

## Interaction between macroions mediated by divalent rod-like ions

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received 22 July 2004; accepted in final form 28 September 2004

published online 27 October 2004

PACS. 41.20.Cv – Electrostatics; Poisson and Laplace equations, boundary-value problems.

PACS. 87.68.+z – Biomaterials and biological interfaces.

**Abstract.** – Attractive interactions between identical like-charged macroions in aqueous multivalent salt solution arise due to ion-ion correlations. The mean-field level Poisson-Boltzmann (PB) theory does not predict such behavior for point-like structureless ions. Various multivalent ions, such as certain DNA condensing agents or short stiff polyelectrolytes, do have an internal, often rod-like, structure. Applying PB theory to the generic case of divalent rod-like salt ions, we find attraction between like-charged macroions above a critical distance between the two individual charges of the rod-like ions. We calculate this distance analytically within linearized PB theory. Numerical results for the non-linear PB theory indicate strong enhancement of the tendency to mediate attractive interactions.

*Introduction.* – Poisson-Boltzmann (PB) theory is a widely used mean-field level method to calculate interactions between macroions in aqueous (salty) solutions. For monovalent salt, its predictions are generally found to agree well with experimental results and computer simulations. However, the presence of *multivalent* ions can affect the nature of the interactions between macroions in a way that qualitatively differs from the PB prediction. A remarkable example is the possibility of *attraction* between two identical, like-charged, macroions that the mean-field approach is unable to predict. This attraction currently receives much interest [1] because it is observed for a number of biologically relevant processes such as condensation of DNA [2], network formation in actin solutions [3], virus aggregation [4] and interactions between lipid membranes that occur during adhesion and fusion. Various theoretical approaches ascribe this attraction to the presence of ion-ion correlations [5,6]. An intuitive understanding of these correlations can be based on the formation of a periodic counterion arrangement in the vicinity of each macroion, similar to a Wigner crystal. The two interlocked counterion-decorated macroions then experience short-ranged attraction.

Multivalent ions are commonly treated as point charges. However, real ions (and particularly organic ones) often possess an internal structure with the individual charges being located at distinct, well-separated positions. Among others [7], a characteristic example is the rod-like backbone structure of various DNA condensing agents such as the tri- and tetravalent ions spermine and spermidine, protamine sulfate, or poly-lysine. Clearly, the spatial separation of the individual charges within a multivalent ion is expected to affect the role that correlations play for the energetics of interacting macroions. That is, large separation is expected to reduce the importance of correlations between different multivalent ions (“inter-ionic” correlations) but retains the steric constraints between the individual charges of the multivalent ions (“intra-ionic” correlations). As is well known, PB theory entirely neglects inter-ionic correlations. Yet, intra-ionic correlations can be accounted for within PB theory. Hence, with growing separation between the individual charges of a multivalent ion, PB theory is expected to become increasingly more applicable. In line with this, a recent simulation study [8] on a mixture of monovalent and rigid dumbbell-like ions observed a substantial decrease in the critical temperature compared to an ordinary 1 : 2 electrolyte of point-like ions. The questions arise, how to apply PB theory [9] and if it is able to predict attraction (or at least an attractive component) for the interaction of like-charged macroions. We note that PB theory offers a particularly simple tool to model the interaction between macroions of *low* dielectric constant immersed in aqueous salt solution. Such systems are not captured by the so-called primitive model where—nevertheless—simulations as well as analytical model calculations have provided valuable information on the structure and phase behavior of electrolyte solutions [10], including their role for biological systems [11]. Obtaining attractive interactions between like-charged macroions is also possible on the level of PB theory if additional order parameters are considered. This is the case, for instance, upon including the solvent structure [12] or the presence of polyelectrolytes [13, 14] into PB theory.

In the present work we formulate PB theory for an electrolyte with an internal structure of the individual ions. For simplicity, we shall focus on the simplest, namely that of a symmetric 2 : 2 electrolyte in which the two charges of each (positive and negative) divalent ion are separated by a distance  $l$ . Figure 1 schematically illustrates the rod-like structure of the divalent ions. More involved cases such as asymmetric electrolytes with higher than divalent ions and with any distribution of the individual charges on the rod-like ion can be treated analogously (but are not expected to give rise to qualitatively new behavior). We shall derive a modified PB equation that takes into account the charge distribution of the rod-like divalent

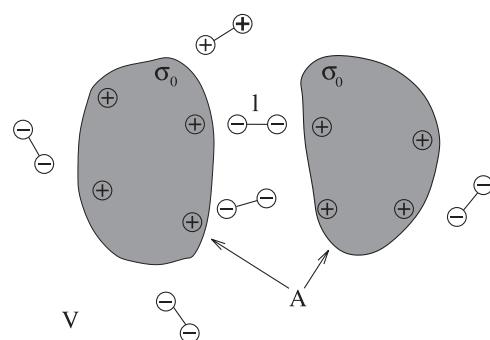


Fig. 1 – Schematic illustration of two like-charged macroions of (bare) surface charge density  $\sigma_0$  and overall surface area  $A$ , interacting in a symmetric 2 : 2 electrolyte solution enclosed in a volume  $V$ . The divalent ions of the electrolyte are rod-like, with a separation  $l$  between their individual charges.

ions up the quadrupolar order. For the generic case of two interacting like-charged planar surfaces we show that the modified PB equation can give rise to an attractive interaction.

*Single rod-like ion in external field.* – Consider first a single rod-like divalent ion, located at fixed position  $\mathbf{r}$  in the external electric field  $\mathbf{E}(\mathbf{r})$ . The two individual charges of the ion are localized at positions  $\mathbf{r}_{1,2} = \mathbf{r} \pm (l/2)\mathbf{t}$ , where the unit vector  $\mathbf{t} = \{\sin \theta \cos \phi, \sin \theta \sin \phi, \cos \theta\}$  describes the instantaneous spatial orientation of the ion. The ion's orientation-dependent interaction energy,  $u_{el}(\mathbf{t}) = e[\Phi(\mathbf{r}_1) + \Phi(\mathbf{r}_2)]$  with the electric field  $\mathbf{E}(\mathbf{r}) = -\nabla\Phi(\mathbf{r})$ , can be written up to quadratic order in  $l$  as

$$u_{el}(\mathbf{t}) = 2e\Phi(\mathbf{r}) + \frac{el^2}{4}\mathbf{t} \cdot [\nabla \circ \nabla\Phi(\mathbf{r})] \cdot \mathbf{t}, \quad (1)$$

where  $e$  denotes the elementary charge and  $\Phi$  is the electrostatic potential. Statistical averaging over all possible orientations yields the free energy up to quadratic order in  $l$ :

$$f_{el} = -\ln \left[ \frac{1}{4\pi} \int_0^{2\pi} d\phi \int_0^\pi d\theta \sin \theta e^{-u_{el}} \right] = 2e\Phi + \frac{el^2}{12}\Delta\Phi, \quad (2)$$

where here and in the following we express all energies in units of  $k_B T$  (Boltzmann constant  $\times$  absolute temperature). Equation (2) confirms a well-known result: the quadrupolar moment of the ion energetically couples to the gradient of the electric field.

*Poisson-Boltzmann theory for rod-like divalent ions.* – Consider next a mixture of positive and negative rod-like divalent ions, contained in a large aqueous solution of volume  $V$ . Also contained in the aqueous solution are one or several macroions of overall surface area  $A$  and bare (fixed) surface charge density  $\sigma_0$ . Denote the local concentrations of positive and negative divalent ions by  $n_+$  and  $n_-$ , respectively. Due to the spatial separation of the charges along the divalent ion, the orientationally averaged volume charge density [15],  $\rho$ , receives contributions not only from the local concentrations but also from their second derivatives:

$$\rho = 2e(n_+ - n_-) + \frac{el^2}{12}(\Delta n_+ - \Delta n_-) \quad (3)$$

and similarly for the surface charge density,

$$\sigma = \sigma_0 + \frac{el^2}{12} \left( \frac{\partial n_+}{\partial n} - \frac{\partial n_-}{\partial n} \right)_A \quad (4)$$

at the macroion surfaces, where  $\partial/\partial n$  denotes the derivative in normal direction. The quantities  $\rho$  and  $\sigma$  define both the electrostatic potential,  $\Phi$ , through the Poisson equation,  $\epsilon\Delta\Phi = -\rho$ , where  $\epsilon$  is the dielectric constant of water, and the boundary condition at the macroion surfaces,  $(\partial\Phi/\partial n)_A = -\sigma/\epsilon$ . Note that the latter is valid in the limit of a low dielectric constant,  $\epsilon_M \ll \epsilon$ , inside the macroions. The corresponding electrostatic free energy can then be written as [15]

$$F_{el} = \frac{\epsilon}{2} \int_V dv (\nabla\Phi)^2 = \frac{1}{2} \int_V dv \Phi\rho + \frac{1}{2} \int_A da \Phi\sigma. \quad (5)$$

Using Green's theorem we re-express  $F_{el}$  as

$$F_{el} = \frac{1}{2} \int_V dv (n_+ - n_-) \left[ 2e\Phi + \frac{el^2}{12}\Delta\Phi \right] + \frac{1}{2} \int_A da \left[ \sigma_0\Phi + \frac{el^2}{12}(n_+ - n_-) \frac{\partial\Phi}{\partial n} \right]. \quad (6)$$

Indeed, eq. (6) appears as the generalization of eq. (2) from one single rod-like ion in an external field to a symmetric 2 : 2 electrolyte of rod-like ions.

To derive the PB equation, we consider the full free energy  $F = F_{el} + F_{tr}$  of the system which contains (besides  $F_{el}$ ) also the translational entropy contribution

$$F_{tr} = \int_V dv \left[ n_+ \ln \frac{n_+}{n_0} + n_- \ln \frac{n_-}{n_0} - (n_+ + n_- - 2n_0) \right] \quad (7)$$

of the rod-like divalent ions, where  $n_0$  denotes the bulk concentration of the divalent ions. We note the reference state  $F(n_+ \equiv n_- \equiv n_0) = 0$ . In thermal equilibrium, the free energy  $F$  must be minimal with respect to the ionic concentrations  $n_+$  and  $n_-$ . To find the corresponding equilibrium distributions, we perform the first variation of  $F(n_+, n_-)$ , resulting in

$$\begin{aligned} \delta F = & \frac{el^2}{12} \int_A da \frac{\partial \Phi}{\partial n} (\delta n_+ - \delta n_-) + \\ & + \int_V dv \delta n_+ \left[ 2e\Phi + \frac{el^2}{12} \Delta\Phi + \ln \frac{n_+}{n_0} \right] + \int_V dv \delta n_- \left[ -2e\Phi - \frac{el^2}{12} \Delta\Phi + \ln \frac{n_-}{n_0} \right]. \end{aligned} \quad (8)$$

Vanishing of  $\delta F$  for arbitrary  $\delta n_-$  and  $\delta n_+$  gives rise to both the Boltzmann distributions

$$n_\pm = n_0 \exp \left[ \mp \left( 2e\Phi + \frac{el^2}{12} \Delta\Phi \right) \right] \quad (9)$$

and the boundary condition at the macroions surfaces

$$\left( \frac{\partial \Phi}{\partial n} \right)_A = 0. \quad (10)$$

Note that eq. (10) implies  $\sigma = 0$ , indicating the tendency of the rod-like ions to fully neutralize the bare charges on the macroion surfaces. This electrostatically preferable complete neutralization can occur only for  $l > 0$  without a prohibitively large entropic penalty of immobilizing the ions onto the macroion surfaces.

Inserting  $n_\pm$  from eq. (9) into the Poisson equation yields the PB equation which we express in terms of the dimensionless electrostatic potential  $\Psi = 2e\Phi$ . In the following, we shall also use dimensionless spatial coordinates,  $\bar{x} = x/l_D$ , etc., scaled by the Debye length  $l_D = 1/\kappa$  with  $\kappa^2 = 4 \times 8\pi l_B n_0$ , where  $l_B = e^2/4\pi\epsilon = 7 \text{ \AA}$  is the Bjerrum length in water. We then obtain a fourth-order, non-linear, partial differential equation:

$$\Delta\Psi = \sinh(\Psi + \xi^2 \Delta\Psi) + \xi^2 \Delta \sinh(\Psi + \xi^2 \Delta\Psi). \quad (11)$$

The PB equation, eq. (11), depends on the dimensionless parameter  $\xi = \kappa l / \sqrt{24}$  that expresses the effective distance between the charges of the divalent rod-like ion. For  $\xi = 0$  the PB equation reduces to  $\Delta\Psi = \sinh\Psi$ , which is the familiar equation used for a symmetric salt solution of structureless, point-like ions.

Solving the PB equation, eq. (11), requires the specification of two boundary conditions at the macroion surfaces. The first one is given by  $(\partial\Psi/\partial n)_A = 0$ ; see eq. (10). To formulate the second boundary condition, it is convenient to express the (local) surface charge density at the macroions,  $\sigma_0 = pe/8\pi l_B l_D$ , in terms of the dimensionless charge density,  $p = \pm 8\pi l_B l_D/a$ , where  $a$  is the (local) area per surface charge (the sign of the macroion charge is determined

by the sign of  $p$ ). The second boundary condition, which follows from insertion of eqs. (4) and (9) into the condition  $\sigma = 0$ , can then be written as

$$\frac{p}{\xi^4} = \cosh(\Psi + \xi^2 \Delta \Psi) \frac{\partial}{\partial n} \Delta \Psi. \quad (12)$$

Upon insertion of the equilibrium distribution for  $n_{\pm}$  into  $F$ , we can show that the free energy can be calculated by the familiar charging process [16]

$$F = \int_A da \int_0^{\sigma_0} \Phi(\sigma'_0) d\sigma'_0 = \frac{1}{16\pi l_B l_D} \int_A da \int_0^p \Psi(p') dp'. \quad (13)$$

In the remainder, we analyze possible consequences of  $\xi > 0$ , first for the linearized and then for the non-linear PB equation.

*The Debye-Hückel limit.* – In the Debye-Hückel (DH) regime the electrostatic potential is small everywhere ( $\Psi \ll 1$ ) and the PB equation (see eq. (11)) linearizes:

$$\xi^4 \nabla^4 \Psi + (2\xi^2 - 1) \Delta \Psi + \Psi = 0, \quad (14)$$

where  $\nabla^4$  is the biharmonic operator. The boundary condition, eq. (12), becomes  $p/\xi^4 = \partial(\Delta \Psi)/\partial n$ .

Consider two large, like-charged, planar surfaces, located at (dimensionless) positions  $\bar{x} = 0$  and  $\bar{x} = \bar{d} = d/l_D$ , each having area  $A/2$  and bare surface charge density  $\sigma_0$  (with corresponding scaled surface charge density  $p$ ). The electrostatic potential depends only on the  $\bar{x}$ -direction, and we must solve the equation  $\xi^4 \Psi''' + (2\xi^2 - 1) \Psi'' + \Psi = 0$  with the boundary conditions  $\Psi'(0) = \Psi'(\bar{d}) = 0$  and  $\Psi'''(0) = -\Psi'''(\bar{d}) = p/\xi^4$ . The solution can be written as  $\Psi(\bar{x}) = \sum_{i=1}^4 B_i e^{-\omega_i \bar{x}}$  with  $\omega_3 = -\omega_1$ ,  $\omega_4 = -\omega_2$  and

$$B_i = \frac{(-1)^i p}{\xi^4 \omega_i (\omega_1^2 - \omega_2^2) (1 - e^{-\bar{d}\omega_i})}, \quad \omega_{1,2} = \frac{1 \pm \sqrt{1 - 4\xi^2}}{2\xi^2}. \quad (15)$$

Most notably, for  $\xi > 1/2$  the potential  $\Psi$  exhibits damped oscillations, whereas for  $\xi < 1/2$  it decays monotonically. For the potential at the surfaces we find  $\Psi(0) = \Psi(\bar{d}) = p C(\xi, \bar{d})$  where the function  $C(\xi, \bar{d})$  is given by

$$C(\xi, \bar{d}) = \frac{1}{\xi^4 (\omega_1^2 - \omega_2^2)} \left[ \frac{1}{\omega_2} \coth \frac{\bar{d}\omega_2}{2} - \frac{1}{\omega_1} \coth \frac{\bar{d}\omega_1}{2} \right]. \quad (16)$$

Upon insertion of  $\Psi(0)$  into eq. (13), we obtain the free energy  $F = p N C(\xi, \bar{d})/2$ , where  $N = (\sigma_0/e)(A/2)$  is the number of fixed charges on each of the two flat surfaces. The function  $C(\xi, \bar{d})$  determines the nature of the interaction between the like-charged macroionic surfaces.

Let us discuss some relevant cases of the DH regime. For two isolated surfaces ( $d \rightarrow \infty$ ; the left diagram of fig. 2 shows the potential for some selected cases) we obtain  $C(\xi, \bar{d} \rightarrow \infty) = 1$ , and the surface potential  $\Psi(0) = p$  as well as the free energy  $F = p N/2$  are independent of  $\xi$ . In fact, this is the familiar DH result for point-like divalent salt ions [16]. Hence, for an isolated flat surface, an influence of the salt structure on  $\Psi(0)$  and  $F$  cannot be seen in the linear DH limit. In contrast to that, the normalized, distance-dependent, integrated charge density of the bare macroion charges and rod-like salt ions

$$Q(\bar{x}) = \frac{1}{\sigma_0} \left[ \sigma + \int_0^{\bar{x}} \rho(x) dx \right] = \frac{\sigma}{\sigma_0} + \frac{1}{p} \sum_{i=1}^2 B_i \omega_i e^{-\omega_i \bar{x}} \quad (17)$$

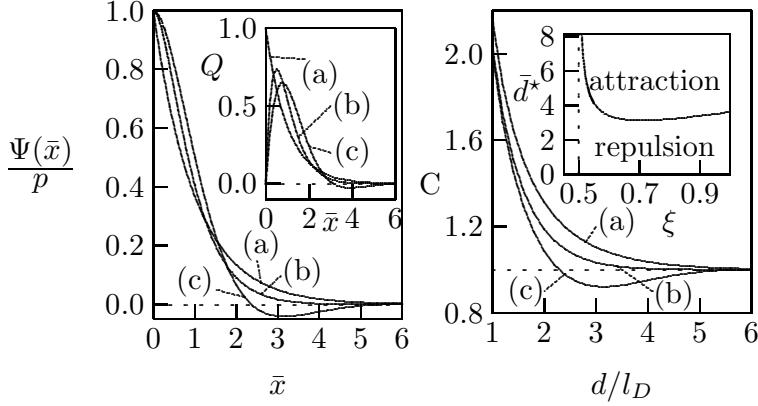


Fig. 2 – Results for the DH regime. Left diagram: the normalized potential,  $\Psi/p$ , of an isolated planar surface as a function of the scaled distance,  $\bar{x} = x/l_D$ , to that surface. The inset shows the normalized, integrated charge density  $Q(\bar{x})$ ; see eq. (17). Right diagram: the normalized free energy  $C = 2F/Np$  as a function of the distance  $\bar{d} = d/l_D$  between two planar surfaces. The corresponding repulsive and attractive regions are marked in the inset. Both diagrams show the cases  $\bar{x} = x/l_D$  for  $\xi = 0$  (a),  $\xi = 0.5$  (b) and  $\xi = 0.7$  (c).

does depend on  $\xi$ , as shown in fig. 2 (inset of left diagram). Note, in particular, that  $\xi > 1/2$  allows for electrical *overcharging* as indicated by  $Q < 0$ .

Consider next the interaction between two like-charged planar surfaces as a function of their mutual distance  $d$ . The corresponding (normalized) free energy  $C = 2F/Np$  is shown in fig. 2 (right diagram) as a function of  $\bar{d} = \kappa d$  for  $\xi = 0, 0.5$ , and  $0.7$ . For  $\xi < 1/2$ , the interaction is always repulsive. For  $\xi = 1/2$ , we obtain  $C(\xi = 1/2, \bar{d}) = \coth \bar{d} + \bar{d}/\sinh^2 \bar{d}$  which still is a monotonously decaying function of  $\bar{d}$ , implying repulsion between the two surfaces. However, for  $\xi > 1/2$ , the interaction turns attractive above a sufficiently large separation  $\bar{d} = \bar{d}^*$  between the two surfaces. The inset in the right diagram of fig. 2 shows position  $\bar{d}^*$  at which  $C(\xi > 1/2, \bar{d}^*)$  adopts a minimum, separating the repulsive from the attractive regime. For example,  $\xi = 0.7$  (corresponding to  $l = 3.4l_D$ ) results in an energetic minimum at  $\bar{d}^* = 3.2$  (corresponding to  $d = 3.2l_D$ ). Hence, the rod-like ions just match

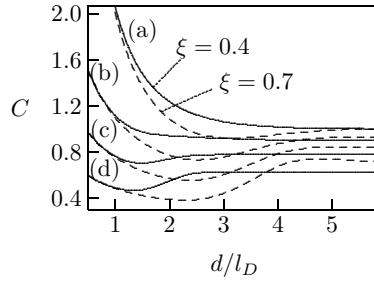


Fig. 3 – Results for the non-linear PB regime. The scaled free energy  $C = 2F/Np$  as a function of the dimensionless distance  $\bar{d} = d/l_D$  for  $p = 0.01$  (a),  $p = 3$  (b),  $p = 6$  (c), and  $p = 12$  (d). The solid and broken lines correspond to  $\xi = 0.4$  and  $\xi = 0.7$ , respectively.

the optimal separation between the macroions, indicating that a bridging mechanism [13] is responsible for the attractive interactions.

*Nonlinear Poisson-Boltzmann theory.* – Analytical solutions of the non-linear PB equation, eq. (11), are not available. To investigate the influence of the non-linearity, we have numerically calculated solutions of eq. (11) and of the corresponding free energy,  $F$ . As for the linear regime, we can express the free energy  $F = p N C/2$  in terms of the coefficient  $C$ . Yet, unlike in the linear regime, the coefficient  $C = C(\xi, \bar{d}, p)$  now depends on  $p$ , the scaled charge density of the macroion surfaces. Figure 3 displays for two cases,  $\xi = 0.4$  (solid lines) and  $\xi = 0.7$  (broken lines), the  $\bar{d}$ -dependence of  $C$  for increasing  $p$ . Two conclusions can be drawn. First, for  $\xi > 1/2$ , the non-linearity of the PB equation enhances the attraction strength between two like-charged surfaces. Second, with increasing  $p$  there appears an attractive region even for  $\xi < 1/2$  which is not predicted in the DH approximation. Hence, attractive interactions between like-charged macroions in salt solution of rod-like divalent ions can be induced through an increase in the surface charge densities of the macroions.

*Conclusions.* – We show that the mean-field level PB theory is generally able to predict attractive interactions between like-charged macroions if the mobile ions possess an internal structure with spatially separated individual charges. Even though we have focused on a symmetric 2 : 2 electrolyte that consists of simple rod-like ions, similar conclusions are valid for other mixtures (including the only-counterion case) and other ionic structures. As is well known, ion correlations provide the general mechanism to induce attraction between like-charged macroions. Our present approach is based on the PB approach and, thus, neglects inter-ionic correlations. Yet, it takes into account intra-ionic correlations through the constraint that the two individual charges of each rod-like divalent ion are separated from each other by a *fixed* distance  $l$ .

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