Simulation of Ion Conduction in the *ompF* Porin Channel using BioMOCA

Kyu-Il Lee, Trudy A. van der Straaten[1], Gulzar A. Kathawala[1], Young June Park, and Umberto Ravaioli[1]
School of Electrical Engineering and Computer Science, Seoul National University, San 56-1 Shillim-Dong, Kwanak-Gu, Seoul 151-744, Republic of Korea
[1] Beckman Institute for Advanced Science and Technology, University of Illinois at Urbana-Champaign, 405 North Mathews Ave., Urbana, IL 61801, USA
E-mail: macjr@bawi.org

Ion channels are natural nanotubes that play a key role in regulating ion transport through the membranes of all biological cells. They have captured the attention of the computational electronics community because they possess functionalities like gating (switching) and filtering that resemble those of electronic devices, and so, have the potential to be used as down-scaled application devices such as single molecule detector. Many channels can also be mutated in the laboratory with atomic precision, allowing the possibility of designing new channels with specific properties and behaviors. Realistic simulation of ion channels is a necessary complement to the experimental effort aimed at understanding the fundamental mechanisms underlying channel function and operation. For this purpose, several standard simulation methodologies have been applied, from the detailed method of Molecular Dynamics (MD) to the efficient Drift-Diffusion (DD) approach. Because the vast computational resources required by MD simulations limit simulation times, while DD schemes sacrifice important molecular detail, coarse-grained particle approaches such as Transport Monte-Carlo (TMC) have recently been proposed as a compromise between numerical efficiency and physical detail.

BioMOCA has been developed at the University of Illinois to simulate ion transport through open channels using the TMC technique. Realistic channel structures with fixed permanent charges (doping) are mapped onto a 3-D mesh using the Cloud-In-Cell (CIC) scheme. The computational speed-up over MD is achieved by modeling water, protein, and lipid as static dielectric background materials and only computing ion trajectories. Electrostatic forces are calculated using the Particle-Particle-Particle-Mesh (P^3M) scheme and pairwise 6-12 Lennard-Jones potential is also considered in order to prevent the unphysical overlap of the finite-sized ions. Ion-water interactions are treated as thermalizing scattering events with scattering rates linked to the ion's diffusivity in bulk electrolyte.

In this paper we report on recent BioMOCA simulations of K^+ and Cl^- transport through the *ompF* porin channel. *OmpF* porin is a highly charged (net charge on the entire porin molecule is $\approx -30|e|$) trimeric protein channel (Fig. 1) found in the outer membrane of the *E. coli* bacterium. It has an unusually stable arrangement that maintains its structural integrity well beyond the normal physiological range of salt concentrations, temperatures, and applied voltages. High-resolution molecular structures for *ompF* and several of its mutants are well-known from X-ray crystallography. About halfway along each pore the channel has a narrow and highly charged constriction region. Mutation studies and DD simulations both indicate that the charge distribution in the constriction region plays an important role in the conductance properties of the channel. We use the BioMOCA simulator to further this line of enquiry using a detailed map for the permanent charge distribution to investigate the conduction properties of *ompF* (Fig. 2).

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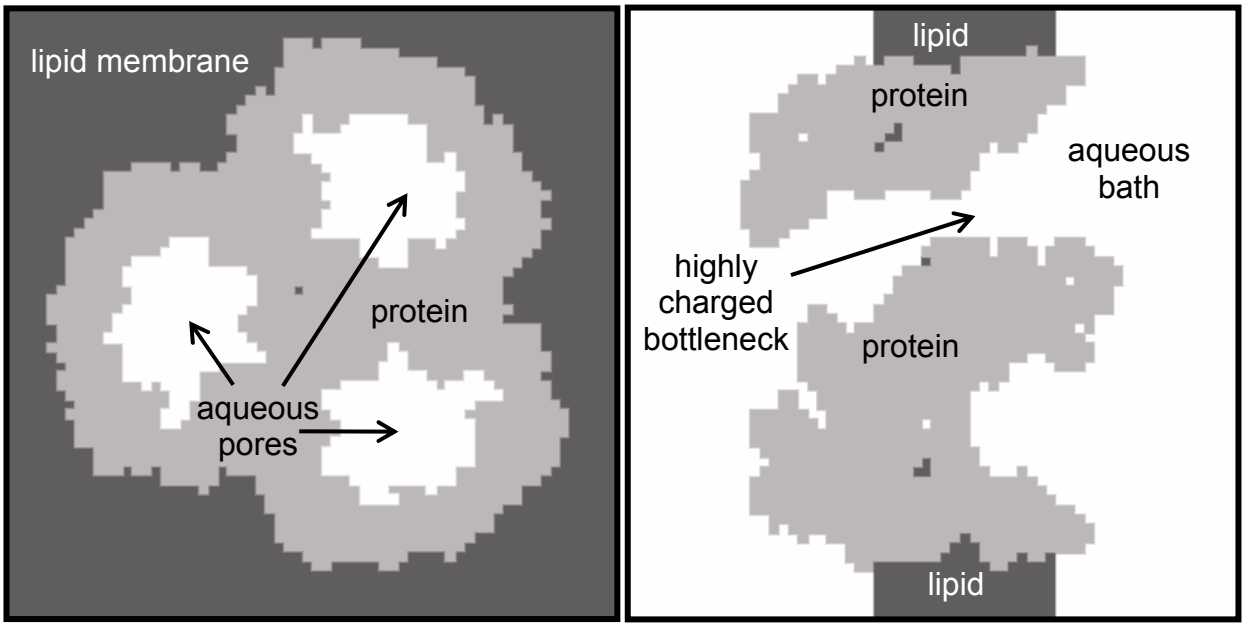

Figure 1. (a) Frontal view of the simulation domain for the *ompF* porin channel showing the trimeric structure with three separate pores. (b) Longitudinal slice through one monomer showing the hourglass shape of each pore.

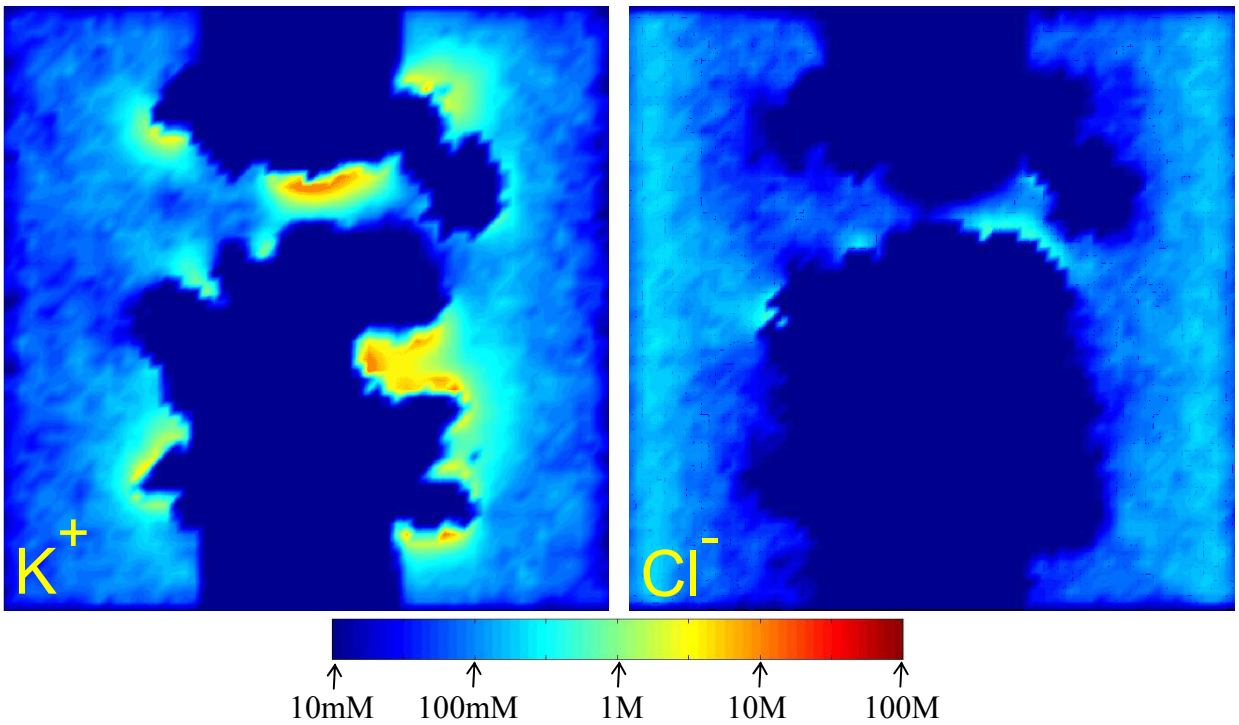

Figure 2. K^+ and Cl^- ion densities in the *ompF* porin channel, on a 2-D slice through the 3-D domain, averaged over 100 ns of BioMOCA simulation under 200mV bias. Negative fixed charges on the pore, particularly in the constriction region attract a very high density of K^+ ions.

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