A Brief History of Chemistry at Yale

Teaching and research in chemistry at Yale began 200 years ago with the appointment of Benjamin Silliman as Professor of Chemistry and Natural History. Chemistry at Yale thus spans the entire life of the science since the Chemical Revolution of the late 18th century. This essay begins by tracing the development of chemistry at Yale from the time of Silliman through the organization of a modern chemistry department by John G. Kirkwood in the early 1950s. It concludes with capsule descriptions of the types of chemical research that have been practiced at Yale during the past 50 years and a few observations on the role of the Chemistry Department in Yale's fourth century.

Benjamin Silliman

When Benjamin Silliman graduated from Yale College in 1796 at the age of 17, chemistry as a modern science was in its infancy. Lavoisier's "Traité Élémentaire de Chimie", the flagship of the Chemical Revolution, had appeared only 7 years earlier. Having grown up in Fairfield on a farm overlooking Long Island Sound, Silliman was fond of nature, but his primary academic interests were classics and theology, and he was looking forward to a career in law. His Yale science training was limited to mathematics, a little astronomy, and one chapel lecture on the heating and freezing of water delivered by Professor Meigs, who had read Lavoisier.

As a tutor and student of law in 1801 Silliman was contemplating a law practice in Georgia, when President Dwight, a former Fairfield neighbor, said to him, "I advise you not to go to Georgia. I would not voluntarily, unless under the influence of some commanding moral duty, go to live in a country where slavery is established; you must encounter moreover, the dangers of the climate, and may die of a fever within two years. I have still other reasons which I will now proceed to state to you."

Dwight then offered Silliman the new Professorship of Chemistry and Natural History. He recognized that the young man would need chemical training, but he wished to avoid the alternative of appointing "a foreigner, with his peculiar habits and prejudices [who,] however able he might be in point of science, would not understand our college system, and might therefore not act in harmony with his colleagues." It is not altogether clear who Dwight would have considered a foreigner. He might have been thinking of the French, since

Lavoisier had made chemistry a predominantly French science, or of the British. But he might well have included in his definition anyone from beyond New Haven, since during the next 126 years only one individual educated elsewhere would be appointed to teach chemistry at Yale.

At first Silliman continued to study law, but he wrote that he "obtained a few books on chemistry, and kept them secluded in my secretary, occasionally reading in them privately." It became obvious to him that he needed exposure to experimental chemistry, so he decided to "resort to Philadelphia, which presented more advantages in science than any other place in our country." There he heard lectures by Benjamin Rush and by John Woodhouse, who, though acquainted with Sir Humphrey Davy, "had not the gift of a lucid mind, nor of high reasoning powers, nor of a fluent diction." Silliman found that his "memory was burdened, and with little satisfaction" by Woodhouse's chemistry, but he learned experimental technique from his fellow boarder Robert Hare, an accomplished brewer of porter who had just invented the oxyhydrogen blowpipe, and he was excited to meet Joseph Priestly, the elderly British expatriate who was a discoverer of oxygen. During brief visits en route between New Haven and Philadelphia he was introduced to contemporary chemical theory by John Maclean, Princeton's professor of chemistry.

In 1804 the Yale Corporation gave Silliman a year's leave to study chemistry and geology in Britain and gave him $10,000 (equivalent to $140,000 today) to purchase scientific books and apparatus . He made the acquaintance of most of the leading British scientists - Dalton, Davy, Banks, Thomson, Brewster - and returned to New Haven inspired to launch Yale's instruction and research in the natural sciences.

Silliman served as Yale's Professor of Chemistry and Natural History for 51 years (a record that still stands), and earned an outstanding reputation as the Father of American Science. His energy was boundless: he wrote text books, was a spellbinding popular lecturer, and founded the *"American Journal of Science and Arts"*. He was professor not only of chemistry, but also of pharmacy, mineralogy, and geology. His contributions to establishing the study of science at Yale were crucial, not least the role he played in assuring that the Library would possess a complete collection of contemporary science journals.

But Silliman's contributions to the science of chemistry itself were very modest, compared, for example, to those of Sweden's Jöns Jakob Berzelius, who was born in the same year and studied many of the same kinds of samples (minerals) with similar techniques. Where Silliman analyzed meteorites, Berzelius provided a bridge between the French founders of modern chemistry and their German successors. Berzelius measured accurate atomic weights, helped establish electrochemistry, and devised the symbols we still use for the elements. It is appropriate that when the Sterling Chemistry Laboratory was constructed in 1923, a statue of Silliman was placed before it, but Berzelius, not Silliman, was included in the honor roll of 24 founders of chemistry whose names were emblazoned on its facade.

By 1845 the Junior Class at Yale was attending "a course of experimental lectures on Natural Philosophy," and the Senior Class had "courses of lectures on Chemistry, Mineralogy, Geology and selected subjects of Natural Philosophy." But these were intended as popular diversions for a general audience rather than as training for prospective scientists.

After the generous initial support for books and apparatus Yale had never provided Silliman adequate space for serious laboratory instruction. Until 1820 he was installed in the "Pit", the cellar of the Lyceum just south of Connecticut Hall, where moisture rusted his apparatus and spoiled his preparations. After 1820 he worked and taught in the "Old Laboratory" a former kitchen/dining hall that at least was above ground level. If these facilities allowed him to do work that placed him in the "front rank of American chemists", it was because he was a superb rhetorician and the competition was slim. His most notable chemical innovations were showing that carbon was volatilized by an electric arc and preparing hydrofluoric acid for the first time in America.

Chemistry in the Sheffield Scientific School
1846-1895

Analytical Chemistry

By 1846 it was clear that America needed individuals trained in chemistry, and especially in analytical chemistry, to support the development of agriculture, mining, and manufacturing. The Yale Corporation responded by establishing a "professorship of agricultural chemistry and of vegetable and animal physiology" and a second "professorship of practical chemistry…in respect to the application of chemistry and the kindred sciences to the manufacturing arts, to the exploration of the resources of the country and to other practical uses."

But to preserve the purity of Yale's classical tradition there were two conditions: neither professor was to provide instruction to undergraduates, and there were to be "no charges to the funds or revenues of the College, compensation to derive exclusively from fees for instruction and for other services." The parsimony of this response would doom Yale science to more than a century of serious organizational problems.

The first unenviable incumbents of these chairs in the School of Applied Chemistry were John Pitkin Norton, age 24, and Benjamin Silliman, Jr., age 30. They were personally responsible for the expense of fitting and equipping a laboratory and providing apparatus and a library. They received no salaries. The Yale Corporation rented them a vacant frame house, where Farnham Hall now stands, for $150/year. It had to serve as laboratory, lecture room, library, and dormitory.

Benjamin Silliman, Jr.

After graduating from Yale College in 1837 Benjamin Silliman, Jr., had remained in New Haven as assistant to his father in chemistry, mineralogy, and geology. He taught a few private students and ultimately generated the proposal for a School of Applied Chemistry to gain official recognition for this enterprise.

Chemistry for the Sillimans, and indeed for almost all Yale chemists, and almost all American chemists until nearly the end of the 19th Century, meant analytical chemistry as applied to one practical area or another. In Silliman Jr.'s case the practical areas were mining, gas illumination, and petroleum production. Like his father, he preferred painting with a broad brush and delighted in projects like preparing a large volume on *"The World of Science, Art, and Industry"* for the 1853 Crystal Palace Exhibition in New York, or an 1871 lecture on *"A Century of Medicine and Chemistry."* He was a member of the New Haven city council and director of the New Haven gas works.

Within three years of launching the School of Applied Chemistry, in 1849, Silliman abandoned New Haven and his colleague Norton for a professorship of medical chemistry and toxicology in Louisville. After his father's retirement he returned to New Haven in 1854 - but not to the struggling School of Applied Chemistry. He took a position in Yale College, as a colleague of his father's son-in-law and successor, the geologist James D. Dana.

Much of Silliman's subsequent work involved evaluating the commercial potential of properties for mining, and particularly for drilling. His enthusiastic 1855 report on the petroleum of Venango County, Pennsylvania, led Drake two years later to drill the well in Titusville that launched the American petroleum industry. Silliman proposed steam distillation and thermal cracking to obtain useful petroleum products, and he worked on perfecting kerosene lighting. His equally enthusiastic report on California petroleum a decade later led to a speculative bubble that burst amid cries of scandal when the deposits were found to be too deep for practical recovery with existing methods.

He was enlisted in Procter & Gamble's efforts to establish the purity of their Ivory Soap and thus to reduce the anxiety of American women who were reluctant to believe that a laundry soap might be used on one's person. An 1882 advertisement quotes him as follows,

> *"This analysis and comparison shows the PROCTER & GAMBLE 'IVORY SOAP' to be of remarkable purity, and in every respect of superior excellence. As a Laundry Soap it has no superior, and it is equaled only by the most select vegetable oil Castile Soap."*

The scientific basis for his claim is questionable.

As in the case of his father, his contributions were much more to the popularization and commercialization of science than to its intellectual development.

John Pitkin Norton

Norton, Silliman's young partner in launching the School of Applied Chemistry, had grown up on a farm and was intent on bending science to the service of agriculture. This interest led him to private study of chemistry with Silliman, Jr., from 1840 to 1843. He then studied agricultural chemistry in Utrecht and Edinburgh, where his chemical analysis of oats and of the oat plant at different growth stages won him a 50 sovereign prize. He returned to the School in New Haven full of enthusiasm and extraordinary knowledge. But the organizational and financial stress of this fledgling enterprise, particularly after Silliman's departure, drained him. Within five years he died at the age of 30. Almost his last act was to give Yale College all the laboratory apparatus, chemicals, books, and notes which he had had to obtain for himself, together with the plaintive request, "I hope it will be kept up; it has cost me a great deal of labor." More importantly he left students who would ultimately establish Yale chemistry on a solid basis.

John Addison Porter and Joseph Sheffield

Survival of the School of Applied Chemistry was in peril, but finally John Addison Porter, who was the same age as the late Professor Norton, agreed to come from Brown University for the 1852-53 year, and ultimately he stayed. After graduating from Yale in 1842 Porter had taught rhetoric at Dartmouth for three years. But, like Norton, he was interested in applying science to improve agriculture, so he had studied analytical and agricultural chemistry at the world's premier laboratory for these subjects, that of Justus Liebig in Giessen.

Yale's 1852 raid on Brown University also netted William A. Norton, who was recruited to establish a School of Engineering. Within two years this School and the School of Applied Chemistry would merge and evolve from the "Department of Philosophy and the Arts" to the "Yale Scientific School". As a dowry Norton brought his students from Brown, swelling the science enrollment of the Department of Philosophy to 55, which was crucial since the Corporation still provided no financial support for the struggling scientific enterprise.

By 1856 two more professors had been appointed, both graduates from the first class in the School of Applied Chemistry - George J. Brush in Metallurgy, and Samuel W. Johnson in Analytical Chemistry. But still there was no financial commitment from the Corporation and no suitable building to house the growing Scientific School.

Fortunately, however, young Professor Porter had brought his wife back to New Haven and had decided to stay. She was the daughter of Joseph Sheffield. Although Porter would teach agricultural and organic chemistry for only 12 years before his death at the age of 42 in 1864, he served long enough to fix Sheffield's generous attention on the Scientific School.

Joseph Sheffield was a practical man, a railroad tycoon who had built the Rock Island and New Haven railways. He also completed the Farmington Canal and converted it to a railway. He understood both the importance of applying science and engineering to the practical arts, and the financial needs of his son-in-law's enterprise. So when the appeal went out in 1856 for funds to support the Scientific School, he responded both with money and with a large building on the northwest corner of Grove and Prospect Streets, near his Hillhouse Street mansion and his Farmington Line. In 1861 the Corportation acknowledged Sheffield's contributions of more than $100,000 by giving his name to the Scientific School.

Chemistry for Agriculture and the Applied Arts

Samuel William Johnson

The most important Yale chemist through the second half of the19th Century was probably Samuel William Johnson (1830-1909), who had come to the Scientific School in 1849 to study chemistry as applied to agriculture with John Pitkin Norton. In 1856, after three years further study in Europe, including in Liebig's Munich laboratory, he returned to Yale, where he taught for the next forty years. As professor of analytical and agricultural chemistry he worked indefatigably in the service of scientific agriculture helping to develop practical commercial fertilizers. Johnson's monographs "How Crops Grow" and "How Crops Feed" were standards for more than forty years. He founded and directed the Connecticut Agricultural Experiment Station as the first such station in America, and was responsible for moving it to New Haven and forging its links with Yale that ultimately helped make New Haven an important center of biological chemistry.

Equally important for the Sheffield Scientific School, the presence of Johnson as a certified agricultural chemist gave it a claim on funds made available by the Morrill Land Grant Act. In 1863 the school became Connecticut's official College of Agriculture and Mechanic Arts. It remained in that capacity until 1893, when Connecticut farmers, over vigorous protests from Yale, convinced the State Assembly to transfer the land grant funds to the new Storrs Agricultural School, now the University of Connecticut.

W. G. Mixter, O. D. Allen, G. J. Brush, and H. L. Wells

Other leading Sheffield chemistry professors during the latter part of the 19th Century included W. G. Mixter, O. D. Allen, G. J. Brush, and H. L. Wells. William Mixter was one of the few Yale chemists before 1900 whose work was not primarily analytical. Having studied in the German laboratories of Bunsen and Hofmann he returned to New Haven in 1874 and taught elementary chemistry to freshmen for the next 38 years. During this period he published more than 50 papers, most of which involved thermochemical measurements with a bomb calorimeter. He is responsible for measuring the heats of combustion of hydrogen and silicon, and the heats of formation of a number of inorganic oxides.

More typical were Oscar D. Allen and George J. Brush who began as analytical chemists but drifted into allied fields by applying analysis to metallurgy and mineralogy, respectively. Lepidolite from a mine in Allen's home town of Hebron, Maine, provided an abundant source of rubidium and cesium, allowing him and Johnson to correct Bunsen's value for the atomic weight of cesium in 1863. Apparently Allen was a memorable teacher, since his student R. H. Chittenden would later write, " to all those who came to know him well, and knowing him forgot or overlooked his peculiarities, he was an inspiration."

From 1885 until 1924 Horace L. Wells, who was in charge of undergraduate instruction in analytical chemistry, became noted for his studies of multiple salts of cesium, including 23 double and 14 triple thiocyanates, which at least one contemporary regarded as opening "a new and important chapter in inorganic chemistry."

Surveying the last hundred years of chemistry in 1918, Wells and his colleague Harry W. Foote wrote,

> *"There came a time towards the end of the nineteenth century when the attention of chemists, particularly in Germany, was so much absorbed by organic chemistry that mineral analysis came near becoming a lost art there. It was during this period that an English mineralogist, visiting New Haven and praising the mineral analyses that were being carried out at Yale, expressed regret that there appeared to be no one in England, or in Germany either, who could analyze minerals."*

From the perspective of pure chemistry at the dawn of the 21st Century, 19th Century chemistry in the Sheffield Scientific School seems largely irrelevant. Chemistry in the School had made practical contributions to contemporary agriculture and industry, had helped make Yale an important center for the development of mineralogy, and had trained many leaders of American education and industry, but the School had made no innovative, fundamental contribution to the development of chemistry as we know it today. Analysis had dominated chemistry for a century, and the age when it would rule, rather than serve, had come to an end. This fact was clear to all by 1923, when the honor roll of 24 founders of chemistry on Sterling Chemistry Laboratory's facade included not one Yale chemist.

Chemical Science in Yale College

J. Willard Gibbs

But the chemistry laboratory's honor roll appropriately included a Yale physicist, J. Willard Gibbs, who like his philologist father, was associated not with the Scientific School but with Yale College. His contributions to statistical thermodynamics in the last quarter of the 19th Century made American contributions to pure science respectable in the academic centers of Europe and still serve as the cornerstone of theoretical physical chemistry. His legendary character and career are covered elsewhere in this volume. From the perspective of Yale chemistry we can only regret that his retiring nature, and the lack of imagination of his Yale contemporaries, kept Yale from establishing a school of theoretical physical chemistry that would survive Gibbs. Although its fledgling physical chemists worked on experiments related to the phase rule after 1900, Yale's distinction in this area would be regained only half a century after Gibbs's seminal work.

Analytical Chemistry and F. A. Gooch

Because of the curious College/Scientific School bifurcation, undergraduate chemical instruction and research were carried out in Yale College, as well as in Sheffield, just as language and literature were taught in Sheffield, as well as in the College. The faculties were duplicate and independent.

In 1888 the impressive Kent Laboratory was constructed on the current site of Jonathan Edwards College to house Yale College chemistry and its new professor Frank Austin Gooch. Gooch was an alumnus of Harvard, where he had developed the filtering crucible that would make his name famous to quantitative analysis students for the next 75 years. In the 85 years since Silliman's conversation with President Dwight, Gooch was the only "foreigner" appointed to teach chemistry at Yale, and he would retain that distinction for another 41 years. By 1915 the Kent Laboratory had been enlarged twice and was offering laboratory instruction to over 400 Yale undergraduates.

During his 33 years at Yale Gooch made a large number of important contributions to the methodology of analytical chemistry, including inventing the rotating electrode, which made determination of many metals rapid and cheap.

Initiatives in the New Sheffield Laboratory 1895-1923

Throughout the 19th Century chemistry at Yale had been the handmaiden of geology, applied science, and technology - metallurgy, mining, and agriculture. Aside from Gibbs's work in physics, there had been no discoveries that a 21st Century chemist, or a contemporary European chemist, would regard~~ed~~ as crucial for the development of chemistry as a pure science. The same could be said of other American universities until the last decade of the century. As the Sheffield Scientific School's new Sheffield Chemistry Laboratory opened in 1895, the style of chemistry had begun to change with the appointment of organic chemist Henry L. Wheeler in 1894 and of physical chemists Bertram B. Boltwood in 1896 and Harry W. Foote in 1900.

Physical Chemistry

Bertram Borden Boltwood

After receiving his undergraduate degree in chemistry and studying inorganic chemistry for two years in Munich, Boltwood returned to New Haven in 1894 as an assistant in analytical chemistry, working on the double salts of H. L. Wells. After another term abroad, this time in Ostwald's Leipzig laboratory, the center of the new discipline of physical chemistry, he rejoined Yale as instructor of analytical chemisty. He promoted physical chemistry at Yale by translating textbooks and developing new apparatus including a new type of pump and "Boltwax," a wax with low melting point and good mechanical properties.

Boltwood developed an interest in separating rare earth salts (including those in pitchblende, which had recently been discovered to be radioactive) and studying their phase behavior. In 1900 he left Yale to establish "Pratt and Boltwood, consulting mining engineers and chemists" on Orange Street in New Haven, but continued working on rare earth minerals in his private laboratory. He was broadly interested and well informed, and soon was providing chemical evidence to support Rutherford and Soddy's revolutionary 1903 theory on the disintegration of radioactive elements.

After Rutherford's visit to Yale in 1904, he and Boltwood formed a close scientific relationship. This raised Boltwood's profile in the physics community, and he was made assistant professor of physics in Yale College. His chemical skills and intellectual powers soon produced a wealth of fundamental contributions to the physics and chemistry of radioactive elements. He proved that radium came from uranium, developed other genetic relationships in different radiochemical series, demonstrated the existence of isotopes, and originated the idea of dating minerals by measuring the ratios of elements (uranium/lead). This work, arguably the most significant chemistry that had originated from Yale, is discussed in more detail in the physics chapter of this volume.

After a leave with Rutherford in Manchester in 1910, Boltwood was offered a continuing position in England, but returned to Yale College as professor of radio-chemistry in the Physics Department. Unfortunately for his science, his good nature and energy were soon exploited for administrative duties. After supervising construction of the Sloan Physics Laboratory and serving as its acting director, he was chosen to succeed Gooch as acting professor of chemistry and director of the Kent Chemical Laboratory. When the chemistry departments of Sheffield and Yale College were amalgamated in 1918, he became chairman and was given responsibility for planning and constructing Sterling Chemistry Laboratory, at the time America's largest academic building dedicated to chemistry. This work broke his health. After a leave and several bouts of depression he took his own life in 1927.

Sloan Physics Laboratory and Sterling Chemistry Laboratory stand as impressive monuments to Boltwood's dedication and energy. One can see his touch not only within the Chemistry Laboratory, where there is a small radiochemistry facility, but also on its facade where physicist Rutherford is the youngest member of the chemical honor roll, and where number 86 in the frieze of chemical elements, now called Radon, is labeled Ra/Em, for Radium Emanation.

Harry W. Foote

When Boltwood left Yale temporarily in 1900, Harry Ward Foote, recently returned from postdoctoral training in physical chemistry in Germany, succeeded him as the first Sheffield instructor appointed specifically to teach physical chemistry. In 1912 Foote was appointed to the new chair of physical chemistry which he occupied until 1942. As Boltwood had done, he began his research working with Mixter on double salts, although he later branched out to studies of colloids and the dissociation of metallic oxides. Like many contemporary physical chemists, he harvested where Gibbs had sown, working on the phase behavior of inorganic solids, but he did not have the flair or the luck to make his work as formative for chemical science as Boltwood's.

Organic Chemistry in Sheffield

William J. Comstock

Even before the introduction of physical chemistry, chemistry at Yale was showing signs of modernization in the introduction of instruction in organic chemistry. Most of the laboratory work at Sheffield was in mineral and ore analysis which, according to Russell Chittenden, “to many was merely another name for a rather plebeian workshop.” But “in 1881 there was a decided increase of interest in the study of chemistry as a pure science, without regard to its application to industrial pursuits or its use in other professions.” As a result synthetic organic chemistry laboratory work was introduced, including 20 hours of laboratory instruction per week and the possibility for original research.

For 29 years, beginning in 1888, William J. Comstock (S ’79) who had trained in Baeyer’s Munich laboratory, was responsible for organic laboratory instruction. Although he never advanced beyond the rank of instructor, he was popular and effective, and he trained his more prominent successors well in organic chemistry.

Henry L. Wheeler

Sheffield’s first noted organic chemist was Henry Lord Wheeler (S ’90, Ph.D. 1893). He joined the Sheffield faculty after postdoctoral work with Baeyer in Munich and Nef at Chicago, the world’s, and the nation’s most respected and productive organic chemistry laboratories. In 1898 he was appointed assistant professor, and his student T. B. Johnson was appointed instructor. Comstock, Wheeler and Johnson began to attract graduate students, and organic became the most popular branch of chemistry for graduate study. Wheeler taught no undergraduates, but by 1901 his “phenomenal activity” had generated 28 papers on the synthesis of pyrimidines, on rearrangements, and on the natural products uracil, cytosine, and thymine. He had been introduced to these areas of chemistry during his postdoctoral work, but his own contributions, and those of Johnson, made Yale an important center of activity in the area of nitrogen containing heterocyclic natural products. While studying nucleic acids, Kossel in Germany had isolated a new base which he called cytosine. In 1903 Wheeler and Johnson proved its structure by synthesis, as Emil Fischer in Berlin would do for uracil and thymine.

Although Wheeler’s productivity continued through the first decade of the 20th Century, he retired at the age of 44 in 1911, presumably because of failing health, and died two years later.

Treat B. Johnson

By the time of Wheeler's death, Treat B. Johnson had been promoted to professor of organic chemistry and was establishing an important school of synthetic organic chemistry. In 1913, ten of Sheffield's 25 chemistry graduate students were working on organic chemistry with Johnson, and over his 41 year career at Yale he trained 94 graduate students. During this time he produced 358 books and papers, 182 of them on pyrimidines, the class of compounds he had begun studying as a student with Wheeler. During Johnson's lifetime this devotion to pyrimidines was best justified by Robert Williams's 1936 discovery of the structure of thiamine. This first vitamin of known structure, was a substituted pyrimidine. In the long run it would turn out that Johnson's concern with the composition and structure of nucleic acids would play an even more important role in biology. He developed techniques for separating uracil and thymine and a specific color test to distinguish uracil and cytosine from thymine.

Johnson also worked with proteins and amino acids and carried out a long research project supported by the National Tuberculosis Association to study the nucleic acids and proteins of tuberculosis bacilli. He profited from interaction with the community of Yale physiological chemists, including Chittenden, Vickery, and Osborne, whose work is discussed elsewhere in this volume, as well as with his colleague Rudolf Anderson, who is mentioned below.

In the 1930s Johnson began working on synthetic drugs, but his most important practical contribution was a 1921 modification of the Gattermann synthesis that made a series of 4-alkylresorcinols accessible. Ultimately the effectiveness of hexylresorcinol as a topical antiseptic used in cleansing wounds and in mouthwashes and throat lozenges, together with the "business acumen he inherited from his Yankee forebears" made him a wealthy man, and the legacy he left to be expended by Yale's organic chemists continues to play an important role in supporting lectureships and instrumentation in the Chemistry Department.

United Department - Sterling Chemistry Laboratory

The profound restructuring of Yale after the First World War led to the effective demise of the Sheffield Scientific School as an independent entity, and to amalgamation of the Sheffield and Yale College Chemistry Departments in the new Sterling Chemistry Laboratory, one of many glorious products of Sterling's $40 million bequest. Dedication of the laboratory in

1923 was an event of national significance, marked by a national meeting of the American Chemical Society in New Haven and the commissioning of a series of chemical essays that were collected as the first two volumes of *Chemical Reviews*, a journal that remains influential after more than three quarters of a century.

Bertram Boltwood first chaired the new department. Upon his death in 1927 Arthur J. Hill, a former student of T. B. Johnson, succeeded to the chairmanship, a position he occupied until 1957. Hill was an organic chemist of no particular distinction, and his stewardship of the department was not marked by creative vision. Younger faculty members remembered ruefully the pride he would take each year in sharing with his colleagues the fact that he had been able to save and return to the central administration a significant fraction of the department's annual budget.

Organic Chemistry in Sterling Laboratory

Rudolph Anderson and Werner Bergmann

Although Hill was chairman, Johnson exercised special influence, particularly in organic chemistry. In 1926 he attracted Rudolph Anderson from Cornell to Yale to collaborate on the National Tuberculosis Association sponsored studies of the tubercle bacillus. The next year Anderson became the second non-Yale graduate to become a Yale chemistry professor, and he served with distinction for the next 21 years.

At the age of 13 Anderson had emigrated alone from Sweden to America. He came slowly to science through a career marked by poverty, catch-as-catch-can education, and bad luck that included failing to complete his doctorate in Emil Fischer's Berlin laboratory because of the outbreak of the First World War. He remembered sadly how, upon hearing the announcement of mobilization, his laboratory mates had swept all their precious samples and equipment from the benchtops to the floor and marched off singing "Deutschland über Alles." He finally completed his doctorate at Cornell five years later, at the age of 39.

Anderson's career was marked by a number of agile changes in research direction. When he began to investigate the pollen of the corn plant with the goal of studying plant nucleic acids, he found that early extractions produced a number of fats and unknown sterols that seemed more interesting, and more tractable, than the nucleic acids.

It was Anderson’s work on these sterols that attracted the attention of Johnson, who hoped that Anderson could isolate and identify important sterols in the tubercle bacillus. In fact when Anderson had fractionated 4 kilograms of dried tubercle bacilli from two thousand culture bottles, he found no trace of any sterol-like substances. So he studied what he had found and isolated a new substance, phthioic acid, which was shown at the Rockefeller Institute to bring about the formation of massive amounts of artifical tubercular tissue when injected into animals.

Ultimately Anderson isolated a very large number of new fats, waxes and sterols from tubercle and leprosy bacilli, which were said to be “of the greatest assistance to all students of tuberculosis.” He was equally well known in the biochemistry community as managing editor of the *Journal of Biological Chemistry* for 21 years.

Werner Bergmann, born and educated in Germany, practiced a closely related style of natural product organic chemistry at Yale beginning in 1931. His specialty was phospholipids and marine natural products. In the 1950s he began attempting to establish evolutionary relationships among marine invertebrates by analyzing their nucleic acids. Unfortunately his death in 1959, at the age of 45, cut short this promising line of research.

Yale’s organic chemists in the period between the wars were respected, and they provided strong training of graduate students, but from today’s perspective most of their work does not seems to have been centered on the most important developments in the science. German efforts on isolation and structure elucidation of steroid hormones bore much richer fruit. During the second half of the 20th Century improvements in chromatographic separation and spectroscopic structural elucidation displaced this type of search for new natural products from most academic laboratories to industrial and pharmaceutical ones.

By the 1960s the rows and rows of neatly labeled sample bottles in display cases that lined the corridors of Sterling Chemistry Laboratory had begun to disappear, and the comprehensive display of lipid fractions isolated from the tubercle bacillus had become neglected and was ultimately dismantled. This marked the end of natural history as a dominant theme in Yale chemistry.

Physical Chemistry in Sterling Laboratory

As Yale chemistry began to open its faculty ranks to the outside world in the late 1920s, the department had gained national prominence in organic chemistry, but it would play a more significant role in the development of science through physical chemistry The crucial first step was hiring Herbert Harned, head of the Physical Chemistry Division at Pennsylvania, in 1928.

Herbert S. Harned

As an undergraduate student of classics at Penn, Harned was attracted to chemistry by the possibility of making precise measurements. Sturtevant has written that Harned's passion became to

> *"search for the most fundamental quantity you can find and then measure it with the highest accuracy you can achieve. Some years later he discovered this quantity, the chemical potential of Josiah Willard Gibbs, and the major portion of his research involved the accurate measurement of this quantity."*

Harned had established a vigorous program in electrochemical research at Pennsylvania, but he was attracted to Yale by the space available in the new Sterling Laboratory and the commitment of President Angell and graduate dean Wilbur Cross to upgrade the Graduate School. Harned oriented the Yale physical chemistry program toward pure research, and over the next 30 years he oversaw development of the world's leading school of the physical chemistry of electrolyte solutions. In fact by 1937 chairman A. J. Hill, the organic chemist whose perspective was nothing if not parochial, defined physical chemistry as "a field which in a broad sense may be defined as a study of the thermodynamics of electrolytic solutions."

Although financial and administrative support declined soon after Harned's arrival at Yale, he had chosen an intrinsically inexpensive technique, and financial times were difficult everywhere in the early 30s. So he was able both to maintain his own research productivity and to attract an extraordinary set of students and colleagues.

The crown jewel of his research was developing techniques that allowed him to determine the dissociation constant of pure water, arguably the most important single number in all of solution chemistry, with an accuracy that remained unmatched for many decades. Moreover he measured the constant over a wide enough range of temperature to determine the enthalpy of dissociation to high precision.

During his first 20 years Harned assembled a team of solution physical chemists that included experimentalists Gösta Åkerlof, Benton Owen, Henry Thomas, Andrew Patterson, and Philip Lyons. In 1945 he recruited Raymond Fuoss, whose experimental and theoretical work at the General Electric

Laboratories had already won him the American Chemical Society's Langmuir Award (now called the Award in Pure Chemistry).

But Harned's greatest coup came early in his Yale career when he was contacted from Providence in 1933 by a young faculty member whose position had been eliminated because Brown University, facing financial retrenchment, had decided to dismiss unmarried junior faculty members. Within hours Harned had arranged to offer a Sterling Fellowship to Lars Onsager, who 35 years later would become Yale's first Nobel Laureate.

Lars Onsager

Onsager was much more than Yale's most outstanding chemist, and its most outstanding scientist as well, save Gibbs. He was the sort of giant who appears only a few times in a century. If he had not won the Nobel Prize for irreversible thermodynamics, he could have won it for any of two or three other strikingly original contributions. Onsager was a worthy successor of Gibbs, and his contributions to 20th Century thermodynamics and dynamics are unparalleled. But like Gibbs his strength was not in classroom teaching. Probably he had difficulty relating to the limitations of most of his colleagues and students, although he was legendarily kind and patient, and when an eager, serious questioner would be persistent in admitting his inability to understand, Onsager could ratchet his explanation down step by step until he could establish effective communication.

Outstanding scientists in all fields, when they had a chance to interact with Onsager, recognized him as not quite of this world in the breadth of his knowledge of fact and in the depth of his analytical insight. Yale's Physics Department was proud to have Onsager as a joint appointee, but disappointed that his invariable evaluation of all prospective faculty appointments was, "The candidate is very good." It finally dawned on the department chair that Onsager must be candidly rating candidates on a logarithmic scale in which he included himself, making all faculty candidates, however distinguished, indistinguishable from one another.

When Onsager came to Yale at the age of 30, after studying chemical engineering in his native Norway, and conducting research at Zurich, Johns Hopkins, and Brown, he had already done the work in irreversible thermodynamics that would earn him a Nobel Prize in 1968. At Yale he piled success on success in a wide range of fields, with contributions to understanding the Wien effect, thermal diffusion, quantized vorticity in superfluids, spontaneous magnetization, the electrical conductivity of ice, and especially the possibility of sharp phase transitions in a regular array of particles with only nearest-neighbor interactions. After World War II Wolfgang Pauli wrote a physicist colleague, who had been cut off from work in the Allied countries, that he had missed nothing except Onsager's beautiful solution of this latter "Ising" problem.

All of Onsager's publications involved deep and original analysis. He was unwilling to publish anything routine, and averaged only one paper a year during most of his time at Yale.

Although physical chemists recognized that Onsager's irreversible thermodynamics was the key to understanding the behavior of solutions, it was not an easy subject for them to grasp. When it became time for Harned and Owen to prepare the third edition of their classic monograph "The Physical Chemistry of Electrolytic Solutions", the editor insisted that the authors include a section on Onsager's theory that would supplement their extensive descriptions of its experimental verification.

So, as Harned later described the process, he hesitantly wrote down what he thought might be the thread of Onsager's story, backing it up with equations copied straight from Onsager's paper in such a way that they had at least the virtue of being serially correct. When Victor LaMer, Harned's long-time colleague and rival at Columbia, had read the passage, he surprised Harned by complimenting him, saying that it was the best write-up on irreversible thermodynamics that he had ever seen. In response, as Harned liked to recount, "I just smiled."

Many Onsager legends relate to his predilection for providing oracular hints to leading scientists who were struggling with problems that Onsager himself had solved but never published. One of his tersest responses was to a physicist at MIT who asked him after a seminar how he had derived a certain equation he had mentioned. Onsager erased a small portion of the blackboard and wrote the Schrödinger equation, $H\Psi = E\Psi$. He stared at it a moment, and then wrote the equation in question underneath. For Onsager the derivation was self-evident.

Although Onsager was a great theoretical physicist, he considered himself a physical chemist, and he reveled in solving practical problems, like designing a conductance cell that would supply Harned the most reliable data most easily, or advising a physicist on the design of insulation for a thermal diffusion cell.

In considering Onsager's influence on the Yale Chemistry Department one thinks of Falstaff's claim,

I am not only witty in myself,
but the cause that wit is in other men.

Most of the useful research by the electrochemistry group at Yale involved studying something that Onsager had either emphasized or alluded to. This influence extended beyond Yale. Lewis Longsworth, a leading solution phase physical chemist from Rockefeller University once said, “For the last twenty years I have done nothing more than pursue leads from one Onsager paper.”

Onsager’s chemical interests were catholic and his influence was felt in other areas of the department. In the early 1950s, when Wilkinson and Woodward at Harvard first announced the revolutionary “sandwich” structure of organometallic complexes, such as ferrocene, Onsager stopped in Cambridge to ask whether the chromium compounds prepared 20 years earlier by the German chemist Hein might possess analogous structures. After consulting with a distinguished local theorist, the Harvard consensus was that Onsager must not only be wrong, but that in this case, as one of them was heard to remark, “The old guy has lost it.”

Onsager persuaded Harold Zeiss, a junior organic chemist at Yale to repeat Hein’s work. Zeiss’s structural data vindicated Onsager’s hypothesis and constituted the first report on these chromium compounds, the independent discovery of which would earn E.O. Fischer a share of Wilkinson’s subsequent Nobel Prize. Onsager was no doubt pleased, but certainly he did not insist even on the footnote in which his name was mentioned in Zeiss’s paper that announced these results.

Onsager influenced contemporary Yale chemistry in another less-technical way. For more than thirty years his office was a monk’s cell, barely large enough for his cluttered desk lit by a pull-chain desk lamp, with no window but a tiny skylight. We see in retrospect that this was a scandal, but it helped generate a persistent local pride in the intellectual distinction of Yale Chemistry divorced from any elements of gaudy display. It also helped chairman Hill generate his annual refund from the department’s budget to the central administration.

Early Efforts in Spectroscopy

Not all branches of physical chemistry could be conducted as parsimoniously as pencil-and-paper theory or measurements of electrochemical potentials and conductances. In the late 30s Yale recruited two outstanding young spectroscopists, George Murphy and Bryce Crawford. But before long they left because Yale did not provide the support their research required.

Crawford, who would become America's premier infrared spectroscopist at the University of Minnesota, stayed only one year.

World War II

The war interrupted the course of research but offered new opportunities at Yale, as it did elsewhere. Most of the physical chemists stayed at Yale during the war to work on isotope separation under Harned's direction. Although Onsager's ideas were crucial to the ultimate success of the isotope separation efforts, he was not allowed to take part in this research because some of his in-laws were German citizens. His own wartime work involved solving the Ising problem.

While Yale Chemistry did not profit institutionally from war research as some universities did, its youngest physical chemists worked away from Yale in labs where they learned to use modern equipment that would revolutionize their subsequent research. Julian Sturtevant, who had begun as an organic research student of A.J. Hill, worked on radar at MIT, while Andrew Patterson worked on sonar in New London.

This experience was richly rewarding for Patterson, who devised a number of important new experiments in the postwar years. The most important of these involved his use of pulsed electric fields to test, without heating the sample, Onsager's theory of the Wien effect on high-field conductivity. Patterson and his student Gledhill noticed that after the pulse there was a delay before the conductivity returned to a steady low-field value, and they correctly interpreted this as the time required for ion recombination. They had discovered a new technique for studying ultra-fast kinetic processes. Although Patterson went on to other research projects, and other university responsibilities, application and generalization of his approach in another lab led to a Nobel Prize in Chemistry for fast kinetics.

In 1945 Raymond Fuoss came to Yale from General Electric Laboratories, to rejoin Onsager, with whom he had collaborated as graduate student at Brown. Although Fuoss came as an experimental and theoretical researcher with the unique understanding that he would not have responsibility for teaching undergraduates, he took teaching quite seriously. He taught courses that made curricular sense to himself and to others, unlike many of the other senior figures in the department who were comfortable teaching courses in their specialty to graduate students. Systematic undergraduate teaching was left to junior colleagues, each of whom taught three courses and three laboratories Monday through Saturday. This would soon change.

By the 1940s the gap between physical and organic chemistry at Yale had become almost as wide as the gap between the teaching responsibilities of senior and junior faculty. A physical chemist overheard Treat B. Johnson, passing Harned's laboratory during a tour for a visiting dignitary, as he announced with his signature lisp, "Here's where my physical chemistry is done." Harned sometimes referred to his organic colleagues as " bezazzled," which rhymed with bedazzled and referred to their interest in bis azole compounds. This too would soon change.

A.J. Hill was surely not solely responsible for the sorry state of the department by 1950. Over the 30 years of his chairmanship other powerful department members appeared to be too narrowly focused on their own work or too comfortable to insist on change. Before the presidency of Whitney Griswold, the university administration had been out of touch with the role of science in a university curriculum and was apparently all too content with Hill's annual refund from the chemistry department's budget.

The Kirkwood Revolution 1951-1959

When Hill stepped down as chairman in 1951, the year after Griswold's inauguration as Yale president, it was decided that he should be replaced by a dynamic researcher who had the vision to make the department achieve its potential. That man was John G. Kirkwood, a theoretical chemist at Caltech.

As the first chairman who was not a Yale graduate, Kirkwood completely reshaped the Chemistry Department. He insisted on first-class research from all faculty members, and he reduced the teaching responsibilities of junior faculty members to make that expectation reasonable. He gave authority that had previously resided in nonfaculty functionaries to faculty members. No longer would junior faculty members have to apply to the chairman's secretary for permission to use a piece of glassware.

In conducting the department, as in conducting his research group, Kirkwood had unquestioned authority, but he was straightforward and fair. He had a special talent for encouraging young scientists, giving them responsibility, and convincing them that they could succeed.

When Kirkwood died, at the age of 52, in 1959, he had set the Department on the road to the future. Sputnik had flown, and the period of substantial federal support for chemical research in universities had begun.

Within six years the department would expand into a modern research laboratory, the Kline Chemistry Laboratory, more that half the cost of which had been raised from government grants.

Kirkwood was succeeded as chairman by Julian Sturtevant, the first in a series of citizen-soldiers who have guided the department so effectively for more than 40 years.

Current Research in Yale's Department of Chemistry

Within a decade of Kirkwood's chairmanship the Yale Chemistry Department had a modern subdisciplinary structure very similar to the one it has today with emphasis on biophysical, inorganic, organic, physical and theoretical chemistry. The balance of this essay is a brief survey of the progress of Yale Chemistry within these subdisciplines since Kirkwood's arrival at Yale.

Theoretical Chemistry and Chemical Physics

Kirkwood was a brilliant theoretician, and would probably have shone as the brightest star in the Yale Chemistry firmament but for Onsager, especially had he not died prematurely. As a team they were unmatched in theoretical physical chemistry making Kirkwood's eight years the Golden Age of chemical theory at Yale. Unlike Onsager, Kirkwood was an unparalleled organizer and mentor of graduate students and postdoctorals, and the team he assembled and led went out from Yale to dominate the field of statistical mechanics in America.

Before his work was cut off, Kirkwood had pioneered the statistical mechanics of artificial and biological polymers, and he introduced a number of approaches in the statistical mechanics of fluids that remain productive today.

In the decade between Kirkwood's death and Onsager's retirement, emphasis on theory in Yale Chemistry Department survived in the quantum mechanics of Oktay Sinanoglu and the polymer statistical mechanics of Kirkwood's former postdoctoral Marshall Fixman. But Fixman left New Haven, and during the succeeding twenty years this line of research, so compatible with the Yale tradition of deep analysis and careful thought about chemical phenomena, faded from prominence at Yale.

Happily, theoretical chemistry has reemerged at Yale during the past decade with the appointments of William Jorgensen, whose research spans a wide range of computational chemistry including fluids and reactions, molecular and protein modeling, and synthesis design, and of John Tully, whose research emphasizes developing new analytical and computational tools to study dynamical processes such as energy transfer and chemical reaction at surfaces, in condensed-phases, and in biological environments, especially when the ubiquitous Born-Oppenheimer simplification fails.

Experimental physical chemistry was succeeded by chemical physics, which most certainly did not fit Hill's definition of "the study of the thermodynamics of electrolytic solutions." Under Kirkwood's leadership Yale appointed Richard Wolfgang in 1956. Finally financial support was available for this kind of work at Yale, and Wolfgang established a leading center in hot-atom chemistry, but it was unable to survive his premature death a dozen years later.

An attempt to establish a subdiscipline of nuclear chemistry in the mid-70s misfired, but gas phase chemical physics has become a permanent feature of Yale research with William Chupka's work on atomic spectroscopy, James Cross's studies of cross beam reactions and fullerene chemistry, and Mark Johnson's investigations of the structure and dynamics of cluster ions. For more than 20 years spectroscopist Steven Colson helped lead the effort create a distinguished chemical physics group.

Patrick Vaccaro and Charles Schmuttenmaer provide strength in four-wave mixing and pulsed laser techniques for studying structure and dynamics in gaseous and fluid phases. Kurt Zilm, together with biophysical chemist James Prestegard, helped make the Yale Chemistry Department a national leader in nuclear magnetic resonance spectroscopy with very high field capability for studies in materials science and biophysical chemistry.

Biophysical Chemistry

The time since Kirkwood's chairmanship has seen a steady and dramatic rise in the importance of biological chemistry within chemistry departments, and the biophysical group in Yale's department have been in the vanguard of that transformation.

By the time Kirkwood was initiating theoretical studies on the statistical mechanics of biological polymers, Julian Sturtevant was already on his way to convincing biochemists that thermochemistry is as central to their discipline as to all other branches of chemistry. In a career that is unprecedented in Yale chemistry he continued experimental research as an emeritus professor until his 90th year, supplying valuable calorimetric results on subtle biochemical systems that would have been inaccessible without his instruments and technique.

The two biophysical chemists appointed to Yale as junior faculty members in Kirkwood's time, Jon Singer and Jui Wang, established important research programs and were promoted to tenure. But ultimately both were lured away by other institutions.

When Donald Crothers joined the faculty as a biophysical chemist in 1964, his was the first chemistry appointment of a Yale graduate in a quarter century. His loyalty to Yale has been amply demonstrated by his repeated willingness to provide leadership as department chair, despite which extra burden he has produced a body of research on the physical chemistry of nucleic acids that has provided key insights for understanding the regulation of function and gene expression. His work, particularly with gel electrophoresis and NMR, showed that the DNA that biochemists had been accustomed to viewing as a rigid, double helical rod is in fact bent through interaction with proteins and drug molecules, and that the bending is crucial to how the molecule functions.

Peter Moore, the other former Yale undergraduate on the biophysical chemistry faculty, has made equally distinguished contributions to biochemistry. When he joined the faculty in 1969, Moore chose a research problem that would appear almost foolhardy to a less single-minded individual, because its importance was equaled by its difficulty. It was to determine the structure of the ribosome, life's intricate Jacquard loom for transcribing genetic information into proteins. Patiently, methodically, and imaginatively over the years he developed techniques that first allowed locating the protein constituents of the ribosome in collaboration with Donald Engelman and then allowed determining the atomic locations of all of its atoms in collaboration with Thomas Steitz. This most recent work has confirmed what could not even have been guessed at the outset of Moore's quest, that the machinery is most centrally composed of the RNA components of the assembly, not of its proteins. Moore's work has required painstaking application of neutron diffraction, NMR spectroscopy, and X-ray diffraction.

Like Moore, Gary Brudvig chose a piece of biological machinery of key importance, Photosystem II, and he has used electron paramagnetic resonance as well as inorganic and biological chemistry to study how it works. Together with inorganic chemist Robert Crabtree, Brudvig developed the first manganese cluster capable of modeling photosynthesis by splitting water and oxidizing it to gaseous oxygen.

During 27 years on the faculty James Prestegard helped build Yale's reputation in NMR spectroscopy and used this technique in fundamental studies of membrane structure and function.

Although the biophysical group within Yale's Chemistry Department has never been large, it has contributed special research distinction, as well as extraordinary leadership, to the department as a whole.

Inorganic Chemistry

Inorganic coordination chemistry began to flourish in Britain in the decades following World War II. After an influential visit by Joseph Chatt in 1965, the Yale department enthusiastically moved for representation in this field by hiring John Faller as Assistant Professor in 1967. Robert Crabtree joined Faller in 1977, and John Hartwig in 1992.

All three of these inorganic chemists have made substantial contributions to organometallic chemistry on the basis of carefully designed, mechanism-based research. Faller has specialized in developing new chiral transition metal catalysts and reagents for asymmetric organic synthesis. Crabtree made landmark contributions in alkane C-H activation and invented the first homogeneous transition metal catalyst system capable of dehydrogenating alkanes. In collaborations with Brudvig he also prepared the manganese cluster capable of splitting water as in photosynthesis. Hartwig has developed a rhodium/boron catalyst system that activates linear alkanes and selectively functionalizes them to give primary alkyl boron derivatives. The synthetic versatility of borane intermediates, and the selectivity of their preparation by this procedure are particular advantages over functionalization by less selective free-radical processes that typically yield secondary products.

Physical-Organic Chemistry

When Kirkwood arrived as chairman in 1951, the Yale senior faculty had no representation in one of chemistry's most rapidly growing research areas, physical-organic chemistry, which since the mid-30s had been harnessing the techniques of physical chemistry to provide a logical underpinning for the venerable, but empirical, discipline of organic chemistry.

Kirkwood's first recruit to Yale was William Doering, who had established a leading research program in physical-organic chemistry at

Columbia, and whose student Harold Zeiss was already a Yale instructor. Doering brought a large, productive research group with him in 1952. Over the next 16 years he expanded his elegant studies on the mechanism of carbene reactions to include studies of molecular rearrangements such as the Cope and Claisen rearrangements - processes that were central to the development of organic chemistry in that period.

Between 1955 and 1969 the department made two additional senior appointments in physical-organic chemistry and four junior appointments, two of whom were subsequently tenured. Since 1990 two more physical-organic chemists have joined the department to maintain strength in this area in the face of retirements.

When Kenneth Wiberg and Jerome Berson came to Yale in the 1960s, the department became the world's leading center for physical-organic chemistry, despite Doering's departure in 1967. Yale trained the next generation of leaders in this field. The strength of physical-organic chemistry has proven beneficial for the department as a whole. As an interdisciplinary area it has helped to bridge among subdisciplines and to promote collaboration, where in many chemistry departments there would be factionalism.

A prime example of collaboration is provided by the research of Martin Saunders. Although his own group has never been a large one, Saunders has made an extraordinary number of fundamental contributions to physical-organic chemistry, many of them through enthusiastic collaboration with other scientists who have the experimental facilities to implement his ideas. Over a period of 46 years he has coauthored research papers with more than a dozen different Yale chemistry colleagues and many colleagues from other institutions and disciplines. His innovative contributions have ranged from measuring the first NMR spectra of proteins to predicting, discovering, and developing rare-gas inclusion complexes of fullerenes. His spectroscopic studies of the rearrangements of simple organic cations were particularly significant and led to his innovative technique of isotopic-perturbation to solve the thorny but ubiquitous problem of distinguishing between equilibrating and "resonant" structures.

Kenneth Wiberg and Jerome Berson had both earned their doctorates in Doering's Columbia laboratory, and early in their careers both did important work on the formation and rearrangement of carbon cations. Wiberg has become particularly noted for the range of physical and computational techniques he skillfully brings to bear on determining the properties of carbon-carbon bonds, especially when they are strained by inclusion in small-ring polycyclic compounds. He not only succeeded in preparing compounds that many organic chemists thought incapable of existence, but also determined their spectroscopic and thermodynamic properties and used these results to test and improve computational methods. Berson’s hallmarks have been elegant kinetic and structural studies of reaction mechanism, usually involving subtle design and painstaking synthesis of isotopically and stereochemically labeled compounds. His comprehensive study of trimethylenemethanes and other “non-Kekulé” molecules has shed light on the most fundamental questions of chemical bonding and molecular reactivity.

Michael McBride has used a variety of physical methods to study reaction mechanism in organic crystals as a means of gaining detailed understanding of intermolecular influences on chemical dynamics. William Jorgensen has developed computational techniques for studying solution phase thermodynamics, molecular reactivity, and the design of organic syntheses. Most recently Andrew Hamilton has extended physical-organic studies from host-guest compounds to bioorganic chemistry and materials science.

Synthetic and Bio-Organic Chemistry and Chemical Biology

When Harry Wasserman came to Yale as an instructor in 1948, he was the sole practitioner of modern synthetic organic chemistry, but over the next 35 years he helped build one of the world’s leading departments of organic chemistry. Wasserman’s own research involved harnessing very unstable species - singlet oxygen, cyclopropanone, vicinal tricarbonyls - for use as practical reagents for the synthesis of natural products. He also enhanced the prominence of organic chemistry at Yale by editing *Tetrahedron* and *Tetrahedron Letters* for nearly 40 years.

Two Yale synthetic chemists, Frederick Ziegler and Samuel Danishefsky have made notable contributions in developing pericyclic reactions for synthesis of natural products. Ziegler used such reactions to prepare alkaloids and polypropionates, and he developed tandem procedures to approach other natural products. During 13 productive years at Yale Danishefsky developed hetero Diels-Alder reactions for synthesizing a variety of carbohydrates and other important classes of natural products. He has been particularly noted for his success in devising elegant new approaches to solving the most complex and challenging problems in natural products synthesis.

Stuart Schreiber began his career at Yale in 1981 as a synthetic organic chemist. Over the next decade he developed a number of innovative methods to achieve new levels of stereochemical and regiochemical control. His method for differenting functional groups after ozonolysis proved particularly powerful. His early success in synthesizing periplanone-B, the sex-attractant of the cockroach, led him to seek collaboration with biologists, and since that time he has become the world's leading figure in the rapidly developing area of chemical biology. Although Schreiber left Yale in 1990, two of his postdoctoral students, John Wood and David Austin, have subsequently joined the Yale Chemistry faculty and another, Craig Crews, is a joint appointee.

John Wood has made remarkable contributions to the synthesis of natural products and their analogues, developing rhodium carbenoids as important reagents for many of these syntheses.

Yale's involvement in bioorganic chemistry can be traced back 150 years to Samuel Johnson, Treat Johnson, Rudolf Anderson, and Werner Bergmann, but the modern era began in 1969 with the appointment of Ian Scott. During his decade at Yale, Scott was responsible for dramatic advances in understanding the mechanism of the biosynthesis of alkaloids and of vitamin B_{12}.

Not long after Scott's departure, Stuart Schreiber began developing a new type of chemical biology at Yale. Since 1988 Alanna Schepartz has made the department a center for using the tools of synthetic, biophysical, and physical-organic chemistry to study how proteins and synthetic molecules bind to nucleic acids so as to influence their structure and biological function. With the participation of Jorgensen, Hamilton, and Austin, bioorganic research has become a dominant theme within organic chemistry at Yale.

The Future

Although life-science students have been required to study chemistry for two hundred years, only in recent decades has the chemical understanding of biology truly progressed to the molecular level. It seems certain that branches of chemistry related to the life sciences, bioorganic chemistry, biophysical chemistry and bioinorganic chemistry, will continue to grow vigorously at Yale. Yale is already well represented in these area both by senior faculty and by recently appointed assistant professors David Austin, Patrick Loria, and Ann Valentine. Assistant professor of theoretical chemistry Victor Batista, whose primary interest is in applying quantum mechanics to fundamental studies of reaction dynamics, has an important research project on light harvesting by rhodopsins. Yale's efforts in chemistry, both in research and in teaching, will certainly continue to lay the foundation for rapid progress in biology, biotechnology, and molecular medicine.

Academic chemistry is also showing the way as industrial research in the United States shifts from a traditional emphasis on simple commodity chemicals to the development of specially designed materials, such as those for optical and electronic applications. Yale's Chemistry Department will certainly become more deeply involved in this effort.

Although the chemistry of the complex systems of biology and materials science will continue to grow in importance, improved fundamental understanding of the behavior of simple systems will be necessary to provide a rigorous chemical base that can support sound innovation in all the molecular sciences. Only chemistry can discover at a fundamental level why molecules behave as they do, or predict the behavior of completely unknown molecules, and only chemists can make them.

Since the mission of deepening our understanding of molecules and their reactions, and of providing a sound infrastructure for more applied areas, is a unique responsibility of chemistry departments, it is certain that Yale will continue to provide leadership in the areas of its traditional strength - physical and theoretical chemistry, physical-organic chemistry, organic synthesis, and inorganic chemistry - as well as in the areas where chemistry merges with biology and materials science.

The maxim "Build it and they will come" is amply born out by the development of chemistry at Yale for more than a century. The impending construction of the Kent Laboratory was a key factor in bringing Gooch to Yale College from Harvard in 1885. The facilities of the new Sterling Chemical Laboratory attracted Harned from Pennsylvania in 1928, ushering in Yale's golden age of electrolyte physical chemistry. Construction of Kline Chemistry Laboratory during the 1960's was crucial in bringing both biophysical and physical-organic chemistry at Yale to international prominence. One can anticipate that the recent gift from Yale's Class of 1954 to allow construction of a new chemistry research laboratory will be equally effective in helping to launch a fruitful third century of chemistry at Yale.

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