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Brownian Dynamics Simulation of Calcium Channels

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Calcium-selective ion channels play a crucial role in many biological functions allowing the selective flux of calcium ions into the cytoplasm from storage sites inside the cell or from the extracellular environment. They feature high selectivity for calcium ions even if the calcium concentration is hundreds of times smaller than other monovalent cations (sodium, potassium).

We studied ion permeation properties through calcium channels, using a simplified channel model and Brownian Dynamics simulations with Grand Canonical-Monte Carlo control regions in the baths.

The physical mechanisms related to ion permeation were investigated under physiological conditions, with calcium ions only on one side of the membrane.

The Brownian Dynamics approach was used to describe ion motion in the simulation domain. The electrostatic forces impinging on the ions were evaluated at run-time, solving Poisson's equation with the Induced Charge Computation method (ICC) that provided better accuracy in our hands than look-up tables. Different dielectric constants were assigned to the protein and the permeation pathway. Polarization effects were computed by the ICC method, which leads to an accurate description of the electrostatics. The transmembrane potential and the ion concentrations were imposed by a Grand Canonical Monte-Carlo algorithm.

The carboxylate-rich selectivity filter of calcium channels was modeled with 8 independent half-charged oxygens. Oxygens were treated as ions, but they were confined in the central region of the pore. Transport properties were determined by the competition between

electrostatic forces and steric repulsion due to charge crowding. This simple channel model allowed us to investigate the physical mechanisms responsible for the selective conduction of divalent cations over monovalent cations.

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