Variational Analysis of Ionic Systems: Biology and Electrochemistry

Bob Eisenberg
Mathematics and Computer Science Division, Argonne National Laboratory, IL
Department of Molecular Biophysics, Rush University & Medical Center, Chicago, IL

Biological systems contain interacting components on a range of scales from atoms (Ångstroms) to proteins (nm), to cells (µm), to tissues (mm) that function on the msec time scale. A handful of atoms often control vital functions, so it is natural to try to exploit the burgeoning capabilities of computational science to directly compute macroscopic properties from molecular dynamics. However, the gap between molecules and biology are all ~10^{10} in volume, time, and concentrations. All gaps must be dealt with at once so direct simulation is not easy. A multiscale analysis of interacting components is needed in biological, as in engineering applications.

The variational principles of mechanics provide a selfconsistent framework for studying interactions in conservative systems, but biological systems are not conservative. Biology occurs in mixtures of ions in water, and nothing can move in these systems without friction and dissipation.

Recently, the mathematician Chun Liu, building on the work of many others, has constructed a variational method that derives the full Navier Stokes equations from an energy principle: it combines dissipation (of Rayleigh/Onsager) with Hamiltonôs action. Existence and uniqueness are proven.

The variational method is well suited to problems involving ions. All ions interact with each other through the electric field. Ions, unlike holes and electrons of semiconductors, have finite diameter and interact through steric forces. Steric interactions are dramatic in proteins, ion selective membranes, or close to electrodes. Most biological and electrochemical function occurs where number densities and steric interactions of ions are very large, approaching that of solid NaCl. óEverythingô interacts with everything else in these systems. **It is important to use mathematics that deals naturally with interactions instead of an idealization that assumes no interactions.** Sadly, classical analysis in biology uses the ólawô of mass action that assumes no interactions and no flow. Classical analysis in electrochemistry deals cavalierly with flow and interactions. Biology without flow is usually death. We use Chun Liuôs variational approach that analyzes flow and interactions with well-defined mathematics.

The Energy Variational Principle *EnVarA* has been applied to ions in solutions and proteins as they control a wide range of biological function. Channel proteins control flow of ions across otherwise insulating membranes. They have a role in biology similar to transistors in computers. ***EnVarA* allows realistic treatment of ions interacting in solutions**, including finite diameter and flow by migration, diffusion, and bulk transport and electrical interactions across scales.

Variational analysis of ionic solutions yields partial differential equations for ions of finite diameter (Journal of Chemical Physics (2010) 133, 104104) coupled to the (global) Poisson equation.

$$\frac{\partial c_n}{\partial t} = \nabla \cdot \left[D_n \left\{ \nabla c_n + \frac{c_n}{k_B T} \left(z_n e \nabla \phi - \text{ Steric Repulsion (Lennard Jones) Terms} \right\} \right] \right.$$

These equations have been integrated in bulk solutions to describe interactions of ions in flowing systems used in desalination and detoxification. These equations have been integrated for ions in protein channels as ions flow and control electrical signals of nerves and heart. These equations have been integrated for ions and water in cells of changing volume, as in kidney, blood vessels, and intestine. Related equations are solved for viruses and cell organelles as they change shape and make pores.

The variational method has a particular advantage in biological models of complex multiscale systems. **Components are added self-consistently, so that complexity can be built up step by step**, component by component, maintaining consistency with simpler models and their successes.

The variational method *EnVarA* provides a well-defined computational framework for the complex systems of biology and engineering that involve many components at different scales.