

Molecular Dynamics Simulation of Membrane Channels

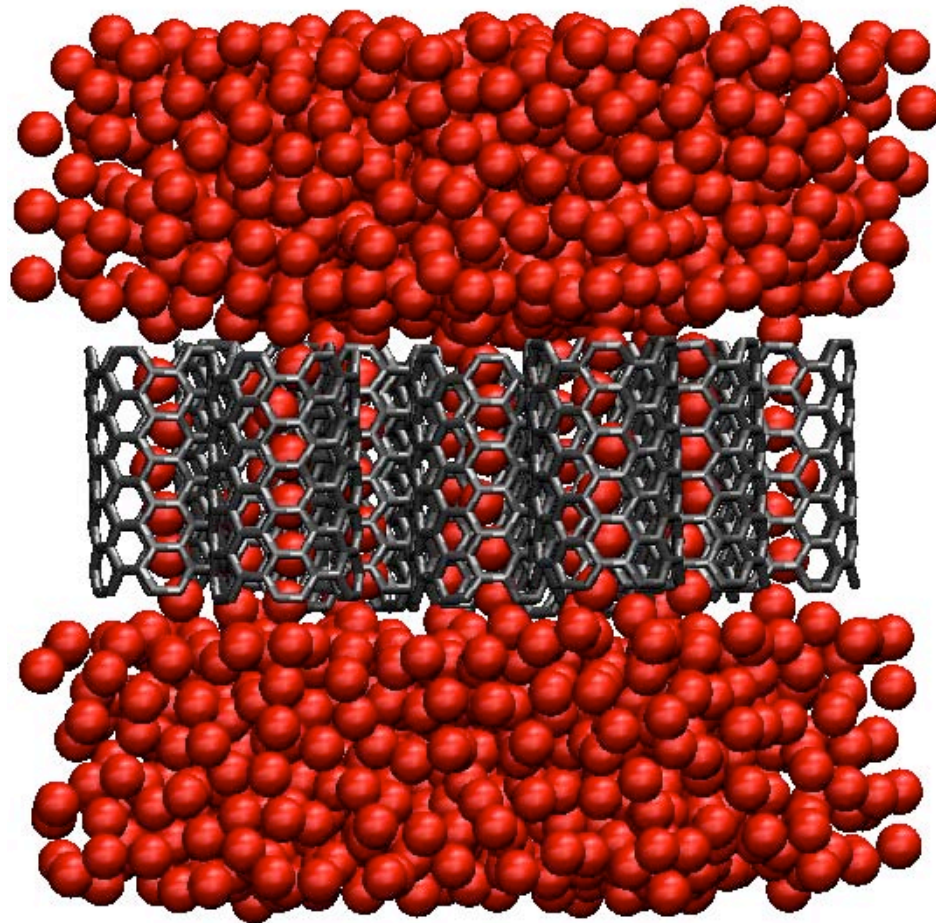
Part III. Nanotubes
Theory, Methodology

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Summer School on Theoretical and Computational Biophysics
June 2004, University of Western Australia

Carbon Nanotubes

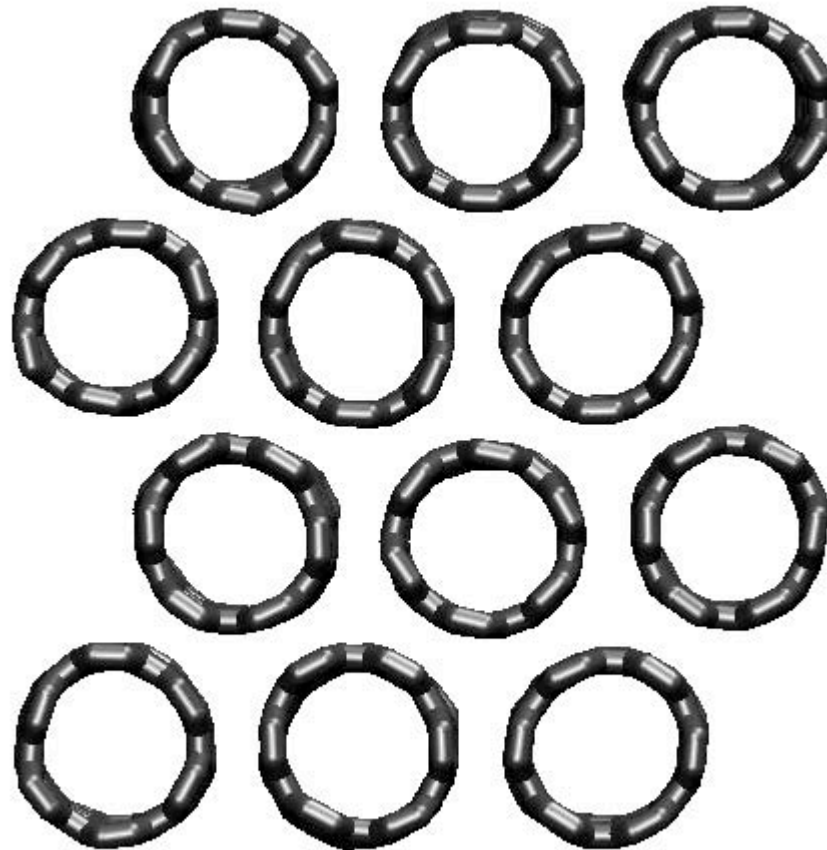
Hydrophobic channels - Perfect Models for Membrane Water Channels



A balance between the size and hydrophobicity

Carbon Nanotubes

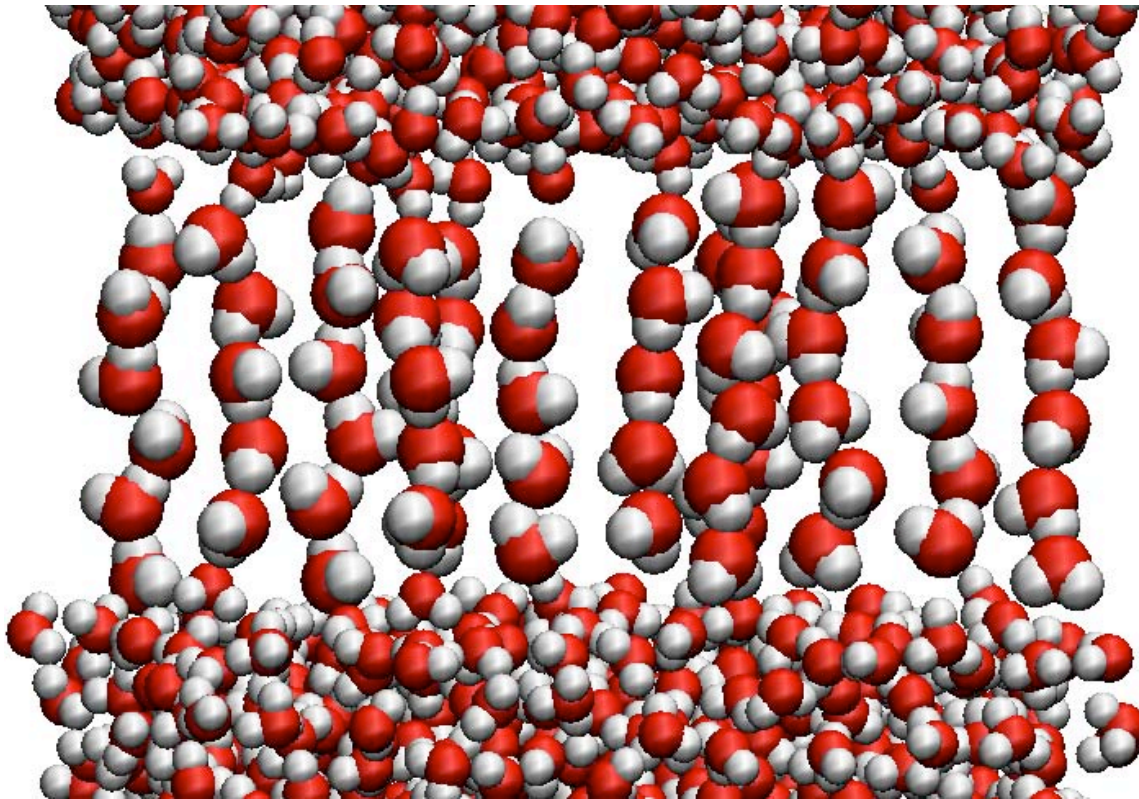
Hydrophobic channels - Perfect Models for Membrane Water Channels



- Much better statistics
- No need for membrane and lipid molecules

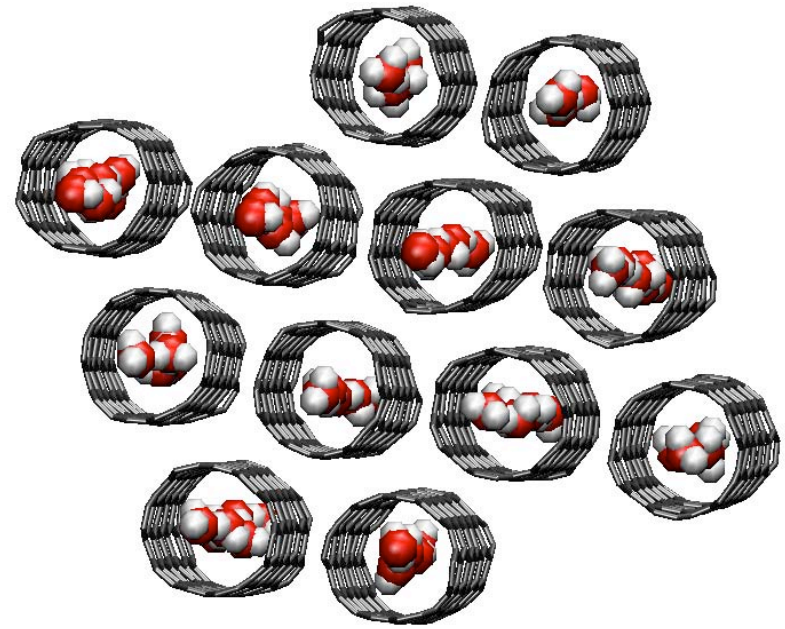
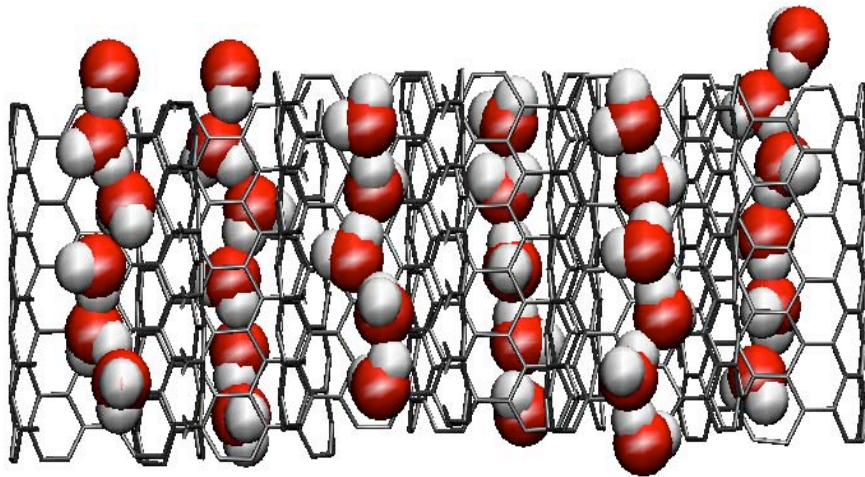
Carbon Nanotubes

Hydrophobic channels - Perfect Models for Membrane Water Channels



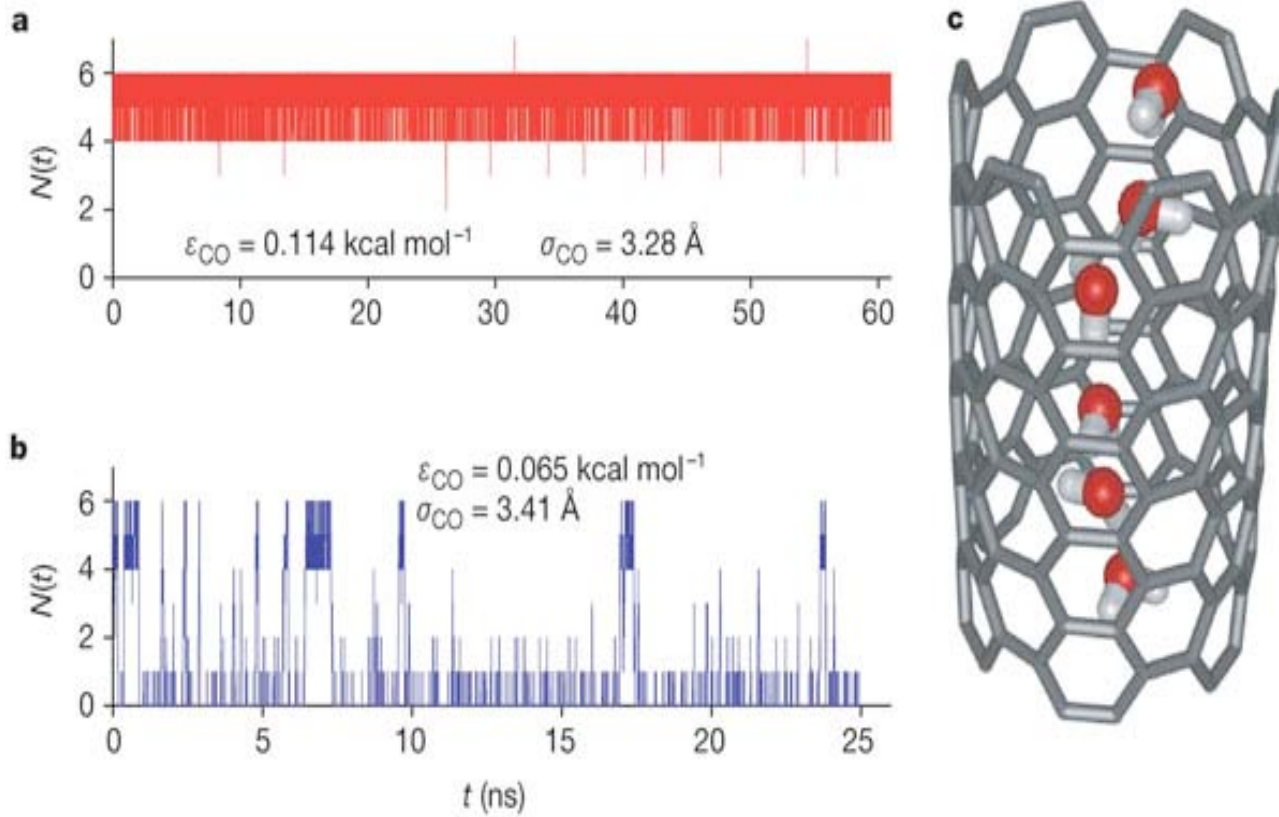
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Water Single-files in Carbon Nanotubes

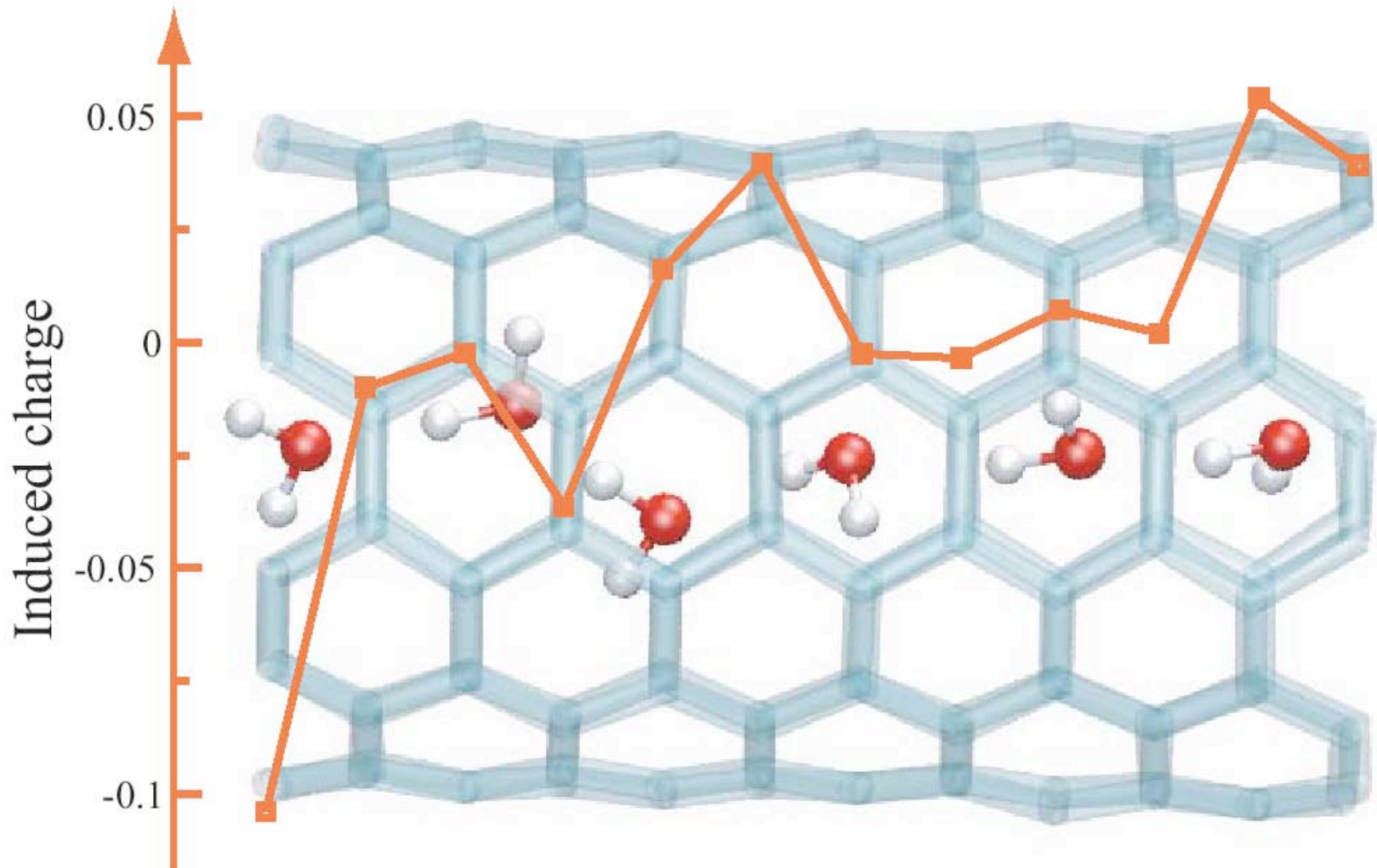


Water files form polarized chains in nanotubes

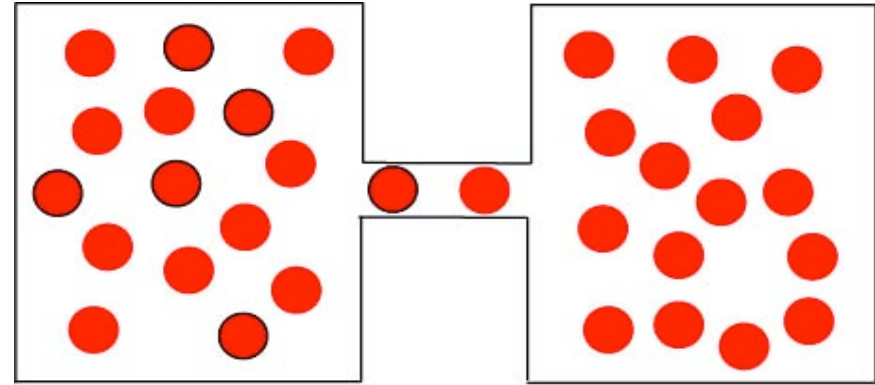
Water-Nanotube Interaction can be Easily Modified



Tight-Binding Self-Consistent Field Model for Nanotube Wall Electrons



Calculation of Diffusion Permeability from MD

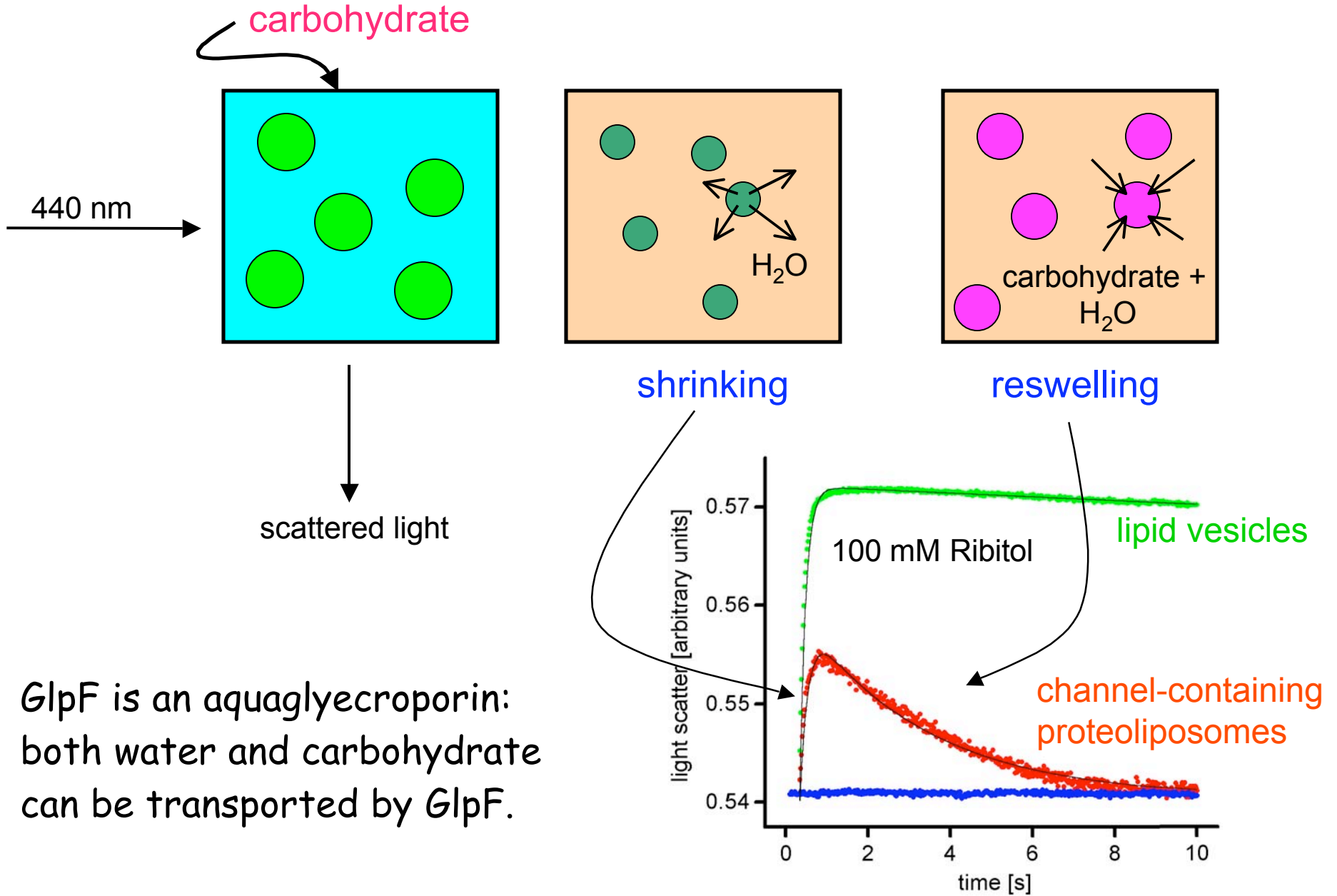


Φ_0 : number of water molecules crossing the channel from the left to the right in unit time

$$P_d = \frac{V_w}{N_A} \Phi_0$$

Φ_0 can be directly obtained through **equilibrium MD** simulation by counting “full permeation events”

Liposome Swelling Assay



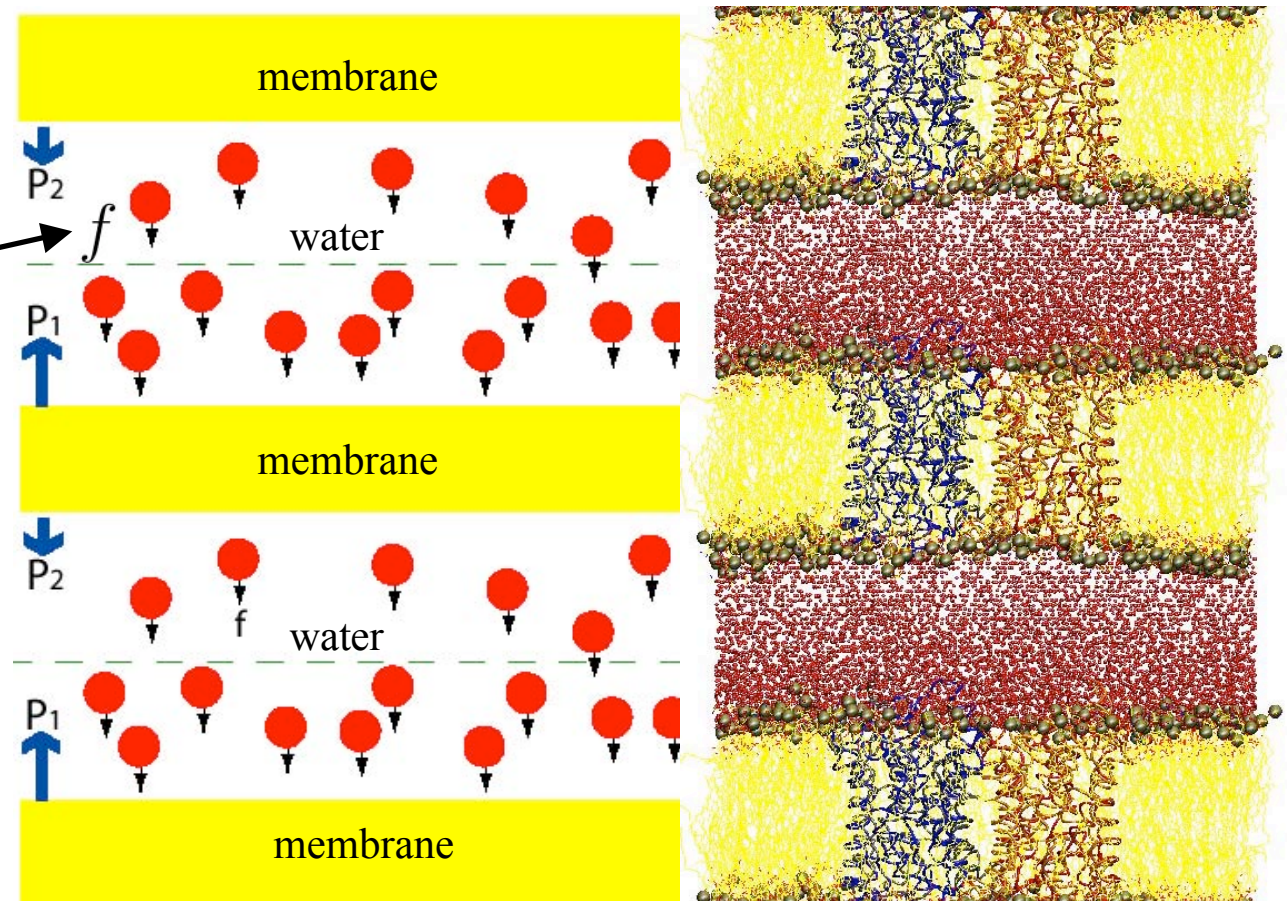
GlpF is an aquaglyecoporin: both water and carbohydrate can be transported by *GlpF*.

Realizing a Pressure Difference in a Periodic System

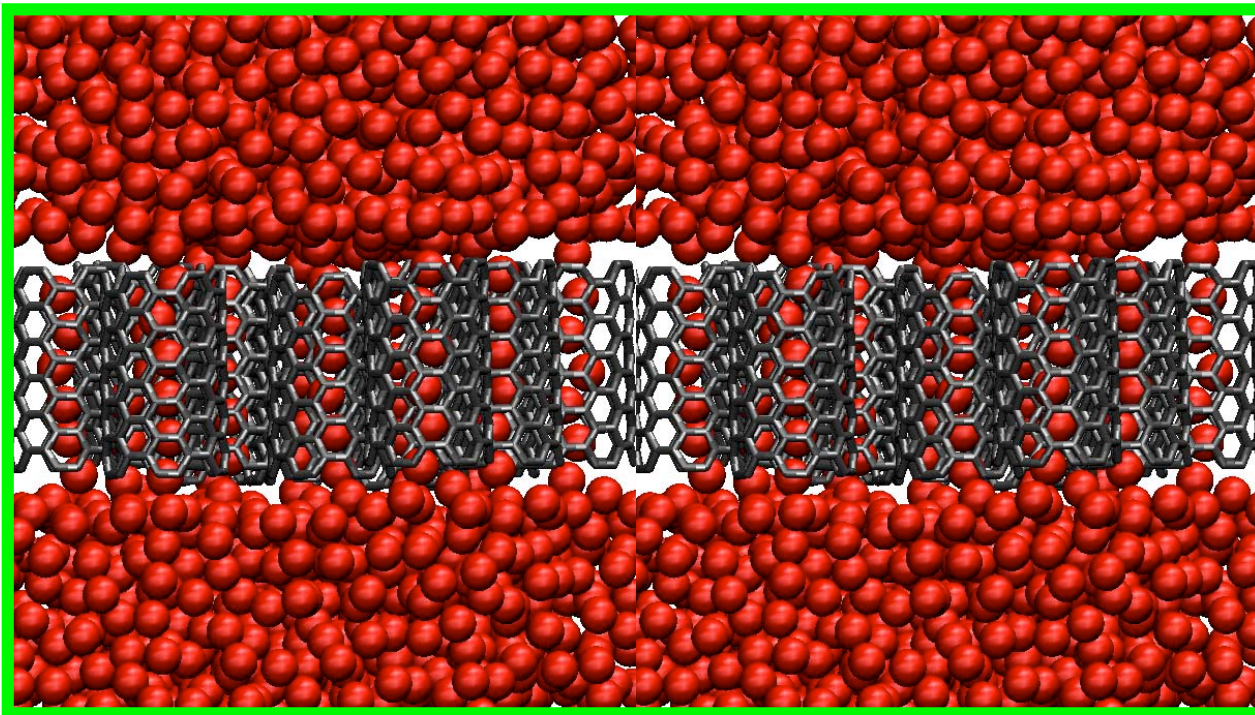
Fangqiang Zhu

f is the force on each water molecule, for n water molecules

The overall translation of the system is prevented by applying constraints or counter forces to the membrane.



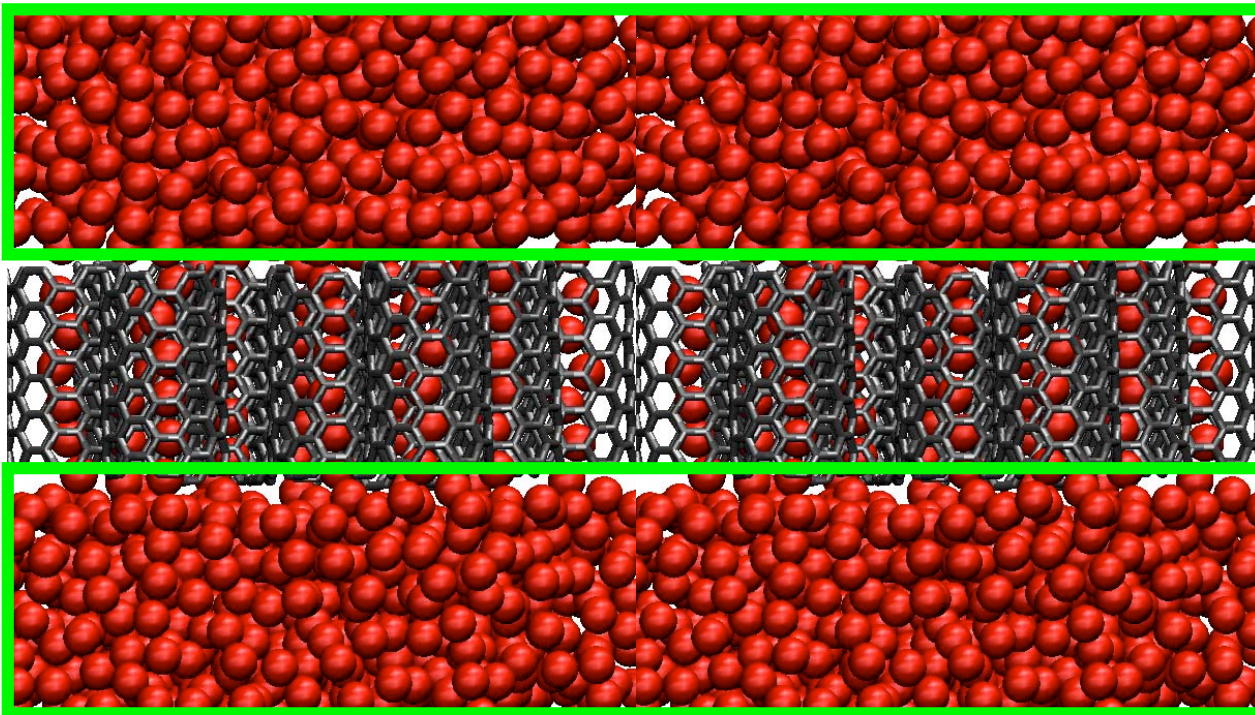
Applying a Pressure Difference Across the Membrane



Applying force on all water molecules.

Not a good idea!

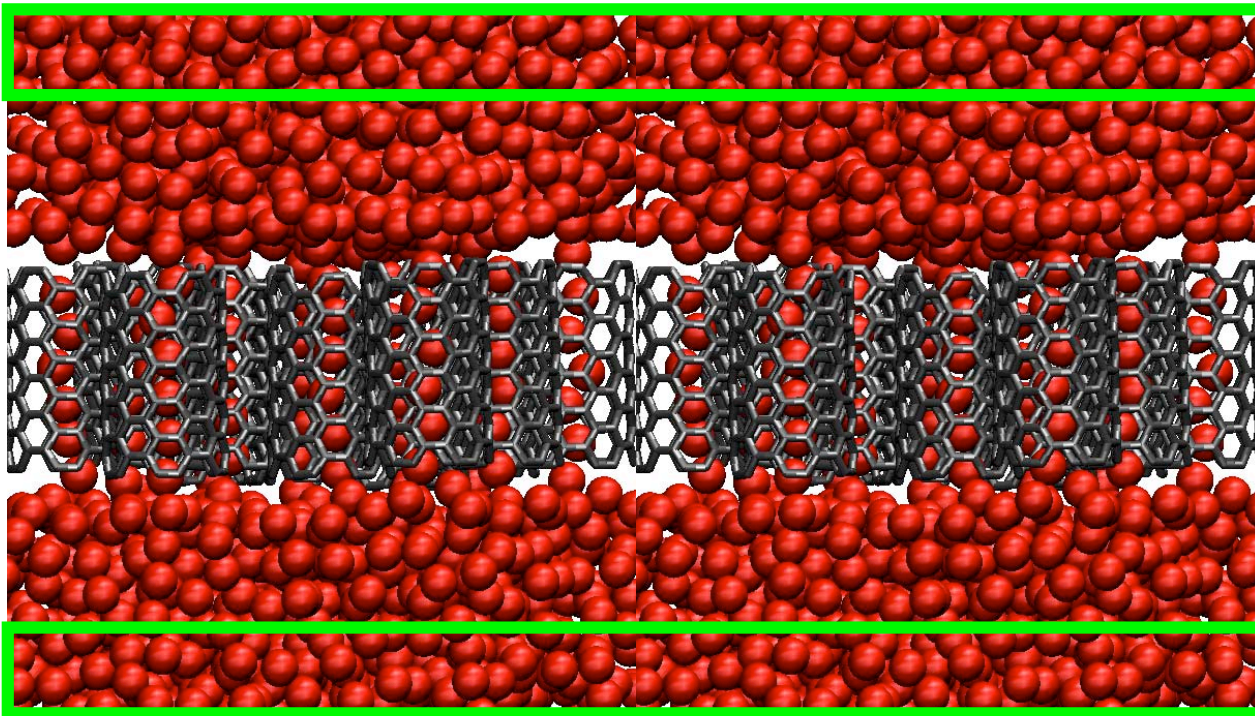
Applying a Pressure Difference Across the Membrane



Applying force on bulk water only.

Very good

Applying a Pressure Difference Across the Membrane

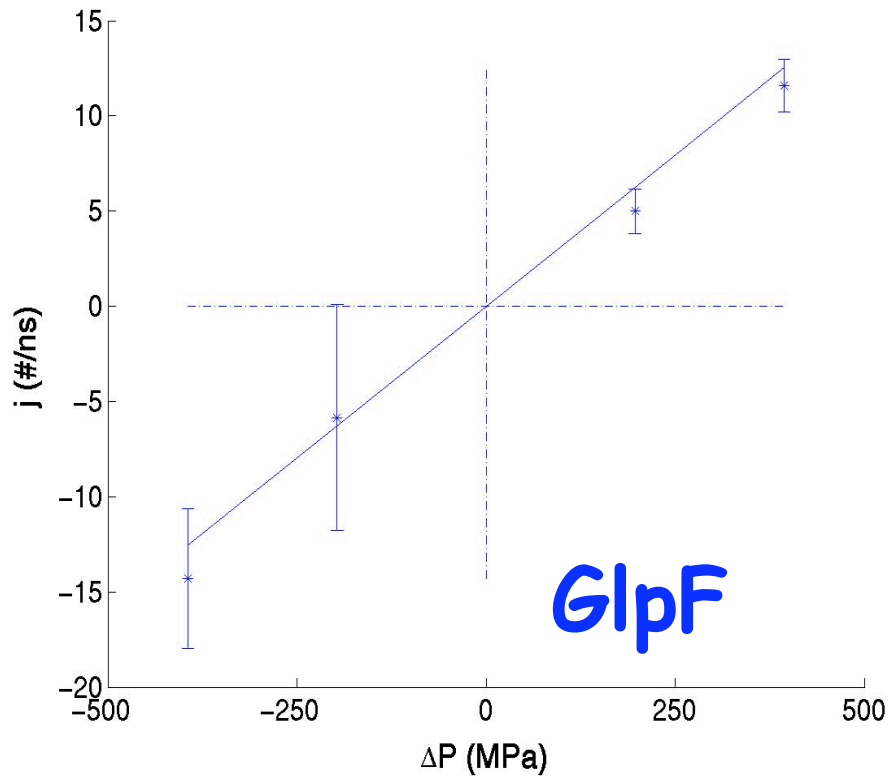


Applying force only on a slab of water in bulk.

Excellent

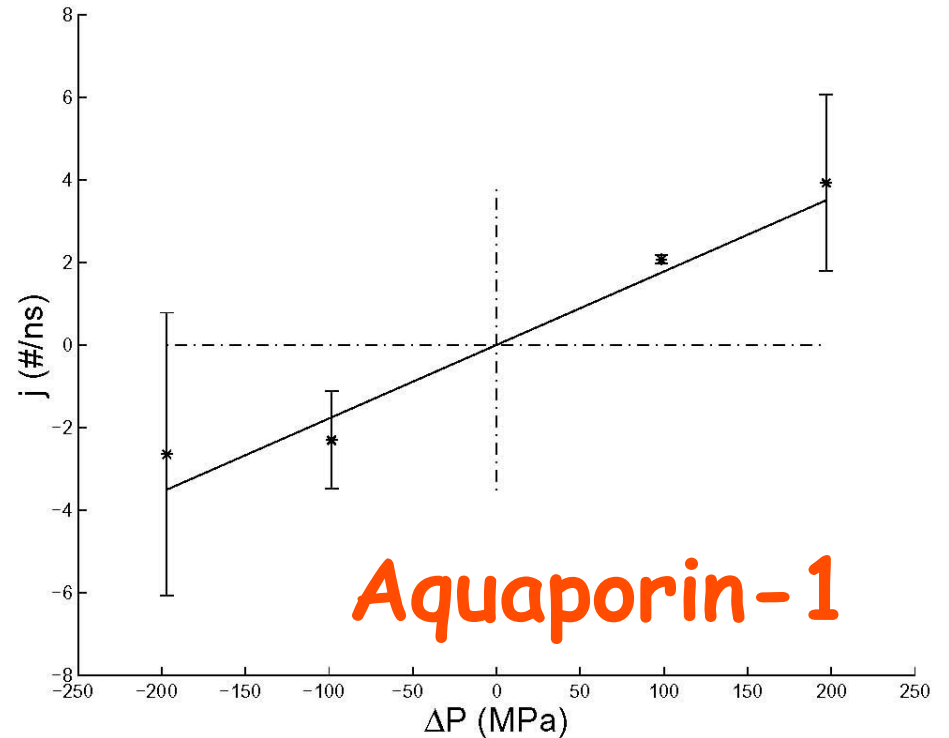
P_f can be calculated from these simulations

Calculation of osmotic permeability of water channels



GlpF

$p_f: 1.4 \times 10^{-13} \text{ cm}^3/\text{s}$



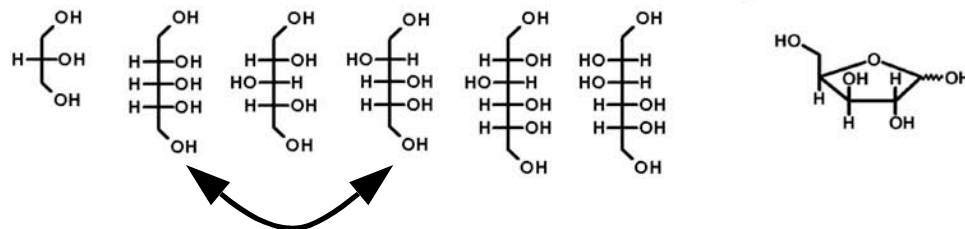
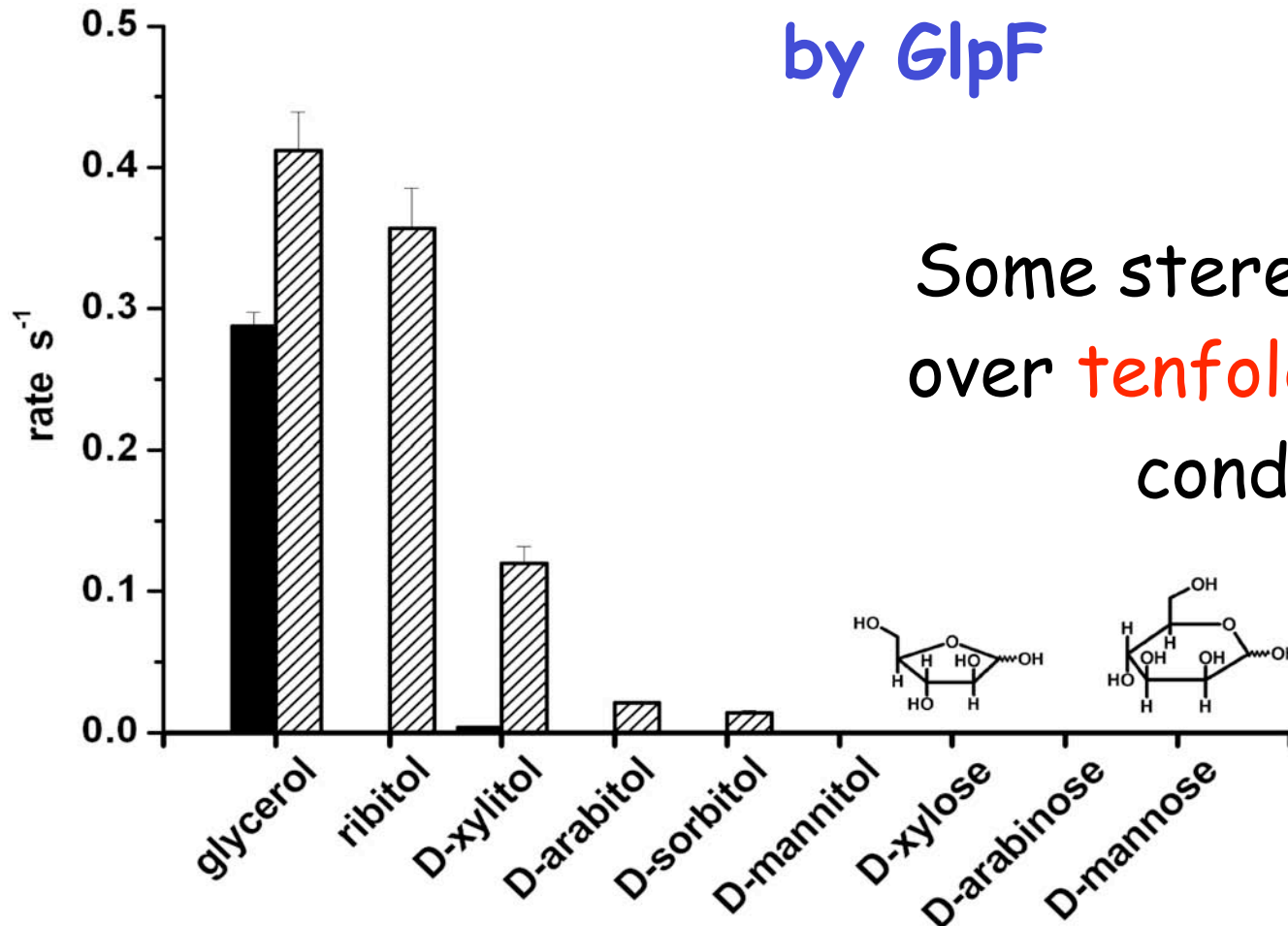
Aquaporin-1

$p_f: 7.0 \pm 0.9 \times 10^{-14} \text{ cm}^3/\text{s}$

Exp: $5.4 - 11.7 \times 10^{-14} \text{ cm}^3/\text{s}$

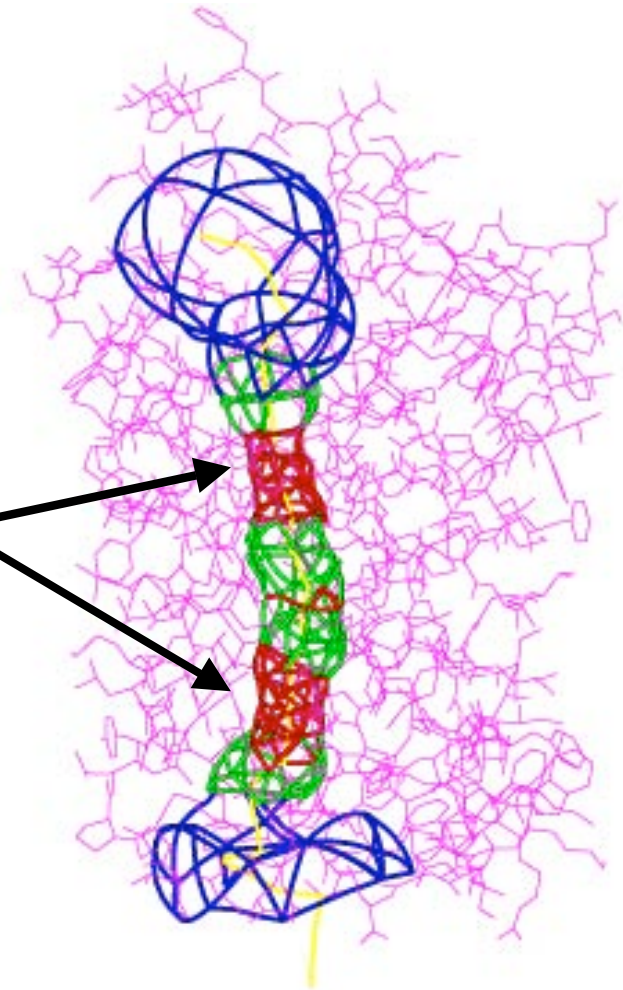
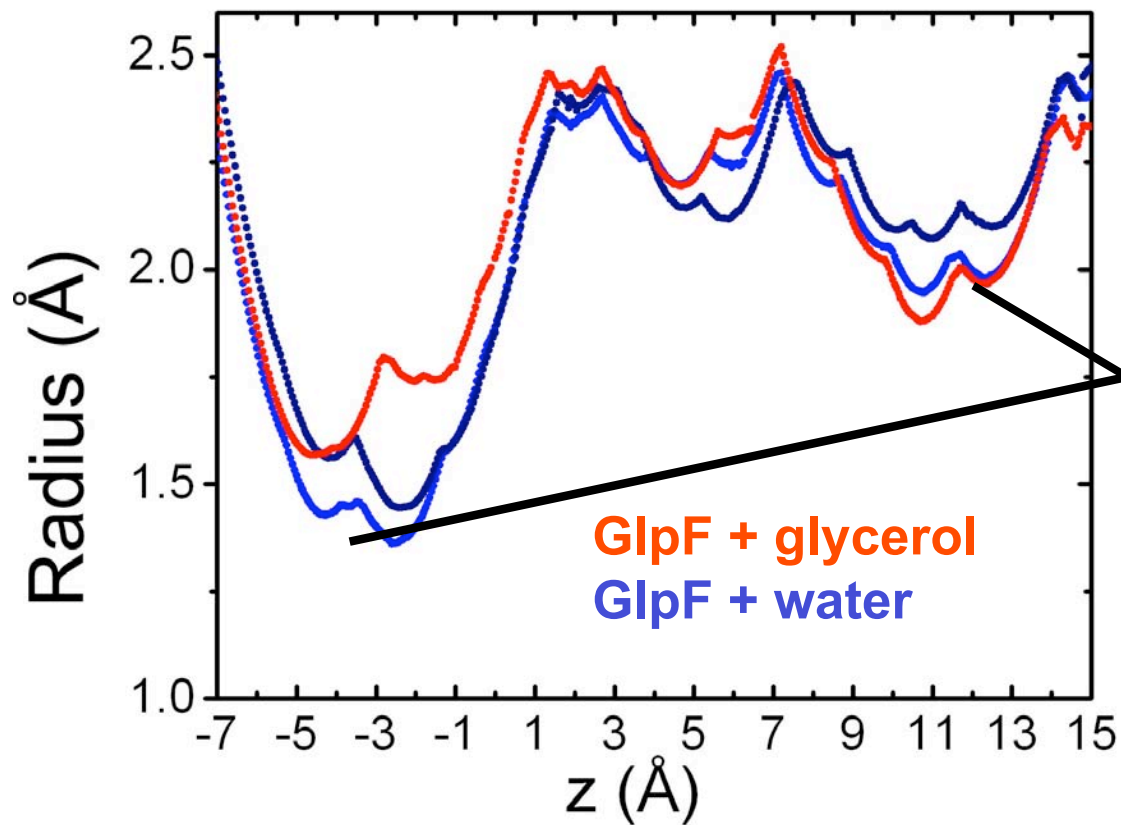
Stereoselective Transport of Carbohydrates by GlpF

Some stereoisomers show over **tenfold** difference in conductivity.



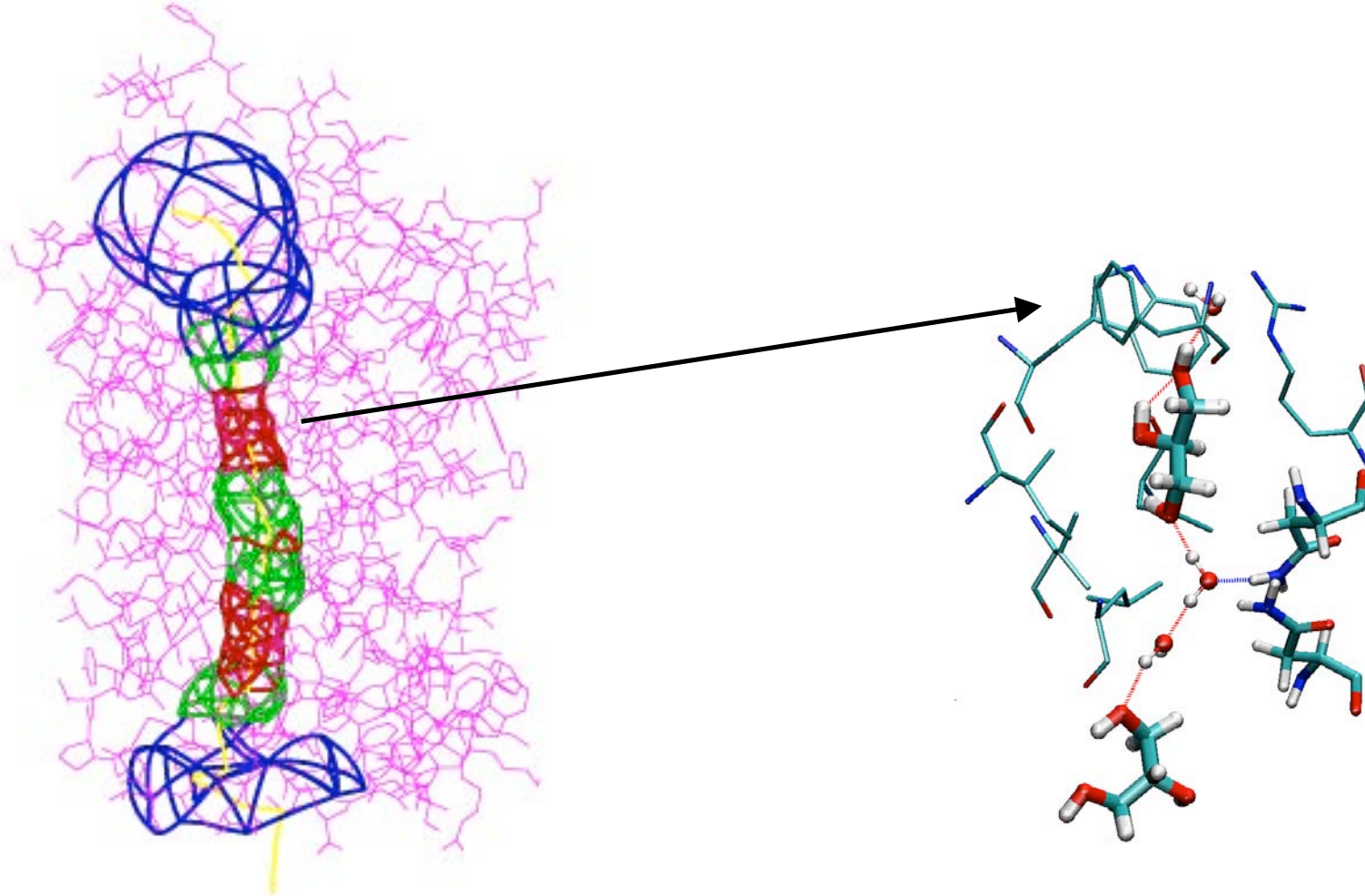
stereoisomers

Channel Constriction



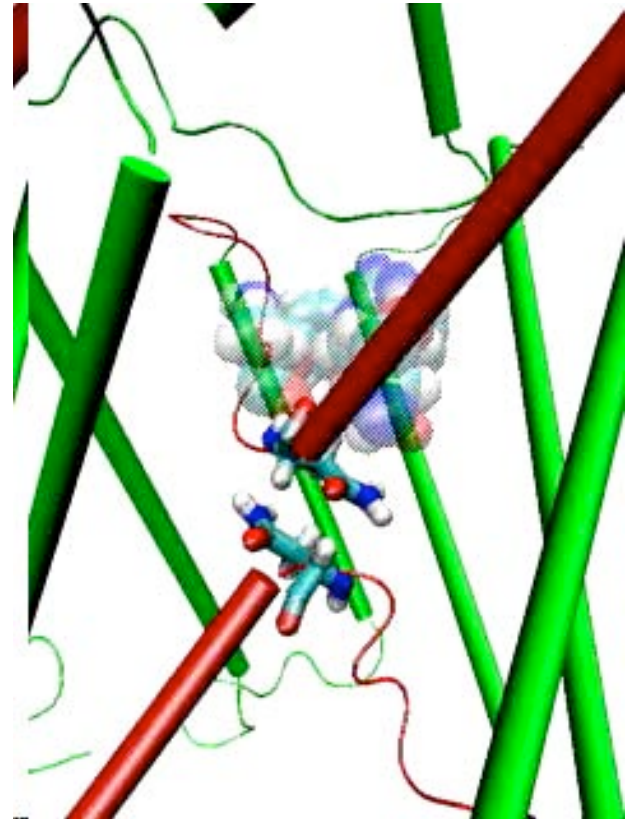
red < 2.3 Å
2.3 Å > green > 3.5 Å
blue > 3.5 Å

Selectivity filter

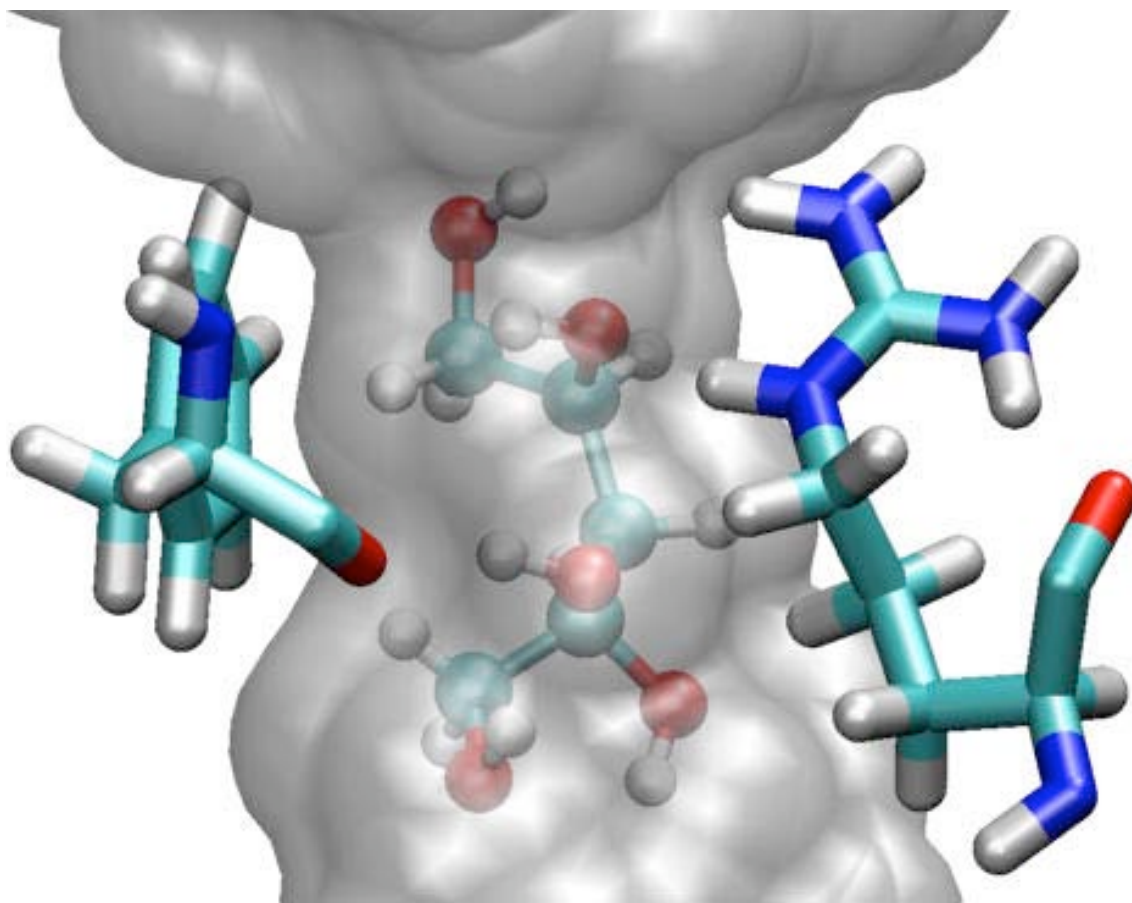


Interactive Molecular Dynamics

VMD \longleftrightarrow **NAMD**

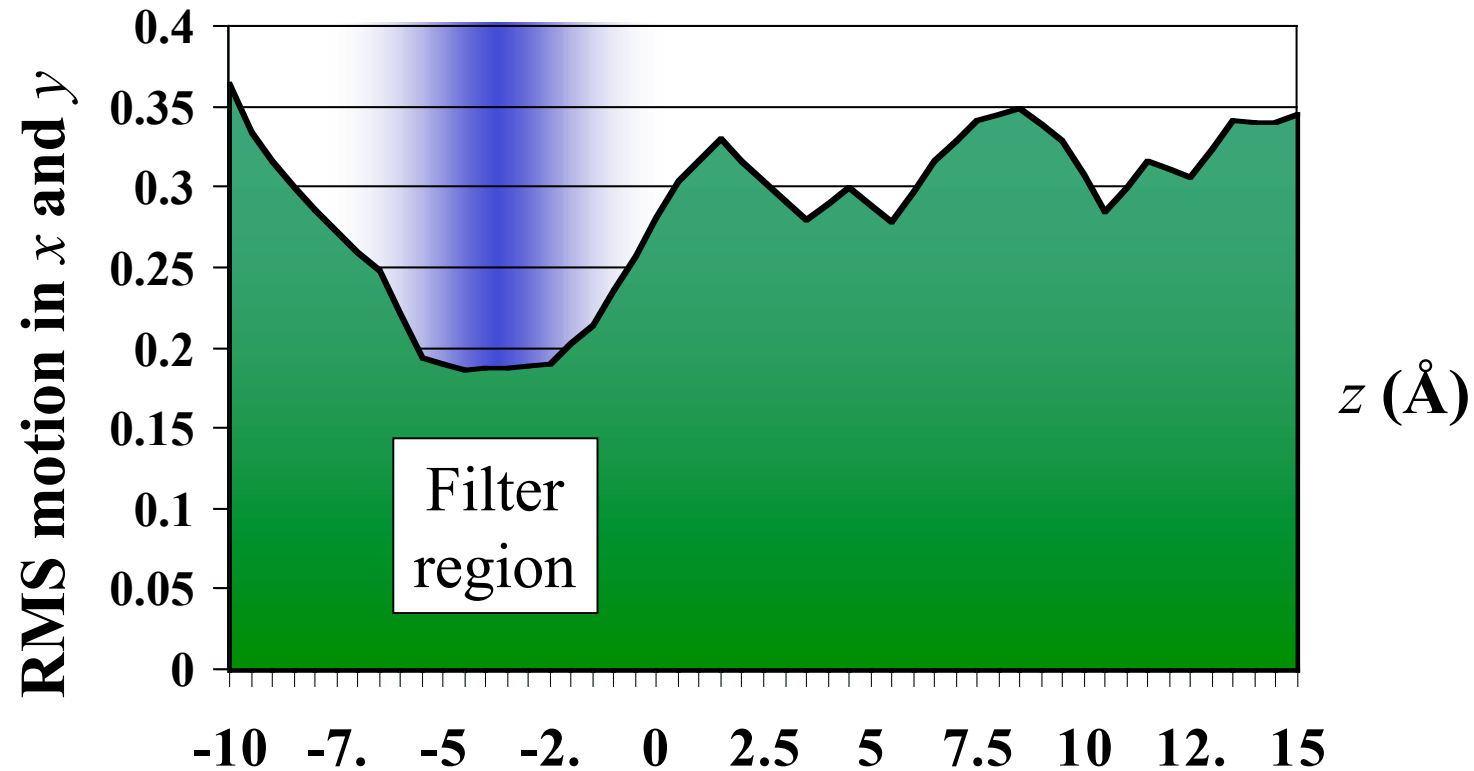


Observed Induced Fit in Filter



Confinement in Filter

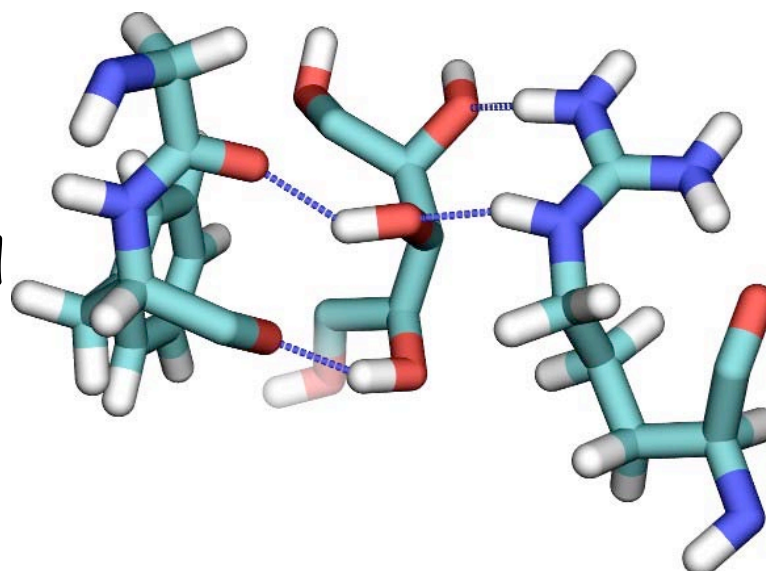
- Selection occurs in most constrained region.
- Caused by the locking mechanism.



Evidence for Stereoselectivity

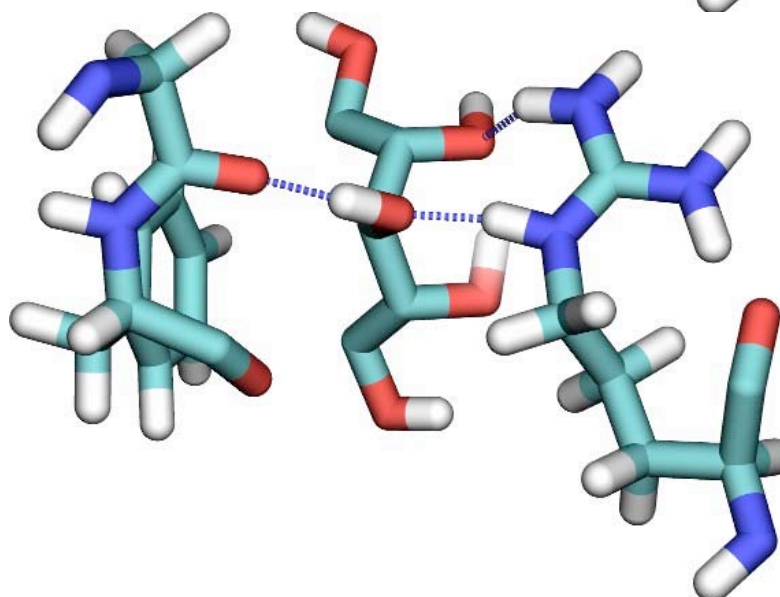
Ribitol

Optimal hydrogen bonding and hydrophobic matching



Arabitol

10 times slower



Dipole Reversal in Channel

- Dipole reversal pattern matches water.
- Selects large molecules with flexible dipole.

