

# 3-D FE steady-state electrodiffusion model of Ionic Channels

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## Abstract

A 3-D Finite Element steady-state electrodiffusion (Poisson-Nernst-Planck) model is presented and applied to the analysis of the ion transport across ionic channels of cellular membrane. The model allows us to obtain an accurate description of ion flow across the cell membrane. An example of application to the case of a K channel is also illustrated. The resulting current-voltage curve for the K channel shows excellent agreement with experimental measurements.

## 1 Introduction

The exchange of signals between living cells takes place mainly through the cellular membrane, which represents a selective permeable barrier between the cell and extracellular environment. The flow of substances across cell membranes takes place through membrane channels, which are typical hydrophobic regions having a size of the order of few Å, where the membrane lipid bilayer exhibits openings. Among interesting substances, ions are of paramount importance since activation of several critical signalling pathways depends on ionic concentrations (especially  $\text{Ca}^{++}$  and  $\text{K}^+$ ) and therefore a number of cellular functions are activated by specific ion concentrations. For these reasons, the ion transport across cell membranes and the electrolytic equilibrium between the cells and their environment have a fundamental role in biological systems.

The simulation of the mechanism of ion flow across ionic channels is a very complicated task, for a number of reasons including the lack of accurate descriptions of channel structure, the difficulty of modeling the behaviour of the proteic chains constituting the channel walls, the very high number of atoms, the very short time scale of the involved dynamical phenomena, etc. Nevertheless several attempts have been made to build coherent representations of ion flow across ionic channels, in accordance with experimental measurements. In literature [2] several approaches have been followed for this purpose and in particular the most used technique are Molecular Dynamic (MD), Brownian Dynamic (BD), Langevin-Lorentz-Poisson (LLP) particle model, and a continuum model named Poisson-Nernst-Planck (PNP). Differently from MD, BD and LLP, the PNP model does not consider explicitly ion motion, being based on the electrodiffusion theory describing the average ionic

flux due to gradients of ion concentrations and electric fields. Recently the PNP model has been successfully applied to obtain the V-I characteristic curve of different ionic channel [3-5]. Usually the solution of the PNP equation is performed by using 2-D model and finite difference method, which involves several limitations in the description of ionic channel geometry. In this paper a fully 3-D Finite Element (FE) discretization of steady-state PNP equation is presented. The use of irregular FE mesh allows us to model the 3-D channel geometry with a lower number of degree of freedom with respect to FD. The obtained results are in good agreement with experimental data available in literature.

## 2 FE PNP modeling of ionic channels

In the PNP model the flow of ions across the cellular membrane is mathematically described by means of the diffusion equations of the several ion species and the Poisson equation for the electrostatic potential:

$$\begin{aligned}\frac{\partial n_i}{\partial t} + \nabla \cdot \mathbf{J}_i &= 0 \\ \mathbf{J}_i &= z_i \mu_i n_i \mathbf{E} - D_i \nabla n_i \\ \nabla(\varepsilon \nabla \varphi) - eN + \sum_i q_i n_i &= 0 \\ \mathbf{E} &= -\nabla \varphi\end{aligned}$$

where  $e$  is the proton charge,  $\varepsilon$  is the dielectric coefficient, and where for each ion species  $i$ ,  $n_i$  is the ion spatial density,  $\mathbf{J}_i$  is the particle flux,  $q_i$  is the ionic charge,  $z_i = q_i/e$ ,  $\mu_i$  is the mobility coefficient, and  $D_i$  is the diffusion coefficient. The total electric current density (charge flux) is

$$\mathbf{J} = \sum_i q_i \mathbf{J}_i$$

In our analysis we are interested in the steady state solution of the PNP model and consequently we remove the time dependence from the above equations obtaining the following system (the second equation must be written for each ionic species):

$$\nabla(\epsilon\nabla\varphi) - eN_{fixed} + \sum_i q_i n_i = 0$$

$$\nabla \cdot (z_i \mu_i n_i \nabla \varphi + D_i \nabla n_i) = 0$$

The ionic channel can be described by adding two funnels located at channel extremities in such a way as to take into account the effects of the two baths representing the environment inside and outside the cell. The size of the funnels are chosen to guarantee that the ion densities and the electrostatic potential assume their asymptotic values in the baths. In order to guarantee this condition their size must be larger than some Debye length (of the order of 1nm). The boundary conditions for this model are

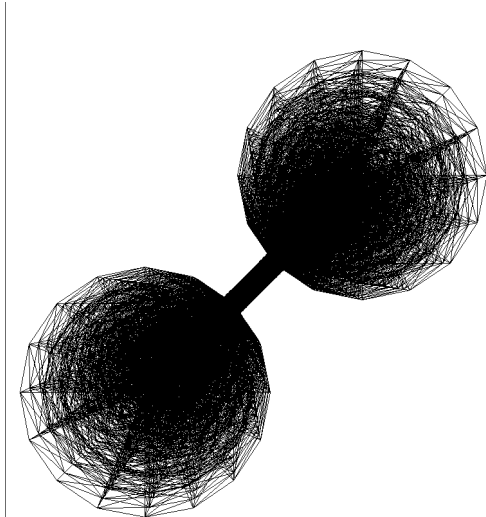
$$n_i = N_i, \varphi = 0 \text{ (left bath left boundary)}$$

$$n_i = N_i, \varphi = V \text{ (right bath right boundary)}$$

$$\mathbf{n} \cdot \nabla n_i = 0, \mathbf{n} \cdot \nabla \varphi = 0 \text{ (noflux)}$$

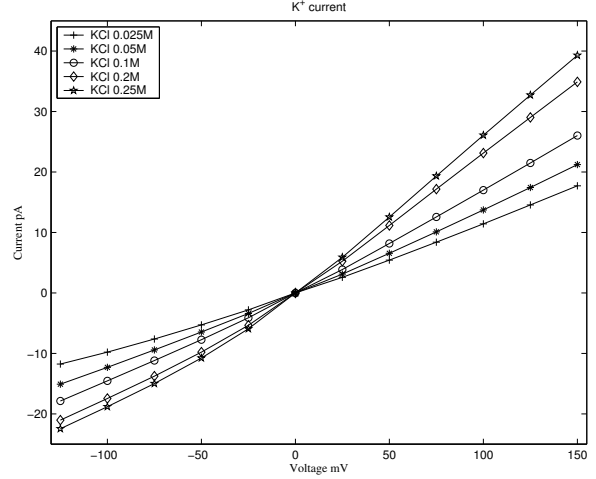
where  $\mathbf{n}$  is an unit vector normal to the boundary. The solution of the system of coupled equations is achieved by using the finite element method, in such a way as to approximate inside each tetrahedron the ion density of each specie  $n_i$ , and the electrical potential  $\varphi$  by means of the nodal FE approximation using Lagrange polynomials. In this way for each mesh node we have  $N+1$  unknown, where  $N$  is the number of ionic species considered in the analysis. The solving system is obtained by applying the Galerkin method, which gives

$$\begin{cases} [S][\varphi] + \sum_i q_i [T][n_i] - e[T][N_{fixed}] = 0 \\ [M_i(\varphi, n_i)] - [C_i][n_i] = 0 \quad i = 1 \dots N \end{cases}$$



**Fig. 1** 3D plot of FE mesh for a K channel

In order to solve the above coupled non linear system we adopt an iterative scheme based on the Newton Method, which solves the equations simultaneously, through a generalization of the Newton-Raphson method for determining the roots of an equation. A more accurate description of the solving procedure will be given in the full paper.



**Fig. 2** V-I curve for different KCl concentrations

The 3-D FE steady-state electrodiffusion model has been used for the simulation of a K channel, for which the geometrical description and electrical data (V-I curve) are available in literature [3]. Fig. 1 show the 3-D mesh for the considered K channel. The resulting current-voltage curve presented in fig. 2 shows excellent agreement with experimental measurements.

## 4 Literature

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