Brief Scientific Autobiography of Robert A. Alberty

The Early Years

I was born June 21, 1921, in Winfield, Kansas, to Luman Harvey and Mattie Alice (Arnold) Alberty, who had grown up in southern Kansas. My father was a teacher of industrial arts, and my mother had been a teacher before they became engaged. My brother Bryce was born in 1922, and my sister Monica was born in 1924. When I was about five years old, my father had the opportunity to become Superintendent of Industrial Arts in Lincoln, Nebraska, and so we moved there and I started school in Lincoln. Because of my father's field, I had experience using tools from an early age, and this affected my hobbies as a boy. We had a shop and a dark room in the basement, and so using a wood lathe and photography were early hobbies. My brother and I built a shack in the backyard. We were fortunate that the telephone company was willing to give us used telephones (the hand-cranked variety) and lots of wire. We built crystal sets and put up antennas. My parents bought me a Gilbert Chemistry Set and a simple microscope. I visited the chemistry laboratory at the State Capitol, and the chemist gave me graduated cylinders and flasks with chipped necks, and so I had quite a laboratory in the basement. All these experiences made science easy for me at school. Miss Gere, who taught chemistry at Lincoln High School, was an inspiring teacher. I can still remember that one day she said she had talked with a professor at the university who said a chemical bond contains two electrons that are spinning. In high school, I was president of the chemistry club and Lillian Wind, later to become my wife, was secretary. My high school science project was on hydroponics.

While I was a boy, my father earned a master's degree in industrial arts by going to summer school five summers at the University of Wisconsin in Madison. Some summers, we lived in a tent on the lake, and I loved the swimming and fishing. In Lincoln, I was active in the Boy Scouts and loved the outdoors.

When I registered at the University of Nebraska in September, 1939, I intended to be a chemical engineer. However, when I heard that this meant I had to take drafting and surveying, I decided to major in chemistry during the registration process. Actually, I enjoyed taking drafting in high school and my grandfather, who had been a pioneer in southern Kansas, had given me a simple transit, but these requirements made me realize that I was interested in the science of chemistry. At the university, I quickly became acquainted with Professor Deming, who taught freshman chemistry, and I helped with proofreading his introductory textbook. I did undergraduate research with Professor Roger Washburn on spreading pressures of films using a Langmuir balance, and Irving Langmuir of General Electric Research Laboratories was my career model at that time. I planned to be an industrial scientist and was fortunate to have a job one summer at the Eastman Kodak Co. in Rochester, New York. I worked on cellulose acetate film and learned for the first time about polymers. When I was working on my bachelor's degree (May, 1943), I was deferred because I was studying science as an undergraduate, and when I was working on my master's degree (May 1944), I was also deferred because I was also teaching freshman chemistry to students in uniform. My master's thesis was on the phase equilibrium of the benzene−isobutyl alcohol−water system.

In the spring of 1944, I wrote several universities where I heard war-related research was going on and received an offer from Prof. Jack Williams at the University of Wisconsin to work on a secret project involving the ultracentrifuge and electrophoresis. On May 22, 1944, Lillian received a bachelor's degree and I received a master's degree. The same day, we were married and left for the University of Wisconsin. The NSRD (National Science Research and Development) project, which was part of a larger project at Harvard Medical School headed by Prof. E. J. Cohn, was making new medical products from expired blood collected by the Red Cross. The part of the project in Madison was concerned with the fractionation of plasma proteins to isolate the gamma globulins, which are antibodies. The gamma globulins were precipitated from aqueous solutions at a specified pH and ionic strength by adding ethanol at low temperatures, and the Svedberg ultracentrifuge and Tiselius electrophoresis apparatus, which had been given to the university by the Rockefeller Foundation, were used as analytical tools. A major focus of the project involved isolating albumin, which could be pasteurized, could be stored at room temperature, and was needed on the battlefield to combat shock. The purified gamma globulins, which could also be stored at room temperature, were used to help provide immunity. My doctoral thesis (1947) with Professor J. W. Williams was on reversible boundary spreading in the electrophoresis of gamma globulins. The standard deviation of the mobility distribution corresponds to a net charge of about three electrons. The gamma globulins are different from most other proteins, which are homogeneous. During the 1944−1947 period, I was fortunate to become acquainted with John Edsall, Lewis Longsworth, Larry Oncley, and Michael Heidelberger. After the war was over, I was nearly drafted, but by then, there was concern about the diseases that the veterans might bring back from overseas, and so deferments were continued for medical researchers.

Our daughter Nancy was born on December 18, 1945, our son Steven was born April 8, 1947, and our daughter Catherine was born January 25, 1952.

Teaching and Research at the University of Wisconsin

In the spring of 1947, the Head of the Department of Chemistry at the University of Wisconsin, Prof. J. H. Mathews, offered me an instructorship, and I accepted. All universities were desperate in their efforts to hire new faculty because there were very few new PhD's and the veterans were coming to the universities and colleges on the GI bill. I had a very heavy teaching load, but I was promised a year's leave after teaching three years. During this period, I became a coauthor of Daniels, Mathews, and Williams, "Experimental Physical Chemistry". I continued my research on electrophoresis with emphasis on the theory of the moving boundary method that had been opened up by Lewis Longsworth at the Rockefeller Institute. Electrophoresis was developed to analyze mixtures of proteins, but I also used it to detect impurities in adenosine triphosphate (ATP) preparations that were just then becoming commercially available.

By 1950, I was anxious to move on to enzyme kinetics. I was inspired by Linus Pauling's ideas about enzymes being complementary to their substrates like antibodies are complementary to their antigens. Pauling invited me to spend a year

10.1021/jp103554e
Published on Web 12/09/2010

in his laboratory at Cal Tech. I received a Guggenheim Fellowship and some support from the University of Wisconsin. As preparation, I spent half of the summer of 1957 with Van Potter at the McArdle Cancer Laboratory and the other half of the summer with David Green at the new Enzyme Institute. During the time I was at Cal Tech, Pauling announced his structures for peptide polymers, and I got started on studies of the mechanism of the fumarase reaction using the first Beckman DU Spectrophotometer that recorded an expanded absorbance scale in the ultraviolet on a rather fast strip chart recorder.

My research had been supported by grants from the Graduate School with funds from the Wisconsin Alumni Research Foundation (WARF), but I needed more support. When Warren Weaver, President of the Rockefeller Foundation, visited Madison, I had an opportunity to ask him about possible sources of research support. He suggested that I apply to the Office of Naval Research. I did so, and was soon surprised to receive one of the first grants from the National Science Foundation that had just been funded. To get as fast a start as possible, NSF had simply taken over some of the proposals that had been made to the Office of Naval Research.

In the early 1950s, Farrington Daniels was Head of the Chemistry Department at the University of Wisconsin, President of the American Chemical Society, and Vice President of the National Academy of Sciences while he was trying to prepare a new edition of his textbook "Outlines of Physical Chemistry". I became a coauthor of the edition that appeared in 1955, and we renamed the book "Physical Chemistry".

I became increasingly impressed with the interesting research on enzyme kinetics going on in Europe. In 1957, Lillian and I took our children out of school for the spring term and spent a month each in Sweden, Denmark, Cambridge, and Oxford, with shorter stays in Germany and France. We later spent the spring semester of 1961 in Gottingen, Germany, so I could learn about relaxation kinetics from Manfred Eigen, who received the Nobel Prize soon after.

In looking back on my research at the University of Wisconsin, here are some things that stand out: In 1953, Bob Bock and I demonstrated the relation between the Michaelis constants and maximum velocities of the forward and reverse reactions and the equilibrium constant for the fumarase reaction, an idea which had been suggested by Haldane. Bob Bock was one of my first graduate students, and later, he became my successor as Dean of the Graduate School. In 1954, Carl Frieden crystallized fumarase and determined its physical properties soon after joining my groups of graduate students. In 1954, Vince Massey and I showed how plots of maximum velocities versus pH could be interpreted in terms of acid dissociation constants in the catalytic site. In 1956, Smith and I determined the stability constants of ionic complexes of magnesium and calcium ions with various adenosine phosphates. In 1957, our group used proton nuclear magnetic resonance to show that water is added to the double bond of fumarate stereospecifically. In 1958, Hammes and I applied the theory of diffusion-controlled reactions in solution to the rate of binding of fumarate and malate to the enzymatic site of fumarase and showed that this is a diffusion-controlled reaction. In 1960, Hammes and I published on the kinetic relaxation spectrum of simple enzymatic reactions. In 1962, Bloomfield, Peller, and I wrote about multiple intermediates in enzyme-catalyzed reactions involving more than a single reactant and product.

In 1955, I received the Eli Lilly Award from the American Chemical Society for my research on enzyme kinetics.

I worked hard on teaching and research, but I must have had some spare time because I learned to fly an airplane in 1960. However, I gave that up when I became increasingly involved in university administration.

University Administration

While I was in Gottingen, I heard that Dean Mark Ingraham of the College of Arts and Sciences had resigned. I was surprised and disappointed because he was an excellent Dean. When I got back to Madison, I learned that his resignation was a result of a difference between him and the President of the University about how to deal with an attempt of Northwestern University to hire four members of the faculty in particle physics. The new Dean was Edwin Young, an economist, and I soon heard from my friend Charlie Heidelberger of the Cancer Laboratory that Dean Young was looking for an Associate Dean in the sciences. I said I was not interested, but Charlie came back saying he hoped I would be willing to have lunch with him and Dean Young because Dean Young needed advice about the science departments. As a result, I became an Associate Dean of Letters and Science in 1961 and Dean of the Graduate School in 1963.

The Dean of the Graduate School at the University of Wisconsin is fortunate to be Chairman of the Research Committee, which receives an annual grant from the Wisconsin Alumni Research Foundation (WARF). WARF was created when Prof. Steenbach of the Department of Biochemistry realized that his patent on putting vitamin D in milk by irradiation was going to produce a larger income than he felt he needed. WARF invested the patent income, and, according to its charter, used the income to support research only at the University of Wisconsin. It also developed patents on research of faculty members. Prof. Link, also of the Department of Biochemistry, synthesized warfarin, which is used both as a "blood thinner" and a rat poison. His patents were developed by the Foundation and also brought in a large income. Many of the grants made to faculty members by the Research Committee were "seed corn" in the sense that they helped develop research ideas to be the basis for requests to Federal agencies.

In 1965, I was elected to the National Academy of Sciences. In 1968, I became a member of the American Association of Arts and Sciences. In 1967, I received honorary doctorates from Lawrence College and the University of Nebraska. While I was Dean of the Graduate School, I continued to have graduate students and postdocs, but my time was increasingly taken up with all-university affairs and frequent trips to Washington, DC. I remember being in the Pentagon on the weekend of the Cuban missile crisis.

We bought a small sailboat and enjoyed using it on Lake Mendota. Later, we wanted more exercise and bought two aluminum canoes, which we could carry to other lakes and rivers. In 1965, we bought a lot on Lake Vermilion near Cook, Minnesota, and in the summer of 1966, my son and I built a 10 foot by 18 foot cabin of plywood with our own hands there. We enjoyed the beautiful lake, the canoeing, and the construction process so much that we began to plan a 24 foot by 24 foot cabin of plywood. When we moved to Cambridge in January 1967, we had to reconsider this plan, but we decided that, since it was a family enterprise, we would proceed with construction of the large cabin. In August 1967, we built the larger cabin with our own hands in 30 days and nailed it shut until the next summer. We have had wonderful vacations there for over 44 years, but sometimes while I was a Dean, we could get out there for only two weeks.

In the fall of 1966, Howard Johnson called me and said he was the new President of the Massachusetts Institute of Technology and that Jerry Wiesner, who had been Dean of Science, was the new Provost. "Would I be willing to come and talk?" I said "yes". Although we were very happy in Madison and never expected to leave, the new job and institution looked very interesting, and I agreed to become Dean of Science as of February 1, 1967. In my first year at MIT, I was very busy getting acquainted with a new institution, and so I did not continue my research grants. I did write several more papers on the thermodynamics of the hydrolysis of adenosine triphosphate (ATP) with the assistance from the Laboratory of Computer Science, but very quickly the campus activism against the war in Vietnam built up. Howard Johnson asked me to be the administration's representative on the Student Center Committee. There was a strong tradition at MIT that the students ran the Student Center, but the Student Center Committee had one place for a faculty member. As a result, I spent many days and evenings at the Student Center, and even slept there on the floor during the periods of the most intense demonstrations against the war. I was also the first cochairman of the new exchange program with Wellesley College.

At about the time I arrived at MIT, Dr. James Shannon, the Director of the National Institutes of Health came to the administration of MIT and urged it to consider establishing a Medical School. Since Harvard had a group of teaching hospitals, this discussion quickly involved Harvard University. Starting a new Medical School was judged to be too expensive, but MIT and Harvard joined together to establish a joint PhD-MD program, and MIT established a Health Sciences Program. A Cancer Research Center was also established at MIT with the leadership of Salvador Luria (Nobel Laureate). Gobind Khorana accepted a joint appointment in Chemistry and Biology at MIT before he received the Nobel Prize. I became a member of the Institute of Medicine in 1973.

In 1974−1977, I chaired the Human Resources Division of the National Research Council that produced the Annual Survey of Doctorates with the support of the National Science Foundation.

After World War II, there was increasing recognition of the adverse health effects of exposure to chemicals, both in the environment and in the laboratory. The National Research Council organized a study of chemical safety in the laboratory chaired by Prof. Herbert House at MIT, and I was on the committee that wrote "Prudent Practices in the Chemical Laboratory (1981)". The National Academy Press sold more copies of this report than any of its previous publications. I chaired the committee that wrote the second report "Prudent Practices for the Disposal of Chemicals in the Laboratory (1983)". At MIT, we instituted new procedures for working with chemicals, and I chaired the Institute Committee on Environmental Health and Safety until I left the Dean's Office.

In 1972, The Dreyfus Foundation for the Chemical Sciences invited Jack Roberts, Conrad Block, and me to a meeting in New York to discuss recommendations that had been made to them by a distinguished group of academic administrators, including Jay Stratton from MIT, Detlev Bronk from the Rockefeller Institute, and Terman from Stanford. They urged the foundation to use its resources to support the best young faculty members in chemistry at about the time they were being considered for tenure, but only those who had demonstrated their interest and ability in being outstanding teachers. The Teacher-Scholar program was the Foundation's first program, but later others were developed as well, and I was privileged to be an advisor to the Foundation for 30 years.

In 1978, I became a Director of Colt Industries and served on that board for ten years. George Harrison, a physicist at MIT, who had been Dean of the School of Science before Jerry Wiesner, had just retired from the Colt Board, and George Harrison had done such a good job that they invited the current Dean to be his successor.

I was a Trustee of the Institute for Defense Analysis from 1980 to 1986.

During the first five years, I was Dean of the School of Science I reported to Jerry Weisner, and when he became President of MIT, I reported to Walter Rosenblith who was also an electrical engineer. They were both very able administrators, and I enjoyed working with them on new educational and research projects. During this time, there were many changes in the undergraduate programs and increased emphasis on Undergraduate Research Opportunities (UROP). While I was Dean, I taught Biophysical Chemistry for several years with Paul Schimmel and Philip Sharp, who were both my scientific grandsons, but I was too busy to do this for very long. In my fifteenth year as Dean, I began to feel the need to return to teaching and research in physical chemistry, and I left the Dean's Office in the spring of 1982.

Teaching and Research on Thermodynamics of Petroleum Processing

While I was Dean, I was too busy to keep up with my previous area of research, enzyme kinetics. Since I had to start over after being away from research for almost 20 years, I had considerable latitude in my choice, but I was sure of one thing and that was I wanted to utilize the increasing power of computers to make calculations on complex systems. During the "oil shock" in about 1972, I had begun to worry about fuel sources as petroleum sources became depleted. So when I went back to teaching and research, I wrote a research proposal on coal liquifaction and sent it to a new program of the Department of Energy, where it was turned down. However, I was persistent and soon received support from the Department of Energy to make thermodynamic calculations on petroleum processing using the concept of isomer groups. In homologous series like the alkanes, alkenes, alkyl benzenes, etc., the number of isomers increases rapidly with carbon number. For example, there are about 120 isomers of $C_{10}H_{22}$. Pitzer's group had used a semiempirical statistical mechanical approach to make tables of the standard thermodynamic properties of all the alkane isomers from methane to decane, and I used their values to calculate the isomer group thermodynamic properties assuming the isomers to be in equilibrium. After methane and ethane, these isomer group properties turned out to be linear in carbon number, and that made it possible to calculate equilibrium compositions of mixtures that had significant mole fractions of isomer groups above $C_{10}H_{22}$. I used Sidney Benson's group additivity approach to estimate standard thermodynamic properties of gaseous alkenes, alkynes, alkanols, alkylbenzenes, alkylnaphthalenes, thiols, and polycyclics. Another innovation I developed was to make equilibrium calculations at specified partial pressures of hydrogen, ethylene, or acetylene. For example, at a specified partial pressure of ethylene, all the various alkyl benzenes form a single pseudoisomer group and the distribution of carbon numbers is represented by a partition function. In writing a couple of papers on this, Irwin Oppenheim and I realized that the constraint of holding the partial pressure of a species constant is equivalent to using a Legendre transform to define a new thermodynamic potential, the transformed Gibbs energy G', that is minimized at equilibrium. In 1989, Oppenheim

and I published on the use of semigrand ensembles in chemical equilibrium calculations in complex organic systems. After using this approach with hydrocarbon mixtures, I suddenly realized that this concept was needed in my previous research area of the thermodynamics and kinetics of enzyme-catalyzed reactions, since the pH is held constant. Hydrogen ions are involved in most enzyme-catalyzed reactions, and so the equilibrium that is reached depends on the pH. Therefore, pH has to be treated as an independent intensive variable like temperature and pressure. In 1991, I defined a transformed Gibbs energy for use in biochemistry as the Gibbs energy minus the product of the conjugate variables, chemical potential of hydrogen ions, and the total amount of hydrogen atoms in the system. I immediately submitted a research proposal to the NIH to make a new kind of thermodynamic table for enzyme-catalyzed reactions just as I became 70 and an Emeritus Professor, as required by the State of Massachusetts. Since I was active in the International Union of Pure and Applied Chemistry (IUPAC) (President of the Physical Chemistry Division, 1991−1993), I got IUPAC and IUBMB (International Union of Biochemistry and Molecular Biology) to jointly sponsor a report on the uses of Legendre transforms in biochemistry. This report was published in 1994. In retrospect, I feel very fortunate to have spent ten years working on the thermodynamics and statistical mechanics of petroleum processing because I learned a lot of thermodynamics that I do not think I would have learned if I had returned directly to the thermodynamics of biochemical reactions after being Dean of Science for fifteen years.

Retirement and Research on Thermodynamics of Biochemical Reactions

As an Emeritus Professor, I wanted to continue my research and continue to work on Silbey and Alberty "Physical Chemistry". When Bob Silbey joined me in writing the edition that appeared in 1992, we started the numbering of editions over, as Daniels and I had done in 1955. Our second edition appeared in 1997 and our third edition in 2001. Moungi Bawendi became a coauthor in 2005. The Department of Chemistry has been very cooperative in providing me an office as an Emeritus Professor.

Biochemical thermodynamics needs Legendre transformed thermodynamic properties because the pH is an independent variable like temperature and pressure. The remarkable thing about the Legendre transform used to define G' is that it automatically introduces a transformed enthalpy H' and a transformed entropy S' for a system. It also introduces a transformed chemical potential $\mu'(j)$ for each species j. Since the species ATP^{-4}, $HATP^{-3}$, and H_2ATP^{-2} of adenosine triphosphate, for example, have the same transformed chemical potential at a specified pH, the fundamental equation for the transformed Gibbs energy can be written in terms of the total amount of ATP, rather than the amounts of the three species. This means that the expressions for apparent equilibrium constants of reactions involving ATP can be written in terms of the total concentration of ATP, rather than concentrations of the three species. This led to new types of thermodynamic properties for calculating apparent equilibrium constants K' and heats of biochemical reactions. In 1992, Robert Goldberg joined me in writing an article for Biochemistry on equilibrium calculations on systems of biochemical reactions.

In 1993, I showed that systems of biochemical reactions, like glycolysis and the citric acid cycle, can be treated quantitatively by use of a further transformed Gibbs energy G'', defined by subtracting products of conjugate variables calculated using the steady state concentrations of coenzymes. This provides a more global view of a system of biochemical reactions by yielding the equilibrium concentrations that will be reached at specified concentrations of coenzymes. In 1996, I extended these considerations to the binding of ligands by macromolecules. In 2001, I put standard thermodynamic properties of 131 biochemical reactants up on the web at MathSource.

My book "Thermodynamics of Biochemical Reactions" appeared in 2003. The last half of the book gives *Mathematica* printouts of solutions to problems in biochemical thermodynamics. *Mathematica* is a wonderful language for the thermodynamics of biochemical reactions because it is convenient for deriving functions of multiple variables and taking partial derivatives. When the transformed Gibbs energy or further transformed Gibbs energy of a system can be expressed as a function of its natural variables, all the other thermodynamic properties of the system can be obtained by taking partial derivatives. My research on biochemical thermodynamics profited so much from the use of *Mathematica* that it led to a second book "Biochemical Thermodynamics: Applications of Mathematica" (Wiley, 2006). This book was written in *Mathematica* and has a CD in the back that contains the whole book. This makes it possible to use the programs and databases in the book to make thermodynamic calculations on other reactions at other temperatures, pH's, and ionic strengths.

My research on biochemical thermodynamics led me to rapid-equilibrium enzyme kinetics because this treatment of velocities is based on the assumption that the reactions prior to the rate-determining reaction are at equilibrium. *Mathematica* is especially useful in rapid-equilibrium enzyme kinetics because Solve can be used to derive the general expression for the concentration of the enzyme−substrate that yields products. Solve is also useful for implementing the suggestion by Duggleby (1979) that the kinetic parameters can be estimated using the number of velocity measurements that corresponds with the number of kinetic parameters.

Since *Mathematica* is so useful in rapid-equilibrium enzyme kinetics, I have written a second book in *Mathematica*: "Enzyme Kinetics: Rapid-Equilibrium Applications of Mathematica" (Wiley, 2010). This book has chapters on seven types of enzyme kinetics mechanisms, three types of inhibition, activation, and modification. The last chapter is on systems of enzyme-catalyzed reactions. There is a CD in the back of the book that contains the whole book. Thus, experimental velocity data can be inserted into rate equations in the CD to estimate the values of the kinetic parameters.

As I look back, I realize that my two research careers, which were separated by about 20 years of administration, were of about the same length and yielded about the same number of publications.

During the past decade, I have been active in the American Academy of Arts and Sciences and have and have been cochairman of the Development Committee and a Councilor.

Lillian and I have enjoyed our relationships with our three children and their spouses, nine grandchildren, and five great grandchildren. I would like to dedicate this autobiography to Lillian for all that she has done.

Robert A. Alberty

JP103554E