

PRESIDENTIAL ADDRESS.

Delivered at the ANNUAL GENERAL MEETING held on March 30th, 1939.

The Rôle of Osmotic Pressure in the Development of Chemical and Biochemical Science.

By FREDERICK G. DONNAN, C.B.E., D.Sc., LL.D., F.R.S.

It was a fortunate moment for the development of chemical science when De Vries turned van 't Hoff's attention to the quantitative measurements of osmotic pressure which the German botanist Pfeffer had already made, for van 't Hoff, following up this clue, was led to the discovery of the general law relating the osmotic pressure of a dilute solution to the molecular concentration of the solute and the absolute temperature. It is not my purpose to discuss van 't Hoff's famous equation, $PV = iRT$, where P is the osmotic pressure, V the volume of the solution containing 1 gram-mol. of the solute, R the universal gas constant, and T the absolute (Kelvin) temperature. Suffice it to say that in the case of dilute solutions of non-electrolytes the factor i was found to be nearly unity, and its strikingly higher values for dilute solutions of electrolytes in water formed one of the strongest arguments for the general validity of Arrhenius' theory of ionisation in aqueous solution. The important point to notice is that van 't Hoff was now in possession of a weapon which enabled him to apply the firmly established laws of thermodynamics to solutions. He already knew that he could, provided the gas laws were known, place the law of chemical equilibrium in a mixture of gases on a simple and sure thermodynamic basis. His method lay in carrying out reversible operations with gases by means of semipermeable membranes and gas pistons. Van 't Hoff saw that a precisely similar method could now be applied to dilute solutions, *i.e.*, by means of osmotic pistons and semipermeable membranes, since the laws relating to osmotic pressure in such cases were now known.

The results obtained by van 't Hoff were presented to the Royal Swedish Academy of Sciences on October 14th, 1885, and were published in 1886 in volume 21 of the *Transactions* of the Academy. This famous paper can be read in volume 110 of Ostwald's "Klassiker der exakten Wissenschaften," edited with notes by G. Bredig. Needless to say, I have no intention on the present occasion of discussing the details of van 't Hoff's work, and must content myself by remarking that he obtained the general law of chemical equilibrium in dilute solution, showed by thermodynamical reasoning that, in the case of a volatile solute which obeyed Henry's law, $i = 1$, and that from measurements of the lowering of vapour pressure of a solvent or the depression of its freezing point, caused by a solute in dilute solution, the value of i could be calculated. He found in this way that for a non-electrolyte, such as cane sugar, in dilute aqueous solution the value of i was practically equal to unity.

Two very important practical results flowed from van 't Hoff's osmotic-thermodynamic treatment of dilute solutions. In the first place, the approximate molecular weights of non-electrolytes could be securely determined from measurements of the lowering of vapour pressure (or the elevation of boiling point) and the depression of freezing point of dilute solutions, since the theory of these methods was now placed on a sure basis. This result was of very great importance for organic chemistry, and, as is well known, Beckmann, by means of his delicate variable-zero thermometer, soon brought this method into common laboratory use. Secondly, in the case of electrolytes in aqueous solution, the same technique enabled approximate values for the degree of ionisation to be determined. This method was of great importance in connection with the then rapidly developing theory of Arrhenius, though, owing to the deviation of ions from van 't Hoff's laws in ordinarily "dilute" solutions, the results, as we know now, were not so easy to interpret, and led to various discrepancies, especially in the case of aqueous solutions of multivalent ions. I do not think that van 't Hoff himself or any of his immediate collaborators made any direct measurements of osmotic pressure, since in the case of most substances of moderate molecular weight it is difficult to obtain semipermeable membranes. In the work of van 't Hoff, osmotic pressure and the laws relating to it played essentially a theoretical conceptual part, which enabled him to apply the laws of thermodynamics to the properties of solutions in a simple

manner which could be easily understood by the chemists and physicists of his day. I need scarcely remind this audience that in subsequent years very elaborate direct measurements of the osmotic pressure of solutions were made, especially by Morse and Frazer in the United States, and by the Earl of Berkeley and his collaborators in England. These investigations were more particularly directed to the measurement of osmotic pressures of relatively concentrated solutions, and required the construction of special membranes which could withstand high pressures. The results showed how the osmotic pressure of these relatively concentrated solutions, for example, of cane sugar, deviated from the simple $PV = RT$ law. Writers of textbooks often refer to such results as deviations from "van 't Hoff's law," but it is to be noted that van 't Hoff's law was $PV = iRT$. Only in the case of a volatile solute which obeyed Henry's law in the range of concentrations employed was it possible for van 't Hoff to prove by thermodynamical reasoning that $i = 1$. In the vast majority of cases such a test was not possible, so that it was a matter of experiment to determine at what degree of "dilution" the value $i = 1$ could be employed (for non-ionised substances). From many conversations which I had with van 't Hoff, I know that he considered the $PV = RT$ law to be a "limiting law," which possessed approximate applicability (in the case of a non-electrolyte) only to very dilute solutions.

The theory of solutions as elaborated by van 't Hoff, Arrhenius, Ostwald, and Nernst played an important part in the development of biochemistry. For an exhaustive account of this I cannot do better than refer you to the two volumes of H. J. Hamburger's "Osmotischer Druck und Ionenlehre in den medicinischen Wissenschaften" (Bergmann, Wiesbaden, 1900—1904) and, for a later account, to R. Höber's "Physikalische Chemie der Zelle und der Gewebe" (Engelmann, Leipzig, 1922). Although the ordinary chemist may be only indirectly interested in the subject of osmotic pressure, since, so far as his practical operations are concerned, he has seldom to do with semipermeable membranes, the physiologist and biochemist are deeply concerned with the phenomena produced by the semipermeable membranes occurring in living organisms. Owing to the wealth of results obtained in this important field of investigation, I can only refer to one or two matters of special interest to the biochemist. Physiological measurements have shown that the average hydrostatic pressure of the blood in the capillaries is higher than that in the intercellular fluid which bathes the cells of the tissues and organs and which is separated from the capillary blood by the endothelial cells of the capillary walls. Since these capillary wall membranes are permeable to the non-protein contents of the blood, it occurred to the renowned English physiologist Starling that a rapid ultrafiltration from blood to intercellular fluid must occur, unless there was some counterbalancing force. It was known that the total osmotic pressure of blood, amounting to about 6.5 atmospheres, was chiefly due to the inorganic salts and organic "crystalloids" dissolved in the plasma. It was obvious that the osmotic pressure due to these substances could play no part in the production of any counterbalancing pressure-difference, since the capillary membranes are permeable to them. Up to the time of Starling, physiologists had neglected the possibility of the existence of an osmotic pressure due to the non-permeating proteins of the blood, but Starling perceived that herein lay the true explanation, and by his pioneer measurements of this osmotic pressure provided a complete experimental proof of the correctness of his view. The work of later investigators has fully corroborated the validity and importance of Starling's great discovery, and demonstrated that there is no "secreting" action of the endothelial cells of the capillary membranes. In this connection I must refer you to the important work of Krogh and to his book "The Anatomy and Physiology of the Capillaries" (Yale University Press, 1922).

The second example to which I wish to refer relates to the secretion of urine by the kidney. The *final* action, as everybody knows, is the separation from the circulating blood of an aqueous solution of some of its constituents, chiefly the waste products of cell metabolism. It is an interesting and important problem to calculate the net minimum osmotic work involved in such a separation. This problem was solved by A. V. Hill in the case of solutes obeying van 't Hoff's law and by means of a very ingenious adaptation of van 't Hoff's osmotic-thermodynamic method. You will find an account of Hill's calculation on pages 94—96 of Barcroft's "Respiratory Function of the Blood" (Cambridge University

Press, 1914). Owing to the work of many investigators, amongst whom I would specially mention A. R. Cushny and A. N. Richards, a great deal is now known about the secretion of urine. Those of you who are interested in the matter will find a masterly account in Richards' Croonian Lecture, entitled "Processes of Urine Formation" (*Proc. Roy. Soc.*, 1938, B, 126, 398). It appears that the first process is simply an ultrafiltration of the permeable constituents of the blood through the cell membrane of the glomerulus. This takes place against the "colloid osmotic" pressure of the protein constituents of the blood, the necessary difference of hydrostatic pressure being supplied by the action of the heart. There is no question of any metabolic "secreting" action in this first stage. In the second stage, however, the valuable blood constituents, *e.g.*, water, glucose, salt, etc., are in varying degrees taken back into the blood stream through the cell membranes of the tubules. This second process cannot be explained on the basis of osmotic pressure and diffusion gradients, since the regulative and composition-varying actions of the tubule cells are obviously linked with metabolic processes (oxidative and other) which supply free energy. In this case, as in all the cases of true "secretion," the physico-chemical mechanism of the linkage is quite unknown and remains a master problem for the biochemistry and biophysics of the future. In many such cases we may not have to deal with systems which are in or near a state of thermodynamic equilibrium, but with "stationary" states due to the concurrence and interlinkage of free energy-supplying and free energy-dissipating processes. This point has been recently emphasised by A. V. Hill, and in recent years Straub and Teorell have described simple *in vitro* models of certain stationary states.

Naturally the existence of the master problem to which I have referred has not escaped the attention of physiologists and biochemists. Anyone interested will find a very valuable and relevant account of the energetics of cell processes in Otto Meyerhof's monograph "Chemical Dynamics of Cell Phenomena" (Lippincott, Philadelphia and London, 1924), though, as might be expected, later investigations require a modification of some of the statements contained in this book.

The last example which I shall quote in this part of my Address is the case of the red blood cells. Since it appears that the metabolic processes in these cells are at a rather low ebb, it is probable that the contents of the red cells are, at any moment, not far removed from thermodynamic equilibrium with the circumambient blood plasma. Some ten or twelve years ago, D. D. van Slyke and L. J. Henderson (together with their collaborators) attacked this problem from the point of view of osmotic and ionic membrane equilibria, with very encouraging results. For the state of these investigations as they stood up to 1927 I must refer you to van Slyke's monograph "Factors Affecting the Distribution of Electrolytes, Water and Gases in the Animal Body" (Lippincott, Philadelphia and London, 1926) and to Henderson's book "Blood, A Study in General Physiology" (Yale University Press, New Haven, 1928). Although later investigations in this field appear to indicate that the problem is perhaps not so simple as was at first thought, there can be little doubt that the mode of attack initiated by these pioneer investigations of van Slyke and Henderson is fully justified, provided that the metabolic activity of the red cells can be practically neglected, and that the existence of a cell membrane with the assumed and constant selective permeability is experimentally verified.

In dealing, at the beginning of this Address, with the part played by osmotic pressure in van 't Hoff's work on the theory of dilute solutions, I omitted to mention that this osmotic method constituted an essential part of Nernst's theory of the electrical potential-differences between metals and solutions of their salts, and led him to his famous logarithmic equation. Although nowadays we should deal with this question in a different manner, we cannot afford to ignore a method which led to a result of such great importance in the development of chemical science. I must also not fail to mention that the theoretical work of Nernst, Kohlrausch and many others on the diffusion of electrolytes, which led, for example, to various well-known formulæ for diffusional potential differences, depended essentially on deriving the purely diffusional driving forces from osmotic gradients and the laws of osmotic pressure. If I may be allowed a personal reference, I employed this method many years ago in deriving equations for the Hall effect in dilute aqueous solutions of electrolytes. Curiously enough, these equations received their first verification from the

experimental work of Marx and of Moreau on the Hall effect in flames, and of Wilson on the Hall effect in rarefied gases. I cannot discuss such matters on the present occasion, but anyone who is interested may be referred to L. L. Campbell's monograph on "Galvanomagnetic and Thermomagnetic Effects" (Longmans, Green & Co., London, 1923).

It is probably well known to everyone at the present day that the fundamental basis of the (thermodynamic) theory of osmotic pressure was given to the scientific world by J. Willard Gibbs some ten years before the publication of van 't Hoff's Swedish Academy paper. Indeed Gibbs was obliged, in later years, to point out that van 't Hoff's approximate equations could have been deduced from his own more general results when applied to the special case of dilute solutions. Since the general and exact theory of osmotic and membrane equilibria on the basis of Gibbs' method has been dealt with very fully by E. A. Guggenheim and myself in two relatively recent papers in the *Zeitschrift für physikalische Chemie* (1932, A, 162, 346; 1934, A, 169, 369), and since E. A. Guggenheim has given an excellent and comprehensive treatment of this subject in his contribution to volume I of the "Commentary on the Scientific Writings of J. Willard Gibbs" (Yale University Press, New Haven, 1936) and in his "Modern Thermodynamics by the Methods of Willard Gibbs" (Methuen, London, 1933), I need not say very much concerning this matter on the present occasion. I must, however, ask your permission to say a little, since the practical use of the equations for osmotic pressure will have an important bearing on what I shall have to say later on.

From Gibbs' point of view, the phenomenon of simple osmotic pressure equilibrium is an example of the equalising of an original difference of chemical potentials by a difference of hydrostatic pressures. If, for the sake of simplicity, we agree to neglect the compressibilities of the liquid phases, the matter can be stated very briefly and simply. Denoting the pure solvent phase by the numerical suffix 1, and the solution phase by the numerical suffix 2, let us denote the molar chemical potential of the solvent by μ , and the hydrostatic pressure by P . Then for the osmotic equilibrium of the solvent $\mu_1 = \mu_2$, and $P_2 - P_1 = \pi$ (the osmotic pressure), where π is a positive quantity and $P_2 > P_1$. In the case of an ideal solution we may write $\mu_2 = \phi(T) + P_2 v_0 + RT \log N_0$, where v_0 is the volume of one mol. of the pure liquid solvent at the given temperature T and at zero pressure, and N_0 is the mol.-fraction of the solvent in the solution phase 2. The second term on the right-hand side of this equation can be justified on general thermodynamical grounds, and the third term follows from one of the (defined) properties of an ideal solution, namely, that the partial molar fugacity of the solvent in the vapour phase in equilibrium with the solution (at the given pressure and temperature) is proportional to the mol.-fraction of the solvent in the solution. For μ_1 we have now $\mu_1 = \phi(T) + P_1 v_0$, and hence since $\mu_1 = \mu_2$, $(P_2 - P_1)v_0 = -RT \log N_0$. The equation for the osmotic pressure is therefore $\pi = P_2 - P_1 = (RT/v_0) \log (1/N_0)$. In the usual case of a non-ideal solution, we can indicate the deviation from ideality by introducing the "activity" coefficient f_0 and writing $\mu_2 = \phi(T) + P_2 v_0 + RT \log N_0 f_0$. For the present purpose it is, in general, more convenient to employ, instead of f_0 , Bjerrum's osmotic coefficient g , defined by the equation $g \log N_0 = \log N_0 f_0$, and so write $\mu_2 = \phi(T) + P_2 v_0 + gRT \log N_0$. Then we have $\pi = P_2 - P_1 = (gRT/v_0) \log (1/N_0)$. This is the most general equation (neglecting compressibilities) for the osmotic pressure in the case of simple osmotic equilibrium. I make no excuse for entering into this brief discussion on the present occasion, since certain recent publications exhibit a profound ignorance of the present state of knowledge in this branch of chemical science.

In the case of very dilute solutions, that is to say, solutions which are so dilute that the mol.-fractions of all the solute species are very small in comparison with that of the solvent, the general equation for the osmotic pressure admits of great simplification.

Denoting any solute species by the suffix s and mol.-numbers by m , we may in those cases make the following approximations :

$$\begin{aligned} \log (1/N_0) &= -\log (1 - \sum_s N_s) = \sum_s N_s \\ N_s &= m_s / (m_0 + \sum_s m_s) = m_s / m_0 \\ V &= m_0 v_0 \end{aligned}$$

where V is the volume of the solution. Introducing these approximations, the general equation takes the approximate form $\pi = (gRT/V)\sum_s m_s = gRT\sum_s C_s$, where C_s denotes the molar volume concentration of a solute species. It will be seen that this equation is the same as that of van 't Hoff, with Bjerrum's osmotic coefficient g playing the rôle of van 't Hoff's factor i . It will be recollected that van 't Hoff proved that $i = 1$, if the single solute which he was thinking of obeyed his form of Henry's law. In the modern statement, $g = 1$ for an ideal solution, *i.e.*, in the case where the partial molar fugacity (in the vapour phase) of every constituent is proportional to its mol.-fraction in the solution. If van 't Hoff had employed the modern exact form of Henry's (and Raoult's) law, his thermodynamic deduction would have been very similar to that given above, although following a different procedure.

Modern chemical interest in the subject of osmotic pressure arises from a series of discoveries which concern substances of very high molecular weight. The first impulse came from the physiologists and biochemists, whose investigations have led them to study very closely certain important classes of naturally occurring substances such as the animal and vegetable proteins and various complex carbohydrates, *e.g.*, cellulose and starch. Another impulse has come from the industrial use of synthetic polymers, which play such an important part in the production of new materials of construction. It will not be denied, I think, that in the investigation of this new world of "megamolecules" (to borrow an expression from Dr. Wrinch) much has been learned by means of physical and physico-chemical methods which could not have been obtained by the classical methods of "pure" organic chemistry. In this connection the method of X-ray analysis has proved of very great importance, but a great deal of new and valuable knowledge concerning the particle or molecular weight, volume, and shape of these "giant" molecules has been gained by a study of their behaviour in solution. In the chief position of honour we must place the ultracentrifugal method of Svedberg, but measurements of osmotic pressure, viscosity, rate of diffusion, cataphoresis, and double refraction due to streaming and to electric and magnetic fields have all played a notable part.

In consonance with the theme of this Address, I shall confine myself to saying something about only one of these physico-chemical methods, namely, the determination of osmotic pressure. Here the direct measurement has come into its own, and has been of great value in the ascertainment of molecular (or particle) weights in solution. We may ascribe this to several practical reasons, namely (*a*) the impracticability of the usual freezing- and boiling-point methods, (*b*) the comparative facility in obtaining semi-permeable membranes for substances of very high molecular weight, (*c*) the smallness of the osmotic pressures in question, and (*d*) the simplicity and cheapness of the apparatus required.

As regards (*a*), the following remark may be made. Let us consider a non-ionising substance of only "moderately high" molecular weight, say, 40,000. The lowering of freezing point for a solution containing 20 grams per litre would then be about 0.001°, and the osmotic pressure, measured in cm. of water, would amount approximately to 10. An approximate calculation of this sort demonstrates very clearly the practicability of the osmometric method and the impracticability of the ordinary (Beckmann) thermometric methods.

The pioneer exact work on the osmotic pressure of proteins is due to Sørensen in Copenhagen, whilst we must ascribe the great modern development of this particular field to the researches of Adair in Cambridge. In the intervening period the classical investigations of Loeb were made in New York, though Loeb, as is well known, was chiefly concerned with the demonstration of the effects due to the unequal distribution of the freely diffusible ions, and not with the determination of the molecular weights of definite protein species. For an account of this branch of work in the field of proteins (up to 1935), I may refer you to the interesting summary published by Madame Andrée Roche, entitled "Le Poids moléculaire des Protéines" (Conférence faite devant la Société de Chimie biologique, le 7 mai, 1935). The various types of osmometers employed (up to 1929) have been described by Dr. Marie Wreschner in an article entitled "Methoden zur Bestimmung des kolloid-osmotischen Druckes in biologischen Flüssigkeiten," published in Abderhalden's "Handbuch der biologischen Arbeitsmethoden" (Abt. III, Teil B, s. 757—774, 1929). Since the date of this

article, special types of osmometers have been described by P. van Campen (*Rec. Trav. chim.*, 1931, **50**, 915) and by H. B. Oakley (*Trans. Faraday Soc.*, 1935, **31**, 137; 1937, **33**, 372; *Biochem. J.*, 1936, **30**, 868). Oakley's type of osmometer has been developed and somewhat simplified by R. C. Rose (work shortly to be published). Those who are interested in the theory as well as the practice of osmotic and membrane equilibria of substances of high molecular weight may be referred to the account of the Faraday Society Discussion on Colloidal Electrolytes (published as a separate volume, January, 1935, or *Trans. Faraday Soc.*, 1935, **31**, 4).

Owing to the great extent of this comparatively new branch of chemical science, I have so far been obliged to confine my remarks to the somewhat dry method of giving a few references to important summaries. In the remaining portion of this Address, I propose to say something about a particular aspect of it, in which I have been personally interested during the last few years. This concerns the determination of the molecular weights (in solution) of the salts of polybasic acids of high molecular weight, such as are encountered, for example, in gum arabic and the salts of alginic acid. We are not able, in these cases, to reduce the free ionisation by working near the isoelectric point, as in the case of proteins. Hence we are obliged to compensate for the large osmotic effect of the free (alkali) cations by using as large a concentration as possible of a freely diffusible salt, such as sodium chloride. Moreover, as it is not generally possible to obtain a complete compensation by this device, it is desirable to work at such low molarities of the high-molecular salt that graphical extrapolation to the zero concentration limit becomes practicable. This means that extremely delicate and sensitive osmometers have to be employed, since the osmotic pressures to be measured are very small.

Let us represent the high-molecular acid by the formula H_nA , where A stands for the high-molecular "colloid" radical. Complete ionisation of the sodium salt Na_nA in dilute aqueous solution may then be represented by the equation $Na_nA = nNa^+ + A^{n(-)}$. In this case, if the dilution be sufficiently great, it follows (from what I have said in the earlier part of this Address) that $\pi = gRT(n+1)C/M$, where C is the volume concentration (say in grams per litre) of the salt and M its molecular weight.* Of course, if the ionisation be not complete, we must replace n by q , where $q < n$. Now in the limit $C \rightarrow 0$, we have $g \rightarrow 1$ and $q \rightarrow n$, so that we may write $\text{Lt.}_{C \rightarrow 0} \pi/C = RT(n+1)/M$. This equation contains two unknown quantities, namely, n and M . In fact, if $n \gg 1$, as will usually be the case for these high-molecular polybasic acids, the equation just given reduces to the very good approximation $\text{Lt.}_{C \rightarrow 0} \pi/C = RT/Q$, where Q is the equivalent weight of the acid (or salt). Since Q can be easily determined by simple chemical analysis, the osmotic pressure measurements become pointless. A good example of this state of affairs may occur in the case of high-molecular polymeric acids and salts. Q is now the molecular weight of the monomer, so the osmotic pressure results become independent of the degree of polymerisation, provided, of course, that the polymerisation factor (which is n) is large compared with unity. In proof of this theoretical conclusion, I may refer you to the recent interesting work of Werner Kern on the osmotic pressures of aqueous solutions of the sodium salts of the polyacrylic acids (*Z. physikal. Chem.*, 1938, *A*, **181**, 271).

The method of surmounting this difficulty, and thus conferring significance on the measurement of osmotic pressure, is now fairly well known, so I need refer to it only very briefly. In the presence of a sufficiently high *relative* concentration of a freely diffusible salt, such as sodium chloride, there occurs, at equilibrium, an unequal distribution of these diffusible ions, which has the effect of setting up a counter osmotic pressure which tends to compensate, partly or wholly, for the large osmotic pressure due to the free alkali cations of the high-molecular salt. If, as frequently happens in the case of these high-molecular polybasic acids, the "polybasicity" is high, then, in spite of the very high molecular weight, the equivalent weight may be comparatively low. Under these conditions it is not generally possible to employ an equivalent concentration of sodium chloride or other such salt which is sufficiently great, compared with the equivalent concentration of the high-molecular salt,

* From the value of M so obtained, that of the corresponding acid can be derived from the results of chemical analysis.

to secure the desired high compensation of the osmotic effect of the alkali "gegenions" and at the same time avoid agglomeration or actual precipitation.

This difficulty can, however, be surmounted by working as near as possible to the zero concentration limit of the high-molecular salt, for at this limit (which we may reach by graphical extrapolation) the former equation $\text{Lt. } c \rightarrow 0 \pi/C = RT(n+1)/M$ becomes $\text{Lt. } c \rightarrow 0 \pi/C = RT/M$, since, for any finite concentration of the diffusible salt, the ratio of its equivalent concentration to the equivalent concentration of the high-molecular salt becomes infinite in the limit $C \rightarrow 0$. According to views recently expressed by Brønsted and by G. S. Hartley, the osmotic coefficient g , in the case of low molarities of the high-molecular salt and a sufficiently high relative concentration of the freely diffusible salt (*e.g.*, sodium chloride), may be put equal to unity. If that be so, then graphical extrapolation to the $C \rightarrow 0$ limit may not be necessary if a sufficiently high compensation has been attained at finite values of C .

The majority of writers who have been kind enough to refer to the unequal distribution of the freely diffusible ions as the Donnan (or the Gibbs-Donnan) effect seem to labour under the misapprehension that, in the osmotic pressure phenomena which I have described, this unfortunate "Donnan effect" can be comfortably obliterated by the use of a "swamping" excess of the diffusible salt. Such is, however, not the case. This mistaken view arises from the common mathematical error of assuming that when the ratio of two quantities tends to unity their difference must tend to zero. I cannot go further into this matter here, and must refer anyone interested to the article I wrote for the Faraday Discussion to which I have previously referred. It will be seen at once that the uncomfortable Donnan effect persists in the "swamped" limit, and that it is precisely its non-zero difference value at this limit which does the trick! I regret having had to make this personal reference, but, having been kindly credited with the D-effect, I am unwilling to surrender it in just those circumstances where its existence (or persistence) is of most practical value to chemical science.

Before closing this brief theoretical discussion, I should like to mention one or two points. If we make use of only the first two approximations mentioned on p. 710, it will be seen that we arrive at the (approximate) equation $\pi = gRT \sum_s m_s / m_0 v_0$, which may be written $\pi = gRT \sum_s \gamma_s$, where γ_s denotes the ratio of the mol.-number of a solute species to the volume of the pure solvent used in making up the solution. This equation is a better approximation than the equation $\pi = gRT \sum_s C_s$, which was obtained by identifying the total volume V of the solution with $m_0 v_0$ (third approximation on p. 711). The more accurate equation must be used in the case of more concentrated solutions of high-molecular substances, where, although the mol.-fractions of the solute species may be very small compared with the mol.-fraction of the solvent, the volume of the high-molecular solute species may not be negligible.

The rather precise chemical formulation given in the preceding discussion does not imply that we must be necessarily dealing with "true" molecules, *i.e.*, with solution units which are held together solely by purely chemical bonds. These units may be colloid "micelles," although, of course, the equations which I have given assume that, within the range of their applicability, the micelles do not break up, and do not "agglomerate" to units of higher mass.

It is necessary also to note that the molecular or micellar weights obtained by the osmometric method are necessarily mean values which may refer to mixtures of molecules or micelles of varying mass. It is one of the great advantages of Svedberg's ultracentrifugal method that it reveals the presence of such mixtures.

I conclude this discussion by quoting very briefly a few of the results of investigations in which I have been personally interested during the last four or five years. I suggested to Dr. H. B. Oakley that he should investigate the molecular (or micellar) weight in the case of the alkali salts of the acid of gum arabic by means of the osmometric method. Here is one result taken from his work. Molecular weight 240,000, maximum electrovalency (basicity) 200, equivalent weight 1200. Subsequently to this work, Oakley and

F. G. Young applied the same technique to aqueous solutions of rabbit liver glycogen, rabbit muscle glycogen, and methylated rabbit liver glycogen. The results indicated a particle weight of the order of two millions.

Another example of a high-molecular polybasic acid is the alginic acid discovered in certain seaweeds by Stanford in 1883. At my request, Dr. R. C. Rose has made an interesting and comprehensive study of the sodium alginates. As this work is not yet published, I must restrict myself to stating that Rose, employing the osmometric method, has found, in the case of aqueous solutions of the sodium salt of different grades of alginic acid, particle (or molecular) weights varying from about 50,000 to 180,000. I may remark that both the gum arabic acid and alginic acid are carboxylic derivatives of complex carbohydrates. It is interesting to note that gum arabic (or gum acacia) was one of the substances classed as a true colloid by Thomas Graham in 1862. It would, no doubt, have greatly interested him to know that some seventy-two years later the molecular weight would be determined at University College, London.

I cannot conclude this highly condensed sketch of the part played by osmotic pressure in the development of chemical and biochemical science without at least a passing reference to the comprehensive work of Schreinemakers on osmosis. To this, in the main, theoretical investigation Schreinemakers devoted the last fourteen years of his active life at the University of Leiden. We may describe it as a logical deductive study based on thermodynamics and geometry, of which sciences Schreinemakers has always been a master. I think that this work, when it becomes better understood, is destined to exert an important influence on the future development of physiology and biochemistry. Recently Schreinemakers has summarised the results of his investigations in a book entitled "Lectures on Osmosis" (Naeff, The Hague, 1938).

In this my swan song as the retiring President of the Chemical Society, I fear I have chosen a subject which may have comparatively little attraction for the eager young chemists of the present day. In the rushing tide of new discoveries and everchanging and developing theories, there is but little time, and perhaps even less inclination, for the quiet contemplation of the older and simpler things. No doubt this very statement betrays that serenity (or is it ignorance?) of age, which loves to listen to the music of the past and cares but little for the thunder and fury of the wonderful present. Be that as it may, I have tried to show, in some small measure, and in one very particular field, that the old things, when true and useful, never really lose their linkage with the wheel of Time, and so are always new and present.