Permeation in Gramicidin Ion Channels by Directly Estimating the Potential of Mean Force Using Brownian Dynamics Simulations

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ABSTRACT We present a method for estimating the 'best-fit' potential of mean force encountered by an ion permeating across the gramicidin-A ion channel. The proposed method does not require explicit use of a dielectric constant and can be applied to other ion channels. The potential of mean force is parameterized and its parameters are estimated using a stochastic optimization algorithm that control Brownian dynamics simulations. A loss function measuring the differences between currents simulated using Brownian dynamics and currents observed at various applied potentials and ionic concentrations is calculated to compare between possible candidate parameters of the potential of mean force. The results obtained indicate that several possible potentials of mean force with barrier-heights and well-depths in the vicinity of $6\ kT$ and $4.5\ kT$ provide optimal fits to the observed currents. Using both "brute-force" search and stochastic optimization, a sensitivity analysis is conducted to show the effect of potential of mean force (PMF) parameter variations on the simulated currents fit to the observables. We illustrate the methods using the gramicidin channel as a test case and show that the results closely match the profiles of potential of mean force reported in the literature.

Keywords: Adaptive control; Brownian dynamics; stochastic optimization; stochastic search algorithms; gramicidin channels; ion permeation; potential of mean force

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