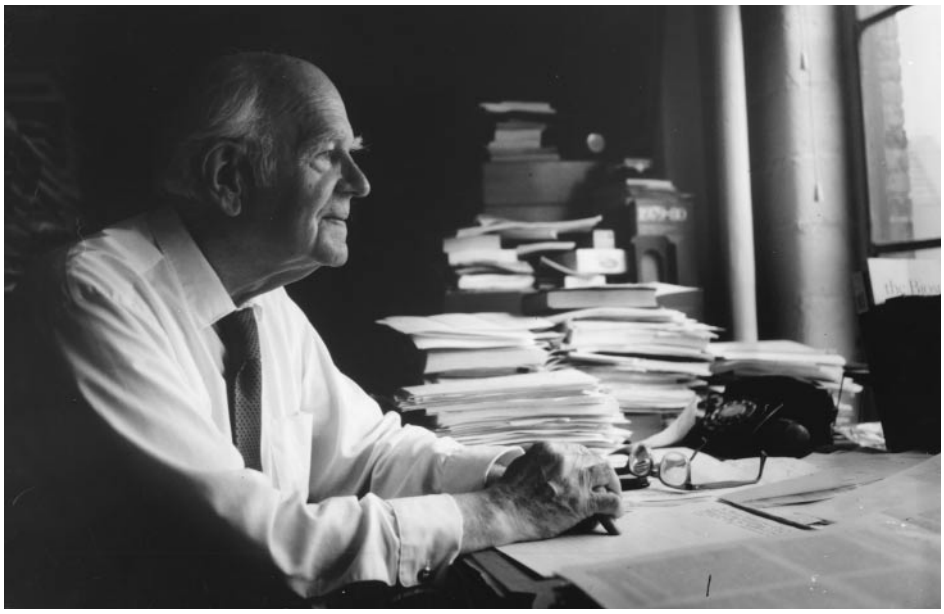
Obituary

John Tileston Edsall (1902–2002)



Photograph of John T. Edsall by Rick Stafford, taken during the 1970s

John Edsall died on 12 June 2002, five months before his 100th birthday. His long career spanned the major years of protein discovery and characterization. To say only that he was a leading contributor in this field does not convey his central importance to the enterprise. Before many others, he realized the essential biological role of proteins, and appreciated that physical chemistry was crucial to understanding their structures and functions. Beyond his own laboratory work, he edited, synthesized and explained the new discoveries on proteins in three coauthored monographs and the review series *Advances in Protein Chemistry*, which he co-founded and co-edited for 55 years. He also made major contributions to the *Journal of Biological Chemistry*, of which he was Editor-in-Chief from 1958 to 1967. Edsall recruited generations of new scientists into his field, guiding them, and helping them overcome obstacles along the way. He had the ability to focus on his work as well as the society around him, and when he saw biological research imperiled by McCarthyism in the 1950s, he bravely spoke out to set things right. His great achievements were dependent on his character, which combined a Puritan discipline and formality of speech and dress, with modesty and diffidence; he gave, in the words of his lifelong friend Jeffries Wyman, the 'impression of unbounded benevolence.'

Edsall's youth was privileged, but far from trouble-free. His American ancestry on both sides stretched back to the 17th century. His mother, who died when John was 10-years-old, was an honors graduate of Radcliffe. His father was an academic physician who became Dean of Harvard Medical School (Boston, MA, USA) when John was 15, and it was simply assumed that John would attend Harvard and Harvard Medical School. Edsall was close to both his busy, scientific father and his attentive, literary mother. When he was young, his mother read poetry to him, and by the age of nine he knew the *Rime of the Ancient Mariner* by heart, and was familiar with several Shakespearian plays. His early love of literature stayed with him throughout his life, as his books and Editorships attest. Shortly before his 96th birthday, when my wife and I visited Edsall in his home, we found him at his desk, reading a book of philosophy in French.

When his mother died of pneumonia, Edsall was sent to the Milton Academy in suburban Boston, where he never felt at home. He recalled in oral history interviews with F.L. Holmes (Yale University, New Haven, CT, USA) during 1990–1991, that, aged more than a year younger than his classmates, he was shy, awkward and inept at sports in a school that placed great emphasis on athletics. His high grades did not relieve this situation. Compounding his concerns was growing short-sightedness, which, although no one else noticed, depressed him. Nearly 80 years later he recalled his distress when the school posted the scores of a 'strength test', with his score appearing at the very bottom. Clearly, this test was the poorest predictor ever for what became a long and vigorous life.

Entering Harvard at 16-years-old, Edsall made efforts to emerge from his shell, but at first continued to suffer from bouts of depression. He majored in chemistry and met Jeffries Wyman; thus began a lifelong friendship and collaboration. Edsall joined the Harvard Liberal Club, and became founding editor of their journal *The Gadfly*, the name of which was suggested by another undergraduate friend, Robert Oppenheimer, who later became a brilliant quantum physicist, and later still the leader of America's vast World War II program to build the atomic bomb.

The first two years of medical school were tedious for Edsall. He recalled that 'the two occasions in my life when I felt the greatest sense of relief were when I passed my anatomy and second when I was accepted by my wife'. The tedium of medical school was relieved by two years (1924–1926) studying biochemistry at Cambridge University (UK), along with Wyman. There, Edsall also renewed his friendship with Oppenheimer. Returning to medical school in the fall of 1926, Edsall was bored by his rotations in clinical medicine, and happily found an opportunity to do research on muscle proteins in the Harvard Medical School Laboratory of Physical Chemistry, under the forceful directorship of Edwin J. Cohn. Soon, with Alex von Muralt he discovered that the muscle protein myosin was bi-refringent when oriented by flow, and derived the biophysical analysis that showed the protein elongated in solution, as it is in muscle. Edsall completed medical school in 1928, but declined an internship in favor of continued research in the Cohn laboratory. The following year he married Margaret Dunham, and together they raised three

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sons and remained married until her death in 1987.

Edsall's academic career can be roughly divided into four periods. The first spanned from 1930 to 1940, when he and the other talented scientists in the Cohn laboratory studied the biophysical properties of amino acids and peptides. Edsall's special contribution to this effort was the application of Raman spectroscopy, a newly discovered tool that showed, unequivocally, that amino acids occur as doubly-charged ions in solution. Furthermore, he compiled and analyzed data generated by the Harvard group for many amino acids (including thermodynamic, structural, spectroscopic, chemical, dielectric, diffusion and sedimentation, and acid–base properties). He summarized this immensity of work in monograph, co-authored with Cohn, which he finished during a sabbatical at Caltech during 1940–1941, entitled: *Proteins, Amino Acids, and Peptides, as Ions and Dipolar Ions*. Nearly 60 years after its publication, this monograph remains an indispensable source of information for scientists working in the field. In addition, the monograph on *Biophysical Chemistry* that Edsall co-authored a decade later with Wyman, is still enjoying a long and useful life.

Returning to Harvard Medical School in the fall of 1941, Edsall found that Cohn was preparing the laboratory for a role in the coming war. This was the second major period of Edsall's career: he and others in the Cohn laboratory discovered methods to fractionate plasma into its components to enable storage, transport and reconstitution on the battlefield, or wherever needed. They found that plasma can be fractionated by precipitating its component proteins by changes in pH and in the concentration of cold ethanol. A pilot-plant was set up in the medical school basement to test the whole procedure on a large scale before being turned over to commercial firms. One wonders how many human lives have been saved by the blood products derived from these procedures.

In 1953, Edsall – by now a full professor – moved across the Charles River from Harvard Medical School to his own laboratory in the Biology Department at Harvard's main campus in Cambridge (MA, USA). He had requested this move, as his appetite for the big science of the Cohn laboratory had decreased. One factor had been Cohn's refusal to critically examine some of his own ideas. Cohn had come up with a fanciful numerology to predict the sequences of proteins. Edsall, with the search for truth being the core of his life, could not accept these ill-founded notions, nor could he hide his views from Cohn. More comfortably situated in his own laboratory, Edsall began his third major phase of research by exploring another mystery of blood-proteins: how carbonic anhydrase, found in red blood cells, catalyzes the combination of the respiratory product CO_2 with water to form bicarbonate, which is highly soluble in blood.

No sooner was Edsall set up in his own Harvard laboratory, than he was propelled into leadership of the scientific community by a crisis brought about by the anti-Communist hysteria of the McCarthy era. In 1954, biological scientists learned that the US Public Health Service [the parent of the National Institutes of Health (NIH)] was revoking research grants of some scientists because of secret information in their security files. Edsall, along with Philip Handler (Duke University, Durham, NC, USA), Wendell Stanley (University of California, Berkeley, CA, USA) and a few others, drafted a resolution asking the National Academy of Sciences to investigate the situation. When the response was slow in coming, Edsall decided to publish an article in *Science* outlining the threat to basic rights, and announcing a personal resolution. He took care to present, in more than three full journal pages, a balanced picture of events, and then warmed to his resolution in Tom-Paine-like tones: 'Certainly I do not share the fears of the alarmists who believe that our society is rapidly becoming totalitarian; the fact that articles like this one can be published and freely discussed is good disproof of such ideas. Yet the trend toward totalitarian procedures is present in the arbitrary actions that I have discussed; and the time for resistance is now, not later…Under the circumstances, I shall neither ask for nor accept funds from any Government Agency that denies support to others for unclassified research for reasons unconnected with scientific competence or personal integrity'.

Possibly partly because of Edsall's leadership, the Eisenhower administration called on all government agencies to restore proper procedures. The revoking stopped, and within a year Edsall had applied for and received research support from the NIH. The biochemical community responded with gratitude and esteem for Edsall, who was subsequently elected President of the American Society of Biological Chemists, and was asked to serve as President of the International Congress of Biochemistry held in New York in 1964.

Another issue confronted by Edsall during the McCarthy period, was President Eisenhower's order to place 'a blank wall' between any classified information and Robert Oppenheimer, Edsall's long-standing friend, and the subsequent decision to revoke Oppenheimer's security clearance. This decision was made despite Oppenheimer's successful leadership of the atomic bomb project, and in part because Oppenheimer had at one point advised against a crash program to build the hydrogen bomb. Edsall considered the handling of the Oppenheimer case outrageous, and protested in letters to the *New York Times* and to officials involved in the case. However, Edsall recognized that the complexity of Oppenheimer's character was, in part, to blame for the troubles that engulfed him. In a letter to me in 1977, Edsall explained, 'Oppenheimer had great gifts for making both friends and enemies. His brilliance of mind was of course phenomenal. In our student days he was obviously in a class by himself intellectually, in a group that included several people who became distinguished later. His mind seemed to burn like a flame, and his range of interest was very wide. When we were both students in Cambridge (1925–1926) he introduced me to the work of several French poets that I had never read before; he was devouring Dostoyevsky and other authors, while plunging into the new quantum mechanics. Heisenberg's first papers had just come out, and Schroedinger's were soon to follow. Later, his charm and his powers of persuasion were famous; indeed, people who opposed his policy views sometimes distrusted him for this very reason – they felt he was much too persuasive. Yet also he could be arrogant, and cuttingly sarcastic with people whom he did not respect intellectually; and he paid a heavy price for this. He was certainly a

very complex person; his capacity for friendship was certainly great; he was devoted to his close friends, and they to him'.

In 1958, Edsall took on the Editorship of the *Journal of Biological Chemistry*, and guided its post-war expansion. He lifted the standards for authors, reviewers and editors, reading and often revising every letter that went out to authors. He demanded high scientific quality for publication, yet he was sensitive to the feelings of authors who had their papers rejected. A colleague joked that an author, after a cursory reading of a rejection letter from Edsall, might conclude that he had won an award.

During this period, it was my good fortune to be assigned as one of Edsall's undergraduate tutees. We met about twice a month in his office, or occasionally after dinner at his home on the periphery of the Harvard campus. There, his wife Margaret would offer warm words of greeting and would supplement the undergraduate diet with grape juice and cookies. In these sessions, Edsall would answer any of my questions on the reading he had assigned to me at the end of the previous session. During my sophomore year, the readings were from biochemical monographs; the next year, the readings were from scientific reviews and papers; and by my final undergraduate year, Edsall gave me a research project on spectrophotometric properties of human serum albumin, which led to my first scientific paper. Of course, I was just one of many undergraduates whom he coaxed out of scientific ignorance. Edsall was a towering model for students searching for truth in science, and he insured fairness to all involved. Moreover, he was a fine example of a humane, cultured, and socially aware scientist.

Social issues relating to science formed the focus of Edsall's fourth period of research and writing. He stated that 'Until the atomic bombs fell on Hiroshima and Nagasaki, my work in science and my concern with politics ran in different channels. After 1945, that was no longer possible'.

His concerns over the years, which intensified after the closure of his laboratory in 1973, included: atomic, chemical and biological weapons; the pollution of our air, water and countryside; issues that threaten the freedom and integrity of research; punishment of scientific whistle-blowers; and the misuse of applied science. Increasingly, he thought and wrote on such issues, publishing ~80 articles on the history and social responsibilities of science, in addition to his three books and ~110 scientific articles.

Long after the years when most individuals surrender to old age, John Edsall's mind and body remained active. His last published paper appeared during his 90th year. One of the last times I spent in his company was a hot summer day when he was 94. He had traveled from his home in Cambridge, on foot and by subway, to the *Symposium of the Protein Society* in Boston to attend scientific sessions. Other participants stared in awe as the tall, elderly scientist in a blue suit took his seat in the lecture hall, still curious about developments in the field he had helped to shape some 70 years before.

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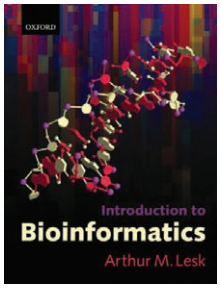
Book Review

Bioinformatics for beginners

Introduction to Bioinformatics
by Arthur M. Lesk Oxford University Press, 2002. £19.99 (320 pages) ISBN 0 19 9251 967



Lesk has worked hard to deliver a broad introductory-level bioinformatics text for students and practicing scientists who need to access information about genes and proteins and their associated software tools. The text is easily accessible to students on a budget and is delightful to read, with Lesk's wry humor interspersed throughout.

The opening chapter of the book gives the reader a summary view of bioinformatics, spanning the distance from central dogma to computers, to phylogeny, past PSI-BLAST and on to a survey of protein structure classification, structure prediction and protein engineering, and winding up with an outlook on the clinical relevance of bioinformatics. While this might cover a lot of ground in a single chapter, it serves the important purpose of providing a stage upon which Lesk can explore the characters and themes in bioinformatics, revealing them in more detail in subsequent chapters.

The text has a very well thought-out set of additional exercises for the beginner bioinformatician. It integrates information from the Internet in the form of problem sets known as 'Weblems'. The exercises in the first chapter cover the span of topics. Many take the form of problems analagous to bioinformatics, such as recovering the order of overlapping fragments of sentences using PERL programming, while others challenge the reader to find facts, such as when the last new species of primate was discovered.

The second chapter delves into genomics and provides a well-rounded discussion of the genomes of the major important model organisms, evolution and horizontal gene transfer. Special topics, such as mapping genes, positional cloning, gene clusters and the most common protein domains, are provided as supplementary boxes. Missing from this chapter are mentions of the role of intein splicing and the importance of modular protein interactions and regulatory networks as components of the proteome.

The third chapter introduces the reader to the 'archives', the term Lesk uses for bioinformatics databases. The reader is provided with a rather primitive 'flatfile' viewpoint of biological information as an introductory point, which might be suitable for many beginners looking for information. However, it would be helpful if Lesk indicated to his readers those bioinformatics standards for archives

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