

Free Energy of Solvation, Interaction, and Binding of Arbitrary Charge Distributions Imbedded in a Dielectric Continuum

B. Jayaram

Department of Chemistry, Indian Institute of Technology, Hauz Khas, New Delhi-110016, India

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A theoretical treatment of solvation and interaction of two arbitrary charge distributions imbedded in a dielectric continuum solvent is presented. The electrostatic component of the total free energy of such a charge assembly contains contributions from the solvation energies of each charge distribution, and modified Coulomb interaction energies between the two charge distributions. The theory developed is illustrated for special cases along with an application to the interaction between two ions in a continuum solvent.

Introduction

The dielectric continuum treatment of solvent in theoretical descriptions of equilibrium properties of aqueous solutions of simple ions, molecules, and biomolecules has received renewed attention in recent years due to its conceptual simplicity and computational expediency. Both analytical and numerical techniques have been exploited to obtain free energies of hydration of solutes, starting from Laplace or Poisson-Boltzmann equations. The stage is now set to tackle problems of binding equilibria with a continuum treatment of solvent. In this article, we present a theoretical treatment of solvation, interaction, and binding of two arbitrary charge distributions imbedded in a dielectric continuum solvent. We have derived expressions for the free energy of interaction between two solutes as mediated by solvent. This amounts to obtaining the electrostatic contribution to the potential of mean force between the solutes, which is not only of interest per se, but also can be used in molecular simulations to incorporate solvent effects. The theory developed is discussed with an application to the interaction between two ions in a continuum solvent.

Background

Attempts seeking analytical solutions to the hydration free energies of arbitrary charge distributions have a long history. Born's model for ion solvation^{1–3} and Onsager's reaction field approach⁴ to dipolar solvation found a generalization in Kirkwood's formulation^{5,6} of the Helmholtz free energy of an arbitrary charge distribution imbedded in a dielectric continuum solvent containing added salt. Beveridge and Schnuelle⁷ reported a concentric dielectric continuum model which can in principle incorporate several layers of solvent with varying dielectric constants to account for saturation effects in calculating solvation free energies of arbitrary charge distributions with an overall spherical symmetry. This theory was subsequently extended to other geometries.^{8,9} Jayaram and Beveridge included ionic strength effects in the concentric dielectric model¹⁰ as an extension to Tanford-Kirkwood theory¹¹ and compared the dielectric continuum model results on solvation with those based on molecular simulations.¹² Solvation and salt effects in the stability of globular proteins, for instance, fall within the purview of such theories.⁶ The SATK (static accessibility Tanford-Kirkwood) model,¹³ which uses a simpler treatment of solvent than that of Beveridge and co-workers but an additional depth parameter, has been extensively applied to study protein titration curves, merits and limitations of which are discussed in several places.^{13,14} States and Karplus¹⁵ developed an electrostatic continuum solvent model to treat hydrogen-exchange behavior in proteins.¹⁶ Gilson et al.¹⁷ categorized the different contributions to electrostatic free energies of macromolecules under two sets. The first set

includes all pairwise interactions, viz. coulombic, boundary polarization effect and a pairwise Debye-Hückel term. The second set includes all self-energies. Gilson and Honig¹⁸ subsequently presented a numerical method to calculate the total electrostatic energy of a macromolecular system. Solvation free energies of DNA-like molecules with an overall cylindrical symmetry in the continuum framework have also been reported.¹⁹ Bashford²⁰ has recently summarized the existing theoretical tools to treat electrostatic effects in biological molecules. Molecular simulations on solvation free energies have provided new insights into the success of continuum models.^{21–23} The above theories deal with solvent and/or salt effects on an ion, molecule, or macromolecule. Dielectric continuum theories, in the above vein, for binding and interaction have not progressed beyond Coulomb's law, although numerical results based on simulations and the integral equation method,²⁴ the protein dipole Langevin dipole (PDLD) approach,^{25,26} the finite boundary element method,²⁷ and finite difference and finite element Poisson-Boltzmann methods^{18,28–30} have been reported. Binding is the next phase in the theoretical approaches.

Consider two arbitrary charge distributions infinitely apart in a vacuum (dielectric constant $\epsilon = 1$). When these two charge distributions are brought together to a distance R , Coulomb's law gives us the interaction energy as a summation over $(q_i q_j / r_{ij})$ -type terms. Now if these charge distributions held at a distance R are transferred to a dielectric medium (e.g., $\epsilon = 80$), the interaction energies are still calculated as $(q_i q_j / \epsilon r_{ij})$, treating each charge distribution as a collection of point charges in a continuum solvent. Suppose each of these charge distributions is imbedded in a low dielectric cavity in a continuum solvent. Coulomb's law is not valid for estimating the interaction energies. The free energy of such an assembly contains contributions coming from the solvation of each charge distribution and its interaction with the other charge distribution as mediated by the solvent. To illustrate this further, let a cation of charge q_+ and radius r_+ represent charge distribution I and an anion of charge q_- and radius r_- represent charge distribution II and consider that they are infinitely apart in a dielectric medium. The free energy of such an assembly in the continuum model may be evaluated as a sum of the Born's self-energy terms or the solvation free energy of each ion. Implicit in Born's formulation is the idea that a point charge is imbedded in a low dielectric cavity which in turn is surrounded by a high dielectric medium. Now when these two ions are brought closer from infinity to a distance R , the solvation free energy terms are modified and there is an additional contribution due to the interaction between the two charges. Coulomb's law obviously is not valid for estimating the interaction energies between the two ions because of the presence of the dielectric boundaries between the two ions. Also, usage of Coulomb's law is inconsistent with the Born model. A theory is needed which accounts for both solvation and interaction as a

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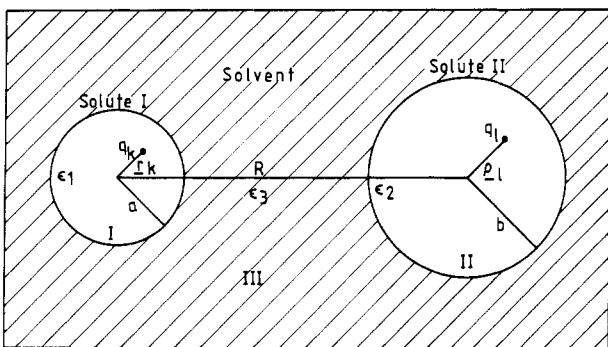


Figure 1. Definition of the parameters for the problem of solvent-mediated interaction of an arbitrary charge distribution enclosed in a sphere of radius a and dielectric constant ϵ_1 with another charge distribution enclosed in a sphere of radius b of dielectric constant ϵ_2 , both separated by a distance R and solvent of dielectric constant ϵ_3 .

function of distance between the two arbitrary charge distributions. The present paper addresses this need.

Theory and Discussion

The model considered in this study is depicted in Figure 1. Region I represents a cavity of radius $r = a$ and a dielectric constant ϵ_1 where in the solute charges q_k are located at sites r_k . Region II similarly represents a cavity of radius $\rho = b$ and a dielectric constant ϵ_2 where in the solute charges q_l are located at sites r_l . Region III contains solvent of dielectric constant ϵ_3 . The distance between the centers of the charge distributions of solutes I and II is denoted as R . The objective here is to obtain an analytical expression for the solvation free energies together with the free energy of solvent-mediated interaction between the two charge distributions as a function of distance between them.

To obtain the solvent contribution to the total free energy of the charge assembly, one starts with the Laplace equation

$$\nabla^2 \Phi = 0 \quad (1)$$

where Φ is the electrostatic potential and ∇^2 is the Laplacian operator. The general solution for eq 1 in polar coordinates is

$$\Phi = \epsilon^{-1} \sum_{n=0}^{\infty} \sum_{m=-n}^{+n} \left(A_{nm} r^n + \frac{B_{nm}}{r^{n+1}} \right) P_n^m(\cos \theta) e^{im\varphi} \quad (2)$$

where $P_n^m(\cos \theta)$ are associated Legendre polynomials, A_{nm} is a constant, and B_{nm} is related to the charge distribution.

The problem considered here involves three regions. The potential inside the cavity I is given as

$$\Phi_1 = \epsilon_1^{-1} \sum_{n=0}^{\infty} \sum_{m=-n}^{+n} \left(A_{nm} r^n + \frac{B_{nm}}{r^{n+1}} \right) P_n^m(\cos \theta) e^{im\varphi} \quad (3)$$

The potential inside cavity II is given as

$$\Phi_2 = \epsilon_2^{-1} \sum_{n=0}^{\infty} \sum_{m=-n}^{+n} \left(C_{nm} \rho^n + \frac{D_{nm}}{\rho^{n+1}} \right) P_n^m(\cos \theta) e^{im\varphi} \quad (4)$$

The potential in the region of bulk solvent, i.e. region III, is given as

$$\Phi_3 = \epsilon_3^{-1} \sum_{n=0}^{\infty} \sum_{m=-n}^{+n} \left(E_{nm} r^n + \frac{F_{nm}}{r^{n+1}} + G_{nm} \rho^n + \frac{H_{nm}}{\rho^{n+1}} \right) P_n^m(\cos \theta) e^{im\varphi} \quad (5)$$

The terms containing $(1/r^{n+1})$ and $(1/\rho^{n+1})$ originate in the multipolar expansion of the two charge distributions with " n " denoting the order of the electrical moments. It may be noted that r , ρ , and R represent lengths of three sides of a triangle. Let

the angle between the sides of length r and R be γ and that between ρ and R be δ . Then according to the law of cosines

$$r^2 = (R^2 + \rho^2 - 2R\rho \cos \gamma) \quad (6A)$$

$$\rho^2 = (R^2 + \rho^2 - 2R\rho \cos \delta) \quad (6B)$$

B_{nm} and D_{nm} contain the characteristics of the charge distributions I and II, respectively:

$$B_{nm} = \frac{(n-|m|)!}{(n+|m|)!} \sum_{k=1}^s q_k r_k^n P_n^m(\cos \theta_k) e^{-im\varphi_k} \quad (7)$$

$$D_{nm} = \frac{(n-|m|)!}{(n+|m|)!} \sum_{l=1}^t q_l \rho_l^n P_n^m(\cos \theta_l) e^{-im\varphi_l} \quad (8)$$

The terms with A_{nm} and C_{nm} in eqs 3 and 4 are due to the reaction field acting on the solute charge distributions I and II, respectively, originating in the polarization of the bulk dielectric continuum, and these are made to include Coulomb potentials as well, due to charge distributions II and I, respectively, as modified by the presence of dielectric discontinuities by a suitable choice of the (general solutions and) boundary conditions. The reaction as well as the modified Coulomb potential acting on the solute charge distribution I is identifiable with

$$\Phi_1^R = \epsilon_1^{-1} \sum_{n=0}^{\infty} \sum_{m=-n}^{+n} (A_{nm} r^n) P_n^m(\cos \theta) e^{im\varphi} \quad (9)$$

Similarly, the reaction as well as the modified Coulomb potential acting on the solute charge distribution II is identifiable with

$$\Phi_2^R = \epsilon_2^{-1} \sum_{n=0}^{\infty} \sum_{m=-n}^{+n} (C_{nm} \rho^n) P_n^m(\cos \theta) e^{im\varphi} \quad (10)$$

The Helmholtz free energy of the system is then obtained as

$$A = \frac{1}{2} \sum_{k=1}^s q_k \Phi_1^R(r_k) + \frac{1}{2} \sum_{l=1}^t q_l \Phi_2^R(\rho_l) \quad (11)$$

The above free energy expression contains solvation free energies of each charge distribution and the free energy of interaction between the two charge distributions. The reference state is the two charge distributions infinitely apart in a vacuum or the absence of solvent.

Thus the problem on hand reduces to evaluating the constants A_{nm} and C_{nm} subject to a specification of appropriate boundary conditions. The boundary conditions for the model considered here are that the potential and the dielectric displacement across the boundaries be continuous and the potential be finite in the bulk solvent region.

$$\Phi_1(r=a) = \Phi_3(r=a) \quad (12)$$

$$\Phi_2(\rho=b) = \Phi_3(\rho=b) \quad (13)$$

$$\epsilon_1 (\partial \Phi_1 / \partial r)_{r=a} = \epsilon_3 (\partial \Phi_3 / \partial r)_{r=a} \quad (14)$$

$$\epsilon_2 (\partial \Phi_2 / \partial \rho)_{\rho=b} = \epsilon_3 (\partial \Phi_3 / \partial \rho)_{\rho=b} \quad (15)$$

$$\Phi_3 \rightarrow 0 \text{ as } r \rightarrow \infty \quad (16)$$

and

$$\Phi_3 \rightarrow 0 \text{ as } \rho \rightarrow \infty \quad (17)$$

Equations 16 and 17 imply that $E_{nm} = 0$ and $G_{nm} = 0$. Equations 3, 5, and 12 lead to

$$\epsilon_1^{-1} \left[A_{nm} a^n + \frac{B_{nm}}{a^{n+1}} \right] = \epsilon_3^{-1} \left[\frac{F_{nm}}{a^{n+1}} + \frac{H_{nm}}{\rho_a^{n+1}} \right] \quad (18)$$

where ρ_a is ρ evaluated at $r = a$, i.e.

$$\rho_a^2 = a^2 + R^2 - 2aR \cos \gamma \quad \rho_a^{-1} = (\mathrm{d}\rho/\mathrm{d}r)_{r=a} \quad (19)$$

Let

$$\epsilon_a = (\epsilon_3/\epsilon_1) \quad (20)$$

With these, eq 18 may be rewritten as

$$F_{nm} = a^{n+1} \left(\epsilon_a A_{nm} a^n + \epsilon_a \frac{B_{nm}}{a^{n+1}} - \frac{H_{nm}}{\rho_a^{n+1}} \right) \quad (21)$$

Equations 3, 5, and 14 lead to

$$nA_{nm} a^{n-1} - (n+1) \frac{B_{nm}}{a^{n+2}} = -(n+1) \frac{F_{nm}}{a^{n+2}} - (n+1) \frac{H_{nm}}{\rho_a^{n+2}} \rho_a^1 \quad (22)$$

Eliminating F_{nm} from eqs 21 and 22 gives

$$H_{nm} = \left(\frac{\epsilon_a}{\epsilon_a - \epsilon_a^1} \right) \left(\frac{\rho_a^{n+1}}{a^{n+1}} \right) \left[A_{nm} a^{2n+1} \left\{ \frac{n + (n+1)\epsilon_a}{(n+1)} \right\} + B_{nm} (\epsilon_a - 1) \right] \quad (23)$$

where

$$\epsilon_a^1 = \frac{\epsilon_a a \rho_a^1}{\rho_a} \quad (24)$$

From eqs 21 and 23, F_{nm} is obtained as

$$F_{nm} = \left(\frac{\epsilon_a}{\epsilon_a - \epsilon_a^1} \right) \left[-A_{nm} a^{2n+1} \left\{ \frac{n + (n+1)\epsilon_a^1}{(n+1)} \right\} + B_{nm} (1 - \epsilon_a^1) \right] \quad (25)$$

Similarly, eqs 4 and 5 together with eq 13 lead to

$$\epsilon_2^{-1} \left(C_{nm} b^n + \frac{D_{nm}}{b^{n+1}} \right) = \epsilon_3^{-1} \left(\frac{F_{nm}}{r_b^{n+1}} + \frac{H_{nm}}{b^{n+1}} \right) \quad (26)$$

where r_b is r evaluated at $\rho = b$.

$$r_b = (b^2 + R^2 - 2bR \cos \delta)^{1/2} \text{ and } r_b^{-1} = (\mathrm{d}r/\mathrm{d}\rho)_{\rho=b} \quad (27)$$

Let

$$\epsilon_b = (\epsilon_3/\epsilon_2) \quad (28)$$

With these, eq 26 may be rewritten as

$$\epsilon_b \left[C_{nm} b^n + \frac{D_{nm}}{b^{n+1}} \right] = \frac{F_{nm}}{r_b^{n+1}} + \frac{H_{nm}}{b^{n+1}} \quad (29)$$

Equations 4, 5, and 15 lead to

$$C_{nm} b^{n-1} - D_{nm} \frac{(n+1)}{b^{n+2}} = -F_{nm} \frac{(n+1)r_b^1}{r_b^{n+1}} - H_{nm} \frac{(n+1)}{b^{n+2}} \quad (30)$$

Eliminating F_{nm} from eqs 29 and 30 gives

$$H_{nm} = \left(\frac{\epsilon_b}{\epsilon_b^1 - \epsilon_b} \right) \left[C_{nm} b^{2n+1} \left\{ \frac{n + (n+1)\epsilon_b^1}{(n+1)} \right\} - D_{nm} (1 - \epsilon_b^1) \right] \quad (31)$$

where

$$\epsilon_b^1 = \frac{\epsilon_b b r_b^1}{r_b} \quad (32)$$

Equations 29 and 31 lead to

$$F_{nm} = \left(\frac{r_b^{n+1}}{b^{n+1}} \right) \left(\frac{\epsilon_b}{\epsilon_b^1 - \epsilon_b} \right) \left[-C_{nm} b^{2n+1} \left\{ \frac{n + (n+1)\epsilon_b}{(n+1)} \right\} + D_{nm} (1 - \epsilon_b) \right] \quad (33)$$

Eliminating H_{nm} from eqs 23 and 31 and F_{nm} from eqs 25 and 33 gives two equations for A_{nm} and C_{nm} in terms of B_{nm} and D_{nm} . Solving for A_{nm} and C_{nm} gives

$$A_{nm} = \frac{(n+1)}{\Theta} \left[(1 - \epsilon_a)(n + (n+1)\epsilon_b) - \left(\frac{ab}{\rho_a r_b} \right)^{n+1} (1 - \epsilon_a^1) \right. \\ \left. (n + (n+1)\epsilon_b^1) \right] \frac{B_{nm}}{a^{2n+1}} + \frac{(n+1)}{\Theta} [(1 - \epsilon_b^1)(n + (n+1)\epsilon_b) - \\ (1 - \epsilon_b)(n + (n+1)\epsilon_b^1)] \left(\frac{\epsilon_b}{\epsilon_b^1 - \epsilon_b} \right) \left(\frac{\epsilon_a - \epsilon_a^1}{\epsilon_a} \right) \frac{D_{nm}}{\rho_a^{n+1} a^n} \quad (34)$$

$$C_{nm} = \frac{(n+1)}{\Theta} [(1 - \epsilon_a^1)(n + (n+1)\epsilon_a) - (1 - \epsilon_a)(n + (n+1)\epsilon_a^1)] \left(\frac{\epsilon_a}{\epsilon_a^1 - \epsilon_a} \right) \left(\frac{\epsilon_b - \epsilon_b^1}{\epsilon_b} \right) \frac{B_{nm}}{r_b^{n+1} b^n} + \frac{(n+1)}{\Theta} [(1 - \epsilon_b)(n + (n+1)\epsilon_a) - \\ \left(\frac{ab}{\rho_a r_b} \right)^{n+1} (1 - \epsilon_b^1)(n + (n+1)\epsilon_a^1)] \frac{D_{nm}}{b^{2n+1}} \quad (35)$$

$$\Theta = \left[(n + (n+1)\epsilon_a)(n + (n+1)\epsilon_b) - \left(\frac{ab}{\rho_a r_b} \right)^{n+1} (n + (n+1)\epsilon_a^1)(n + (n+1)\epsilon_b^1) \right] \quad (36)$$

Using eqs 34 and 35 along with eqs 9–11, the Helmholtz free energy of the charge assembly can be obtained as

$$A = \frac{1}{2\epsilon_1} \sum_{k=1}^s \sum_{n=0}^{\infty} \sum_{m=-n}^{+n} A_{nm} q_k r_k^n P_n^m(\cos \theta_k) e^{im\varphi_k} + \\ \frac{1}{2\epsilon_2} \sum_{l=1}^t \sum_{n=0}^{\infty} \sum_{m=-n}^{+n} C_{nm} q_l \rho_l^n P_n^m(\cos \theta_l) e^{im\varphi_l} \quad (37)$$

Some special cases:

(a) Two charge distributions infinitely apart, $R \rightarrow \infty$. In this limit eqs 34 and 35 become

$$A_{nm} = \left[\frac{(n+1)(1 - \epsilon_a)}{n + (n+1)\epsilon_a} \right] \frac{B_{nm}}{a^{2n+1}} \quad \& \quad C_{nm} = \\ \left[\frac{(n+1)(1 - \epsilon_b)}{n + (n+1)\epsilon_b} \right] \frac{D_{nm}}{b^{2n+1}}$$

These compare exactly with the expressions reported previously for solvation free energies (see eqs 13–19 in ref 7). With the additional condition that $n = 0$, one recovers Born's expressions

for the individual ions.

$$A_{nm} = \left(\frac{1 - \epsilon_a}{\epsilon_a} \right) \frac{B_{nm}}{a} \quad \& \quad C_{nm} = \left(\frac{1 - \epsilon_b}{\epsilon_b} \right) \frac{D_{nm}}{b}$$

Similarly for $n = 1$, one obtains Onsager's expressions for the solvation free energy of dipoles.

(b) Two monopoles (ions) in a dielectric continuum solvent, $n = 0$.

$$A_0 = \frac{1}{\Theta_0} \left[(1 - \epsilon_a) \epsilon_b - \left(\frac{ab}{\rho_a r_b} \right) (1 - \epsilon_a^1) \epsilon_b^1 \right] \frac{B_0}{a} + \frac{1}{\Theta_0 \epsilon_a} (\epsilon_a - \epsilon_a^1) \frac{D_0}{\rho_a} \quad (38)$$

$$C_0 = \frac{1}{\Theta_0} \left[(1 - \epsilon_b) \epsilon_a - \left(\frac{ab}{\rho_a r_b} \right) (1 - \epsilon_b^1) \epsilon_a^1 \right] \frac{D_0}{b} + \frac{1}{\Theta_0 \epsilon_b} (\epsilon_b - \epsilon_b^1) \frac{B_0}{r_b} \quad (39)$$

$$\Theta_0 = \epsilon_a \epsilon_b - \left(\frac{ab}{\rho_a r_b} \right) \epsilon_a^1 \epsilon_b^1$$

$$\gamma = 0; \delta = 0 \quad \rho_a = R - a; r_b = R - b \quad \rho_a^1 = -1; r_b^1 = -1$$

$$\epsilon_a^1 = \epsilon_a (a/(a - R)) \quad \epsilon_b^1 = \epsilon_b (b/(b - R))$$

$$B_0 = q_k \quad D_0 = q_l$$

$$\Delta A = (1/2) [(1/\epsilon_1) A_0 q_k + (1/\epsilon_2) C_0 q_l] \quad (40)$$

(c) Coulomb's law for two point charges imbedded in a dielectric continuum solvent. The infinities arising in the self-energies of point charges are avoided by first taking the limit of homogeneous dielectric continuum, i.e. by equating all the different dielectric constants in the system and then letting the ionic radii go to zero. Setting $\epsilon_1 = \epsilon_2 = \epsilon_3 = \epsilon$, i.e. $\epsilon_a = \epsilon_b = 1$ in eqs 37 and 38 leads to

$$A_0 = [b^2 R / \{(R - a)^2 (R - b)^2\}] B_0 + [R / (R - a)^2] D_0$$

$$C_0 = [a^2 R / \{(R - a)^2 (R - b)^2\}] D_0 + [R / (R - b)^2] B_0$$

The free energy expression then becomes

$$\Delta A = (1/2\epsilon) [b^2 R / \{(R - a)^2 (R - b)^2\}] q_k^2 + (1/2\epsilon) [R / (R - a)^2] q_k q_l + (1/2\epsilon) [a^2 R / \{(R - a)^2 (R - b)^2\}] q_l^2 + (1/2\epsilon) [R / (R - b)^2] q_k q_l$$

Letting $a = b = 0$ in the above equation gives

$$\Delta A = (1/2\epsilon) [q_l q_k / R + q_k q_l / R] = q_k q_l / (\epsilon R)$$

(d) Influence of a vicinal point charge on the solvation free energy of a charge. Recently Kang, Nemethy, and Scheraga³¹ developed a theory to estimate the Helmholtz free energy of polarization of the hydration shell of a charge due to the presence of a neighboring point charge which they identified as $(q_k q_l / 2\epsilon R)$. We consider here a special case of a point charge in the vicinity of a finite-sized ion, as this proves to be a very instructive example in delineating the contributions of each part of the system.

Let $\epsilon_b = 1$ and then $b = 0$ in eqs 38 and 39

$$A_0 = \{(1 - \epsilon_a) / \epsilon_a a\} B_0 + \{(1/\epsilon_a) (R / (R - a)^2)\} D_0$$

$$C_0 = \{a^2 / (R(R - a)^2)\} D_0 + \{1/R\} B_0$$

The Helmholtz free energy is then given as

$$\Delta A = \{(1 - \epsilon_a) / 2a\epsilon_a\} q_k^2 + \{R / (2\epsilon_a(R - a)^2)\} q_k q_l + \{a^2 / (2\epsilon_3 R(R - a)^2)\} q_l^2 + \{1/2\epsilon_3 R\} q_k q_l \quad (41)$$

The system in this case, it may be recalled, consists of a charge q_k embedded in a cavity of radius a and dielectric constant ϵ_1 which is surrounded by solvent of dielectric constant ϵ_3 . There exists a point charge q_l in the solvent region at a distance R from q_k . The ΔA here represents work done for transferring both q_k and q_l from vacuum to solvent and bringing them together to a distance R from infinity. The first term in eq 41 represents Born's self-energy for q_k . There is no such self-energy term for q_l since it is a point charge. The second and fourth terms are the contributions of q_k and q_l to the interaction energy between these two charges. The fourth term is half the Coulomb energy due to the point charge q_l . The second term would reduce to the remaining half of the Coulomb energy if a goes to zero. Thus, to interpret the fourth term $q_k q_l / 2\epsilon R$ as the polarization free energy³¹ due to a point charge does not appear to be justified. This is just half the Coulombic ($1/r$) term in any force field which takes care of charge-charge interactions. Adding this under solvation as well will result in double counting. The second term may be seen as the modified Coulomb energy due to the finite size of the ion of charge q_k . The third term then becomes the correction to the solvation (first term) free energy. In the limit of $\epsilon_a \rightarrow 1$ and $a \rightarrow 0$ both first and third terms vanish. A simple partitioning thus suggests that the first and third (self) terms here and in eqs 34 and 35 deal with solvation free energies while the second and fourth (cross) terms refer to the interaction energies.

Finally, the electrostatic contribution to the interaction energies between a sodium and a chloride ion are plotted in Figure 2 as a function of distance between them along with Coulombic interaction energy. Born's self-energies of the Na^+ ion and Cl^- ions which make a constant contribution to the curve have been subtracted out of the total free energy calculated using eq 40. The radius of the cation and anion are taken to be 1.68 and 1.937 Å;³ $\epsilon_1 = \epsilon_2 = 1$, $\epsilon_3 = 80$. It may be noticed that there is an enhancement in the attractive interactions between the two ions of opposite charge relative to Coulomb's law predictions, a consequence of two opposing trends. Charge 1 polarizes solvent, and this acts back on charge 1. Self-energy is due to this reaction field. Desolvation leads to modifications to the reaction field which increases the total free energy of the system (ΔA becomes less negative). When depicted as in Figure 2, desolvation has the apparent effect of decreasing the net attraction between the two species relative to Coulomb's law. The second source involves charge 2 polarizing solvent, and this refraction field acts on charge 1. Modified Coulomb field originates in this. This decreases the total free energy (ΔA becomes more negative). The contribution of this to the total free energy of the system is larger than the desolvation expense. The net result is an increased attraction between the two ions of opposite charge.

Interesting effects ensue when the distance is less than the sum of the assumed radii of the two ions. In particular, the ion pair problem changes over to a dipole problem. The minimum seen in Figure 2 is reflective of this phenomenon. Such a minimum does not and is not expected to occur with Coulomb's law. The distance at which the minimum occurs in Figure 2 is not indicative of the optimal interaction distance between the two ions. Short-range repulsions (as may be incorporated via a $1/r^{12}$ term) are nonelectrostatic in nature and are beyond the purview of dielectric continuum theories. The present theory may, however, be supplemented by addition of such terms for a comparison with potential of mean force data obtainable from molecular simulations and for the development of a force field which includes solvent effects.

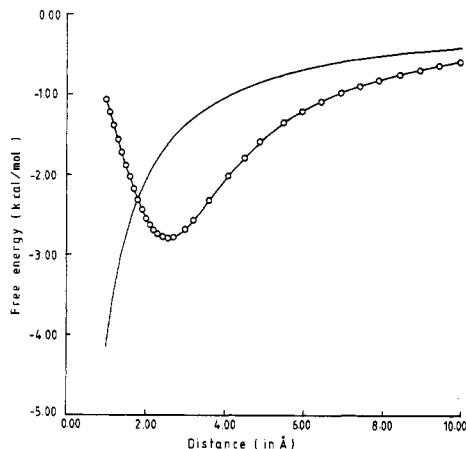


Figure 2. Electrostatic contribution to the total free energy of a system of two finite-sized ions of opposite charge imbedded in a dielectric continuum solvent, calculated using eq 40 (solid line with circles), as a function of distance between the two ions after Born's solvation energies of individual ions have been subtracted out. Interaction energies based on Coulomb's law with $\epsilon = 80$ are also shown (solid line).

Conclusions

A theoretical expression (eqs 34–37) for the total free energy of a charge assembly consisting of two arbitrary charge distributions at a finite distance imbedded in a dielectric continuum solvent is obtained. The free energy arises from the field acting on each charge distribution, and this field has two components: (a) the reaction field which accounts for solvation effects and (b) the refraction field which accounts for modifications to Coulombic interactions due to the presence of dielectric discontinuities in the solution. In general, the refraction field results in an enhanced interaction strength over Coulombic interactions. Like charges repel and unlike charges attract more strongly than in the case of Coulomb's law.

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