Influence of water models on AQP1

Miguel A. Gonzalez[1], Charlotte I. Lynch[2], José Luis F. Abascal[1],
Mark S. P. Sansom[2], and Chantal Valeriani[3]

[1]Universidad Complutense de Madrid, Facultad de Ciencias Químicas, Departamento de Química Física, 28040 Madrid, Spain
[2]University of Oxford, Structural Bioinformatics and Computational Biochemistry Unit, Department of Biochemistry, Oxford OX1 3QU, United Kingdom
[3]Universidad Complutense de Madrid, Facultad de Ciencias Físicas, Departamento de Física Aplicada, 28040 Madrid, Spain

Membrane proteins are vital for the correct functioning of cells, being responsible for cell-cell communication and both active and passive transport of molecules across the membrane [1]. The latter include protein channels and pores, and constitute a large family whose members have different features depending on the nature of the transported molecules. Aquaporins (AQP) are protein pores enabling the passage of water [2] across the membrane, characterised by high selectivity and rates of permeability. Although they have been widely studied, key aspects of the mechanisms relevant for their function remain unclear. Molecular dynamics (MD) is powerful numerical tool for investigating the features of a membrane protein, simulating a full complex system consisting of the membrane protein, the bilayer lipid membrane, water molecules, and ions. In such a system, water plays a key role in the lipid-protein interaction, given that the lipid membrane structure is governed by hydrophobic-hydrophilic forces (as well as the protein structure). Hence, it is essential to properly describe both the water-protein and water-membrane interactions. However, so far in biological simulations, water models have been selected for their ability to reproduce the behaviour of biological molecules, for example, how lipids assemble into a membrane or the dynamics of a protein [3, 4].

In our work, we propose a different point of view: the choice of the water model might influence the predicted transport properties of aquaporins [5, 6]). We will be focusing on newer water models, such as TIP4P/2005 [7] and OPC [8], known to reproduce and to predict the values of a huge range of thermodynamics properties [3, 4]. We have carried out several simulations for AQP1 in combination with TIP3P [9], TIP4P/2005 and OPC as the water potential. We have calculated the water flux through the channel, the water molecule orientation into the channel and the water dipole moment for the three systems. Our preliminary results for all systems reproduce the molecular mechanism described by Tajkhorshid *et al.* [6]. However, the number of water molecules crossing the channel depends on the water model. The thermodynamic properties of the water potential in bulk are extremely different, thus modifying the protein behaviour.

[1] B. Alberts, A. Johnson, J. Lewis, M. Raff, K. Roberts, and P. Walter, *Molecular Biology of the Cell* (Garland Science, 2002).

[2] D. Kozono, M. Yasui, L. S. King, and P. Agre, J. Clin. Invest. **109**, 1395-1399 (2002).

[3] S. L. Rouse and M. S. P. Sansom, J. Phys. Chem. B **119**, 764-772 (2015).

[4] E. J. Denning and O. Beckstein, Chem. Phys. Lipids **169**, 57-71 (2013).

[5] Y. Fujiyoshi, K. Murata, K. Mitsuoka, T. Hirai, T. Walz, P. Agre, J. B. Heymann, and A. Engel, Nature **407**, 599-605 (2000).

[6] E. Tajkhorshid, P. Nollert, M. Ø. Jensen, L. J. W. Miercke, J. O'Connell, R. M. Stroud, and K. Schulten, Science **296**, 525-530 (2002).

[7] J. L. F. Abascal and C. Vega, J. Chem. Phys. **123**, 234505 (2005).

[8] S. Izadi, R. Anandakrishnan, and A. V. Onufriev, J. Phys. Chem. Lett. **5**, 3863-3871 (2014).

[9] M. W. Mahoney and W. L. Jorgensen, J. Chem. Phys. **112**, 8910-8922 (2000).

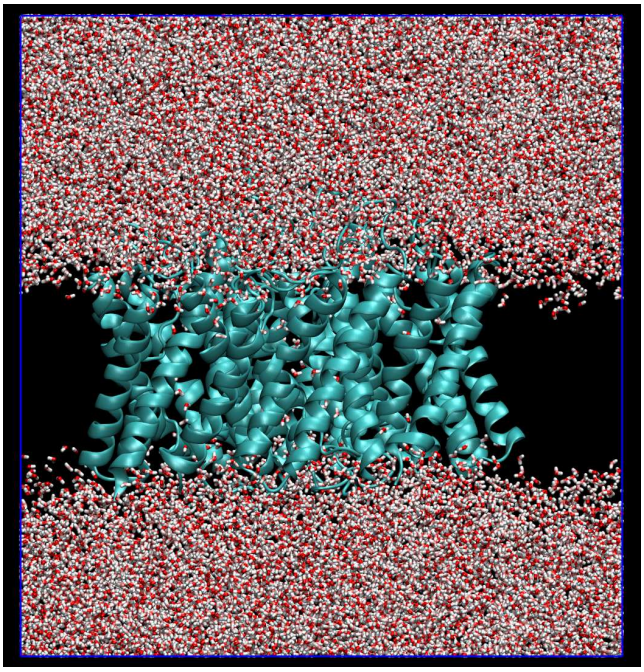

Fig. 1. Snapshot of an AQP1 (in Cyan) embedded into a POPC membrane, lipids from membrane are removed to ease the visualization of the protein).The water is represented by red-white licorice model, red for oxygen and white for hydrogen.