Influence of water models on AQP1

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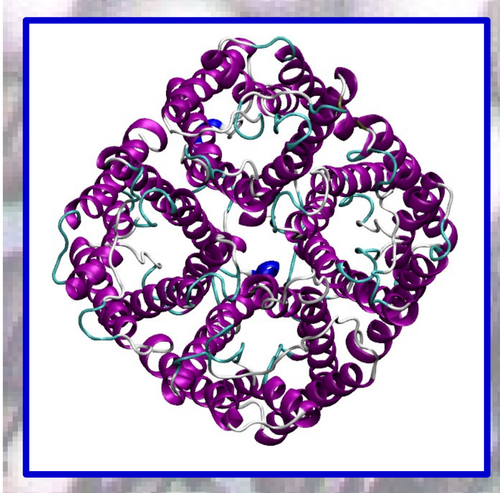
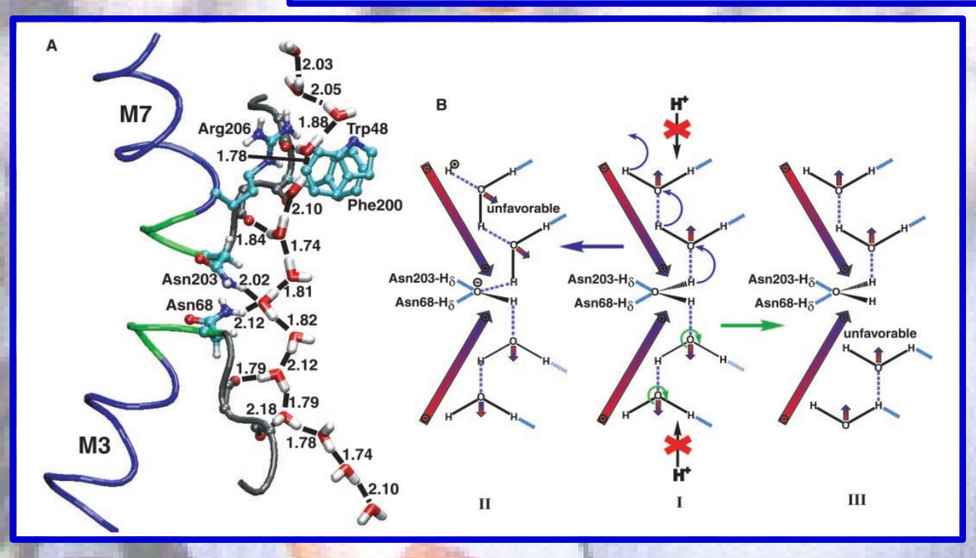
In this work we propose that the choice of the water model might influence the predicted transport properties of aquaporins [1].
We will focus on newer water models, such as TIP4P/2005 [2] and OPC [3], known to reproduce and to predict the values of a huge range of thermodynamics properties [1].
We have carried out several simulations for AQP1 in combination with TIP3P [4], 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.* [5].
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.

Aquaporin-1. Selectivity mechanism



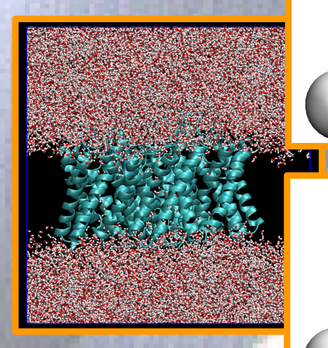


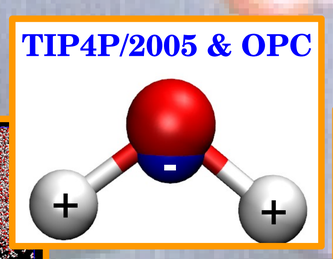
The remarkable property of effective water conductance combined with a strict exclusion of all ions including protons is mediated by two conserved **asparagines** which force a **central water molecule** to act strictly as a **hydrogen bond donor** to its neighboring water molecules.

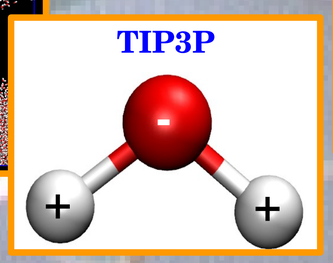
Assisted by the electrostatic potential generated by two half-membrane spanning loops, this dictates **opposite orientations of water molecules in the two halves of the channel**, and thus **prevents the formation of a "proton wire"**, while permitting rapid water diffusion.

Molecular Dynamics Simulation

We have carried out several molecular dynamics simulations using GROMACS 2016.4 software package [6]. The force field used to simulate the protein is CHARMM-36, GROMOS-53A6 for lipids, and the water was modeled with TIP3P, OPC, and TIP4P/2005 force fields. We performed simulations in the NpT ensemble, at 298 K and 1 bar. Long-range electrostatic interactions were treated using the Particle Ewald method [7].







Systems: AQP-1 +

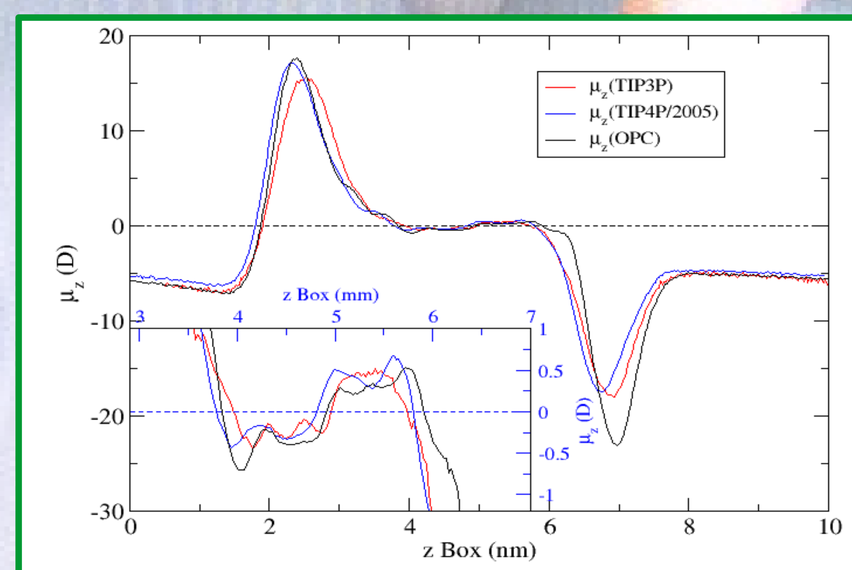
1)TIP3P(100ns)x3 runs

2)TIP4P/2005(100ns)x3 runs

3)OPC (100ns)x3runs

Results

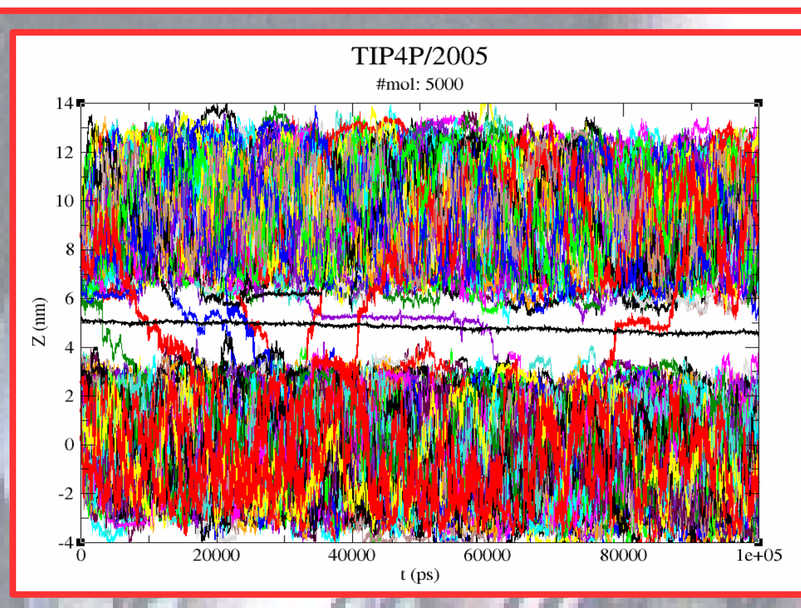
Dipole moment (μ)



Dipolar moment changes inside the AQP1 for every water model.

This could suggest that the issue is not because of an AQP1-water interaction but the force-field used to simulate water.

Diffusion Permeability (p_d)



	EXP.[5,8]	TIP3P	TIP4P/2005	OPC
#water/s x10^9	0.5-3.9	6.17	0.44	0.50
p_d(cm^3/s)	4.5-35.1	55.53	3.96	4.5
D_{Bulk}(298K) (10^{-5} cm^2/s)[9]	2.30	5.19	2.08	2.30

CONCLUSIONS

In this work, we demonstrate that water model choice plays a key role to describe properly the properties of AQP-1.
In combination with CHARMM (to simulate AQP-1), we consider 3 water force-fields (the commonly used TIP3P, TIP4P/2005 and OPC).
We find out that the peculiar mechanism of water through AQP-1 is recovered with all water water models.
However, when computing the water flux and the diffusion permeability, we conclude that the results obtained with TIP4P/2005 and OPC are in better agreement with experiments.
The main reason being the different bulk diffusion coefficient of each of these models.

In order to shed more light on this result, our last goal will be computing the axial diffusion coefficient of water through the AQP-1 channel.

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