A Scandalously Short History of MBB at Yale

William C. Summers

First, let's be clear: Science in America started at Yale. Not at MIT, Caltech, Johns Hopkins, or even Harvard. The current myth that "Yale is a humanities school, not a science school" is a historical distortion of the primary role of Yale in the development of Science, both in the US and in the world. At a time when US higher education focused on the classics: ancient civilizations and theology, Yale was taking the first steps to bring science into the academy. The Sillimans, father and son, were charged with going to Europe and bringing back the "new learning" in scientific subjects to America. By the mid 1800s, a New Haven entrepreneur, Joseph Sheffield, provided Yale with resources to establish a "scientific school" attached to Yale College to study and teach "practical arts" such as agricultural science, chemistry, and military science, among others. Graduate research and education were novel ideas in the America academy, and Yale conferred the first Ph.D. degree in 1861, and the first Ph.D. in engineering in 1863 to J. Willard Gibbs. Interestingly, the curricula in mathematics as well as economics, English, geography, history, modern languages, philology and political science all had their home in what became the Sheffield Scientific School, since such modern and practical subjects were not available in the "Academic Department" as Yale College was called. What we now think of as "the Humanities" were all started by the scientists at Yale! Initially, the program in applied chemistry was located in the Department of Philosophy and the Arts.

Against this arcane background, we find the origins of the current Department of Molecular Biophysics and Biochemistry (MBB). The two recent progenitors of MBB were the Departments of Biochemistry and Physics, but their earlier origins go back to the early days of Sheffield. In the mid 19th century, chemists debated whether the new discoveries of the chemistry of living things deserved its own identity. On one hand it might be called "organic" chemistry, and on the other hand, "iatro" chemistry (the chemistry of medicine). Often iatrochemistry was called physiological chemistry, and in 1874 Yale established a Laboratory of Physiological Chemistry in Sheffield with Russell H. Chittenden, a recent Sheffield graduate, in charge. After two years of study in Heidelberg with the eminent German physiological chemist Willy Kühne, Chittenden developed a broad program that extended physiological chemistry beyond being a handmaiden of medicine, and his students when on to populate many of the medical schools in which research and teaching was the new model. His most important student was Lafayette Mendel, who succeeded Chittenden as head of Physiological Chemistry at Yale in the early decades of the 20th century. Mendel developed an internationally recognized program in nutritional chemistry and the chemistry of growth. He initiated a fruitful collaboration with Thomas Osborne, the analytical chemist at the Connecticut Agricultural Station, which for many years was affiliated with Yale. Osborne's careful identification and quantification of amino acids in various proteins was essential to the new field of protein chemistry as well as nutritional science.

In 1921 Yale reorganized many of its departments and programs, and integrated Sheffield more fully into Yale University. The Physiological Chemistry Laboratory was transferred to the School of Medicine in the newly constructed Sterling Hall of Medicine. A major new direction in the Physiological Chemistry took place in the mid-1930s with the arrival of a German visitor, K.G. Stern, who introduced new styles and new methods from the German schools of Leonor Michaelis and Otto Warburg. From nutrition Yale turned to metabolism. Upon Mendel's death, the medical faculty opted for a more medically oriented leadership of Physiological Chemistry and recruited C.H.N. Long, a biochemical endocrinologist and physician, from McGill. From 1939 until 1941, Long also served concurrently as chair of the Department

of Pharmacology, and in 1947 he became Dean of the School of Medicine while still serving as chair of Physiological Chemistry.

The "modern" history of the medical school origins of MBB begins in 1945 with the arrival of Joseph Fruton. Fruton had worked at the Rockefeller Institute on the mechanisms of enzyme specificity and showed by a tour de force of synthetic chemistry, that pepsin had exquisite specificity for cleavage of only a very few peptide bonds. Fruton's work at Yale had two major impacts: when he became chair in 1947, with the name changed to the Department of Biochemisty, he fostered interests in proteins, their structure, their function, and their synthesis. Second, he and his wife, Sofia Simmons, co-authored the biologically-oriented "General Biochemistry" (1953) which became a best-seller and the canonical textbook of biochemistry for over a decade. Fruton was also well-known for supporting women in science, and two of his early students at Yale, Maxine Singer and Mary-Ellen Jones, when on to become distinguished leaders in the field.

By the 1960s, the new leadership at Yale under President Kingman Brewster, proposed a new Department of Molecular Biology, a move much opposed by both Fruton as head of Biochemistry, and Ernest Pollard as head of Biophysics (see below). However, with the support and advice of an external review committee, Brewster pushed ahead with his plans to develop Molecular Biology at Yale, with the result that Fruton retired as chair of Biochemistry in 1967 and Pollard left Yale. Biochemistry was left in the hands of Joseph Coleman as acting chair. Several failed searches for a new head of the Department of Biochemistry would herald the birth of MBB, as we will soon discuss.

Meanwhile, in the Department of Physics, interesting things were happening. Yale physics was probably the most distinguished department in the US at one time. The reclusive J. Willard Gibbs hosted the likes of Hermann von Helmholtz and other international luminaries who paid visits to the "father of thermodynamics." Somewhat later in the Yale chemistry department was the originator of irreversible thermodynamics, Lars Onsager. E.O. Lawrence, inventor of the cyclotron, was on the faculty, but was lured to California in the 1920s because Yale could not provide the facilities promised by Berkeley (rumored to be year-round tennis facilities). Bertram Boltwood, the inventor of radioactive dating, was one of the few American physicists interested in the new field of radioactivity, and was a collaborator of Marie Curie, who provided Yale with her standardized samples of various radioactive isotopes. In the late 1930s, Yale attracted a young British physicist, Ernest Pollard, a student of James ("Jimmy neutron") Chadwick. Pollard taught atomic physics and build the first cyclotron at Yale for experimental studies in particle physics. Then came World War Two. The American physics community was divided into two research programs: the bomb and radar. Yale's physicists were assigned to radar at MIT (the Rad Lab). Even before the end of the war, Yale's physicists were worried about their post-war future. Clearly, atomic and nuclear physics were where the excitement was heading, yet the physicists working on the bomb would be way ahead, having been in on all the wartime, classified, research. On the other hand, the radar physicists saw themselves relegated to microwave oven research. Pollard organized some discussions about these worries and according to oral recollections, the Yale group saw two possible futures for themselves: cosmology or biophysics. There was a well-established connection between atomic physics and biology through the experimental use of radiation bombardment of biological material using "target theory" models to deduce molecular and atomic processes in biological systems. The future of cosmological work at Yale was apparently discouraged by the then acting chair, Leigh Page. Immediately after the war, then, Pollard established a Biophysics Section in the Department of Physics. He obtained financial backing from private sources, including funds to add a 6th floor on the Gibbs Laboratory of Physics, just for Biophysics.

The Biophysics group flourished in the immediate post war period because of the interest in the consequences of the use of the atomic bomb in the war, but also because of the hope for new and peaceful uses of atomic energy (one of which was the new availability of radioactive tracers for biology and chemistry research). The "Atoms for Peace" program was a major public program promoting interest in radiation biophysics. Pollard and Richard Setlow wrote a widely used textbook "Molecular Biophysics" (1962) which defined the field for a generation and established Yale as a leading institution in this area of research. Like Fruton in Biochemistry, Pollard was rather authoritarian in the way he organized and ran his Section of Biophysics. By 1955, the Section of Biophysics within Physics achieved full departmental status, yet it was still very hierarchical. Setlow, the other full professor in Biophysics chaffed under Pollard and left Yale for Brookhaven National Labs in the late 1950s and Pollard left for Penn State in 1960, taking a substantial fraction of the Biophysics faculty with him. This coincided with Kingman Brewster's initiative to create a Department of Molecular Biology.

One of Pollard's proteges, Franklin Hutchinson, picked up the reins in Biophysics in 1961, but was succeeded in 1963 by Frederick Richards, a protein chemist from the Department of Biochemistry in the School of Medicine, thus planting the seeds of the merger which was to come several years later. In a major change, portending things to come, in 1962 the Biophysics Department became the Department of Molecular Biology and Biophysics (the first version of "MBB"), thus initiating Brewster's modernization plan. Another name change took place in 1964 when a molecular biologist was recruited to lead a new initiative in the department of Biology. To avoid the appearance of overlap or competition, this new chair negotiated the deletion of "molecular biology" from the names of any other department on campus and so "MBB" was renamed the Department of Molecular Biophysics (a simple deletion mutation?). Richards was an effective chair, both internally and externally, getting resources from Yale and recruiting promising faculty from outside, and Molecular Biophysics became the department envisioned by Brewster and his expert advisory committee.

Trouble recruiting a new chair for Biochemistry to succeed Fruton dragged on in the late 1960s. Eventually, one candidate suggested that if Yale would combine the thriving Molecular Biophysics Department with the problematic Biochemistry Department, the job might be more attractive. Apparently, this suggestion was well-received, because the Yale administration promptly proposed the idea to Fred Richards, already chair of Molecular Biophysics, and he accepted (obtaining yet substantially more resources from Yale for the new department, now named Molecular Biophysics and Biochemistry). While the administrative amalgamations between the Faculty of Arts and Science required continual refinements, it was not without precedent. Such a hybrid department already existed in the Department of History of Medicine and Science, which was created in the 1950s, joining the two sides of Yale for mutual benefit.

In 1970 Richards started active recruitments to the new, merged, department. He attracted 10 young molecular biologists, 6 new hires, and 4 recruitments from existing faculty in clinical departments, all in the space of about one year. A complete renovation of the old Biochemistry laboratory space in the basement and first floor of the C-wing of Sterling Hall of Medicine provided the School of Medicine with a new vibrant presence of molecular biology. The connection with the clinical departments involving meaningful joint appointments rather than political "courtesy" appointments was an important step by Richards to improve basic science in the School of Medicine.

As the interplay of macromolecular structure and function became the dominant theme in much of biology over the past 50 years, the once unique research agendas, techniques, and experimental approaches of the MBB department have spread across the biological sciences so that more joint

appointments, joint graduate programs, and (sadly) disputes over “turf” have become common. The once clear differences between the research and teaching programs in Yale’s biological science departments have become blurred. History, however, suggests that such changing scientific landscapes are in the nature of progress, and that as such, might well be embraced rather than resisted.

For further reading:

History of the Sheffield Scientific School of Yale University, 1846-1922, Russell H. Chittenden. New Haven: Yale University Press, 1928.

Science at Yale, ed. S. Altman. New Haven: Yale University, 2002.