

# A SYMPOSIUM ON THE PHYSICAL CHEMISTRY OF THE PROTEINS<sup>1</sup>

## INTRODUCTION TO THE SYMPOSIUM

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At the semi-annual meetings of the American Chemical Society and on other occasions some of the Divisions of the Society, either alone or in collaboration with others, have organized symposia, the purpose of which has been the consideration of the advances in research in the several fields of their scope and the presentation of authoritative and critical summaries of those subjects which are important for the development of pure and applied chemistry. It may be said of the proteins, more than of any other group of compounds, that they are the essence of life, performing as they do in living organisms many important and diverse functions. In recent years data having to do with the nature and behavior of the proteins obtained by physical-chemical observations as distinct from organic-chemical and biochemical methods have been accumulating rapidly, so that it seems a suitable time to attempt to coördinate the knowledge that has become available. The Divisions of Colloid Chemistry and of Physical and Inorganic Chemistry have united their efforts with this end in view.

To study proteins as macromolecules, it is required first of all to learn about their mass, shape, and structure. This is accomplished by the use of experimental procedures such as surface films, surface potential differences, sedimentation, diffusion, osmotic pressure, electrophoresis, viscosity, double refraction of flow, dispersion of dielectric constant, etc. The results arrived at through work along these lines are summarized by the participants in this Symposium.

The chemist is interested in these substances because they have many, if not all, of the properties of molecules. The organic chemist considers their composition, which is derivable from a study of the hydrolytic decompositions. On the other hand, the physical and colloid chemist is

<sup>1</sup> This Symposium was held by the Division of Physical and Inorganic Chemistry and the Division of Colloid Chemistry at the Ninety-sixth Meeting of the American Chemical Society, held in Milwaukee, Wisconsin, September, 1938.

concerned with the molecular weight, molecular form, and solubility relationships, or in a few words, the behavior of these substances as macromolecules. In the reports to follow, the chief concern is the structure and nature of the proteins regarded as physical-chemical units and not as organic compounds.

In the opening paper Langmuir and Schaefer give an account of their recent important work with protein films. After a brief description of the methods used in the formation of the films, their structure is discussed in terms of such measureable properties as thickness, compressibility, insolubility, viscosity, plasticity, and anisotropy after shear or linear compression. Possible explanations are given for certain of these properties in terms of the Wrinch cyclol theory. In the concluding sections there are described some new aspects of the specific reactivities of urease, catalase, and pepsin monolayers.

The extraordinary importance of solubility is universally recognized in chemistry. Recent progress has resulted because investigators are learning how to take into account forces of interaction between ions, dipole ions, and solvent molecules. Experimental and theoretical contributions of distinct merit in these directions have been made by the authors of the next two reports. On the experimental side of the subject, Cohn and his associates have provided data which are indispensable for the development of our subject. In the present report we find a discussion of the parameters in terms of which the structure of protein molecules may be described. Thus, detailed consideration is given to methods by which information is gained regarding the size and shape of protein molecules and by which the number and distribution of the electrically charged groups are determined. Extremely useful tables of certain physical constants for a number of proteins are appended.

Theoretical work by Kirkwood has determined the course of many experiments in protein chemistry. Continuing his work in the statistical mechanics of liquid solutions, the present report reviews and extends the author's work having to do with the electrical interaction of spherical dipolar ions and ordinary ions and extends the theory to give the limiting law for dipolar ions of elongated shape in solution with common electrolytes. The theory is employed to determine from the solubility data the structure and dipole moments of simple dipolar ions.

One of the most characteristic properties of proteins is denaturation. Although the term is used frequently, its exact meaning is still somewhat elusive. The situation has been greatly improved by recent theoretical work. Representative of it is the present contribution of Eyring and Stearn, in which the process of denaturation is pictured as the simultaneous breaking of a number of weak bonds in the protein molecule with

resulting loss of structure, i.e., a large increase in randomness. In this way solvent is eliminated and the solubility is decreased. Activation in denaturation comes from the breaking of these bridge bonds.

The greatly improved technique of electrophoresis measurements due to Tiselius makes possible many important investigations in this field. Longsworth and MacInnes describe several modifications which they have made in this apparatus and give a summary of the conditions necessary for a disturbance-free process. In an important part of their paper these authors have made a study of some of the boundary anomalies which occur, especially with the concentrated protein solutions with which one has to work in preparative investigations.

With the desire to reduce to the absolute minimum the cost of ultracentrifugal analysis of protein and other systems, McBain is developing new types of "spinning top" ultracentrifuges. These are to be contrasted with the suspended rotor types of air turbine ultracentrifuges which have been developed by Beams, Wyckoff, and Bauer. In the new McBain opaque ultracentrifuges, sedimentation equilibrium and sedimentation velocity may be measured accurately by the application of chemical and biological methods after the ultracentrifugation, thus making optical accessories unnecessary. Methods of immobilization are considered, and typical results are cited.

The isolation of certain of the virus proteins by Stanley several years ago was a remarkable achievement. It appears that at least some members of this group of substances are giant molecules of the nucleoprotein type. As such they have been characterized by physical methods. Lauffer and Stanley outline the results of this nature which have been obtained to date with the tobacco mosaic virus protein, and show how data regarding size and shape may be deduced from them. The results of ultrafiltration, x-ray diffraction, and sedimentation studies are in reasonably good agreement with one another.

As Heidelberger remarks, the inclusion of studies on precipitin and agglutinin reactions in such a symposium as this might have occasioned considerable surprise a few years ago. However, one learns from his report that antigen-antibody reactions may follow quantitative equations which are derived from the mass law, assuming an initial bimolecular reaction followed by competing bimolecular reactions leading to large aggregates. Work of this type has led to the isolation and study of pure antibodies and has provided a new conception of the function of salts in these reactions. The molecular kinetic methods of investigation have proved to be useful in the characterization of the antibodies and in studying the nature of the product formed when toxin and antitoxin react.

The Symposium is concluded with a report by Abramson, Gorin, and

Moyer on the polar groups of protein and amino acid surfaces in liquids. As indicated by electrical mobility and isoelectric point data, changes in the relative strength of acidic or basic radicals of organic ampholytes, such as proteins and amino acids, may or may not occur in surface formation, and such substances are classified on this basis. By means of the inter-ionic attraction theory, calculations are made for the electrical charge of proteins. The importance of these methods of approach to problems in biological systems is described.

The breadth of the subject selected for this Symposium has proved to be a source of considerable difficulty, and it has been found impossible to include detailed discussions of such modes of attack as ultracentrifugal sedimentation and x-ray analysis which, after all, have perhaps given the most direct proofs of the existence of the protein molecule. Also, speculations on the constitution of the protein molecule based upon the amino acid composition are of utmost interest. For instance, Bergmann has postulated a general law expressing the constitution of the proteins as a function of the frequency of the occurrence of the several amino acids. The frequency values obtained from the analytical data and the total number of amino acid residues in the molecule are multiples of the powers two and three. These facts are entirely consistent with the grouping by Svedberg of protein molecules into definite molecular weight classes. Svedberg and Bergmann have presented comprehensive summaries of their work in recent volumes of *Chemical Reviews*. Unfortunately, neither of these scientists was available for this Symposium.

However, it is felt that some success has rewarded our efforts to bring together investigators from representative laboratories, because the summaries produced are uniformly authoritative, at least reasonably comprehensive, and highly suggestive. Some deal with selected physical-chemical aspects of the subject, and others show how this information is being applied in biology, pathology, bacteriology, and other sciences.

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