

# STERIC PNP (POISSON-NERNST-PLANCK): IONS IN CHANNELS.

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## Abstract

Ionic solutions are not ideal. **Everything interactions with everything else** through the electric field and steric repulsion.

**Ions are highly concentrated where they are most important**, particularly in the highly concentrated solutions (>10 M) in and near ion channels, active sites, and electrodes (see European Biophysics Journal 41:449-460 (2012) .

A **variational approach** is needed in such interacting systems (see J Chem Phys 133: 104104 (2010). The resulting Euler Lagrange differential equations are difficult to integrate.

Here we present **the first terms of a perturbation expansion** that is much easier to compute and can produce **current voltage curves in complex solutions** and channels in a few hours of time on a notebook computer.

## Poisson Equation

$$-\nabla \cdot (\underbrace{\epsilon \nabla \phi}_{\text{Electric Forces}}) = \underbrace{\rho_0 e}_{\text{Protein Acid/Base}} + \underbrace{\sum_{i=1}^N z_i e c_i}_{\text{Mobile Ions}},$$

$$\underbrace{\frac{\partial c_i}{\partial t} + \nabla \cdot \vec{J}_i}_{\text{Conservation Law 'Continuity' Eqn}} = 0,$$

$$\vec{J}_i = -\underbrace{D_i \nabla c_i}_{\text{Diffusion}} - \underbrace{\frac{D_i c_i}{k_B T} z_i e \nabla \phi}_{\text{Electric Current}}$$

$$-\underbrace{\frac{D_i c_i}{k_B T} \sum_{j=1}^N \epsilon_{ij} \delta^{-12+d} (a_i + a_j)^{12} \nabla c_j}_{\text{Steric Repulsion}}$$

Equations are solved with the multiblock Chebyshev pseudospectral method together with the method of lines: J Computational Physics 231:2498 (2012).

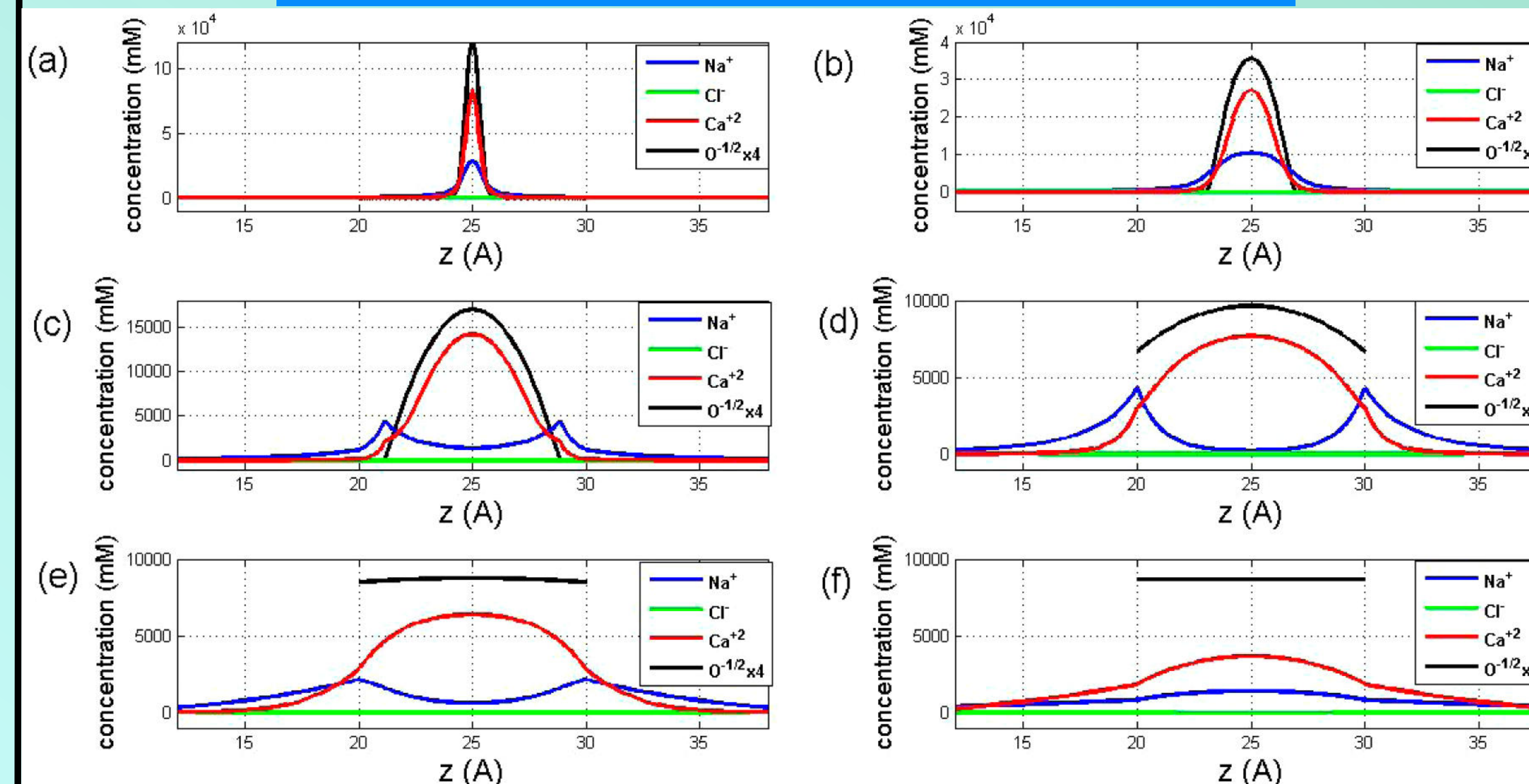
The calcium and sodium channel are represented as in the models introduced by Nonner and Eisenberg<sup>1</sup> that have been used in a series of some 35 papers recently reviewed<sup>2</sup> and extended to deal with current voltage relations of the Ryanodine Receptor by Gillespie<sup>3</sup>, more than anyone else. Most of these papers use the Monte Carlo MC methods of Boda and Henderson<sup>4</sup> and so deal with equilibrium situations. Here we present an **easily computable nonequilibrium treatment** of the same model derived using the energy variational approach EnVarA of Chun Liu and collaborators<sup>5</sup> that allows extension of an equilibrium model to nonequilibrium conditions producing flow. The EnVarA variational approach provides a unique consistent set of differential equations given a model of the conservative and dissipative energetics of the system. Few methods deal consistently with flow, dissipation and friction. Polarization forces are determined by Poisson's equation without approximations used in MC.

Calculations are of properties of the open channel. Models of gating are not yet available, although it is becoming clear that some kinds of gating can arise from instability in models of the open channel. Other properties of gating require explicit models of the energy and dissipation of conformational changes of the electric and steric fields produced by ions, protein structures, and boundary conditions (e.g., membrane potential).

The model used is a one dimensional cylinder of variable diameter. Three dimensional calculations are needed and are in progress. Baths are represented by regions of much larger ("infinite") diameter. The channel protein is represented by primitive models of side chains known to be important for selectivity. Side chains are spheres of different diameter and charge.

Calculations shown here use **Kong combining rules<sup>6</sup> for the first time** to estimate interactions between different types of ions, and ions and side chains. Similar rules are used throughout physical chemistry to describe Lennard Jones forces between different types of ions, for example, in molecular dynamic simulations of bulk solutions. **Interaction terms have profound effects on the coupling of fluxes through the open channel. It seems likely that evolution controls some channel function by controlling these interaction terms.**

## Ions in a Calcium Channel

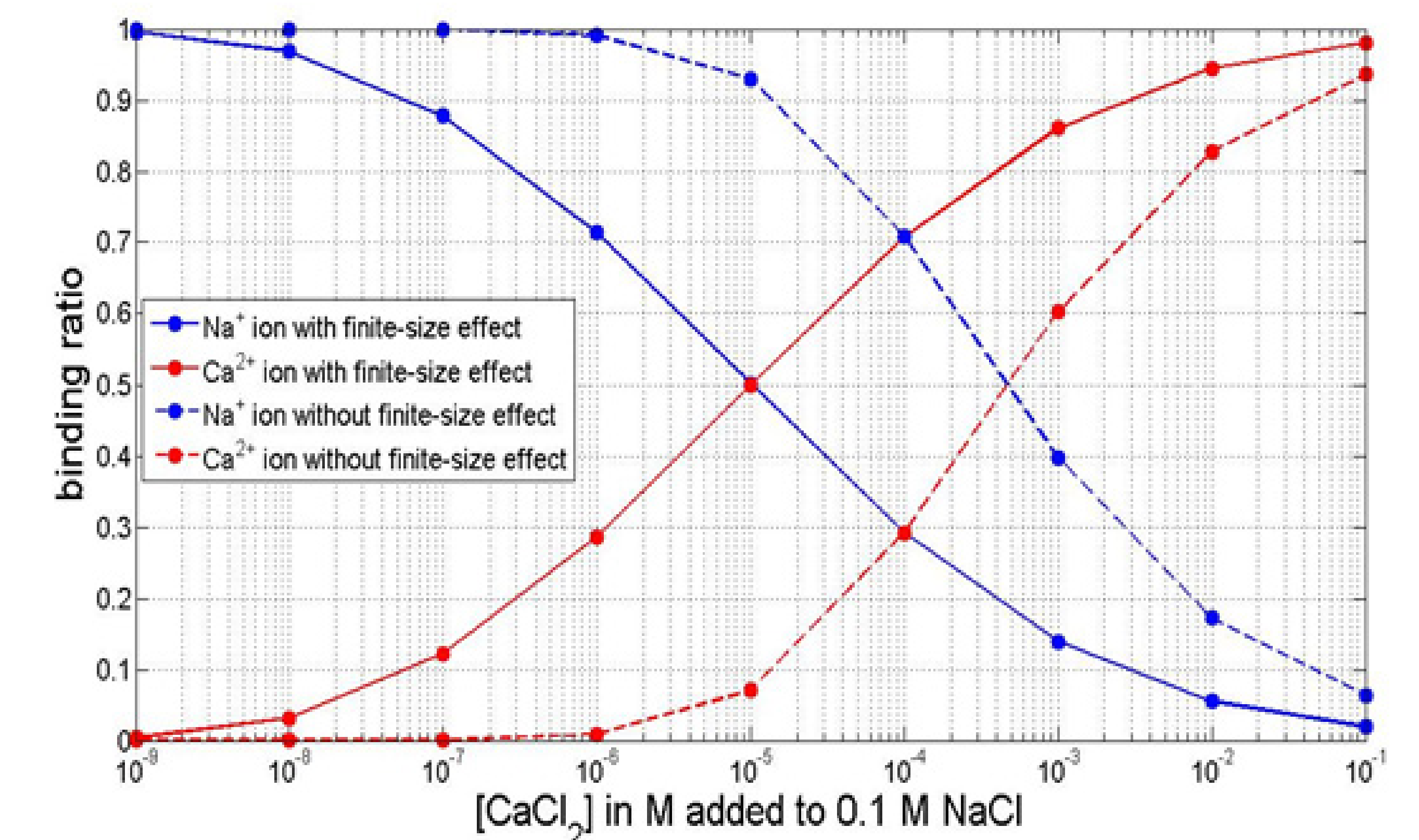


### EEEE Calcium Channel concentration distributions with various interactions.

With : (a) ; Ca<sup>2+</sup> Kong binding ratio=0.60214; (b) ; Ca<sup>2+</sup> binding ratio = 0.59418; (c) Ca<sup>2+</sup> binding ratio = 0.75433; (d) ; Ca<sup>2+</sup> binding ratio = 0.86109; (e) ; Ca<sup>2+</sup> binding ratio = 0.82580; (f) ; Ca<sup>2+</sup> binding ratio = 0.71644 .

Ca<sup>2+</sup> = 1 mM, Na<sup>+</sup>= 100 mM, on both sides. Membrane potential = 0.

## Calcium Binding Curves EEEE



Computations have also been done for DEKA Na and EEEA Ca channels.

Details are in the **Journal of Physical Chemistry B 116:11422-11441 (2012).**

## References

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