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Simulation study of the transport properties of ions through ion channels serving as primary components of a nanobiosensor

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ABSTRACT

Ion channels are naturally occurring pores through the proteins that regulate the passage of ions and thus maintain the concentration of ions inside and outside the cell. The ion channels control many physiological functions and they can show selectivity for a specific ion. Ion channels are mostly observed in nerve cells and muscle cells. The influx of ions into cells can be regulated by a gate, like voltage controlled gate. Here we have investigated the ion transport through an ion channel by Poisson-Nernst-Plank model. In this model, proteins are approximated as cylindrical tubes embedded in a lipid membrane. Different ion channels with different channel radii are taken into consideration. The electrostatic potential, ion concentrations, ion flux and ion current are found. Simulation of ion channel is of vital importance in preparing biosensor where the molecular switching mechanism of ion-channel can regulate the flow of a particular ion in an analyte, if detected. The ion channels show voltage-current relationship similar to that of diodes and transistors. A major challenge in nanomedicine is the quick detection of antigens causing a disease and thus the finding of a novel commercial technique (better than ELISA) is essential. Towards this aim, a nanobiosensor can be devised where an ion-channel may serve as its primary component.

Keywords: *Ion channel, Poisson-Nernst-Plank model, simulation, transport properties, biosensor.*

INTRODUCTION

Ions can be transported inside our body through cell membranes or ion-channels [1] which may be selective for a specific ion. The function of the cells depends on the functioning of ion-channels as they balance the concentration of the electrolytes inside and outside the cells.

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The channel proteins are surrounded by lipid membrane which separates its internal medium from the external medium and the passage of ions through the ion channel is regulated by the potential difference across the membrane, called membrane potential. Ionic currents perpendicular to the membrane is opposed by a longitudinal current which closes the channel pore after a certain interval. It appears due to the difference of concentration of the ions inside and outside of the membrane. The main exploration of the ion propagation as a result of action potential was possible by the studies of Hodgkin and Huxley [2-5] with the squid giant axon. Besides these experiments and some other experimental techniques [6-8] that revealed the transport mechanism and channel structure, latest development on mathematical models and simulation is observed which relate the molecular structure of channel components to the physiological properties of ion channels. In 1998, Molecular Dynamics (MD) simulation was performed by Zhong et al. [9] for a synthetic ion channel consisting of four α-helical peptides. Millar et al. [10] developed a self consistent particle simulation of ion-channels using Poisson and Langevin equations which described the simulation of ion behavior in extremely small pores. An algorithm was developed combining kinetic lattice grand canonical Monte Carlo simulations and mean field theory by Hwang et al. [11]. The molecular switching mechanism of ion-channels can be exploited in the construction of novel biosensors [12, 13].

To study the nature of transport of ions in a sodium or potassium ion channel, we have used the software [14-15] developed on Poisson-Nernst-Planck (PNP) model. The transport properties of ion-channels are similar to that of semiconductors for which PNP equations is proved to be successful simulation model.

MATHEMATICAL MODEL

PNP model approximates proteins as cylindrical tubes embedded in a lipid membrane [14]. Finite difference method is used to solve PNP equations simultaneously and self-consistently. The ions, lipids, protein and water molecules are all described as dielectric continuums. Complex boundary conditions are applied to model an ion-channel and an alpha helical protein structure Figure 1 is simulated.

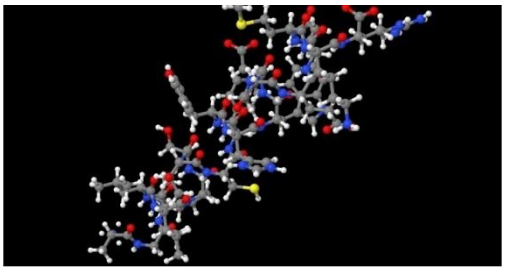

Fig. 1. α-helical peptide structure

RESULTS AND DISCUSSION

First of all, simulation is performed for a peptide channel of radius 3.5 Å using PNP cyclic ion-channel simulator. In PNP theory proteins, membranes, ions and water molecules are considered as continuum dielectric materials and the structure of proteins and lipids are not taken into consideration. As there exits a concentration gradient across the lipid membrane, sometimes the ions can pass through the channel which is generally impossible through the lipid bilayer. The thermal motion of the ions changes their probability of crossing the pore. Once the channel is opened, it allows the ions to flow through it until the potential difference across the membrane balances the flow of ions in the upward and downward direction. This equilibrium potential is called Nernst potential.

The channel is sensitive to Na^+ and Cl^- ions where diffusion coefficients of Na^+ and Cl^- ions in bulk water and in the channel are $2x\ 10^{-5}$ m^2/s and $1x\ 10^{-5}$ m^2/s respectively. Obviously the diffusion coefficients inside the channel are lesser than that of the coefficients outside the channel. For this narrow channel, cation and anion current are obtained as 0.000453845 pA and 5.56853 pA respectively. Three more simulations have been performed with 4 Å, 4.5 Å and 5 Å channel radii.
Cation and anion current are found as-
Channel radius=4 Å
Cation current=0.00124441 pA
Anion current= $1.0661\ e^{-05}$ pA
Channel radius=4.5 Å
Cation current=0.00160074 pA
Anion current= $2.36111\ e^{-05}$ pA

Channel radius=5 Å
Cation current=0.00151038 pA
Anion current= 3.12194 e^{-05} pA
The potential profiles and anion concentrations for different channel radii are shown in Figure 2 and Figure 3.

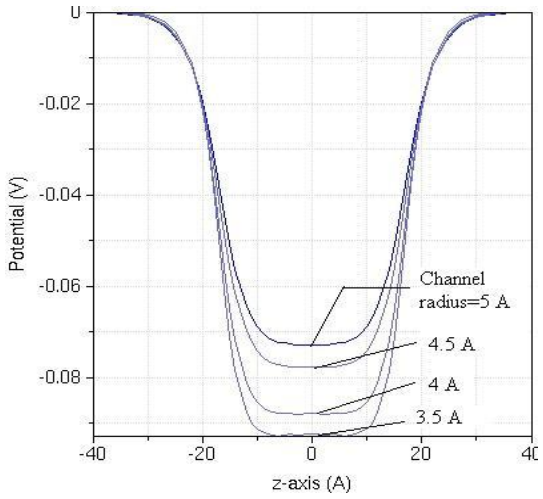

Fig. 2. Variation of potential along z-axis for different channel radii

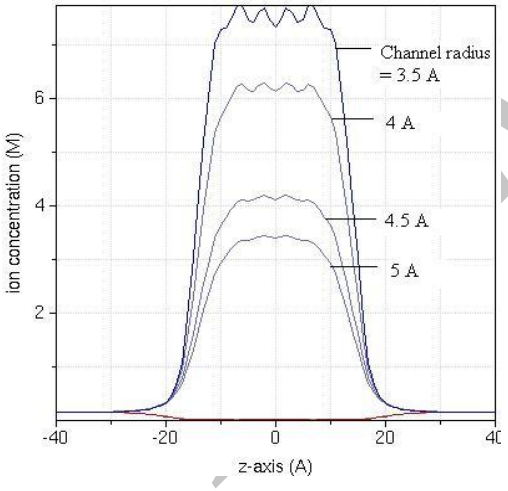

Fig. 3. Variation of anion concentration along z-axis for different channel radii

The radii of Na^+ and Cl^- ions are 102 pm and 181 pm respectively. So, with the increase of channel radii the anion current increases with negligible change in cation current. The ions cross the channel in such a way that when positive ion crosses the channel, the negative ions face a potential barrier. The charge separation across the lipid membrane will build up a potential. The potential increases until a balanced condition is reached. This potential is called the membrane potential and it depends on the concentration of all the permeable ions present there.

However, due to the unpredictability of the opening and closing of the channel, it cannot be definitely said when the channel is really close. It depends on the thermal motion of the protein molecules that decide the fact. The membrane potential changes the probability of opening or closing of the channel. These channels are known as voltage-controlled channels. Such channels (Na and K) are mostly present in neurons. For K^+ and Cl^- ions the voltage current relationship and potential are given in Figure 4 and Figure 5.

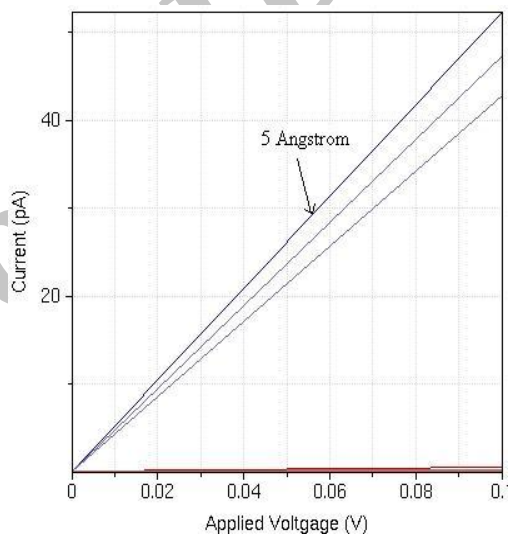

Fig. 4. Voltage-current relationship for different channel radii

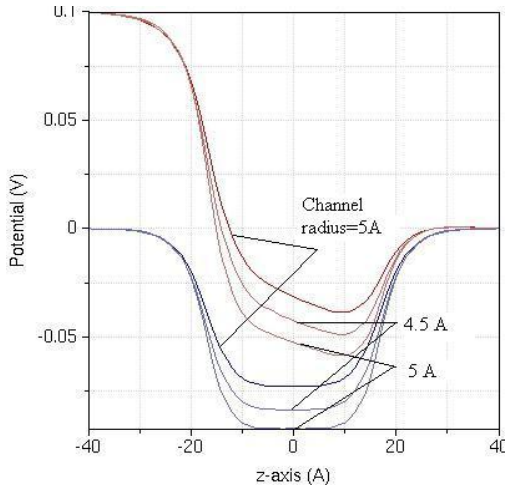

Fig. 5. Variation of potential along z- axis

CONCLUSION

The importance of ion channels in sending fast electronic signals in the nervous system is the motivation behind the considerable research progress in the field of biology and biophysics. Also detection of different biomolecules is of vital importance in the field of nanomedicine. We can regulate the flow of a particular ion through an artificial ion channel which is detected by a biosensor. Thus we can device a novel nano device to regulate the flow of ions to different cells of our body, especially to the nervous system.

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