Poisson-Fermi Formulation of Nonlocal Electrostatics in Electrolyte Solutions

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We present a nonlocal electrostatic formulation of nonuniform ions and water molecules with interstitial voids that uses a Fermi-like distribution to account for steric and correlation effects in electrolyte solutions. The formulation is based on the volume exclusion of hard spheres leading to a steric potential and Maxwell's displacement field with Yukawa-type interactions resulting in a nonlocal electric potential. The classical Poisson-Boltzmann model fails to describe steric and correlation effects important in a variety of chemical and biological systems, especially in high field or large concentration conditions found in and near binding sites, ion channels, and electrodes. Steric effects and correlations are apparent when we compare nonlocal Poisson-Fermi results to Poisson-Boltzmann calculations in electric double layer and to experimental measurements on the selectivity of potassium channels for K^+ over Na^+. The present theory links atomic scale descriptions of the crystallized KcsA channel with macroscopic bulk conditions. Atomic structures and macroscopic conditions determine complex functions of great importance in biology, nanotechnology, and electrochemistry.

Continuum electrostatic theory is a fundamental tool for studying physical and chem-

ical properties of electrolyte solutions in a wide range of applications in electrochemistry, biophysics, colloid science, and nanofluidics [1–6]. For over a century, a great deal of effort has been devoted to improving the Poisson-Boltzmann (PB) theory of continuum models for a proper description of steric (or finite size) and correlation (or nonlocal screening, polarization) effects in electrolytes [7, 8]. We present a continuum model with Fermi-like distributions and global electrostatic screening of nonuniform ions and water molecules to describe the steric and correlation effects, respectively, in aqueous electrolyte solutions.

For an electrolytic system with K species of ions, the entropy model proposed in [9] treats all ions and water of any diameter as nonuniform hard spheres and regards the water as the $(K + 1)^{\text{th}}$ species. It then includes the voids between these hard spheres as the $(K + 2)^{\text{th}}$ species so that the total volume V of the system can be calculated exactly by the identity

$$V = \sum_{i=1}^{K+1} v_i N_i + V_{K+2}, \tag{1}$$

where V_{K+2} denotes the total volume of all the voids, $v_i = 4\pi a_i^3/3$ that gives the volume of each sphere with radius a_i, and N_i is the total number of the ith species particles. In the bulk solution, we have the bulk concentrations $C_i^{\text{B}} = \frac{N_i}{V}$ and the bulk volume fraction of voids $\Gamma^{\text{B}} = \frac{V_{K+2}}{V}$. Dividing the volume identity (1) by V, $\Gamma^{\text{B}} = 1 - \sum_{i=1}^{K+1} v_i C_i^{\text{B}}$ is expressed in terms of nonuniform v_i and C_i^{B} for all particle species. If the system is spatially inhomogeneous with variable electric or steric fields, as in most biological and technological systems, the bulk concentrations then change to concentration functions $C_i(\mathbf{r})$ that vary with positions, and differ from their constant values C_i^{B} at location $\mathbf{r}$ in the solvent domain Ω_s. Consequently, the void volume fraction becomes a function $\Gamma(\mathbf{r}) = 1 - \sum_{i=1}^{K+1} v_i C_i(\mathbf{r})$ as well.

For an electrolyte in contact with electrodes or containing a charged protein, an electric field $\mathbf{E}(\mathbf{r})$ in the solvent domain Ω_s is generated by the electrodes, ionic (free) charges with a displacement field $\mathbf{D}(\mathbf{r})$, and bound charges of polar water with a polarization field $\mathbf{P}(\mathbf{r})$. In Maxwell's theory, these fields form a constitutive relation

$$\mathbf{D}(\mathbf{r}) = \epsilon_0 \mathbf{E}(\mathbf{r}) + \mathbf{P}(\mathbf{r}) \tag{2}$$

that yields the Maxwell's equation $\nabla \cdot \mathbf{D}(\mathbf{r}) = \rho(\mathbf{r}) = \sum_{i=1}^{K} q_i C_i(\mathbf{r})$, $\forall \mathbf{r} \in \Omega_s$, where ϵ_0 is the vacuum permittivity and q_i is the charge on each i species ion [10]. The electric field $\mathbf{E}(\mathbf{r})$ is thus screened by water (in what might be called Bjerrum screening) and ions (in Debye

screening) in a correlated manner that is usually characterized by a correlation (screening) length λ [4, 6, 11]. The screened force between two charges in ionic solutions (at $\mathbf{r}$ and $\mathbf{r}'$ in Ω_s) has been studied extensively in classical field theory and is often described by the screening kernel $G(\mathbf{r} - \mathbf{r}') = \frac{e^{-|\mathbf{r}-\mathbf{r}'|/\lambda}}{4\pi|\mathbf{r}-\mathbf{r}'|}$ [1], which is called Yukawa-type kernel in [4, 12], and satisfies the partial differential equation (PDE) [12]

$$-\Delta G(\mathbf{r} - \mathbf{r}') + \frac{1}{\lambda^2}G(\mathbf{r} - \mathbf{r}') = \delta(\mathbf{r} - \mathbf{r}'), \quad \mathbf{r}, \mathbf{r}' \in R^3 \tag{3}$$

in the whole space R^3, where $\Delta = \nabla \cdot \nabla$ is the Laplace operator with respect to $\mathbf{r}$ and $\delta(\mathbf{r} - \mathbf{r}')$ is the Dirac delta function at $\mathbf{r}'$. The potential $\widetilde{\phi}(\mathbf{r})$ defined in $\mathbf{D}(\mathbf{r}) = -\epsilon_s\epsilon_0\nabla\widetilde{\phi}(\mathbf{r})$ thus describes a local potential of free ions according to the Poisson equation

$$-\epsilon_s\epsilon_0\nabla \cdot \nabla\widetilde{\phi}(\mathbf{r}) = \rho(\mathbf{r}), \quad \forall \mathbf{r} \in \Omega_s, \tag{4}$$

where ϵ_s is a dielectric constant in the solvent domain. We introduce a global electric potential $\phi(\mathbf{r})$ of the screened electric field $\mathbf{E}(\mathbf{r})$ as a convolution of the local potential $\widetilde{\phi}(\mathbf{r}')$ with the global screening kernel $G(\mathbf{r} - \mathbf{r}')$ in the expression

$$\phi(\mathbf{r}) = \int_{R^3} \frac{1}{\lambda^2}G(\mathbf{r} - \mathbf{r}')\widetilde{\phi}(\mathbf{r}')d\mathbf{r}'. \tag{5}$$

However, it would be too expensive to calculate $\phi(\mathbf{r})$ using this equation. Multiplying Eq. (3) by $\widetilde{\phi}(\mathbf{r}')$ and then integrating over R^3 with respect to $\mathbf{r}'$ [12], we obtain

$$-\lambda^2\Delta\phi(\mathbf{r}) + \phi(\mathbf{r}) = \widetilde{\phi}(\mathbf{r}), \quad \mathbf{r} \in \Omega_s, \tag{6}$$

a PDE that approximates Eq. (5) in a sufficiently large domain Ω_s with boundary conditions $\phi(\mathbf{r}) = \widetilde{\phi}(\mathbf{r}) = 0$ on $\partial\Omega_s$ and describes the relation between global $\phi(\mathbf{r})$ and local $\widetilde{\phi}(\mathbf{r})$ electric potentials. From Eqs. (4) and (6), we obtain the fourth-order PDE

$$\epsilon_s\epsilon_0\lambda^2\Delta(\Delta\phi(\mathbf{r})) - \epsilon_s\epsilon_0\Delta\phi(\mathbf{r}) = \rho(\mathbf{r}), \quad \mathbf{r} \in \Omega_s, \tag{7}$$

that accounts for electrostatic, correlation, polarization, nonlocal, and excluded volume effects in electrolytes with only one parameter λ. Thus, when we set $\mathbf{E}(\mathbf{r}) = -\nabla\phi(\mathbf{r})$, we can use Eq. (2) to find the polarization field $\mathbf{P}(\mathbf{r}) = \epsilon_s\epsilon_0\lambda^2\nabla(\Delta\phi(\mathbf{r})) - (\epsilon_s - 1)\epsilon_0\nabla\phi(\mathbf{r})$. If $\lambda = 0$, we recover the standard Poisson equation (4) and the classical field relation $\mathbf{P} = \epsilon_0(\epsilon_s - 1)\mathbf{E}$ with the electric susceptibility $\epsilon_s - 1$ (and thus the dielectric constant ϵ_s) if water is treated as an isotropic and linear dielectric medium [10].

We introduce a Gibbs free energy functional for the system as

$$F(\mathbf{C}, \phi) = F_{el}(\mathbf{C}, \phi) + F_{en}(\mathbf{C}), \tag{8}$$

$$F_{el}(\mathbf{C}, \phi) = \frac{1}{2} \int_{\Omega_s} \rho\phi d\mathbf{r} = \frac{1}{2} \int_{\Omega_s} \rho L^{-1} \rho d\mathbf{r},$$

$$F_{en}(\mathbf{C}) = k_B T \int_{\Omega_s} \left\{ \sum_{i=1}^{K+1} C_i(\mathbf{r}) \left(\ln \frac{C_i(\mathbf{r})}{C_i^{\mathrm{B}}} - 1 \right) + \frac{\Gamma(\mathbf{r})}{v_0} \left(\ln \frac{\Gamma(\mathbf{r})}{\Gamma^{\mathrm{B}}} - 1 \right) \right\} d\mathbf{r},$$

where $F_{el}(\mathbf{C}, \phi)$ is an electrostatic functional, $F_{en}(\mathbf{C})$ is an entropy functional, $\mathbf{C} = (C_1(\mathbf{r}), C_2(\mathbf{r}), \cdots, C_{K+1}(\mathbf{r}))$, $v_0 = \left(\sum_{i=1}^{K+1} v_i \right) / (K + 1)$ an average volume, and L^{-1} is the inverse of the self-adjoint positive linear operator $L = \epsilon_s \lambda^2 \Delta\Delta - \epsilon_s \Delta$ [12]. Taking the variations of $F(\mathbf{C}, \phi)$ at ϕ gives Eq. (7). Taking the variations of $F(\mathbf{C}, \phi)$ at $C_i(\mathbf{r})$ [12] yields Fermi-like distributions

$$C_i(\mathbf{r}) = C_i^{\mathrm{B}} \exp\left(-\beta_i \phi(\mathbf{r}) + \frac{v_i}{v_0} S^{\mathrm{trc}}(\mathbf{r}) \right), \quad S^{\mathrm{trc}}(\mathbf{r}) = \ln\left(\frac{\Gamma(\mathbf{r})}{\Gamma^{\mathrm{B}}} \right), \tag{9}$$

for all $i = 1, \cdots, K + 1$ (ions and water), where $\beta_i = q_i/k_B T$ with $q_{K+1} = 0$, k_B is the Boltzmann constant, and T is an absolute temperature. The distribution is of Fermi type since it saturates. All concentration functions $C_i(\mathbf{r}) < \frac{1}{v_i}$ [9], i.e., $C_i(\mathbf{r})$ cannot exceed the maximum value $1/v_i$ for any arbitrary (or even infinite) potential $\phi(\mathbf{r})$ in the domain Ω_s. In these Fermi distributions, it is impossible for a particle volume v_i to be completely filled with particles, i.e., it is impossible to have $v_i C_i(\mathbf{r}) = 1$ (and thus $\Gamma(\mathbf{r}) = 0$) since that would yield $S^{\mathrm{trc}}(\mathbf{r}) = -\infty$ and hence $v_i C_i(\mathbf{r}) = 0$, a contradiction. For this reason, *we must include the void as a separate species if water and ions are all treated as hard spheres* [9]. Here we do represent water and ions as spheres. Our approach allows other shapes to be used as well.

The nonlocal Poisson-Fermi (PF) Eqs. (7) and (9) have new features, of some importance.

(i) The Fermi-like distribution of uniform spherical ions with voids in ionic liquids was first derived by Bazant et al. [6, 7] using Bikerman's lattice model [13]. The entropy functional in [6] involves a reciprocal of a minimum volume v with a volume fraction Φ that is an empirical fitting parameter and may have to be unrealistically large to fit experimental data in some applications [7]. It is shown in [9] that the entropy functional in [6] does not directly yield classical Boltzmann distributions $C_i(\mathbf{r}) = C_i^{\mathrm{B}} \exp(-\beta_i \phi(\mathbf{r}))$ as $v \to 0$. It can be easily seen from (9) that the entropy functional $F_{en}(\mathbf{C})$ in Eq. (8) consistently yields Boltzmann distributions as $v_i \to 0$ for all i. Our derivation of $F_{en}(\mathbf{C})$ does not employ any

lattice models but simply uses the volume equation (1). The functional $F_{en}(\mathbf{C})$ is a new modification of that in [9], where the classical Gibbs entropy is now generalized to include all species (ions, water, and voids) in electrolytes with the same entropy form. In fact, our $\Gamma(\mathbf{r})$ is an analytical extension of the void fraction $1 - \Phi$ in Bikerman's excess chemical potential [7], where all volume parameters v_i (including the bulk fraction Γ^{B}) are physical not empirical. The adjustable parameter in our model is the correlation length $\lambda \approx 2a_i$ depending on the ionic species i of interest [9, 14]. The PF model was first proposed in [7] without derivation and has been shown to produce the results that are not only comparable to molecular dynamics (MD) simulation or experimental data but also provide insight into nonlinear properties of concentrated electrolytes and ionic liquids [15]. Here, we formally derive the PF model for general electrolytes using a hard-sphere instead of lattice model with the steric potential $S^{\mathrm{trc}}(\mathbf{r})$ first introduced in [14]. As compared with lattice models in [7] and demonstrated, for example, in [9, 16], hard-sphere models significantly improve the agreement between simulation and experiment.

(ii) The fourth-order PDE (7) is similar to those in [6, 11] used in previous papers [9, 14]. However, the physical origin of the PDE is different. In [11], the global convolution is performed only on the charge density of point-like counter ions in contrast to the potential $\widetilde{\phi}(\mathbf{r})$ by Eq. (4) that is generated by all spherical ions. In [6], a more general derivation for electrolytes or ionic liquids with steric effects is given from a free energy function of a gradient expansion of nonlocal electrostatic energy in terms of $\Delta\widetilde{\phi}$. Eq. (7) corresponds to the first term in the expansion. Here, the fourth-order PDE is derived directly from Maxwell's equation with the Yukawa screening kernel. Our result does not depend on the convergence properties of an expansion of nonlocal electrostatic energy.

(iii) Eq. (7) defines an dielectric operator $\widehat{\epsilon} = \epsilon_s\epsilon_0 \left(1 - \lambda^2\Delta\right)$ that in turn implicitly yields a dielectric function $\widetilde{\epsilon}(\mathbf{r})$ as an output of solving Eq. (7) [6, 9]. A physical interpretation of the operator was first introduced in [6] to describe the nonlocal permittivity in a correlated ionic liquid. The exact value of $\widetilde{\epsilon}(\mathbf{r})$ at any $\mathbf{r} \in \Omega_s$ cannot be obtained from Eq. (7) but can be approximated by the simple formula $\widetilde{\epsilon}(\mathbf{r}) \approx \epsilon_0 + C_{\mathrm{H_2O}}(\mathbf{r})(\epsilon_s - 1)\epsilon_0/C_{\mathrm{H_2O}}^{\mathrm{B}}$ since the water density function $C_{\mathrm{H_2O}}(\mathbf{r}) = C_{K+1}(\mathbf{r})$ is an output of Eq. (9). This formula is only for visualizing (approximately) the profile of $\widehat{\epsilon}$ or $\widetilde{\epsilon}$. It is not an input of calculation. The input is the operator $\widehat{\epsilon} = \epsilon_s\epsilon_0 \left(1 - \lambda^2\Delta\right)$ (or the correlation length λ).

(iv) The factor v_i/v_0 multiplying $S^{\mathrm{trc}}(\mathbf{r})$ in Eq. (9) is a modification of the unity used

in our previous work [9]. The steric energy $-\frac{v_i}{v_0}S^{\text{trc}}(\mathbf{r})k_BT$ [9] of a type i particle depends not only on the emptiness $(\Gamma(\mathbf{r}) = 1 - \sum_{i=1}^{K+1} v_i C_i(\mathbf{r}))$ (or equivalently crowding) at $\mathbf{r}$ but also on the volume v_i of each type of particle. If all v_i are equal (and thus $v_i = v_0$), then all particle species at any location $\mathbf{r} \in \Omega_s$ have the same steric energy and the uniform particles are indistinguishable in steric energy. The steric potential is a mean-field approximation of Lennard-Jones (L-J) potentials that describe local variations of L-J distances (and thus empty voids) between every pair of particles. L-J potentials are highly oscillatory and extremely expensive and unstable to compute numerically.

(v) The global convolution in Eq. (5) may seem similar to those in [4, 12] but it is not. The Poisson equation (4) takes the place of the Fourier-Lorentzian (FL) equation — an integro-differential equation — in the previous work [4, 12] in which the local potential $\widetilde{\phi}(\mathbf{r}')$ in Eq. (5) is replaced by a global electric potential $\Phi(\mathbf{r}')$. Moreover, the factor $1/\lambda^2$ in Eq. (5) is replaced by $(\epsilon_s - \epsilon_\infty)/\lambda^2$, where ϵ_∞ and λ are both adjustable parameters. The choice of three parameters ϵ_s, ϵ_∞, and λ in the FL model is reduced to only one λ here.

The nonlocal PF model is first compared with the modified PB model (mPB) of Borukhov et al. [17] in which ions are treated as cubes without considering void and correlation effects. The classical PB model (with $\lambda = v_i = 0$ for all i, i.e., no size, void, and correlation effects) produces unphysically high concentrations of anions near the charged wall at $x = 0$ as shown by the dashed curve in Fig. 1. The surface charge density is $1e/(50\text{Å}^2)$ in contact with a 0.1 M C_4A aqueous electrolyte, where the radius of both cations and anions is $a = 4.65$ Å in contrast to an edge length of 7.5 Å of cubical ions in [17], e is the proton charge, and $\epsilon_s = 80$. The multivalent ions A^{4-} represent large polyanions adsorbed onto a charged Langmuir monolayer in experiments [17]. The dotted curve in Fig. 1 is similar to that of mPB in [17] and was obtained by the PF model with the size effect but without voids and correlations, i.e., $\lambda = 0$, $V_{K+2} = 0$ (no voids), and $v_{K+1} = v_{H_2O} = 0$ (water is volumeless and hence $\Gamma^B = 1 - \sum_{i=1}^{K} v_i C_i^B$ is the bulk water volume fraction). The voids $(V_{K+2} \neq 0)$ and water molecules $(v_{H_2O} \neq 0)$ have slight effects on A^{4-} concentration (because of saturation) and electric potential (because water and voids have no charges) profiles as shown by the thin solid curves in Figs. 1 and 2, respectively, when compared with the dotted curves. However, correlations (with $\lambda = 2a$ [6]) of ions have significant effects on ion distributions as shown by the thick solid and dash-dotted curves in Fig. 1, where the Stern layer is on the order of ionic radius a [18] and the overscreening layer [6] $(C_{A^{4-}}(x) \approx 0)$ of excess coions $(C_{C^+}(x) >$
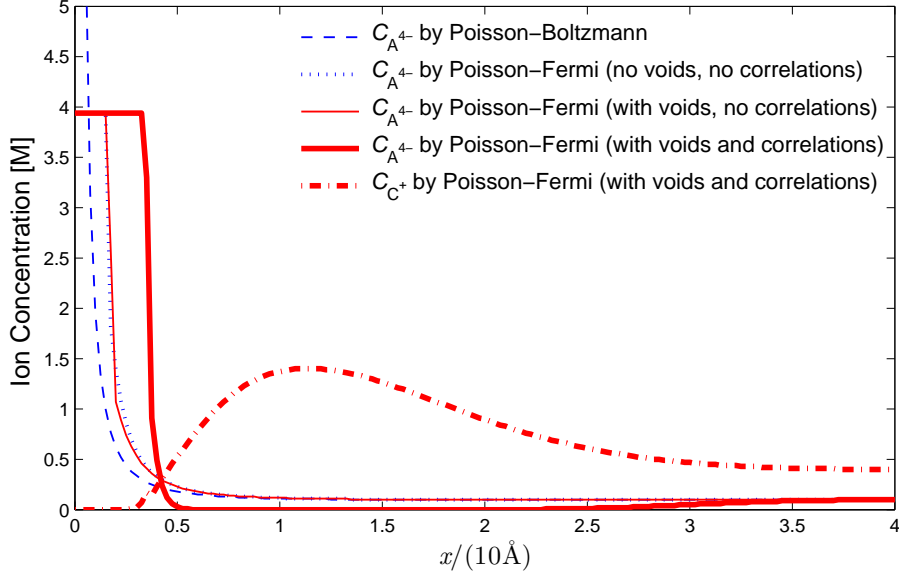
FIG. 1: Concentration profiles of anions $C_{A^{4-}}(x)$ and cations $C_{C^+}(x)$ obtained by various models in a C_4A electrolyte solution with a positively charged surface at $x = 0$.

$C_{C^+}^B = 0.4$ M) is about 18 Å in thickness. The Stern layer is an output (not a prescribed condition) of our model. The electric potentials $\phi(0) = 5.6$ at $x = 0$ and $\phi(11.5) = -1.97$ $k_B T/e$ in Fig. 2 obtained by PF with voids and correlations deviate dramatically from those by previous models for nearly 100% at $x = 0$ (in the Stern layer) and 70% at $x = 11.5$ Å (in the screening layer) when compared with the maximum potential $\phi(0) = 2.82\ k_B T/e$ of previous models.

We next show the size effect of different ions with voids using the crystal structure of the potassium channel KcsA (PDB [20] ID 3F5W [21]) as shown in Fig. 3, where the spheres denote five specific cation binding sites (S0 to S4) [22]. The crystal structure with a total of $N = 31268$ charged atoms is embedded in the protein domain Ω_p while the binding sites are in the solvent domain Ω_s. The exquisite selectivity of K^+ (with $a_{K^+} = 1.33$ Å) over other cations such as Na^+ ($a_{Na^+} = 0.95$ Å) by potassium channels is an intriguing quest in channology. It can be quantified by the free energy (G) difference of K^+ and Na^+ in the pore and in the bulk solution [22, 23]. Experimental measurements [23] showed that the relative free energy [22]

$$\Delta\Delta G(K^+ \to Na^+) = \left[G_{pore}(Na^+) - G_{bulk}(Na^+) \right] - \left[G_{pore}(K^+) - G_{bulk}(K^+) \right] \qquad (11)$$

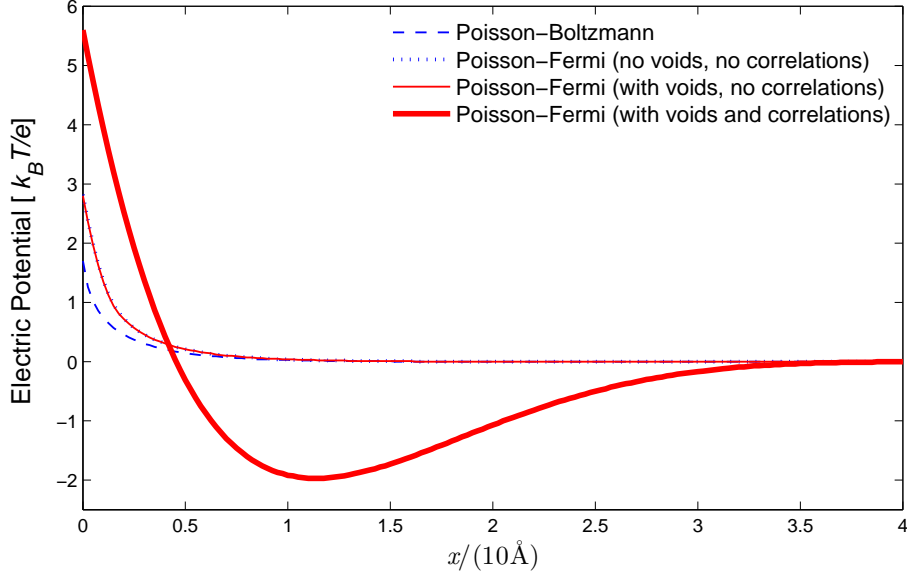FIG. 2: Electric potential profiles $\phi(x)$.

is greater than zero in the order of 5-6 kcal/mol unfavorable for Na^+. The electric and steric potentials at the binding site S2 (as considered in [22]) can be calculated on the atomic scale using the following algebraic formulas

$$\phi_{S2} = \frac{1}{4\pi\epsilon_0}\left(\frac{1}{6}\sum_{k=1}^{6}\sum_{j=1}^{N}\frac{q_j}{\epsilon_p(r)|c_j - A_k|} + \frac{q_{S2}}{\epsilon_b a_{S2}}\right), \quad S_{S2}^{\text{trc}} = \ln\frac{1 - \frac{v_{S2}}{V_{S2}}}{\Gamma^B}, \quad (12)$$

where $S2 = Na^+$ or K^+ (the site is occupied by a Na^+ or a K^+), q_j is the charge on the atom j in the protein given by PDB2PQR [24], $\epsilon_p(r) = 1 + 77r/(27.7 + r)$ [25], $r = |c_j - c_{S2}|$, c_j is the center of atom j, A_k is one of six symmetric surface points on the spherical S2, $\epsilon_b = 3.6$, and $V_{S2} = 1.5v_{K^+}$ is a volume containing the ion at S2. The crucial parameter in (12) is the ionic radius $a_{S2} = 0.95$ or 1.33 Å (also in $|c_j - A_k|$) that affects ϕ_{S2} very strongly but S_{S2}^{trc} weakly. We obtained $\Delta\Delta G = 5.26$ kcal/mol in accord with the MD result in [22], where $G_{\text{pore}}(Na^+) = 4.4$, $G_{\text{bulk}}(Na^+) = -0.26$ [26], $G_{\text{pore}}(K^+) = -0.87$, $G_{\text{bulk}}(K^+) = -0.27$ kcal/mol [26], $G_{\text{pore}}(S2) = q_{S2}\phi_{S2} - \frac{v_{S2}}{v_0}S_{S2}^{\text{trc}}k_BT$, $T = 298.15$, $\phi_{Na^+} = 7.5$ k_BT/e, $\frac{v_{Na^+}}{v_0}S_{Na^+}^{\text{trc}} = 0.23$, $\phi_{K^+} = -1.93$ k_BT/e, $\frac{v_{K^+}}{v_0}S_{K^+}^{\text{trc}} = -0.59$, and $C_{Na^+}^B = C_{K^+}^B = 0.4$ M.

In summary, a nonlocal Poisson-Fermi model is proposed to describe global electrostatic and steric effects that play a significant role of ionic activities in electrolyte solutions especially in high field or large concentration conditions. The model is based on Maxwell's field theory and nonuniform hard spheres of all ions and water molecules with interstitial voids.
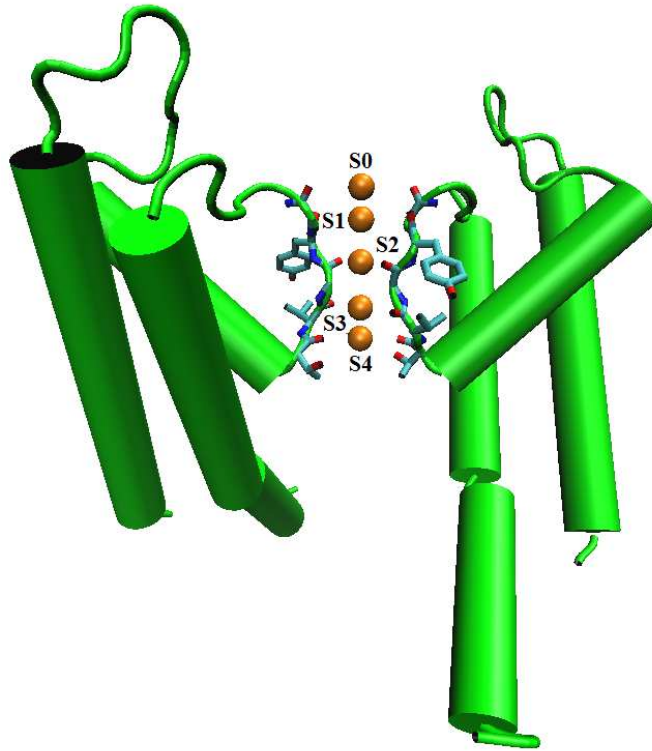
FIG. 3: The crystal structure of the K^+ channel KcsA (PDB ID 3F5W) [21] with five cation binding sites S0, S1, S2, S3, and S4 [22] marked by spheres.

The Fermi-like distribution formula can describe the distribution of nonuniform spherical ions and water molecules with interstitial voids. The steric potential is a mean-field description of Lennard-Jones potentials between particles. Poisson's equation is self-consistent with Fermi distributions and global electrostatics. The present theory can be used to describe complex functions of biological or chemical structures on both atomic and macroscopic scales with far field bulk and boundary conditions. Comparisons with experimental data are promising but incomplete.

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