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Full Length Research Paper

Nanomolecular simulation of the voltage–gated potassium channel protein by gyration radius study

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Molecular dynamics simulations may be used to probe the interactions of membrane proteins with lipids and with detergents at atomic resolution. Examples of such simulations for ion channels and for bacterial outer membrane have already been studied. The molecular potassium channel function is universally conserved. Potassium channels allow potassium flux and are essential for the generation of electric current across excitable membranes. Potassium channels are also the targets of various intracellular control mechanisms, such that the suboptimal regulation of channel function might be related to pathological conditions. Realistic studies of ion current in biologic channels, present a major challenge for computer simulation approaches. In this work, to characterize protein behavior, we observed quantities such as gyration radius and energy average. We studied the changes of these factors for voltage – gated potassium channel protein in gas phase with native conformation by Monte Carlo, Molecular and Langevin Dynamics simulations. Monte Carlo simulation is a stochastic method and therefore, is the best method to evaluate the radius of gyration. When the temperature is increased the kinetic energy is increased too and its correlation is linear. All the calculations were carried out By Hyperchem 8.0 program. The determination of gyration radius is spectacular for configuration of a macromolecule. It also reflects molecular compactness shape. The radius of gyration is calculated by VMD 1.8.7 software.

Key words: Monte Carlo simulation, molecular dynamics simulation, Langevin dynamics simulation, protein folding, gyration radius.

INTRODUCTION

Nature provides us with a very large number of channels or nanopores embedded in cell membranes. The function of channels is to allow selectivity and specificity for a variety of molecular species, transport across the cell membrane (Kaczmarek and Perney, 1991; Doyle and Morais, 1998; Heginbothom, 1999; Hille et al., 1999). These channels, included (a) ligand-gated channels, b) voltage-gated channels, c) second messenger gated channels, d) mechanosensitive channels, e) Gap jucnctions: porins not gated (Mackinnon, 1991; Hille, 2001).

The first step in understanding the physical mechanism of potassium transport through this protein nanopore is the determination of the molecular distribution of water along the axial length of the pore ion channels, which are membrane proteins that mediate flux between the outside of the cell, through a small, water-filled hole in the membrane-a pore. Ion- selective pores were originally proposed to explain separate components of Na^+, K^+ and leak currents in the classic experiments of Hodgkin and Huxley (Chone, 2002).

Potassium channels are the most diverse group, of the ion channel family (Kaczmarek and Perney, 1991). The recent determination of the crystallographic structure of a bacterial K^+ channel, from *Streptomyces lividans* (KcsA) (Doyle and Morais, 1998), has provided the molecular basis for understanding the physical mechanisms controlling ionic selectivity, permeation and transport through various types of K^+ channels (Heginbothom, 1999; Hille et al., 1999).

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In all cases, the functional K^+ channel is a tetramer (Mackinnon, 1991), typically of four identical subunits, folded around a central port (Heginbothom, 1999). Voltage–gated potassium (Kv) channels are members of the voltage–gated ion channel superfamily (Kaczmarek and Perney, 1991; Doyle and Morais, 1998) which is important for initation and propagation of action potentials in excitable cells. They are composed of four identical or homologous subunits, each containing six transmembrane segments, S1 to S6. Segments, S1 to S4, form the voltage- sensing domain (VSD) and segments S5 and S6 connected by the P loop, which is involved in ion selectivity, comprise the pore- forming domain (PD), S4 has four gating–charge carrying arginines (R1 to R4) spaced at intervals of three amino acid residues, which are highly conserved and are thought to play a key role in coupling changes in membrane voltage, to opening and closing of the pore (Heginbothom, 1999; Hille et al., 1999; Mackinnon, 1991).

In the Kv channels 13 electronic charges across the membrane electrical field per channel between the closed and open states (Hille, 2001; Chone, 2002; Yu and Catterall, 2004). Arginine residues interacting with lipid phosphate groups play an important role in stabilizing the voltage-sensor domain of the KvAP channel within a bilayer. Simulations of the bacterial potassium channel kcsA, reveal specific interactions of phosphatidylglycerol with an acidic lipid-binding site on the interface between adjacent protein monomers.

All currently studied VGC (the voltage- gated Ion channel) family channels assemble in the membrane to form functional tetramers. For sodium and calcium channels, the tetrameric organization arises from the folding in the membrane of the α - subunit, a single polypeptide with four internal hydrophobic repeats. For voltage- gated potassium channels, four individual α – subunit, a single polypeptide with four internal hydrophobic repeats. For voltage–gated potassium channels, four individual – subunit monomers associate in the membrane.

MD (molecular dynamics) simulations of membrane proteins provide a valuable complement to experimental studies. Earlier simulations provided only limited information on membrane-lipid interactions as simulation times were rather short. However, current simulation times are in the order of 10 to 100 ns and so enable more reliable analysis of lipid-protein and detergent-protein interactions; a number of experiments implicate acidic head groups of phospholipids in the structural integrity and function of the bacterial potassium channel KcsA. The electron density in the crystal structure of KcsA reveals a lipid-binding site but only a fragment of a lipid molecule is present in the co-ordinates.

Significantly, the presence of negatively charged lipids is required for ion conduction through the kcsA potassium channel, suggesting that binding of lipid to kcsA is important for channel function. Spectroscopic studies also support a specific acidic lipid binding site at the interface between two monomers in the tetrameric channel structure.

Several methods are available for computional studies of protein-ligand interactions, ranging from the simplest docking methods (Doyle and Morais, 1998; Heginbothom, 1999) to Langevin dynamics (LD) and the more sophisticated molecular dynamics (MD) simulations (Mackinnon, 1991; Hille, 2001; Chone, 2002). The aim of the docking methods is to predict the binding configurations and energies of a large number of ligands, for a given receptor with minimal computional effort. This makes them very fast but also limits their accuracy (Yu and Catterall, 2004). An accurate and detailed description of the binding/ unbinding processes requires explicit representation of water molecules, which is possible only in MD simulations. The primary approach used to simulate the dynamic behavior of lipid systems is the molecular dynamics (MD) simulation technique, in which Newton's equations of motion are integrated numerically for a set of interacting particles, to generate the time evolution of the system.

Knowledge of the protein folding mechanism will result in a huge advance in general bioscience, especially in the fields of drug design and pharmaceutical chemistry .for example, Alzheimer's disease and Prion disease, have been found to be caused by miss folding of proteins (Armstrong and Brezanilla, 1974; Onuchic et al., 1997). Gyration radius and end to end distance, predict the dimensions of a macromolecule by statistical mechanics science. The characterization of the protein folding process represents one of the major challenges in protein chemistry. Large theoretical and experimental research efforts have been devoted to this end (Armstrong and Brezanilla, 1974).

Molecular and Langevin dynamics simulation, as well as Monte Carlo simulation have been used to investigate protein folding pathways with some success. The metropolis Monte Carlo was originally developed for calculating equilibrium properties of physical systems (Prusine, 1997; Liu et al., 2001; Lee, 2004; Metropolis et al., 1953). The metropolis algorithm performs a sample of the configuration space of system, starting from a random conformation and repeating a large number of steps. Molecular dynamics simulation, is one of the most promising approaches for solving the protein folding problem .In this method, we observe the time behavior of atoms of the system, in MD simulation, new positions of atoms are calculated by numerical integration of Newton's equation of motion (Chan and Dill, 1994; Kolinski and Skolnick, 2004; Hyperchem, 2007; Humphrey et al., 1996).

When studying proteins, it is important to know how much space a strand takes up at various times. The radius of gyration is one way of parametrizing the "size" of a chain. It is a scalar quantity with units of length, defined as:

$$R = \sqrt{\frac{1}{N}\sum_{i=1}^{N}(\vec{r}_i - \vec{r}_{CM})^2}$$

where i *r* is the vector to each bead and CM *r* is the center mass of the bead. Plotting the radius of gyration for different configurations versus the time interval of the snap shots taken, will show you how the radius of gyration changes over time. The maximum radius of gyration is when the chain is in a perfectly straight line, in which case it can be shown that:

$$R_{max} = L/2\sqrt{3}$$

where L is the length of the chain. It may be interesting to determine the radius of gyration as a fraction of this maximum value and plot this versus time.

METHODS

With an efficient way of evaluating the free energy surface of the system, we can turn to the calculation of its time evolution. As stated in the introduction, it is impractical to use direct MD simulations, as a general way for evaluating ion current in ion channels.

However, the related Langevin dynamics (LD) and Monte Carlo (MC) simulations can be used effectively with our Semi-macroscopic free energies.

For this work a small protein (PDB cod; 1ho2) consisting of only 20 amino acid residues was selected. By using the VMD software, we opened this file and by Ramachandran plot, determined torsion angles for every amino acid and then in Hyperchem 8.0 program, designed this protein with these angles (Hyperchem, 2007). Then we optimized voltage gated potassium channel protein by Monte Carlo simulation with amber force field, at 300 k to 400 k and by using VMD software, gyration radius was determined (Humphrey et al., 1996). It is essential to say that, Hyperchem uses the Metropolis method. By Monte Carlo simulations kinetic, potential and total energy were calculated. Then, by Molecular and Langevin dynamics simulation, we optimized protein with MM^+ force field, in 300 k to 400 k and after optimizing, determined gyration radius. The present work is limited to simulations of ion flow under gas and water phase conditions that maintain a constant concentration gradient.

RESULTS AND DISCUSSION

An alternative replaces the discrete water molecules by "virtual water"- an infinite continuum medium with some of the dielectric and "hydrophobic" properties of water. These continuum implicit solvent models, have several advantages over the explicit water representation, especially in molecular dynamics simulations. Implicit solvents are often less expensive and generally scale better on parallel machines. There is no need for the lengthy equilibration of water that is typically necessary in explicit water simulations; implicit solvent models correspond to instantaneous solvent dielectric response. Continuum simulations generally give improved sampling, due to the absence of viscosity associated with the explicit water environment; hence, the macromolecule can more quickly explore the available conformational space.

There are no artifacts of periodic boundary conditions. The continuum model corresponds to solvation in an infinite volume of solvent. New and simpler ways to estimate free energies become feasible, because solvent degree of freedom are taken into account implicitly, estimating free energies of solvent structures is much more straight forward than with explicit water models.

Implicit models provide a higher degree of algorithm flexibility. For instance, a Monte Carlo move, involving a solvent exposed side chain would require nontrivial rearrangement of the nearby water molecules, if they were treated explicitly with an implicit solvent model thus complication does not arise. Of course, all of these attractive features of the implicit solvent methodology, come at a price at whose effects are often hard, If not impossible, to estimate. Some familiar descriptors of molecular interaction, such as solute-solvent hydrogen bonds, are no longer explicitly present in the model; instead, they come in implicitly, in the mean-field way via a linear dielectric response and contribute to the overall solvation energy. However, despite the fact that the methodology presents an approximation at fundamental level, it has in many cases been successful in calculating various macromolecular properties (Valiyaveetil et al., 2002; Alvis et al., 2003; Armstrong and Hille, 1998).

In many molecular modeling applications and in molecular dynamics (MD), the key quantity that needs to be computed, is the total energy of the molecule in the presence of solvent. This energy is a function of molecular configuration; its gradients with respect to atomic positions determine the forces on the atoms. The total energy of a solvated molecule can be written as $E_{tot} = E_{vac} + \Delta G_{solv}$, where E_{vac} rents molecules energy in vacuum (gas phase), and ΔG_{solv} is the free energy of transferring the molecule from vacuum into solvent, that is, solvation free energy. To estimate the total solvation free energy of a molecule, one typically assumes that it can be decomposed into the electrostatic and non-electrostatic parts (Tiana et al., 2007).

Initial hydration of the voltage-gated potassium channel has been accomplished using our pervious techniques. The simulation box, complete with the hydrated potassium channel, is shown.

Utilizing canonical ensemble molecular dynamics simulation, we are conducting detailed simulations of the expected water molecular distribution inside and proximal to the nanopore, the transport of potassium ions through the nano-channel, including the external electrical potential or cell membrane potential. A hypothesis of selective ion transport through a potassium channel has been presented by T.W.Allen, S.kugcak, and S.H.chung based on the K^+ channel of *S. lividans* (Kaczmarek and

Perney, 1991) the K^+ channel in the open position, acts as a selectivity filter in exchanging the K^+ ions hydration layer, in favor of carbonyl oxygen along the lining of the pore. Na^+ ions that are also present are too small to shed their hydration layers in an energetically favorable way. With the additional feature of a hydrophobic region within the channel, the Na^+ ion-water complex cannot pass through the pore.

Structural modeling of the Kv channel suggests that, the open state conformations of the voltage sensors of these channels are significantly different whereas the voltage sensors may be similar in conformation in their closed states. This finding potentially explains the different magnitude of the S4 translational movement observed experimentally for these channels (Armstrong and Hille, 1998).

Monte Carlo simulation is commonly used to compute the average thermodynamic properties of a molecule and have been employed extensively in the study of the structure and equilibrium properties of molecules (Metropolis et al., 1953). Monte Carlo calculations evaluate the averages of the ensemble directly, by sampling configurations from the statistical ensemble. If the run takes enough time, Monte Carlo and Molecular Dynamics must give the same average results for the same system, such as rotational frequencies or transitional rates (Allen and Tildesley, 1987). Monte Carlo is better in sampling the allowed states of a system, thus, it can often calculate the average properties more quickly and accurately. The Run step and delta max for Monte Carlo simulation were 20000 and 0.001, respectively. The Run time and time step for Molecular Dynamics simulation were 30 ps and 10^{-3} ps, respectively. The time step and friction coefficient for Langevin simulation were 10^{-3} ps and 0.1 ps^{-1}, respectively (Warshel and Parson, 2001; Monajjemi et al., 2006; Haeri et al., 2007; Aghaie et al., 2008). All simulations were at different temperatures. The total energy of the system, in these methods is called Hamiltonian, which is the sum of kinetic and potential energy:

$$E = K + V$$

In Table 1, the total energy, potential and kinetic energy are calculated by Monte Carlo simulations. The total energy increase when temperature rises from 300 until 400K (Figure 1).

In Tables 2 and 3, the total energy, potential and kinetic energy are calculated by Molecular and Langevin dynamics simulations. The total energy increases as the temperature rises from 300 until 400K (Figures 2 and 3).

In Table 4, the total energy, potential and kinetic energy are calculated by Monte Carlo, Molecular and Langevin dynamics simulations. The diagram of kinetic and potential energy has been drawn as a function of temperature for the native structure of the potassium channel protein. Kinetic energy increases as the temperature rises and its diagram is linear in each three methods. The calculated potential energy by, Molecular dynamics approaches Langevin dynamics simulation at 340 K. Molecular dynamics simulation, as well as kinetic energy shows some deviations for potential energy at less than 330 K and after that proceeds constantly (Figures 4 and 5).

Table 1. The total, potential and kinetic energy (kcal/mol) voltage-gated potassium channel protein calculated for native structure by Monte Carlo (MC) simulations in gas phase, (E_{kin} = Kinetic energy, E_{pot} = potential energy, E_{total} = total energy, K = Kelvin temperature).

T(K)	Monte Carlo		
	E_{kin}	E_{pot}	E_{total}
300	287.0498	356.708	643.7578
310	296.6182	371.7409	668.3591
320	306.1865	361.8538	668.0403
330	315.7548	376.8506	692.6054
340	325.3232	372.2094	697.5326
350	334.8915	386.1546	721.0461
360	344.4598	397.1236	741.5834
370	354.0281	386.3405	740.3686
380	363.5965	383.9712	747.5677
390	373.1648	391.4145	764.5792
400	382.7331	409.5067	792.2398

Experimentally, gyration radius for the Voltage–gated potassium channel protein is 9.409 A^o. In Tables 5 and 6 gyration radius for the Voltage - gated potassium channel protein calculated in Gas and Water phase. Gyration radius diagram as a function of temperature for each three method in Figures 6 and 7, shows that Monte Carlo simulation is the best method to evaluate gyration radius as well. Considering the gained values from Monte Carlo, Molecular and Langevin dynamics simulation calculations for α – helix conformation and little deviations from the experimental values, it can be understood that the second structure of mentioned protein is α – helix folding. An accurate description of the aqueous environment is essential for realistic biomolecular simulation but may become very expensive computationally. For example, an adequate representation of the solvation of a medium-sized protein, typically requires thousands of discrete water molecules to be placed around it.

Conclusion

Movements of ions through specific transmembrane channels underlie many important biological functions ranging from oxidative phosphorylation to electric signaling in neural and muscular systems. Although, a large amount of electrophysiological data, provides crucial information about the action of such channels, a detailed molecular picture of the control of ion permeating, is still a partially unresolved problem. The

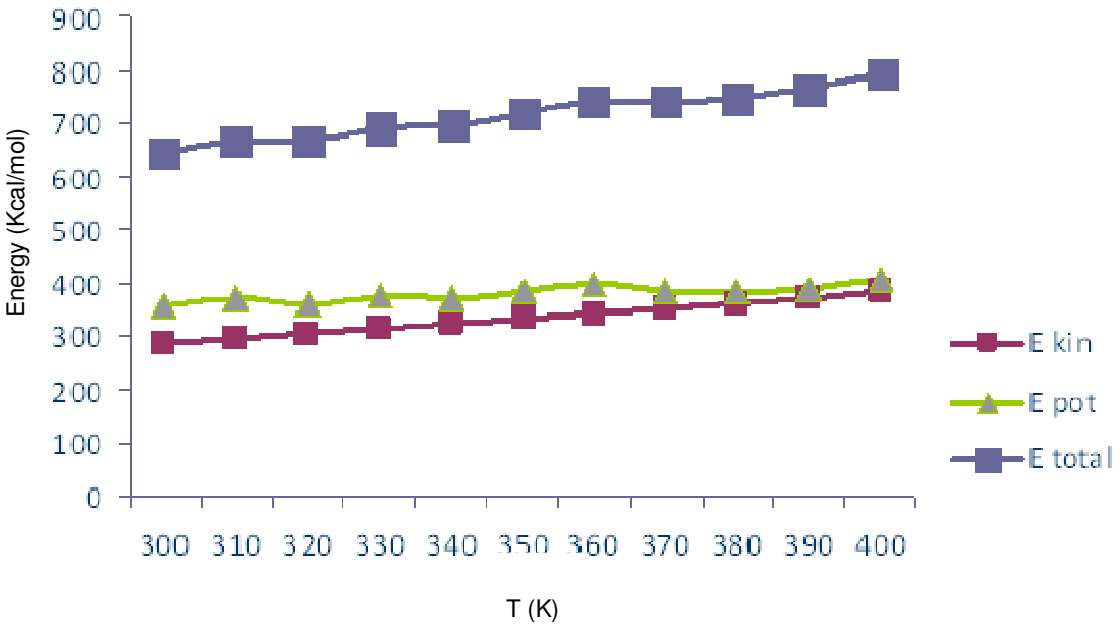

Figure 1. The total , potential and kinetic energy (kcal/mol) voltage-gated potassium channel protein calculated for native structure by Monte Carlo (MC) simulations in gas phase, (E kin = kinetic energy, E pot = potential energy, E total = Total energy, K = Kelvin temperature).

Table 2. The total , potential and kinetic energy (kcal/mol) voltage-gated potassium channel protein calculated for native structure by Molecular Dynamics (MD) in gas phase, (E_{kin} = Kinetic energy, E_{pot} = potential energy, E_{total} = total energy, K = Kelvin temperature).

T(K)	Molecular Dynamics		
	E_{kin}	E_{pot}	E_{total}
300	287.4327	167.5387	454.9714
310	287.9202	179.4714	467.3916
320	327.5925	166.47	494.0625
330	318.9188	216.3305	535.2493
340	343.5757	180.8505	524.4262
350	329.8648	188.917	518.7818
360	355.7188	204.7182	560.437
370	366.925	225.3215	592.2465
380	361.1101	236.0545	597.1645
390	387.9107	220.9124	608.8231
400	377.8991	247.2193	625.1183

Table 3. Total, potential and kinetic energy (kcal/mol) voltage-gated potassium channel protein calculated for native structure by Langevin dynamics (LD) simulation in gas phase, (E_{kin}=Kinetic energy, E_{pot}=Potential energy, E_{total}=total energy, K = Kelvin temperature).

T(K)	Langevin dynamics		
	E_{kin}	E_{pot}	E_{total}
300	296.0033	155.8173	451.8206
310	288.845	178.2814	467.1264
320	322.5929	150.7509	473.3438
330	318.3283	175.2207	493.5491
340	338.2884	208.7121	547.0005
350	333.6071	235.8896	569.4967
360	357.5419	206.8461	564.388
370	358.1902	224.5632	582.7535
380	363.3971	257.4407	620.8378
390	368.2416	278.2447	646.4863
400	403.1537	261.9066	665.0603

ability to simulate ion current is instructive and potentially important. Yet, the overall penetration time, seems to be determined mainly by the energetics of the rate-determining state elucidated, it is possible to evaluate the activation barrier along the corresponding reaction path and apply transition-state theory with a correction that reflects the corresponding transition factor.

In this work, to characterize protein behavior, we observe quantities such as gyration radius and energy average. We studied the changes of these factors for voltage-gated potassium channel. In general, Langevin dynamics simulations are the same as molecular dynamics simulation .There are differences due to the presence of additional forces. Most of the earlier discussion on simulation parameters and strategies for Molecular Dynamics, had been applied to Langevin dynamics. We found that Monte Carlo simulation is the

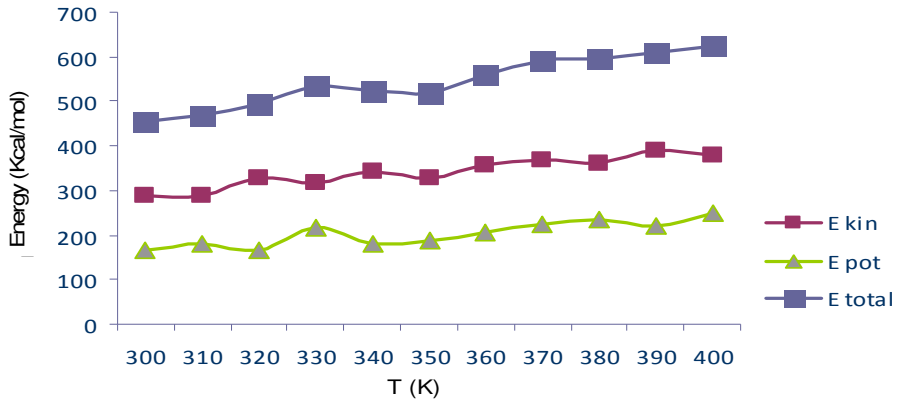

Figure 2. The total, potential and kinetic energy (kcal/mol) voltage-gated potassium channel protein calculated for native structure by Molecular Dynamics in gas phase, (E_{kin}= kinetic energy, E_{pot}= potential energy, E_{tot}= total energy, K = Kelvin temperature).

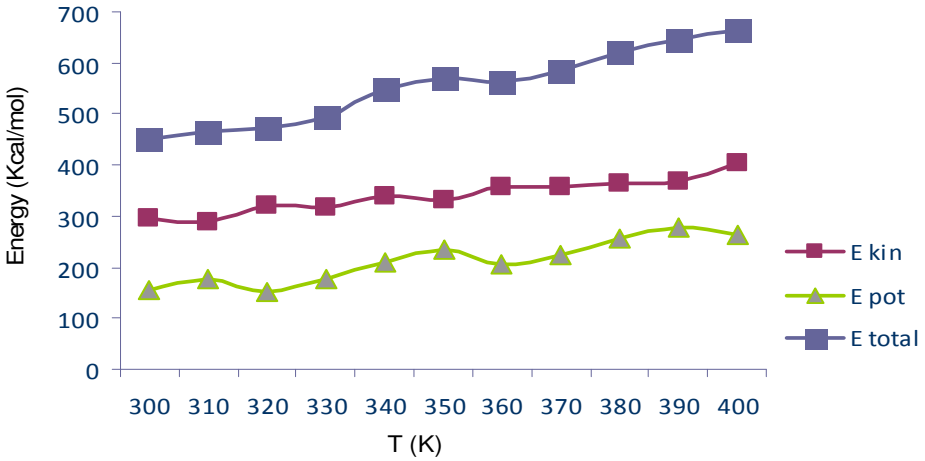

Figure 3. Total, potential and kinetic energy (kcal/mol) voltage-gated potassium channel protein calculated for native structure by Langevin simulation in gas phase (E_{kin}=kinetic energy, E_{pot} = potential energy, E_{total} = total energy, K = Kelvin temperature).

Table 4. The total, potential and kinetic energy (kcal/mol) voltage-gated potassium channel protein calculated for native structure by Monte Carlo (MC), Molecular (MD) and Langevin dynamics (LD) simulations (E_{kin} = kinetic energy, E_{pot} = potential energy, E_{total} = Total energy, K = Kelvin temperature).

T(K)	Monte Carlo			Molecular dynamics			Langevin dynamics		
	E kin	E pot	E total	E kin	E pot	E total	E kin	E pot	E total
300	287.0498	356.708	643.7578	287.4327	167.5387	454.9714	296.0033	155.8173	451.8206
310	296.6182	371.7409	668.3591	287.9202	179.4714	467.3916	288.845	178.2814	467.1264
320	306.1865	361.8538	668.0403	327.5925	166.47	494.0625	322.5929	150.7509	473.3438
330	315.7548	376.8506	692.6054	318.9188	216.3305	535.2493	318.3283	175.2207	493.5491
340	325.3232	372.2094	697.5326	343.5757	180.8505	524.4262	338.2884	208.7121	547.0005
350	334.8915	386.1546	721.0461	329.8648	188.917	518.7818	333.6071	235.8896	569.4967
360	344.4598	397.1236	741.5834	355.7188	204.7182	560.437	357.5419	206.8461	564.388
370	354.0281	386.3405	740.3686	366.925	225.3215	592.2465	358.1902	224.5632	582.7535
380	363.5965	383.9712	747.5677	361.1101	236.0545	597.1645	363.3971	257.4407	620.8378
390	373.1648	391.4145	764.5792	387.9107	220.9124	608.8231	368.2416	278.2447	646.4863
400	382.7331	409.5067	792.2398	377.8991	247.2193	625.1183	403.1537	261.9066	665.0603

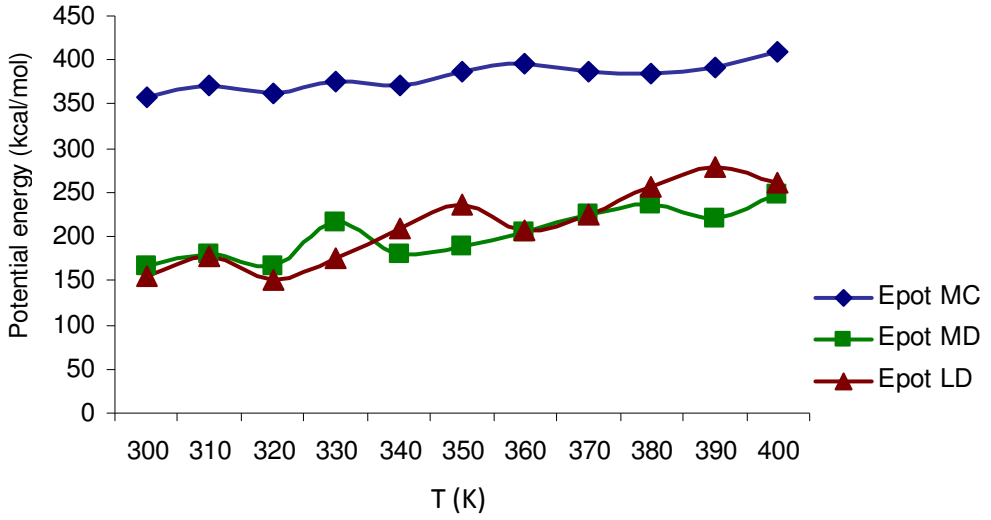

Figure 4. The potential energy(kcal/mol) voltage- gated potassium channel protein calculated for Native structure by Monte Carlo (MC) , Molecular dynamics (MD) and Langevin dynamics (LD) simulations (E kin=Kinetic energy, E pot=Potential energy, E total= total energy, K=Kelvin temperature).

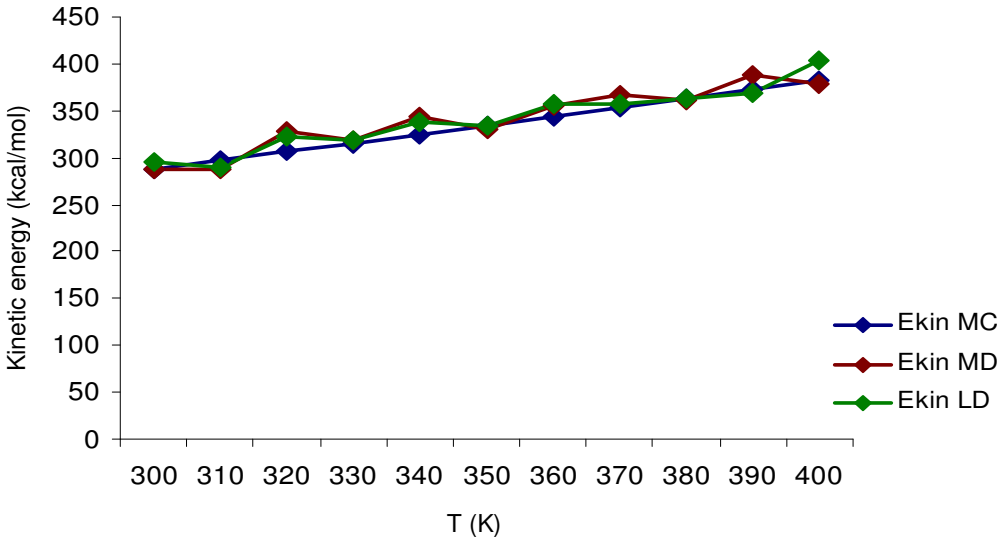

Figure 5. The kinetic energy(kcal/mol) voltage-gated potassium channel protein calculated for native structure by Monte Carlo (MC) , Molecular dynamics (MD) and Langevin dynamics (LD) simulations E_{kin}= Kinetic energy ,E_{pot} = Potential energy ,E_{total} = Total energy, K = Kelvin temperature).

best method to assess and find the value of gyration radius, because Monte Carlo is a stochastic method. Our results show that, kinetic energy is enhanced when the temperature is increased and kinetic energy plot is linear. Monte Carlo calculations evaluate the averages of the ensemble directly by sampling configurations from the statistical ensemble. Molecular dynamics is the key quantity that need to be computed is the total energy of the molecule in the presence of solvent.

The resolution of the atomic structure o f the ion-conduction pathway of voltage-gated potassium channel protein, has served as a spring-board from which we have gained a clear understanding of the underlying principles of ion selectivity and permeation. A huge challenge for the field will now be to understand the structural mechanisms of voltage gating and inactivation. In this regard, examples of conformational coupling between the pore and the cytoplasmic domains of potassium channels are already helping, to gain new insight into the fundamental mechanisms of channel regulation. A nano-

Table 5. Gyration radius (A°) calculated for native structure of voltage gated potassium channel protein by Monte Carlo, Molecular and Langevin simulation (T = temperature, K = Kelvin).

T (K)	Gyration radius (A°) by Monte Carlo	Gyration radius (A°) by Molecular dynamics	Gyration radius (A°) by Langevin dynamics
300	9.413558753	9.66700859	10.01329648
310	9.411185612	9.966947879	9.851894063
320	9.418555544	8.831177035	10.10882701
330	9.418725177	9.252583762	10.13588086
340	9.414216313	10.57210635	10.40001586
350	9.411349084	10.84853185	9.434896554
360	9.414914405	8.151026598	9.439490888
370	9.410921112	10.11491778	9.571484006
380	9.418607994	10.03344007	8.549397494
390	9.417448272	10.69537599	9.948055121
400	9.414307694	10.61029408	8.549995299

Table 6. Gyration radius (A°) calculated for native structure of voltage gated potassium channel protein by Monte Carlo, Molecular and Langevin simulation in water phase (T = temperature, K = Kelvin).

T (K)	Gyration radius (A°) by Monte Carlo -H_2O	Gyration radius (A°) by Molecular dynamics -H_2O	Gyration radius (A°) by Langevin dynamics -H_2O
300	21.4818621	17.31635723	17.6520483
310	21.58852352	16.91597306	17.55157923
320	21.39599083	17.57434703	16.84032627
330	21.46492897	17.72400316	17.18950163
340	21.54416689	17.03781601	18.02533949
350	21.6264298	17.03781601	15.40373283
360	21.50909629	17.95172194	16.22586182
370	21.47100515	16.27805412	15.64075074
380	21.51417015	16.54949375	16.7183823
390	21.49389942	16.73447501	16.42751765
400	21.56286606	16.33872913	17.9001883

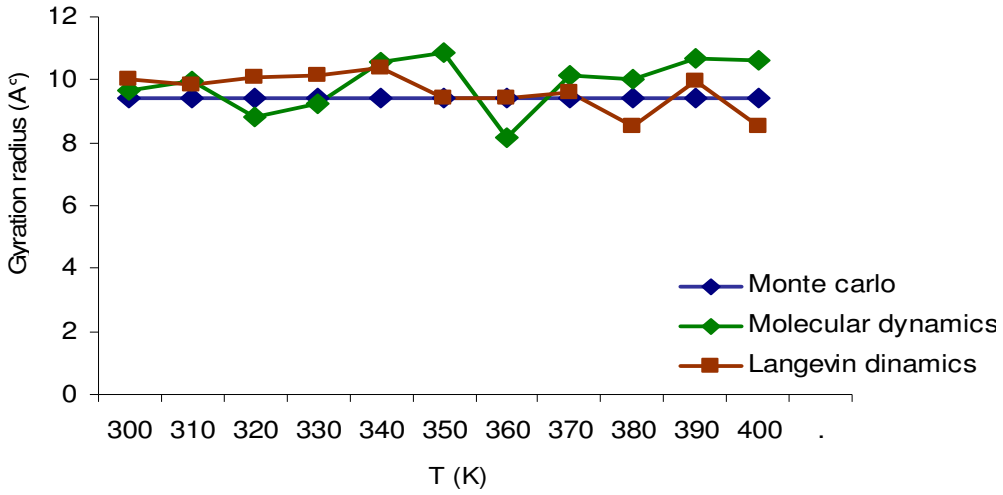

Figure 6. Gyration radius (A°) of voltage gated potassium channel protein for native structure as a function of temperature (Kelvin) in gas phase.

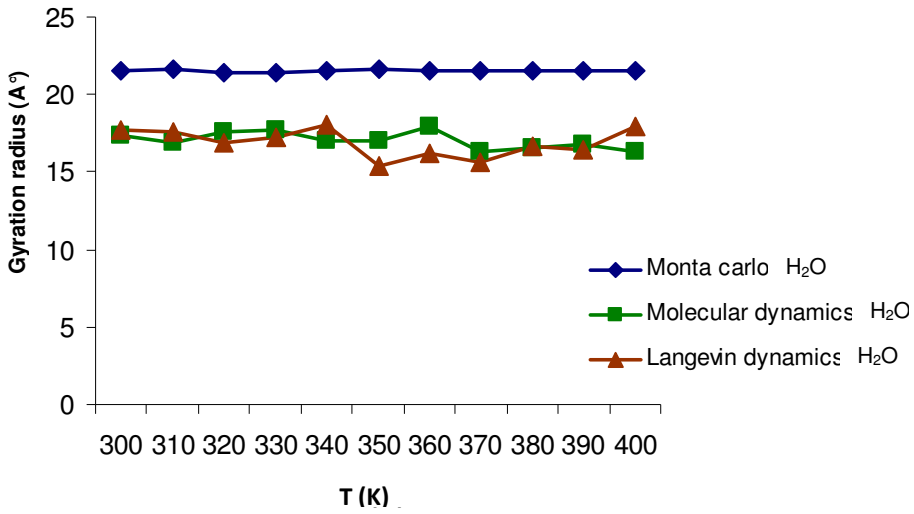

Figure 7. Gyration radius (A°) of voltage gated potassium channel protein for native structure as a function of temperature (Kelvin) in water phase.

molecular understanding of these processes will be instrumental in elucidating the mechanisms that underlie the higher-order activity of neunal networks.

The structure and function of the membrane proteins are central problems in molecular biology and are attracting tremendous interest. However, the cooperative process of lipids and proteins occurring within the membrane is still very difficult to understand. Recent advances in computer technology have proved the molecular simulation approach to be very promising in various fields of research.

REFERENCES

Aghaie H, Gholami MR, Monajjemi M, Ganji MD (2008). Electron transport phenomenon simulation through the carborane nano-molecular wire Physica E: Low-Dimensional Syst. Nanostruct., 40(9): 2965-2972.

Allen MP, Tildesley DJ (1987). Computer Simulation of Liquids. Clarendon Press; Oxford; Ch. 9: 261.

Alvis SJ, Williamson IM, Lee AG (2003). The potassium channel KcsA and its Interaction with the lipid bilayer Biophys. J., 85: 3828-3838.

Armstrong CM, Brezanilla F (1974). Charge movement associated with the opening and closing of the activation gates of the Na channels. J. Gen. Physiol., 63: 533.

Armstrong CM, Hille B (1998). Voltage-gated ion channels and electrical excitability. Neuron 20: 371-380.

Chan HS, Dill KA (1994). Transition states and folding dynamics of proteins and Folding dynamics of protein and heteropolymers. J. chem. phys., 100: 9238-9257.

Chone S (2002). Potassim channel structures.

Doyle DA, Morais cabral J (1998). The structure of the potassium channel: molecular basis of K+ conduction and selectivity. Science 280: 69.

Gainesville (2007). Hyperchem 8.0, Hypecube Inc, FL, USA. folding :the energy landscape perspective.Annu. Rev. Phys. Chem., 48: 545-600.

Haeri HH, Hashemianzadeh SM, Monajjemi M (2007). A kinetic Monte Carlo simulation study of inositol 1,4,5-trisphosphate receptor (IP3R) calcium release channel Computat Biol. Chem., 31(2): 99-109.

Heginbothom L (1999). Growing momentum in the molecular study of ion channels, Nat. Struct. Biol., 6: 811.

Hille B (2001). Ion channels of Excitable membranes.

Hille B, Armstrong CM, Mackinnin R (1999). Ion channels: from idea to reality Nat.med 5: 1105.

Humphrey W, Dalk A, Schulten L (1996). VMD Visual molecular dynamics. J. Mol. Graphics. 14: 33-38.

Kaczmarek LK, Perney TM (1991). The molecular biology of K+ channels . Curr. Opin. Cell Biol., 3(4): 663-670.

Kolinski A, Skolnick J (2004). Reduced models of proteins and their applications. Polymers, 45: 511-524.

Lee AG (2004). Protein- Lipid Interactions: New Approache and Emerging Concepts. Biochim. Biophys. Acta, 1666: 62-87.

Liu H, Elstner M, Kaxiras E, Frauenheim T, Hermans J, Yang W (2001). Quantum mechanics simulation of protein dynamics on long timescale Proteins: Structure, function, and Genetics, 44: 484- 489.

Mackinnon M (1991). Potassium channels: a computer prediction of structure and selectivity. Nature, 350: 232.

Metropolis N, Rosenblth AW, Rosenblth MN, Teller E (1953). equation of state by fast computing machines. J. chem.. phys., 21: 1087- 1092.

Monajjemi M, Ketabi S, Amiri A (2006). Monte Carlo Simulation Study of Melittin: Protein Folding and Temperature Dependence Russian J. Phys. Chem., 1: 55-62.

Onuchic J, luthey-schulten Z, wolynes P (1997). Theory of protein

Prusine SB (1997). Handbook of stochastic Methods for physics and chemistry. Science, 278: 417.

Tiana G, Sutto L, Broglia RA (2007). Use of the Metropolis algorithm to simulate the dynamics of protein chain. A physica, 380: 241.

Valiyaveetil FI, zhou Y, Mackinnon R (2002). Lipids in the structure, folding, and function of the KcsA K+ channel Biochemistry 41: 10771-10777.

Warshel A, Parson WW (2001). Dynamics of biochemical and biophysical reactions: insight from computer simulations. Q Rev. Biophys., 34: 563-679.

Yu FH, Catterall WA (2004). The VGL-chanome: a protein superfamily specialized for electrical signaling and ionic homeostasis. Sci., STKE.