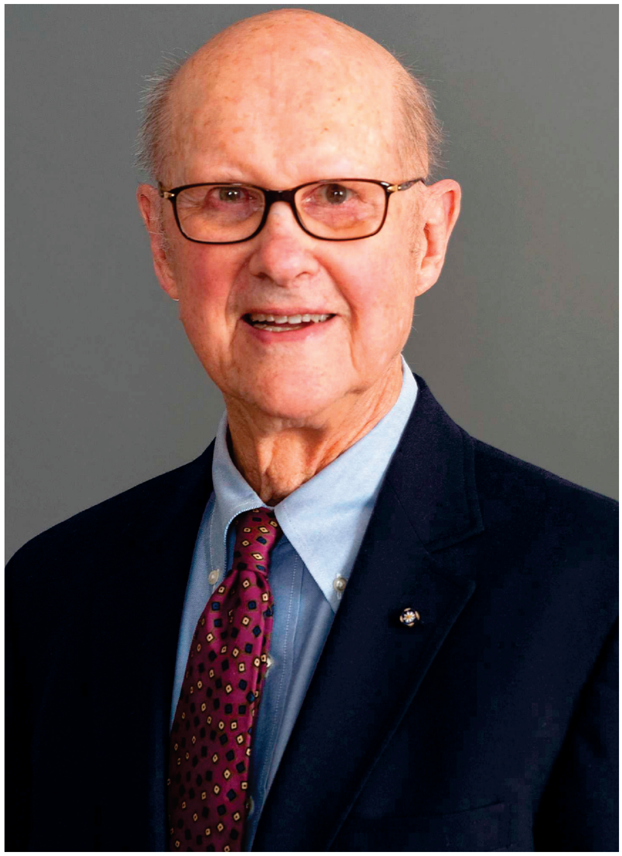

Professor Robert A. Alberty—A Legacy of Excellence

Professor Robert A. Alberty has created a legacy of excellence both in scientific research and in university education and administration. His career spans 67 years, during which time he has made many critical and seminal contributions in the areas of thermodynamics and kinetics—the vast majority of it dealing with biochemical reactions.

The complexity of biochemical substances is largely attributable to the fact that a biochemical reactant is very often made up of a multiplicity of species. Thus, aqueous adenosine 5′-triphosphate or ATP is generally a mixture of species such as ATP^{4-}, $HATP^{3-}$, H_2ATP^{2-}, Mg_2ATP^0, $MgATP^{2-}$, $MgHATP^-$, $CaATP^{2-}$, $CaHATP^-$, etc. Alberty recognized this important fact early on and in the 1950s was one of the first to provide rigorous thermodynamic treatments to deal with it. Alberty's papers published in 1968 and 1969 were the first to predict the complex dependency of the apparent equilibrium constant K' and related quantities ($\Delta_r H'^\circ$, $\Delta_r S'^\circ$, and $\Delta_r C_p'^\circ$) on pH, temperature, and the concentrations of other species such as free Mg^{2+} and Ca^{2+} for the hydrolysis of ATP, a very complex and important biochemical reaction. In particular, he developed Maxwell relationships that clearly demonstrate the interrelationships of the aforementioned quantities. He later applied numerical methods to solve the simultaneous nonlinear equations that are needed to describe the thermodynamics of biochemical reactions. He also developed and used the methods of isomer group thermodynamics and Legendre transforms to make fundamental progress in biochemical thermodynamics. In applying these methods, he provided a rigorous justification for the apparent equilibrium constant K', the standard transformed Gibbs energy change $\Delta_r G'^\circ$, the change in binding $\Delta_r N(X)$ of a ligand X (e.g., $X = H^+$, Mg^{2+}) in a biochemical reaction, as well as other transformed thermodynamic properties such as the standard apparent electromotive force E'°. Rigor and attention to detail were characteristic of Alberty's publications.

Alberty was one of the first to apply computer methods to problems in biochemical thermodynamics. During the past decade, he developed a useful set of computer codes as well as an extensive database for biochemical species and reactants. His methods have been applied to many complex biochemical systems such as the binding of oxygen to hemoglobin and even to entire metabolic pathways. His books *Thermodynamics of Biochemical Reactions* and *Biochemical Thermodynamics: Applications of Mathematica* are important to read for research scientists active in biochemical thermodynamics.

At the beginning of the 1950s, the kinetic study of enzyme-catalyzed reactions had barely advanced beyond the state in which Michaelis and his collaborators had left it more than thirty years earlier. The idea of a steady state had appeared, but studies of pH, inhibition, reactions of multiple substrates, temperature dependence, kinetics of isotope exchange, and fast reactions remained rudimentary. Alberty was one of a small number of scientists who realized that the subject was ripe for development, and he undertook the task with all the energy and enthusiasm that has characterized his whole career. Although others also made major contributions, he was probably the only one who has left his mark on every one of the aspects mentioned.

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Alberty's series of papers on the kinetics of fumarase from 1953 to 1964 remain a model of how an enzyme mechanism should ideally be characterized. Not content with studying one or two aspects of this enzyme, he and his collaborators set out to construct a complete picture of its mechanism. These studies of fumarase include studies of the relationship between kinetics and equilibrium, effects of buffer composition and concentration on ionization, specificity of the enzyme, inhibition, temperature dependence, and the time course of the reaction. Some years passed before there was a comparably complete study of another enzyme.

Fumarase is, of course, a one-substrate one-product enzyme (not counting water). However, during this period Alberty also recognized that most enzymes have more than one substrate and more than one product, and made strenuous efforts to classify the different ways in which a two-substrate reaction can occur, and to understand and analyze the effects of different mechanisms on observed kinetic behavior. His landmark publication with Peller in 1959 demonstrated exactly what mechanistic information can be obtained from steady state kinetics and the relationship between steady state kinetic parameters and individual rate constants. Various different and, to some degree, incompatible ways of symbolizing the different kinetic constants for such reactions appeared in the 1950s. None of these has survived unchanged until today, but the system that Alberty used in his article in *Advances in Enzymology* is still recognizable in the modern symbols. Half a century afterward, Alberty is again contributing to our understanding of the kinetic behavior of enzymes.

Along with his impressive contributions to research, Robert Alberty was a consummate educator. He especially is interested in the development of young scientists. Many graduate students and postdoctorals who worked in his laboratory have gone on to outstanding research careers of their own. Among his trainees are members of the National Academy of Sciences, and even two scientific "grandsons" in the National Academy of Sciences. His style of mentoring was designed to train students how to become independent thinkers. He would throw out a number of possible research problems, and then allow the students to proceed on their own, with just enough guidance to ensure that they would be successful. He also was an outstanding classroom teacher at both the undergraduate and graduate level.

Professor Alberty was the author/coauthor of physical chemistry textbooks that were, and are, widely used. In the late 1940s, he became a coauthor of *Experimental Physical Chemistry*, a laboratory textbook that was popular nationwide. However, the undergraduate textbook he first coauthored with Farrington Daniels in 1955, *Physical Chemistry*, has proved to be his most monumental textbook. Its history traces back almost a century, beginning with a physical chemistry text by Getman in 1913. He eventually became the sole author and later took on coauthors. His participation in the writing of this textbook spans over 50 years, with the most recent edition being in 2004 and a new edition to appear soon. This book has been widely used: many thousands of students have learned their physical chemistry with this textbook. The modern version bears no resemblance to the first volume, as Alberty, and most recently with coauthors, continually brought the book up to modern day standards. Because of his reputation in the laboratory textbook field, he participated in (1981) and chaired (1983) National Research Committees concerned with laboratory safety standards and chemical disposal. The reports that resulted were widely distributed and set the standards for the country.

Robert Alberty was a triple threat faculty member, outstanding in teaching, research, and administration. His first taste of administration at the university level was as Associate Dean of Letters and Sciences at the University of Wisconsin in 1961. In 1963, he became Dean of the Graduate School at the University of Wisconsin. This position was one of the most powerful on campus because of the Wisconsin Alumni Research Foundation funds that were available to support graduate students and research. In this position, he participated in the global development of graduate study and research at the University of Wisconsin which is widely recognized as one of the great research universities in this country.

Because of his many accomplishments at the University of Wisconsin, he was invited to become Dean of Science at MIT in 1967, a position he occupied until 1982. This was a bittersweet undertaking for Professor Alberty, as he abandoned his laboratory research at MIT. The late 1960s were tumultuous times for universities because of the Vietnam War, and he became directly involved in leading MIT through these difficult times. Among his many accomplishments as Dean of Science was participation in the development of a joint MIT-Harvard MD-PhD program, an unprecedented level of cooperation between the two schools. The now well-known Cancer Research Center was also established at MIT during his tenure. The success of his leadership is reflected in the worldwide reputation of MIT in all fields of science.

Finally, in keeping with his interest in the development of young scientists, his influence as an advisor to the Camille and Henry Dreyfus Foundation should be mentioned. He and others recommended that the Foundation use its resources to support young faculty members in chemistry. This advice was followed with the creation of several programs: the best known is probably the Dreyfus Teacher-Scholar Award, one of the most prestigious awards a young faculty member can attain.

This is but a brief account of the many accomplishments of Robert Alberty in the field of education. These accomplishments cover an enormous range: undergraduate and graduate classroom teaching, mentoring of graduate students and postdoctorals, authorship of influential textbooks, and high level university administration.

On behalf of all of his students and colleagues, we wish Bob Alberty continued success in and enjoyment of his scientific endeavors.

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