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Simulating Biological Ion Channels using Computational Electronics Methods

Karl Hess
Beckman Institute, University of Illinois, Urbana, Il 61801
e-mail: k-hess@uiuc.edu

In this presentation a review is given covering recent developments in the simulation of biological ion channels. Biological ion channels perform important functions ranging from the destruction of cancer cells to electrically enabling heart beat. Correspondingly a detailed understanding of ion channel function is desirable and the only way for this detailed understanding is offered by numerical simulation using a multi-scale simulation tool, for the processes that need to be understood range from the molecular dimensions of the constituting proteins to the macroscopic ion concentrations and membrane potentials. A multi-scale approach, as it is available for semiconductor devices in TCAD has not existed for ion channels in the past and is only now being developed in analogy to the TCAD tools. Ion channels have been treated in the past mainly by Molecular Dynamics as pioneered by K. Schulten and coworkers, a method very demanding with respect to computational resources. Alternatively the so called PNP method has been used that corresponds in essence to the drift diffusion approach (plus equation of Poisson) of semiconductor theory. In-between methods such as Brownian Dynamics have been applied by Jakobsson, Roux and others. Monte Carlo solutions of the Boltzmann transport equation have recently been developed by Ravaioli and his group.

The case that the methods of computational electronics may be used for ion channel simulation was mainly made by R. Eisenberg and is based on the fact that the ion transport properties in channels should be describable by the Boltzman transport equation for a variety of reasons, including: (i) The large ion mass and corresponding small de Broglie wavelength around room temperature and (ii) the dilute ion concentrations and small ion numbers that are at any instance in a channel which permits one to think of an ion “gas”. Counterarguments to the use of the Boltzmann transport equation center on the fact that chemical forces lead sometimes to ion localization and hopping and, more importantly on the fact that the ions are mostly surrounded by water molecules. While treatments of ions in bulk water has been well researched and is largely understood, the case of a few water and ion molecules in narrow channels is not; except, of course, for the results of molecular dynamics methods that typically require large computational resources.

I will show in my review that the localization of ions in channels can be treated by the semiconductor methods developed by Shockley, Read and Hall. This method had not been applied by bio-physics researchers of ion channels and has been shown to expand the PNP method significantly for channels such as Gramicidin. Furthermore it will be shown that the Monte Carlo method as used in semiconductor electronics can be extended to include important ion properties such as their finite size and that this method may serve as a link between continuum methods and molecular dynamics. It will also be discussed that the question of how to treat water is still open and that interesting possibilities exist. On the molecular level a few examples will be given how other methods such as density functional theory are advantageously being used to understand natural and also certain artificial channels such as carbon nanotubes and how the knowledge of both types of channels currently expands through simulation.

In summary, this presentation will show the fruitfulness of an interdisciplinary approach to develop new simulation tools and to modify known tools from different research areas to achieve a more extensive and precise multi-scale simulation tool. A few insights will also be given on the interdisciplinary difficulties and the barriers that exist when such a broad subject is approached.

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