Conductance of Ion Channels – Theory vs. Experiment

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Transmembrane ion channels mediate a number of essential physiological processes in a cell ranging from regulating osmotic pressure to transmission of neural signals. Kinetics and selectivity of ion transport is of critical importance to a cell and, not surprisingly, it is a subject of numerous experimental and theoretical studies. In this presentation we will analyze in detail computer simulations of two simple channels from fungi – antiamoebin and trichotoxin. Each of these channels is made of an α-helical bundle of small, non-genomically synthesized peptides containing a number of rare amino acids and exhibits strong antimicrobial activity.

We will focus on calculating ionic conductance defined as the ratio of ionic current through the channel to applied voltage. From molecular dynamics simulations, conductance can be calculated in at least two ways, each involving different approximations. Specifically, the current, given as the number of charges transferred through the channel per unit of time, can be obtained from the number of events in which ions cross the channel during the simulation. This method works well for large currents (high conductance values and/or applied voltages). If the number of crossing events is small, reliable estimates of current are difficult to achieve. Alternatively, conductance can be estimated assuming that ion transport can be well approximated as diffusion in the external potential given by the free energy profile. Then, the current can be calculated by solving the one-dimensional diffusion equation in this external potential and applied voltage (the generalized Nernst-Planck equation). To do so three ingredients are needed: the free energy profile, the position-dependent diffusion coefficient and the diffusive flux of ions into the channel. All these quantities can be obtained from molecular dynamics simulations. An important advantage of this method is that it can be used equally well to estimating large and small currents. In addition, once the free energy profile becomes available the full current-voltage dependence can be readily obtained.

For both channels we carried out calculations using both approaches. We also tested the main assumptions underlying the diffusive model, such as uncorrelated nature of individual crossing events and Fickian diffusion. The accuracy and consistency of different methods will be discussed. Finally we will discuss how comparisons between calculated and measured ionic conductance and selectivity of transport can be used for determining structural models of the channels.