Differential geometry based ion transport models

Qiong Zheng1, Zhan Chen1, Kelin Xia1, Duan Chen1, Zixuan Cang1 and Guo-wei Wei1,2,3

1Department of Mathematics, Michigan State University, MI 48824, USA
2Department of Electrical and Computer Engineering, Michigan State University, MI 48824, USA
3Department of Biochemistry and Molecular Biology, Michigan State University, MI 48824, USA

Introduction

Ion channels are pore-forming proteins presented in cell membranes, usually allowing specific ions to pass across membranes and maintaining proper intracellular ion compositions. They are crucial to cell survival and functions, and are key components in many biological processes such as nerve and muscle excitation, resting and action potential generation, sensory transduction, learning and memory, to name a few. Dysfunctional ion channels can cause many diseases: deafness, blindness, migraine headaches, and cardiac arrhythmias. Ion channels are frequent targets for drug design.

The mathematical model

Total energy functional

\[ G_{tot}(\Phi, n, \eta) = \left[ \text{Geometric} + \text{Electrostatics} + \text{Chemical} \right] \eta \]

- Geometric = \( \gamma \| \nabla \Phi \| + p S + p_0 \left( 1 - S/|U_{GS}| \right) \)
- Electrostatics = \( S \left[ \frac{e_s(r)}{2} \| \nabla \Phi \|^2 + \phi \sum \Omega_\delta(r - r_j) \right] \) + \( (1 - S) \left[ \frac{e_s(r)}{2} \| \nabla \Phi \|^2 + \phi \sum \frac{n_\delta \eta}{r_{\delta}} \right] \)
- Chemical = \( (1 - S) \sum n_\sigma \left[ \ln \frac{n_\sigma}{n_{\sigma 0}} + \frac{n_\sigma}{n_{\sigma 0}} - 1 \right] - \mu_\sigma \)

- Geometric: Surface energy, mechanical work and solvent-solute interactions.
- Electrostatics: Electrostatic energy in protein and in solvent.
- Chemical: Chemical potential energy.

\( \gamma \) is the surface tension, \( \Phi \) is the characteristic function indicates the solvent/solute domain, \( \phi \) is the hydrodynamic pressure, \( \eta \) is the surface tension, \( c_s \) and \( c_m \) are the dielectric constants of the solvent and solute, and \( \gamma_s \) denotes the concentration of ionic solute species.

Simulation results: I

Numerical simulations are carried out based on the molecular structure of Gramicidin A Channel which is one of the most widely studied channels and implicit membrane representation to study the ion transport. The surface defined by \( S \) is shown below:

Gramicidin is a heterogeneous mixture of six antibiotic compounds, Gramicidin A, B and C, making up 80, 6, and 14 percents respectively, all of which are obtained from the soil bacterial species Bacillus brevis. Gramicidin A ion channel selectively passes monovalent cations. All experimental data are from Cole et al., 2002, Biophysical Journal.

Simulation results: II

The electrostatic potential and ion concentration contours of \( S \) along the channel pore direction:

Conclusion

The differential geometry based ion transport model is presented and numerical algorithms are developed for solving the coupled equations in the biomolecular context. Numerical convergence is validated and simulation results are compared well with experimental measurements.

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Reference