

Tanford-Kirkwood Theory for Concentric Dielectric Continua: Application to Dimethylphosphate

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Synopsis

The Tanford-Kirkwood theory for evaluating the electrostatic free energy of a discrete charge distribution in the presence of ion atmosphere is extended to concentric dielectric continua. The theory is applied to study the conformational preferences with respect to phosphodiester torsion angles in the dimethylphosphate anion (DMP^-) and the sodium dimethylphosphate ion pair (Na^+DMP^-), in the absence and presence of ion atmosphere and at varying local dielectric constants. Results indicate that phosphodiester torsion angles in DMP^- prefer the *gauche-gauche* conformation in aqueous solutions.

INTRODUCTION

The dielectric continuum as a description of environmental effects on the equilibrium properties of aqueous solutions, and on the structure and conformation of biomolecules, has received much attention over the last several decades due to its conceptual simplicity and computational convenience. Beveridge and Schnuelle, in an earlier publication,¹ described the evaluation of Helmholtz free energy of polarization of an arbitrary charge distribution imbedded in concentric dielectric continua, generalizing the models of Born^{2,3} for ion solvation and of Onsager⁴ for dipole solvation, within the framework of Kirkwood's reaction potential formalism.^{5,6} This can be useful for including electrostriction or bound-water effects in a dielectric-continuum treatment of solvent. In the following we present an extension of this treatment to incorporate ion atmosphere, thus combining the work on extended Debye-Huckel theory discussed by Tanford⁷ with that in Ref. 1 to provide an extended continuum scheme to treat environmental effects. The theory is illustrated by investigating the conformational preferences of the dimethylphosphate anion and the sodium dimethylphosphate ion pair in aqueous solutions with respect to phosphodiester torsion angles.

BACKGROUND

The continuum approach is motivated physically by a separation of spatial scales involved in the problem. If the dimensions of the solute are much larger

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compared to solvent and counterions, the environment (i.e., solvent and counterions) may be treated as a homogeneous medium. The continuum formalism is characterized mathematically by an appropriate differential equation for the potential of interest. For electrostatic potential, one starts with the Laplace equation for treating solvent effects and the Poisson-Boltzmann equation for considering the effects due to ion atmosphere. Usage of the linearized Poisson-Boltzmann (P-B) equation for the ion atmosphere, while involving an approximation discussed extensively in the literature,⁸ makes the problem analytically tractable.

$$\nabla^2 \Phi = 0 \quad (\text{Laplace equation}) \quad (1)$$

$$(\nabla^2 - x^2)\Phi = 0 \quad (\text{Linearized P-B equation}) \quad (2)$$

Here Φ is the electrostatic potential and ∇^2 is the Laplacian operator. The ionic strength enters the theoretical treatment through x , the Debye reciprocal length parameter. The general solution for Eq. (1) in polar coordinates,⁹ suitable for the symmetry of the problem of solute in a spherical cavity considered here, is

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

and for Eq. (2) it is⁵

$$\Phi = \sum_{n=0}^{\infty} \sum_{m=-n}^{+n} \left[\frac{C_{nm}}{r^{n+1}} e^{-xr} X_n(xr) \right] P_n^m(\cos \theta) e^{im\phi} \quad (4)$$

where $P_n^m(\cos \theta)$ are the associated Legendre polynomials, B_{nm} and C_{nm} are constants, E_{nm} is related to the charge distribution and

$$X_n(xr) = \sum_{s=0}^n \left[\frac{2^s n! (2n-s)!}{s! (2n)! (n-s)!} \right] (xr)^s \quad (5)$$

The form of Eqs. (3) and (4) is due to an expansion of the solutions of Eqs. (1) and (2) in terms of Legendre polynomials, which constitute a set of linearly independent functions.

The problem as extended to concentric dielectric continua¹ considers three regions with solvent treated as a polarizable dielectric continuum. Region A with a dielectric constant of ϵ_i is the cavity of a radius a containing the solute represented as a discrete charge distribution, region B vicinal to the solute contains solvent of dielectric constant ϵ_{loc} in a spherical shell of thickness $(b-a)$, and region C represents the bulk solvent of dielectric constant ϵ_0 and extends radially from b to infinity. Thus for the problem dealt with in Ref. 1, the potential inside the cavity is

$$\Phi_i = \epsilon_i^{-1} \sum_{n=0}^{\infty} \sum_{m=-n}^{+n} \left(B_{nm} r^n + F_{nm} r^n + \frac{E_{nm}}{r^{n+1}} \right) P_n^m(\cos \theta) e^{im\phi} \quad (6)$$

where the $1/r^{n+1}$ terms originate in the multipolar expansion of the central charge distribution, with n denoting the order of the electrical moments. E_{nm} contains the characteristics of the central charge distribution:

$$E_{nm} = \left[\frac{(n - |m|)!}{(n + |m|)!} \right] \sum_{k=1}^n q_k r_k^n P_n^m(\cos \theta_k) e^{-im\phi} \quad (7)$$

The terms B_{nm} and F_{nm} are due to the reaction field acting on the solute charge distribution, originating in the polarization of the local dielectric shell and the bulk dielectric continuum, respectively. The reaction potential acting on the solute charge distribution is identifiable with

$$\Phi_R = \epsilon_i^{-1} \sum_{n=0}^{\infty} \sum_{m=-n}^{+n} (B_{nm} r^n + F_{nm} r^n) P_n^m(\cos \theta) e^{im\phi} \quad (8)$$

The continuity of the potential and its first derivative across the boundaries between the three regions were employed to specify the boundary conditions. The coefficients B_{nm} and F_{nm} were determined in terms of E_{nm} . Helmholtz free energy of polarization was obtained as

$$A = \frac{1}{2} \sum_k q_k \Phi_R(r_k) \quad (9)$$

$$= \frac{1}{2\epsilon_i} \sum_{n=0}^{\infty} \left\{ \left[\frac{(n+1)(1-\epsilon'_a)}{(n+1)\epsilon'_a + n} \right] \frac{Q_n}{a^{2n+1}} + \left[\frac{(n+1)(1-\epsilon_b)}{(n+1)\epsilon_b + n} \right] \left[1 - \frac{n(1-\epsilon'_a)}{(n+1)\epsilon'_a + n} \right] \frac{Q_n}{b^{2n+1}} \right\} \quad (10)$$

where

$$Q_n = \sum_k \sum_l q_k q_l r_k^n r_l^n P_n(\cos \theta_{kl}) \quad (11)$$

and

$$\epsilon'_a = \epsilon_a \left/ \left(1 + \frac{(n+1)(1-\epsilon_a)(1-\epsilon_b)}{[(n+1)\epsilon_b + n]} \frac{a^{2n+1}}{b^{2n+1}} \right) \right. \quad (12)$$

This model was a step beyond the earlier continuum models for solvation free energies in recognizing the special nature of solvent close to the surface of the solute. A similar extension of Kirkwood and Tanford's treatment is presented below.

THEORY

The model considered in the present treatment consists of three regions as in Ref. 1 (cf. Fig. 1) but could of course be generalized further. Region A, represents a cavity of radius $r = a$, and a dielectric constant of ϵ_i wherein the

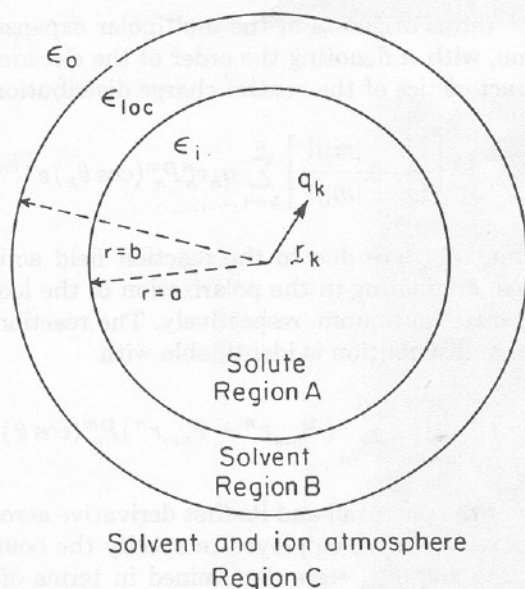


Fig. 1. Definition of the parameters for the concentric dielectric continuum problem.

solute charges q_k are located at sites r_k . Region B, extending from $r = a$ to $r = b$, represents the region of the solvent vicinal to the solute and contains solvent of dielectric constant ϵ_{loc} . Region C, ranging from $r = b$ to $r = \infty$ contains both the counter and coions, i.e., the ion atmosphere and the solvent of dielectric constant ϵ_0 . This partitioning of the system, besides being physically realistic for spherical solutes at low ionic strengths, provides a unified scheme to combine the other models mentioned above. The objective here is to consider analytically the solute-solvent interactions as well as solute-ion atmosphere interactions at the continuum level. The appropriate equations to solve are the Laplace equation [Eq. (1)] in regions A and B, and the linearized Poisson-Boltzmann equation [Eq. (2)] for region C. The notation adopted in the following is as similar as possible to that of Ref. 1.

The potential inside the cavity is given by Eq. (6), where now the F_{nm} terms also include the reaction field due to the ion atmosphere. The reaction potential at the solute charge site r_k is given by Eq. (8). The potential in the local region (region B) is

$$\Phi_{loc} = \epsilon_{loc}^{-1} \sum_{n=0}^{\infty} \sum_{m=-n}^{+n} \left(F_{nm} r^n + \frac{G_{nm}}{r^{n+1}} \right) P_n^m(\cos \theta) e^{im\phi} \quad (13)$$

The potential in the outermost region (region C) is

$$\Phi_0 = \epsilon_0^{-1} \sum_{n=0}^{\infty} \sum_{m=-n}^{+n} \left[\frac{C_{nm}}{r^{n+1}} e^{-xr} X_n(xr) \right] P_n^m(\cos \theta) e^{im\phi} \quad (14)$$

The boundary conditions for the model considered are

$$\Phi_{\text{loc}}(r=b) = \Phi_0(r=b) \quad (15)$$

$$\Phi_i(r=a) = \Phi_{\text{loc}}(r=a) \quad (16)$$

$$\epsilon_{\text{loc}}(d\Phi_{\text{loc}}/dr)_{r=b} = \epsilon_0(d\Phi_0/dr)_{r=b} \quad (17)$$

and

$$\epsilon_i(d\Phi_i/dr)_{r=a} = \epsilon_{\text{loc}}(d\Phi_{\text{loc}}/dr)_{r=a} \quad (18)$$

Equations (13)–(15) lead to

$$\epsilon_{\text{loc}}^{-1} \left(F_{nm} b^n + \frac{G_{nm}}{b^{n+1}} \right) = \epsilon_0^{-1} \left[\frac{C_{nm}}{b^{n+1}} e^{-xb} X_n(xb) \right] \quad (19)$$

$$\text{or} \quad \epsilon_b \left(F_{nm} b^n + \frac{G_{nm}}{b^{n+1}} \right) = C_{nm} Y_b$$

where

$$\epsilon_b = \epsilon_0/\epsilon_{\text{loc}} \quad (20)$$

and

$$Y(r) = e^{-xr} X_n(xr)/r^{n+1} \quad Y_b = [Y(r)]_{r=b}; \quad Y'_b = [dY(r)/dr]_{r=b} \quad (21)$$

Equations (13), (14), and (17) lead to

$$nF_{nm} b^{n-1} - (n+1) \frac{G_{nm}}{b^{n+2}} = C_{nm} Y'_b \quad (22)$$

Eliminating C_{nm} from Eqs. (19) and (22),

$$F_{nm} = \left[\frac{(n+1)Y_b + \epsilon_b b Y'_b}{nY_b - \epsilon_b b Y'_b} \right] \frac{G_{nm}}{b^{2n+1}} \quad (23)$$

Similarly, Eqs. (6) and (13) together with Eq. (16) give

$$\epsilon_i^{-1} \left(B_{nm} a^n + F_{nm} a^n + \frac{E_{nm}}{a^{n+1}} \right) = \epsilon_{\text{loc}}^{-1} \left(F_{nm} a^n + \frac{G_{nm}}{a^{n+1}} \right) \quad (24)$$

$$\text{or} \quad \epsilon_a \left(B_{nm} a^n + F_{nm} a^n + \frac{E_{nm}}{a^{n+1}} \right) = \left(F_{nm} a^n + \frac{G_{nm}}{a^{n+1}} \right)$$

where

$$\epsilon_a = \epsilon_{\text{loc}}/\epsilon_i \quad (25)$$

and Eqs. (6), (23), and (18) lead to

$$nB_{nm}a^{n-1} - (n+1)\frac{E_{nm}}{a^{n+2}} = -(n+1)\frac{G_{nm}}{a^{n+2}} \quad (26)$$

Eliminating F_{nm} using Eqs. (23) and (24) gives

$$G_{nm} = \epsilon'_a (B_{nm}a^{2n+1} + E_{nm}) \quad (27)$$

where

$$\epsilon'_a = \epsilon_a \left/ \left\{ 1 + \left(\frac{a^{2n+1}}{b^{2n+1}} \right) (1 - \epsilon_a) \left[\frac{(n+1)Y_b + \epsilon_b b Y'_b}{nY_b - \epsilon_b b Y'_b} \right] \right\} \right. \quad (28)$$

Combining Eqs. (26) and (27) gives

$$B_{nm} = \left[\frac{(n+1)(1 - \epsilon'_a)}{(n+1)\epsilon'_a + n} \right] \frac{E_{nm}}{a^{2n+1}} \quad (29)$$

and from Eqs. (27) and (29),

$$G_{nm} = \left[1 - \frac{n(1 - \epsilon'_a)}{(n+1)\epsilon'_a + n} \right] E_{nm} \quad (30)$$

and from Eqs. (23) and (30),

$$F_{nm} = \left[\frac{(n+1)Y_b + \epsilon_b b Y'_b}{nY_b - \epsilon_b b Y'_b} \right] \left[1 - \frac{n(1 - \epsilon'_a)}{(n+1)\epsilon'_a + n} \right] \frac{E_{nm}}{b^{2n+1}} \quad (31)$$

The reaction potential is

$$\begin{aligned} \Phi_R = \epsilon_i^{-1} \sum_{n=0}^{\infty} \sum_{m=-n}^{+n} & \left\{ \left[\frac{(n+1)(1 - \epsilon'_a)}{(n+1)\epsilon'_a + n} \right] \frac{r^n}{a^{2n+1}} \right\} + \left[\frac{(n+1)Y_b + \epsilon_b b Y'_b}{nY_b - \epsilon_b b Y'_b} \right] \\ & \times \left[1 - \frac{n(1 - \epsilon'_a)}{(n+1)\epsilon'_a + n} \right] \frac{r^n}{b^{2n+1}} \left\{ E_{nm} P_n^m(\cos \theta) e^{im\phi} \right\} \end{aligned} \quad (32)$$

The electrostatic free energy is

$$\begin{aligned} A = \frac{1}{2\epsilon_i} \sum_{n=0}^{\infty} & \left[\frac{(n+1)(1 - \epsilon'_a)}{(n+1)\epsilon'_a + n} \right] \frac{Q_n}{a^{2n+1}} + \left[\frac{(n+1)Y_b + \epsilon_b b Y'_b}{nY_b - \epsilon_b b Y'_b} \right] \\ & \times \left(1 - \frac{n(1 - \epsilon'_a)}{(n+1)\epsilon'_a + n} \right) \frac{Q_n}{b^{2n+1}} \end{aligned} \quad (33)$$

The above results transform into those of Ref. 1, in particular, Eq. (33) reduces to Eq. (10) in the limit of vanishing ionic strength. For $x = 0$,

$$Y_b = 1/b^{n+1} \quad \text{and} \quad Y'_b = -(n+1)/b^{n+2} \quad (34)$$

Essentially, the terms F_{nm} and ϵ'_a are redefined from those in Ref. 1 to include ion atmosphere through the Debye's reciprocal length parameter x .

For $n = 0$, Eq. (33) reduces to

$$A_0 = \frac{1}{2\epsilon_i} \left[\frac{(1 - \epsilon'_a)}{\epsilon'_a} \frac{Q_0}{a} + \frac{1 - \epsilon_b(1 + xb)}{\epsilon_b(1 + xb)} \frac{Q_0}{b} \right] \quad (35)$$

Substituting for ϵ'_a and setting $\epsilon_b = 1$ results in

$$A_0 = (A_{\text{Born}} + A_{\text{DH}}) = \frac{Q_0}{2\epsilon_i\epsilon_a a} \left[(1 - \epsilon_a) - \frac{xa}{(1 + xb)} \right] \quad (36)$$

In comparing Eq. (36) with the Debye-Huckel result (see, for instance, Eqs. (26)–(30) of Ref. 7) it must be borne in mind that the reference state here is the discrete charge assembly in free space as in Born's model for ion solvation. By letting $x = 0$ and $\epsilon_i = 1$ in the above equation, Born's charging energy is recovered,

$$A_0 = \frac{Q_0}{2a} \left(\frac{1 - \epsilon_a}{\epsilon_a} \right). \quad (37)$$

Similarly, for $n = 1$, $Q_1 = \mu^2$, and

$$A_1 = \frac{1}{2\epsilon_i} \left[\frac{2(1 - \epsilon'_a)}{(2\epsilon'_a + 1)} \frac{\mu^2}{a^3} + \left(\frac{2Y_b + \epsilon_b b Y'_b}{Y_b - \epsilon_b b Y'_b} \right) \left(1 - \frac{(1 - \epsilon'_a)}{(2\epsilon'_a + 1)} \right) \frac{\mu^2}{b^3} \right] \quad (38)$$

where

$$\epsilon'_a = \epsilon_a / \left[1 + \frac{a^3}{b^3} (1 - \epsilon_a) \left(\frac{2Y_b + b\epsilon_b Y'_b}{Y_b - b\epsilon_b Y'_b} \right) \right] \quad (39)$$

$$Y_b = (e^{-xb}/b^2)(1 + xb) \quad (40)$$

$$Y'_b = (-e^{-xb}/b^3)(2 + 2xb + x^2 b^2) \quad (41)$$

Now by setting $\epsilon_b = 1$, $\epsilon_i = 1$, and $x = 0$ in Eq. (38),

$$A_1 = \frac{(1 - \epsilon_a)}{(1 + 2\epsilon_a)} \frac{\mu^2}{a^3}. \quad (42)$$

This is the familiar Onsager's dipolar contribution to the solvation free energy.

CALCULATIONS

Model calculations are performed on dimethylphosphate anion (DMP^-) and sodium dimethylphosphate ion pair (Na^+DMP^-) in the *gauche-gauche* (*gg*), *gauche-trans* (*gt*), and *trans-trans* (*tt*) conformations as systems of previous interest in this laboratory.¹⁰⁻¹⁴ Literature on the conformational preferences of phosphodiester torsion angles, and on the hydration of DMP^- and Na^+DMP^- , is summarized in an earlier publication.¹⁰ Equation (33) in the limiting case was seen to reproduce the hydration free energies of monoatomic ions (Table 2.9 of Ref. 3), and here we consider a polyatomic conformationally flexible molecular ion. All calculations were performed at a temperature of 298 K and varied ionic strengths. Center of the first non-vanishing moment is chosen as the origin for the solute. The inner radius $r = a$ was taken to be 3.2 Å and the outer radius $r = b$ as 6.0 Å. These values are based on the solute-water radial distribution functions calculated from the previous Monte Carlo simulations.¹⁰ The inner radius as estimated from the partial molar volumes was ~ 2.87 Å, but was observed to lead to divergences in the computed free energies since some solute charges lie outside the inner sphere. The choice for the outer radius also agrees with the value of $b = a + 2R_w$, where R_w is the radius of the water molecule. The geometry and charge distribution for DMP^- were identical to those of Alagona et al.,¹⁵ where the charges were chosen as fits to the quantum mechanically calculated electrostatic potentials and reproduce the moments of the electronic charge distribution well. The sodium ion for the ion pair was placed in the anionic POO^- plane on the bisector of the OPO angle at a distance of 2.21 Å from the anionic oxygens, with a unit positive charge, following Liebmann et al.¹⁶ The inner dielectric constant ϵ_i was taken to be 1. A choice close to 2 for the local dielectric constant (ϵ_{loc}) used in conjunction with the values of outer radii obtained from Monte Carlo simulations¹⁷ was observed to reproduce the experimental free energies of hydration¹⁸ of alkali metal cations and halide anions. Some of the estimated ϵ_{loc} values are 1.58 for Na^+ , 1.72 for K^+ , 2.25 for Cl^- , 2.16 for Br^- , and 1.82 for I^- (b is taken as $a + 2R_w$ for Br^- and I^-). This prompted a choice of 2 for ϵ_{loc} for the present study. A value of 4 for the local dielectric constant has some precedence in the work of Kollman et al.¹⁹ However, calculations were also performed with $\epsilon_{\text{loc}} = 10$, and 78.3.³ Different concentrations were employed to study the effect of ionic strength on the conformational preferences.

RESULTS AND DISCUSSION

Results on the hydration free energies of the anion (DMP^-) are collected in Table I as a function of the number of terms considered in the multipole series expansion in Eq. (33). Conformational trends are seen to converge much faster than the absolute magnitudes. The calculations predict an ordering of $gg > gt > tt$ for the relative conformational preferences of phosphodiester torsions in DMP^- in aqueous solutions. Table II summarizes the influence of explicit counterion and the effects of variations in local dielectric constant on the conformational stabilities. The local dielectric constant provides an indirect handle on the ionic strength in the vicinity of the solute. The conformational differences are much smaller for the ion pair than for the anion, particularly

TABLE I
 Convergence of Hydration Free energies of DMP^{-a}

n^b	gg	gt	tt
1	-39.43	-39.43	-39.43
2	-39.43	-39.43	-39.43
3	-39.85	-39.93	-40.27
4	-40.28	-40.45	-40.52
5	-40.71	-40.77	-40.71
10	-42.00	-41.36	-41.00
20	-43.38	-41.66	-41.05
30	-43.98	-41.70	-41.05
40	-44.24	-41.71	-41.05
45	-44.31	-41.71	-41.05

^aEnergies are in kcal/mole; temperature 298 K; ionic strength = 0.0; $a = 3.2 \text{ \AA}$, $b = 6.0 \text{ \AA}$, $\epsilon_i = 1.0$, $\epsilon_{\text{loc}} = 2.0$, and $\epsilon_0 = 78.30$.

^bNumber of terms considered in the multipole expansion.

for gg and gt conformations. A smaller value for the local dielectric constant brings the conformations free energetically even closer. Indeed, for the ion pair, if the dipolar contributions ($n = 2$ and $\epsilon_{\text{loc}} = 2$) alone are considered, the hydration free energies (in kcal/mole) are -11.57 for gg , -13.40 for gt , and -15.21 for tt , suggesting a trend of $tt > gt > gg$ for the ion pair in concurrence with the studies of Bleha, Mlynek, and Tvaroska²⁰ on H^+DMP^- and with our previous Monte Carlo studies.¹⁰ Changes in ionic strength in the outer region on the hydration free energies as presented in Table III are seen to have little or no influence on the conformational trends.

An attractive feature of the present model is its generality. It combines solvent effects and ion atmosphere, and is particularly suited for incorporating a vicinal solvent zone and changes in the ionic strength. The applicability of the present model to biopolymers is to be judged in terms of the overall symmetry of the charge distribution, specifically the shape parameter $[(\text{Area}^{1/2})/(\text{Volume}^{1/3})]$. For other shapes, a similar extension of the spheroidal model²¹ is possible. Soumpasis²² discussed the influence of ion atmosphere on a periodic charge distribution with cylindrical symmetry and this has been

 TABLE II
 Hydration Free Energies of DMP^- and Na^+DMP^- as a Function of Local Dielectric Constant^a

	ϵ_{loc}	gg	gt	tt
DMP^-	78.30	-64.79	-57.32	-55.37
Na^+DMP^-	78.30	-58.20	-55.97	-49.85
DMP^-	10.00	-60.62	-54.32	-52.68
Na^+DMP^-	10.00	-50.87	-49.09	-44.03
DMP^-	4.00	-54.07	-49.41	-48.21
Na^+DMP^-	4.00	-39.99	-38.82	-35.25
DMP^-	2.00	-44.31	-41.71	-41.05
Na^+DMP^-	2.00	-25.28	-24.85	-23.07

^aEnergies are in kcal/mole.

TABLE III
Environmental Free Energies^a of DMP⁻ and Na⁺DMP⁻

	<i>C</i> ^b	<i>gg</i>	<i>gt</i>	<i>tt</i>
DMP ⁻	0.00	-44.31	-41.71	-41.05
Na ⁺ DMP ⁻	0.00	-25.28	-24.85	-23.07
DMP ⁻	0.01	-44.37	-41.77	-41.11
Na ⁺ DMP ⁻	0.01	-25.29	-24.85	-23.07
DMP ⁻	0.10	-44.45	-41.85	-41.18
Na ⁺ DMP ⁻	0.10	-25.30	-24.86	-23.08
DMP ⁻	1.00	-44.55	-41.95	-41.28
Na ⁺ DMP ⁻	1.00	-25.33	-24.89	-23.12

^a Energies are in kcal/mole.

^b Ionic strengths are reported as concentration *C* (in molarities) of 1:1 electrolyte.

extended²³ further to discrete charge distributions incorporating a vicinal solvent zone. The size of the molecule needs to satisfy two mutually conflicting criteria. The solute molecule must be big enough for the bulk environment, and in particular, for the vicinal solvent to be treated as dielectric continua. The charges in the interior of the cavity must not be too close to the boundary, for the spherical symmetry of the potential assumed, and in particular, because the multipolar expansion of the potential converges slowly in this region.²⁴ Studies on the applicability of the concentric dielectric continuum to globular proteins are on hand.

Investigations on the conformational preferences of phosphodiester torsion angles in dimethylphosphate anion indicate that *gauche-gauche* conformation is preferred in aqueous solutions. This is in accord with the experimentally observed preponderance of the *gg* conformations for the diverse phosphodiester torsions (Refs. 10, 14, and references therein). The conformational differences in the hydration free energies are smaller for the ion pair relative to the anion as expected. Variations in the ionic strength in the outer region are not energetically significant, probably due to the large distance (6 Å) from the origin. Changes in the local dielectric constant have a pronounced effect on the magnitudes of the hydration free energies but not on the relative conformational preferences.

This research was supported by NIH grant GM 24914 and by NSF grant CHE-8203501.

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Received December 29, 1986

Accepted September 28, 1987