General Differential Contact Identities for Macromolecules

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We discuss general Maxwell identities relating a macromolecule's charge, the forces acting at its surface, and the osmotic pressure of the solution in which it sits. The identities are closely related to the contact value relations that hold for certain special geometries, but are more general. In particular, the Maxwell identities can be applied to any macromolecule geometry, and they hold both within and outside of mean-field theory. Examples illustrate that combining the identities with approximate treatments of screening can often return simple, accurate osmotic pressure estimates.

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Introduction.—There are two geometries for which a closed-form contact value theorem holds relating the total number of screening ions associated with a macromolecule —its excess sum—to the density of ions at its surface: the isolated planar [1] and cylindrical geometries [2]. In the former case, the contact identity holds in general, while in the latter the identity holds only in the mean field. These theorems are quite useful in that they allow for the determination of a dilute solution's global osmotic pressure—which is a function, Eq. (10) below, of the excess sums—through single-molecule measurements of local contact properties. In this Letter, we introduce a set of thermodynamic Maxwell identities that also relate a macromolecule's excess sum to local properties at its surface. These differential identities can be used to derive the contact value identities that hold for the isolated cylindrical and planar geometries, but are more general. In particular, they can be applied to characterize ion associations with macromolecules of any geometry, and they also always hold, both within and outside of mean-field theory. When combined with approximate treatments of screening, they can be used to obtain simple osmotic pressure estimates for general geometries.

Differential contact identities.—We consider here a general isolated macroion of total charge Q characterized by some set of coordinate configuration degrees of freedom $\{\mathbf{x}_i\}$. We write $q_i \equiv Q\bar{q}_i$ for the charge at $\mathbf{x}_i$, and suppose that the macroion sits within a bulk electrolyte containing salt in excess. We take the ions of species j to have charge ez_j and to be at bulk concentration $c_j \equiv c\bar{c}_j$, with c a scale factor common to all present species. Using standard arguments—see, e.g., [3] for the derivation of a similar relation—one can show that the free energy $\mathcal{F}$ of a large volume V surrounding the macroion satisfies

$$d\mathcal{F} = \sum_i \{\langle \mathbf{f}_i \rangle \cdot d\mathbf{x}_i + \langle \phi(\mathbf{x}_i)\rangle dq_i\} - \sum_j \langle N_j \rangle d\mu_j. \qquad (1)$$

Here, $\mathbf{f}_i$ is the force acting on coordinate $\mathbf{x}_i$, $\phi(\mathbf{x}_i)$ is the electrostatic potential at coordinate $\mathbf{x}_i$, N_j is the number of ions of species j within V, μ_j is its associated chemical potential, and brackets denote a thermal average. The first term above is associated with mechanical work, the second with charging the macroion, and the third with varying the ion concentrations. The $\{d\mu_j\}$ in Eq. (1) are not linearly independent as they are linked through the bulk's Gibbs-Duhem relation, which at fixed pressure and temperature reads $\sum_j c_j d\mu_j = 0$ [4]. Using this equation to solve for the change in solvent chemical potential, $d\mu_W$, and now assuming that c is sufficiently small that we can write $\mu_j = T \log c_j$, the variation of c at fixed $\{\bar{c}_j\}$ gives

$$d\mathcal{F} = \sum_i \{\langle \mathbf{f}_i \rangle \cdot d\mathbf{x}_i + \langle \phi(\mathbf{x}_i)\rangle dq_i\} - \frac{T}{c}\sum_j \langle n_j \rangle dc. \qquad (2)$$

The sum over j in Eq. (2) is now over solute species only, and n_j, the excess of species j, is given by

$$n_j = N_j - c_j V - \frac{c_j}{c_W}\{N_W - c_W V\}. \qquad (3)$$

Because we assume that c is small, the third bracketed term above can be neglected. In this case, Eq. (3) shows that the excess of species j is essentially equal to the number of molecules of species j near the macroion, N_j, minus the number that would be in an equivalent volume of the bulk electrolyte, $c_j V$.

Equating the mixed partials of Eq. (2) returns a very general set of Maxwell relations that can be quite useful. In particular, if one of the partials is taken with respect to c, a differential identity is obtained relating the global excess sum to a local quantity characterizing the macroion. The two fundamental identities of this sort are

$$\partial_c \langle \phi_i \rangle = -(T/c) \partial_{q_i} \sum \langle n_j \rangle, \tag{4}$$

$$\partial_c \langle \mathbf{f}_i \rangle = -(T/c) \nabla_{\mathbf{x}_i} \sum \langle n_j \rangle, \tag{5}$$

the main results of this Letter. These identities can be applied to characterize the relationship between the excess sum and the contact properties of any macromolecule. For the special case of cylindrical and planar macroions, we show in an appendix that they can be used to efficiently derive the contact value theorems. In this sense, Eqs. (4) and (5) can be considered generalizations of these prior results.

In previous works, we derived and applied some system-specific identities related to special cases of Eqs. (4) and (5): in [3,5–7], we applied a conjugate of the second line above to analyze single-molecule experimental data. By considering variations with respect to an applied tension force—rather than position coordinate, as in Eq. (5)—we were able to determine the excess sum of various nucleic acids as a function of their end-to-end extension. In [8], we found that for a thin line charge macroion sitting in an arbitrarily complex electrolyte, the symmetries of the mean-field equations can be exploited to obtain an exact evaluation of the left side of a special case of Eq. (4). This allowed us to efficiently derive the universal limiting law sum rule that holds for thin line charges, a result first derived in [9] through a much more challenging analysis of the Poisson-Boltzmann equation. These prior works demonstrated the significant potential utility of the Maxwell relation approach, as applied to some special cases. Below, we illustrate more general utility, showing that Eqs. (4) and (5) can be applied whenever approximate evaluations of the contact properties are available, e.g., by means of simulation, numerical estimate, or series expansion. We focus in some detail on the linear response approximation, which provides some insight into general properties of screened systems.

General linear response forms.—For weakly charged macroions, screening is well modeled as linear, giving $\phi_i = Q\bar{\phi}_i$, with $\bar{\phi}_i$ independent of Q. In this case, if we vary the net charge Q of the macroion at fixed $\{\bar{q}_i\}$ (i.e., uniformly scale the macroion's charge), Eq. (4) gives

$$\partial_Q \sum \langle n_j \rangle = -\frac{c}{T} Q \partial_c \sum_i \bar{q}_i \bar{\phi}_i \equiv -\frac{c}{T} Q \partial_c \bar{\phi}_S. \tag{6}$$

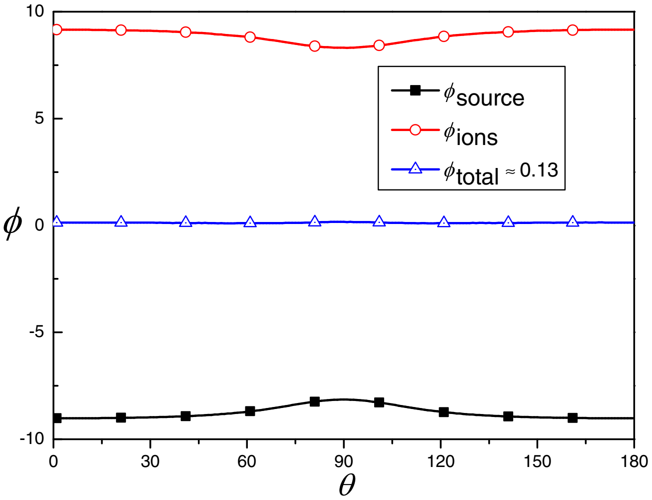

FIG. 1 (color online). Many-body simulation results: Potential ϕ as a function of polar angle θ at the surface of a uniformly charged ellipsoid with major radius 20.8 nm, minor radius 6.9 nm, source charge $Q = 1000e$, and screened by its counterions—simulated as in [10]. The condensed ions are mobile. Consequently, the total potential ϕ_{total} at the surface, which is the sum of that from the ions and the source charge, is nearly uniform.

A similar expression can also be obtained for highly charged macroions if we apply counterion condensation theory [10–12]. This is an approximate treatment of screening that supposes linear screening for all Q up to some critical value Q^*. However, for bare charge $Q > Q^*$, counterions from the bulk are supposed to condense onto the macroion's surface, renormalizing the charge of the macroion back down to its critical value Q^*. The critical value Q^* can be estimated by setting the bulk chemical potential equal to the electrostatic energy gained by a counterion when it condenses onto the surface: it does not matter where on the surface, since the condensed, mobile counterions work to establish an effectively constant surface potential boundary condition [10]—Fig. 1 provides an example. Equating the two energies gives

$$Q^* \bar{\phi}_S e z^* \approx T \log c^*, \tag{7}$$

where c^* and ez^* are the bulk concentration and charge of the condensing species. Combining Eqs. (7) and (4) gives

$$\partial_Q \sum \langle n_j \rangle = -\frac{c}{T} \partial_c (Q^* \bar{\phi}_S) = -\frac{1}{ez^*}, \tag{8}$$

the high-charge analog of Eq. (6).

Integrating Eqs. (6) and (8) with respect to Q provides us with the following approximate expression for the excess sum associated with a positively charged macroion:

$$\sum \langle n_j \rangle = \begin{cases} -\frac{cQ^2}{2T} \partial_c \bar{\phi}_S, & \text{for } Q < Q^* \\ -\frac{cQ^{*2}}{2T} \partial_c \bar{\phi}_S + \frac{Q - Q^*}{|ez^*|}, & \text{for } Q \geq Q^* \end{cases}. \tag{9}$$

This formula is very general and often accurate. Indeed, Eq. (9) is exact for the special case of thin line charges in the mean-field limit [8,9]. For other geometries, this is not precisely the case, but Eq. (9) can always be used to provide reasonable estimates to the excess sum. This, in turn, allows for the osmotic pressure Π of a volume V of dilute solution to be estimated, via the expression [13]

$$\frac{\Pi V}{T} = N_M + \sum_j (N_j - N_M n_j). \tag{10}$$

Here, N_j is the number of molecules of species j in the volume—with N_M the macroion number—and n_j is the excess of species j associated with each macroion. This result holds because a macroion and its screening cloud translate as a single complex.

While the Q dependence of the estimate is explicit in Eq. (9), evaluation of its c dependence requires an estimate of $\partial_c \bar{\phi}_S$. This factor can depend sensitively on macroion geometry. However, it is not particularly sensitive to the makeup of the electrolyte: within the linear screening approximation, the surface potential $\overline{\phi_S}$ depends on the makeup of the electrolyte only in so far as the screening length does. This means that the sum is a function of the screening length only, and any two electrolytes having the same screening length will return a common excess sum. This implies that knowledge of the excess sum for one electrolyte composition, at varying salt concentrations, is sufficient to estimate the sum for any other electrolyte composition. We consider some explicit examples below.

Spheres, planes, and cylinders.—Linear screening is governed by the Debye-Hückel equation [14]

$$\nabla^2 \phi = \kappa^2 \phi - 4\pi \rho_S. \tag{11}$$

Here, $\kappa^2 \equiv 4\pi l_B \sum_j c_j z_j$, κ^{-1} is the screening length, ρ_S is some source charge, and $l_B = (e^2/\epsilon T)$ is the Bjerrum length. Three macroion geometries where closed-form solutions to this equation can be obtained are given by the uniformly charged spherical (radius a), planar (area $A \gg \kappa^{-2}$), and cylindrical (radius a, length $L \gg \kappa^{-1}$) macroion geometries [15]. Assuming electrolyte-excluding macroion interiors, solving Eq. (11) for these geometries returns surface potential estimates given by

$$\phi(\text{surface}) = \begin{cases} \frac{Q}{a}\frac{1}{1+\kappa a}, & \text{sphere} \\ \frac{4\pi\sigma}{\kappa}, & \text{plane} \\ \frac{2\lambda}{\kappa a}\frac{K_0(\kappa a)}{K_1(\kappa a)}, & \text{cylinder} \end{cases}. \tag{12}$$

Here, $\sigma \equiv Q/A$, $\lambda \equiv Q/L$, K_0 and K_1 are modified Bessel functions, and we assume the electrolyte sits only in the upper half-space in the planar case. Combining Eqs. (12) and (9) returns the following excess sum estimates:

$$\sum \langle n_j \rangle = \begin{cases} \frac{Q^2}{4T}\frac{\kappa}{(1+\kappa a)^2}, & \text{sphere} \\ \frac{\sigma^2 \pi A}{T}\frac{1}{\kappa}, & \text{plane} \\ \frac{\lambda^2 L}{2T}\left[1 - \left(\frac{K_0(\kappa a)}{K_1(\kappa a)}\right)^2\right], & \text{cylinder} \end{cases}. \tag{13}$$

The expressions in Eq. (13) are valid in the small charge limit. For $Q > Q^*$, the sum is always linear in Q, as in Eq. (9).

Although the Q dependence is similar in each line of Eq. (13), the κ dependence is not: the planar and cylindrical estimates are both monotonically decreasing functions of κ, but the spherical geometry has an excess sum maximum at $\kappa = a^{-1}$. This κ value determines the Q-independent, finite salt-concentration scale where inclusion of spherical macroions will most dramatically reduce the osmotic pressure, Eq. (10), of a solution. A plot of the spherical estimate, Eq. (13), is shown in Fig. 2(a). This is for a sphere of radius of $a = 2.5$ nm and charge $Q = 20e$. Also shown in the plot are excess sum estimates obtained from a full, many-body (non-mean-field) simulation of a spherical macroion of the same size and charge sitting within a monovalent electrolyte [16]. The two generally agree within error, and both are nonmonotonic. We note that this effect might be observed experimentally, perhaps using the scattering approach discussed in [17,18]: for 2–3 nm globular proteins, the peak should sit at about 10 mM monovalent salt.

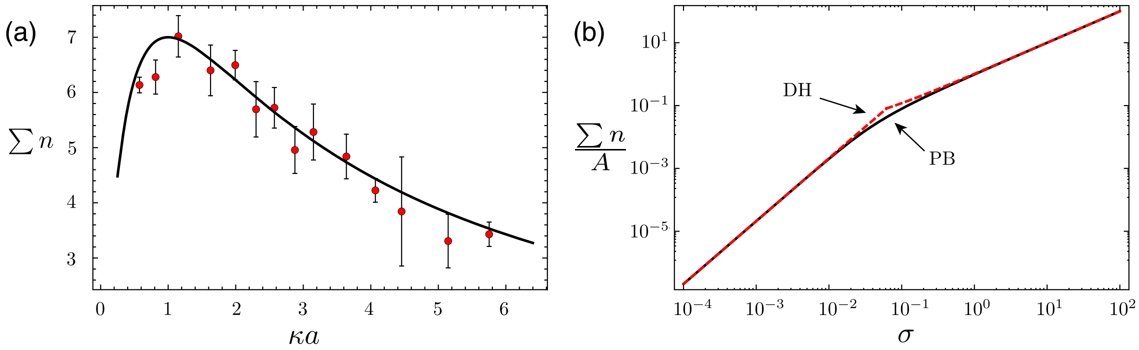

FIG. 2 (color online). (a) Debye-Hückel (black curve) and simulation (red points) excess sum estimates for a sphere of charge $Q = 20e$ and radius $a = 2.5$ nm at various monovalent salt concentrations. (b) Poisson-Boltzmann (PB, black) and Debye-Hückel (DH, red dashed) excess sum estimates as a function of planar surface charge σ ($e/[\text{ nm}^2]$), 1 mm monovalent salt. A crossover is apparent at a critical value of σ: below this value, the excess sum is quadratic in the charge, above it is linear.

Tests of the cylindrical expression given in Eq. (13) were carried out in [8], where the estimate was found to agree well with simulation results (there, we derived this expression using a similar, but less general method that cannot be extended beyond linear response). We can also conveniently test the planar expression in Eq. (13), making use of the known solution to the full, nonlinear Poisson-Boltzmann equation in monovalent salt [19]. This is

$$\phi(z) = -\frac{2}{el_B}\log\left(\frac{1+\gamma e^{-\kappa z}}{1-\gamma e^{-\kappa z}}\right), \tag{14}$$

where $\gamma = \sqrt{(\kappa\mu)^2+1}-\kappa\mu$, $\mu \equiv (e/2\pi l_B|\sigma|)$, and z is the height above the plane. Combining Eqs. (14) and (4) gives

$$n_+ + n_- = \frac{Q\gamma}{e}. \tag{15}$$

We plot this expression alongside Eq. (13) in Fig. 2(b). The two agree well except very near the crossover at Q^*. In the Debye-Hückel plot, the crossover point was estimated using Eq. (7). We have found that by varying Q^* slightly around this approximation—which is only intended to provide an order of magnitude estimate—even better agreement can be obtained between the two.

Discussion.—In this article, we have presented the general Maxwell identities, Eqs. (4) and (5), that relate a macromolecule's global excess sum to local properties at its surface. These results can be of high utility. For example, in [8] we found that a special case of Eq. (4) can be used to obtain the exact mean-field excess sum associated with a line charge—despite the fact that general analytic expressions for the potential and ion density profile have not yet been found for this system. The generalizations that we have presented in this work extend the applicability of the Maxwell identity approach to all geometries. As applied to the cylindrical and planar cases, we have shown in an appendix that the identities imply the contact value theorems [1,2]. As a more general application, we have shown that combining the Maxwell identities with counterion condensation theory [10–12] provides a straightforward method for obtaining excess estimates—with Eq. (9) the formal, general result and Eq. (13) giving some explicit examples. Analytic evaluations of Eq. (9) are also possible for any geometry where the Green's function is known: convoluting this over a source distribution, one can quickly evaluate a molecule's surface potential. It would be interesting to apply this approach to study how the excess sum associated with a polymer depends upon its conformation—perhaps making use of a flexible line charge-Yukawa potential model for the polymer. Another exciting case that might be considered is the dielectric ellipsoid. Making use of the series expansion for this geometry's Green's function [20], one could quickly explore how a globular macroion's excess sum changes with deformations away from the spherical limit, as well as with its degree of source charge heterogeneity, or "patchiness." More generally, the results, Eqs. (4) and (5), can also be combined with numerical solutions to the Poisson-Boltzmann equation, non-mean-field simulation results, or any other source of contact measurements.

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APPENDIX: CONTACT VALUE IDENTITIES

Here, we present efficient derivations of the planar and cylindrical contact identities using Eqs. (4) and (5). Similar identities hold for other geometries, but cannot be written in closed form without knowledge of the surface potential. Planes: Consider an isolated planar charge distribution sitting at $z = z_0$, with an electrolyte in the upper half-space $z > z_0$. For this geometry, at fixed c, Eq. (2) reads

$$d\mathcal{F} = \phi_{z_0} d\sigma + \left(P_{\text{ext}} + \sum_i \frac{c_i(z_0)}{l_B} - 2\pi\sigma^2\right) dz_0. \tag{A1}$$

The second mechanical work term above—associated with moving the location of the plate—takes into account the external pressure force, the local osmotic pressure force at the planar surface, and the attractive electrostatic interaction of the plane with the electrolyte. We assume there are no other interactions between the plane and the solution. From Eq. (A1), we have

$$\partial_{z_0}\phi_{z_0} = \partial_\sigma\left(\frac{1}{l_B}\sum_i c_i(z_0) - 2\pi\sigma^2\right). \tag{A2}$$

The left side here is zero; ϕ_{z_0} is independent of z_0 since we assume a semi-infinite electrolyte. Integration gives

$$\sum_i c_i(z_0) - 2\pi l_B\sigma^2 = \sum_i c_i, \tag{A3}$$

the isolated planar contact identity [1]. Cylinders: The cylindrical contact identity holds only in the mean-field limit, in which the potential takes the following scaling form, which follows directly from the homogeneity of the Poisson-Boltzmann equation [8]:

$$\phi \equiv \frac{1}{el_B} y(\kappa r; \kappa a; \lambda l_B; \{z_j, \bar{c}_j\}). \tag{A4}$$

Letting $\rho_i \equiv n_i/L$, Eq. (2) reads

$$d\mathcal{F} = \phi_a d\lambda - \frac{1}{c l_B}\sum_i \rho_i dc + 2\pi a\left[P_{\text{ext}} + \frac{1}{l_B}\sum_i c_i(a) - \frac{\lambda^2}{2\pi a^2}\right] da. \qquad \text{(A5)}$$

The mechanical work term is now associated with adjusting the cylinder's radius. This contains an external pressure term, a local pressure term, and a cylindrical self-repulsion term. Consider now the two relations

$$a\partial_a \phi_a = 2\pi a^2 \partial_\lambda \left(\frac{1}{l_B}\sum_i c_i(a) - \frac{\lambda^2}{2\pi a^2}\right),$$
$$\partial_c \phi_a = \frac{1}{2c}\{r\partial_r \phi|_a + a\partial_a \phi|_r\}_a = -\partial_\lambda \sum_i \frac{\rho_i}{c l_B}. \qquad \text{(A6)}$$

The first equality in the second line follows from Eq. (A4). Further, the left side of the first line is evaluated with r set to a, and so equates to the bracketed term in the second. Combining the two equations gives

$$\partial_\lambda \left(\sum_i c_i(a) - \frac{l_B \lambda^2}{2\pi a^2} + \frac{1}{\pi a^2}\sum_i \rho_i\right) = 0, \qquad \text{(A7)}$$

or

$$\sum_i c_i(a) - \frac{l_B \lambda^2}{2\pi a^2} + \frac{1}{\pi a^2}\sum_i \rho_i = \sum_i c_i. \qquad \text{(A8)}$$

This is the cylindrical contact identity, as first derived by Anderson and Record through the use of an asymptotic analysis of the Poisson-Boltzmann equation [2].

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[16] The electrolyte was modeled using a grand canonical Monte-Carlo simulation performed within the primitive model. The spherical macroion was associated with a hard sphere boundary condition. The outer boundary was also chosen spherical, with radius $R = 11.6$ nm. The ion radii were set to 2 Å, and the solvent was modeled as uniform with dielectric constant $\epsilon = 80$. 10^5 steps were used for equilibration and 10^6 steps for data production. The excess sum was estimated using the definition, Eq. (3).
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