NATIONAL ACADEMY OF SCIENCES

WILLIAM MANSFIELD CLARK

1884—1964

A Biographical Memoir by
HUBERT BRADFORD VICKERY

Biographical Memoir

NATIONAL ACADEMY OF SCIENCES
WASHINGTON D.C.

W. Mansfield Clark

WILLIAM MANSFIELD CLARK

August 17, 1884–January 19, 1964

BY HUBERT BRADFORD VICKERY

WILLIAM MANSFIELD CLARK, late DeLamar Professor of Physiological Chemistry in The Johns Hopkins University School of Medicine, was a biochemist to whom accuracy in the measurement of physicochemical quantities and in the statement of the conclusions to be drawn from them was an abiding and controlling principle. Throughout a long life of research, beginning as a student with summer work at Woods Hole, Clark devoted himself to measurements, to the design and improvement of apparatus with which the measurements were made, and to the exposition of the results in papers and books uniformly characterized by clarity of expression and thoroughness of treatment. His book *The Determination of Hydrogen Ions,* the first edition of which appeared in 1920, brought about what amounted to a revolution in bacteriological laboratories and exerted a profound influence upon all aspects of biochemistry where the measurement and control of acidity are matters of importance. With characteristic modesty, Clark denied in the preface to the first edition that he had any special qualification for writing the book. In commenting on it in later life, he wrote, "This book put in convenient form what anyone could have found in the literature if he took the trouble to search," and indeed the principles developed in it were largely based upon the fundamental work of Sörensen and of Michaelis. But the organization, the exposition, the brilliant illustration, many of the data, and the profound scholarship are pure Clark. He has recorded occasional embarrassment "by the mention of this book as the chief item in citations accompanying some honors." He needed to feel no distress. The book laid a foundation for a distinguished career of helpfulness not only to biochemistry but to many allied fields as well as to industry. We are all and always shall remain in his debt.

William Mansfield Clark was born August 17, 1884. His father was James Starr Clark (1822-1914), whose ancestry can be traced back to James Clarke, one of the signers in 1639 of the Fundamental Articles of Agreement at New Haven, Connecticut. The Starr name traces through three generations of Barnums and five of Starrs to Dr. Comfort Starr[1] (1589-1659), who came to America in 1634 and settled in what is now Cambridge, Massachusetts; later he removed to Boston where he practiced medicine for many years.

Clark's mother was Caroline Scoville Hopson (1840-1928) of Poultney, Vermont, the daughter of an Episcopal clergyman. Among her early ancestors was William Leete (1613-1683), a governor of the New Haven Colony and, toward the end of his life, of Connecticut. Her family of two daughters and a son was born at Myersville in the township of Tivoli, New York. The son was named for her oldest brother William, who had settled in Georgia and who fought on the Confederate side in the Civil War (a second brother fought on the Union side), and for the Reverend Richard Mansfield, another family connection.

James Starr Clark was also an Episcopal clergyman. He graduated from King's College (now Columbia University) in

---

[1] The writer can likewise trace a line of descent through his maternal grandmother to the oldest son of Dr. Comfort Starr, his common ancestor with W. M. Clark, who was thus a seventh cousin.

1850 and received the honorary degree of S.T.D. in 1872. He established or administered a succession of boys' schools. Trinity School in Tivoli, New York, founded by him in 1867, flourished until the financial panic of 1893. It was conducted on military principles, and the elder Clark became influential in the community through his example of progressive practices on the farm and in the orchards connected with the school. He provided every possible facility for athletics for the boys, but also implanted in them the love of learning and the high appreciation of scholarship so well exemplified in his son.

Clark received his elementary education at the Trinity School and at several other schools during successive moves after the family left Tivoli, but finally obtained a scholarship at The Hotchkiss School in Lakeville, Connecticut. Here he excelled in English and in mathematics, was a member of the debating team, and was captain of the intramural gymnasium team in his final year. He was also class poet when he graduated in 1903. Then followed four years at Williams College where he became interested in chemistry, initially through reading Remsen's textbook in preference to a more elementary text advocated by his teacher, Professor Leverett Mears. Although this departure from conventional behavior earned him the nickname "Remmie" among his fellow students, his initiative brought him special attention and led in turn to his taking advanced courses in chemistry. During his senior year he taught chemistry in the Williamstown High School and, after graduation, was invited to remain another year as an assistant and candidate for the M.A. degree, which he received in 1908. On the recommendation of Professor Mears, he then applied for admission to The Johns Hopkins University and was accepted as a graduate student by Professor Harmon Morse.[2]

---

[2] Elected to the National Academy in 1907; see *Biographical Memoirs,* Vol. XXI.

Clark has recorded that the situation in the chemistry department during the two years he spent there was somewhat less than inspiring. The lectures in organic chemistry by President Remsen[3] had lost something of their earlier polish, and he found Professor Morse's lectures dull. Furthermore, the long-standing differences of opinion between two of the other professors created an atmosphere in the department which Clark often found extremely uncomfortable. Professor Morse employed him as a student assistant and not only excused him from much of the course in analytical chemistry but also arranged to have him skip the laboratory work in organic chemistry and some of that in physical chemistry. As a partial compensation he was given serious responsibilities in the care and maintenance of the complex equipment used by Morse for the measurement of osmotic pressure, inasmuch as the dissertation problem assigned to him was a redetermination of the osmotic pressure of cane sugar solutions at 20°C. He has recorded that this restriction of his activities was satisfactory to him at the time, and that he "became the willing and worshipful slave of the finest experimenter I have known." Later, however, he felt that he had been deprived of much course work that would have provided valuable experience. Nevertheless, it is quite possible that his teachers realized, as the event proved, that their brilliant student was quite capable of mastering any needed aspect of chemistry with little help from them and, whether or not he was adequately prepared, the coveted Ph.D. degree was awarded in 1910.

WOODS HOLE AND THE DAIRY DIVISION

During his college years, Clark spent several summers in the laboratory at Woods Hole where his brother-in-law Francis B.

---

[3] Elected to the National Academy in 1882; see *Biographical Memoirs,* Vol. XIV.

Sumner[4] was in charge of the local station of the United States Fish Commission. When a chemical research laboratory was set up under Carl Alsberg, then teaching physiological chemistry at Harvard, Clark became his assistant, and it was this relationship which first turned Clark's attention to biochemistry. Alsberg's discussions of the early days of biochemistry in Europe aroused the interest of his young assistant and stimulated him to read extensively. Alsberg was succeeded as head of the chemical laboratory at Woods Hole by D. D. Van Slyke[5] in 1909, and Clark has recorded an incident at this time which had a significant bearing on his later career.

Van Slyke was taken ill at the start of the season, and Clark was left alone in the laboratory. Knowing that his chief would need accurately standardized solutions on return from the hospital, he prepared a solution of redistilled ammonia and titrated it with standard acid. To make sure of the titre, he tested the equivalence point with every indicator dye available, as well as with several histological stains, and found, to his bewilderment and disgust, that hardly any two dyes yielded the same result. As a further example of the unsatisfactory state of the subject at that time, Clark has mentioned that a question regarding the behavior of phenolphthalein, asked during his oral doctoral examination at Johns Hopkins not long afterwards, gave rise to a wrangle between two of his examiners which occupied a substantial and very welcome fraction of the examination period.

Clark's first full-time job, for which he had been warmly recommended by Alsberg, was in the department of L. A. Rogers, the head of the research laboratories in the Dairy Division of the United States Department of Agriculture. When

---

[4] Elected to the National Academy in 1937; see *Biographical Memoirs,* Vol. XXV.

[5] Elected to the National Academy in 1921.

Clark reported for work in July 1910 and asked what he was to do, he was told, "That is for you to find out." As soon as he realized that his new chief meant this literally, he independently began a study of the composition of the gases in the characteristic "eyes" of cheese of the Emmental or Swiss type.

This early work was characterized by resourcefulness and skill in the design and construction of special apparatus for the manipulation and analysis of the gases produced by bacterial fermentation. Clark became a master glass blower. His techniques were of immediate assistance in his chief's extensive investigations of the group of bacteria found in milk, in bovine feces, and also occurring on grain, the classification of which was an important contemporary problem. Two broad groups of organisms (the colon-aerogenous groups) were distinguished, of which one gave small volumes of gas containing carbon dioxide and hydrogen in approximately equal amounts; the other gave large volumes of gas in which carbon dioxide predominated. The two groups also differed with respect to their ability to ferment various carbohydrates and other substances commonly used in the classification of bacteria.

One of the conventional tests used in the examination of the innumerable culture solutions was a titration with alkali. The results served as evidence of the capacity of the organism to ferment the sugar in the culture medium. Clark has reported, "It was while I worried over the lack of clarity in discussions of acid development in cultures and in milk products that I recalled the work done at Hopkins by my fellow student [N. Edward] Loomis with the hydrogen electrode. While I had read of the hydrogen electrode in the text of physical chemistry, the instrument had never been real to me, and I had never discussed it with Loomis. . . . I knew enough only to search the literature and there came across the excellent papers of Sörensen. Then a great light broke and, with the encouragement of Rogers, I began my own systematic studies."

The first fruit of this new approach was a paper published early in 1915 in the *Journal of Medical Research.* In it Clark discussed in detail the objections to the then common medical practice of modifying cows' milk used in infant feeding by the addition of alkali, usually calcium hydroxide but occasionally magnesium oxide. The alleged purpose was "to correct the high acidity of cows' milk." The practice was based upon the observation that more alkali was needed to titrate cows' milk to neutrality to phenolphthalein than was needed by human milk. In a closely reasoned argument, Clark showed that the hydrogen ion concentrations of the two kinds of milk were nearly the same, the difference in titration being attributable to the higher salt and protein content of cows' milk. The term "buffer" and the symbol "pH" were used by Clark for the first time in this paper. The conclusion was that the modification of cows' milk for infant feeding by the addition of alkali was "based upon wrong principles."

A paper on the adjustment of the reaction of culture media also appeared in 1915 in which Clark discussed the elements of the measurement of hydrogen ion concentration and showed typical titration curves of various acids, then somewhat of a novelty. He exposed the fallacies in the customary methods of adjusting the reaction by titration and advocated the substitution of a colorimetric method for this purpose.

Clark was joined at this time by H. A. Lubs, a skillful organic chemist. Together they showed that the organisms of the colon-aerogenes family, which could be differentiated in terms of the ratio of carbon dioxide to hydrogen in the gas produced, could be equally well and far more easily differentiated by measurements of the hydrogen ion concentration of the culture medium with the electrode, or by means of an indicator. This was the basis of the simple so-called "Clark and Lubs methyl-red test" still commonly used in studies of the organisms of this group.

To a suggestion that they should next assemble and study all of the indicators they could find, Lubs's reply was, "Why fool with old indicators. Let's make some new ones." It chanced that S. F. Acree at Hopkins had studied phenolsulphonphthalein and with the aid of his students had prepared several new derivatives of it. The exceptional brilliance of these dyes had attracted Clark's attention, and samples were obtained and tested. Lubs prepared additional homologues, and there began the patient survey of the whole field that ended in the selection of some thirteen dyes which could be used as indicators to cover nearly the entire range of pH, and which were reliable in the presence of salts or of proteins. The first description of some of these indicators appeared in 1915, as did the description of the well-known Clark hydrogen electrode vessel.

Clark next turned to the subject of buffer mixtures, and in a paper, published in 1916, he and Lubs described the series of phthalate, phosphate, and borate mixtures which are used as standards to this day. The extreme precautions taken in the purification of the salts and in the measurements of the potentials of the solutions were described in detail and established new standards for work in this field.

The following year a comprehensive paper on the colorimetric determination of hydrogen ion concentration and its application in bacteriology appeared in three parts in successive issues of the *Journal of Bacteriology*. The paper ran to 106 pages, and copies were soon in such demand that these issues of the journal were completely exhausted. To the proposal by the publisher that the papers should be reprinted, Clark countered with the suggestion that he should gather all of the appropriate material in the form of a book since the subject was much broader than was indicated in the paper. How much broader it turned out to be may be roughly estimated from the fact that the bibliography of the paper contains about

160 references while that of the first edition of *The Determination of Hydrogen Ions* in 1920 has well over 1,200 titles. The second edition of 1923 contains about 2,000. These figures perhaps provide sufficient commentary on Clark's remark quoted earlier that anyone who took the trouble to search the literature could have found what was in the book. Although this is possibly true, the fact remains that the writing of the book required nearly two years, and it is quite clear that the previous literature need never be searched again.

Clark's interest in the measurement of oxidation-reduction potentials was aroused initially as the result of a chance conversation in 1915 with his friend L. J. Gillespie, at that time working in the Bureau of Soils. Gillespie had set up a calomel half-cell against an electrode of mercury overlaid by a culture of bacteria, and had noted that the mercury electrode became progressively more negative as the culture developed. He recognized that he was observing a reduction potential and became interested in possible applications to the study of water-logged soils. Clark saw at once that the technique offered promise in the study of the differential reduction of dyes often seen in cultures of bacteria. As he put it a few years later, ". . . there was hope that a method had been revealed whereby it might be possible to accumulate *quantitative* data and, step by step, build up exact evidence upon one of the manifold aspects of the general problem."

As opportunity offered, therefore, he repeated, verified, and extended Gillespie's observations. Since difficulties were encountered with bacteria under the conditions then used, the work with biological systems was suspended, and a comprehensive study was begun of the potentials of various dyes in equilibrium with their reduction products.

Although several other investigators also took up the study of oxidation-reduction systems at about this time, Clark has noted that with but one exception none of the early workers had provided conditions for the attainment of stable and definitive potentials. The use of buffer solutions had become routine in Clark's laboratory and, as a consequence, his earliest experiments were carried out at constant pH. Stable and reproducible potentials were at once obtained, and the observations "lined up beautifully on a diagram like nothing seen before. I was elated. I recall saying to myself: 'This general subject will keep me busy for years.' It did."

The results of these preliminary studies appeared in 1920 in a brief paper dealing with indigo sulfonate and methylene blue. In the introduction to this paper, Clark wrote, "So far as the writer is aware such indicators have not been regarded in their possible relation to oxidation-reduction potentials in a manner analogous to the now well-systematized relation of hydrogen-ion indicators to hydrogen-electrode potentials. That such a relationship if established will aid in the interpretation of various biochemical phenomena will be evident, but the significance of such data is of broader scope, because the efforts that have previously been made to bring organic compounds within the range of potential measurements have yielded few data of value." Thus Clark outlined the field of research which became his lifework.

THE HYGIENIC LABORATORY

In 1920 Clark was made Chief of the Division of Chemistry of the Hygienic Laboratory of the United States Public Health Service. After some delay while a new laboratory was built, Clark, with the aid of a number of enthusiastic and gifted colleagues, began the systematic study of the oxidation-reduction potentials of dye systems. The first ten papers appeared as Public Health Reports between 1923 and 1926. Then, because the demand for copies had exhausted the supply, they were reprinted in 1928 as Hygienic Laboratory Bulletin No. 151, a book of 340 pages.

It is perhaps a fortunate circumstance that these papers were written for publication in what was to a certain extent a "house journal." Aside from the formal approval of superior officers in the service, there was no restriction on space; no editor or referee demanded that minor details be more briefly treated, or that fewer tables be used. As a consequence Clark was able in the first two papers to present the theory of oxidation-reduction potentials in full detail and in terms addressed to a reader unfamiliar with the subject, at that time an essential precaution. The techniques were next described, and then measurements of the potentials of each of a series of dyes were made over a broad range of pH. The dyes chosen included the indigo sulfonates, a long series of substituted indophenols, methylene blue, and a group of so-called meriquinones (semiquinones). These dyes were selected to provide as wide a range of potentials as possible and were either synthesized for the purpose or were obtained by careful purification of commercially available material.

The data accumulated consisted in general of measurements of the potential during titration of the oxidized dye with a suitable reducing agent at a series of carefully buffered pH values, the converse operation on the reduced form of the dye, and of measurements of the potential of equimolecular or other known mixtures of the oxidized and reduced form over a broad range of pH. The solutions were sufficiently dilute with respect to the dye so that its effect upon the independently determined pH of the buffer solution was negligible. The data were presented both in tabular and in plotted form, and the results were analyzed in terms of percentage reduction and of the dissociation constants of both forms of the dye, this at times requiring the development of highly complex equations. In a review paper published in 1925 the significance of the observations was pointed out as follows: "With a convenient method of formulating the somewhat complex relations . . . we shall not only gain a better understanding of how it is that accurate data on organic systems are now being obtained, but we shall also see that the potentiometric methods are furnishing precise data on free energy relations, opening new methods of analyses, broadening the methods of determining hydrion concentration, aiding in the solution of problems in structural chemistry, furnishing valuable data on the effects of substitution, and suggesting new approaches to fundamental problems of biological oxidation-reduction."

The papers contained many discussions of applications of the results, and there were many sometimes sharply critical examinations of fallacious or misleading statements or procedures in the current literature. Taken together, this group of papers established Clark as the leading investigator in the field and led naturally into the next phase of his career.

THE JOHNS HOPKINS UNIVERSITY

Clark has recorded that he had been interviewed occasionally with respect to appointment to a university chair. He had invariably declined on the grounds that "I had had no formal training in any of the subjects I was supposed to 'profess'." Early in 1927, however, he was notified—without any preliminary consultation—that he had been appointed DeLamar Professor of Physiological Chemistry in the School of Medicine at The Johns Hopkins University in succession to Professor Walter Jones,[6] who had retired.

During a visit to Baltimore shortly thereafter he remarked to Professor Abel[7] that he "did not know, for example, the difference between the thymus and the thyroid glands and knew less

---

[6] Elected to the National Academy in 1918; see *Biographical Memoirs,* Vol. XX.

[7] Elected to the National Academy in 1912; see *Biographical Memoirs,* Vol. XXIV.

of their function." Abel replied, "My dear boy, that is why we want you."

Clark accepted the appointment in spite of the fact that, as he later wrote, "I had had no formal training in biochemistry, had an inadequate appreciation of the needs of medical students, and [that] I inherited laboratory equipment and space totally deficient in what was required for my research and student instruction. I needed support desperately. It was given effectively. Funds were provided for equipment needed immediately. I was allowed to modify plans for a new building, and then everyone left me completely alone as a token of confidence." It is characteristic of his approach to problems that he shortly enrolled in the class in gross anatomy and dissected a cadaver along with the students to whom he was teaching chemistry.

Clark served as DeLamar Professor for twenty-five years during a period in which physiological chemistry, or biochemistry as it more generally came to be called, developed into a major branch of chemistry. He was concerned from the start with the problem, faced by all teachers of biochemistry in medical schools, of deciding which aspects of the subject to include in the course. His decision was that "to provide a basis on which the students could build we should pick up the threads of thought in basic chemistry before weaving them into biochemistry. . . . In the 30's it was estimated that about half of the entering students had had inadequate instruction in those more elementary parts of physical chemistry that are involved in almost all parts of the science, and that are essential in a first approach to an understanding of matters of clinical importance."

To meet this difficulty Clark later wrote his second book, *Topics in Physical Chemistry,* the first edition of which appeared in 1948. It carries the subtitle "A supplementary text for students of medicine." The book was not intended as a course textbook but was designed to provide material to be studied as needed to fill out gaps in knowledge or experience. The book was so widely used that a second edition was called for in 1952.

Clark became a distinguished teacher. He invariably insisted upon a clear knowledge of fundamental principles. One of his colleagues, Professor Philip Bard,[8] has recorded, in a Minute recently prepared for the Advisory Board of the School, "To some students he appeared at times stern; he demanded precision and definition, for his approach was necessarily a quantitative one. Many students with an insufficient background in chemistry, especially quantitative chemistry, had a hard time in his course. But he was as fair to such individuals as he was encouraging to the good students. He liked the students and they, conscious of his high scientific repute and integrity, admired and respected him. . . . There can be no doubt that he was a great force for good teaching in this Medical School."

The program of research in Baltimore, after the new laboratory had been established, was continued for several years along the lines followed at the Hygienic Laboratory. A number of dyes which broadened the observed range of potentials were studied, and Clark mentioned in his Harvey Lecture in the fall of 1933 that 64 different oxidation-reduction systems had been measured up to that time. These yielded a system of indicators available for the colorimetric estimation of electrode potential comparable in versatility with the better-known system of acid-base indicators.

Although his interest in the field of oxidation-reduction had been aroused by Gillespie's early experiments on the potentials observed in suspensions of bacteria in culture solution, Clark for the most part left to his colleagues and to others the detailed investigation of biological systems. However, in occasional review papers or lectures, he brought together examples of the rapidly increasing mass of reliable biological data for compari-

---

[8] Elected to the National Academy in 1944.

son with the model systems he himself preferred to deal with. He repeatedly emphasized the thermodynamic implications of the measurements, pointing out that "the potentiometric method . . . is only a special means—sometimes available and sometimes not, sometimes of the highest accuracy and sometimes not—of obtaining data upon changes of free energy and heat content, data for which we have pressing need. . . . The electrode potential is a function of the chemical potentials which persist in the absence of the configuration of the electric cell, and it is this function which determines the *possibility* of a reaction between a given system and another whose characteristic theoretical electrode potential is known." In many of these papers he reproduced a diagram showing the position on the scale of potential of the curves for percentage oxidation of an increasing number of dye systems in relation to such biological oxidation-reduction systems as epinephrin, ascorbic acid, phthiocol, the succinate-fumarate and lactate-pyruvate pairs in the presence of the appropriate catalytic enzyme, and a few others. To quote from a symposium lecture given in 1937, "Thus thermodynamics provides certain critical data on the components of biological catalysts without touching the mechanism by which passive resistance to interaction is overcome. The path for action being open, the relative potentials define what reaction can use the path—thus ordering and simplifying the subsequent kinetic treatment."

In presenting the data for the potential of certain dye systems, Clark as early as 1924 made occasional use of three-dimensional diagrams. These were constructed from two plots. One showed potential against percentage reduction at a succession of constant pH values which gave a series of S-shaped curves. The other was a plot of the potentials at fixed percentages of reduction against pH, a function giving straight lines which changed in slope at each of the pH levels corresponding to the magnitude of the acid dissociation constants of the substance and thus furnishing estimates of these quantities. When combined, these diagrams defined a surface, for which an equation was provided, points on which give the potential of any mixture of the oxidant and reductant at any pH within the limits of the diagram.

From time to time papers appeared from other laboratories in which the oxidation-reduction behavior of various naturally occurring pigments was described. Clark was especially interested in the early work of J. B. Conant[9] at Harvard on the nemoglobin-methemoglobin system and on a few hemochromogens, and in its extension during the 1930s at the hands of E. S. G. Barron and his associates to the study of the potentials of coordination compounds of heme with nitrogenous bases. It was clear that the potentials of the dye systems he had studied earlier were functions of the pH and of the relative proportions of the oxidized and reduced forms of the dye under examination. An additional parameter entered the system in the case of the compounds of heme with bases, since the potential was also a function of the degree of coordination of the metalloporphyrin with base. This was a function entirely distinct from the acid-base relationships of the carboxyl groups present on the porphyrin molecule. The system thus became four-dimensional even at constant temperature and pressure.

It was this line of thought which induced Clark to undertake the studies of the metalloporphyrins to which he devoted the greater part of his time at Johns Hopkins. These compounds were obviously concerned with respiration (cytochrome), with the transport of oxygen, and with many enzyme processes in the living cell. Each system must be characterized by a certain electron escaping tendency. In a lecture given in 1952, Clark set forth the problem he had faced as follows: "What modification

[9] Elected to the National Academy in 1929.

of the electron escaping tendency, exhibited by the prosthetic system, follows the incorporation of oxidant and reductant in complexes? Second: suppose the complexes form reversibly so that in the same solution there will be uncombined prosthetic compound in both oxidized and reduced states, uncombined ligand, and both oxidized and reduced complexes. Suppose also that each component can serve as a proton donor or as a proton acceptor in one or another region of pH. How shall we formulate the equilibrium states of so complex a system in such a way as to make them subject to experimental evaluation?"

Although in the living cell a specific protein frequently plays the role of coordinating substance with the metalloporphyrin, Clark saw that more stable substances would be required for the experimental studies necessary. He therefore turned to the examination of the coordination compounds of a number of available metalloporphyrins with such bases as pyridine, nicotine, cyanide, and various imidazoles. There was no attempt to use these systems as catalysts nor to find practical applications. The motivation was entirely the elucidation of the general principles which controlled the interactions among the components. For this, stable reproducible model systems were obviously to be preferred.

Clark's mastery of the mathematical intricacies involved in the general theory of the subject is most clearly shown by the first paper in the long series on metalloporphyrins. This was published in the *Journal of Biological Chemistry* in 1940. In this paper the theoretical relations were considered in detail in the form of a series of sixteen propositions dealing with the five types of reactions which can occur. A general equation for the potential was derived which contained five logarithmic terms. In addition, an equation was derived for the use of spectrophotometric data in determining various constants. He then discussed the simplifications which can be made so that graphical methods can be used in analyzing the data. In the subsequent papers of the series, these theoretical considerations were used in the exposition.

The experimental difficulties were formidable. It was necessary to work in alkaline solutions, there was frequently a tendency toward polymer formation, and certain components of some of the systems had low solubilities so that measurements were often frustrated by precipitation occurring in the system. Sometimes the data were open to various alternative interpretations, but Clark was usually able, by manipulation of the necessary equations, to devise a mathematical or graphical test which led to a judgment.

In a general discussion of this work in 1952, he emphasized the following points. To the criticism that he had made use of models rather than natural systems he replied: "We have done enough with one natural system to appreciate both the inherent difficulties in handling it and the probability that we might have been far off the beam had we not had experience with the artificial, model system. . . . The structural features of most natural systems differ very greatly from those of components of our artificial system. There may also be great differences in the nature of bondings. It remains to be seen how far we are 'off the beam.' I have faith that our little beam will serve as a direction finder in local flights at least."

He went on to develop a concept that informs all of his work, the idea, based upon the smooth behavior of the electrode even in complex systems, of what he called a "chemical continuum." Proton donors and their conjugate acceptors form an acid-base continuum. A more complex system that contains potential oxidants and reductants constitutes an oxidation-reduction acid-base continuum involving electron and proton transfers, and sometimes the incorporation of oxygen. Further, there are cases where the oxidant, the reductant, or both enter into processes of coordination. Where such still more complex systems occur in nature, there is an at least four-dimensional continuum. The experimentalist works on this continuum by a series of zigs and zags since he must control all parameters save the one under investigation. Nature is under no such restriction. As Clark put it when considering the degrees of freedom open to the metabolism of the amoeba,

I once met a lively young cell
Whom I then proceeded to tell
Of pH, electrons,
P wiggles and protons;
To which he replied: "Go to ———."

It will be recalled that Clark was his class poet at Hotchkiss!

WAR WORK

Clark made important scientific contributions to national defense in both world wars. As a member of the Dairy Division staff during World War I, he was faced with the problem of the manufacture of casein for the glues essential to make the plywood used in the wings and other parts of the airplanes of the period. Most of the casein was imported from Argentina, American-made casein being rejected by the glue manufacturers on the grounds of lack of uniformity. At the time, Clark was fresh from his studies of the papers of Sörensen and knew that proteins pass through a minimum of solubility at their isoelectric points. Accordingly, when supervising the precipitation of casein from the skim-milk in a huge vat, he insisted that the addition of acid should be continued until the pH of the whey reached the isoelectric point of casein in spite of the fact that all of the casein appeared to have separated long before this point was reached. As a result the casein aggregated into large firm granular curds which could be easily washed free from the whey and secured in a reproducible and adequately pure form. This material was entirely satisfactory for glue manufacture. A troublesome and difficult problem thus received a simple solution. There were few young chemists in America at the time who would have known how to solve it so promptly.

During World War II, Clark was a member of the Executive Committee of the National Academy of Sciences, and from 1941 to 1946 was Chairman of the Division of Chemistry and Chemical Technology of the National Research Council. He has recorded that, when he took over this last position, "there was nothing of importance to defense on the agenda of this august institution which had been established to serve the Government."

This situation soon underwent change. The first problem involved investigations concerning the physiological action of toxic gases, a matter of grave concern early in the war. The Division was next called upon to examine the purity of the supplies of the antimalarial agent quinacrine (Atebrin) of domestic origin, since toxicity was suspected which was attributed to impurities. The outcome of studies at the hands of a number of investigators was that all samples of domestic or foreign origin were satisfactorily pure, and that the drug itself is somewhat toxic.

The importance of research on malaria soon led to the formation under the Division of an office of information known as the Survey of Antimalarial Drugs. One of its important functions was to screen for antimalarial use the enormous number of drugs submitted by pharmaceutical manufacturers. The published tables which appeared after the war contained information on some 15,000 substances. Several new and useful antimalarial drugs were found.

A further part of the Division's work involved the organization of new synthetic work on drugs and, as a result of Clark's administrative skill, this was prosecuted with great vigor. Still another part was concerned with problems arising in connection with requests for improvement of quartermaster's stores. Clark was also for a while chairman of an Academy committee on biological warfare which was called upon to solve problems of defense against possible use of biological agents by the enemy. His broad acquaintance with gifted scientists in many fields enabled him to assemble *ad hoc* committees to deal satisfactorily with these widely varied challenges.

He later recorded his uneasiness throughout this period because of the paucity of basic knowledge and the necessity of resorting to empirical solutions of the problems. The only relief was that "I saw an abundance of goodwill as made evident by the fact that everyone, without exception, followed advisory committees' requests which I had the honor to transmit in the name of the National Research Council."

RETIREMENT

Clark retired in 1952, becoming DeLamar Emeritus Professor and Research Professor of Chemistry. He transferred his office and much of his specialized equipment to the Remsen laboratory at the Homewood campus of the University. Here for a few years he occupied himself with the investigation of a few problems in which he was interested, but which did not lead to publication. For several years he also gave a course of lectures on physical chemistry to graduate students. Finally, however, he settled down to the task of writing his last book, *Oxidation-Reduction Potentials of Organic Systems,* a monograph for which he felt there was a need.

The book appeared in 1960. It is dedicated to his associates and students, twenty-five in number, who, he wrote, "I trust, enjoyed our cooperative survey of fascinating terrain." It consists of fourteen chapters, beginning with a consideration of the parts of thermodynamics essential for the development of the theory of the subject, with illustrations in the form of tables or plots of data drawn mainly from his own vast experience. There followed a full description of standardizations and techniques, and a chapter on the criteria for the reliability of measurements, a chapter which ends with the one-line conclusion: "More experiments are needed."

The last chapter takes up nearly one third of the book. It consists of a compilation of all of the data in the literature of oxidation-reduction potential which Clark considered to be reliable. An appendix gives a number of tables useful in the computations, and the bibliography contains more than twelve hundred titles.

This monograph is definitely in the *magnum opus* class. Here is gathered together the knowledge and experience gained in a lifetime of practical investigation and scholarly research in a recondite field. It stands today as the final authority in this field and will doubtless remain so for many years. In his first paper on oxidation-reduction, Clark in 1923 had written regarding biological oxidations: "Contesting schools offer postulates which are easily interchanged without revealing any decisive addition to our knowledge . . . and the impartial student despairs of finding the quantitative data which alone can establish the relative importance of the differing viewpoints." Clark had corrected this situation by 1960.

HONORS

Clark received many honors in recognition of his accomplishments. He was President of the Society of American Bacteriologists in 1933 and of the American Society of Biological Chemists in 1933 and 1934. He was elected to the National Academy of Sciences in 1928 and to the American Philosophical Society in 1939. He was given honorary degrees by Williams College (1935) and the University of Pennsylvania (1940). The Albany Medical College of Union University conferred upon him its first Honorary Lectureship Award in 1957. He received the Nichols Medal of the New York Section of the American Chemical Society in 1936, the Borden Award in 1944, and the Passano Award in 1957. He was Remsen Memorial Lecturer in 1952 and Dakin Memorial Lecturer at Adelphi University in 1958, and was Consultant of the Office of Scientific Research and Development from 1941 to 1945. In October 1963 he received the Award of Merit of the Maryland Section of the American Chemical Society.

Now may I be allowed to drop the style of an impersonal biographer and talk about my honored friend Bill Clark. There perhaps has emerged a picture of a hard-working scientist and scholar who had few interests aside from the measurement of potentials. Nothing could be further from the fact. I first met him during a meeting of the Federation of Biological Societies in Washington in 1924. I had gone to the Hygienic Laboratory where Van Slyke was to demonstrate his then recently developed manometric apparatus for the determination of gases in blood, and Bill was in the group watching the demonstration. Later, we came into contact as members of the Editorial Board of the *Journal of Biological Chemistry* to which Bill had been appointed in 1933 and to which I was appointed some years later. No one who was privileged to attend the annual dinners given by the late Rudolph Anderson to the members of the Editorial Board of the *Journal* and the Editorial Committee of the American Society of Biological Chemists will ever forget the occasional shouts of "Yea, Rudolph!" from Bill's end of the table, and the necessity to drink still another toast to our beloved Managing Editor.

Bill was a skilled editor and critic of manuscripts. The difficult ones which involved mathematics and physical chemistry were almost automatically assigned to him, and none passed through his hands without being improved both in diction and in accuracy of statement; and he could be ruthless when necessary. He served on the board of the *Journal* until 1952 and later was frequently asked for referee opinions. This is an inconspicuous service to science, and is often a thankless one; but few activities contribute more to the quality of what is published in scientific journals.

Bill was not a gregarious person. Even as a student at Williams he is recorded as being "a great reader, fond of his pipe and of walking, and quiet and thoughtful in his ways." But he had an unusual capacity for friendship, as all who have been associated with him can testify.

He married Rose Willard Goddard of Salisbury, Connecticut, in 1910, and two daughters were born while they lived in Washington. Mrs. Clark died in 1958.

Bill was a golfer and a gardener. The highlights of his life were two holes-in-one made in games with friends. He was neither an expert nor a duffer but could be a keen opponent. He had a garden in Washington and later bought a summer home in Lakeville, Connecticut, where he developed another that was a joy not only to himself but to all who visited him. He went in for unusual varieties of flowers and shrubs and knew and used their scientific names. What he did with succulents and vines on the abrupt faces of the rock cliffs by his house was little short of phenomenal. His vegetable garden was a mingled joy and trial, and his stories of the perennial battle with woodchucks, rabbits, insects, and diseases have convulsed many audiences.

His vast reading had developed in him a strong sense of the history of his subject. This is shown repeatedly in the introductions to his papers and books. In his last book he begins his account of oxidation with Lavoisier, Priestley, and Scheele; he defines ion, anode, cathode, electrolyte, and correlative terms by quoting Faraday, who invented the words, but translating Faraday's Greek. His puckish sense of humor comes out in a footnote to this last-mentioned paragraph where he states he had heard that "one librarian classified the author's book on hydrogen ions under Greek mythology." Evidently "ions" still meant "wanderers" to this person.

Another product of his reading was the beautifully chosen quotations with which he embellished the chapter headings of his books. A chapter on the standardization of potentials carries this quotation from Deuteronomy: "Thou shalt not have in thine bag divers weights, a great and a small. Thou shalt not have in thine house divers measures, a great and a small. But thou shalt have a perfect and just weight, a perfect and just measure shalt thou have." A chapter on techniques carries a Turkish proverb: "Don't descend into the well with a rotten rope."

Bill Clark came close to the ideal of what a professor in an American university should be. Modest and unassuming though he was, his strength of character, his total mastery of his subject and enthusiasm for it, his independence of thought, and his personal magnetism impressed themselves on all who came into contact with him. In the words recorded by Dr. Bard of one of his senior colleagues on the faculty at Hopkins, he was "worthy to walk with the great founders of the Medical School, Welch, Howell, Abel, and Halsted." This opinion is shared by all of his friends.

In preparing this account, I have had access to a document by Clark prepared for the use of his biographer and deposited with the Academy as long ago as 1935. This, together with a chapter entitled "Notes on a Half-Century of Research, Teaching and Administration" in Volume 31 of the *Annual Review of Biochemistry, 1962,* provided the main facts. I am grateful to Dr. Murray Luck for per-

mission to quote liberally from the latter. Dr. Leslie Hellerman kindly made available to me a copy of Dr. Philip Bard's "Minute" from which I have also quoted.

In addition, I have had the use of Clark's bound set of reprints together with copies of his books kindly loaned to me by Miss Miriam Clark, to whom I am most indebted. From these I have also quoted freely. My laboratory copies of *The Determination of Hydrogen Ions,* first and third editions, are tattered, stained, and worn beyond description although still usable. Their condition attests to their value. Finally, I have the warm recollection of many conferences and visits in Baltimore, in Lakeville, here in New Haven, and elsewhere with a man I admired deeply and miss more than I can readily say.

BIBLIOGRAPHY

The bibliography has been compiled from Clark's personal file of bound reprints together with references in *Chemical Abstracts.* A complete list of the papers in the series "Studies on Oxidation-Reduction" and in the series "Metalloporphyrins," which contain papers by his colleagues and students, is to be found in the bibliography of his book *Oxidation-Reduction Potentials of Organic Systems.*

KEY TO ABBREVIATIONS

Abstr. Bacteriol. = Abstracts of Bacteriology
Cold Spring Harbor Symp. Quant. Biol. = Cold Spring Harbor Symposia on Quantitative Biology
Hyg. Lab. Bull. = Hygienic Laboratory Bulletin of the United States Public Health Service
Ind. Eng. Chem. = Industrial and Engineering Chemistry
J. Am. Chem. Soc. = Journal of the American Chemical Society
J. Bacteriol. = Journal of Bacteriology
J. Biol. Chem. = Journal of Biological Chemistry
J. Infect. Diseases = Journal of Infectious Diseases
J. Wash. Acad. Sci. = Journal of the Washington Academy of Sciences
Public Health Rept. = Public Health Reports of the United States Public Health Service

1910

A contribution to the investigation of the temperature coefficient of osmotic pressure: a redetermination of the osmotic pressures of cane sugar solutions at 20°. Ph.D. Dissertation, Johns Hopkins University.

1912

A study of the gases of Emmental cheese. United States Department of Agriculture, Bureau of Animal Industry, Bulletin, 151.

1913

A humidity regulator. United States Department of Agriculture, Bureau of Animal Industry, Circular, 211.

An improved thermoregulator. J. Am. Chem. Soc., 35:1889.

A note on Penfold's modification of *Bacillus coli communis.* Science, 38:669.

1914

With L. A. Rogers and Brooke J. Davis. The colon group of bacteria. J. Infect. Diseases, 14:411.

With L. A. Rogers and Alice C. Evans. The characteristics of bacteria of the colon type found in bovine feces. J. Infect. Diseases, 15:99.

With Carl L. Alsberg. The solubility of oxygen in the serum of *Limulus polyphemus L.* and in solutions of pure *Limulus* haemocyanin. J. Biol. Chem., 19:503.

1915

The reaction of cows' milk modified for infant feeding. Journal of Medical Research, 31:431.

The "reaction" of bacteriologic culture media. J. Infect. Diseases, 17:109

With L. A. Rogers and Alice C. Evans. The characteristics of bacteria of the colon type occurring on grains. J. Infect. Diseases, 17:137.

With Herbert A. Lubs. The differentiation of bacteria of the colon-aerogenes family by the use of indicators. J. Infect. Diseases, 17:160.

The final hydrogen ion concentrations of cultures of *Bacillus coli.* J. Biol. Chem., 22:87.

With Herbert A. Lubs. On some new indicators for the colorimetric determination of hydrogen ion concentration. J. Wash. Acad. Sci., 5:609.

A hydrogen electrode vessel. J. Biol. Chem., 23:475.

1916

With L. A. Rogers and Alice C. Evans. Colon bacteria and streptococci and their significance in milk. American Journal of Public Health, 6:374.

With Herbert A. Lubs. Hydrogen electrode potentials of phthal-

ate, phosphate, and borate buffer mixtures. J. Biol. Chem., 25:479.

With Herbert A. Lubs. A note on the sulphone-phthaleins as indicators for the colorimetric determination of hydrogen-ion concentrations. J. Wash. Acad. Sci., 6:481.

With Herbert A. Lubs. The colorimetric determination of the hydrogen-ion concentration of bacteriological culture media. J. Wash. Acad. Sci., 6:483.

1917

With Herbert A. Lubs. The colorimetric determination of hydrogen-ion concentration and its applications in bacteriology. J. Bacteriol., 2:1, 109, 191.

With Herbert A. Lubs. Improved chemical methods for differentiating bacteria of the coli-aerogenes family. J. Biol. Chem., 30: 209.

With Herbert A. Lubs. A substitute for litmus for use in milk cultures. Journal of Agricultural Research, 10:105.

On the formation of "eyes" in Emmental cheese. Journal of Dairy Science, 1:91.

1918

The acid production of *Bacillus bulgaricus,* Abstr. Bacteriol., 1:59.

With B. Cohen. Influence of the pH of media upon the reproduction of some common bacteria. Abstr. Bacteriol., 2:10.

Differentiation of bacteria of colon-aerogenes family. Journal of the American Water Works Association, 5:26.

1919

With B. Cohen. The growth of certain bacteria in different hydrogen-ion concentrations. J. Bacteriol., 4:407-27.

Reduction potential in its relation to bacteriology. Abstr. Bacteriol., 4:2.

1920

The Determination of Hydrogen Ions. Baltimore, Williams & Wilkins Co. 317 pp.

Studies on technical casein. I. Introduction. Ind. Eng. Chem., 12:1162.

With H. F. Zoller, A. O. Dahlberg, and A. C. Weimar. Studies on technical casein. II. Grain curd casein. Ind. Eng. Chem., 12:1163.

Reduction potentials of mixtures of indigo and indigo-white and of mixtures of methylene blue and methylene white. J. Wash. Acad. Sci., 10:255.

1921

Reply to Wherry and Adams' article on methods of stating acidity. J. Wash. Acad. Sci., 11:199.

With H. F. Zoller. A series of oxidation-reduction indicators. Science, 54:557.

1922

Instability of phthalate potentials. J. Am. Chem. Soc., 44:1072.

1923

The Determination of Hydrogen Ions. 2d ed. Baltimore, Williams & Wilkins Co. 480 pp.

Pasteur—an appreciation. (An address made to the staff of the Hygienic Laboratory at the celebration of the one-hundredth anniversary of the birth of Pasteur.) Public Health Rept., 38:91.

With Emery J. Theriault. An experimental study of the relation of hydrogen-ion concentrations to the formation of floc in alum solutions. Public Health Rept., 38:181.

The determination of hydrogen ions. Transactions of Fourth Annual Antimalaria Conference. U.S. Public Health Service Bulletin, 137:3.

Studies on oxidation-reduction. I. Introduction. Public Health Rept., 38:443. Reprint No. 823.

With B. Cohen. Studies on oxidation-reduction. II. An analysis of the theoretical relations between reduction potentials and pH. Public Health Rept., 38:666. Reprint No. 826.

With B. Cohen. Studies on oxidation-reduction. III. Electrode potentials of mixtures of 1-naphthol-2-sulfonic acid indophenol and the reduction product. Public Health Rept., 38:933. Reprint No. 834.

With M. X. Sullivan and B. Cohen. Studies on oxidation-reduction. IV. Electrode potentials of indigo sulfonates, each in equilibrium with its reduction product. Public Health Rept., 38: 1669. Reprint No. 848.

1924

With Elias Elvove. A study of the acid-base equilibria of arsphenamine solutions. Hyg. Lab. Bull., 135:2.

With B. Cohen and H. D. Gibbs. Studies on oxidation-reduction. V. Electrode potentials of simple indophenols, each in equilibrium with its reduction product. Public Health Rept., 39:381. Reprint No. 904.

With B. Cohen and H. D. Gibbs. Studies on oxidation-reduction. VI. A preliminary study of indophenols: (A) Dibromo substitution products of phenol indophenol; (B) Substituted indophenols of the ortho type; (C) Miscellaneous. Public Health Rept., 39:804. Reprint No. 915.

Life without oxygen. J. Wash. Acad. Sci., 14:123.

1925

Recent studies on reversible oxidation-reduction in organic systems. Chemical Reviews, 2:127.

With B. Cohen. Indicators of anaerobiosis. Abstr. Bacteriol., 9:11.

The determination of hydrogen- and hydroxyl-ion concentrations and their significance. Journal of the American Leather Chemists' Association, 20:544.

With B. Cohen and H. D. Gibbs. Studies on oxidation-reduction. VIII. Methylene blue. Public Health Rept., 40:1131. Reprint No. 1017.

1926

With B. Cohen and H. D. Gibbs. Studies on oxidation-reduction. IX. A potentiometric and spectrophotometric study of meriquinones of the *p*-phenylenediamine and benzidine series. Public Health Rept., Suppl. No. 54:1.

With R. K. Cannan and B. Cohen. Studies on oxidation-reduction. X. Reduction potentials in cell suspensions. Public Health Rept., Suppl. No. 55:1.

Standard buffer solutions and acid-base indicators. International Critical Tables, 1:81.

1927

With M. Phillips and B. Cohen. Studies on oxidation-reduction. XI. Potentiometric and spectrophotometric studies of Bindschedler's green and toluylene blue. Public Health Rept., Suppl. No. 61:1.

With B. Cohen and M. X. Sullivan. Studies on oxidation-reduction. XII. A note on the Schardinger reaction (in reply to Kodama). Public Health Rept., Suppl. No. 66:1.

"Synthetic milk" as a basis for research. Journal of Dairy Science, 10:195.

Reversible oxidation-reduction reactions in organic systems. (Lecture delivered at Columbia University in the Summer Session, 1926, on the occasion of the opening of the Chandler Chemical Laboratories.) New York, Columbia University Press.

1928

The Determination of Hydrogen Ions. 3d ed. Baltimore, Williams & Wilkins Co. xvi + 717 pp.

With H. D. Gibbs and W. L. Hall. Studies on oxidation-reduction. XIII. Preparation of indophenols which may be used as oxidation-reduction indicators. Public Health Rept., Suppl. No. 69:1.

With Alice T. Merrill. Some conditions affecting the production of gelatinase by proteus bacteria. J. Bacteriol., 15:267.

With the staff of the Division of Chemistry, Hygienic Laboratory. Studies on oxidation-reduction I-X. Hyg. Lab. Bull. No. 151, 340 pp. (A reprint of the first ten papers.)

Oxidation-reduction potentials of dye systems and their significance in bacteriology. In: *The Newer Knowledge of Bacteriology,* ed. by Jordan and Falk. Chicago, University of Chicago Press.

1929

Oxidation-reduction in relation to biochemistry. Proceedings of the International Congress of Plant Sciences, 1:225.

1931

With E. G. Ball. A potentiometric study of epinephrine. Proceedings of the National Academy of Sciences, 17:347.

1932

With M. E. Perkins. Studies on oxidation-reduction. XVII. Neutral red. J. Am. Chem. Soc., 54:1228.

1933

With R. D. Stiehler and T.-T. Chen. Studies on oxidation-reduction. XVIII. Simple safranines. J. Am. Chem. Soc., 55:891.
With R. D. Stiehler. Studies on oxidation-reduction. XIX. Aposafranines. J. Am. Chem. Soc., 55:4097.
With L. Hellerman and M. E. Perkins. Urease activity as influenced by oxidation and reduction. Proceedings of the National Academy of Sciences, 19:855.

1934

The potential energies of oxidation-reduction systems and their biochemical significance. Harvey Lectures, 1933-1934, p. 67. Also in Medicine, 13:207.
Evolution toward a mature scientific literature. J. Bacteriol., 27:1.

1935

Walter Jones. Obituary notice. Science, 81:307.

1936

Report of the committee on undergraduate courses in chemistry. Johns Hopkins Alumni Magazine, 24:235.
A little of the perspective of acid-base and oxidation-reduction equilibria. Ind. Eng. Chem., 28:620.

1938

With J. F. Taylor, T. H. Davies, and R. Lewis. Coordination of metalloporphyrins with nitrogenous bases. Comptes rendus des travaux du Laboratoire Carlsberg, Série chimique, 22:129.

Potential energies of biologically important oxidation-reduction systems. Journal of Applied Physics, 9:97.

John Jacob Abel: 1857-1938. Obituary notice. J. Biol. Chem., 124:(not paged; follows p. 572).

Biographical memoir of Walter (Jennings) Jones: 1865-1935. National Academy of Sciences, *Biographical Memoirs,* 20:79.

1939

Some elementary aspects of the potentiometric study of oxidation-reduction equilibria. Cold Spring Harbor Symp. Quant. Biol., 7:1.

Potentiometric and spectrophotometric studies of metalloporphyrins in coordination with nitrogenous bases. Cold Spring Harbor Symp. Quant. Biol., 7:18.

Professor S. P. L. Sørensen. Obituary notice. Science, 89:282.

1940

With J. F. Taylor, T. H. Davies, and C. S. Vestling. Metalloporphyrins. I. Coordination with nitrogenous bases. Theoretical relations. J. Biol. Chem., 135:543.

With J. F. Taylor. Metalloporphyrins. II. Cobalt and manganese mesoporphyrins in coordination with nitrogenous bases. J. Biol. Chem., 135:569.

With M. E. Perkins. Metalloporphyrins. V. A spectrophotometric study of pyridine coproporphyrin I. J. Biol. Chem., 135:643.

1941

A challenge to scholarship (printed lecture). University of Pennsylvania Bicentennial Conference. Philadelphia, University of Pennsylvania Press.

1947

With Judson J. Van Wyk. The luminosity and chromaticity of indicators as a function of pH. J. Am. Chem. Soc., 69:1296.

With J. Shack. Metalloporphyrins. VI. Cycles of changes in systems containing heme. J. Biol. Chem., 171:143.

1948

Topics in Physical Chemistry. Baltimore, Williams & Wilkins Co. xv + 738 pp.

With T. H. Davies, C. C. Porter, J. F. Taylor, J. J. Shack, C. S. Vestling, and J. R. Weisiger. A systematic treatment of coordination complexes of metalloporphyrins and nitrogenous bases. Federation Proceedings, 7:499.

1949

With J. Harris and L. L. Rosenberg. Coordination of proteins with ferromesoporphyrin. J. Biol. Chem., 178:1009.

1950

Leonor Michaelis: 1875-1949. Science, 111:55.

1952

Topics in Physical Chemistry. 2d ed. Baltimore, Williams & Wilkins Co. xviii + 777 pp.

Studies on a chemical continuum. Bulletin of the Johns Hopkins Hospital, 90:228.

With R. W. Cowgill. Metalloporphyrins. VII. Coordination of imidazoles with ferrimesoporphyrin. J. Biol. Chem., 198:33.

Barnett Cohen: 1891-1952. An appreciation. Bacteriological Reviews, 16:205.

1953

With L. L. Rosenberg. Metalloporphyrins. VIII. Coordination of ferromesoporphyrin with proteins. J. Biol. Chem., 205:617.

1955

Introduction to: Symposium on electron transport in the metabolism of microorganisms. Bacteriological Reviews, 19:234.

1956

With H. J. Lowe. Studies on oxidation-reduction. XXIV. Oxidation-reduction potentials of flavin adenine dinucleotide. J. Biol. Chem., 221:983.

1960

Oxidation-Reduction Potentials of Organic Systems. Baltimore, Williams & Wilkins Co. xi + 584 pp.

1963

A critique of certain parts of the 1961 report of the commission on enzymes. Science, 141:995.