



CLASSICS | VOLUME 277, ISSUE 33, P29351-29354, AUGUST 2002

John T. Edsall: Biochemist, Teacher, *Journal of Biological Chemistry* Editor, and Responsible Scientist

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Open Access • DOI: [https://doi.org/10.1016/S0021-9258\(18\)75587-7](https://doi.org/10.1016/S0021-9258(18)75587-7)

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Studies in the Physical Chemistry of Muscle Globulin. II. On Some Physicochemical Properties of Muscle Globulin (Myosin)^[SEP] (Edsall, J. T. (1930) *J. Biol. Chem.* 89, 289–313)

Studies in the Physical Chemistry of the Proteins. XI. The Amphoteric Properties of Zein^[SEP] (Cohn, E. J., Edsall, J. T., and Blanchard, M. H. (1933) *J. Biol. Chem.* 105, 319–326)

John Tileston Edsall (1902–2002) was born in Philadelphia to families that had emigrated to the United States in the 17th century. His mother, Margaret Tileston, was a teacher, and his father, David Linn Edsall, was a Professor of Medicine at the University of Pennsylvania Medical School. In 1918, David Linn Edsall became the Dean of Harvard Medical School, a position he held for 17 years. The move from Philadelphia to Boston and Harvard marked, for John, the beginning of a lifelong association with Harvard. At the age of 13, he was fascinated by a science class at Milton Academy which, along with being raised in a medical family, helped to guide him toward medical school and a career in science. John enrolled in Harvard College to study chemistry at age 16 and he was, by his own admission, an average student. In his last two years, however, he was inspired by two teachers/scientists, the organic chemist E. P. Kohler, and the biochemist Lawrence J. Henderson, who was the Chairman of the Department of Physical Chemistry at Harvard Medical School (1).



After completing his undergraduate studies in 1923, Edsall entered Harvard Medical School, where his interest in science and research was further stimulated by Otto Folin's biochemistry course. (Folin is the author of an earlier *Journal of Biological Chemistry* (JBC) Classic (2).) Most important during his first year of medical school was the opportunity to do research with Alfred C. Redfield, Director of the Woods Hole Oceanographic Institute, on the physiology of heart muscle function. This work initiated a career-long interest in the structure and function of muscle proteins. In 1924, Edsall, along with Jeffries Wyman his college friend and colleague (and author of a future JBC Classic), began two years of study at Cambridge University in the Department of Biochemistry chaired by F. Gowland Hopkins (author of a previous JBC Classic (3)). He took biochemistry courses and did some research but, more importantly, came under the influence of G. S. Adair who, Edsall wrote, was his "most important contact" at Cambridge (4). Adair was in the process of determining the molecular weight of hemoglobin, describing hemoglobin oxygen dissociation curves, and applying physicochemical principles to the study of proteins. Adair's work was reported in a previous JBC Classic (5).

Edsall returned to Harvard in 1926 as a third year medical student to begin his clinical training, much of which he felt was "trivial and stupid" (1). In spite of this view, however, he decided to complete his medical degree and in free time from his clinical studies began to work with Edwin J. Cohn in the Department of Physical Chemistry in Harvard Medical School and the author of a previous JBC Classic (6). Cohn was interested in protein physical chemistry and guided Edsall to examine the globulins of muscle. During his early experiments with myosin, in fact actomyosin, it was observed by refractive index measurements that myosin solutions forced to flow through a capillary exhibited streaming birefringence (7, 8). This ordering, induced by capillary flow, was compared to the ordered morphology observed in intact muscle cells by his colleague Alexander von Muralt suggesting that the extracted protein(s) represented a basic unit of muscle structure. At that time, there was no good theory that related flow birefringence to the size and shape of the molecules producing it, but Edsall determined from hydrodynamic considerations that the dimensions of the myosin molecules must be long and thin in order to explain the ordering induced by capillary flow.





John T. Edsall. Photo courtesy of the National Library of Medicine.

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In addition to work on muscle proteins, Edsall and his colleagues in the Department of Physical Chemistry, including Jeffries Wyman, began systematically to study the physical and solution properties of amino acids and small peptides. One of Edsall's contributions was the description of an amino acid as a dipolar ion or, as he preferred, ionic dipole (4). Using Raman spectroscopy, he showed that both the amino and carboxyl groups of amino acids were charged at isoelectric pH (9), which supported evidence obtained with other methods.

The two papers reprinted in this installment of JBC Classics are intended to represent a body of work focused on the physical chemistry of proteins. As was common in Edsall's time, much of his work was published in the chemical literature. The first paper examines primarily the solubility and viscosity of myosin as a function of ionic strength and pH. Further it is reported that the viscosity of myosin in solution was much greater than that of plasma proteins such as albumin. The

paper presents titration data for the protein zein and reports the pK values for the titratable groups, primarily the carboxyl groups and the imidazole of histidine. The titrations were carried out only to pH 8 so the ionization of the lysine and arginine residues were not observed as Edsall pointed out.

Edsall was a devoted teacher and because the Department of Physical Chemistry in the Medical School had few formal teaching responsibilities, he volunteered to be a tutor at Harvard College, a position he held from 1928 to 1968. This program was an integral part of the Harvard biochemical sciences teaching program and covered all aspects of biochemistry. He met with small groups of undergraduates and advised seniors on their honors research projects. Edsall served as Chairman of the Board of Tutors from 1931 to 1968, a few years before his retirement. Among the students in Edsall's groups were R. Gordon Gould, I. Herbert Scheinberg, Alton Meister, Alexander Rich, Gary Felsenfeld, Jared Diamond, W. French Anderson, Eliot Elson, Michael Chamberlain, David Eisenberg, Robert Eisenberg, and Joel Huberman. All were to have successful careers in science and medicine (1). He also taught a formal course in the Biology Department of Harvard College on biophysical chemistry.

With the beginning of World War II, work in the Department of Physical Chemistry was redirected to support the war effort. Led by Edwin J. Cohn, this group spearheaded the national plasma fractionation program. The large scale fractionation procedures they developed provided many protein products to meet the needs of the war including clotting factors and human albumin as a "plasma extender" for transfusions (6). This applied research also produced valuable fundamental knowledge of protein solubility properties and techniques for fractionation.

After Cohn's death in 1953, Edsall moved to Harvard College where he continued both his research and teaching without the necessity of the four-mile trips between the Medical School and College. For much of the remainder of Edsall's career, his research was focused on carbonic anhydrase. In 1954, he was invited to become a member of the Editorial Board of the JBC, and in 1958 he was asked to succeed Rudolph J. Anderson as Editor. He accepted and served as Editor until 1967. The editorial office of the Journal was set up at Harvard, and the basic structure of the JBC manuscript review process as it exists today was established. In 1958, the Journal page was enlarged to enable presentation of 2.4 times the content of the previous, smaller format. The result was a thinner Journal but only for a short time. Edsall was responsible for the first appointments of women to the Editorial Board, Mildred Cohn, Sarah Ratner, and Sofia Simmonds.

During Edsall's 10-year term, the size of the Editorial Board doubled from 26 to 54 members. (In here are about 500 members of the editorial board.) The number of pages published by the Journal had also doubled reaching 5800 during his tenure. He believe < so >

sort of limit made it likely that the JBC would become divided into subspecialty journals. It survived that period of growth without fission, however, and remains a general journal of biochemistry and molecular biology. (In 2002 the Journal will publish over 50,000 pages.) During Edsall's last year as Editor, page charges of \$35 were instituted and were then, as they are now, somewhat controversial albeit essential to the financial health of the Journal. (Page charges in 2002 are \$65.) Edsall was succeeded as Editor by William H. Stein, who was stricken by a crippling paralytic illness and served only a short term. Herbert Tabor became Acting Editor, and in 1971 with Stein's resignation was appointed Editor, a position he occupies in 2002 ([1](#), [10](#)).

Among Edsall's many roles was that of a vigorous advocate for freedom of scientific inquiry as well as the responsible conduct of research and usage of applied science. At the Annual Meeting of the American Society of Biological Chemists (ASBC) in 1954, it was reported that the United States Public Health Service (USPHS) was withholding research support from some investigators because their security files contained unevaluated, adverse information. The investigators were not made aware of this information nor were they given any opportunity to respond to the allegations, which were irrelevant in any case, Edsall felt, because none of the research was classified. With a general sense of outrage, Edsall, along with Philip Handler, Wendell Stanley, and a few others ([1](#)), prepared a resolution to send to the National Academy of Sciences asking for an investigation of this action by the USPHS. At the general business meeting of the ASBC, the resolution was passed unanimously.






The National Academy, after a thorough investigation, recommended to President Dwight D. Eisenhower that grants for unclassified research should be awarded solely on the basis of scientific merit. The Eisenhower administration made this policy effective in all federal granting agencies. During the months of preparation of the National Academy report, Edsall undertook a personal protest. He wrote an article that was published in *Science* ([11](#)), condemning the actions of the USPHS and declaring his refusal to accept support from the USPHS for his research as long as their practices continued ([1](#)). Not until two years later, with assurance that they had stopped, did he apply for and accept research support from the USPHS. Edsall played an important role also in the establishment of the Committee on Scientific Freedom and Responsibility (CSFR) of the American Association for Advancement of Science (AAAS). His article published in *Science* in 1975 "Scientific Freedom and Responsibility" ([12](#)) is a seminal statement of issues confronting scientists and citizens that is still relevant.

Throughout his long career, Edsall continued to be an informed, articulate, and effective voice of
n regarding nuclear, biological, and chemical agents for war, environmental dec < on >



the relationship of technology to society. He died on June 12, 2002, five months before his 100th birthday.

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Article Info

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DOI: [https://doi.org/10.1016/S0021-9258\(18\)75587-7](https://doi.org/10.1016/S0021-9258(18)75587-7)

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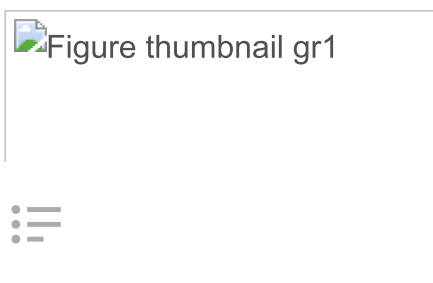
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