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Solvent Effect on Aquaporin4

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ABSTRACT

Aquaporins are integral membrane proteins from a larger family of major intrinsic proteins that form pores in the membrane of biological cells. Aquaporins form tetramers in the cell membrane with each monomer acting as a water channel.In this research, the AQP4 tetramer was modeled from its PDB structure file, then, we have performed the intraction of aquaporin4 in different temperatures (298k, 300k, 302k, 304k, 306k, 308k and 310k) with OPLS and Amber force field in molecular mechanic (MM) method. The Total energy (E_t), Potential energy (E_p) and Kinetic energy (E_k) in (Kcal/mol), were examined, with Amber and OPLS in force field in molecular mechanic (MM) method. In this investigation HyperChem professional release 7.01 was used for the quantum chemical calculations. We have performed geometry optimization and Monte Carlo simulation by this software.

Keywords: Aquaporin; Quantum monte carlo (QMC); Force field

INTRODUCTION

There are 13 homologous aquaporins identified in mammals, of which 6 subtypes (Aquaporin1, Aquaporin3, Aquaporin4, Aquaporin5, Aquaporin8 and Aquaporin9) have been reported in the dynamic regulation of brain water homeostasis and in the regulation of cerebrospinal fluid production [1-2]. Aquaporins selectively conduct water molecules in and out of the cell, while preventing the passage of ions and other solutes [11–12]. The different aquaporins contain differences in their peptide sequence, which allows for the size of the pore in the protein to differ between aquaporins.Each of the aquaporins has an essentially unique pattern of expression among tissues and during development [14]. A summary of these attributes and some of the important potential or known functions is presented in the following table [15]:

The X-ray derived crystal structure of AQP4 was obtained from the Protein Data Bank (PDB code 3GD8) [3-23]. AQP4 has two alternative splice variants resulting from differential translation initiation either at the first methionine (AQP4M1, 323 aa) or at the second methionine (AQP4M23, 301 aa) [25].

The structure of rat AQP4M23 was determined by electron crystallography of two-dimensional (2D) crystals [26]. This packing of AQP4 contrasted with that of the AQP0 arrays, which were stabilized by lipid–protein interactions [27–28].

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	Major Sites of Expression	Comments
Aquaporin-1	Red blood cells	Osmotic protection
	Kidney: proximal tubule	Concentration of urine
	Eye: ciliary epithelium	Production of aqueous humor
	Brain: choriod plexus	Production of cerebrospinal fluid
	Lung: alveolar epithelial cells	Alveolar hydration state
Aquaporin-3 *	Kidney: collecting ducts	Reabsorbtion of water into blood
	Trachea: epithelial cells	Secretion of water into trachea
Aquaporin-4	Kidney: collecting ducts	Reabsorbtion of water
	Brain: ependymal cells	CSF fluid balance
	Brain: hypothalamus	Osmosensing function?
	Lung: bronchial epithelium	Bronchial fluid secretion
Aquaporin-5	Salivary glands	Production of saliva
	Lacrimal glands	Production of tears
Aquaporin-8	Testis, pancreas, liver, others	
Aquaporin-9 *	Leukocytes	

* an aquaglyceroporin

AQP4 is a specific water channel that is predominantly expressed in the brain [6] (Fig.1). This aquaporin has gained much attention due to its putative role in the physiopathology of brain disorders including ischemia, epilepsy and traumatic brain disease [13], tumor-induced brain swelling, infections and hydrocephalus [4–5]. Although the major role of AQP4 is to control water movements into and out of the brain, it has been suggested to play roles in the generation of brain edema, astrocyte migration, neuronal activity, cell adhesion between astrocytes and endothelial cells, and so forth [24].

This Aquaporin is predominantly expressed in astrocytes and ependimal cells. The specificlocalization of AQP4 appears to contribute to facilitate the bidirectionalwater flow across blood–brain interfaces [7-8].The solvated AQP4 tetramer was then placed in a model of the biological membrane [31]. Although AQP4 is expressed in many tissues, its expression level is limited, which made it difficult to use native sources to purify sufficient

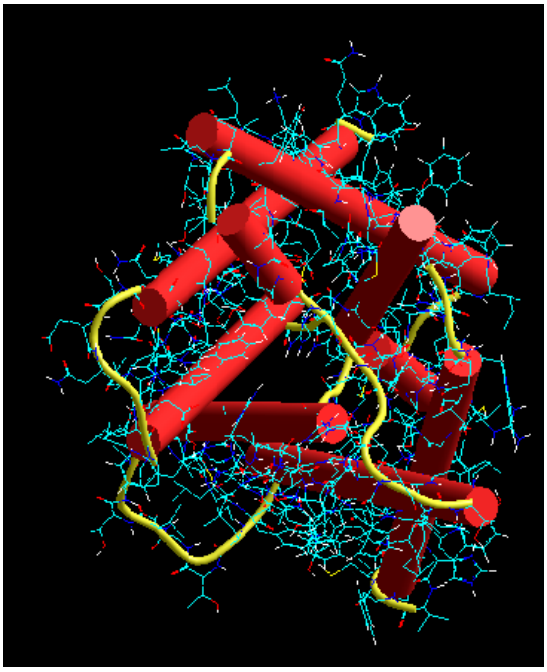

Fig.1. Aquaporin4 (2D57).

amounts of the protein for structural studies.AQP4 is also expressed in glial lamellae of the hypothalamus, [9] where it may play a role in osmo, thermo- and glucose-sensing [10]. The importance of AQP4 as the predominant water channel in brain [29-30] and its propensity to form ordered arrays made AQP4 an attractive target for structure analysis by electron crystallography.

COMPUTATIONAL TECHNIQUES

Molecular Mechanics (Monte Carlo Simulation)

Monte Carlo'' is a term used in many fields of science, engineering, statistics and mathematics to mean entirely different things. The one (and only) thing that all Monte Carlo methods have in common is that they all use random numbers to help calculate something. Monte Carlo simulations are widely used in the fields of chemistry, biology, physics and engineering in order to determine the structural and thermodynamic properties of complex systems at the atomic level. Thermodynamic averages of molecular properties can be determined from Monte Carlo methods, as can minimum-energy structures [16].

Also, it should be noted that constraining potentials (which keep the cluster components from straying too far from a cluster's center of mass) are sometimes used [17].

At finite temperature, clusters have finite vapor pressures, and particular cluster sizes are typically unstable to evaporation. Introducing a constraining potential enables one to define clusters of desired sizes. The Monte Carlo method is one of the most broadly and commonly used numerical techniqual, with application in statistical physics, quantum mechanics, field theory and others [18].Monte Carlo simulation, which can generate a canonical ensemble, is applied when systems have difficult integrals to be solved and should generate some random number to generate uniform independent values statistically [19-20].In the Monte Carlo method, a metropolis algorithm is applied more than other algorithm because of its simplicity [21]. The accuracy of the algorithm is determined by random displacement. In trivial displacements, all moves can be accepted, but in large cases the rate of acceptable moves is small. In this investigation, differences in force field are illustrated by comparing the calculated energy by using force fields AMBER and OPLS. In this investigation HyperChem professional release 7.01 is used for the quantum chemical calculations [22].

The Model of Theory and Computational Details

The Monte Carlo method is one of the most broadly and commonly used numerical techniqual, with application in statistical physics, quantum mechanics, field theory and others [28]. In this investigation, the quantum chemical study was carried out using Monte Carlo simulation. In this paper, we investigate Solvent effects (water, methanol, ethanol and DMSO) at seven temperatures (298k, 300k, 302k, 304k, 306k, 308k and 310) on interaction of Aquaporin4, with OPLS and Amber force field in molecular mechanic (MM) method. The temperature ranges from 298 to 310 Selected based on the ambient temperature and the temperature of the human body. Two different force fields (AMBER, OPLS) are available in the Macro Model program. Choosing a force field that is well parameterized for the molecular system under study is very important [22]. The calculations were carried out using HyperChem professional release 7.01 package of program. The Total energy (E tot), Potential (E pot) and

Kinetic (E kin) energy (kcal/mol), calculated by Monte Carlo simulation (AMBER, OPLS) by solvent effects in different Temperature (298k, 300k, 302k, 304k, 306k, 308k and 310k). We performed geometry optimization and Monte Carlo simulation by this software [11].

RESULTS AND DISCUSSION

At the first, it's very important to Know Location AQP4 tetramer in a membrane. The AQP4 tetramer solvates in different solvents then placed in a model of the biological membrane. This membrane contains a palmitoyloleoyl- phosphatidyl-choline (POPC) lipid bilayer generated. It was necessary to make room for the AQP4 in the membrane bilayer so that the protein doesn't overlap any lipid molecules.

In this investigation, the interaction energies between aquaporin and Different solvents (water, methanol, ethanol and DMSO), were calculated utilizing these force fields (AMBER, and OPLS) in different Temperature (298k, 300k, 302k, 304k, 306k, 308k, and 310) have been performed. First, a molecule Select the appropriate geometry of a molecule and then a calculation method and its associated options are selected. As shown in Table.1 and 2, the calculations of the interaction between aquaporin with Ethanol. Total energy (E tot), Potential (E pot) and Kinetic (E kin) energy (kcal/mol), calculated by Monte Carlo simulation with Amber and Opls force field in different Temperature (298k, 300k, 302k, 304k, 306k, 308k, 310k), The Total energy, Potential and Kinetic energy (kcal/mol). In (fig3) E kin (kcal/mol) calculated versus different Temperature by Monte Carlo simulation (Amber force field). As shown in (fig3), with increasing Temperature Kinetic energy also increases, the largest amount of kinetic energy is observed at 310. In this diagrams, the slope of the line is more, will be more stable and in (fig3), Epot (kcal/mol) calculated versus different Temperature. In this research, differences in force fields are illustrated by comparing the computed energy using various force fields such as Amber and OPLS (Table 1 and 2, Figure 2 and 3). The theoretical energy values are attained by using different force fields.

As shown in Table.3 and 4, the calculations of the interaction between aquaporin with Methanol. The Total energy (E tot), Potential (E pot) and Kinetic (E kin) energy (kcal/mol), calculated by Amber and OPLS force field.in fig 4 and 5, EKin (kcal/mol) and E pot (kcal/mol) Shown Compare energy. As shown in Table.5 and 6, the calculations of the interaction between aquaporin with DMSO and in Table.7 and 8, the calculations of the interaction between aquaporin with Water. In this paper, we examined Energy values from interaction of aquaporin with Different solvents (water, methanol, ethanol and DMSO) in different temperature. Calculations of the Total energy, potential energy and kinetic energy by Monte Carlo simulation (AMBER, OPLS) have been to solvents (water, methanol, ethanol and DMSO) in different temperature and in Different number of solvents (n= 0, 5, 10, 15, 20, 25). Since the two different force fields have been utilized, the calculated energy of molecules will not be the same. Thus, comparing the computed energy of one molecule by using a particular force field with the energy of another molecule, which is calculated by another force field, is neither rational nor possible.

As you can see, in all solvents with increasing Temperature Kinetic energy also increases and also DMSO is the most amount of Energy among different solvents (water, methanol and ethanol).We found, that the amino acid residues involved in during the simulations,

Because of this, in during the simulations, the aquaporin exhibited significant fluctuation.

CONCLUSION

In this work, we have studied the effects of different solvents (water, methanol, ethanol and DMSO) on Aquaporin4 in different Temperature (298k, 300k, 302k, 304k, 306k, 308k and 310k) and in Different number of solvents (n= 0, 5, 10, 15, 20, 25) by each force field (AMBER and OPLS) have been performed. At the beginning, the calculations were performed by HyperChem program. Our studies concerning the influence of increasing temperature in potential energy show that, when the temperature increases, the potential energy will increase and stability declines. The Total energy (E tot), Potential (E pot) and Kinetic (E kin) energy (kcal/mol), calculated by Monte Carlo simulation (Amber and Opls force field) in different Temperature. The calculated data as shown in tables and figures are corresponding with some behavior of aquaporin. Because of this, the aquaporin exhibited significant fluctuation during the simulation. Use of the solutions for characterization of motions and determination of the properties or dynamics of the molecules of interest requires a number of theoretical or computational steps and all of which are current activities of research. Therefore in this paper we summarize the method and describing the reasons for the choices.

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