

Abstract

We derive
A continuum model of biological calcium channels,
Poisson-Fermi equation,
designed to deal with crowded systems
in which ionic species and side chains nearly fill space.

The model is evaluated in three dimensions. It includes steric and correlation effects and is derived from classical hard-sphere lattice models of configuration entropy of finite size ions and solvent molecules. **Formulae are given for ionic species with different sizes and valences.**

Unphysical overcrowding does not occur with the Fermi-like distribution, unlike the Boltzmann distribution.

Fermi-like distributions deal automatically with saturation effects

We provide analytical descriptions of implicit dielectric ('primitive') models of ionic solutions. Poisson-Fermi equations are local, dealing with different correlations at different places. **Correlations produce spatial variations of dielectric permittivity and chemical potential.**

We give global and local formulae for the chemical potential and permittivity (as outputs).

Results are consistent with Monte Carlo binding curves and illustrate **the anomalous mole fraction effect of calcium channels,** a blockage of sodium binding by a tiny concentration of calcium ions.

Details are in Publications

Jinn-Liang Liu: J. Computational Physics (2013) **15**: 88

Liu and Eisenberg: J. Phys. Chem. B (2013) **117**: 12051-12058

Poisson-Fermi Equation

Poisson-Fermi field equations are a fourth order partial differential equation

$$\underbrace{\epsilon_w (l_c^2 \nabla^2 - 1)}_{\text{Dielectric Operator}} \nabla^2 \phi = \sum_{i=1}^K q_i C_i = \rho$$

or a pair of second order partial differential equations

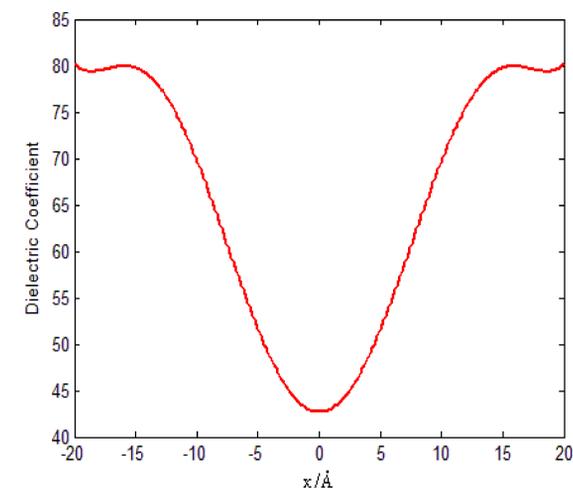
$$\begin{cases} \nabla^2 \phi = \Psi, \\ \underbrace{\epsilon_w (l_c^2 \nabla^2 - 1)}_{\text{Dielectric Operator}} \Psi = \rho, \end{cases}$$

Boundary conditions appropriate for these equations are derived in J. Computational Physics (2013) **15**:88

Numerical methods are developed and tested there and also used in J. Phys. Chem. B (2013) **117**:12051-12058

Inappropriate boundary conditions lead to unphysical results. Inappropriate numerical methods lead to uncomputable models, particularly in three dimensions

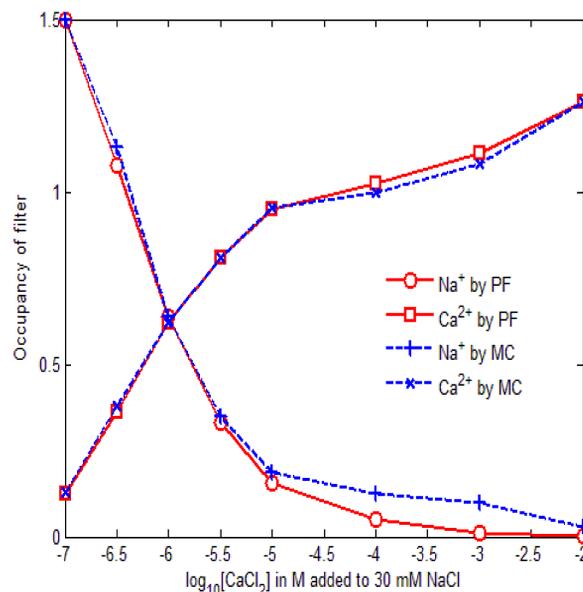
Dielectric Properties i.e., polarization charges Vary Significantly with position



Variables

ϕ is the electrostatic potential, $q_j = z_j e$ is the charge on ion of type j , radius a_j , $\beta_j = q_j / k_B T$ is the electrostatic energy with e the charge on a proton. C_j is the concentration of j . k is the Boltzmann constant, T is the absolute temperature, l_c is a correlation length chosen to fit data (see publications), ϵ_w is the dielectric coefficient of water; ρ is charge density.

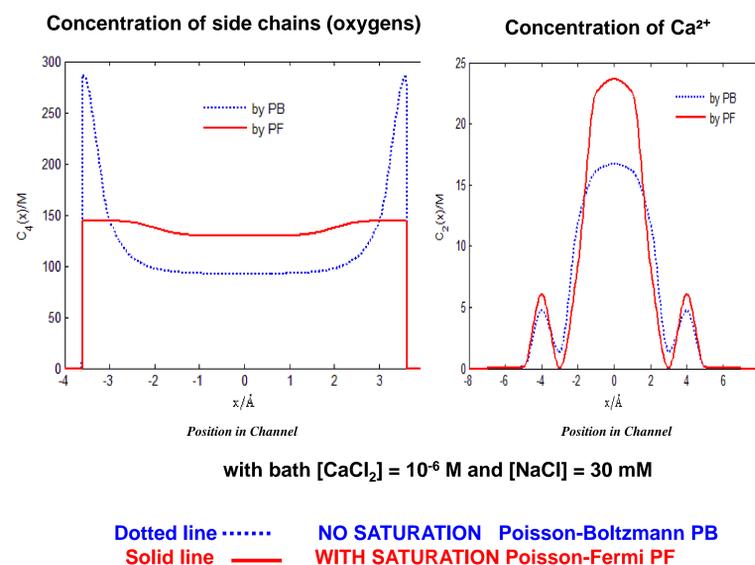
Results Agree Quantitatively with INDEPENDENT Monte Carlo Simulations



The average number of Ca^{2+} and Na^+ in the selectivity filter varies with increasing $[\text{CaCl}_2]$ added to a fixed $[\text{NaCl}] = 30$ mM background electrolyte.

The Monte Carlo MC curve is reproduced from Fig. 6c in Boda, et al, Biochimica et Biophysica Acta (BBA) - Biomembranes (2009) **1788**, 2471-2480

Saturation is Important Poisson Fermi deals well with Saturation



CONCLUSION
Poisson-Fermi continuum model
deals with finite size and saturation
as does the
Monte Carlo discrete model

Equilibrium Properties

S_{trc} Steric Excess Potential

$$S_{\text{trc}} = \log_e \left[\frac{\left(1 - \sum_{j=1}^K v_j C_j\right)}{\left(1 - \sum_{j=1}^K v_j C_j^B\right)} \right]$$

$v_j = \frac{4}{3} \pi a_j^3$ = volume of ion

Steric excess potential S_{trc} is different for each ionic species — beyond ideal dilute solutions.
Concentration of each species depends on concentration of **all other species.**

$$C_j = \frac{C_j^B \exp(-\beta_j \phi)}{1 - \sum_{j=1}^K v_j C_j^B} \left(1 - \sum_{j=1}^K v_j C_j \right) = C_j^B \exp(-\beta_j \phi + S_{\text{trc}}),$$

**'EVERYTHING' INTERACTS WITH EVERYTHING
in crowded systems like ions in channels**