NATIONAL ACADEMY OF SCIENCES

LEWIS GIBSON LONGSWORTH

1904—1981

A Biographical Memoir by
ROBERT A. ALBERTY

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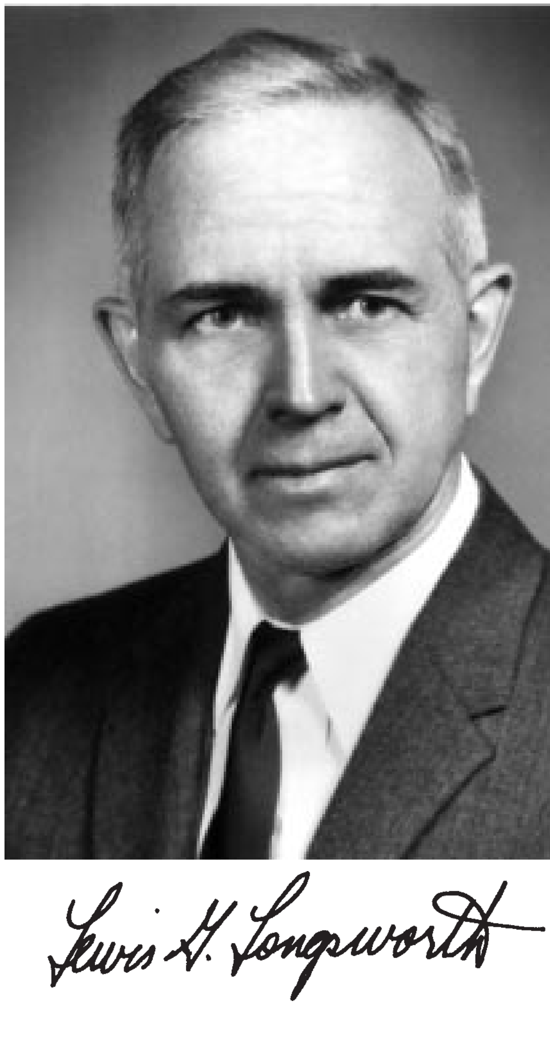

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November 16, 1904—August 8, 1981

BY ROBERT A. ALBERTY

THE FOCUS OF Lewis Longsworth's scientific research was the measurement of mobilities of ions and molecules in liquid media. Initially, he studied small ions under the influence of an electric field by the moving boundary method, and then he extended his research to the study of proteins and nucleic acids and then complexes. He made major contributions to the analysis of mixtures of proteins by electrophoresis.

Later in his career Longsworth studied the diffusion of neutral molecules in solution, where the gradient of the chemical potential provides the driving force. Diffusion affords a means for the study of the mobility of a nonelectrolyte in any medium in which it is soluble. He provided an early model of separation methods in laboratories to obtain purified biological substances. His experimental work was characterized by great care, high precision, and innovation of new experimental methods.

Longsworth spent his whole career at the Rockefeller Institute, where MacInnes, Shedlovsky, and Longsworth created one of the world's outstanding centers of electrolyte research and brought it to bear on biological problems.

THE EARLY YEARS

Lewis Longsworth was born in Somerset, Kentucky, on November 16, 1904, and spent his first dozen years in this community. His father operated a lumber mill, using hardwoods, especially the local hickory, until his death in an industrial accident in 1916. Lewis moved with his mother to Lexington, Kentucky (1916-18), and then to Winfield, Kansas (1918-25). This living in Winfield increased the warmth of the personal relationship I had with Lewis Longsworth, starting thirty years later, because I had been born in Winfield, and had left in 1925 when my family moved to Lincoln, Nebraska. Lewis mentioned in his autobiographical sketch[1] that Winfield "had been awarded a prize for being the best community in Kansas in which to raise children."

Lewis was salutatorian of his high school class when he graduated in 1922. His interest in science was kindled by his high school physics teacher. Lewis attended Southwestern College in Winfield, where he came under the influence of Larry Oncley, head of the Chemistry Department and father of a member of the National Academy of Sciences with the same name. Lewis concentrated on his studies, graduated from college in three years, and went to Kansas University for graduate work, where he earned his Ph.D. in three years.

Lewis did his doctoral research under the direction of H. P. Cady, the discoverer of helium in the natural gas from Dexter, Kansas, that wouldn't burn. His thesis was on the measurement of ion mobilities in liquid ammonia. He used the moving boundary method in which the movement of an interfacial region between solutions in a U-shaped tube is measured when an electric potential difference is applied across the tube. Upon completion of his doctoral work in 1928, Lewis was awarded a two-year term as a National Research Council fellow. In 1929 he was married to Helen Francis Cady, the youngest daughter of his research advisor.

FORTY-TWO YEARS AT THE ROCKEFELLER INSTITUTE

As a National Research Council fellow, Lewis went to the Rockefeller Institute to join the electrochemistry group started by Duncan A. MacInnes.[2] MacInnes had moved there from the Massachusetts Institute of Technology in 1926 at the suggestion of Dr. W.J.V. Osterhout, a physiologist, who felt that physiology could benefit from the advancement of fundamental electrochemistry. The laboratories of MacInnes and Osterhout were adjacent. MacInnes had gone to MIT in 1917 to join the Research Laboratory of Physical Chemistry, and had been appointed a professor in 1925. At the time he moved he was measuring transference numbers and the potentials of galvanic cells containing liquid junctions. One of the first things he did at the Rockefeller Institute was to hire Theodore Shedlovsky,[3] who had been his student at MIT. Longsworth and Shedlovsky were closely associated with MacInnes throughout nearly the entire period of his career at the Rockefeller Institute and Rockefeller University.

Longsworth stayed at the Rockefeller Institute until he retired as a professor emeritus in 1970. From 1930 to 1939 he had the rank of assistant, from 1939 to 1945 associate, and from 1945 to 1949 associate member, becoming a member in 1949 and a professor in 1954, when the Rockefeller Institute became Rockefeller University.

In his first years at the institute, Longsworth used the moving boundary method for increasingly precise measurements of transference numbers and ionic mobilities. These studies form the basis for current tables of these properties in aqueous electrolyte solutions. Many of the papers were published under his name alone, but he also published papers with Duncan MacInnes and Theodore Shedlovsky, who was making precise measurements of electric conductivities of electrolyte solutions and testing the applicability of the interionic attraction theory of Debye and Hückel in 1923, as later modified by Onsager in 1927 to include the relaxation effect and the electrophoretic effect. In addition, Lewis was involved in improving pH measurements and using them in physiologic studies. Longsworth and MacInnes published on bacterial growth with automatic pH control and on the apparent oxidation-reduction potential, acid production, and population studies of *Lactobacillus acidophilus*.

In 1937 an important new development occurred when Arne Tiselius published his method for studying the electrophoresis of proteins. The study of protein mixtures by the moving boundary method is more difficult than the determination of mobilities of small ions because the boundaries are more easily disrupted by the convection resulting from the temperature gradient across the cell due to ohmic heating. When the moving boundary method is applied to strong electrolytes, the electric forces within the moving boundary keeps it sharp, but when protein molecules move in buffer solutions the moving boundaries were easily disrupted by convection. Tiselius's solution to this problem was to carry out the electrophoresis experiments at about 2°C, the temperature of maximum density of the buffer solution. Tiselius received a Nobel Prize in 1948. Tiselius used a schlieren band method for photographing boundaries between colorless solutions. A knife edge in the focal plane of the schlieren lens was used to cut off light from the cell that had been deflected by the refractive index gradient of a boundary. Actually the displaced slit "images" produce Gouy interference patterns in the focal plane of the schlieren lens, which I will refer to later. In 1938 Philpot showed that by adding a diagonal slit in the focal plane of the schlieren lens and a cylindrical lens to focus the plane of the slit on the photographic plate, a plot of refractive index gradient versus height in the electrophoresis cell could be obtained. This is referred to as the astigmatic camera. The term electrophoresis was originally introduced to mean the migration of charged colloidal particles in an electric field. Later it was generally applied to the movement of charged particles under the influence of an electric field.

Longsworth was well prepared to make contributions to the study of proteins by electrophoresis because he had been making precise measurements on electrolytes and understood the underlying theory of moving boundaries. He made a number of improvements in the Tiselius apparatus. His first experiments with proteins were in collaboration with Dr. Karl Landsteiner, an immunochemist, who was puzzled by the inability of the physical measurements then available to distinguish between proteins that could be readily identified by the antigen-antibody reaction. In an article published in 1938 Landsteiner and Longsworth found that the egg albumins of several closely related birds and the hemoglobin of a variety of animals had different electrophoretic mobilities. Longsworth also used electrophoresis to obtain purified biological substances.

During World War II Longsworth's electrophoretic studies were interrupted by an Office of Scientific Research for Defense project that led to a patent assigned to the U.S. government and some unclassified research on the electrochemistry of uranyl salt solutions.

In his research Longsworth obtained more accurate analyses of mixtures of proteins, such as blood plasma. In 1945 he published analyses of maternal and fetal plasmas and sera with R. M. Curtis and R. M. Pembroke. It was in this period that I became acquainted with Longsworth. I was working on a wartime medical research project on the isolation and purification of plasma proteins under the direction of Prof. J. W. Williams at the University of Wisconsin. This was part of a large project of Prof. Edwin J. Cohn at Harvard Medical School. It was Cohn's idea to separate and purify human blood proteins (selected ones) and use them in the treatment of medical and surgical conditions in the Armed Forces and also in the civilian population. Prof. John T. Edsall was the senior associate to Cohn, and Larry Oncley, Larry Strong, and John Ferry were important leaders in the project. One of my activities was to determine the purity of serum albumins and gamma globulins isolated from blood collected by the Red Cross. I used the University of Wisconsin's Tiselius apparatus, which had come from Sweden. The number of samples to be analyzed was so great that Lewis Gosting, who was also in the Wisconsin project, and I built the improved optical systems for the electrophoresis of proteins.

The 1940s was a very active time both for the development of the theory required for the quantitative interpretation of experiments in moving boundary electrophoresis and the improvement of equipment. Longsworth made major contributions both to theory and experimental techniques.

THEORY OF MOVING BOUNDARY ELECTROPHORESIS

When an interface is formed between two homogeneous electrolyte solutions, and an electric current is passed through the system, moving boundaries are formed. When the current has been passed for a long enough time, there are homogeneous regions between the boundaries. The theory of moving boundaries in electrolyte solutions starts with

Kohlrausch in 1876. He showed that the sum of ratios of ion concentrations to ion mobilities is constant throughout a moving boundary system, and this sum is called the regulating function. Longsworth made the next contribution to the theory of moving boundaries in 1945 by deriving the moving boundary equation, which relates the concentrations of an ion on either side of a boundary to the volume moved through by the boundary and the relative mobilities on either side of the boundary. The general solution to the problem of predicting the compositions of new solutions and the displacements of the separated boundaries was provided by Vincent Dole,[4] also of the Rockefeller Institute. Vincent Dole was a young medical doctor who had come to the Rockefeller Institute to work with D. D. Van Slyke and became acquainted with Longsworth, Shedlovsky, and MacInnes because of his mathematics background as an undergraduate and his interest in using the electrophoresis of plasma in the clinic. Vincent Dole understood that moving boundary systems are constrained by electroneutrality and mass balance. He showed that these constraints led to a relation between the volumes moved through by the various boundaries and the concentration changes across boundaries, subject only to constant relative ion mobilities. His demonstration dramatically changed the understanding of complicated moving boundary systems. According to Dole's equations, a system containing n ions will, in general, form a maximum of n – 1 boundaries, one of which is a stationary boundary. If a system contains p anions and q cations, there will generally be p – 1 boundaries with negative velocities and q – 1 boundaries with positive velocities. Dole showed that the volumes moved through by boundaries can be obtained as solutions of polynomials.

Starting in 1946 I corresponded with Longsworth a great deal about the moving boundary method and in 1947 I wrote my thesis with Prof. J. W. Williams on electrokinetic characterization of the gamma globulins from normal human blood plasma. I vividly remember several trips to the Rockefeller Institute to consult with Longsworth about the equipment and the interpretation of electrophoretic schlieren patterns. I was very much impressed with his knowledge about the moving boundary method, the high standards that he set for himself, his kindness and helpfulness, and his having lunch with me in the dining room of the Rockefeller Institute. I want to acknowledge my gratitude to Lewis Longsworth for his wise and patient counsel during the time (1946-60) that I was at the University of Wisconsin-Madison and was in frequent communication with him. Longsworth was basically a gentle man, and I can remember that he never told me that I was wrong, although he did tell me when he was skeptical. When he told me he was skeptical, I took it very seriously. Longsworth visited Madison in June 1952 to give an All University Lecture.

ELECTION TO THE NATIONAL ACADEMY OF SCIENCES

Longsworth became a member of the National Academy of Sciences in 1947. In 1953 he was appointed by President Bronk to serve on an Academy committee on battery additives. The formation of this committee had been requested by Secretary of Commerce Sinclair Weeks shortly after the head of the National Bureau of Standards A. V. Astin had been dismissed, thereby disturbing the scientific community. The head of a private company was promoting a certain battery additive, but on the basis of the Bureau's tests Astin thought the claims were false and repudiated them. Secretary Weeks fired Astin and forced him out of the Bureau. The scientists were outraged because this seemed to them a blow to honest science, and they petitioned the

Academy to carry out an investigation. The four months' interval from the time of appointment of the committee on June 24, 1953, to the release of its report on October 30 was devoted to the reading and appraisal of the many reports on the battery additive AD-X2 and the meetings of the committee under the direction of Zay Jeffries. The release of the report supporting Astin was not the end of the committee's duties. The subsequent action of the Federal Trade Commission against Pioneers, Inc., makers of AD-X2, involved Lewis Longsworth and two other members of the committee as witnesses in January 1955. Although the charge of false advertising made by the Federal Trade Commission against Pioneers, Inc., was dropped on May 16, 1956, the work of the committee had been a factor in the reinstatement of Astin as head of the National Bureau of Standards in October 1953. It was not until December 1961 that the suit Pioneers, Inc., brought against the U.S. Court of Claims in 1959 was rejected and science finally prevailed over politics.

Longsworth also served the Academy as a member of a committee that President Seitz appointed in August 1962 to evaluate the merits of a classified project of the Bureau of Ships.

DIFFUSION OF ELECTROLYTES AND PROTEINS

In the mid-1950s Longsworth's interests shifted from moving boundary measurements with electric fields to measurements of diffusion constants in aqueous solutions. The reason for this was that it was becoming increasingly clear that moving boundary measurements in free solution for analyses of biochemical mixtures of both low and high molecular weights were going to be replaced by zone techniques in stabilized media. Longsworth's interests in diffusion had been kindled in 1944 by the organization of a conference on this subject under the auspices of the New York Academy of Sciences, for which he prepared a historical survey. In this survey he included a photograph he had taken of the interference fringes that had been obtained by G. L. Gouy in 1880, but which had not been subsequently used. When a boundary is formed between two solutions and a substance is diffusing from the lower solution to the upper solution, the image of an illuminated horizontal slit is spread out into a rectangular pattern of interference fringes. The lower edge is formed by the light that has passed through the solution where the gradient of a refractive index is the steepest. Interference fringes are formed by rays that pass through layers of equal gradient above and below the center of the boundary for which the path difference gives constructive interference. Thus, Longsworth revived the use of Gouy fringes for determining diffusion coefficients, which was brought to its highest level by Prof. L. J. Gosting and associates in the Enzyme Institute at the University of Wisconsin.[5,6] Gosting had spent a year at the Rockefeller Institute in the MacInnes-Longsworth-Shedlovsky group.

Longsworth was a member of the American Chemical Society, Electrochemical Society, Harvey Society, and Sigma Xi. He was the recipient of the 1968 American Chemical Society Award in Chromatography and Electrophoresis. In 1978 he was cited by *Lab World* for his "important contributions to the ever-increasing and expanding adaptations of electrophoresis and chromatography in laboratory medicine." In 1978 he received an honorary doctorate of science degree from Rockefeller University at its commencement ceremony.

Longsworth was very dedicated to his research and did not have much time for hobbies. He and Helen had three children (Anne Louise, Ralph Cady, and Stella Caroline). The Longsworths spent their summer vacations in Estes

Park, Colorado, hiking in the Rocky Mountain National Park and visiting other parks and natural forests in the west. They worked at hiking at increasing elevations, and the ascent of Long's Peak at an elevation of 14,256 feet was frequently the climax of their vacation. Helen climbed Long's Peak on fifteen different occasions, whereas Lewis's count was thirteen. Lewis Longsworth died of a stroke during a vacation in Estes Park.

Longsworth provided a standard of excellence in the measurement of mobilities of ions and molecules from low molecular masses to those of proteins and nucleic acids. His first contributions were to the transference numbers of inorganic ions, but this led to improvements in both the theory and experimental methods for the electrophoresis of proteins. In his later years he turned to the measurement of mobilities using diffusion in free solution. He supported and encouraged many others working on these problems, and his criticisms and suggestions were welcomed by many people working on the determination of the properties of proteins and nucleic acids and the analysis of mixtures.

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