

APPENDIX I

The Model of the Biological Fixed-Charge System

(Reproduced from Chapter 4 of Ling, 1962)

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4.1. Introduction—The 1951–52 Model

In 1951 and 1952, the author presented a version of the present hypothesis. According to this early version, selectivity of one alkali-metal ion over another is achieved by a difference in association energy and by an enhanced degree of ionic association through fixation of one species of ion; the fixed ions were called “fixed charges.”

In the early model, the author followed Bjerrum’s theory of ion-pair formation (1926). The treatment differed from that of Bjerrum in that it included the effect of dielectric

saturation, a phenomenon of particular importance to the present case. If dn is the average number of counterions within a spherical shell of thickness dr and at a distance r from the center of a fixed ionic group, then

$$dn = \frac{N_{\pm}}{V} 4\pi r^2 \exp\left(\frac{-Z_1 Z_2 \epsilon^2}{D(r) k T r}\right) dr. \quad (4-1)$$

Here N_{\pm} is the number of counterions in the volume V ; Z_1 and Z_2 are the valences of the charges; ϵ is the electronic charge; k is the Boltzmann constant; T is the absolute temperature; and $D(r)$ is the effective dielectric value, which varies with r as a result of the freezing in (dielectric saturation) of the water molecules in the intense field immediately surrounding an ion (Sack, 1926, 1927; Debye, 1929; Webb, 1926; Hasted *et al.*, 1948; Grahame, 1950). We considered pdr ,

$$pdr = \frac{dn}{N_{\pm}/V} \quad (4-2)$$

as the probability of finding a counterion within the shell. Using the values of 2.0Å for the radius of the hydrated K^+ ion and 2.8Å for the hydrated Na^+ ion and a microcell radius of 20Å, we estimated a selectivity ratio K^+/Na^+ of 7. The details of this calculation are given in Appendix C; Figure 4.1 presents the results. We have reproduced Bjerrum's curve showing the probability of finding a cation in a shell r Å (abscissa) away from the anion as part B of this figure. The shaded area corresponds to the volume within the microcell of 12Å radius illustrated in part A.

This earlier model served many useful purposes, but the theory, as such, had serious limitations. First, despite its general acceptance (Fowler and Guggenheim, 1939; Harned and Owen, 1958; Kortüm and Bockris, 1951), the concept of hydrated ionic radii lacks clear physical significance. The hydrated ionic radius is usually only a few tenths of an angstrom unit larger than the crystal radius although a single water molecule is 2.7Å in diameter (see Appendix C; interpretation according to the present model is given in Section 4.4D). The use of the hydrated ion concept thus prevented quantitative improvement of the model. Second, the rigidity imposed upon the theory by the acceptance of a set of hydrated diameters of constant magnitude, and hence a fixed order of preference for different ions, is at variance with an increasing amount of evidence demonstrating the variability of ionic preference.

It was not until some years after 1952 that I became aware of any system, living or non-living, that shows an unequivocal selective ionic accumulation of alkali-metal ions in any order other than $K^+ > Na^+$. Thus my early model seemed adequate. In the years that followed, however, it gradually became clear that, in a number of other systems in which ionic selectivity is a matter of greater simplicity, different and opposite orders of preference exist. Investigators in these fields had, in fact, already offered qualitative explanations to account for the diverse orders of preference observed for the monovalent cations.

Following the work of Wiegner and Jenny (1927), Jenny (1932) concluded from studies of clays and permutites that "the observed irregularities in the lyotropic series of natural aluminum silicates may be interpreted as various stages in the reversal of the normal hydration order of the exchanging cations. From the viewpoint of hydration of ions, it is

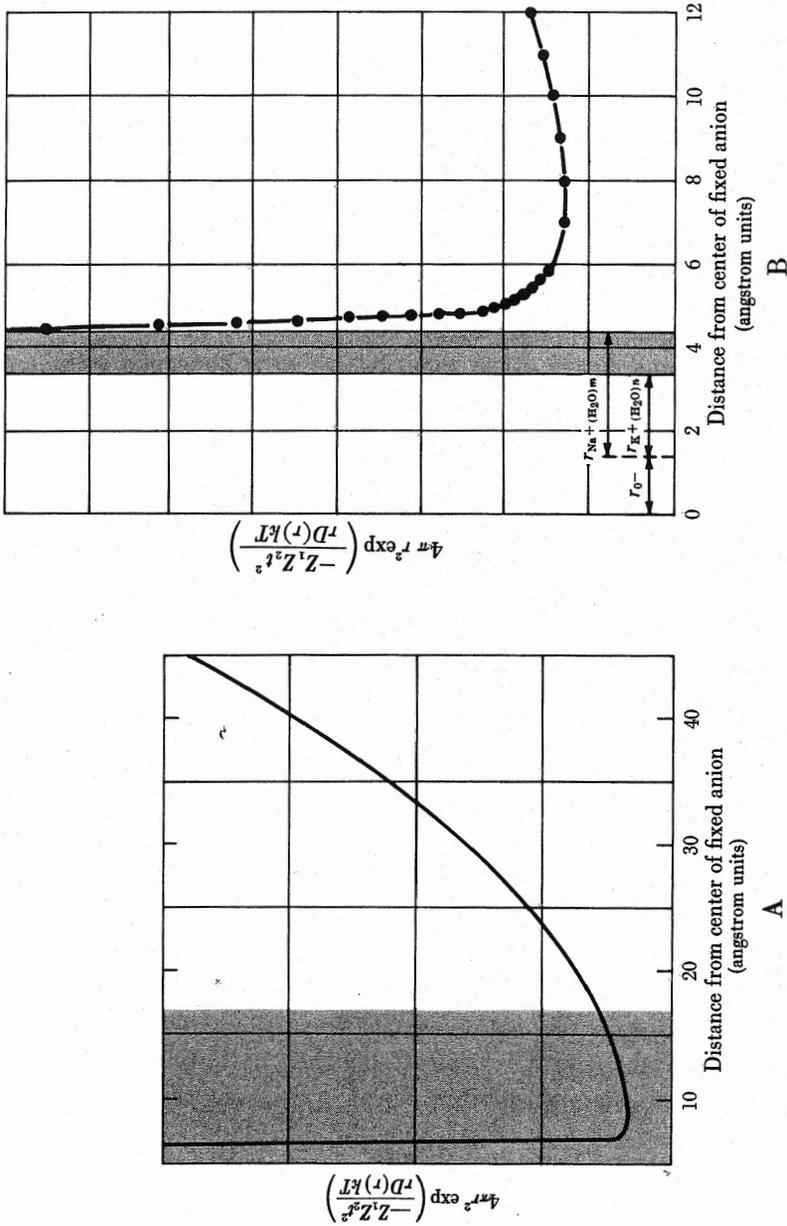


FIGURE 4.1. The probability of finding a counterion at various distances from the center of a microcell. The shaded area in A represents the volume available to the smaller hydrated K^+ ion (radius = $r_{K^+(H_2O)_n}$) but not to the larger hydrated Na^+ ion (radius = $r_{Na^+(H_2O)_n}$); r_0 stands for the radius of the singly charged oxygen. In B, taken from Bjerrum (1926), the shaded area corresponds to the volume of a microcell of the size shown in A.

logical to connect the reversal of the lyotropic series with a dehydration of ions." Bungenberg de Jong (1949) ascribed the difference in the order of selectivity for different ions among systems possessing unlike functional groups to the different polarizabilities of these groups (see also Bregman and Murata, 1952; Bregman, 1953). After Eisenman *et al.* (1957),* as quoted by Isard (1959), postulated that the variation in the lyotropic series was due to a change in the electrostatic field strength of the fixed anionic sites, a convincing system could be erected to explain the selectivity orders observed in nature. These investigators hypothesized that with the increase of the field strength the interacting cations would lose their hydration shells in an orderly fashion, the least hydrated cations losing their hydration shells first.†

Eisenman and co-workers postulated eleven orders out of the 120 possible permutations for the five alkali-metal ions. They then showed that these eleven orders could account for a large number of the "irregular" lyotropic orders encountered in various ionic studies.** This hypothesis led to refinements in the calculation of the association energies of the various ions mentioned in the introduction (for an abstract, see Ling, 1957).

4.2. The Present Model

A. THE DEFINITION OF c - AND c' -VALUES AND THEIR ANALOGUES

Acids bearing the same carboxylic groups may have widely varying acid-dissociation constants: the pK value of acetic acid is 4.76, but the pK value of trichloroacetic acid is less than 1.0; the pK value of the carboxyl groups of uncharged glycine $\text{NH}_2\text{CH}_2\text{COO}^-$ is 4.30 (Edsall and Blanchard, 1933), that for the charged glycine $\text{NH}_3^+\text{CH}_2\text{COO}^-$ is 2.31 (Zief and Edsall, 1937). Thus, although the three substituent chlorine atoms of trichloroacetic acid and the amino group of glycine are spatially separated from the dissociating carboxyl group, they markedly weaken the attractive force between the carboxyl group and its proton. This phenomenon is called the inductive effect.

G. N. Lewis in 1916 and 1923 proposed that the inductive effect is a result of an electrical dissymmetry caused by the unequal sharing of electrons between unlike atoms. Pairs of shared electrons are thus displaced without being dissociated from their original atomic octets; this produces a similar displacement in the next link and the effect is propagated along a multiatomic molecule. The electronegativity of an atom or group in a molecule is the measurement of the tendency of this atom or group to draw electrons toward itself (Pauling, 1948). Substitution of hydrogen atoms by the more electronegative chlorine atoms, as in trichloroacetic acid, leads to withdrawal of electrons from an attached residue and hence a reduction of electron density in it. This is a negative inductive effect, $-I$ -effect. The NH_3^+ group which is electronegative also exerts a $-I$ -effect. Substitution

* The theories of Jenny and Bungenberg de Jong, as well as that of Eisenman, and coworkers, up to 1957 all dealt with the effects of hydration and dehydration in a qualitative manner. In deriving a quantitative theory one must take into account the effects of dielectric saturation as well as the hydrated diameters; only in this way can a significant selectivity between K^+ ion and Na^+ ion be theoretically derived.

† This order of dehydration is the reverse of that envisioned by Jenny (1932); he stated that the most hydrated ion will be the first affected by the dehydration process.

** Eisenman (1962) has summarized the views of these authors.

of hydrogen by less electronegative groups releases electrons and increases the electron density of a connected atom creating a + *I*-effect (Ingold, 1953).

The inductive effect is an electrostatic effect mediated through intervening atoms and intimately dependent upon their number, polarizability, and other characteristics. Another electrostatic effect emanates from substituent groups and is transmitted through space along the axis of shortest separation of the interacting atoms. This is called a direct effect, *D*-effect. The difference between the acid dissociation constants of acetic acid and of glycine may be accounted for by the combined *D*-effect and *I*-effect, together termed the *F*-effect. This nomenclature, used mostly by European authors (see Hermans, 1954), has been adopted in this monograph for its simplicity.

Let us begin with a singly charged and isolated oxygen ion O^- and assume that it is associated with a monovalent cation G^+ (Figure 4.2A). Let us also assume that the equilibrium distance between the "center of gravity" of the extra electron of this singly charged oxygen and the geometrical center of the cation is r_f . We now build up a complex molecule such as that shown in Figure 4.2B, bearing one or more chains of varying dipolar groups as well as single charges. These groups interact with the cation G^+ ; their interaction energy may be analyzed and resolved into three terms.

(1) Direct electrostatic effects produced by charge-bearing monopolar or dipolar groups and transmitted through the shortest spatial distance. Resolving the dipoles into single charges one may represent this class of effects by

$$\sum_{i=1}^n \frac{Z_G Z_i \epsilon^2}{D_i r_i}$$

Here Z_G and Z_i are the valences; ϵ is the electronic charge; r_i is the shortest distance in space between the charge-bearing group and the center of the cation G^+ ; and D_i is the effective dielectric constant for that particular interaction.

(2) The *I*-effect, which produces induced dipoles along the whole molecule. The induced dipoles may again be resolved into single charges and absorbed in the first term.

(3) The *I*-effect and the *M*-effect (mesomeric or resonance effect), which create a change of electron density and a displacement of the center of gravity of the electron cloud of the oxygen atom on the functional group. This displacement of the center of gravity of the functional group is analogous to other induced dipoles mentioned under (2); it too will be absorbed in the first term. The varying electron density may be represented by a varying charge $\eta\epsilon$, where η is a positive number and ϵ is the electronic charge located at a distance r_f from the center of the cation G^+ . D_f is the effective dielectric constant within this distance. The net effect corresponds to the sum of (1) the *D*-effect, and (2) and (3), the *I*-effects:

$$\frac{Z_G \eta \epsilon^2}{D_f r_f} + \sum_{i=1}^n \frac{Z_G Z_i \epsilon^2}{D_i r_i}$$

Although the detailed meaning of this expression may be quite complex, its net effect is an increase, a decrease, or no change in the energy of interaction between the anion and the cation G^+ . Exactly the same increase or decrease may be simulated by assuming a

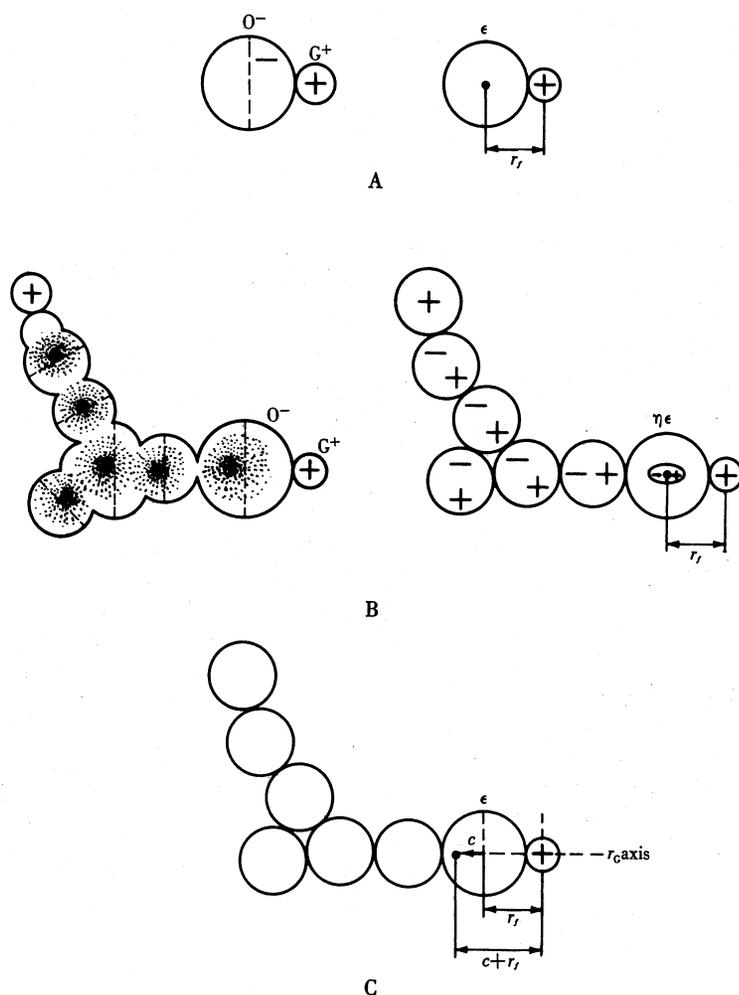


FIGURE 4.2. The definition of the c -value.

constant unit excess charge (valence electron) on the anion and by moving this excess charge along the r_G axis toward or away from G^+ . This change in the separation of the unit excess electron from G^+ may be represented in angstrom units; it will be called c . The distance c is positive if the excess electron is displaced toward G^+ , negative if it is displaced away from G^+ . Thus, the total separation, as shown in Figure 4.2, will be $r_f - c$. We may then set $Z_G\epsilon^2 / (r_f - c)$ equal to the combined actions of the three terms above. Cancelling $Z_G\epsilon^2$ and rearranging, we have the definition of the c -value:

$$c = r_f - \frac{1}{\frac{\eta}{D_f r_f} + \sum_{i=1}^n \frac{Z_i}{D_i r_i}}. \quad (4-3)$$

In this treatment, the c -value is defined to be independent of the nature of the cation G^+ and its exact location. That part of the interaction which does depend on the nature and location of G^+ is absorbed in another variable, the group polarizability α (see Section 4.3A).

A fall of the c -value (a change from 0 to -1\AA) parallels a decrease in the electron density of the functional group; for example, acetic acid (a weak acid) \rightarrow trichloroacetic acid (a strong acid). A rise of c -value parallels an increase of electron density; for example, trichloroacetic acid \rightarrow acetic acid. A c' -value may be formulated for a change in the density of the excess positive charge on an amino group; we use a hypothetical NH_3^+ group. Here, a rise of c' -value parallels a decrease of electron density and a fall of c' -value parallels an increase of electron density.

We can broaden the concepts of the c - and c' -values so that their application will include proton-accepting and proton-donating groups such as alcoholic, amide, ester, and ether groups as well as charged or dipolar groups other than O^- and NH_3^+ . In these cases, the particular group is matched by a hypothetical, singly charged O^- or NH_3^+ group with the equivalent c - and c' -values. These values are then called the c - and c' -analogues of these different groups.

B. THE LINEAR MODEL AND THE FOUR CONFIGURATIONS

Having defined the c -value, the c' -value, and their analogues, let us insert a hypothetical cylindrical cavity in a microcell of a fixed-charge system. One end of the cavity encloses a negatively charged oxyacid group, represented as a negatively charged oxygen atom (Figure 4.3). Adjacent to the oxygen atom and near the middle of the cavity, we place a cation; farther away, we place two water molecules in a linear array. This configuration is called configuration 0. We then insert, between the fixed anion and its countercation, one, two, and three water molecules successively and call these configurations, respectively, configurations I, II, and III.* We assume that all the water molecules within this cavity are completely frozen in (dielectrically saturated) and that variation of polarization outside the cavity from one configuration to another may be neglected.

C. THE VALUE OF THE DIELECTRIC COEFFICIENT D

Dielectric saturation in the immediate vicinity of an ion has long been recognized (Sack, 1926, 1927). According to the Debye theory of dielectric saturation (1929), the radial dielectric coefficient has a constant value of 3 in the space extending from the center of a monovalent ion radially to a distance of about 3\AA , where it begins to rise gradually to the macroscopic value of 81, at about 16\AA . The more recent calculations of Hasted *et al.* (1948) and of Grahame (1950) show a more abrupt rise of dielectric coefficient immediately beyond the first layer of water. Nevertheless, the consensus of opinion is that the first layer of water is almost completely saturated dielectrically.

Hasted assumed that the first layer of water around an anion is much less saturated than the first layer around a cation. This opinion is quite widely held (Hasted *et al.*, 1948;

* There is not enough room to accommodate the two water molecules distal to the anion within the microcell of 20\AA radius. However, the linear arrangement is a model of the three-dimensional system in which water molecules are joined, not end-to-end, but in a zigzag. In that case, the problem disappears. Calculations were also made with the two distal water molecules removed from the model; the results showed no significant change except that the crossover points, to be discussed later, occurred at lower c -values.

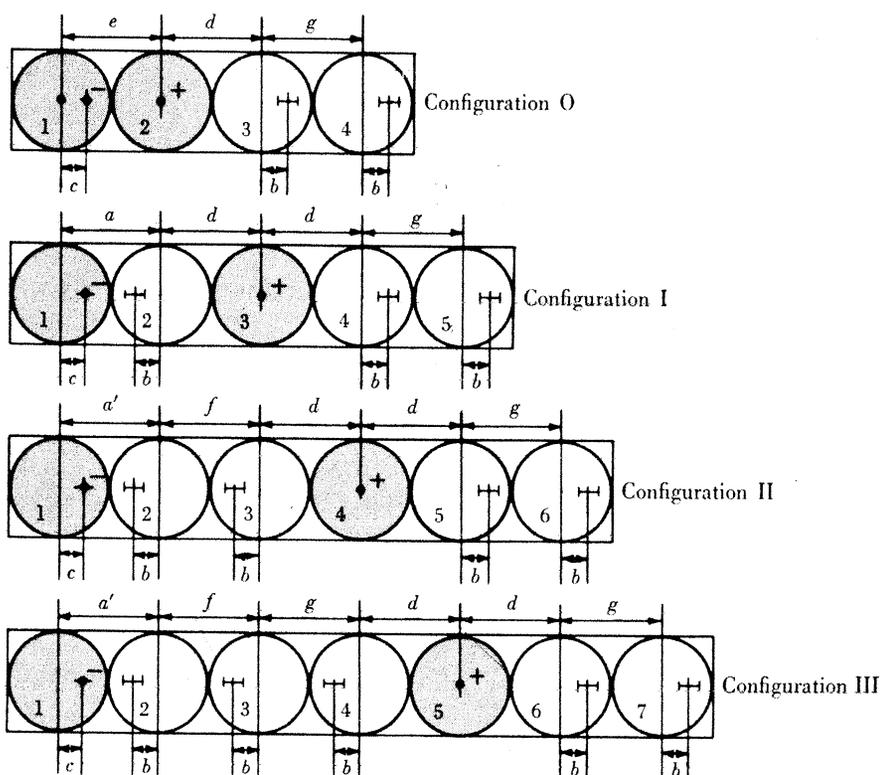


FIGURE 4.3. The linear model. The interaction energies were calculated for each of the monovalent cations in each of the four configurations of fixed anions and water.

Grahame, 1950). I adopted this assumption in my treatment of the 1951–52 model; however, little experimental evidence exists to support this view. Lorenz and Posen (1916) presented measurements of the mobilities of a large number of polyatomic organic anions. Applying Stokes' law, they calculated the effective volume of the ions and then compared these effective volumes with the molecular volume and concluded that no room could be left for an additional layer of water. Judging from the uncertain applicability of Stokes' law and the large ionic size, one sees no conclusive evidence for a general lack of hydration around anions, although the particular contention of these authors may prove correct. On the contrary, anions are known to possess both greater heats of hydration and greater entropies of hydration than cations of equal size; for example, K^+ (crystal radius = 1.33\AA) has a ΔH of -75 kcal/mole and a ΔS of -11 cal/deg/mole; the corresponding values for F^- (crystal radius = 1.36\AA) are -121.5 kcal/mole and -26 cal/deg/mole, respectively (Ketelaar, 1953, Table 13; Verwey, 1942). Water molecules oriented in the first hydration shell of an anion should thus be more rigidly frozen and have less freedom than water molecules around a cation of equal size. We may conclude that the first layer of water in immediate contact with either anions or cations is dielectrically saturated. Therefore, the water molecules between the anionic oxyacid group and a cation in configurations I and II should be completely saturated.

The third water molecule in configuration III, found between the two water molecules immediately adjacent to the carboxyl group and the cation, should also be completely saturated dielectrically. The following facts suggest that this middle water molecule is more polarized than any second-nearest neighboring water molecule around a single isolated cation or anion: (1) The interaction between the permanent dipole moment of a water molecule and the cation and that between the permanent dipole moment of the water molecule and the anion are additive. (2) The interaction between induced dipole and permanent dipole and that between induced dipole and induced dipole are enhanced through reinforcement of cationic and anionic induction. (3) These effects combine to shorten the equilibrium distances between the interacting molecules and ions, and thereby secondarily further intensify the cohesive forces of all these as well as those of the London dispersion energies.

4.3. Calculation of the Association Energies and Distribution Ratios

The difference in thermodynamic internal energy between the appropriately defined associated and dissociated states ($\Delta E = E_{\text{assoc}} - E_{\text{dissoc}}$) is represented by ΔE , which is usually a negative quantity. The terms “association energy” and “dissociation energy” are both used in this monograph. These energies are equal in absolute magnitude but differ in sign. We have chosen to represent the association energy by ΔE ; the dissociation energy, then, is given by $-\Delta E$. We use the terms “adsorption energy” and “association energy” as synonyms. Having presented the basic assumptions of the linear model, we can calculate the association energy ΔE for each cation at varying c -values. Two steps are involved in this process; first, given a cation, a particular c -value of the fixed anion, and an unlimited number of water molecules, we want to find the statistical probability of having no water molecule, one water molecule, two, or three water molecules between the cation and the fixed anion pair; that is, we want to determine the probability of finding each of the configurations 0, I, II, III. To evaluate this, we must find the total of all energies between cation and anion, between ions and water, between water and water on an absolute basis for each configuration. By comparing the total energies of the various configurations, we can calculate their relative abundance at a given temperature. Having found this, we can calculate the association energy ΔE for each particular cation in its particular statistical distribution (for example, 95 per cent in configuration III, 4 per cent in configuration II, and 1 per cent in configuration I). The association energy ΔE is the difference between the energy of the cation in the fixed-charge system as a counterion of a fixed anion of a given c -value and the energy of the same cation in an infinitely dilute solution at an infinite distance. In a truly accurate three-dimensional model, ΔE could be obtained by comparing the energy calculated from the first step, properly weighted statistically, with the experimentally measured energy of the hydrated cation extrapolated to infinite dilution. Since we have only a linear model, this comparison cannot be made; instead we use the charging method of Born (1920). Since the major energy difference between the associated ion pair and the dissociated ion pair is the electrostatic interaction energy between the cation and the fixed anion, we can determine the approximate ΔE by evaluating the work done in bringing the cation from infinity to the particular equilibrium location estimated in the first part of our calculation. Once the association energies have been evaluated we can find the macroscopic equilibrium distribution ratios between various ion pairs.

A. CALCULATION—PART I. THE EVALUATION OF THE STATISTICAL WEIGHTS OF THE VARIOUS CONFIGURATIONS AT EQUILIBRIUM

We shall follow the treatment of ionic hydration of Moelwyn-Hughes (1949). We represent a water molecule as one that has a permanent dipole located $b\text{\AA}$ away from the geometrical center of an otherwise spherically symmetrical molecule. The repulsion constant between the oxygen end of the water molecule and a cation is then assumed to be similar to that between the same cation and a fluoride ion (which resembles oxygen, Moelwyn-Hughes); the repulsive field is represented as inversely proportional to the ninth power of the distance between the centers of the two interacting atoms. The whole array is first assumed to be at 0°K . The total potential energy 0u of a particular configuration can be calculated from the equation:

$$\begin{aligned}
 ^0u = & \sum_i \sum_{j>i} \frac{Z_i Z_j \epsilon^2}{|r_{ij}|} - \sum_i \sum_{j \neq i} \frac{Z_i \epsilon \mu_j (r_{ij} + b_j)}{|r_{ij} + b_j|^3} \\
 & (1) \qquad (2) \\
 & - \sum_i \sum_{j \neq i} \sum_{k \neq i} \frac{\alpha_i Z_j Z_k \epsilon^2 r_{ji} r_{ki}}{2|r_{ji}|^3 |r_{ki}|^3} - \sum_i \sum_{j>i} \frac{2\mu_i \mu_j}{|r_{ij} - (b_i - b_j)|^3} \\
 & (3) \qquad (4) \\
 & - \sum_i \sum_{j \neq i} \sum_{k \neq i} \frac{2\alpha_i Z_j \epsilon r_{ji} \mu_k}{|r_{ji}|^3 |r_{ki} - b_k|^3} \\
 & (5) \qquad (4-4) \\
 & - \sum_i \sum_{j>i} \frac{2}{|r_{ij}|^3} \left(\sum_{k \neq i} \frac{\alpha_i Z_k \epsilon r_{ki}}{|r_{ki}|^3} \right) \left(\sum_{l \neq j} \frac{\alpha_j Z_l \epsilon r_{lj}}{|r_{lj}|^3} \right) \\
 & (6) \\
 & - \sum_i \sum_{j>i} \frac{9}{4} \frac{\alpha_i \alpha_j}{|r_{ij}|^6} \frac{U_i U_j}{U_i + U_j} + \sum_i \sum_{j>i} \frac{A_{ij}}{|r_{ij}|^9} \\
 & (7) \qquad (8)
 \end{aligned}$$

In succession, the terms on the right-hand side of the equation represent (1) the classical energy of interaction between charge and charge, (2) the energy of interaction between charge and permanent dipole, (3) the energy of interaction between charge and induced dipole, (4) the energy of interaction between permanent dipole and permanent dipole, (5) the energy of interaction between permanent dipole and induced dipole, (6) the energy of interaction between induced dipole and induced dipole, (7) the London dispersion energy, and (8) the Born repulsion energy.

We number the ions and molecules consecutively from the fixed site to the end of the linear array, and define the positive direction as that of increasing numbers. The valency (0, +1, or -1) of the i th entity is represented by Z_i ; ϵ is the electronic charge; r_{ij} is a scalar quantity representing the distance from the i th to the j th entity and is positive if $i < j$; μ_j is the scalar permanent dipole moment of the j th entity and is positive or negative as the dipole lies parallel or antiparallel to the positive direction; b_j is equal to $\pm b$, the sign being determined by the direction of displacement of the permanent dipole from the geometrical center of the species in a particular configuration. Thus the quantity

$$\frac{b_j}{\pm b} = \frac{\mu_j}{|\mu_j|} \quad (4-5)$$

depends only upon the orientation of the dipole within the species. We determine the equilibrium orientation of the dipoles with respect to the linear system by minimizing the total energy as a function of the possible orientations. The polarizability of the j th entity is represented by α ; A_{ij} is the specific energy constant of the repulsive field between the i th and j th entities in immediate contact; U_j is the zero-point energy of the j th entity. The zero-point energy of a cation is taken as the second ionization potential; that of an anion is taken as the electron affinity (see J. E. Mayer, 1933). The zero-point energy for water molecules is calculated from the value of refractive indices of Tilton and Taylor (1938) to be 20.92×10^{-12} ergs per molecule.* This agrees closely with the ionization potential of water, 21.1×10^{-12} ergs per molecule (International Critical Tables).

In calculating the dispersion energy, we introduce the additional factor of 3/2 into the London expression,

$$-\frac{3}{2} \frac{\alpha_i \alpha_j}{|r_{ij}|^6} \frac{U_i U_j}{U_i + U_j}$$

following Born and Mayer (1932) and Bernal and Fowler (1933). Other constants adopted and their sources are listed in Table 4.1.

Constant	H	Li	Na	K	NH ₄	Rb	Cs	H ₂ O	Carboxyl oxygen
$d \times 10^8$ cm	1.61	2.21	2.50	2.90	3.06	3.09	3.38		
$g \times 10^8$ cm	2.42	2.50	2.53	2.55	2.55	2.56	2.58		
$\alpha \times 10^{24}$ cm	0 ^c	0.075 ^d	0.21 ^d	0.87 ^a	1.65 ^b	1.81 ^d	2.79 ^d	1.444 ^e	0.876 ^e
$U \times 10^{12}$ erg/mole	0 ^c	120.6 ^d	75.4 ^d	50.7 ^d	50.7 ^c	43.8 ^d	37.5 ^d	20.9 ^e	3.4 ^f
$\mu \times 10^{18}$ e.s.u.								1.834 ^g	
$A \times 10^{82}$ erg/cm ⁶									
(against oxygen end of water molecule)	0.208 ⁱ	3.38 ⁱ	8.5 ^h	26.5 ^h	35.01 ⁱ	42.5 ^h	82.5 ^h	14.14 ⁱ	14.14 ⁱ
(against fluoride ion)			(6.29) ^k	(28.4) ^k		(49.4) ^k	(90.3) ^k		

Table 4.1. PHYSICAL CONSTANTS USED IN THE COMPUTATION OF INTERACTION ENERGIES.

^a B. E. Conway, 1952 (Table II 3).

^b Ketelaar, 1953.

^c See text.

^d Handbook of Chemistry and Physics, 1956-57 (p. 2347, II).

^e Calculated from refractive indices of Tilton and Taylor, 1938.

^f Latimer, 1952 (p. 18).

^g Moelwyn-Hughes, 1949.

^h Calculated from experimental heat of hydration, Moelwyn-Hughes, 1949.

ⁱ Calculated.

^j Calculated from Searcy, 1949.

^k Calculated from Lennard-Jones, 1936 (Table 32, p. 327).

* Sellmeier's equation of the form

$$n_i = 1 + \frac{a}{\nu_0^2 - \nu_i^2}$$

was used. Here n_i is the refractive index at wave length λ_i ; ν_i is the corresponding frequency; ν_0 is assumed to be the only natural frequency; and a is a constant. The wave lengths λ_i chosen correspond to the following: 7065.2Å (He), 5892.6Å (Na), 4861.3Å (H), 4046.6Å (Hg), and $\nu_i = c_{\text{light}}/\lambda_i$ (c_{light} is the velocity of light). The ν_0 values calculated for each pair of frequencies were averaged, giving 20.92×10^{-12} ergs per molecule.

(1) The polarizability, zero-point energy, and other constants

The value α , assigned to the oxyacid group, represents the polarizability of the negatively charged oxygen and includes contributions from nearby atoms and other secondary effects (see the top of page 60). Consequently, we choose two values representing a reasonable range, rather than a single value. The lower value is arbitrarily taken as $0.876 \times 10^{-24} \text{ cm}^3$. This is not an unreasonable lower limit since the carboxyl oxygen has a polarizability of $0.84 \times 10^{-24} \text{ cm}^3$; the fluoride ion has a polarizability of $0.81 \times 10^{-24} \text{ cm}^3$; the hydroxyl oxygen, $0.59 \times 10^{-24} \text{ cm}^3$; and the ether oxygen, $0.64 \times 10^{-24} \text{ cm}^3$ (Ketelaar, 1953, Table 9). For the upper limit, we choose the value $2.0 \times 10^{-24} \text{ cm}^3$ (the OH^- group has a polarizability of $1.89 \times 10^{-24} \text{ cm}^3$, Ketelaar, 1953).

The H^+ ion is given zero values for both its polarizability and its zero-point energy. The zero-point energy for the ammonium ion NH_4^+ is not available. Mulliken (1933) pointed out the chemical similarity between the ammonium ion and the potassium ion, and showed that the ionization potential of the NH_4^+ ion is very close to that of the potassium ion. We have assumed that the NH_4^+ ion has the same value for its second ionization potential as the potassium ion has. The best approximation for oxyacid oxygen is that of the electron affinity of a singly charged oxygen atom (Latimer, 1952).

The Born repulsion constants for the Na^+ ion, the K^+ ion, the Rb^+ ion, and the Cs^+ ion against either the oxyacid oxygen or the oxygen end of a water molecule were calculated from experimentally determined heats of hydration using Moelwyn-Hughes' equation 3 (1949, p. 479). For comparison, the repulsion constants between alkali-metal ions and the fluoride ion (which resembles oxygen) are also listed (Lennard-Jones, 1936, p. 327). We calculate the repulsion constant between water molecules from the data of Searcy (1949), who equated the repulsion term to C/r^{12} , while we use the approximation A/r^9 . The value of C a constant, is obtained from Searcy. The equilibrium distance r between water molecules in ice is 2.76 \AA (Pauling, 1948). Equating C/r^{12} to A/r^9 , we obtain $A = 14.14 \times 10^{-82} \text{ erg cm}^9$. We assume the same value for the repulsion between the hydrogen end of a water molecule and an oxyacid oxygen atom.

(2) Calculation of equilibrium distances

Figure 4.3 represents a scheme for the linear arrangement in the cylindrical cavity mentioned earlier and the designation of the distances: a , a' , b , d , e , f , g . The next step is to select or calculate the equilibrium values of these distances. The value of b , the distance between the center of a water molecule and the center of its permanent dipole moment, is 0.274 \AA ; d -values (roughly the sum of the radii of the cation and a water molecule) for the Na^+ ion, the K^+ ion, the Rb^+ ion, and the Cs^+ ion are, respectively, 1.55 \AA , 1.57 \AA , 1.61 \AA , and 1.69 \AA greater than their respective Pauling crystal radii. Adding the average value of 1.61 \AA to the crystal radius of zero for proton and of 1.45 \AA for the ammonium ion (Ketelaar, 1953, Table 3E), we obtain an equilibrium d -value equal to 1.61 \AA for the H^+ ion and to 3.06 \AA for the ammonium ion. Substituting these into a_0 of equation 3 of Moelwyn-Hughes, we obtain the repulsion constant A with a value of $0.208 \times 10^{-82} \text{ erg cm}^9$ for the H^+ ion and $35.0 \times 10^{-82} \text{ erg cm}^9$ for the NH_4^+ ion. It now remains only to find the values of a , a' , e , f , and g .

(a) *The distance g.* The g -value represents the center-to-center distance between the two water molecules distal to the anion (Figure 4.3). Since this distance is far removed

from the anionic charge we assume that it varies only with the nature of the cation and that it does not depend on the anion. Neglecting the less important terms, we solve for the equilibrium distance g by assuming d constant for each cation and equating the repulsion force to the combined cohesive forces* due to the dispersion energy and to the energy of interaction between ion and dipole. We obtain

$$\frac{9A}{g^{10}} = \frac{2\epsilon\mu_w}{(d+g+b)^3} + \frac{6\alpha_w\mu_w\epsilon}{(g+b)^4d^2} + \frac{6\mu_w^2}{g^4} + \frac{54}{8} \frac{\alpha_w^2 U_w}{g^7} \quad (4-6)$$

where A represents the repulsion constant, equal to 14.14×10^{-82} erg cm⁹ between a pair of water molecules; and the subscript w refers to the water molecule. The equation is then solved for the different cations with the results given in Table 4.1. These and following equations are solved by the method of successive approximation.

(b) *The distance e .* After similar simplification by neglecting less important terms, one obtains at equilibrium

$$\frac{9A'}{e^{10}} = \frac{\epsilon^2}{(e-c)^2} + \frac{2\alpha_- \epsilon^2}{e^5} + \frac{2\alpha_+ \epsilon^2}{(e-c)^5} \quad (4-7)$$

where A' is the repulsion constant between a cation and the oxygen end of a water molecule; and the subscripts $+$ and $-$ refer to the cationic and anionic groups, respectively. Defining a variable k by the equation $e-c=ke$, we substitute ke for $(e-c)$. Rearranging the above equation, we obtain

$$e^8 + \left(2\alpha_- k^2 + \frac{2\alpha_+}{k^3}\right) e^5 - \frac{9A'k^2}{\epsilon^2} = 0 \quad (4-8)$$

which we then solve for different cations and different k -values. From the relation $e-c=ke$, we find the value of c that corresponds to each k -value; a plot of e versus c for each alkali-metal ion is shown in Figure 4.4.

(c) *The distances a and a' .* Letting $a-c=k'a$, we find that

$$\frac{9A}{a^{10}} = \frac{2\alpha_w \epsilon^2}{(k')^5 a^5} + \frac{2\mu_w \epsilon}{(k')^3 \left(a - \frac{b}{k'}\right)^3} + \frac{27}{2} \frac{\alpha_- \alpha_w U_- U_w}{U_- + U_w} \frac{1}{(k')^7 a^7} + \frac{\epsilon^2}{(k')^2 \left(a + \frac{d}{k'}\right)^2} \quad (4-9)$$

Calculations of a -values using the above equation, first with the smallest d -value for the H⁺ ion and then with the largest d -value for the Cs⁺ ion, show that these differences of d -value affect the a -value very little. We decided to use the average d -value of 2.68Å for all cation calculations and 2.68 + 2.7Å (2.7Å is the diameter of a water molecule) = 5.38Å for the calculation of all a' -values. The result is also given in Figure 4.4.

* Both the repulsion force and the combined cohesive forces are derived from equation (4-4) for the various energies and from the relation that the force between two interacting particles is equal to the derivative of the energy between them with respect to r , the distance of separation.

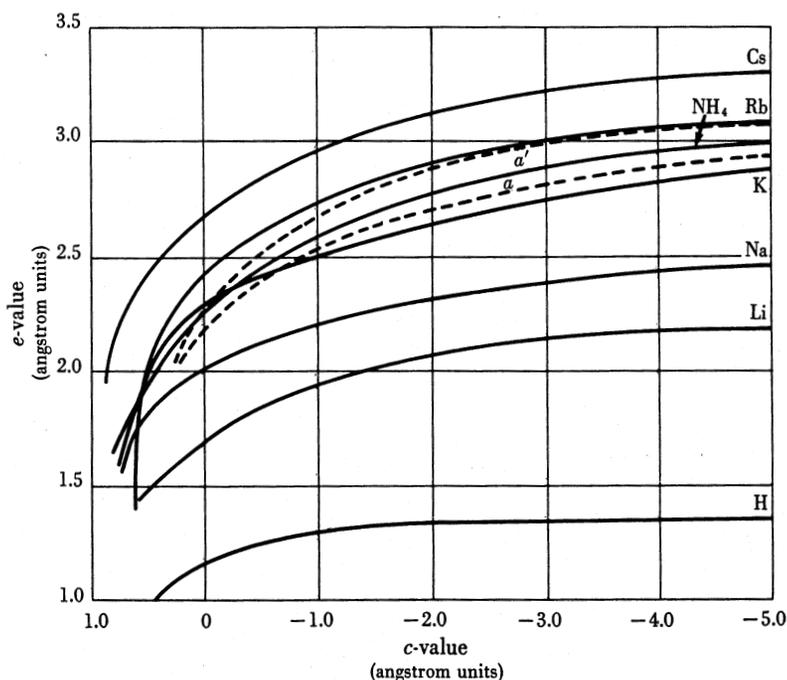


FIGURE 4.4. The relation between the c -value and the computed value of e , a , and a' . The equilibrium distance e between the centers of the fixed anion and the counterion in the 0-configuration is represented by the solid line. The dotted lines show the distances a and a' as functions of the c -value. Here a is the distance between the center of the fixed anion and the first water molecule in configuration I and a' is the analogous distance in configurations II and III.

(d) The distance f . Following the same reasoning as above, and again neglecting the lesser terms, we derive

$$\frac{9A}{f^{10}} = \frac{2\mu_w \epsilon}{(d+f)^3} + \frac{\epsilon^2}{(d+f+a-c)^2} + \frac{6\mu_w^2}{f^4} \quad (4-10)$$

for configuration II. The same i -values were used for configuration III. The results are plotted in Figure 4.5.

(3) The calculation of the total potential energies of the various configurations

Having determined all the equilibrium distances, we calculate the total potential energies of the various configurations. In summing the individual terms, we neglect a particular term in equation (4-4) only after computing that term for each cation and finding that the term for the ion with the highest value is less than 0.15 kcal/mole. The total energy for each ion at each c -value is then plotted against the c -value after subtracting the value $n \times 4.98$ kcal/mole; here n represents the number of water molecules inserted between the cation and the anion for that configuration and 4.98 kcal/mole corresponds to the energy

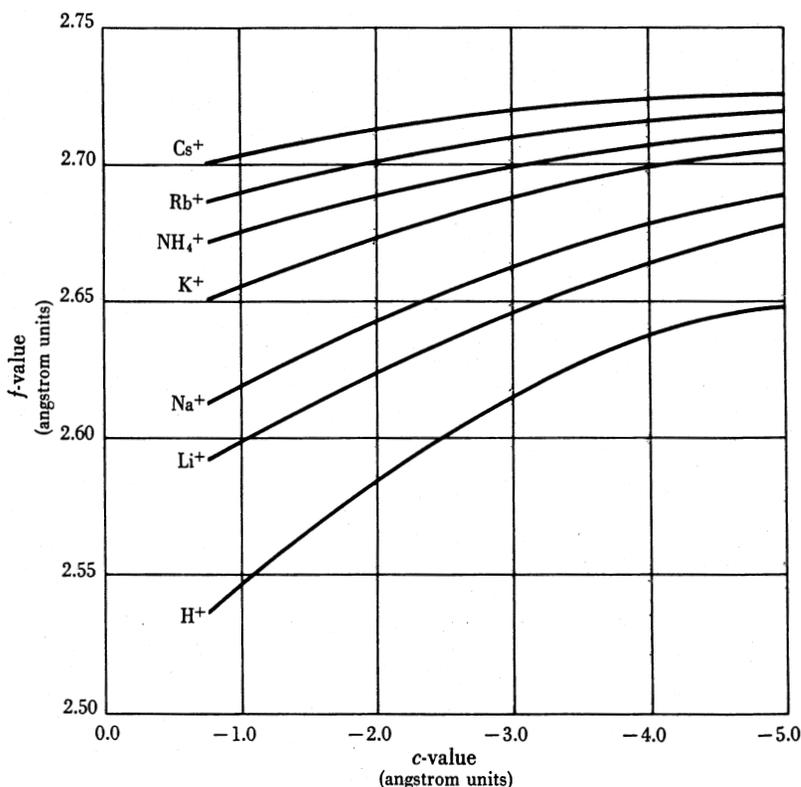


FIGURE 4.5. The relation between the c -value and the computed value of f . The distance between the first and second water molecules in configurations II and III is represented by f .

needed to bring a water molecule from pure liquid water at an infinite distance into the linear array.*

Figures 4.6, 4.7, and 4.8 plot the computed energies of the various configurations of the different ions against the c -value. In Figure 4.6, the polarizability of the oxyacid group is assumed to be $0.876 \times 10^{-24} \text{ cm}^3$; in Figure 4.7, $1.25 \times 10^{-24} \text{ cm}^3$; and in Figure 4.8, $2.0 \times 10^{-24} \text{ cm}^3$.

(4) The calculation of the contributions of different configurations

For each ion at a particular c -value, one configuration represents a state of lowest energy. In general, the relationship for each ion is such that at lower c -values the higher configuration with a greater number of water molecules intervening between the fixed anion and the counteranion is preferred. As the c -value increases, the preference is shifted to lower

* Each oriented water molecule possesses a total energy equal to the latent heat of vaporization (9.955 kcal/mole) minus RT (0.582 kcal/mole at 20°C). Each water molecule has four "half bonds" (coordination number = 4, each bond counted twice) of 2.489 kcal/mole each. We assume that two of these half bonds are altered in transplanting one water molecule to the linear array.

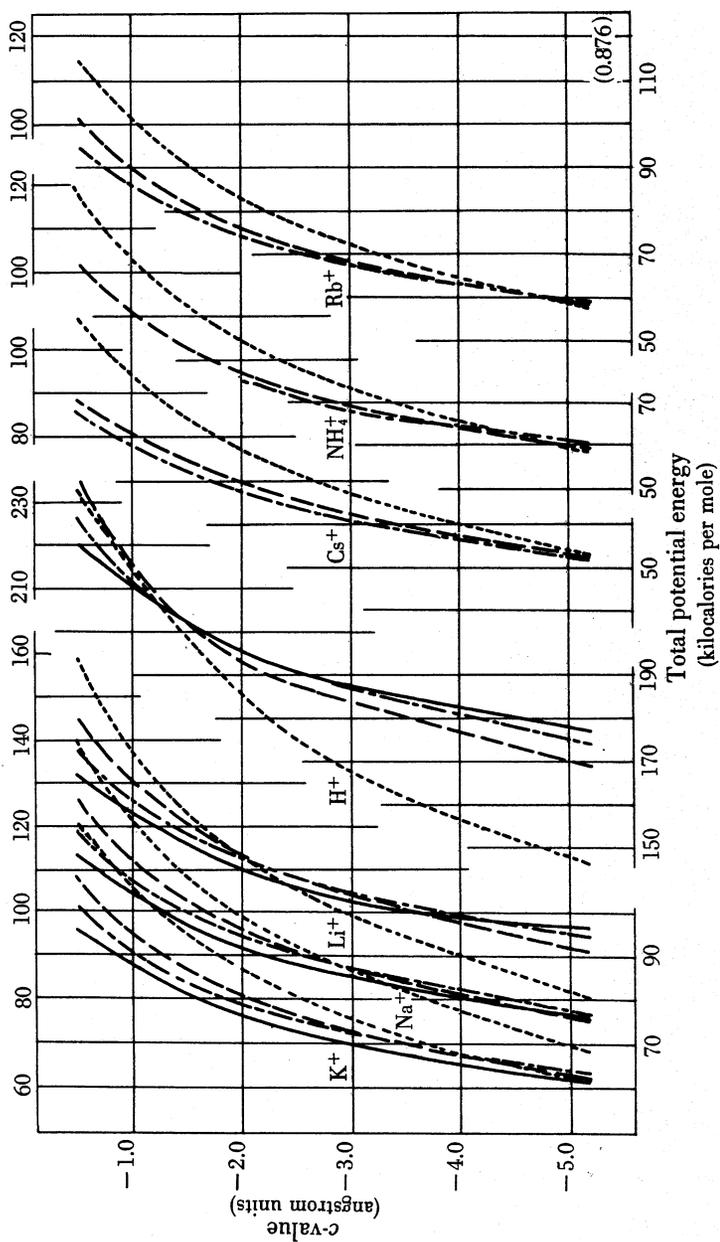


FIGURE 4.6. The variation of the total potential energy \mathcal{U} of the fixed anion-counteranion-water systems as a function of the c -value at 0°K. In this figure, the fixed anion has a polarizability of $0.876 \times 10^{-24} \text{ cm}^3$. Values are plotted for each cation in each of the configuration 0 - - -, I - · - ·, II - - - - -, III —.

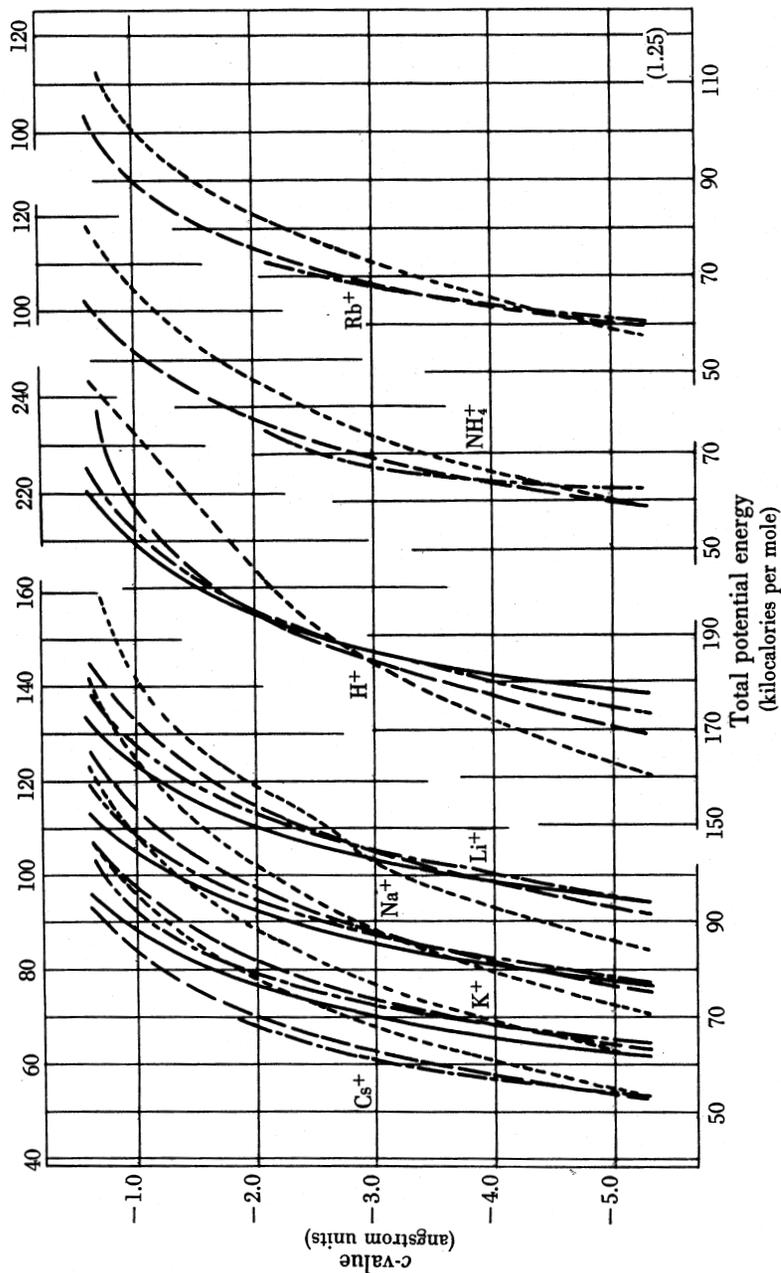


FIGURE 4.7. The variation of the total potential energy \mathcal{U} of the fixed anion-counterion-water systems as a function of the c-value at 0°K. In this figure, the fixed anion has a polarizability of 1.25×10^{-24} cm³. Values are plotted for each cation in each of the configuration 0 ---, I ---, II - · - · -, III —.

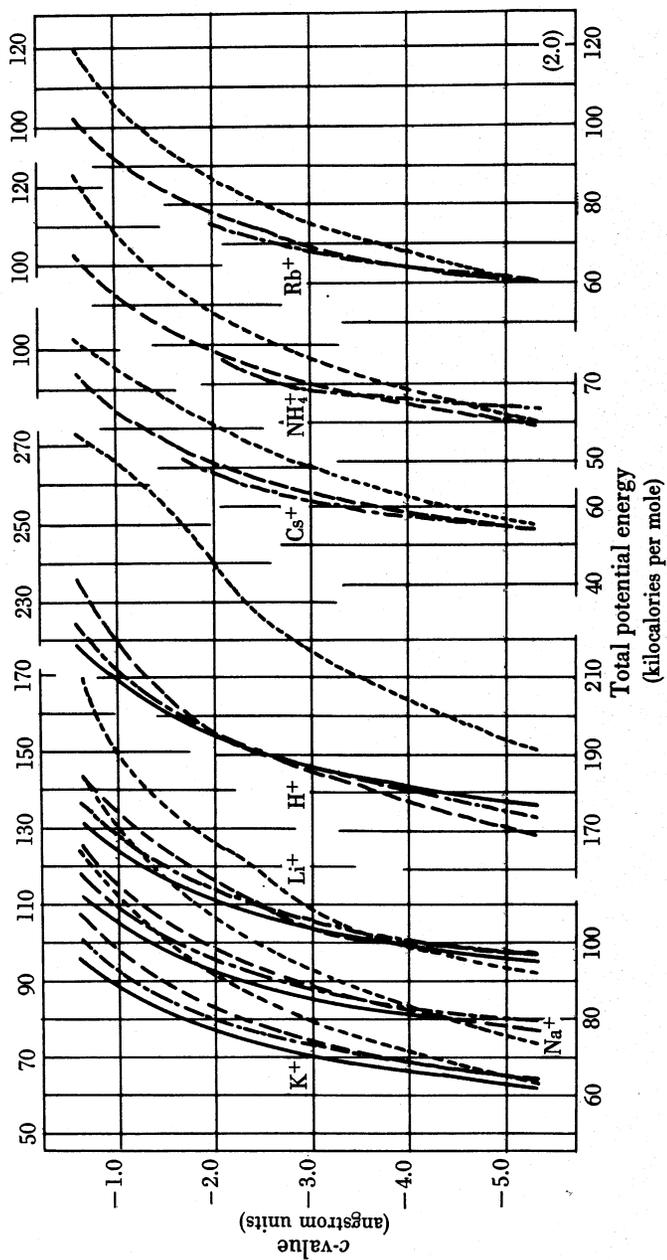


FIGURE 4.8. The variation of the total potential energy \mathcal{U} of the fixed anion-counteranion-water systems as a function of the c-value at 0°K. In this figure, the fixed anion has a polarizability of $2.0 \times 10^{-24} \text{ cm}^3$. Values are plotted for each cation in each of the configuration 0 ---, I ---, II - · -, III —.

and lower configurations until eventually, at the highest c -value, the 0-configuration is invariably the preferred one. This trend is followed by each ion, although the c -value at which the preference changes from one configuration to another varies from ion to ion.

From Appendix B, we derive for the species p_i

$$\frac{n_i^s}{\sum_{s=0, I, II, III} n_i^s} = \frac{(\mathbf{p.f.})_i^s \exp(-\mathfrak{u}_i^s/RT)}{\sum_{s=0, I, II, III} (\mathbf{p.f.})_i^s \exp(-\mathfrak{u}_i^s/RT)} \quad (4-11)$$

where n_i^s is the number of p_i ions in a particular configuration s ; $(\mathbf{p.f.})_i^s$ is the partition function for that ion in that configuration; and \mathfrak{u}_i^s is the total energy of the i th ion assembly in configuration s .

If we assume that only the configurational partition function varies significantly among the associated ions (see Section 2.4), the relative distribution of the same ion p_i in the different configurations would be

$$\frac{n_i^s}{\sum_{s=0, I, II, III} n_i^s} = \frac{\rho_i^s \exp(-\mathfrak{u}_i^s/RT)}{\sum_{s=0, I, II, III} \rho_i^s \exp(-\mathfrak{u}_i^s/RT)} \quad (4-12)$$

where ρ_i^s is the number of sites (see Section 2.4A) available to p_i in configuration s , a function of the species of the ion, its configuration, and the c -value as shown in Figures 4.6 to 4.8. If r_i^s is the equilibrium distance from the center of p_i in configuration s to the center of gravity of the negative charges ($r_f - c$), on first approximation the ion may be assumed to be constrained to move within a spherical shell of radius r_i^s and thickness h . We make the further assumption that the empirical equation

$$h = \left(\frac{RT}{\mathfrak{u}}\right)^{1/2} \text{ \AA}$$

which holds for almost all diatomic molecules, also applies to the fixed anion-counterion pair (see Mayer and Mayer, 1940). In this equation, \mathfrak{u} stands for the absolute magnitude of the energy of the bond and one may write for ion p_i in configuration s

$$\rho_i^s = 4\pi \left(\frac{RT}{\mathfrak{u}_i^s}\right)^{1/2} (r_i^s)^2.$$

Substitution into equation (4-12) yields

$$\frac{n_i^s}{\sum_{s=0, I, II, III} n_i^s} = \frac{[(r_i^s)^2/(\mathfrak{u}_i^s)^{1/2}] \exp(-\mathfrak{u}_i^s/RT)}{\sum_{s=0, I, II, III} [(r_i^s)^2/(\mathfrak{u}_i^s)^{1/2}] \exp(-\mathfrak{u}_i^s/RT)} \quad (4-13)$$

In the present case, since only those configurations with the greatest (negative) total energies count, the ratio of $(\mathfrak{u}_i^s)^{1/2}$ for two such configurations is always close to unity; hence

$$\frac{n_i^s}{\sum_{s=0, I, II, III} n_i^s} = \frac{(r_i^s)^2 \exp(-\mathfrak{U}_i^s/RT)}{\sum_{s=0, I, II, III} (r_i^s)^2 \exp(-\mathfrak{U}_i^s/RT)} \quad (4-14)$$

This equation gives us the percentages of different configurations of the ion-fixed-charge pair at a particular value of c .

B. CALCULATION—PART II. THE CALCULATION OF THE ASSOCIATION ENERGIES OF VARIOUS IONS AT DIFFERENT c -VALUES

The problem of ionic association is always ambiguous because it depends intimately upon the definition of a state of association and the definition of a state of dissociation. The problem becomes even less clear when we deal with a fixed-charge system in equilibrium with a free solution. In this case, the dissociation of a counterion-fixed-charge pair could mean the assumption of a new position by the dissociated counterion either inside or outside the fixed-charge system. If it migrates out of the fixed-charge system, the process is complicated by the development of surface potentials (see Section 10.2 on cellular potential). Further, the association energy depends, in general, on both the spatial position of the counterion in the fixed-charge system and the history of the fixed-charge system itself. To eliminate these complications, we regard as associated any counterion that assumes one of configurations 0, I, II, or III. The fixed-charge system with its complete assortment of counterions is then brought from 0°K to the ambient temperature. We now define the association energy, ΔE , to be the difference between the energy of the associated counterion and the energy of the first counterion that diffuses out of the fixed-charge system to an infinite distance in an infinitely dilute aqueous phase. This energy is not significantly different from that obtained if we compare the associated counterion in configuration 0, I, II, or III with a similar counterion in a hypothetical "beyond III" configuration within the fixed-charge system. The limit of association (equivalent to r_2 of Section 2.4A) in this case refers to the radius at which there is a sharp increase in the dielectric coefficient of the medium such that a volume of water which is not dielectrically saturated intervenes between the two charged particles (see Ling, 1952, inset of Figure 6).

Taking into account the freezing-in of the water molecules between the fixed ion and its counterion (Section 4.2B), we calculate the association energy by evaluating the work performed when the counterion is brought from infinity through a medium having the dielectric properties of water into a microcell at the equilibrium distance which that particular ion assumes. Instead of using a macroscopic dielectric coefficient, we take Debye's value for the dielectric coefficient $D(r)$ at a distance r from the center of a univalent ion.* In the present case, however, the sharp increase of dielectric coefficient with increase of r does not begin until r corresponds to a distance three water molecules away from the anion. Thus, within a region of 8.1Å ($3 \times 2.7\text{Å}$) between the cation and anion in configuration III, we assume a uniform dielectric constant of three.

The energy of association of each ion at each c -value is then

* No significant variation would be created if the curve of Grahame (1950) or of Hasted *et al.* (1948) were used for the rising part of the effective dielectric coefficient.

$$\Delta E = \sum_{s=0, I, II, III} \frac{n_i^s}{\sum_{s=0, I, II, III} n_i^s} \int_{r_i}^{\infty} -\frac{\epsilon^2}{D(r)r^2} dr \quad (4-15)$$

where $n_i^s / \sum_{s=0}^{III} n_i^s$ is given by equation (4-14). In Figures 4.9 to 4.11, the computed association energies of the various cations against anions of differing c -values are presented. For Figure 4.9, the polarizability of the oxyacid functional group is taken to be $0.876 \times 10^{-24} \text{ cm}^3$; for Figure 4.10, as $1.25 \times 10^{-24} \text{ cm}^3$; and for Figure 4.11, as $2.0 \times 10^{-24} \text{ cm}^3$. We believe that Figure 4.9 gives the closest approximation to ion interaction with biological fixed-charge systems; most of this discussion will be based on this figure.

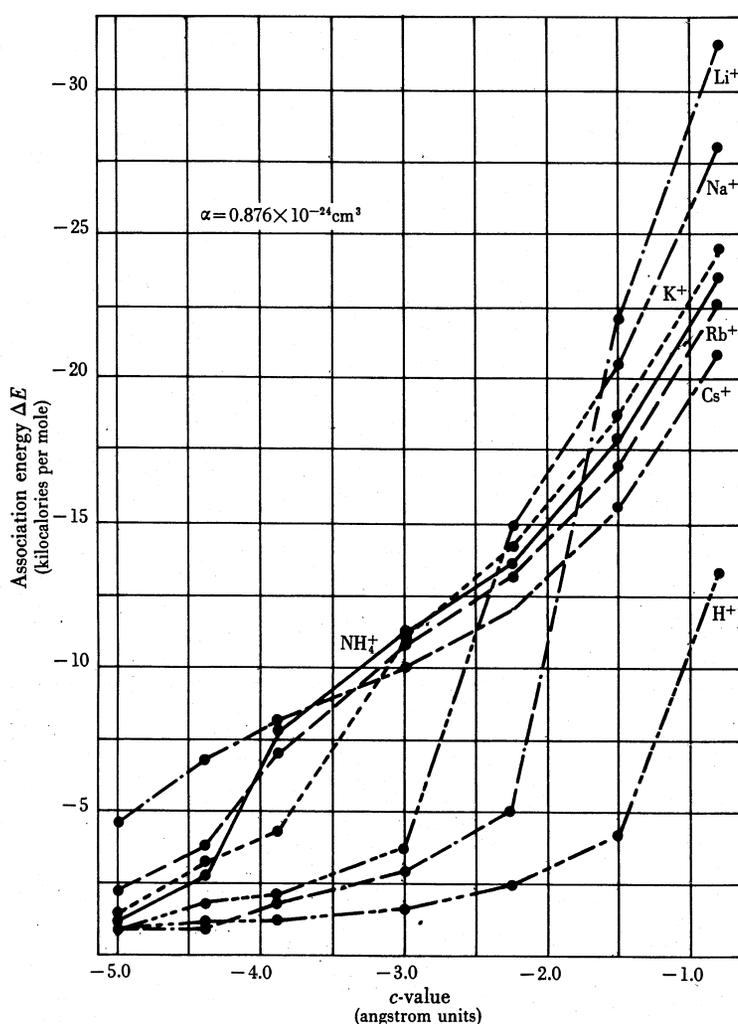


FIGURE 4.9. The relation between the calculated association energy ΔE of various cations and the c -value of the anionic group. The polarizability α is $0.876 \times 10^{-24} \text{ cm}^3$.

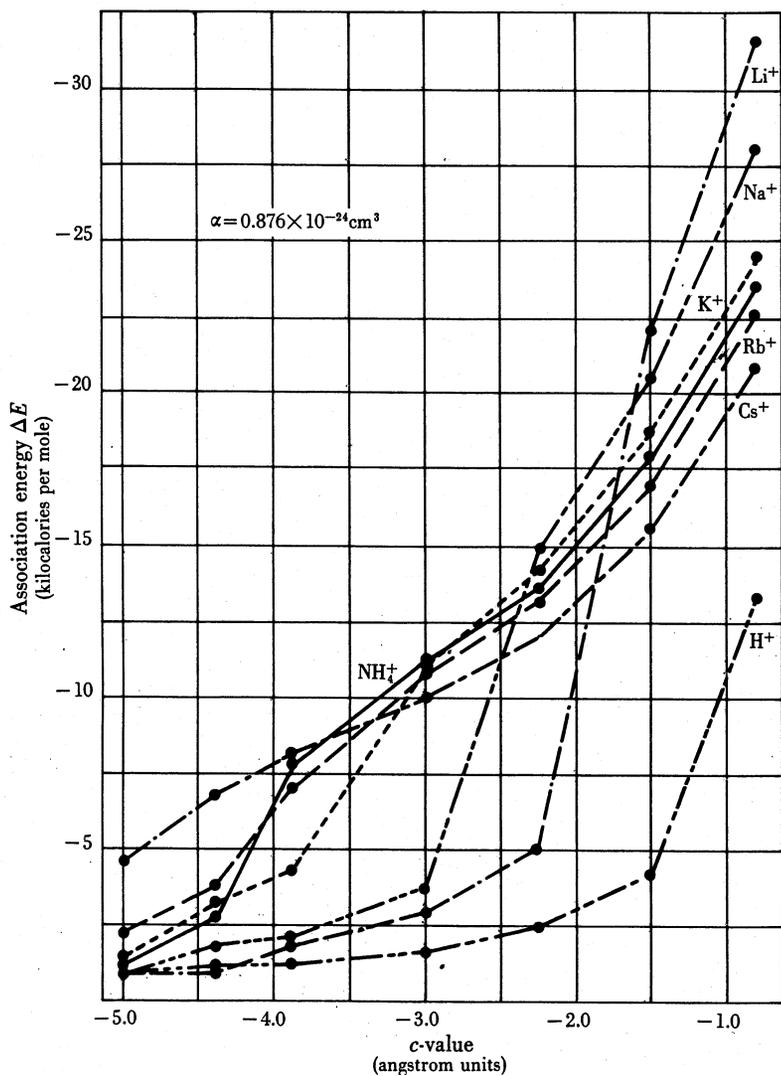


FIGURE 4.10. The relation between the calculated association energy ΔE of various cations and the c -value of the anionic group. The polarizability α is $1.25 \times 10^{-24} \text{ cm}^3$.

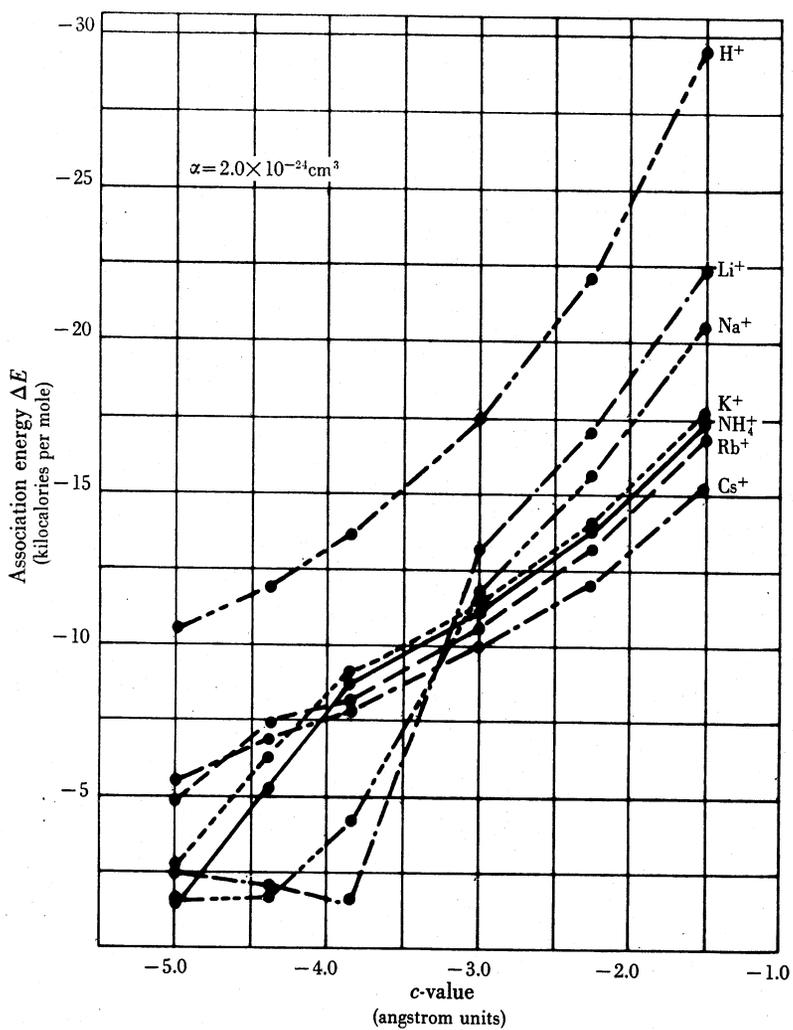


FIGURE 4.11. The relation between the calculated association energy ΔE of various cations and the c-value of the anionic group. The polarizability α is $2.0 \times 10^{-24} \text{ cm}^3$.

4.4. Discussion and Comment on the Present Model

A. THE TENTATIVE NATURE OF THE ABSOLUTE c -VALUE AND ASSOCIATION ENERGIES

The adoption of the present linear model is a concession to the forbidding complexity associated with a three-dimensional model. Since transforming the linear model to a three-dimensional model would involve symmetrical changes only, one would not expect the ΔE -versus- c -value plot to involve any disorderly disturbance of the relations calculated, but only changes of absolute magnitude.

The linear model does discriminate against the higher configurations. Thus the calculation of the total energies of the 0-configuration would be virtually the same in the linear as in a three-dimensional model. On the other hand, for configurations I, II, and III, the energies calculated are a great deal less in the linear model than they would be in a three-dimensional one; in these higher configurations, a large part of the energy arises from the interactions between the ions and water molecules and these water molecules are obviously coordinated in three dimensions. In the linear model, therefore, only a fraction of the coordinated water molecules is taken into account; the higher the configuration the greater the discrepancy.

Another aberration is created by the adoption of the Born charging method for the determination of association energies. The assumption that the total hydration energy of the ions remains the same in the dissociated and associated states is implicit in this procedure. This assumption is closer to the truth for ions in the higher configurations than for ions in the 0-configuration. If we neglect the partial loss of ion-water interaction in the 0-configuration the calculation overestimates the 0-configuration energy. Consequently, (1) the aberration from the first part of the calculation is accentuated and this causes the crossover points to fall on lower c -values than they should, and (2) the dissociation energy at high c -values is overestimated.

When the three-dimensional model is developed, we do not expect the shape of the ΔE -versus- c -value plot to be changed significantly; but the c -values should be much higher than the present tentative values which we have calculated. One must remember that the c -value, as defined, is not a spatial location of a particular electron; thus, comparison of its value with, say, the diameter of an oxygen atom is quite meaningless and leads to erroneous conclusions.

The heat of hydration in kcal/mole is 114.6 for Li^+ , 89.7 for Na^+ , 73.5 for K^+ , 67.5 for Rb^+ , and 60.8 for Cs^+ (Latimer *et al.*, 1939). The coordination numbers of these ions range from 6 for Li^+ to 2 for Cs^+ (B. E. Conway, 1952, Table III, p. 53). The overestimation of the energy of the 0-configuration thus consists essentially of one-sixth to one-half of the heat of hydration, a value that ranges from -20 to -30 kcal/mole. Therefore, the corrected association energies for the alkali-metal and ammonium ions at high c -values should have values no greater than -20 kcal/mole. For a rough quantitative estimation involving these association energies, we halve the calculated association energies. Figure 4.12 shows the distribution ratios (with K^+ as the reference ion) for an anion polarizability equal to $0.876 \times 10^{-24} \text{ cm}^3$. (Compare with Figure 4.13, where the uncorrected values were used.)

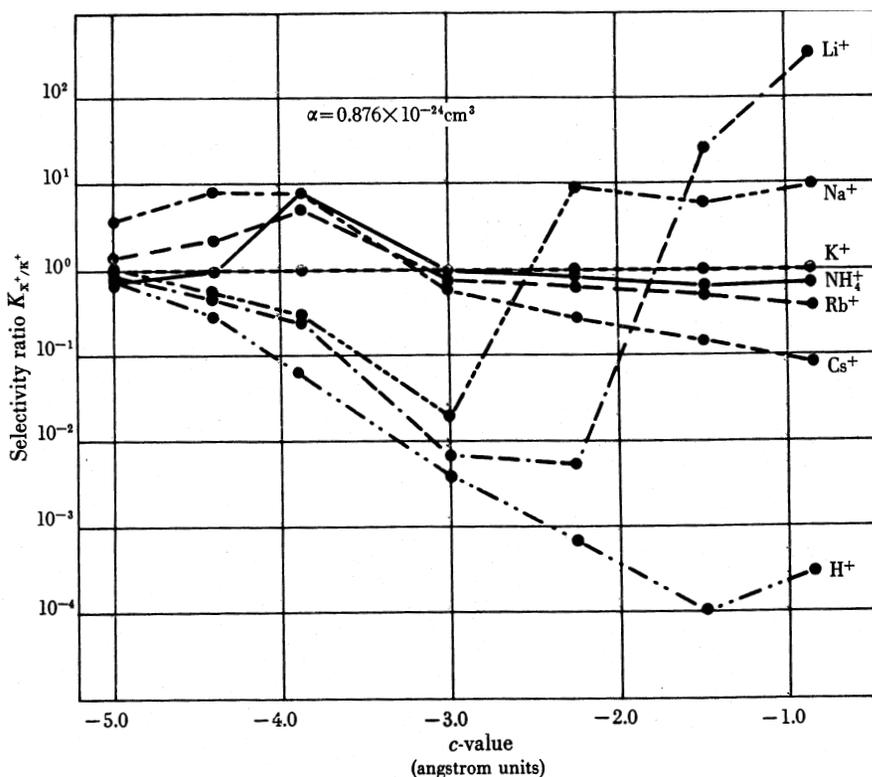


FIGURE 4.12. The relation between the selectivity ratios of various cations and the c -value. The K^+ ion is taken as unity and selectivity ratios are calculated from the association energies given in Figure 4.9, divided by 2 (see Section 4.4A).

B. INTERNAL ENERGY COMPARED WITH FREE ENERGY

Calculated as work, the association energy ΔE is equivalent to a standard free energy of association in a dilute salt solution. It does not correspond to the standard free energy of association in a fixed-charge system because a large positive entropy of dissociation that is not included in the free energy found by the Born charging method contributes greatly to the true free energy of adsorption. This large entropy change arises from the configurational- and rotational-entropy gain experienced by a counterion when it is taken from the associated state in a fixed-charge system to the dissociated state in free solution. The free energy that we obtained approximates the association energy ΔE more closely than the free energy of association ΔF . Since we are interested primarily in the relative values of the association energies with reference to other counterions, we do not need the absolute ΔF and have not attempted to calculate it.

C. THE HYDROGEN ION

Although the O—H bond in an alcoholic group is almost entirely nonionic, resonance greatly increases the ionic nature of the O—H bond in the carboxylate ion (Pauling, 1948; Branch and Calvin, 1941). In the present treatment, we do not take account of the covalent

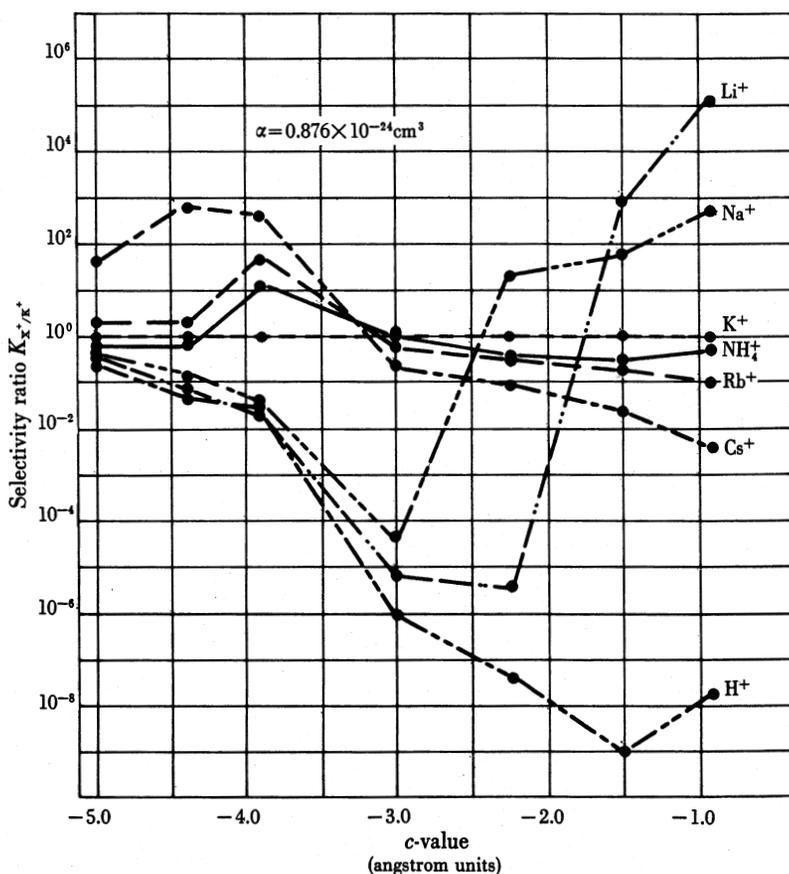


FIGURE 4.13. The relation between the selectivity ratios of various cations and the c -value. The K^+ ion is taken as unity and selectivity ratios are calculated from the association energies given in Figure 4.9. Here, the anionic polarizability is $0.876 \times 10^{-24} \text{cm}^3$. The assumption is made that all ions are completely associated and that there is no difference among the partition functions of the various adsorbed states (configurations) other than the configurational entropy.

contribution to the bond between the H^+ ion and the carboxyl oxygen; we assume that it is constant with respect to variation in c -value. This is justified. The pK 's of a list of oxyacids vary from less than 1 (HIO_3) to 11 (HPO_4). Kossiakoff and Harker (1938) showed that variation in the nonexchange electrostatic part of the interaction energy alone can produce this wide pK variation. Thus the dissociation of an oxyacid with a pK -value between 1 and 11 may involve little additional contribution due to variation of the exchange energy. Bregman (1953) has shown that the sulfonic ion exchange resin (which has an average pK -value of about 1.6 for its sulfonate radicals) selects alkali-metal ions in the order $\text{Cs}^+ > \text{Rb}^+ > \text{K}^+ > \text{Na}^+ > \text{Li}^+$, whereas a carboxylic resin (with a pK -value of about 6.0) selects them in the reverse order, $\text{Li}^+ > \text{Na}^+ > \text{K}^+$ (see Chapter 9). This shows that the range of c -value variation corresponding to pK -value variation from 1.6 to 6.0 includes roughly the entire range of c -value variation for which we have made calculations. The wider range of variation that Kossiakoff and Harker demonstrated to be dependent only

on electrostatic variation assures us that it is safe to assume that variation of the covalent contribution has very little effect on variation of the acid dissociation within the pK range of interest to us.

The constancy of the covalent contribution does not reflect its magnitude. Although this constancy makes comparison between ΔE -values calculated at varying c -values valid, the absolute value for ΔE may not be so reliable. Neglecting the exchange energy has two untoward effects: (1) the 0-configuration is de-emphasized, and (2) the association energy is reduced. Thus, if we were to evaluate it properly for a particular ionic group, the exchange energy would be added to the 0-configuration both in the calculation of the total energies of the system (step I) and in the electrostatically calculated association energy (step II). The net result of adding the exchange-energy contributions may be simulated by increasing the polarizability value α of the anionic group, a change which primarily affects the 0-configuration. The result of this manipulation differs little from the change brought about by transposing the H^+ -ion curve from Figure 4.10 (or even from Figure 4.11, with the higher polarizability) to Figure 4.9, without disturbing the values of the curves of the other ions.

D. THE STATISTICAL INTERPRETATION OF THE MEANING OF "HYDRATED IONIC RADII" IN THE CLASSICAL LYOTROPIC SERIES

At the lowest c -value, the free energy of association follows the same order as the classical lyotropic (Hofmeister) series, $Cs^+ > Rb^+ > K^+ > Na^+ > Li^+$; this order was found to depict the relative effectiveness of the action of these ions on colloidal systems as well as their mobilities in dilute aqueous solution (Hofmeister, 1888; Höber, 1945). From the point of view of the present theory, this is due entirely to the statistical nature of the number of water molecules found between the cation and the fixed anion. Thus if the same number of water molecules intervenes between the different cations and the same anion, the cation with the smallest crystal radius will always have the highest free energy of association. In fact, however, at the lowest c -value, the largest ion (Cs^+) has the highest energy of association because, statistically, it prefers to have fewer water molecules between it and the anion.

The water molecules between the cation and the anion clearly do not belong, as hydration water, to either the cation or the anion, exclusively. If we arbitrarily assign these water molecules to the cation only, the statistical nature of the water of hydration would explain the fact that a hydrated ion may have a radius only a fraction of an angstrom unit larger than its crystal radius although the water molecule has a diameter of 2.7\AA . To calculate the hydrated diameter of a cation, one must include the crystal radius of the cation plus the statistical number of water diameters. For $c = -5.0\text{\AA}^*$ and $\alpha = 0.876 \times 10^{-24} \text{ cm}^3$, given 2.7\AA as the diameter of each water molecule, the theoretical, curve would give the hypothetical hydrated cation diameters: Li^+ , 8.57\AA ; Na^+ , 7.10\AA ; K^+ , 6.67\AA ; Rb^+ , 5.64\AA ; and Cs^+ , 3.52\AA .

The order of this series is the same as that in the classical lyotropic series. As the c -value changes, the relative preference for different counterions also changes. This variation includes both a reversal of preference for one or another of a pair of cations (for

*The hydrated radii of dissociated cations in free solution correspond to the case in which $c \rightarrow -\infty$. To approximate this condition the lowest value of c equal in our calculation to -5.0\AA has been chosen for illustration.

example, a system may go from a class for which $\text{Na}^+/\text{K}^+ < 1$ to a class for which $\text{Na}^+/\text{K}^+ > 1$, and a wide variation in the selectivity coefficient within any class of preferences. Thus, in a mixture of Na^+ and K^+ at a given c -value (let it fall within the range that gives $\text{Na}^+/\text{K}^+ < 1$) the counteraction population would be represented by both K^+ ions and Na^+ ions in all configurations. However, K^+ ions would be selectively accumulated because statistically more Na^+ ions would assume higher configurations than K^+ ions and consequently the K^+ ion would have a higher association energy. Conversely, there are high c -values at which there is no water between most of the Na^+ ions and the fixed anions (configuration 0), while K^+ ions remain mostly in configurations I and II. The selectivity coefficient for Na^+/K^+ would be very much higher ($\text{Na}^+/\text{K}^+ \gg 1$) than at the c -values discussed above. At very high c -values, both K^+ and Na^+ assume the 0-configuration and the absolute energies of association are much higher; however, the Na^+/K^+ ratio again decreases because the interconfigurational advantages have vanished. But the ratio cannot fall to unity because the crystal radius of Na^+ is smaller than that of K^+ .

E. THE IMPORTANCE OF THE PHYSICAL PROPERTIES OF WATER

It is perhaps obvious that the physical properties of the water molecules intervening in the various configurations are of critical importance because of their effect on short-range interactions. Thus the substitution of deuterium oxide (D_2O) for water (H_2O) affects acid dissociation constants, as mentioned in the introduction, and has a profound effect on the c -value versus total-potential-energy plots of the various ions in Figures 4.6 to 4.8. Such changes in interaction energies are the basis of the functional and morphological changes of cells kept in D_2O media, discussed on page xxviii.

F. THE CRITICAL IMPORTANCE OF AN OPTIMAL MICROCELL SIZE

Very high selectivity ratios have been calculated for the ratios of K^+ , NH_4^+ , Rb^+ , or Cs^+ to Na^+ or Li^+ at various c -values. The reason is that at these c -values, Li^+ and Na^+ ions prefer high configurations, whereas K^+ , NH_4^+ , Rb^+ , and Cs^+ ions prefer low configurations. A high configuration subsumes a sufficient microcell volume to permit a sizable number of water molecules around the ion pairs. If the fixed ionic sites are too close together, the preference for the higher configurations by, say, Na^+ or Li^+ , is lost and the selectivity ratio falls. If the microcell is excessively large, the counterions will be dissociated and there will then be a loss of ionic selectivity. Thus, for optimal selectivity, a microcell is needed in which, for the particular association energies involved, there will be both a high degree of ionic association and sufficient water to allow the assumption of the higher configurations. It seems that nature has anticipated this need by providing living cells with an average microcell 20Å in diameter, and by providing effective charge fixation with a profusion of anchoring sites in the form of H-bonding and ionic groups.

G. THE OPTIMAL c -VALUE FOR MAXIMUM SELECTIVITY

Given an optimal microcell size, one can calculate the theoretical selectivity ratios for a particular pair of ions from the association energies given in Figures 4.9 to 4.11. Results of such calculations are illustrated in Figure 4.13, which demonstrates that for the maximal ratio of, say, Na^+/K^+ , a particular range of optimal c -values exists. Variation in c -value beyond this range in either direction causes a decline in selectivity.

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