Selectivity and conduction of a model calcium channel studied by the NP+LEMC method

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ABSTRACT

We present results for the steady-state diffusion of ions (electrodiffusion) through a three-dimensional model of a calcium channel studied by a recently proposed technique [1] in which the Nernst-Planck (NP) transport equation of electrodiffusion is coupled to the Local Equilibrium Monte Carlo (NP) method (NP+LEMC). The NP equation provides the flux as a function of the concentration, electrochemical potential, and diffusion coefficient profiles. The LEMC method performs Grand Canonical Monte Carlo (GCMC) simulations for small volume elements of the system using a parameter for each subvolume that we identify as the electrochemical potential of the given subvolume. If local equilibrium exists in the volume elements, this identification is exact; otherwise, it a practical assumption.

The LEMC simulations provide the concentration profile for a given electrochemical potential profile. We also assume that the gradient of this electrochemical potential profile is the driving force of the steady-state diffusion as given by the NP equation. An iterative procedure has been developed [1] to find the electrochemical potential profile that (together with the resulting concentration profile) provides a flux that satisfies the continuity equation (conservation of mass).

The diffusion coefficient profile is an external, adjustable parameter of the method that can be fitted to experimental data or to results obtained from direct simulation methods. Such a direct simulation method is the Dynamical Monte Carlo (DMC) technique. The calcium channel studied in this work was simulated by the DMC method by Rutkai et al. [2]. In this work we adjust the diffusion coefficient profiles to the results from their DMC simulations.

These DMC simulations do not use the LEMC technique. They simulate the transport between two control cells (Dual Control Volumes, DCV) in which GCMC simulations are performed to maintain the concentration difference between the two sides of the membrane (DMC+DCV method). Coupling the DMC simulations to the LEMC method (DMC+LEMC) is presented by another contribution of this conference.

Our results for the calcium channel show the importance of the clear distinction between binding affinity and dynamical selectivity. Binding affinity describes the ratio of the probabilities that calcium and sodium ions bind to the binding site (the selectivity filter) of the channel. The dynamical selectivity describes the ratio of fluxes carried by these two ionic species.

REFERENCES

[1] Boda, D., Gillespie, D., "Steady state electrodiffusion from the Nernst-Planck equation coupled to Local Equilibrium Monte Carlo simulations", Journal of Chemical Theory and Computation., **8** (3), 824-829 (2012)
[2] Rutkai, G., Boda, D., Kristóf, T., "Relating binding affinity to dynamical selectivity from dynamic Monte Carlo simulations of a model calcium channel", Journal of Physical Chemistry Letters, **1** (14), 2179-2184 (2010)