Molecular Dynamics Simulation of Membrane Channels

Part III. Nanotubes

Theory, Methodology

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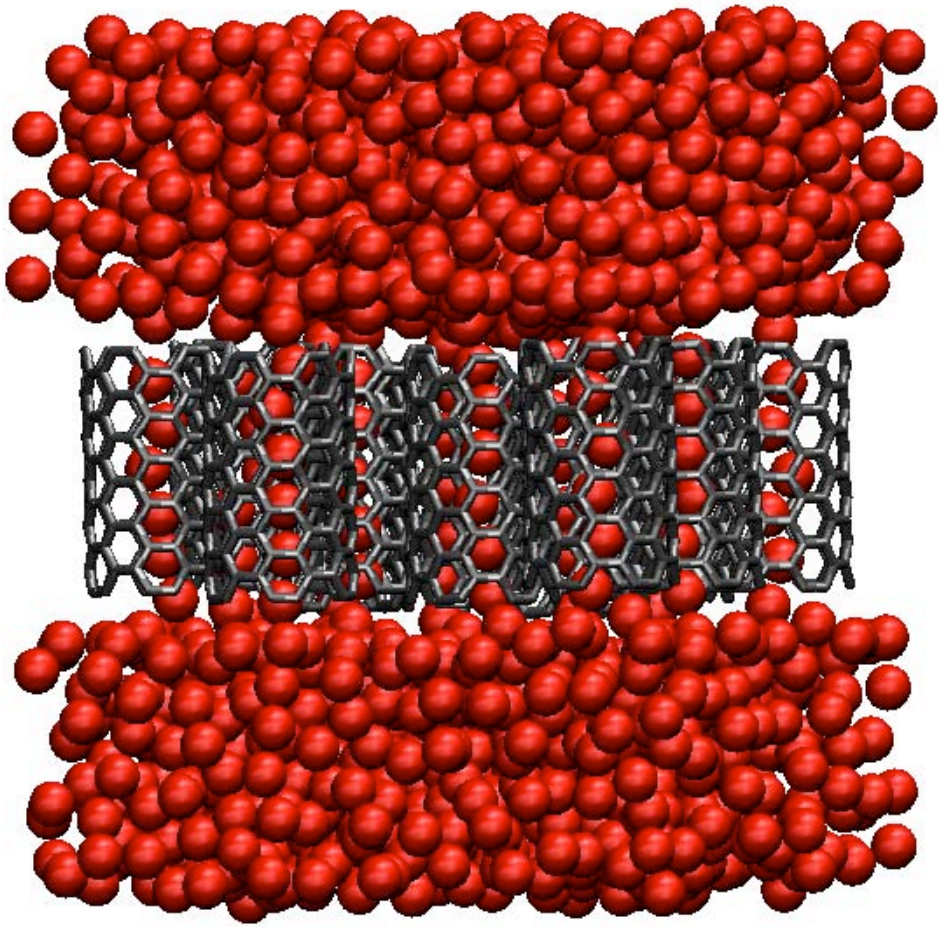
Carbon Nanotubes
Hydrophobic channels - Perfect Models for Membrane Water Channels

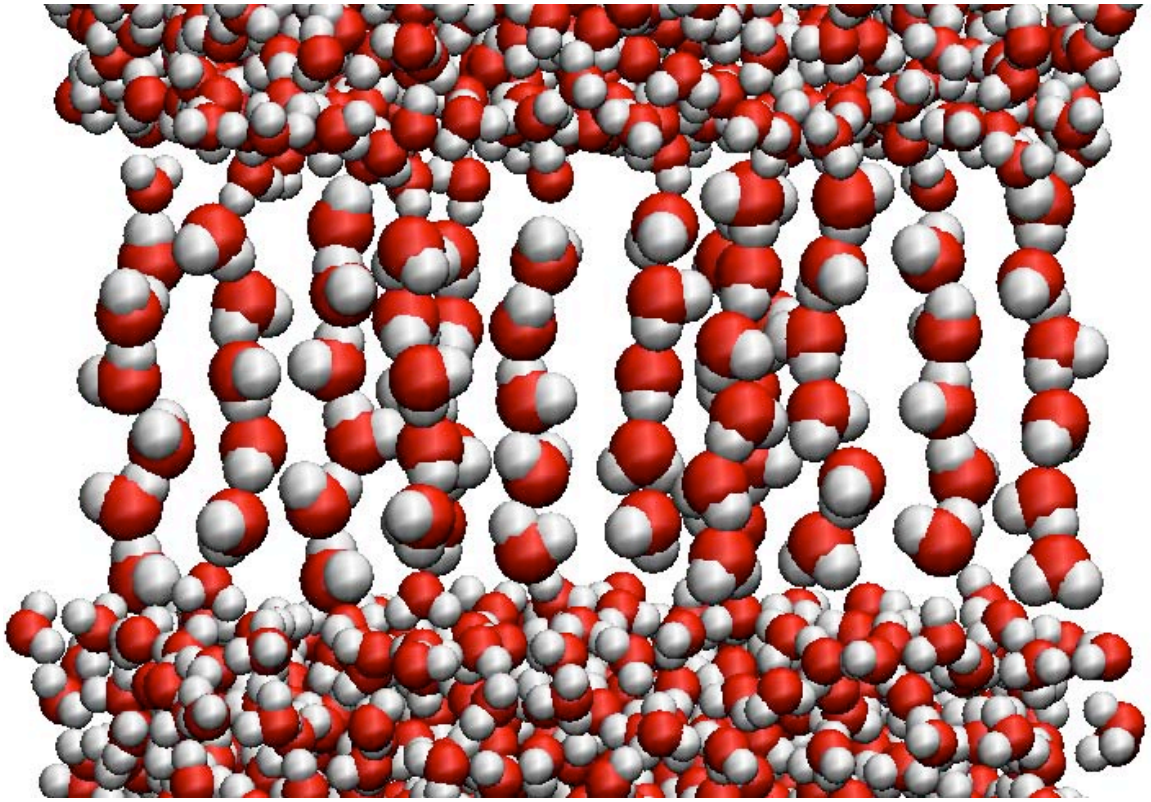


A balance between the size and hydrophobicity

Carbon Nanotubes
Hydrophobic channels - Perfect Models for Membrane Water Channels

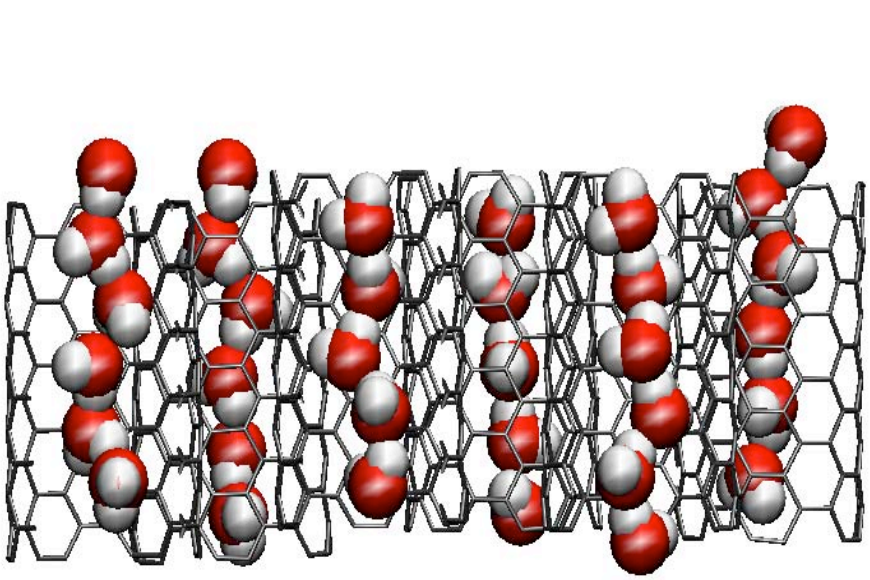
- Much better statistics
- No need for membrane and lipid molecules

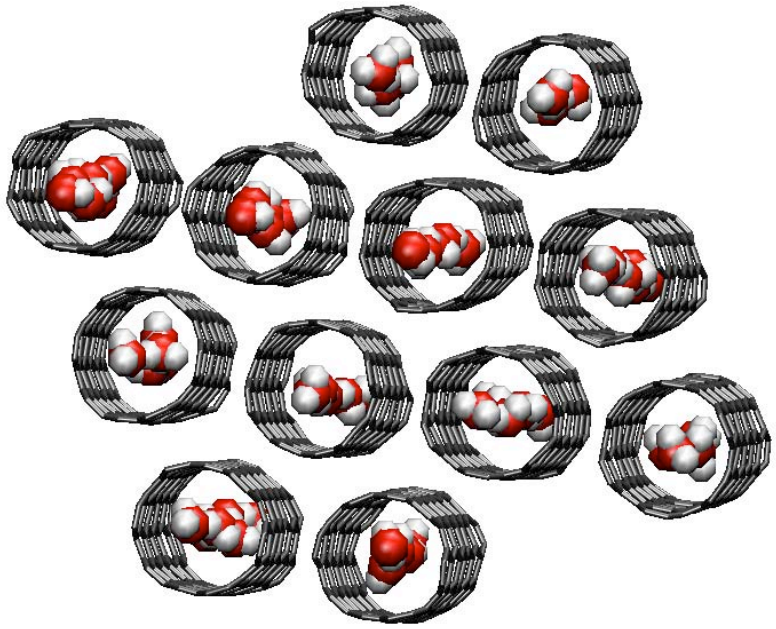
Carbon Nanotubes
Hydrophobic channels - Perfect Models for Membrane Water Channels



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

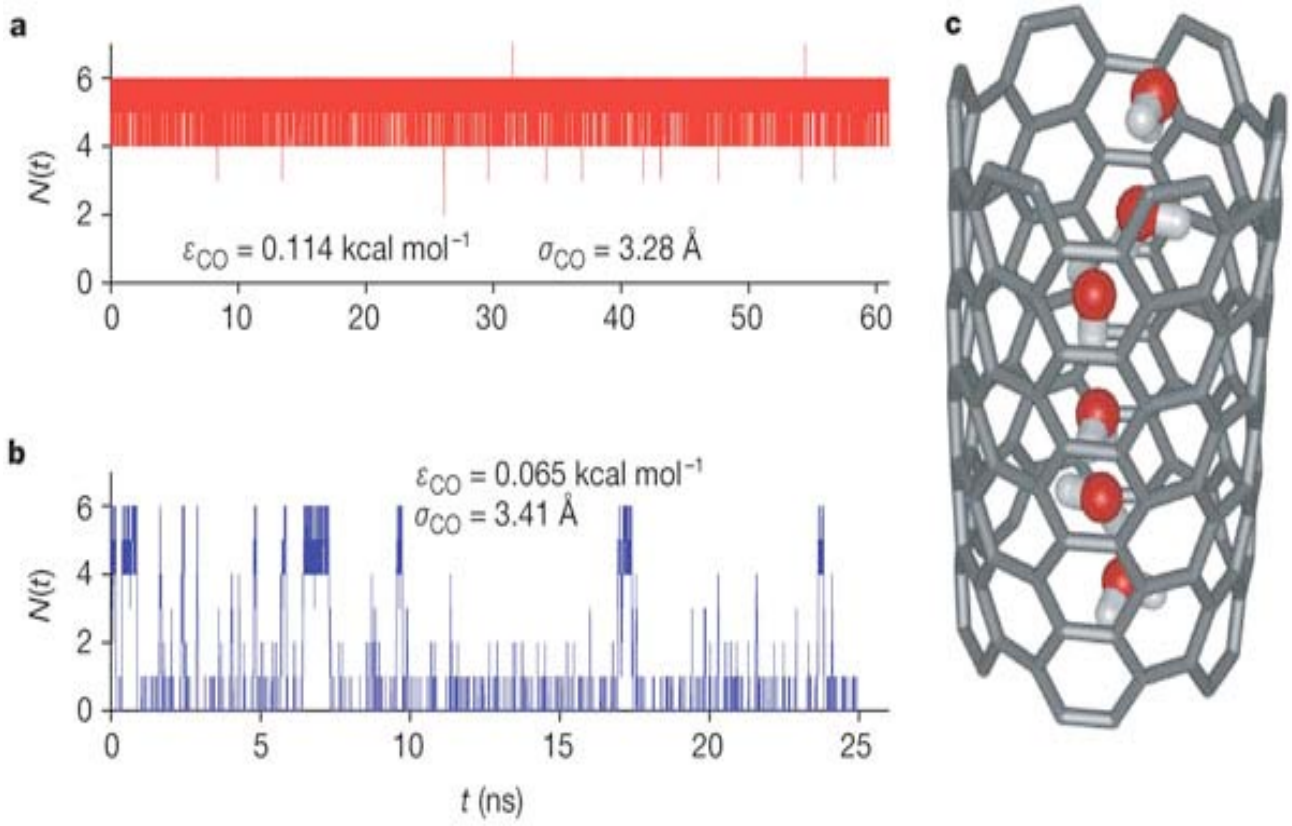
Water Single-files in Carbon Nanotubes





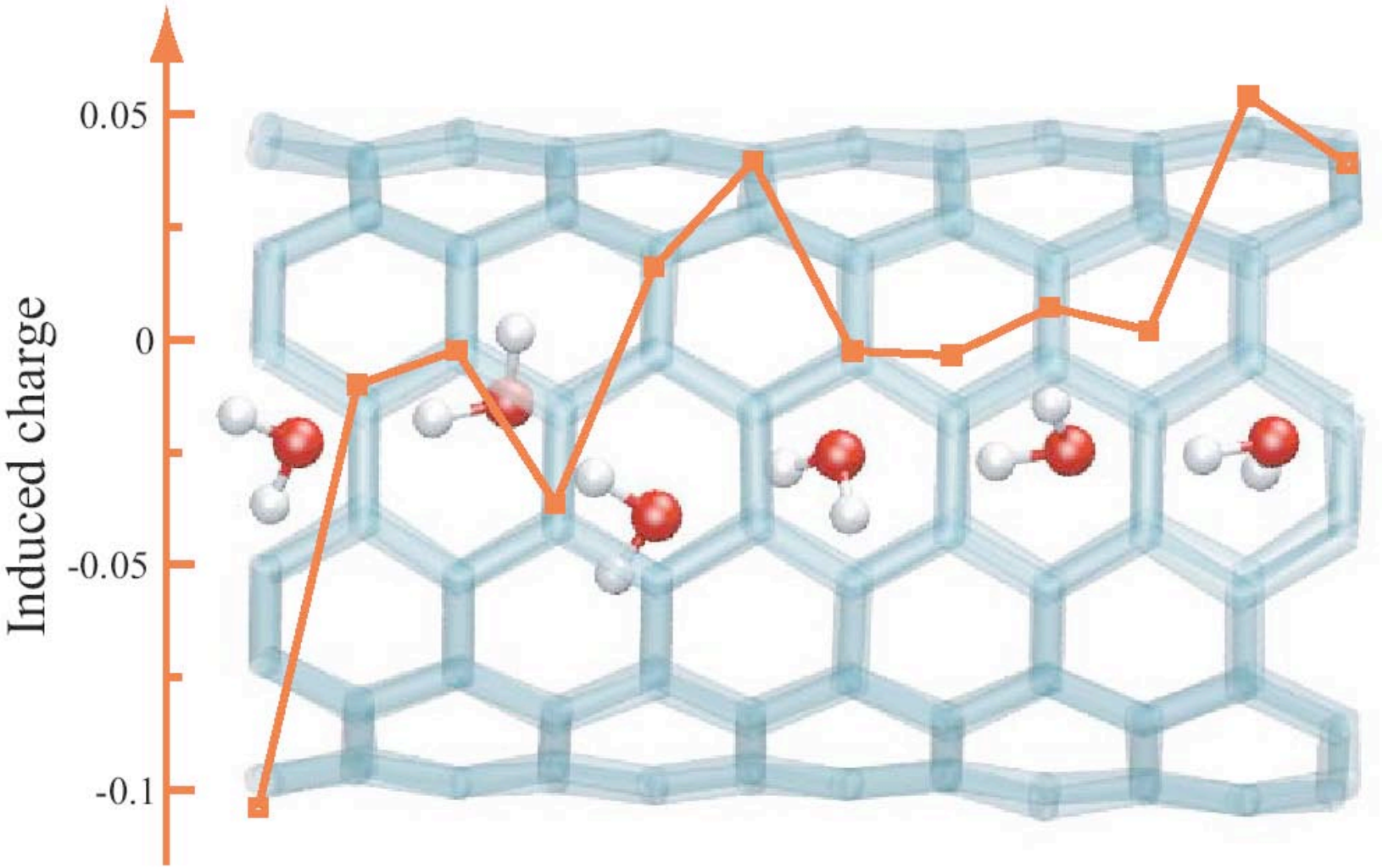
Water files form polarized chains in nanotubes

Water-Nanotube Interaction can be Easily Modified

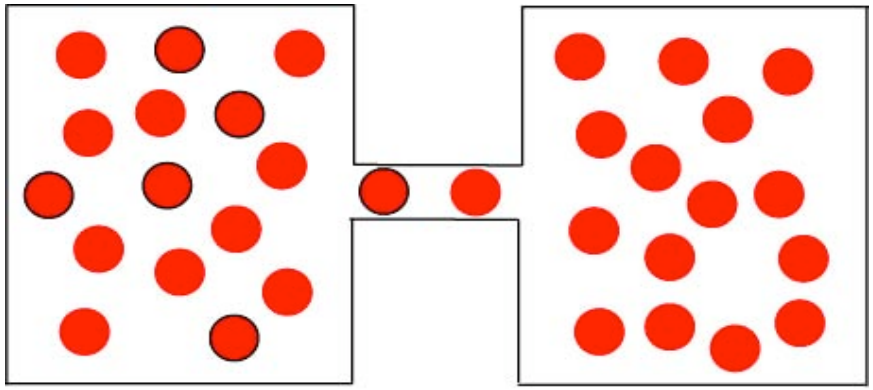


Hummer, et. al., Nature, 414: 188-190, 2001

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



Calculation of Diffusion Permeability from MD

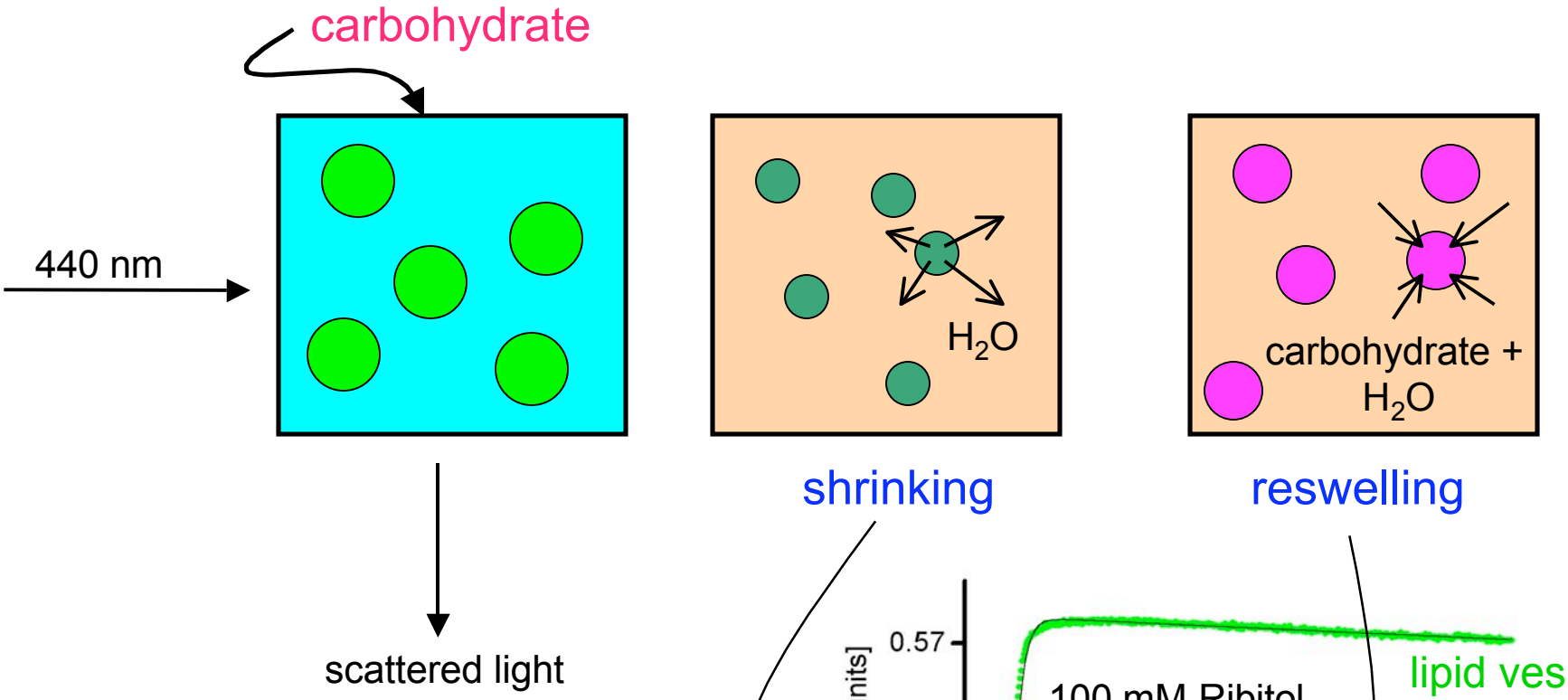


Φ_0: number of water molecules crossing the channel from the left to the right in unit time

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

Φ_0 can be directly obtained through equilibrium MD simulation by counting "full permeation events"

Liposome Swelling Assay



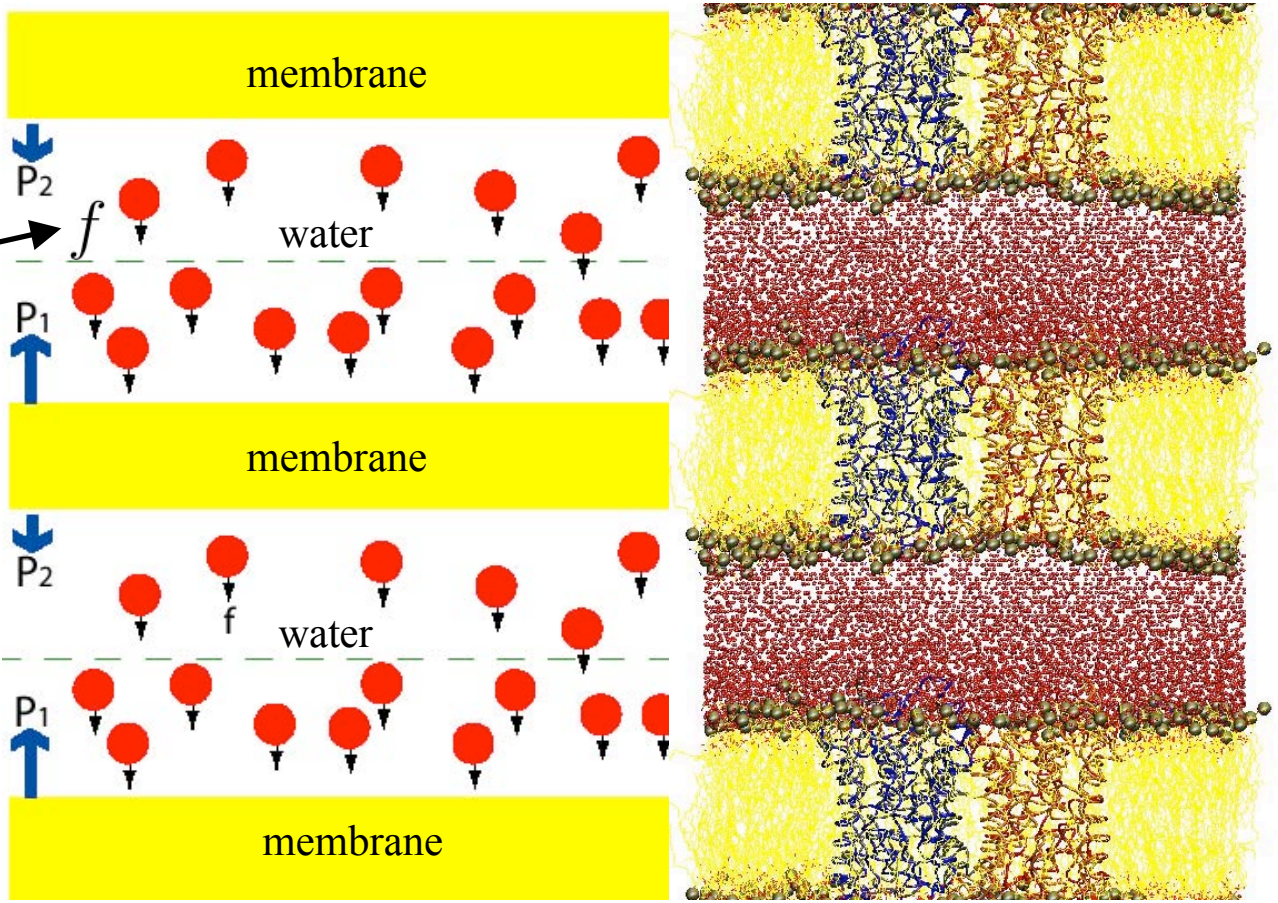
GlpF is an aquaglyecroporin: both water and carbohydrate can be transported by GlpF.

Realizing a Pressure Difference in a Periodic System

Fangqiang Zhu

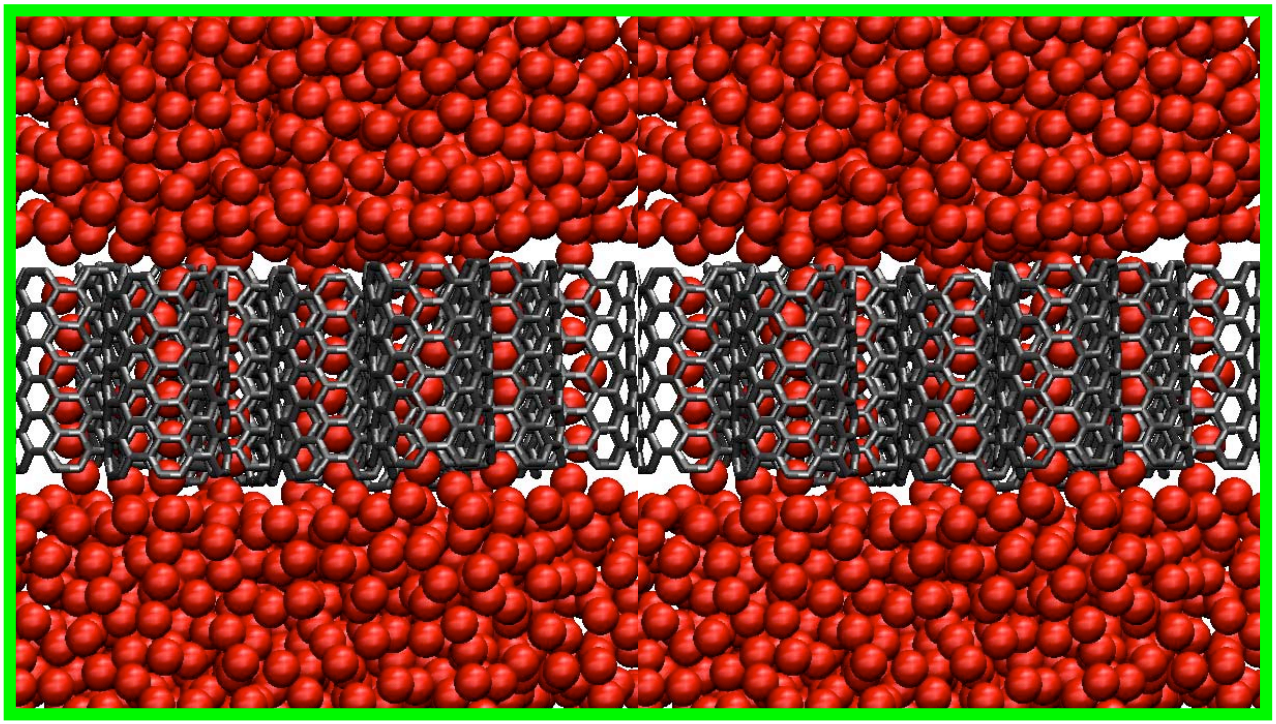
f is the force on each water molecule, for ***n*** water molecules

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



F. Zhu, et al., *Biophys. J.* 83, 154 (2002).

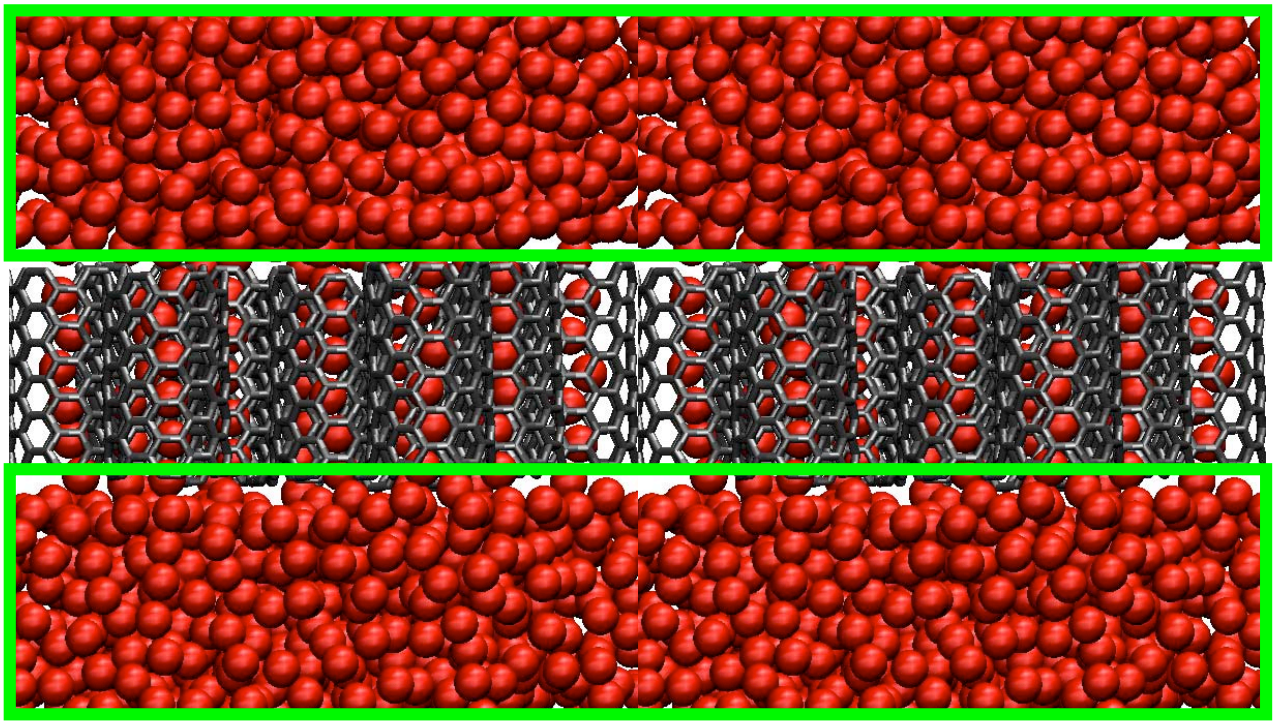
Applying a Pressure Difference Across the Membrane



Applying force on all water molecules.

Not a good idea!

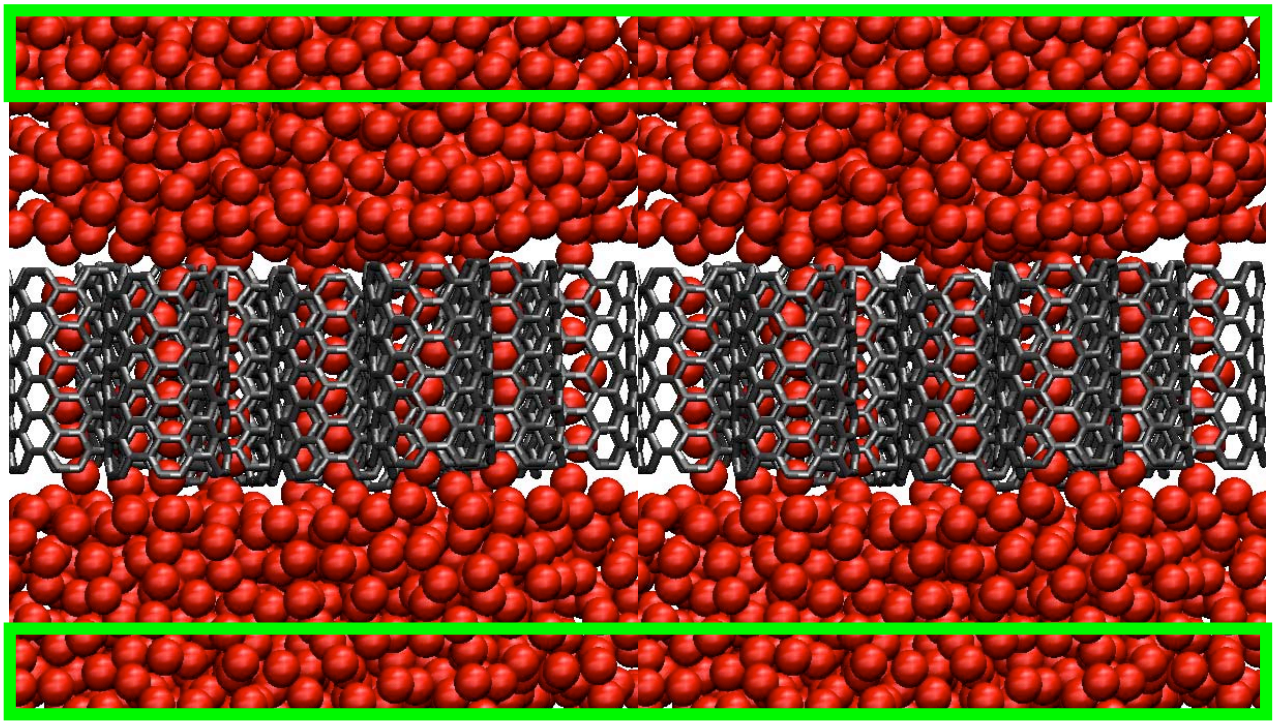
Applying a Pressure Difference Across the Membrane



Applying force on bulk water only.

Very good

Applying a Pressure Difference Across the Membrane

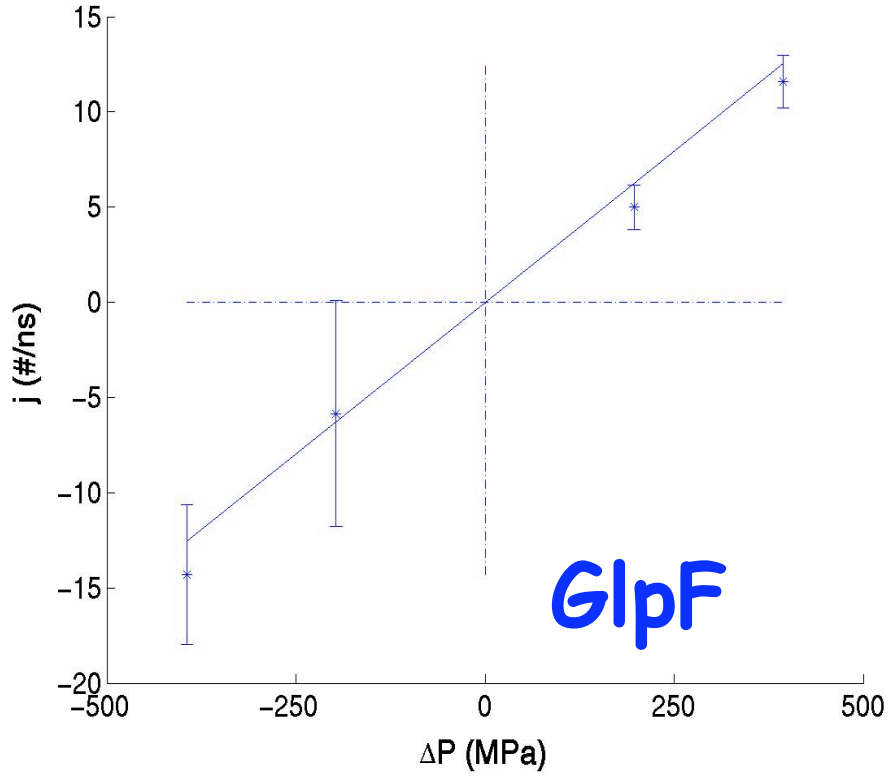


Applying force only on a slab of water in bulk.

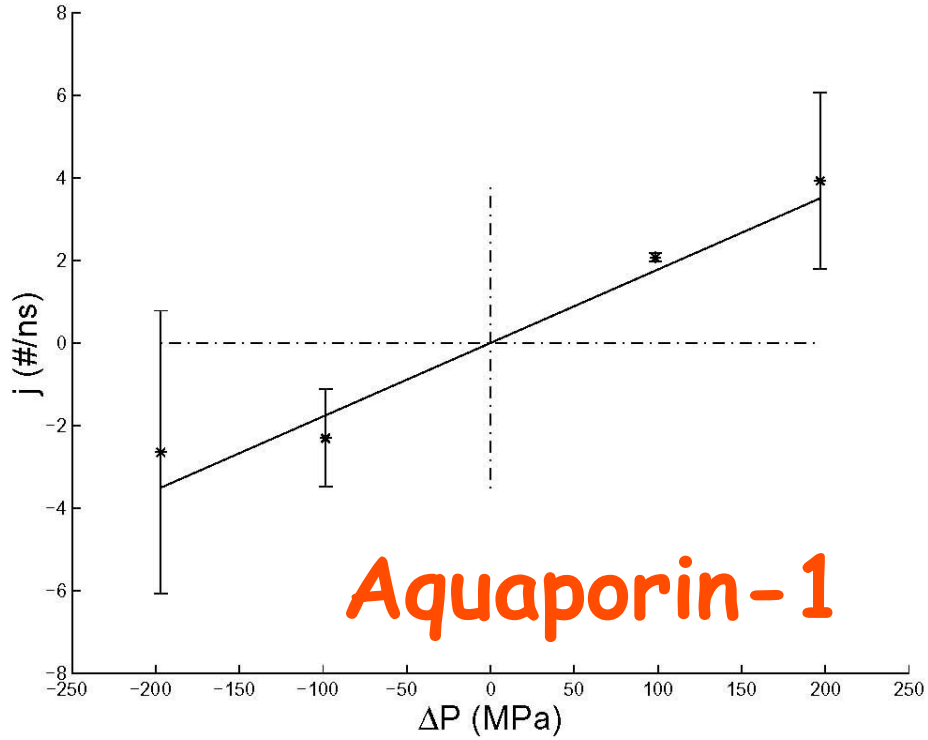
Excellent

P_f can be calculated from these simulations

Calculation of osmotic permeability of water channels

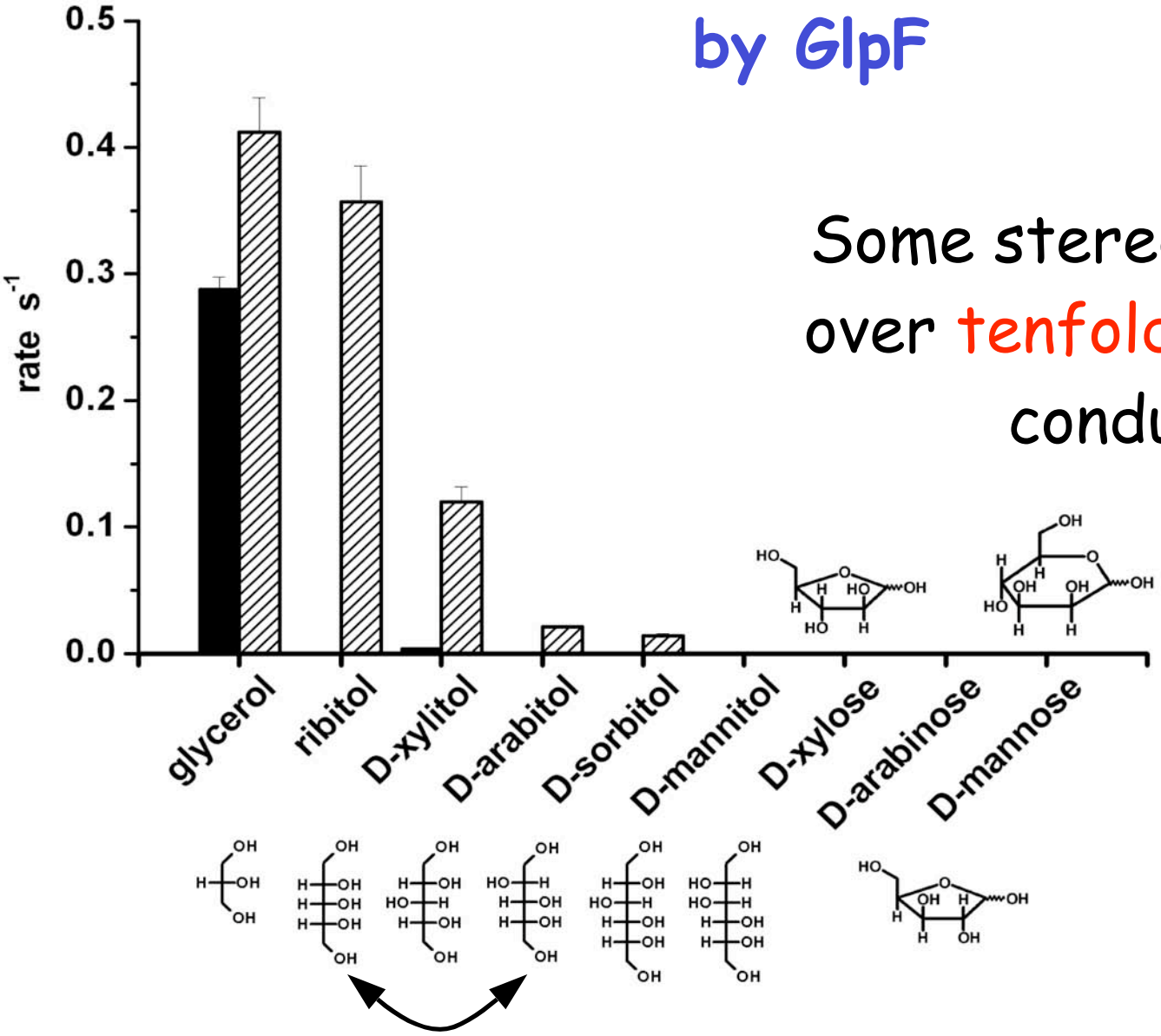


p_f: 1.4×10^{-13} cm^3/s



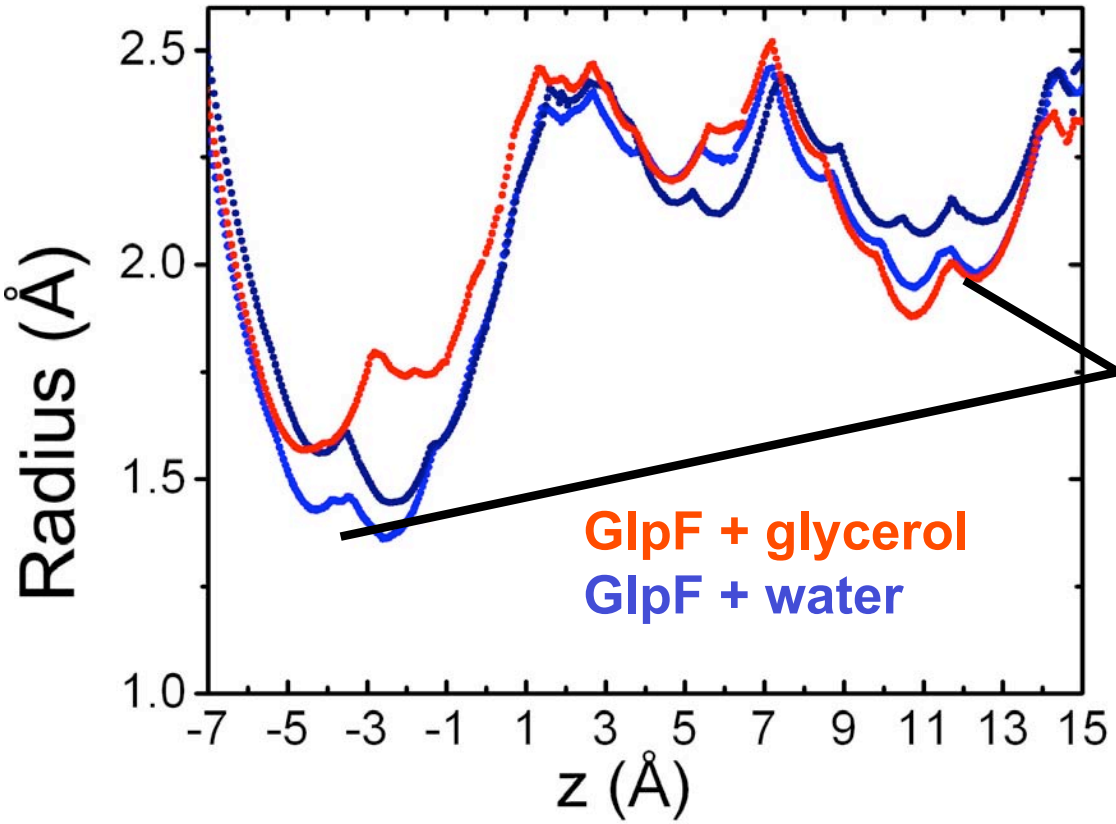
p_f: 7.0 ± 0.9 × 10^{-14} cm^3/s
Exp: 5.4 – 11.7 × 10^{-14} cm^3/s

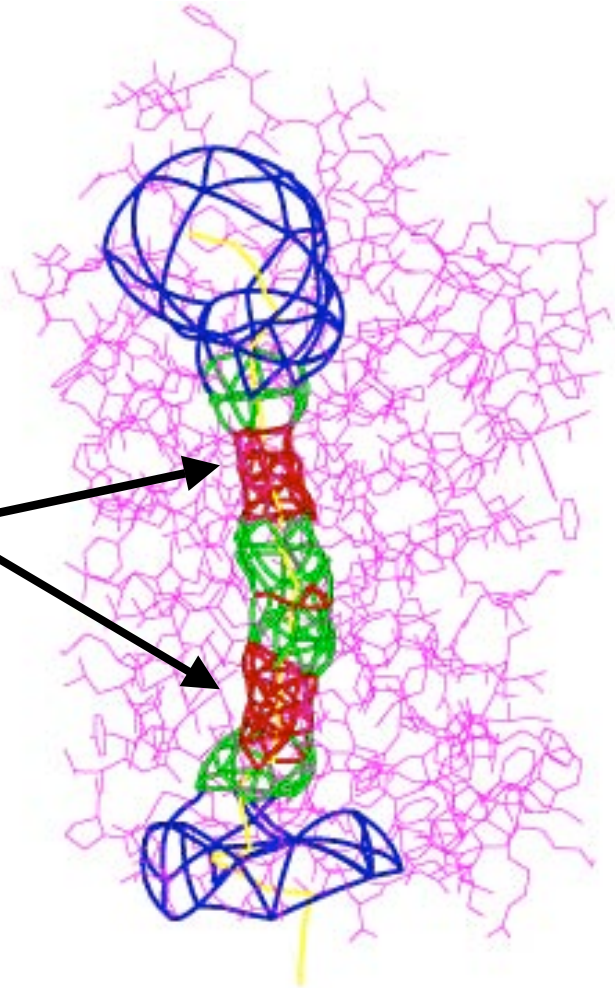
Stereoselective Transport of Carbohydrates by GlpF



Some stereoisomers show over tenfold difference in conductivity.

Channel Constriction

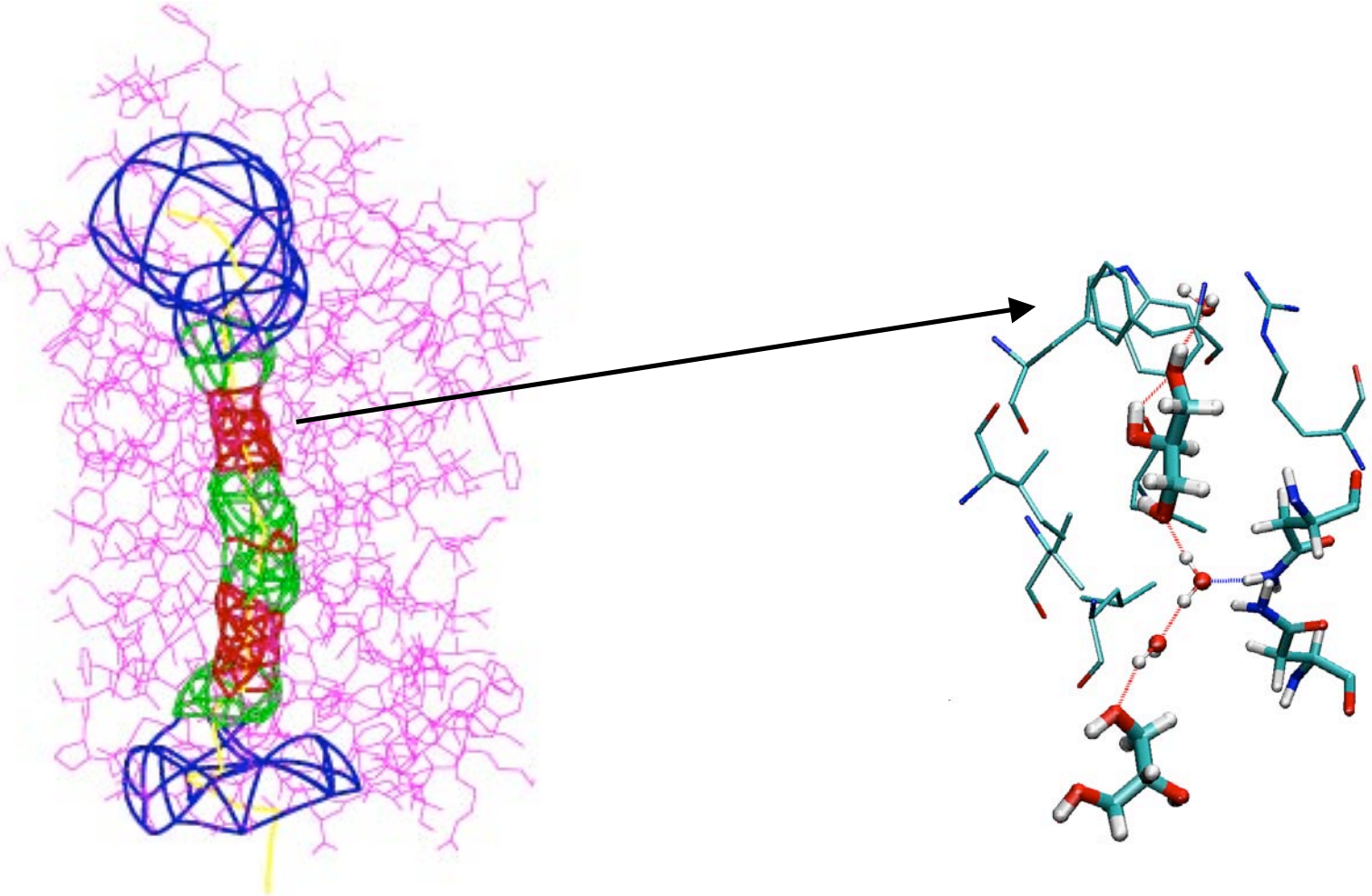




red < 2.3 Å
2.3 Å > green > 3.5 Å
blue > 3.5 Å

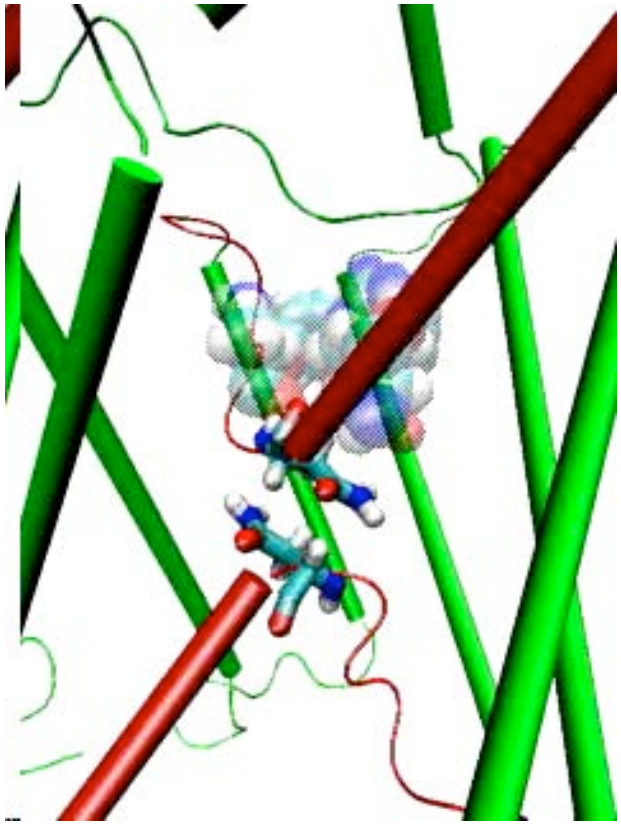
HOLE2: O. Smart et al., 1995

Selectivity filter

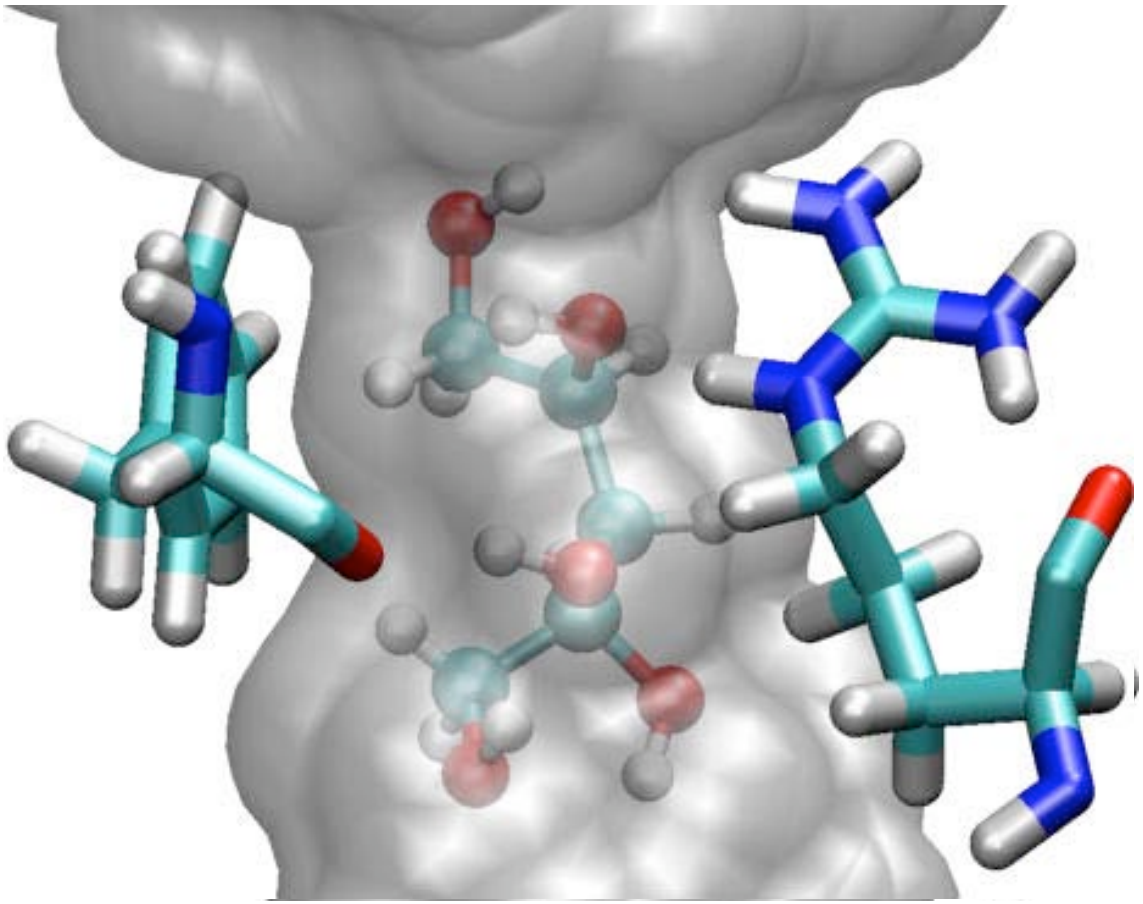


Interactive Molecular Dynamics

VMD ◄·····► NAMD

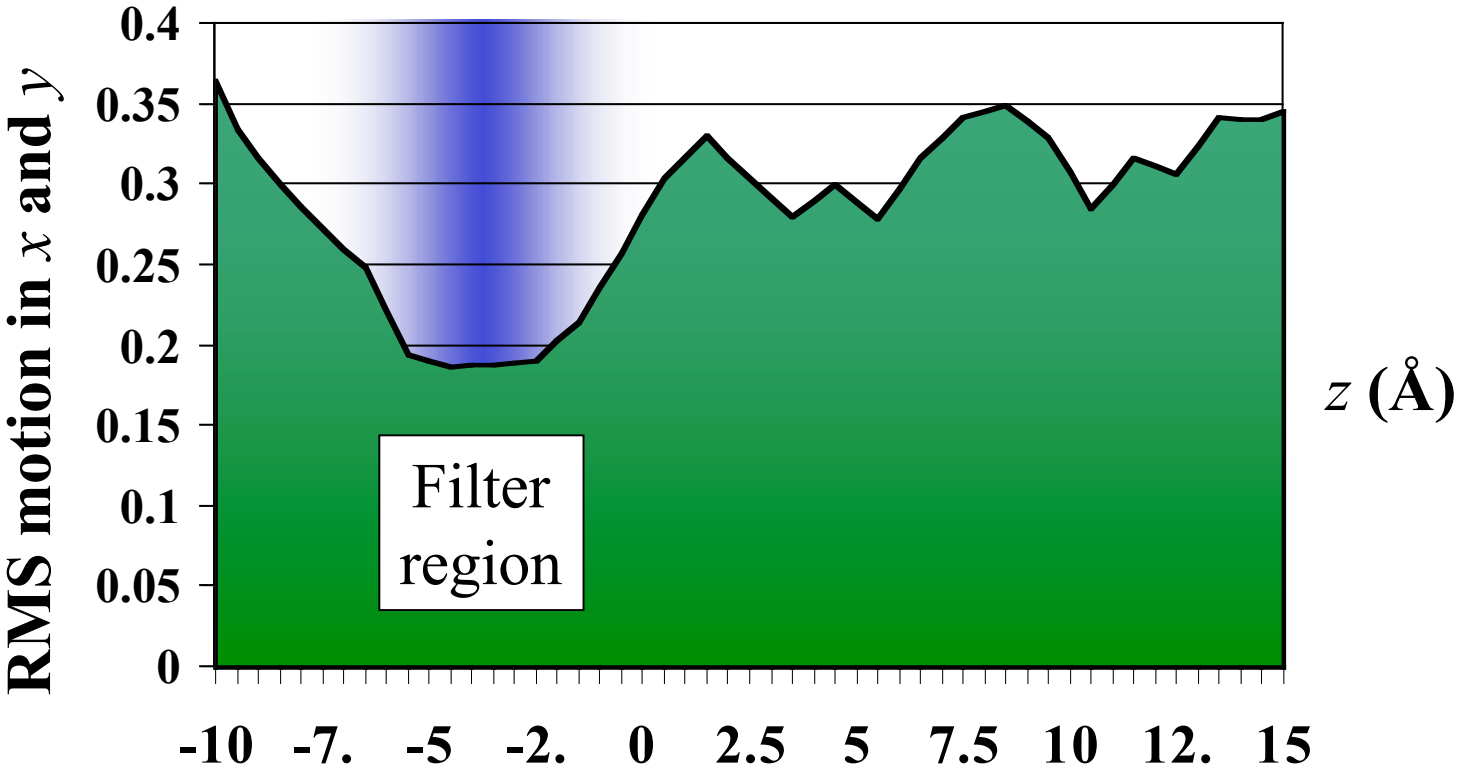


Observed Induced Fit in Filter



Confinement in Filter

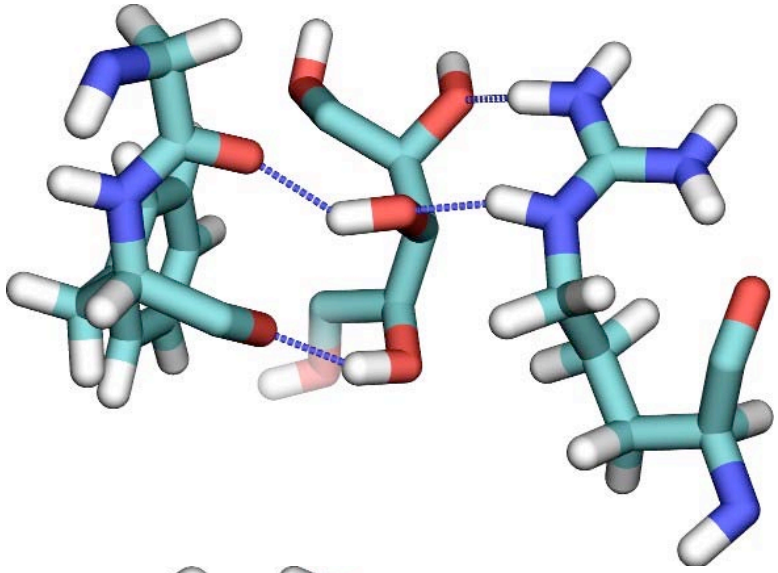
- Selection occurs in most constrained region.
- Caused by the locking mechanism.



Evidence for Stereoselectivity

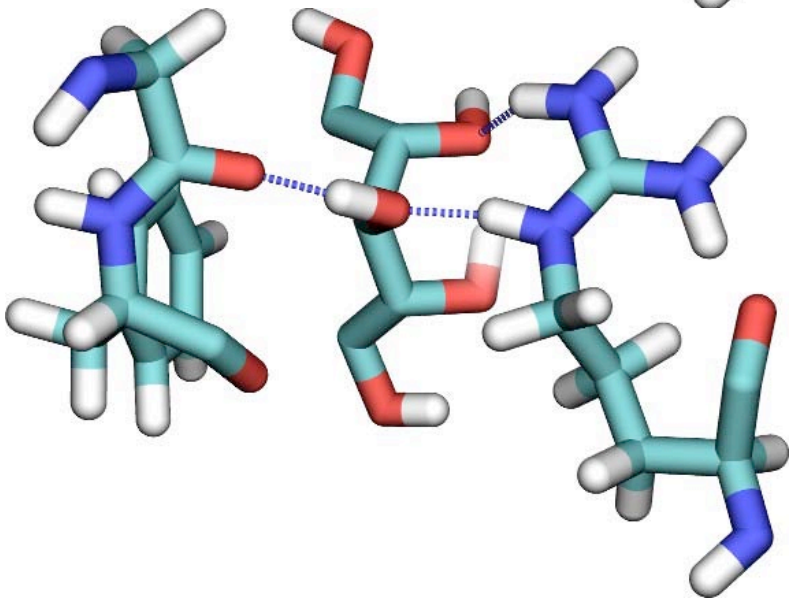
Ribitol

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.