Poisson-Nernst-Planck Equations for Simulating Biomolecular Diffusion-Reaction Processes II: Size Effects on Ionic Distributions and Diffusion-reaction Rates

(Supplementary Material)

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S1 Numerical implementation of the SMPNP equations

S1.1 The free energy functional is convex

We will first show that the free energy functional 24 of the SMPNP system is convex. Since ϕ is determined by the ion densities through the PE

$$\rho = L\phi,$$

we note the dependence of ϕ on p as $\phi[p] = L^{-1}\rho$, where $\rho = \rho^f + \lambda\sum_i z_i e p_i$ is the total charge density, and $L = -\nabla\cdot\varepsilon\nabla$ is the partial differential operator corresponding to the Poisson equation. By taking the first-order variation of the functional 24 with respect to δp_i we get

$$(\delta F[p])_i = \int \left[q_i\phi + k_B T \ln(p_i a_i^3) - k_B T a_0^{-3} a_i^3 \ln(1 - \sum_l^K a_l^3 p_l) - \mu_i \right] \delta p_i dx. \quad \text{(S1)}$$

The second order functional variation with respect to δp_j is

$$(\delta F[p])_{i,j} = \int \left[q_i \delta p_i (L^{-1} q_j \delta p_j) + k_B T \frac{\delta_{ij}\delta p_i \delta p_j}{p_i} + k_B T a_0^{-3} \frac{a_i^3 a_j^3 \delta p_i \delta p_j}{1 - \sum_l^K a_l^3 p_l} \right] dx. \quad \text{(S2)}$$

It is known that that the elliptic operator L (hence L^{-1}) is definite positive because ε is piecewise constant. Let H be the Hessian $\frac{\delta^2 F[p]}{\delta p_i \delta p_j}$. For any non-zero variation in densities p (densities are always positive $p_i > 0$), i.e. $p \to p + \delta p$,

$$\begin{aligned} \delta p \cdot H \delta p &= \int \left[(\sum_i^K q_i \delta p_i)(L^{-1} \sum_i^K q_i \delta p_i) + \sum_i^K k_B T \frac{(\delta p_i)^2}{p_i} + k_B T \frac{a_0^{-3} (\sum_i^K a_i^3 \delta p_i)^2}{1 - \sum_l^K a_l^3 p_l} \right] dx \\ &\geqslant 0. \end{aligned} \quad \text{(S3)}$$

Therefore, H is symmetric, semi-positive definitive. It follows that $F[p]$ is convex. This guarantees a unique solution for the SMPNP equations. This fact will be used in the subsection 2.4 of the paper to make sure that the SMPBE model can be obtained from the solution of the SMPNP equations at certain conditions.

S1.2 Finite element method for the NP equations

We write Eq. 34 in a brief form:

$$-\nabla \cdot J_i = -\nabla \cdot \left[\sum_j a_{ij}(r, p(r)) \nabla p_j(r) + b_i(r) p_i(r) \right] = 0, \quad \text{(S4)}$$

tetrahedral finite elements. Functions in the space

$$H^1_{0_i} = \left\{ v \in H^1(\Omega_s) : v = 0 \text{ on } \partial\Omega, v = 0 \text{ on } \Gamma_{D_i} \right\}$$

satisfy the Dirichlet boundary condition on the exterior boundary $\partial\Omega$ and the essential or Dirichlet boundary condition on the molecular surface Γ if there is one. We assume that the finite elements are regular and quasi-uniform. The weak formulation of the problem of the whole PNP system now is:
Find $u = p \in S$ such that

$$\langle F(u), v \rangle = 0, \quad \forall v \in S. \tag{S9}$$

The weak form of Eq. S4 is

$$\langle F(p), v \rangle|_i = \int_{\Omega_s} (J_i \cdot \nabla v_i) dx = \int_{\Omega_s} \left[\sum_j a_{ij}(r,p) \nabla p_j + b_i p_i \right] \cdot \nabla v_i dx \tag{S10}$$

and the Newton-type iterations necessitate its bilinear form defined by the Gâteaux derivative $DF(u)$

$$\begin{aligned} \langle DF(p)w, v \rangle_i &= \frac{d}{dl} \langle F(p + lw), v \rangle_i |_{l=0} \\ &= \int_{\Omega_s} \left[\sum_j a_{ij} \nabla w_j \cdot \nabla v_i + \sum_j \frac{\partial a_{ij}}{\partial p_k} w_k \nabla p_j \cdot \nabla v_i + b_i w_i \cdot \nabla v_i \right] dx, \end{aligned} \tag{S11}$$

where w is functions from the same basis as v.

The derivatives (Gateaux) of a_{ij} are:

$$\frac{\partial a_{ij}}{\partial p_k} = \frac{D_i k_i \delta_{ik} a_j^3}{1 - \sum_l a_l^3 p_l} + \frac{D_i k_i p_i a_k^3 a_j^3}{(1 - \sum_l a_l^3 p_l)^2}. \tag{S12}$$

The first term in Eq. S11 leads to a symmetric stiffness matrix, but the latter two will not.

S1.3 Treatment of singular charges in Poisson equation

Two common issues exist in the solution of biomolecular electrostatic governed by either the PE 5 or the traditional PBE. These are (i) the point charge singularity, (ii) the dielectric discontinuity across a molecular surface. For a rigorous treatment

of the singular charges we introduce the Green's function for the Laplace equation and a harmonic function; the summation of these functions amounts to the zeroth order approximation to the solution to solve the point charge singularity problem. The potential is decomposed into three parts $\phi = \phi^s + \phi^h + \phi^r$. It defines a singular potential ϕ^s only in the domain Ω_m,

$$\begin{aligned} \phi^s &= G|_{\overline{\Omega}_m} \text{ in } \overline{\Omega}_m, \\ \phi^s &= 0 \text{ in } \Omega_s, \end{aligned} \tag{S13}$$

where the singular potential G solves $-\varepsilon_m \Delta G = \rho^f$ in $\mathcal{R}^3$, and uses a harmonic component ϕ^h to compensate the discontinuity of ϕ^s on Γ

$$\begin{aligned} \Delta\phi^h &= 0 \text{ in } \Omega_m, \\ \phi^h &= -\phi^s \text{ on } \Gamma. \end{aligned} \tag{S14}$$

Subtracting these two components from the PE 5, one obtains the equation for the regular potential ϕ^r:

$$\begin{aligned} -\nabla\cdot(\varepsilon\nabla\phi^r) - \lambda\sum q_i p_i = 0 \text{ in } \Omega, \\ [\phi^r] = 0, \ \left[\varepsilon\frac{\partial\phi^r}{\partial n}\right] = -\varepsilon_m\left(\frac{\partial\phi^s}{\partial n} + \frac{\partial\phi^h}{\partial n}\right) \text{ on } \Gamma. \end{aligned} \tag{S15}$$

Similarly the regular part for the nonlinear PBE satisfies:

$$-\nabla\cdot(\varepsilon\nabla\phi^r) + \kappa^2\sinh(\phi^r) = 0 \text{ in } \Omega. \tag{S16}$$

Numerical experiments illustrating the stable convergence are shown in (*S2*). The weak form, bilinear form, and more details of FEM solution of the PBE can be seen in (44) and (*S3*).

S1.4 Relaxed Gummel iteration for the SMPNP equations

A standard Gummel iteration proceeds as following: given any initial solution function ϕ^0 (or p^0), solve the NP equations Eqs. 34 (or the PE 35) to get a solution p^0 (ϕ^0), then solve the PE (NPEs) with these p^0 (ϕ^0) to get an updated solution ϕ^1 (p^1), and with ϕ^1 get an updated solution of NPEs p^2 (ϕ^2 of the PE), continue this iteration until approaching a converged solution (p,ϕ) of the PE and the NPEs.

It is found that the standard Gummel iteration converges slowly, and may diverge in some circumstances. A γ-iteration procedure for the iteration between the NP and PE as used in our former PNP solution (43) appears also helpful in as-

sisting convergence of solution for our SMPNP system. When obtained a solution (p_n, ϕ_n) of the SMPNP equations at the n-th step during the iterations between solutions of the PE and SM NPEs, we modify them for use in next iteration step by a γ-relaxation

$$p_i^n = \gamma p_i^n + (1-\gamma) p_i^{n-1}, \tag{S17}$$

$$\phi^n = \gamma \phi^n + (1-\gamma) \phi^{n-1}. \tag{S18}$$

It is found that usually under-relaxation, i.e. $\gamma < 1$ is necessary for the SMPNP system, while over-relaxation does not help the convergence.

S2 Substrate concentration dependency of the rate coefficient

We first perform simulations of the substrate diffusion-reaction process using the PNP model that does not have the size effects. As shown previously (*S4*, *S5*) the rate coefficient is dependent on substrate bulk density, even for a fixed ionic strength (see Fig. S1 for the sphere case). In particular, for attractive substrate, increasing of substrate density can speed up the diffusion process and thus increase the rate coefficient significantly. The sphere model shows the same tendency of the rate-concentration dependence as that in the enzyme model (*S5*) for the similar underlying physics.

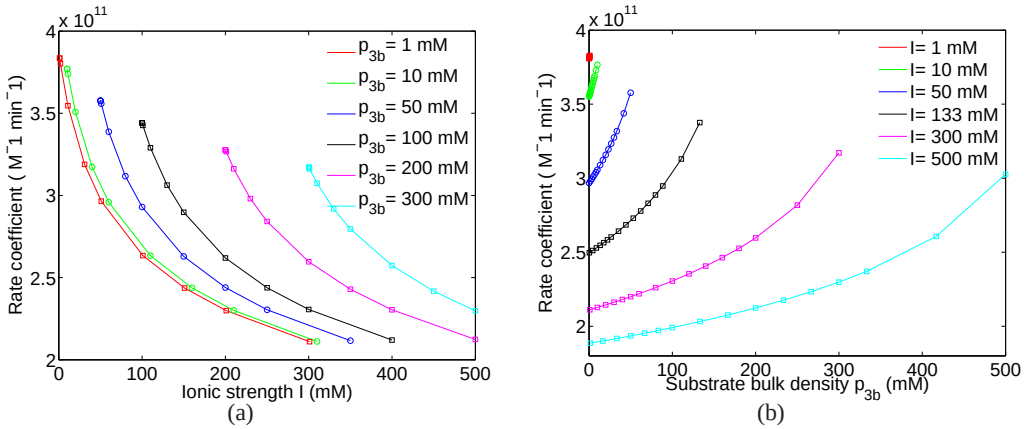

Figure S1: Rate coefficients from PNP model for a spherical case. The bulk ion densities and the substrate density keep charge neutral.

References

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