Ions in Channels

Bob Eisenberg

Dept of Molecular Biophysics, Rush Univ Medical Center, Chicago, IL 60612, USA, E–mail: beisenbe@rush.edu

Channels are proteins with a hole down their middle that control a wide range of biological function because they control the flow of ions and thus electric charge in and out of cells: channels produce the electrical properties of the nervous system; they control the heart beat and muscle contraction; channels control secretion of hormones and urine. A substantial fraction of drugs act on channels. Thousands of biologists study channels every day, recording current voltage (IV) relations from single molecules in a variety of solutions and concentrations. The genetic code and amino acid sequence for hundreds of channels are known, and new three-dimensional structures are reported every few months. Ion channels are appealing objects for physical investigation because conformation changes are not involved in channel function, once the channel is open. Ions move in a structure that does not vary even by $0.1\AA$ on the biological time scale of 10^{-5} sec. Open channels are appealing objects for chemical study because they effectively select among chemically similar ions, under unfavorable circumstances. Channels are appealing objects for physical study because they contain an enormous density of charge, fixed, mobile, and induced. Channels are lined with a large density of induced and fixed charge, say 4 charges in a length of $20\AA$, diameter of $5\AA$, with a nearby ionic atmosphere of 10**M** concentration. Direct simulation of channel behavior is difficult if not impossible, because ion transit takes 10 nsec; concentrations of μM must be accurately represented, and macroscopic electric fields and concentration gradients produce substantial flows, making equilibrium analysis unhelpful. Lower resolution theories are surprisingly successful in describing selectivity and IV relations: mean field treatments do quite well if they include electric field, crowded charge, and induced charge, although the proper treatment of correlated motions is a challenge. The future seems to require simulations to evaluate parameters and establish bounds of validity for lower resolution theories. Simulations are more helpful if they are calibrated in standard situations and thereby shown to deal reliably with crowded charge, electrostatic fields, and induced charge away from equilibrium.