Simulating Ion Transport through Selective and Rectifying Ion Channels Using Local Equilibrium Monte Carlo

Desző Boda¹, Dirk Gillespie², Mónika Valiskó³, Zoltán Ható⁴, Tamás Kristóf⁵


Motivation

Systems of interest:
- ion channels in biological membranes
- synthetic nanopores
- silicate membranes

Phenomena of interest:
- Selective transport and/or adsorption
- Rectification

Models:
- Molecular models – coarse grained to some degree

Methods:
- Simulations – combined with transport equation

Nernst-Planck equation

\[ \mathbf{j}^\alpha(r) = -\frac{1}{\mathcal{V}} \mathbf{D}^\alpha(r) c^\alpha(r) \nabla \mu^\alpha(r) \]

- \( \mathbf{j}^\alpha(r) \) – flux density
- \( \mathbf{D}^\alpha(r) \) – diffusion coefficient profile
- \( c^\alpha(r) \) – concentration profile
- \( \mu^\alpha(r) \) – electrochemical potential profile (contains the external electric field)
- We need a statistical mechanically correct relation between \( c^\alpha(r) \) and \( \mu^\alpha(r) \).

Local Equilibrium Monte Carlo

- Suggestion: divide the domain of solution (blue line) into volume elements, \( V_i \).
- Perform Grand Canonical Monte Carlo simulation using the local \( \mu_i^\alpha \) in \( V_i \).
- Key: assume LOCAL EQUILIBRIUM in \( V_i \) [1-3].
- Acceptance probability: \( \lambda = 1 \) for insertion/deletion

\[ \rho_i^\alpha(r) = \frac{N_i^\alpha V_i^X}{\rho_i^\alpha} \exp \left( -\frac{\Delta\mu^\alpha(r) - \mu_i^\alpha - \mu_i^\alpha}{kT} \right) \]

The algorithm:

\[ \mu_i^\alpha[n] \xrightarrow{LEMC} c_i^\alpha[n] \xrightarrow{NP} \mathbf{j}_i^\alpha[n] \xrightarrow{\nabla \cdot \mathbf{j}_i^\alpha = 0} \mu_i^\alpha[n + 1] \]

Rectifying ion channel motivated by a mutated OmpF porin

Motivation: experiments of Miedema et al. [6] for an OmpF porin channel.

- The wild-type OmpF porin has been mutated (RREE) into a rectifying channel.
- All-atom molecular dynamics simulations failed to reproduce this behavior.

Let us try a reduced model! It contains the positive & negative amino acids in order to mimic the PN junction of a rectifying diode.

Ryanodine Receptor (RyR) Ca²⁺-release calcium channel

- Output: current-voltage curves for various compositions of electrolytes on the two sides of the membrane:

Experimental values in the baths – the pore embedded in a membrane – access regions – bulk regions (control cells)

Boundary conditions: voltage and concentrations are prescribed in the baths

Anomalous mole fraction experiment: voltage is fixed, electrolyte composition is varied

CaCl₂ is added to 100 mM CsCl on the SR side at -20 mV.

Results of NP+LEMC calculations

Conclusion

- NP+LEMC is an efficient combined transport equation & simulation method that is able to compute steady state diffusion through pores.
- Advantage: fast and it gives correct relation between \( c^\alpha(r) \) and \( \mu^\alpha(r) \).
- Disadvantage: dynamics is hidden in \( \mathbf{D}^\alpha(r) \)
- Solution: a dynamical simulation method can be used instead of NP [7].

References


Acknowledgment

Supported by OTKA NN113927 and TÁMOP-4.1.4-C-12/1/KONV-2012-0017

Experimental data and NP+DFT results of Gillespie are from Refs. [4-5].

Experimental data and NP+DFT results of Gillespie are from Refs. [4-5].