composed or two or more rings. While muscone and Du Pont's musk Astrotone are macrocyclic, a number of synthetic musks from the 1950s onwards are polycyclic, including International Flavors and Fragrances' Galaxolide, the synthetic most widely used in the early twenty-first century. Kraft (note 10): 147, 152-155.

[12] Walbaum, H. Das natürliche Moschusaroma. *Journal für praktische Chemie.*: **73**, 488–493.

[13] Oberkofler (note 8): 61.

[14] Oberkofler saw Ruzicka as emotionally attached to academia. Oberkofler (note 8): 63.

[15] Leopold Ruzicka (1887-1976) was born in the Austo-Hungarian Empire, in Vukovar, Croatia. At Karlsruhe he was also taught by Fritz Haber and completed both an Engineering Diploma and a doctorate studying ketenes under Staudinger. Prelog and Jeger (note 8): 411- 412.

[16] For a study of Staudinger's career and the foundation of polymer studies, see Yasu Furukawa's 1998 work: *Inventing Polymer Science: Staudinger, Carothers and the Emergence of Macromolecular Chemistry.* (Philadelphia: University of Philadelphia Press).

[17] Prelog and Jeger (note 8): 412. Terpenes are a class of compounds very important in natural products; they consist of arrangements of isoprene units. Isoprene is a hydrocarbon of the formula C_5H_8, with the IUPAC name 2-methyl-1,3-butadiene.

Staudinger curtailed continued support when Ruzicka expressed his intention to work on more independent projects and so at an early stage in his career the latter was obliged to seek outside financial assistance to develop his own line of research.[18] Ruzicka's first industrial contact, Haarmann and Reimer was established in Holzminden, Germany in 1874, by chemists who had trained under Hofmann in Berlin, to manufacture synthetic vanillin. However Ruzicka's first project on fragrance materials was unsuccessful; in his period of work for Haarmann and Reimer, 1917-1920, he was unable to synthesise irone, an aroma chemical of violet. However, the project allowed Ruzicka to become more experienced with a certain type of structural change occurring in chemical reactions, a rearrangement of atoms called the Wagner-Meerwein rearrangement, which would be foundational for his future work.[19]

Ruzicka had been in contact with Chuit and Naef in 1919, but did not agree to undertake direction of research until January 1921, beginning "a highly propitious and productive symbiosis".[20] From the start Chuit and Ruzicka worked together closely, and together compiled a list of six interesting molecules to investigate, that is, to determine structures and synthesise possible substitutes, as a research programme: nerolidol, jasmone, farnesol, irone, civetone and muscone.[21] Ruzicka's choice of industrial partners indicates the status of perfumery as a scientific industry, a viable partner not only for funding and temporary projects but for sustained research.

From the funding allotted by Chuit and Naef, Ruzicka hired assistants. While he did not receive funding from the ETH, he did hold honorary appointments of Privatdozent from 1918 and Titular Professor from 1923, so that he was able to have his own students and space. Ruzicka and his group only worked on-site at the Geneva laboratories of Chuit and Naef for a year from March 1925, when relations with Staudinger became strained.[22] In 1927, Ruzicka obtained an academic position at the University of Utrecht, but continued to maintain a close relationship with Chuit and Naef during his career.

The chemistry of terpenes as well as macrocyclic compounds was not trivial and the list of molecules which Chuit and Ruzicka agreed upon was not lacking in ambition; Ruzicka promised Martin Naef, "For the first time we have before us a rare chance to do something really novel in perfume chemistry."[23] Macrocyclic compounds such as muscone were considered to be very unstable and impossible to synthesise, based on Adolf von Baeyer's strain theory, and carbon rings of more than eight carbons had not yet been identified.[24] However, Ruzicka's series of papers in 1926 based on work he had begun a few years earlier with Chuit and Naef countered that understanding. He elucidated the structure of civetone to

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[18] Prelog and Jeger (note 8): 413.
[19] Prelog and Jeger (note 8): 413, 428.
[20] Prelog and Jeger (note 8): 413.
[21] Oberkofler (note 8): 61-62. Chuit proposed the same list, but with nerol for nerolidol. The compounds are components of a number of essential oils, but the predominant origin is as follows: nerolidol from orange blossom oil, jasmone from jasmine, farnesol from acacia blossoms, and irone from iris essential oil.
[22] Ruzicka was also Privatdozent at the University of Zurich from 1920. Prelog and Jeger (note 8): 413-414; Oberkofler (note 8): 62.
[23] Cited in Prelog and Jeger (note 8): 425.
[24] Prelog and Jeger (note 8): 413, 425.

be a large ring and then conjectured that muscone must also be of a similar structure before experimental confirmation.[25] In synthesis experiments, he was able to identify a reaction which produced large-ringed ketones and synthesised a series of these compounds from 9 to 29 carbons, of which the 14-18 membered rings had the strongest musk odour. The reaction was dry distillation of thorium and cerium salts of certain dicarboxylic acids. Chuit and Naef were most likely quite pleased with these results, as one of the rings was successfully marketed: cyclopentadecanone/*nor*-muscone with the trade name Exaltone. This was almost identical to natural musk but was missing a methyl (CH_3) group.[26] Ruzicka then embarked on a study of related macrocyclic compounds, ketones, lactones, ketoximes, lactams, imines, amines and alcohols produced through various steps of reduction, oxidation and rearrangements, to determine general properties and stereochemistry and develop theoretical insights into large rings and multi-ringed compounds. Ruzicka showed that large ring compounds could exist, were not subject to a special strain and indeed could have lower heats of combustion than small rings.[27]

The commercial import of the work on musks is evidenced by the competition to release a synthetic to market. For example, Haarmann and Reimer, a strong competitor against Chuit and Naef, strove to gain a market in musk substitutes. In 1927 one of their researchers, Max Kerschbaum, isolated a vegetal musk, a macrocyclic lactone identified as 15-pentadecanolide, from Angelica root oil.[28] However Chuit and Naef were first to be able to produce the molecule on an industrial scale, branding it Exaltolide®.[29] It was synthesised by an oxidation step (a Baeyer-Villiger reaction) from Ruzicka's first commercial musk for Chuit and Naef, Exaltone. Kerschbaum also isolated another vegetal musk, ambrettolide from Ambrette seed oil, which Haarmann and Reimer were able to sell, synthesising it from shellac.[30]

Ruzicka's work on terpenes continued in earnest at Chuit and Naef with studies into synthesising farnesol and determining the structure of and synthesising nerolidol. Many terpenes important in perfume are sesquiterpenes, which are composed of three isoprene units, of which farnesol and nerolidol are examples. As Prelog and Jeger noted, the "interest in this field was by no means pecuniary."[31] When Ruzicka began work on the sesquiterpenes, there was scant understanding of their structure and no sesquiterpene found in nature had yet been synthesised. He developed a different procedure to determine structure and satisfied the latter with synthesis of nerolidol. Building on the work of German chemist and Nobel laureate in Chemistry (1910) OttoWallach, Ruzicka found further evidence for three isoprene units as the structure of sesquiterpenes.[32] Ruzicka continued work on sesquiterpenes after returning to academic positions both at Utrecht and Zurich, especially in the late 1920s and 30s but also

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[25] Prelog and Jeger (note 8): 431.

[26] It was later identified to be a naturally-occurring compound in the scent gland of the Louisiana muskrat. Kraft (note 10): 146.

[27] Prelog and Jeger (note 8): 425. Specifically, heats of combustion per methylene group of 15- and 30-member hydrocarbon rings (cycloalkanes) were lower than for cyclohexane and cyclopentane.

[28] Kerschbaum also determined the structure of farnesol in 1913, one of the compounds Ruzicka worked to synthesise at Chuit and Naef. Prelog and Jeger (note 8): 437.

[29] Kraft (note 10): 147.

[30] Kraft (note 10): 147, 149.

[31] Prelog and Jeger (note 8): 437.

[32] Prelog and Jeger (note 8): 437-438.

into the 1950s, working on constituents of such natural products as the oils of sandalwood, eucalyptus, celery and clover.

The fragrance industry was a very propitious site for investigating this complicated chemistry as it was able to gain favourable margins on its products and thus supply a large amount of financial support for these experiments. The reaction yields of Ruzicka's musks were very low, from 0.1% to 6%, but though the reactions were expensive these were still very profitable in the musks market where a kilogram of muscone cost 300,000 Swiss francs.[33] Chuit and Naef's financial backing allowed Ruzicka to build a research group, some members of which made their careers in perfume-related research and moved between industry and academia, such as Max Stoll and Hans Schinz. Max Stoll remained at Chuit and Naef (to be renamed Firmenich in 1934) as head of research from 1927 when Ruzicka left Geneva to continue his work on terpenes and macrocyclic compounds as Chair of Organic Chemistry at the University of Utrecht.[34] Hans Schinz joined Ruzicka at the ETH and had doctoral students of his own, one of whom was Albert Eschenmoser, who completed his thesis on sesquiterpene chemistry and later synthesised vitamin B_{12} in collaboration with Harvard.[35] Chuit and Naef's later incarnation as Firmenich continued to heavily support the work of Ruzicka's team; Eschenmoser, who remained a consultant for them, remembered that "For many years they [both Firmenich and CIBA] have supported my group very generously, without any strings attached," their funding "was very important for us."[36]

Ruzicka's study into chemically interesting fragrance molecules led him to consider research questions in the wider field of terpenes and terpenoids then into steroids and hormones, as Prelog and Jeger attested. One of Ruzicka's major contributions to the chemistry of terpenes was his establishment of the Isoprene Rule, a proposal made by Otto Wallach in 1887 but not considered significant. It was thus Ruzicka's work for a perfume company which provided much of the impetus and the foundation for his Nobel-Prize winning research.

Perfume in industrial research: the Du Pont Experimental Station

Moving from the laboratories of a small but profitable Swiss synthetics firm, Ruzicka's research was taken up by the chemists of the largest chemical company in the United States, Du Pont.

Following the *mensis mirabilis*, as Hounshell and Smith labelled April of 1930, the Carothers group delved more deeply into the theoretical consequences and new avenues posited by their accomplishments of the synthesis of neoprene and a laboratory-made polyester fibre, one avenue of which, namely further studies into polymerisation, led to the synthesis of fragrant macrocyclic molecules. From the late 1920s Carothers had been working on synthesising substances of high molecular weight, higher than previous successes – these substances were

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[33] Prelog and Jeger (note 8): 425.
[34] Prelog and Jeger (note 8): 414. Ruzicka returned to ETH when he was hired as Chair in 1929, after the previous Chair, Richard Kuhn, left for the Kaiser Wilhelm Institute for Medicinal Chemistry in Heidelberg.
[35] Oral history interview with Albert Eschenmoser, 1985, Chemical Heritage Foundation: 6-7.
[36] Eschenmoser (note 25): 30.

polymers, synthesised through a process of polymerisation.[37] Carothers published a series of papers in the *Journal of the American Chemical Society* presenting his group's work on polymerisation. As noted above, polymerisation was a very active field of study in the 1920s, though in a "disorganised" state before the formulation of Carothers' theory, according to organic chemist Roger Adams.[38]

In 1932, Carothers together with Julian W. Hill developed a research project on cyclic molecules. Hill was the member of Carothers' group sharing responsibility for the linear condensation polymers/synthetic fibre synthesis. Condensation reactions, where water is released as a by-product of a reaction (in this case the functional groups of two or more substances react and result in covalent bonds), were the group's primary means of building polymers. In his project to build high-weight polyester chains, Hill facilitated the synthesis by realising that a molecular still could overcome the current impediment – Carothers conjectured that water formed during polyester reactions hindered formation of longer chains and needed to be removed. The still could be used to trap and remove the water.[39] The still did indeed lead to the formation of polymers of much higher molecular weight and subsequently was also decisive in the synthesis of aroma chemicals. Specific aroma chemicals, of a large-ring macrocyclic structure, became of great interest to Carothers and Hill as these molecules exist in equilibrium between ring and long-chain polymer forms.

Ruzicka's research was the foundation for Hill and Carothers' work; no one outside his group had yet taken Ruzicka's "finished and very striking researches on the constitution of the musks" further.[40] Carothers was very deliberate in his intention to develop the field of macrocyclic molecules.[41] The standard set-up for a polymerisation reaction was between dibasic (diprotic) acids and glycols. The Du Pont researchers proceeded to try a series of synthetic reactions, systematically making macrocyclic compounds of increasing size in as many combinations of various dibasic acids and glycols as available. Hill recollected that musky odours were detected in almost any combination of glycols and acids, as long as the ring was within a certain size.[42] Already by July of 1932, Carothers reported that these molecules could be commercialised as "substitutes for one of the most costly type of perfume materials."[43] Among the different series, the most powerful odour came from a reaction with the hexamethylene glycol. Another researcher, Frank J. Van Natta, was conducting the reactions, presuming that the crystalline substance deposited on his apparatus was distilled excess glycol; Hill recollects himself realising that the substance was probably a large ring, cyclic hexamethylene carbonate, which resulted in a camphoraceous odour.[44] Based on

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[37] For a detailed account of Carothers' polymer research, see Furukawa (note 16) and Hounshell and Smith (note 3): 223-248.

[38] Adams, Roger. 1939. Biographical Memoir of Wallace Hume Carothers. *National Academy of Sciences, Biographical Memoirs* **20**: 301.

[39] Furukawa (note 16): 136-138; Hounshell and Smith (note 3): 236-237.

[40] 14 January 1930, Carothers to Charles Stine. Accession 1784, Box 18, Hagley Museum and Library, Wilmington, DE 19807.

[41] Oral history interview with Julian Hill, 1982, Hounshell and Smith oral history interviews, 1982-1988, Accession 1878, Hagley Museum and Library: 33.

[42] Hill (note 41): 36.

[43] July 1932 report: 4. Accession 1784, Box 18, Hagley Museum and Library.

[44] Hill (note 41): 35.

Ruzicka's research, larger rings synthesised from larger molecules of methylene carbonate would be predicted to have a musk odour. Hill himself performed the synthesis using the larger glycol tetradecamethylene, which yielded the very musky tetradecamethylene carbonate.[45] By August 1933 the group had not yet succeeded in isolating the compounds, but Carothers sent samples of the pungent products to Bolton and Stine. Bolton was apparently ready to dismiss the project as a 'hoax'.[46]

The work on large rings was very fruitful for Carothers and his colleagues. Julian Hill's letter nominating Carothers for the American Chemical Society's William H. Nichols Medal in 1934 enumerates the outcomes of the research as: new method of synthesising many-membered cyclic compounds, several new types synthesised, and new data for studying and conceptualising ring formation.[47]

Tetradecamethylene carbonate was the original Astrotone, Du Pont's commercial synthetic musk. It was first introduced as a synthetic musk in the 1933 meeting of the American Chemical Society and described in the Carothers publication series on polymers. The trade name Astrotone was announced in the November 1934 issue of Du Pont Magazine, and was available for purchase at $200 per pound. The Purity Hall musk was further developed for marketable production by another member of the Carothers group, Edgar Spanagel. Indeed, when he joined Du Pont in 1933, on his first day of work Spanagel was assigned to the on-going perfume project.[48] This project was recently expanded through sponsorship from the Organic Chemicals Department (Orchem), to determine whether any of the cyclic molecules could be viable on a larger scale. Orchem decided that tetradecamethylene carbonate was the only promising compound at that time.[49] Spanagel was put to task on optimising the synthesis of the musky macromolecules, specifically a 17-member ring, as yields were very small and inconsistent. After maintaining at a specific pressure the vacuum in which the starting polymer was heated, Spanagel recalled that the macrocyclic compound was produced consistently and yielded as much as 100 grams per batch.[50] Spanagel then travelled to the Organic Chemical plant in New Brunswick, New Jersey to work on further streamlining the reactions and preparation of intermediate reagents.[51] From November 1933, Spanagel was suspended from direct work on tetradecamethylene carbonate until Orchem would decide that manufacturing would be undertaken, but continued to work on cyclic molecules.

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[45] Hill (note 41): 35.
[46] Hill (note 41): 35.
[47] Julian Hill to J.M. Weiss, 28 August 1934, Records of the DuPont Company's Central Research and Development Department, 1902-1985, Accession 1784, Box 18, Hagley Museum and Library.
[48] Oral history interview with Edgar W. Spanagel, 1997, Chemical Heritage Foundation: 9.
[49] Carothers to Bolton, New Project on Substituted Bifunctional Esters, 10 November 1933, Records of the DuPont Company's Central Research and Development Department, 1902-1985, Accession 1784, Box 18, Hagley Museum and Library.
[50] Spanagel (note 48): 9 -10; Carothers to Bolton, New Project on Substituted Bifunctional Esters, 10 November 1933, Records of the DuPont Company's Central Research and Development Department, 1902-1985, Accession 1784, Box 18, Hagley Museum and Library.
[51] Carothers to Bolton, New Project on Substituted Bifunctional Esters, 10 November 1933, Records of the DuPont Company's Central Research and Development Department, 1902-1985, Accession 1784, Box 18, Hagley Museum and Library.

However, what is now known as Astrotone is a molecule called ethylene brassylate, synthesised by Spanagel. In the search for a range of different glycols and dibasic acids as starting materials for polymerisation, Carothers asked a colleague at Cornell, John R. Johnson in May 1932, whether the ozonisation methods he was developing could produce a good yield of higher weight dibasic acids.[52] Johnson sent the directions for production of the compound his group had found interesting, dimethyl brassylate. Spanagel then worked on the ring formation with this compound and produced ethylene brassylate, a 17-member ring with a strong musk odour, using tin chloride as a catalyst.[53] Spanagel's patent including this synthesis covered the more general ground of preparing cyclic esters of 7 or more members, using catalysts he determined were effective, of which tin chloride is one type.[54] From the 37 new cyclic esters listed in his patent, he used three as examples of musk or civet substitutes, suggesting that those with 15-17 member rings were most suitable: ethylene brassylate, nonamethylene adipate and hexamethylene azelate. According to Spanagel, ethylene brassylate was much easier to make than tetradecamethylene carbonate, especially with the catalysts described in his patent, and so perhaps for this reason was the more successful commercial Astrotone.[55] The tetradecamethylene carbonate Astrotone was made by Orchem for a brief period. According to Merlin Brubaker's account of the laboratory legend, 300 pounds of tetradecamethylene carbonate were produced, but Orchem was unable to sell it until a Rhone-Poulenc representative evinced interest. Rhone-Poulenc then resold "for some fabulous price" after diluting it by fifty percent and adding diethylamine, a strongly unpleasant smelling compound, which measures seem to have proved beneficial as it was then allegedly used in a successful French perfume.[56]

The Carothers group perfume project was a small but vibrant part of Du Pont's fundamental research section. Apart from the macromolecules, Hill, Brubaker and Carothers also worked on smaller questions such as substitution for perfume intermediates.[57] It incurred little expenditure compared to other projects, $7,484 in 1933 and less costs thereafter.[58] Projects continued until 1938, such as research on derivative of pinene and camphor in 1937, and condensation of terpenes with phenols in 1937 and 1938. The number of scientists involved was sizeable, Carothers and two of his colleagues, Julian Hill and Edgar Spanagel.

In conclusion, perfume materials were not only of commercial interest to companies, but certain compounds were of high chemical interest in the academy, as evidenced by the work of Ruzicka. The chemistry of these compounds was not ordinary or trivial, but was situated in

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[52] Carothers to Johnson, 24 May 1932, Records of the DuPont Company's Central Research and Development Department, 1902-1985, Accession 1784, Box 18, Hagley Museum and Library.
[53] Hill (note 41): 36.
[54] Edgar W. Spanagel, 'Process of Preparing Cyclic Esters', US 2092031, 1937.
[55] Spanagel (note 48): 11; Hermes (note 6): 165.
[56] Oral history interview with Merlin Brubaker, 1982, Hounshell and Smith oral history interviews, 1982-1988, Accession 1878, Hagley Museum and Library: 20.
[57] E.g. o-toluic acid for benzoic acid. 8 August 1934, Paul Austin to Carothers, Records of the DuPont Company's Central Research and Development Department, 1902-1985, Accession 1784, Box 18, Hagley Museum and Library.
[58] Fundamental Research Expenditure. Perfume Chemicals, Account S-1408-B-2, project number 1635, Records of the DuPont Company's Central Research and Development Department, 1902-1985, Accession 1784, Box 18, Hagley Museum and Library.

the field flourishing at the time, polymer chemistry, and study of these compounds led to new insights in polymerisation and understanding of macrocyclic molecules, as seen also in Carothers' research.

Polanyi's Physical Adsorption: One of the Early Theories of Quantum Chemistry

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Michael Polanyi is known as a philosopher who presented such ideas as tacit-knowledge or personal knowledge, generally speaking. But before changing his profession to philosophy, he had been an extremely active physical chemist, who dealt with diverse fields such as adsorption theory, chemical kinetics, X-ray diffraction, dislocation theory and so on. We find that he is even more extreme when we look at his key students and colleagues. Needless to say, John Polanyi is Michael's son. Eugene Wigner was his doctor student. Herman Mark, Karl Weissenberg, Egon Orowan, Henry Eyring, M. G. Evans, and Melvin Calvin were members of his research team, or colleagues. It could be said that it was Polanyi who raised the next generation of leaders in modern physical chemistry from the 1930's.

John Polanyi says this of his father:

> If he were ever boastful, Michael Polanyi would have described himself as a scientist of the second rank. The first rank, in his terminology, constituted the pillars on which the edifice of science rested…He was equally bold in his choice of topics. He was anxious to make use of the freedom that his amateur status gave him. His family cultivated young Hungarian painters, poets, novelists and scholars. "I grew up in this circle," Michael wrote, "taking it for granted that I could do great things."

This saying is actually supported by Michael Polanyi himself. Polanyi replied to Kuhn when he was asked why he left the sciences:

> I thought that I would make my discoveries in science before the Great War and afterwards I would go on and do something in philosophy of science. And actually when I wrote my theory of adsorption I thought I had made a great discovery. I had made a discovery, but not a very great one. And so that didn't help me to establish myself definitely as a scientist.

It is quite obvious that Polanyi was a first tier scientist, but the question of first or second is not really the point here. The point is that Polanyi thought his adsorption theory to be his greatest discovery, even though it is his reaction kinetics that is generally regarded to be his representative work as a scientist.

Polanyi's adsorption theory was not chemisorption but physisorption, in present terminology. He assumed porous solids to be adsorbent and gas to be adsorbate; the binding force to the adsorbent he thought to be potential spatially fixed, caused by intermolecular attraction; and multi-layer adsorption continuing to liquefy the compressed layer. At first, he proposed this theory in 1914 under the supervision of George Bredig when he studied at Karlsruhe TH, eventually basing his doctoral thesis on it in 1916. His theory was supported by other chemists such as Herbert Freundlich, but on the other hand resulted in severe criticism from Fritz Haber and Albert Einstein for reasons I will explain in just a moment. Polanyi kept developing this theory intermittently and presented the final version with Fritz London in 1930.

Although Langmuir proposed the adsorption theory at the same time Polanyi first proposed his theory, Polanyi was not aware of it, because of the communication difficulties under the influence of the war. Langmuir's theory assumed the plane surface of metal to be adsorbent and the binding force he thought to be electrostatic force. The adsorbates are captured in distant cite, so that the force between adsorbates is negligible, forming a mono layer on the surface. This theory was apparently conditionally limited for the phenomena but simple and easy to apply. An electrostatic view of chemical reaction was popular for the chemists at that time, and also G. N. Lewis proposed the chemical valence theory in 1916. Most physicists at that time, such as Haber and Einstein, followed this line of thinking.

In actuality, setting at that time was not so simple. Polanyi himself summarized the situation at that time:

> During the very years in which the theory was born, there occurred a dazzling series of insights into the nature of things. Debye's discovery of fixed dipoles, Bohr's atomic model, and the ionic structure of sodium chloride found by W. H. Bragg and W. L. Bragg, established the pervasive function of electrical interaction. A number of theories were put forward on these lines. Keesom suggested an electrostatic interaction of fixed quadrupoles; Debye, an interaction of quadrupoles with induced dipoles. Kossel's attempt to explain all chemical bonds as attraction between positive and negative ions also belongs to this period.

> This view of atomic forces made my theory of adsorption untenable. Electrical interactions could not be derivable from a spatially fixed potential; they would be screened off by the presence of other molecules in the field.[1]

The electrostatic view was not uniquely created by chemists, but was also being approached concurrently by physicists as well. It was the result of the sudden development of atomic theory in accordance with the development of quantum theory in physics. Unlike chemistry, the idea of the "atom" was very new for physics. Although the existence of the electron was already accepted, the electron was not recognized as a part of the atom's structure. Atomic theory, more precisely atomic structure theory including electrons, was not accepted until Bohr's model in 1913. For physicists, the atom had been just a particle in their own mechanics. In 1911, the need for energy quanta was first confirmed during the famous Solvay Conference, and in the same year Rutherford proposed the atomic model on which Bohr expanded just afterwards. Valence theory was gradually accepted as an extension of the atomic structure theory in physics. As a result, Freundlich dealt with both Langmuir's theory and Polanyi's theory in his book in 1922. Even so, the fusion of valence chemistry and atomic structure physics was not yet to be.

Here, let us clarify the situation and terminology. There were two schools of chemists: those who referred to valency to explain chemical reaction or chemical structure, and those who did not during the 1910's. The latter included electrochemists, thermochemists, and scientists on kinetic theory of gases, mainly in Europe. They were physicists rather than chemists in that sense, or one might say chemical physicists. European chemistry at that time was organic synthetic chemistry. Ostwald already used the term "physical chemistry" with regards to his unique philosophical idea. However, it generally meant nothing more than to differentiate it from organic synthetic chemistry when it referred to a discipline.

But by the 1920's, as John W. Servos has pointed out, the former became powerful in the U.S.[2] They developed their theories independently of what was going on in Europe, which

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[1] Polanyi Michael, p. 88.
[2] Servos, pp. 202-250.

was the development of atomic structure theory in accordance with quantum theory. Valency was, however, gradually adopted in Europe during the 1920's as well. The final push towards fusion was given by the physicists' side; Heitler and London in 1927.

Polanyi was a chemical physicist. His approach to adsorption was completely through chemical physics, as I have explained. Indeed, Mary Jo Nye pointed out that "Polanyi's approach lay thoroughly within the framework of nineteenth-century classical thermodynamics."[3] But he was not "classical" in a Whiggish sense. His approach derived from the very heart of the topic at that time. In Polanyi's theory, gas molecules, through equation of state, would become liquefied when adsorbed under high pressure. This was the biggest difference from Arnold Eucken's theory, which assumed direct gas adsorption under high pressure. This hypothesis came from Polanyi's interest in early quantum theory.

As Scott pointed out:

> Polanyi's proposal to Bredig came out of a careful study of Planck's treatise on thermodynamics and of the work of Einstein in establishing the concept of the quantum of energy. His creative contribution was to see, by an act of the imagination, a joint consequence that was not separately obvious in either piece of work. Planck had explained Nernst's theorem that the entropy (the disorder of the component molecules) of a substance would approach zero as the temperature approached absolute zero. Polanyi's new idea was that the same would be true if, instead of lowering the temperature in order to decrease the random motion of the gas molecules, pressure were increased instead. The closer the pressure came to infinity the more motion of the molecules would be restricted, thus decreasing entropy to zero at infinite pressure.[4]

It is apparent that Polanyi applied Nernst's heat theorem, in the context of specific heat, to adsorption. He also took into account Van der Waals equation for application. Certainly he did not use quantum theory directly, but despite that at the time only few scientists such as Einstein and Nernst knew the significance between quantum theory, Nernst's heat theorem and low temperature physics, Polanyi was putting it into practice within the field of adsorption.

From 1900 to 1907, Max Planck's energy quanta were just a hypothesis. But in 1907, Einstein proposed a quantum theory on solids. Unlike the light quanta, this quantum theory had a quick reaction in the scientific community. Nernst noticed the significance of Einstein's theory, because for his heat theorem, which was proposed in 1906, he needed to clarify the reason how and why specific heat at low temperature goes down. By this time, quantum theory was no longer a mere hypothesis, but only for the select few. Also they needed more experimental evidence. It was brought by Kamerlingh Onnes in 1908. He liquefied helium through Van der Waals equation. It was due to this that they could examine quantum effects at low temperature. Thus, this became the main theme of the 1st Solvay Conference, which was organized by Nernst himself. This was the context under which Polanyi proposed his adsorption theory.

Even though Polanyi himself was not good at mathematics of quantum mechanics, he was one of its early adopters. This is why he could follow along with Einstein and Nernst's discussion on specific heat. Polanyi had been interested in specific heat since reading a book by Nernst during Gymnasium. Polanyi regarded the paper on specific heat he wrote at Gymnasium to be 'nonsensical', however, that was the year 1907 and according to Scott, there was a correspondent at the University of Vienna who offered to discuss it with him. As John Polanyi

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[3] Nye, p. 89.
[4] Scott & Moleski, p. 27

described, Polanyi was bold with his choice of topics. And the greatest topic for him had been adsorption[5].

Even after being attacked by Einstein and Haber, Polanyi did not abandon his adsorption theory. He contacted London right after London had proposed his dispersion theory in 1929. Polanyi immediately asked such questions of London: 'Are these forces subject to screening by intervening molecules? Would a solid acting by these forces possess a spatially fixed adsorption potential?'[6] Even though Polanyi himself was not good at mathematics of quantum mechanics, he recognized the impact of London's work and applied it with London to his adsorption in 1930; he proved that adsorption potential changes depending on the distance from the wall as he suggested in 1916.

As I have explained so far, Polanyi's theory only makes sense when applied within the context of early quantum theory. He was definitely an early adopter of quantum theory. This can be seen by his choice of topic and application of London dispersion force to his adsorption theory. Also as Gavrogru and Simoes argued, one is unable to follow any story by focusing on one discipline alone, especially during this era in history. It is for this reason I would like to propose in lieu of disciplines such as physics, chemistry, physical chemistry or chemical physics, a *topic* instead be used to describe this study. Perhaps quantum theory (not quantum mechanics) or property of matter would be good candidates.

When we intentionally remove the confines of discipline and examine Polanyi in the context of quantum theory, we can see intention behind Polanyi's choice of research topic. In previous studies, Polanyi's life seemed to be dictated by coincidence, however, he might have made very carefully planned choices. Study on colloids was one main theme of electro chemistry at that time. Colloid was a topic common to both mentors Tangl in the medical school of Budapest University, and Bredig in Karlsruhe TH. Even though Polanyi was forced to turn to medical study on the advent of his father's death in order to make a living, he began as an unpaid assistant to Tangl. Rare at that time, Tangl put emphasis on physics and chemistry. Polanyi had held interest in thermodynamics since his time in gymnasium.

Polanyi says to Kuhn in the same interview I quoted in the beginning:

> As to myself, it was an idea that although I had no change of becoming a scientist, at least I would have some form of scientific occupation—being a doctor—and then I could read and perhaps do some work on the side. But it turned out that I became scientist.

When we think from this perspective, we can understand how happy he was when his idea on liquefaction of gases was approved by Einstein. Polanyi wrote "Bang! I was created a scientist."[7]

To re-examine Polanyi in this way lead me to re-examine the history of early quantum theory as well. For example, it was in fact specific heat that was the central topic for early quantum theory, even though normal history of quantum mechanics had until now only been examined at the simplest level. During that time only a few scientists knew the significance of specific heat for quantum theory, and it was they who were its' paradigm builders.

With Polanyi as the catalyst, I started focusing on the history of quantum mechanics as the beginning of the research programs for property of matter.

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[5] Scott & Moleski, p.16.
[6] Polanyi Michael, pp. 89-90.
[7] Scot & Moleski, p. 28.

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From Physical Chemistry to Chemical Physics, 1913-1941

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There has never been one unique name for the intersection of chemistry and physics. Nor has it ever been defined by a single, stable set of methods. Nevertheless, it is possible and arguably rewarding to distinguish changes in the constellation of terms and techniques that have defined the intersection over the years. I will speak today about one such change, the advent and ascendancy of chemical physics in the interwar period.

When the young Friedrich Wilhelm Ostwald first began to formulate his campaign for "physical chemistry" in 1877, he used the term almost interchangeably with two others, "general chemistry" and "theoretical chemistry." According to his vision of what would soon become a new chemical discipline, physical chemistry would investigate and formulate the general principles that underlie all chemical reactions and phenomena. The primary strategy that he and his allies used to generate these principles was to formulate mathematical "laws" or "rules" generalizing the results of numerous experiments, often performed using measuring apparatus borrowed from physics. Their main fields of inquiry were thermochemistry and solution theory, and they avoided and often openly maligned speculations regarding structures or mechanisms that might underlie the macroscopic regularities embodied in their laws.[1]

In the first decades of the 20th-century, the modern atomic theory was firmly established, and with only a slight delay, the methods of 19th-century physical chemistry lost a considerable proportion of their audience. Theories relying upon atomistic thinking began to reshape the disciplinary intersections of chemistry and physics, and by the end of the 1930s, cutting-edge research into the general principles of chemistry looked quite different than it had at the turn of the century. For one, quantum mechanics had become the basis not only for a range of new theories, but also for a wide array of promising, if still primitive, new instrumental methods. In addition, the "homeland" of physical chemistry, the bulk of its leading research centers, was moving increasingly further from the German-speaking universities, as research centers in Great Britain and the USA as well as Japan took the lead in developing these new methods. This marked a disciplinary transformation both intellectually and institutionally, leading to tensions between older physical chemists and those employing the new methods. It also spawned a new disciplinary label, "chemical physics," meant to include not only quantum chemistry, but also modern reaction kinetics, diffraction techniques (both x-ray and electron), and molecular spectroscopy, among other fields.

In this talk, I will provide an overview of the rise of chemical physics, albeit a brief one, and I will argue that the intellectual and geographical peculiarities of its establishment, especially its deep instrumental entanglement and its early reliance upon a relatively small, widely distributed research network are important keys to understanding the postwar development of chemistry, particularly chemical modeling and theory. The talk will be divided into three parts. The first part will cover how chemical physics differed from traditional physical chemistry and what this might tell us about the intersections between chemistry and physics in the interwar period. The second part provides some examples of how the methods that

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[1] For an overview of this development see John W. Servos, *Physical Chemistry from Ostwald to Pauling: The Making of a Science in America* (Princeton: Princeton University Press, 1990).

collectively made up chemical physics moved simultaneously between countries and between scientific disciplines. Most of these methods originated in Germany, and I will focus primarily on movement between Germany, Great Britain, and the United States, as these are the cases I know best. However, it would be remiss to leave out the Japanese case, as several Japanese researchers contributed decisively to these methods. The final section, will argue for two possible benefits of closer attention to the advent of chemical physics. First, it provides a vital basis for understanding the epistemological changes attendant on the widely discussed "instrumental revolution" or "second chemical revolution."[2] Second, it helps to delimit the field of plausible explanations for why several prominent new methods at the intersection of chemistry and physics, though they originated in Germany, developed more rapidly in other countries between the mid-1930s and the 1950s

One of the classic signs of a new scientific discipline is the founding of new journals. The first issue of *The Journal of Chemical Physics* appeared in 1933. The journal was, in part, a response to the reluctance of Wilder Bancroft, a colloid chemist and editor of the well-established *Journal of Physical Chemistry*, to publish articles on the new quantum chemistry or technical articles on x-ray crystallography, electron diffraction, or molecular spectroscopy.[3] In the first issue of the new journal, Harold Urey, the American physical chemist and radioactivity researcher, as well as the new journal's first editor, justified its establishment based on the following observation:

> Men who must be classified as physicists on the basis of training and of relations to departments or institutes of physics are working on the traditional problems of chemistry; and others who must be regarded as chemists on similar grounds are working in fields which must be regarded as physics.[4]

In light of the articles that the *Journal of Chemical Physics* would host, it's hard to disagree with Urey's assessment. Chemists, like Linus Pauling, published on quantum mechanics; while, physicists, like John Slater, explained idiosyncratic structural transitions of specific compounds.

However, disciplinary labels at the intersection of chemistry and physics at the time were even more fluid than Urey's assessment might lead one to believe. It was not simply that chemists were employing physicists' methods and vice versa. The very same methods often belonged to physics (specifically molecular physics) in one location and chemistry (specifically physical chemistry) in another. I will provide some examples shortly, but first let me point out some concrete consequences of this sharing of research methods (in the sense of methods developed by Gaston Bachelard)[5] across disciplines. It meant that, to stay up to date in their field, physicists and chemists working with these new methods frequently read articles from journals outside their discipline. Many also attended conferences across the disciplinary divide, and some, such as Robert Mulliken, even pursued a disciplinarily ambiguous career.

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[2] On the instrumental revolution see, among others, Peter J. Morris, ed., *From Classical to Modern Chemistry: The Instrumental Revolution* (Cambridge: The Royal Society of Chemistry, 2002); Davis Baird, *Thing Knowledge: A Philosophy of Scientific Instruments* (Berkeley: University of California Press, 2004); and Carsten Reinhardt, *Shifting and Rearranging: Physical Methods and the Transformation of Modern Chemistry* (Sagamore Beach: Science History Publications, 2006).
[3] Servos, "A Dissenter's Decline," *Physical Chemistry from Ostwald to Pauling*, ch. 7.
[4] Harold Urey, "Editorial," *Journal of Chemical Physics* 1 (1933), p. 1.
[5] See Gaston Bachelard, "Le Problème Philosophique des Méthodes Scientifiques (1951)," in *L'Engagement Rationaliste* (Paris: Presse Universitaires de France, 1972).

(Mulliken completed both his B.Sc. and his Ph.D. in chemistry before becoming a professor of physics at the University of Chicago but then received the Nobel Prize in Chemistry in 1963.)

As to the methods with dubious disciplinary identities that would make up the new field of chemical physics, the best researched is quantum chemistry—in the now standard sense of determining the electronic structure and energy of molecules. Kostas Gavroglu and Ana Simões, among others, have published several excellent studies on the origins of this field; how the term "quantum chemistry" came to be associated with just this, relatively narrow, application of quantum mechanics to chemical problems; and how the field shifted disciplinary identities between physics (in Germany), chemistry (in the USA) and applied mathematics (in Great Britain) before establishing itself as a relatively stable and independent discipline.[6]

But quantum chemistry was not the only new method reliant upon quantum theory and with dual citizenship in chemistry and physics. X-ray crystallography and electron diffraction also clearly fit the bill. X-ray diffraction was famously discovered by the physicists Max von Laue, Walter Friedrich, and Paul Knipping but soon attracted the attention of physical chemists such as Hans Georg Grimm. Its applications to crystals and chemistry were developed further in Britain under the guidance of the physicists, William and Henry Bragg, who soon took to employing chemists as assistants. Then, in the United States, it became one of the main research foci for physical chemists at the California Institute of Technology; although, the techniques first employed there were extensions of the photographic technique developed by the Japanese physicist Shoji Nishikawa.

A strikingly similar story lies behind the development of molecular spectroscopy in this period. In Copenhagen, Niels Bjerrum made it one of the central pursuits of his Physical Chemistry Institute. In the United States, on the other hand, molecular spectroscopy became a hallmark of at least three leading physics departments, at Harvard, the University of Michigan, and the University of California, Berkeley.[7] While in Japan, at least one of the early centers for molecular spectroscopy research was the physical chemistry laboratory of San-Ichiro Mizushima.

The case of reaction kinetics, particularly transition state or activated complex theory, was somewhat different. The researchers who developed this theory did remain almost exclusively in institutes for physical chemistry. But especially early on they encountered considerable resistance from older physical chemists, who, in some cases, not only did not accept the new theory but also hindered the professional advancement of those who did. These tensions were clearly visible in the 1937 Annual Faraday Society Meeting, whose main topic was reaction kinetics,[8] and in a published protest by the physical chemist Henry Edward Armstrong against that appointment of Michael Polanyi, one of the founders of transition state theory, to a physical chemistry post in Manchester.[9] Again, it would be interesting to know more about

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[6] Kostas Gavroglu and Ana Simões, *Neither Physics nor Chemistry: A History of Quantum Chemistry* (Cambridge, MA: MIT Press, 2012).

[7] Assmus, Alexi, "The Molecular Tradition in Early Quantum Theory," *Historical Studies in the Physical and Biological Sciences* 22, no. 2 (1992): 209-31, and "The Amrericanization of Molecular Physics," *Historical Studies in the Physical and Biological Sciences* 23, no. 1 (1992): 1-34.

[8] See Mary Jo Nye, *Michael Polanyi and his Generation: Origins of the Social Construction of Science* (Chicago: University of Chicago Press, 2011) p. 128-130.

[9] Henry Edward Armstrong, "Physical Chemistry in the University of Manchester," *Nature* 132 (1933) p. 67, and Polanyi to Bragg, 14 July 1933, Folder 2.12, Michael Polanyi Papers, Regenstein Library, University of Chicago.

how chemists working with these theories were received in Japan, in particular Juro Horiuti, who worked early in his career with Polanyi both in Berlin and in Manchester.

One thing all of the methods just discussed had in common was their reliance upon quantum theory, if not quantum mechanics. This, if nothing else, distinguished them from the bulk of the physical chemistry that came before them.[10] In the case of quantum chemistry, this connection is clear. In the case of the various instrumental methods, the relationship to quantum theory might appear more distant, but as Carsten Reinhardt has pointed out "the use of [new] methods in scientific experiments was closely bound to *accepting* the theoretical underpinning of the apparatus,"[11] and beneath all of the instrumental methods classified as chemical physics lay quantum theory.

Moreover, for a new generation of chemists (and physicists) interested in developing theories covering the whole of chemistry, the quantum mechanics became not only a tool, but also a grail after which to quest. Dudley Herschbach, who received his Ph.D. in Chemical Physics and later shared the 1986 Nobel Prize in Chemistry with Yuan Lee and John Polanyi, sketched a rather entertaining cartoon depicting his own, historicized version of this quest.[12] Representing the progress of field as a mountain being ascended, Herschbach placed at its base "thermochemistry." From this base the field developed (ascended) toward theories of "structure," a term that, in light of the names given in the sketch (Lewis and Pauling), clearly includes quantum chemistry, and then onward to "dynamics," a term that, for Herschbach, includes transition state theory (Eyring and Polanyi) as well as his own later work on chemical kinetics. The figure that gives the cartoon meaning, though, is an angel holding a psi at the peak of the mountain, representing the Schrödinger equation, and symbolizing the eventual goal of tying all of these theories directly to quantum mechanics. This in spite of the fact that it was (and is) unclear how (or if) this linkage can be achieved in many cases.

As already mentioned, most of the new methods discussed originated in Germany. This is certainly true of x-ray crystallography, gaseous electron diffraction, and quantum chemistry, and arguably true of the chemical application of molecular spectroscopy; though, one might also claim it originated in Denmark. It is also true for transition state theory, which, though initially developed by the American Henry Eyring and the Hungarian Michael Polanyi, took shape while the two were working at Fritz Haber's institute in Berlin. By 1941, however, one would be hard pressed to argue that Germany dominated any of these fields. The United States, Britain, and Japan all had prominent research groups, that arguably individually, and certainly if taken together, outweighed the German influence. Hence, the redefinition of research on the borders of chemistry and physics around these methods also came to mean, rather early on, a distancing of the methods of chemical physics from their "Germanic" roots. This phenomenon was closely wedded to the dual disciplinary identity of many of these methods, as it was often in crossing national boundaries that research methods acquired new disciplinary identities. This section will close with a few examples of these two-fold border crossings. Thereafter, I will argue briefly for the significance of these methods to the development of postwar chemistry, especially chemical models and theories. Then I will touch upon *some* of the reasons why those developing these methods in Germany might have seen progress there as lagging behind advances in the United States and in other European nations beginning in the mid-1930s.

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[10] One exception to this generalization is clearly Walther Nernst's work in heat theory, in particular his development of the Third Law of Thermodynamics.

[11] Reinhardt, *Shifting and Rearranging*, p. 11.

[12] Dudley Herschbach, "Chemical Reaction Dynamics and Electronic Structure" in Ahmed Zewail, ed., *The Chemical Bond: Structure and Dynamics* (San Diego: Academic Press Inc., 1992), p. 175.

Quantum chemistry has become the classic, if not the only, well-researched example of how these new methods crossed oceans and changed disciplines. Several physicists, primarily but not exclusively German, worked on solutions to the Schrödinger equation for simple molecules during late 1926 and 1927.[13] Historians generally credit the first complete and practicable solution to the problem to Walter Heitler and Fritz London, but many also argue that it would be remiss to overlook the earlier papers of Friedrich Hund. All three were physicists, working in physics departments and were trained in German universities. When quantum chemistry came to the United States in the 1930s, however, largely through the efforts of Linus Pauling and Robert Mulliken, it found a home in chemistry, or perhaps, more precisely, on the borders of chemistry. Pauling and Mulliken both had difficulties publishing in the *Journal of the American Chemical Society* due to the technical nature of their articles; neither one published in the *Journal of Physical Chemistry*, and both would become contributors to the *Journal of Chemical Physics* after its launch in 1933.

In other cases, like transition state theory, it is quite clear that the inclusion of quantum theory and the move toward chemical physics, though developed in the German context, relied from the outset upon the work of foreign researchers. Neither the Hungarian Michael Polanyi nor the American Henry Eyring stayed long in Berlin after they completed their collaboration on chemical kinetics. In 1933, Polanyi would move to Manchester, England; while, Eyring returned to the USA and a post at Princeton University in 1931. Hence, in a sense, the rapid dissemination of transition state theory was built into the very conditions of its first formulation.

A different, less corporeal form of international exchange can be seen in the case of gaseous electron diffraction. The important step in this case was not the discovery of the phenomenon of electron diffraction itself, which occurred independently and near simultaneously in the USA and Great Britain. Rather, the key to developing a technique relevant to chemistry was the use of this phenomenon to create gaseous diffraction patterns. Herman Mark and his assistant Raimond Wierl were the first to manage this technical feat, in a BASF laboratory in Ludwigshafen.

For this technique to make it from Germany to the United States, however, researchers had to transport not only theoretical knowledge, but also apparatus designs and operation procedures. The technique was first established in the USA at Caltech, under the guidance of Linus Pauling, whom Mark had personally given plans for a gaseous diffraction apparatus in 1931. But it was Pauling's student, Lawrence Brockway, who actually built a copy of the apparatus with the help of the Institute mechanic.[14] I know less about how these instruments and their associated research methods came to Japan, but I would feel very negligent if I did not mention the work begun by Yonezo Morino, who built a gaseous electron diffraction apparatus with the help of Shigeto Yamaguchi. However, Morino was not the first Japanese scientists to publish on gaseous electron diffraction. As far as I know, that distinction belongs to Hazime Oosaka, but there are very few sources in English on Oosaka and how he managed to replicate this technique.[15]

I have granted the example of gaseous electron diffraction a bit of extra attention because, along with x-ray diffraction, it was one of the key experimental techniques used to determine the parameters of space-filling models (specifically covalent radii). As I have discussed

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[13] See Jeremiah James and Christain Joas, "Subsequent and Subsidiary? Rethinking the Role of Applications in Establishing Quantum Mechanics," *Historical Studies in the Natural Sciences*, forthcoming (2015).

[14] Jeremiah James, "Naturalizing the Chemical Bond: Discipline and Creativity in the Pauling Program, 1927-1942" (Harvard University, 2007), p. 263-74.

[15] See the contribution by Mari Yamaguchi in these proceedings.

elsewhere, these models and the ideas about the interactions between atoms within molecules which they embodied, were among the most visible ways in which methods from chemical physics affected the broader chemistry community.[16] Chemists built into these models not only the "raw" instrumental results of new chemical physics techniques but also their "theoretical underpinnings," to use Reinhardt's terminology.

Furthermore, the adoption of these generally implicit theoretical underpinnings could and did contribute to the development of later, explicit chemical theories. In the case of electron diffraction, there are clear ties between the method and the spatial parameters it defined, viz. inter-nuclear separations within molecules, and the postwar development of conformational analysis. Of the two researchers who shared the 1969 Nobel Prize in Chemistry for the development of the theory, Odd Hassel, the experimentalist, if you will, was an electron diffraction specialist, and Derek Barton, the theorist, developed his own personal set of precision chemical models based on results from electron diffraction to aid in his calculations.[17] In the years since the work of Hassel and Barton, conformational analysis has developed into an almost indispensable aspect of organic chemistry. Hence, though electron diffraction did not become a commonplace method for chemists, changing the material and social conditions of their laboratories in the way that instrumental methods such as NMR or mass spectroscopy did, its decisive role in the development of new models and theories did have an epistemological effect similar to that of these standard-bearers of the "instrumental revolution." An analogous argument could be made for x-ray diffraction. Whereas molecular spectroscopy, which *is* one of the standard methods discussed in histories of the instrumental revolution, clearly had roots in the interwar chemical physics community. This epistemological contribution is the first reason that we should take into account interwar chemical physics when discussing the postwar development of the chemical sciences.

The second reason relates to the 'gap' that some chemists and historians have purported in the development of physical and theoretical chemistry in Germany from the late 1930s through the 1950s. According to the computational chemist Sigrid Peyerimhoff,

> in the first decades after the war, the primary users of computers were quantum chemists…this outcome was logical *considering all the work that was stopped in the early 1930s and which was reanimated after the war making use of the new computational tools*.[18]

The most common explanation given for the relatively slow development in Germany is that chemical physics could not find a stable disciplinary home in the existing academic system, in large part due to the shortcomings or resistance of mainstream chemists. As Kostas Gavroglu and Ana Simões summarized the situation:

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[16] Jeremiah James, "Modeling the Scale of Atoms and Bonds: The Origins of Space-filling Parameters," in *Objects of Chemical Inquiry*, ed. Carsten Reinhardt and Ursula Klein (Sagamore Beach: Science History Publications, 2014).

[17] James, "Modeling Scale," p. 310-11.

[18] Sigrid D. Peyerimhoff, "The Development of Computational Chemistry in Germany," *Reviews in Computational Chemistry* 18 (2002): 257-292, quote on 259, emphasis added.

In Germany, there was a sharp division between the chemical and the physical communities, which hardly if ever communicated. And German chemists were in general ill prepared to cope with the challenges of quantum mechanics.[19]

This argument was put in perhaps its most pointed form by Hermann Hartmann, who took part in the ostensible renaissance in chemical physics in Germany in the 1950s, and the British quantum chemist H. Christopher Longuet-Higgins. In their biographical memoir of Erich Hückel, they presented the limited professional success of the, admittedly star-crossed, quantum chemist as the epitome of chemists' resistance to the new field. (In spite of the mentorship of Peter Debye and extensive publications, Hückel first achieved the rank of extraordinary Professor at Marburg in 1937 at 40 years of age and it was another decade until he was promoted to a newly established Chair for Theoretical Physics.) According to Hartmann and Longuet-Higgins:[20]

physicists in [Germany] in any case were not ready to accept investigations about more complicated chemical bond phenomena as a typical contribution of a physicist. Still more difficult was his (Hückel's) relationship to the chemists. Before World War II, especially in the Anglo-Saxon countries, chemical physics and within that field quantum chemistry also was accepted by both physicists and chemists as an interesting new field of science. Chemists in Germany, on the other hand maintained that chemistry is what chemists do. They did not do quantum chemistry and therefore this kind of science did not belong to chemistry.[21]

Implicit in this explanation is that what chemists "did" in Germany was primarily organic chemistry, particularly organic synthesis, which had strong ties to the German chemical industry.

Organic chemistry did predominate in Germany, and the field did have strong ties to the German chemical industry. Moreover, the chemistry community in the United States was more strongly oriented toward physical chemistry. *However*, the problem with using these factors to explain the dearth of chemical physics in Germany is that many German *organic* chemists were willing to grant support to new research methods on the borders of chemistry and physics; while, not all American and British *physical* chemists were so charitable, as illustrated earlier by the examples of Wilder Bancroft, editor of *The Journal of Physical Chemistry* and Michael Polanyi's detractor, Henry Edward Armstrong.

In fact prominent German chemists, including not only the physical chemists Walther Nernst and Wilhelm Ostwald but also the organic chemist Emil Fischer were already concerned in 1905 that Germany was falling behind in general and physical chemistry. This concern was one of the central motivators for the founding of the Kaiser Wilhelm Society (now the Max Planck Society).[22] Furthermore, it was the key reason that the first two Institutes of the

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[19] Gavroglu and Simoes, *Neither Physics nor Chemistry*, p. 86.

[20] More nuanced forms of this argument can be found in Andreas Karachalios, "Die Entstehung und Entwicklung der Quantenchemie in Deutschland," *Mitteilungen, Gesellschaft Deutscher Chemiker, Fachgruppe Geschichte der Chemie* 13 (1997) and *Erich Hückel (1896-1980): From Physics to Quantum Chemistry*, Boston Studies in the Philosophy of Science (Dordrecht: Springer, 2010); and in Gavroglu and Simões, *Neither Physics Nor Chemistry*.

[21] Hermann Hartmann and H. Christopher Longuet-Higgins, "Erich Hückel," *Biographical Memoirs of the Friends of the Royal Society* 28 (1982), p. 153.

[22] See Jeffrey A. Johnson, *The Kaiser's Chemists: Science and Modernization in Imperial Germany* (Chapel Hill:

society were the Institute for Chemistry, led by the physical chemist Ernst Beckmann, and a separate Institute for Physical Chemistry and Electrochemistry, led by Fritz Haber.[23] The structure of the Society would later be a model for RIKEN in Japan, and Fritz Haber's Institute would help guide Setsuro Tamaru, who had worked with Haber in Berlin, in designing the plans for Building No. 1 of RIKEN. Meanwhile in Germany, Haber's institute became one of the central hubs for researchers interested in chemical physics between 1911 and 1933. As already mentioned, Michael Polanyi and Henry Eyring wrote their first paper on transition states there. In addition, Otto Sackur worked there on integrating quantum theory with the thermodynamics of gases, and Paul Harteck and Karl Friedrich Bonhoeffer managed to explain the troubling specific heat of the hydrogen molecule based on the quantum mechanical concept of nuclear spin.

Of course, even in the days before big science, one institute supporting so many new lines of research was unlikely to suffice. But there were clearly other institutes in Germany supporting research into quantum chemistry, into the integration of quantum theory and thermodynamics, and into novel diffraction, spectroscopy, and photochemistry techniques. Although, all together, they numbered maybe a dozen and most were relatively small by comparison to, for example, the main chemistry laboratory at Berlin University,[24] this was not peculiar to Germany. In the United States during the 1920s and early 1930s, research in chemical physics was concentrated in just a few centers such as the California Institute of Technology, the University of Chicago, and the University of California, Berkeley.

Hence, the landscape for chemical physics in Germany, up to the early 1930s, did not look that much friendlier and better populated than the landscape in Great Britain or the United States. The fledgling field found its home in a handful of select research institutes, often highly distinguished but still a small minority. Arguably, the field was only even able to sustain a critical mass of research and researchers thanks to the international exchanges that defined its geographical distribution, if not its deeper character.

However, this thin, internationally distributed network also made chemical physics particularly susceptible to changes in university and science funding policies. In the United States, in 1941, war mobilization stripped Linus Pauling of so much of his staff that he was forced to write his sponsors at the Rockefeller Foundation to explain that he could not continue research in quantum chemistry and molecular structure.[25] In recent years, historians of science have justifiably questioned the notion that totalitarian regimes in general and the German National Socialist regime in particular were inherently detrimental to science,[26] but chemical physics, due to its size and distribution, a was a field particularly sensitive to even small interventions. Moreover, given the *timing* of the initial decline in publications in quantum chemistry and related fields in Germany, it is worth considering the role of the 1933 "Law for the Reform of the Career Civil Service," in the initial onset of the purported German

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University of North Carolina Press, 1990).

[23] For later discussion of the relationship between physical or general chemistry (often used interchangeably) and organic chemistry, particularly in educational reform and debates, see Jeffrey A. Johnson, "The Case of the Missing German Quantum Chemists: On Molecular Models, Mobilization, and the Paradoxes of Modernizing Chemistry in Nazi Germany," *Historical Studies in the Natural Sciences* 43, no. 4 (2013): 391-452.

[24] Carsten Reinhardt, "Zentrale einer Wissenschaft. Methoden, Hierarchie und die Organisation der chemischen Institute," in *Geschichte der Univesität Unter den Linden 1810-2010, Bd. 5,* ed. Rüdiger vom Bruch and Heinz-Elmar Tenorth (Berlin: Akademie Verlag): 575-603.

[25] James, "Naturalizing the Chemical Bond," p. 105-06.

[26] See, among others, Margit Szöllösi-Janze, ''National Socialism and the Sciences: Reflections, Conclusions and Historical Perspectives,'' in *Science in the Third Reich*, ed. Margit Szöllösi-Janze (Oxford: Berg, 2001), 1–35.

lag.[27] The law barring Jews from posts at universities and government research centers, like the Kaiser Wilhelm Institutes, led to the resignation of Fritz Haber and to the removal or resignation of much of his staff, including Michael Polanyi.[28] Other prominent researchers in chemical physics who departed Germany in response included Fritz London, James Franck, Ladislau Farkas, Karl Weissenberg, and Max Born. In addition, Max Bodenstein, Chair for Physical Chemistry at Berlin University, who had hosted Massao Katayama when he visited Germany, was deemed too "friendly" to his Jewish colleagues and upon his retirement in 1936 found himself unwillingly divested of many of his academic obligations.[29] In such a small and widely distributed field, these losses were not easily replaced, and unlike losses of manpower due to military mobilization, they were not easily reversed after 1945. This was due in part, as Jeffrey Johnson has explained, to the structure of German chemical education during the 1930s and 1940s, which did not offer the same grounding in modern physics as advanced chemical education in the United States, for example. However, the difficult material and political conditions for researchers in the immediate postwar should also be taken into consideration.

Once again, my comparison with the Japanese case will be sadly limited, due to a dearth of English-language sources. I would assume that the situation in Japan was quite different from that in Germany *or* in the USA in that there does not appear to be the same reduction in publications relating to chemical physics during the late 1930s and early 1940s. Yonezo Morino published several papers on gaseous electron diffraction during this period, and Masao Kotani, working in quantum chemistry, published important tables of molecular integrals. However, how this was possible and what other duties these men might have had in relation to, for example, military research, are questions I cannot yet answer.

After that caveat, let me conclude with a brief summary of the key features of the rise of chemical physics, at least as it occurred across Germany, Great Britain, and the USA. First, chemical physics was a relatively small-scale, widely internationally distributed, and heterogeneous endeavor before World War II, but one that was clearly different from "classical" physical chemistry, if in no other aspect, than its relationship to atomistic and quantum theory. Second, the methods that constituted the field and their theoretical underpinnings maintained if not increased their importance in the postwar period, in part through their contributions to the so-called instrumental revolution. Finally, the purportedly slow development of the methods of chemical physics in Germany from the mid-1930s through mid-1950s, likely began with the loss of a small number of key research centers and research group leaders in the 1930s that were difficult to replace at the time given international relations and the thin, internationally-distributed research network that supported the field, a situation then prolonged by the path of chemical education reform in Germany. It would be easy, however, to overemphasize this last point, as Germany's "catching up" in the postwar period, though portrayed by some of the actors involved as painfully slow and prolonged, does not appear so far out of step with the postwar development of other scientific fields.[30]

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[27] For a discussion of more enduring factors, with a quite different relation to the National Socialist Regime see Johnson, "The Case of the Missing Quantum Chemists."

[28] Jeremiah James et al., *One Hundred Years at the Intersection of Chemistry and Physics: The Fritz Haber Institute of the Max Planck Society, 1911-2011* (Berlin: De Gruyter, 2011), ch. 2.

[29] Hans-Georg Bartel, "Aus der Geschichte der physikalischen Chemie and der Friedrich-Wilhelms-Universität zu Berlin. Zum 200. Gründungsjubiläum der Alma Mater Berolinensis, Friedrich-Wilhelms-bzw. Humbold-Universität zu Berin," *Bunsenmagazin* 12, no. 3 (2010): 105-10.

[30] See, for example, Dieter Hoffman ed., *Physik im Nachkriegsdeutschland* (Frankfurt am Main: WV Harrie Deutsch GmbH, 2003).

Robert Mulliken and His Influence on Japanese Physical Chemistry

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Introduction

Physical Chemistry underwent a transformation from a science based on thermodynamics to one based on quantum mechanics in the 1920s and the early 1930s. Although quantum mechanics was born in Germany and first applied to a chemical problem, understanding of the covalent bonding in H_2, by two physicists, Walter Heitler and Fritz London[1], the transformation in physical chemistry was mainly made in the US; some young American physical chemists were very active in applying quantum mechanics to chemical problems. Most notable among them were three Nobel Prize winning physical chemists, Linus Pauling, Robert Mulliken and Harold Urey. In particular, Linus Pauling and Robert Mulliken played the most important roles in the development of quantum chemistry in the 1920s and the1930s. Both of them started as experimental physical chemists, Pauling as an X-ray crystallographer and Mulliken as a molecular spectroscopist, but they became pioneers in applying quantum mechanics to chemical problems. However, in their endeavors they took different approaches. Pauling advanced valence bond theory, applying it to explain a variety of chemical bonds. His famous book on the nature of chemical bonds was well received by chemists and became a classic.[2] On the other hand, Mulliken advanced molecular orbital theory in connection with the interpretation of the electronic spectra of small molecules[3]. Before World War II Paulings's valence bond theory was more popular and influential among chemists because of its appeal to chemical intuition. However, in the long run Mulliken's molecular orbital theory has made a much greater influence on chemistry as performance of electronic computer improved rapidly, while Pauling's valence bond theory eclipsed. Among quantum chemists Mulliken made the most important contributions to the transformation of chemistry in the period covering from the 1920s to the 1960s. He also presented a theory on charge transfer (CT) complexes in 1952 that has become very influential in a variety of areas of chemistry.[4] This theory made a particularly strong impact on Japanese Physical Chemistry.

Introduction of quantum chemistry to Japan was also made by physicists. Yoshikatsu Sugiura who made an extension of Heitler-London calculation of the H_2 molecule at Bohr's Institute in Copenhagen returned to Riken in 1927, and introduced quantum mechanics to Japan. Masao Kotani's group in the Physics Department of the University of Tokyo started to evaluate molecular integrals involved in the quantum mechanical calculations of atoms and molecules before World War II, and continued their work after the war. Their efforts resulted in the publication of internationally known *Table of Molecular Integrals"*[5]. However, physical chemists in Japan were not very active in doing theoretical work based on quantum

[1] Heitler, W., and London, F., *Z. Physik*, **44**, 455 - 4472 (1927)
[2] Pauling, F., "The Nature of Chemical Bonds, and the Structures of Molecules and Crystals.", Cornell Univ. Press, 1939.
[3] Mulliken, R. S., *Phys. Rev.* **32**, 186 - 222 (1928)
[4] Mulliken, R. S., *J. Am. Chem. Soc.* **74**, 811 - 825 (1952)
[5] Kotani, M., Amemiya, A., Ishiguro, E., and Kimura, T., "Tables of Molecular Integrals", Maruzen, Tokyo, (1955)

mechanics before World War II, perhaps with an exception of Taikei Ri (later known as Taikyu Ree), assistant professor at Kyoto University, who published a paper with Henry Eyring at Princeton in 1940.[6]

After the war some young Japanese chemists began work based on quantum chemistry. Notable among them were Kenichi Fukui of Kyoto University and Saburo Nagakura of the University of Tokyo. Fukui and coworkers reported their "frontier electron theory" on chemical reactions in 1952[7], the same year as Mulliken published his paper on charge transfer complexes. Fukui's group found a support to their theory in Mulliken's paper. Nagakura and coworkers studied electronic spectra of organic molecules that involve intra and intermolecular charge transfer interactions.[8,9] They were inspired by Mulliken's work. In 1954 Akamatsu, Inokuti and Matsunaga discovered high electrical conductivity in a complex formed between perylene and bromine.[10] It was soon recognized that charge transfer interaction is involved in this complex. Thus studies of charge transfer complexes became a very popular research field in Japan.

In 1953 Kotani organized a satellite meeting on molecular physics in Nikko on the occasion of the international conference of theoretical physics held in Kyoto and Tokyo. Mulliken presented a paper on electronic spectra and molecular structures at the Nikko meeting. There he met Japanese scientists who were working on molecular electronic spectra and quantum chemistry. Since then he had close ties with Japanese physical chemists and physicists, and contributed much to the development of Japanese physical chemistry. From the mid 1950s to the 1960s a number of Japanese scientists including Nagakura worked in Mulliken's laboratory in Chicago.

In this article we first briefly describe Mulliken's biographical background and his work on molecular orbital theory. Then we discuss his charge transfer theory and the influence of this theory on Japanese physical chemistry.

2. Brief Summary of Mulliken's Biographical Background[11, 12] and Achievements[13].

Robert Mulliken was born in Newburyport in Massachusetts on June 7, 1896. His father, Samuel P. Mulliken, was a professor of organic chemistry at the Massachusetts Institute of Technology (MIT). As a young boy Mulliken helped his father by proofreading his father's book on organic analysis. Influenced by his father's academic interests and the scientific ferment of the period, he developed an early interest in science. In high school, he elected the science course, which included biology, chemistry, physics, French, German, and read widely books on science. When he graduated from Newburyport High School in 1913, he was class salutatorian and delivered an essay entitled "Electrons: "What they are and what they do." Amazingly, this topic turned out to be the target of his life-long research.

Mulliken entered MIT to study chemistry in 1913. He did senior research in organic chemistry with J. F. Norris, the result of which was published in *JACS* in 1920. He graduated from MIT in 1917, but the United States was at war and he accepted a job which later came under the Chemical Warfare Service, and worked on the poison gas research under James B.

[6] Ri, T., and Eyring, H., *J. Chem. Phys*. **8**, 433 - 443 (1940)
[7] Fukui, K., Yonezawa, T., and Shingu, H., *J. Chem. Phys*., **20**, 722 - 725 (1952)
[8] Nagakura, S., *J. Chem. Phys.* **23**, 1441- 1445 (1955)
[9] Kuboyama, A., and Nagakura, S., *J. Am. Chem. Soc*., **77**, 2644 - 2646 (1955)
[10] Akamatsu, H., Inokuchi, H., and Matsunaga, Y., *Nature*, 173, 168 - 169 (1954)
[11] Ransil, B., "Robert Mulliken" in "Nobel laureates in Chemistry 1901 - 1922", L. K. James Ed., ACS/CHF (1993)
[12] Adams,D. L., www.chem.umass.edu/~adams/pubs/mullikenweb.pdf
[13] Mulliken, R. S., Nobel lecture (1966), "Spectroscopy, molecular orbitals and chemical bonding" Nobelprize. org. 1966

Conant. Then after working for New Jersey Zinc Company for a while, he went to the University of Chicago to work with William Harkins in the fall of 1919. He wrote his thesis on the partial separation of mercury isotopes by irreversible evaporation. From 1922 to 1923 he continued his work on mercury isotope separation as a National Research Council Fellow. When he reapplied to the National Research Council to continue his work on the isotope separation, the Council told him to propose something different at another institution. He proposed a project to study isotope effects in molecular band spectra, especially that of BN at Harvard's Jefferson Physical Laboratory. This introduced him to the field of molecular spectroscopy. At Harvard Mulliken studied the band spectra of BN and analyzed them carefully. He found that there was a much better fit of the data with theory if the spectra were ascribed to BO rather than BN.

Mulliken made a European tour to meet European spectroscopists in the summer of 1925. He met nearly everybody in Europe who had been doing worthwhile research on band spectra as well as important scientists working on atomic spectra and quantum theory. In particular, he extensively discussed with Friedrich Hund, who was Born's assistant at that time, about molecular spectra. In 1926 he became assistant professor at New York University. Two years later he moved to the University of Chicago as associate professor. Between 1926 and 1932 Mulliken and Hund worked independently with periodic communications with each other. They developed a molecular orbital (MO) model based on the Bohr's model of the atom in which electrons, characterized by individual quantum numbers, were distributed in molecular orbitals that permeate the entire molecule[3,14]. Further development of the MO theory was facilitated by Lennard-Jones's introduction of linear combinations of atomic orbitals (LCAO) in 1929[15]. It appears that his idea of molecular orbital has its root on his attempt to interpret the band structure of the electronic spectra of diatomic molecules. When he accepted the offer of the University of Chicago, he intended to continue his experimental work, but he gradually devoted himself to theoretical studies.

From 1932 Mulliken started to publish a series of fourteen papers, all titled "Electronic structures of polyatomic molecules and valence"[16]. In this series Mulliken used the term "orbital". He also used Hund's symbols for σ and π bonds to describe typical single and double bonds. In Paper VI[17] in this series he outlined the general method of MO theory which was developed by Hund and Mulliken in 1927-28. By these publications Mulliken established the foundation of MO treatment of the electronic structures of small molecules.

Mulliken spent World War II years as an organizer and Director of the Information Division of Manhattan Project at the University of Chicago. After the war he assembled a group of students and associates, and established the Laboratory of Molecular Structure and Spectra (LMSS). Research emphasis was divided between theoretical and experimental work on molecules. In the theoretical group C. C. Roothaan developed a self-consistent field method in which each MO is constructed as LCAO.[18] This LCAO-SCF method opened a way to accurate *ab initio* calculations of atomic and molecular wave functions. With rapid progress of computer technology more and more reliable and accurate calculations on molecules became feasible using MO methods. MO calculations became widely disseminated and appreciated by chemical communities. His laboratory became an international center for molecular spectroscopy and molecular calculations with many visiting scientists, research associates and students from all over the world. A number of Japanese chemists and physicists

[14] Hund, F., *Z. Physik*, **40**, 742 - 764, **42**, 93 - 120 (1927)
[15] Lennard-Jones, J. E., *Trans. Faraday Soc*., **25**, 668 - 686 (1929)
[16] Mulliken, R. S., *Phys. Rev*.,**40**, 55 - 62 (1932)
[17] Mulliken, R. S., *Phys. Rev*., **43**, 279 - 302 (1933)
[18] Roothaan, C. C.,*Rev. Mod. Phys*. **23**, 69 - 89 (1951)

visited his laboratory. Mulliken's great contribution to the developments of molecular science in Japan was well recognized; in 1984 he was decorated by the Japanese Government for his contribution to the training of Japanese spectroscopists. He received the 1966 Nobel Prize in Chemistry for "his fundamental work concerning chemical bonds and electronic structures of molecules". Mulliken died in 1986.

3. Mulliken's Charge Transfer Theory

In addition to the monumental work on molecular orbital theory Mulliken published his seminal paper[4] on charge transfer complexes in 1952 that has made a huge impact on various fields of chemistry. The appearance of strong color on bringing together two colorless or nearly colorless compounds had been well known for many years. In the late 1940s evidence for the formation of molecular complexes between inorganic and organic molecules attracted considerable attention; complex between benzene and iodine studied by Benesi and Hildebrand,[19] those between Ag^+ and aromatic or unsaturated compounds studied by Andrews and Keefer,[20] and such compounds as $R_3N:BF_3$[21] are these examples. Mulliken proposed a simple general quantum mechanical theory to explain the stabilities and electronic spectra of such complexes in terms of the interaction of electron acceptors and donors.[4]

The wave functions for the ground (N) state of a molecular complex A:B was given as,

$$\psi_N = a\psi_0 + b\psi_1 + . . .$$

where ψ_0 is a "no-bond" structure wave function, $\psi_A\psi_B$, product of the wave function of acceptor A and donor B. ψ_1 is the wave function for the ionic state A^-B^+ formed by electron transfer from B to A. The energy of the ground state as well as the energy of formation of the complex were calculated based on the second order perturbation theory, but he mainly treated the cases in which only the first two terms are important. Then the wave function for the excited state, ψ_E, is given as,

$$\psi_E = a^*\psi_1 - b^*\psi_0$$

The existence of an intense absorption spectrum corresponding to the transition $\psi_N \rightarrow \psi_E$ was predicted and called intermolecular charge transfer spectrum. The intensity of the charge transfer spectrum is obtained from the transition moment μ_{EN} which is given by

$$\mu_{EN} = - e \int \psi_E \Sigma r_i \psi_N \, dv = ab^* (\mu_1 - \mu_0) + (aa^* - bb^*)(\mu_{01} - S\mu_0)$$

where $\mu_1 = - e \int \psi_1 \Sigma r_i \psi_1 \, dv$, $\mu_0 = - e \int \psi_0 \Sigma r_i \psi_0 \, dv$, $\mu_{01} = - e \int \psi_1 \Sigma r_i \psi_0 \, dv$, and $S = \int \psi_0 \psi_1 \, dv$.
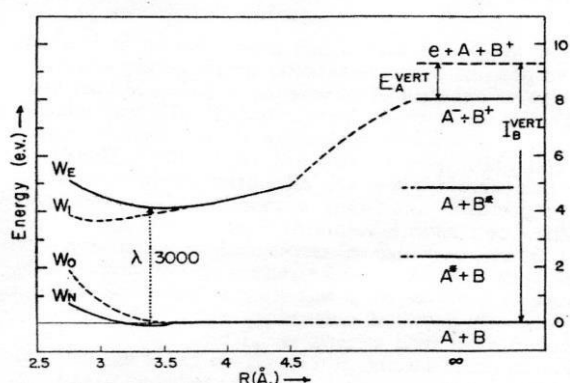

Fig.1 Potential energy curves for the benzene- iodine complex[4].

Mulliken made detailed calculations on the stabilities and structures of the complexes and the intensities of the intermolecular charge transferred spectra for benzene-iodine (Fig. 1), Ag^+ Benzene, and $BX_3:NR_3$ type complexes. He compared the calculated results with the experimental data and showed that the agreements were satisfactory. Mulliken also reported on the hyperconjugation and the spectrum of the Benzenium ion ($C_6H_7^+$), prototype of aromatic carbonium ion. He

[19] Benesi, H. A., and Hildebrand, J. H., *J. Am. Chem. Soc.*, **70**, 2832 - 2833 (1948), 71, 2703 - 2707 (1949)
[20] Andrews, L. J., and Keefer, R. M.., *J. Am. Chem. Soc.* 71, 3644 - 3647 (1949), **72,** 3113 - 3116 (1950)
[21] Brackmann, W., *Rec.trav.chim.*, **68**, 147 (1949)

calculated energy levels and spectrum, charge distribution, bond orders, resonance energy and hyperconjugation energy of the $C_6H_7^+$ ion[22]. This work became important in connection with Fukui's "frontier electron theory" as we see later.

4. Fukui's Frontifter Electron Theory and Mulliken's Charge Transfer Theory

Kenichi Fukui, Japan's first Nobel Prize winner in chemistry, was born in Nara in 1918. He received a B.A. degree in engineering from the Department of Industrial Chemistry of Kyoto University. After two years employment in the Army Fuel Laboratory he returned to Kyoto University in 1943, and started to do applied fuel research. Gifted with mathematical ability he developed a strong interest in quantum mechanics while he was an undergraduate student, and he became a self-taught theoretical chemist. He was also interested in the reaction rate theory, and was stimulated by work being done in the Chemistry Department of the Faculty of Science. In the early 1950s, he built up a small theoretical chemistry group in the Department of Hydrocarbon Chemistry, and started to work on the electronic theory of organic reactions.

In 1952 Fukui, Yonezawa and Nagata presented the "frontier electron theory",[7] the same year as Mulliken presented the charge transfer theory. In Fukui's first paper, they calculated the electron densities of the highest occupied π orbitals (HOMO) in fifteen aromatic hydrocarbons and examined the relationship between the electron densities and chemical reactivities, electrophilic attack of the NO_2^+ to the ring. They found that the positions at which the electron density of HOMO is the largest is most readily attacked by electrophilic or oxidizing reagents. In the subsequent paper they discussed the nucleophilic substitution reactions.[22] In this case the important role of the lowest unoccupied orbitals (LUMO) in determining the reactivity was noted. HOMO and LUMO were referred as "Frontier Orbitals", and they concluded that the frontier orbitals play decisive roles in chemical reactions of hydrocarbons. However, this conclusion was radically different from the way of thinking of the leading theoretical chemists at the time including Longuet-Higgins, Coulson and Dewar; the total electron density is important in determining the chemical reactivity. In their papers theoretical arguments to justify their bold proposal were qualitative and lacked in solid theoretical foundation. Therefore, Fukui and coworkers received considerable controversial comments to their papers. In his Nobel lecture Fukui wrote as follows.[23]

"But the results of such a rather "extravagant" attempt was by no means smoothly accepted by the general public of chemists. The paper received a number of controversial comments. This was in a sense understandable, because, for a lack of my experiential ability, the theoretical foundation for this conspicuous results were obscure or rather improperly given. However, it was fortunate for me that the paper on the charge transfer complex of Mulliken was published in the same year as ours."
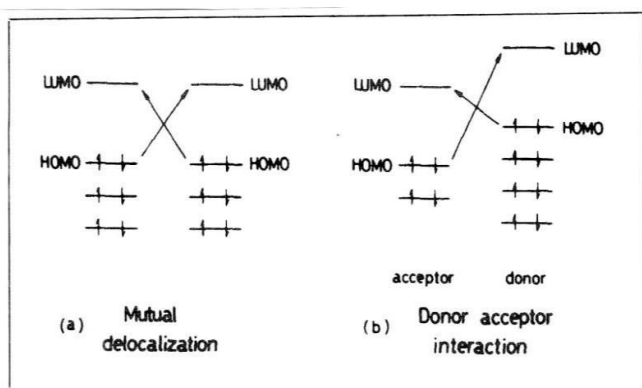

Fig 2.   The mode of orbital interactions[24]

[22]   Muller, N. L., Pickett, W., and Mulliken, R. S., *J. Am. Chem. Soc.*, **76**, 4770 - 4778 (1954)
[23]   Fukui, K., Yonezawa, T., and Nagata, C., *Bull. Chem. Soc.* **27**, 423 - 427 (1954)
[24]   Fukui, K., Nobel lecture, 1981, "The Role of Frontier Orbitals in Chemical Reactions", Nobelprizeorg. 1981

In both Mulliken's charge transfer theory and Fukui's frontier electron theory, HOMO – LUMO interacions shown in Fig. 2 are important. In both cases overlap of orbitals and their orientations are crucial, and HOMO and LUMO play decisive roles. Mulliken's quantum mechanical treatments must have helped Fukui to fortify the theoretical foundations of their work. In 1954 Fukui and coworkers extended frontier electron theory to explain the orientation effects in substitution and addition reactions in heteroaromatic and other conjugated molecules, including electrophilic, nucleophilic or radical type.[25] In the fourth paper on the frontier electron theory by Fukui and coworkers an MO-theoretical investigation on the mechanism of aromatic substitutions was presented.[26] Here detailed quantum mechanical calculations were made on the transition state complexes during the course of reaction which are similar to the bebzenium ion discussed by Mulliken and coworkers.[22] The role of charge transfer in the process of the reaction was discussed in great detail.

Though the criticism to Fukui's frontier electron theory continued through 1950s,[27] the theory gradually gained world-wide recognition as his group extended its applicability to a wide variety of reactions. The advent of the Woodward-Hoffman rule in 1965[28] was decisive in bringing complete recognition. In 1964 Fukui pointed out the importance of the symmetries of the frontier orbitals in the cyclization reaction of diene and dienophile.[29] This preceded the Wood-Hoffman rule. The pioneering role that the frontier electron theory had played in the development of the electronic theory of organic reactions was fully appreciated. Fukui was awarded Nobel Prize in Chemistry in 1981 together with Roald Hoffman.

5. Influence on the Molecular Spectroscopy in Japan

Molecular spectroscopy in Japan gained international reputation under the leadership of Sanichiro Mizushima at the University of Tokyo before World War II. They developed infrared and Raman studies on molecular structures. In particular, the work done by Muzushima and Morino on the rotational isomerism of dichloroethane[30,31] was internationally acclaimed. After World War II a group of young physical chemists in Tokyo became interested in the electronic structures of molecules, and started active research in this field. The leader of this group was Saburo Nagakura who was a student of Mizushima, but was more interested in the electronic structures of molecules rather than the geometric structures. He was interested in the colors of molecules and led to study electronic spectra of aromatic compounds. From 1952 Nagakura's group started to publish papers on the electronic spectra of substituted benzenes and unsaturated compounds containing nitro or carbonyl group.[31] They interpreted the strong absorption bands in the near UV region as arising from the transitions between two energy levels produced by the interaction of the highest occupied levels of the electron donating group with the lowest vacant levels of the electron accepting group, which are regarded as intramolecular charge transfer bands in analogy with Mulliken's intermolecular charge transfer bands.[32−35]

25 Fukui, K., Yonezawa, T., Nagata C., Shingu, H.,*J. Chem. Phys*., **22**, 1433 - 1443 (1954)
26 Fukui, K., Yonezawa, T., Nagata, C., *J. Chem. Phys*., **27**, 1247 - 1259 (1957
27 Fukui, K., Yonezawa, T., Nagata, C.,*J. Chem. Phys*. **28**, 550 -551 (1959) and references therein.
28 Woodward ,R.,Hoffman, R., *J. Am. Chem. Soc*. **87**, 395 – 396, 396 -397, 2045 – 2046, 2046 - 2048 (1965),
29 Fukui, K., in "Molecular Orbitals in Chemistry, Physics and Biology", ed. by Lowdin, P –O., Pullman, B., Academic Press, New York, p. 513 (1964)
30 Mizushima, S., Morino, Y., and Takeda, M., *J. Chem. Phys*. **9**, 826 (1941)
31 Mizushima, S., Morino, Y., *Bull. Chem. Soc. Japan*, **17**, 94 - 99 (1942)
32 Nagakura, S., *Bull. Chem. Soc. Jpn*., **25**, 164 - 168 (1952)
33 Nagakura, S., and Tanaka, J., *J. Chem. Phys*. **22**, 236 - 240 (1954)
34 Nagakura, S.,*J. Chem. Phys*., **23**, 1441 - 1445 (1955)
35 Tanaka , J, and Nagakura, S., *J.Chem. Phys*. **24**, 1274 - 1275 (1956)

Nagakura's group also studied a variety of electron donor-accepter complexes. In 1955 he and Kuboyama reported on the determination of binding energies of molecular complexes formed between p-benzoquinone and various aromatic substances such as hydroquinone and phenol.[9] Subsequently Nagakura studied the complex formation between iodine and triethylamine spectrophotometrically and determined thermodaynamic quantities ($\triangle$H and$\triangle$S) for the complex formation. This work was submitted in 1957 while he was staying in Mulliken's laboratory.[36]

Nagakura and his coworkers made numerous contributions to the studies of charge transfer complexes, but here we only mention the observation of excited triplet states of some charge transfer (CT) complexes as a particularly noteworthy contribution. In 1967 Nagakura's group reported phosphorescence spectra of the CT complexes formed between 1,2,4,5-tetracyanobenzene(TCNB) and benzene or methyl-substituted benzenes.[37] From the EPR spectra they could verify the existence of the excited triplet states of the CT complexes, and determined the degree of the CT character of the triplet state.[38]

In a tribute to a collection of selected papers of Nagakura, Mulliken wrote in 1980 as follows[39],

"For nearly thirty years, Nagakura and his collaborators at frequent intervals have published important experimental and theoretical papers on the structure and spectra of molecules and molecular complexes. They have dealt with large variety of molecules and of complexes for themselves and both in solution at ordinary temperature and in rigid matrices and crystals. In the course of this work, Professor Nagakura has trained many good people who have afterward gone on to do notable work themselves."

Studies of elecronic spectra and electronic structures of molecules were also persued by many other groups and became a very active field of physical chemistry research in Japan in the 1950s and the 1960s.

6. Studies of Organic Conductors

In concluding this article we briefly discuss the work on the organic conducting material that is also related to Mulliken's charge transfer work. In 1954 H. Akamatsu, H. Inokuchi and Y. Matsunaga reported in *Nature* that the complex formed between perylene and bromine shows high electric conductivity comparable to that of some metals.[10] This was an epoch making discovery in the studies of organic conductors. It is interesting to note that their paper did not refer to Mulliken's 1952 paper explicitly, and only stated that the high electric conductivity was ascribed to "some particular electronic state", though Mulliken is now considered as the pioneer in the field of organic conducters. Therefore, it appears that their finding was made during the course of research on organic semicoductors without paying attention to the charge transfer process. However, the charge transfer character of the complex must have been recognized soon. Unfortunately, the perylene-bromine complex was unstable, and the studies of conducting charge-transfer complexes did not progress much until the discovery of high conductivity of TCNQ (tetracyanoquinodimethane) complexes in 1972[39]. Organic metals made of charge transfer complexes have been investigated extensively in Japan since then. This area of research attracted many researchers as an ineresting interdiciplinary area between physics and chemistry. The dicovery that some organic metals

[36] Nagakura, S., *J. Am. Chem. Soc*., **80**, 520 - 524 (1958)
[37] Iwata, S., Tanaka, J., and Nagakura, S., *J. Chem. Phys*. **47**, 2203 - 2209 (1967)
[38] Hayashi, H., Iwata, S., and Nagakura, S., *J. Chem. Phys*. **50**, 993 - 1000 (1969)
[39] Selected Papers of Saburo Ngakura (1981): A commemorative volume published on the occasion of his retirement from the University of Tokyo and Riken.
[40] Ferraris,J. P., Cowen, D. O., Walaska, V., Perlstein, J. H., *J. Am. Chem. Soc.*, **95**, 948 - 949 (1973)

become superconductive at very low temperature further stimulated the research activity of this area.

The 2000 Nobel Prize in Chemistry was awarded to A. Heeger, A. McCdiarmid and H. Shirakawa for their discovery of conducting polymers. Although the success of the production of trans-polyacetyrene film by Shirakawa[41] was the first key step to the development of the conductive polymers, the breakthrough was brought about by the doping of bromine to the polyacetyrene film that was done in collaboration with McCdiarmid and Heeger in the US.[42] This is the case in which collaboration among researchers in different fields resulted in an excellent result. However, this collboration was spured when McCdiarmid accidentaly met Shiwakawa on his visit to Tokyo Institue of Technology where Shirakawa was working at the time. This author feels that the doping experiment could have been done earlier in Japan, if the communication between synthetic polymer chemists and physical chemists was much better in Japan at that time, because the doping of bromine to polyacetyrene was so closely related to the pioneering work done by Akamatsu, Inokuchi and Matsunaga in 1954.

7. Concluding Remarks

In this article we mainly focused on the influence excerted by Mulliken's charge transfer theory on the work by Fukui and Nagakura in the 1950s and the 1960s. The charge transfer theory has become the key concept in understandig manny phenomena in wide areas of chemistry. It played a major role in the tranformation of chemistry in the 1950s and 1960s. Mulliken's work on the charge transfer theory was not mentioned explicitly in the Nobel citation, but its impact was enormous.

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[41] Ito, T., Shirakwa, H., Ikeda, S., *J. Polym. Sci.,Poly. Chem.Ed*. **12**, 11 (1974)

[42] Shirakawa, H.,Loius, E. J., MacDiarmid, A. G.,Chiang, C. K., and Heeger, A. J., *J. Chem. Soc. Chem. Comm*. 578 - 580 (1977)

Program

The International Workshop on the History of Chemistry "Transformation of Chemistry from the 1920s to the 1960s" (IWHC 2015 Tokyo)

March 2-4, 2015, Tokyo Institute of Technology,
West Building No.9

March 2, Monday

12:30 – **Registration**

14:00 – 15:30 **Opening Ceremony (Chair: Masanori Kaji)**

14:00 – 14:30 **Opening Address: Yasu Furukawa** (Nihon University, Japan)

14:30 – 15:30 **Keynote Lecture (1): (Chair: Masanori Kaji)**

> **Jeffrey Johnson** (Villanova University, USA) "From Bio-organic Chemistry to Molecular and Synthetic Biology: Fulfilling Emil Fischer's Dream."

15:30 – 15:45 Coffee Break

15:45 – 16:45 **Session 1: From Local Products to Global Chemistry (Chair: Hiroaki Tanaka)**

> **Masanori Kaji** (Tokyo Institute of Technology, Japan), "The Transformation of Organic Chemistry in Japan: From Majima Riko to the Third International Symposium on the Chemistry of Natural Products."

> ***Victoria Lee** (Max-Planck Institute for the History of Science, Germany), "Screening for Gifts: Japanese Glutamic Acid Fermentation."

16:45 – 17:00 Coffee Break

17:00 – 18:00 **Session 2: Preserving the Chemical Heritage (Chair: Masao Uchida)**

> **Susanne Rehn-Taube** (Deutsches Museum, Germany), "The Nuclear Fission Table in the Deutsches Museum: A Special Piece of Science History on the Eve of World War II."

> **Ronald Brashear** (Chemical Heritage Foundation, USA), "Preserving the Heritage of Modern Chemistry."

18:15 – **Reception**

March 3, Tuesday

8:30 – **Registration**

9:00 – 10:00 **Session 3 (1): Internationalizing Chemistry and the Chemical Community (Chair: Brigitte Van Tiggelen)**

Masanori Wada (Tokyo Institute of Technology, Japan), "The Two International Congresses Held in Tokyo in the 1920s: The Rise of the First Generation of Japanese Scientists."

Danielle M. Fauque (University of Paris Sud, France), "Jean Gérard, Secretary General and Driving Force of the International Chemical Conferences between the Wars."

10:00 – 10:15 Coffee Break

10:15 – 11:45 **Session 3 (2): Internationalizing Chemistry and the Chemical Community (Chair: Jeffrey Johnson)**

Yoshiyuki Kikuchi (The Graduate University for Advanced Studies, Japan), "San-ichiro Mizushima and the Reconfiguration of the International Relations of Japanese Chemistry."

Keiko Kawashima (Nagoya Institute of Technology, Japan), "Female Scientists Whom Nobuo Yamada Encountered: Early Years of Radio Chemistry and the Radium Institute."

Evan Hepler-Smith (Princeton University, USA),"Changing Names and Naming Change: Transformations in the 'International Machinery' of Chemical Information."

11:45 – 13:00 Lunch

13:00 – 14:00 **Keynote Lecture (2): (Chair: Yasu Furukawa)**

Mary Jo Nye (Oregon State University, USA) "A Career at the Center: Linus Pauling and the Transformation of Chemical Science in the Twentieth Century."

14:00 – 14:15 Coffee Break

14:15 – 15:15 **Session 4: Interface between Chemistry and Biology (Chair: Togo Tsukahara)**

Kevin Fujitani (Ohio State University, USA), "A Child of Many Fathers: The Question of Credit for the Discovery of Thiamine, 1884-1936."

Pnina G. Abir-Am (Brandeis University, USA), "Pauling's 'Boys' and the Mystery of DNA Structure: On Mentorship in Structural Chemistry and Molecular Biology."

15:15 – 16:00 Coffee Break

16:00 – 17:30 **Session 5: Instruments and Measurements (Chair: Carsten Reinhardt)**

Pierre Laszlo (École polytechnique, France & Université de Liège, Belgium), "Structure of the NMR Revolution."

Mari Yamaguchi (The University of Tokyo, Japan), "Pursuit of Accurate Measurements: Gas Electron Diffraction from the 1930s to the 1960s."

Makoto Yamaguchi (Japan), "Development of Vibrational Spectroscopy of Polyatomic Molecules in the 1930s and Its Implication to the Emergence of 'Molecular Science'."

18:00 – **Reception**

March 4, Wednesday

8:30 – **Registration**

9:00 – 10:30 **Session 6: Making Theories and Making Methods (Chair: Mary Jo Nye)**

Yasu Furukawa (Nihon University, Japan) ,"From Fuel Chemistry to Quantum Chemistry: Kenichi Fukui and the Rise of the Kyoto School."

*Buhm Soon Park (Korea Advanced Institute of Science and Technology, Korea), "A 'Marriage of Poor Theory and Good Experiment'?: The Origins of the Woodward-Hoffmann Rules."

Carsten Reinhardt (Chemical Heritage Foundation, USA), "Physical Methods in the Twentieth Century between Disciplines and Cultures."

10:30 – 10:45 Coffee Break

10:45 – 11:45 **Keynote Lecture (3): (Chair: Yoshiyuki Kikuchi)**

*Ernst Homburg (Maastricht University, The Netherlands) "On Molecules, Men, and Mirrors: Different Ways to Write a History of the Chemical Industry."

11:45 – 12:45 Lunch

12:45 – 14:15 **Session 7: Synthesis and Production (Chair: Masanori Wada)**

Takashi Mine (Japan), "The Small-Scale Ammonia Production of China in the Day of Mao Zedong."

Ian D. Rae (Australia), " 'Ideal' Gases: Anaesthetics in the Heart of the Twentieth Century."

Galina Shyndriayeva (King's College, UK), "Perfume at the Forefront of Macrocyclic Compound Research: From Switzerland to Du Pont."

14:15 – 15:15 Coffee Break

14:20 – 15:00 A Visit to the University Museum

15:15 – 16:45 **Session 8: Interface between Chemistry and Physics (Chair: Yoshiyuki Kikuchi)**

Shintaro Furuya (Tokyo Institute of Technology, Japan), "Polanyi's Physical Adsorption: One of the Early Theories of Quantum Chemistry."

Jeremiah James (Ludwig-Maximilian University, Germany), "From Physical Chemistry to Chemical Physics, 1913-1941."

Noboru Hirota (Kyoto University, Japan), "Robert Mulliken and His Influence on Japanese Physical Chemistry."

16:45 – 17:00 **Closing Remarks: Makoto Ohno** (Aichi Prefectural University, Japan)

18:45 – 21:00 **Banquet** (Happo-en, 1-1-1 Shirokanedai, Minato-ku, Tokyo)

March 5, Thursday

Optional Tour in Tokyo

Note: Papers with * are not included in this proceedings due to various circumstances.