Non-equilibrium properties from equilibrium free energy calculations

Andrew Pohorille and Michael Wilson
NASA-Ames Research Center
and
Department of Pharmaceutical Chemistry
University of California, San Francisco

Calculating free energy in computer simulations is of central importance in statistical mechanics of condensed media and its applications to chemistry and biology not only because it is the most comprehensive and informative quantity that characterizes the equilibrium state, but also because it often provides an efficient route to access dynamic and kinetic properties of a system.

Most of applications of equilibrium free energy calculations to non-equilibrium processes rely on a description in which a molecule or an ion diffuses in the potential of mean force. In general case this description is a simplification, but it might be satisfactorily accurate in many instances of practical interest. This hypothesis has been tested in the example of the electrodiffusion equation. Conductance of model ion channels has been calculated directly through counting the number of ion crossing events observed during long molecular dynamics simulations and has been compared with the conductance obtained from solving the generalized Nernst-Plank equation. It has been shown that under relatively modest conditions the agreement between these two approaches is excellent, thus demonstrating the assumptions underlying the diffusion equation are fulfilled. Under these conditions the electrodiffusion equation provides an efficient approach to calculating the full voltage-current dependence routinely measured in electrophysiological experiments.