Ionic Selectivity in Channels: complex biology created by the balance of simple physical forces

Bob Eisenberg (Rush University Chicago, USA)

An important class of biological molecules – proteins called ionic channels – conduct ions (like Na^+, K^+, Ca^{2+}, and Cl^-) through a narrow tunnel of fixed charge ('doping'). Ionic channels control the movement of electric charge and current across biological membranes and so play a role in biology as significant as the role of transistors in computers: a substantial fraction of all drugs used by physicians act on channels. Channels can be studied in the tradition of physical science because the ions near and in channels form an ionic plasma in both the biological and physical meaning of the word. Poisson-Drift diffusion equations familiar in physics (called the PNP or Poisson Nernst Planck equations in biophysics) can be extended to describe 'chemical' phenomena like selectivity with some success by including correlations produced by the finite size of the ions. Complex phenomena of selectivity in this reduced model come from the balance of simple attractive (mostly electrostatic) and repulsive (mostly excluded volume) forces. Preformed binding sites and chemical bonds like cation-π interactions play no role in these models. Two parameters (volume and dielectric coefficient) set to invariant values are enough to describe the complex selectivity of DEEA (asp glu glu ala) calcium channels in a wide range of solutions. The same model and identical parameter values describe the very different properties of the DEKA (asp glu lys ala) sodium channel, including selectivity for Na^+ vs. K^+ in a wide variety of solutions. In these reduced models, the structure of 'side chains' is an output of the model, different in different ionic conditions. Binding sites are variable and not preformed. We are unaware of other models – structural, crystallographic, or computational – that deal successfully with measurements of complex selectivity phenomena over a range of concentrations, mutations and channel types.