Simulation of conductance of voltage-gated ion channels and solid-state nanopores

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Ion channels are pore-forming proteins that regulate the flow of ions across the membrane in biological cells, whereas nanopores are nanometer-scale pores in an electrically insulating membrane. Both structures can be used as single-molecule detectors, based on monitoring the ionic current of an electrolyte solution passing through the nanopore, with the passage of molecules causing measurable variations of the ionic current level [1, 2]. Given the biological importance of this process, realistic studies of ionic currents in these structures present a major challenge for simulation approaches.

We perform Brownian dynamics simulations to study ionic currents flowing across a model nanopore under various conditions. According to Langevin's equation, the ions move under two different forces: a random force due to collisions with surrounding water molecules and an electrostatic force due other ions, the external electric field, fixed charges in the channel and the image charges induced at the water-protein boundary. The image charges play a significant role in the electrostatic potential in narrow channels; we calculate their contribution using the method introduced by Levitt [3].

Simulations performed in a simplified model channel with a cylindrical transmembrane segment joined to a catenary vestibule at each side gave satisfactory results, see Fig. 1. Simulations of ion flow through various kinds of synthetic nanopores are underway to determine their conductance under various conditions, which can be compared directly with experimental data. With these simulations we can investigate how parameters like temperature, applied voltage, and nanopore shape affect the translocation dynamics or we can study the ion current rectification mechanism in particular kinds of nanopores [4]. Moreover, simulations of voltage-gated biological channels, such KcsA and alpha hemolysin, are also considered, with channel shapes deduced from crystallography.

Our simulations let us study the mechanism of ion selectivity at atomic level, examine how a variety of cationic channels discriminate between ions of differing charge and investigate more complex conductance properties of ion channels as a consequence of electrostatic interactions.

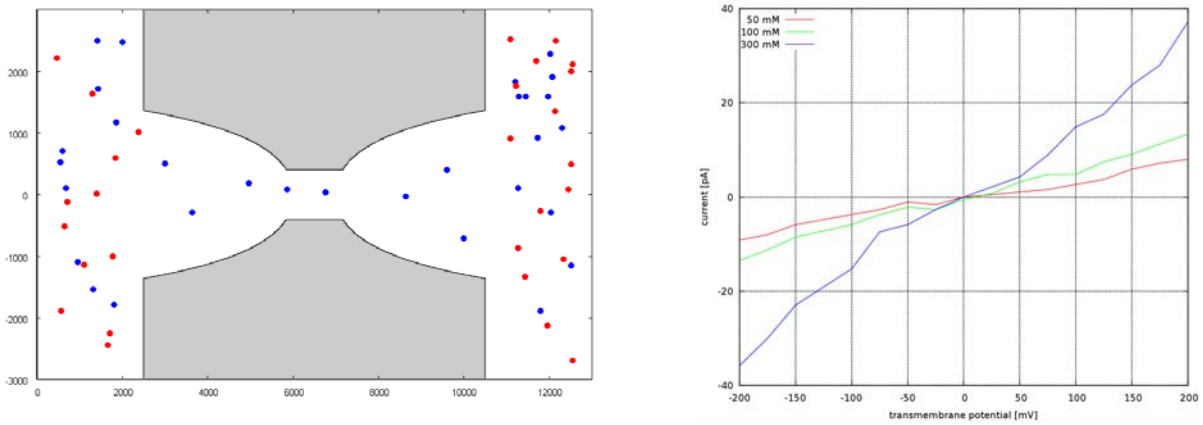

FIG. 1. (a) Simulated section of the catenary channel, with blue and red dots representing cations and anions; (b) catenary channel currents for differing ionic concentrations and transmembrane potentials.

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