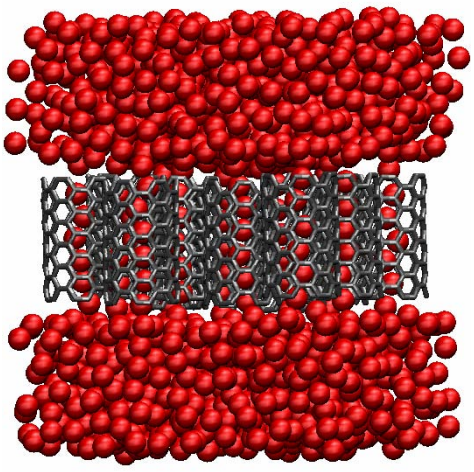
Simulating Membrane Channels

Part III. Nanotubes
Theory, Methodology

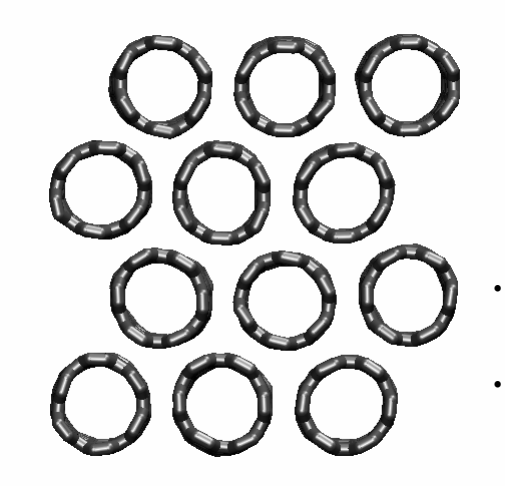
Theoretical and Computational Biophysics
Fall 2004, University of Illinois at Urbana-Champaign
http://www.ks.uiuc.edu/training/SumSchool03/

Carbon Nanotubes
Hydrophobic channels - Perfect Models for Membrane Water Channels



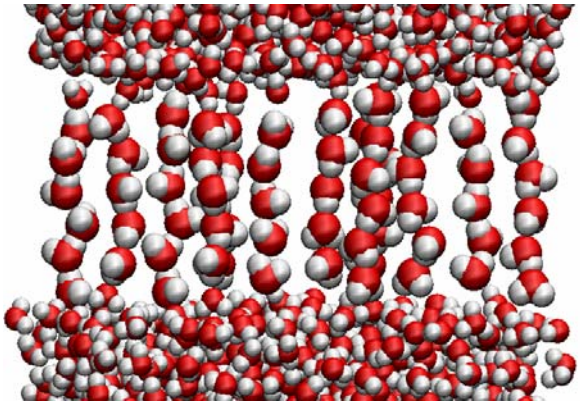
A balance between the size and hydrophobicity

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
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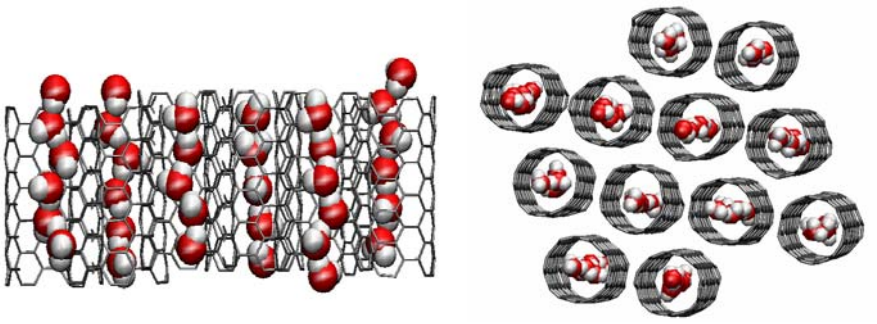
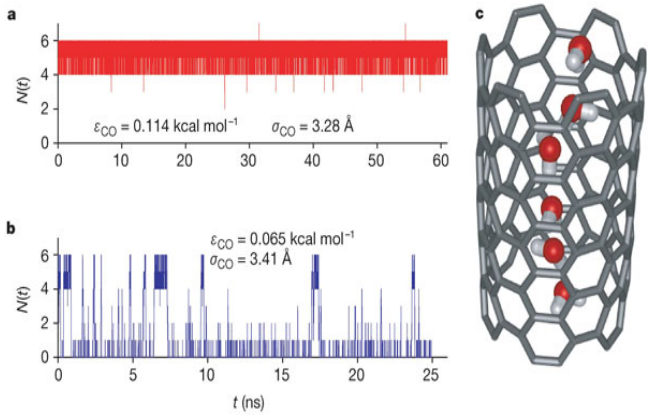
Water Single-files in Carbon Nanotubes



Water files form polarized chains in nanotubes

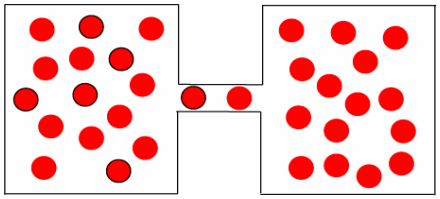
Water-nanotube interaction can be easily modified



Modifying charges
Modifying vdW parameters

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

Calculation of Diffusion Permeability from MD

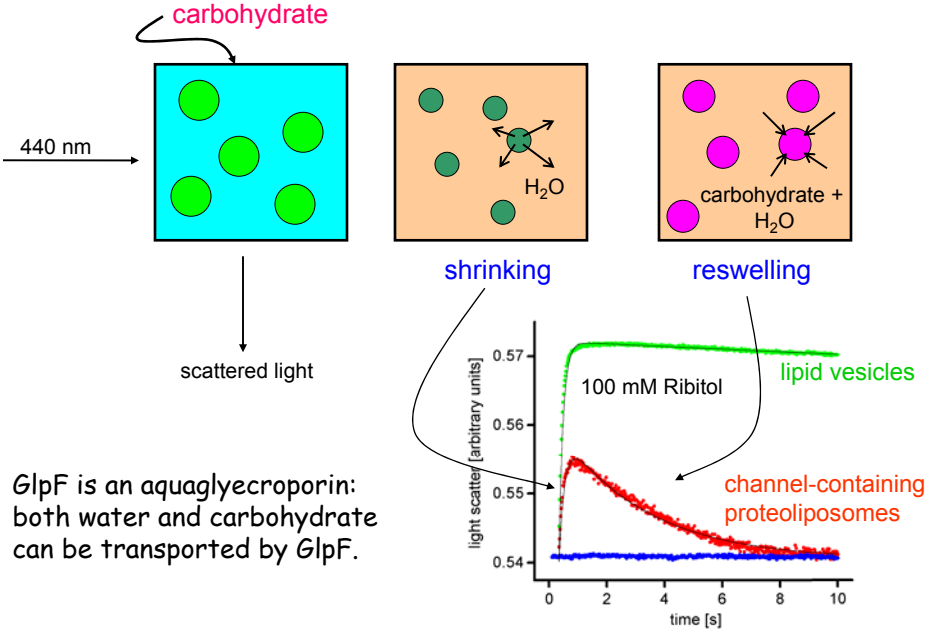


Φ_0: number of water molecules crossing the channel from the left to the right in unit time

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

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.

Chemical Potential of Water

$$\mu_w = \mu_w^o + RT \ln X_w + PV_w$$

μ_w^o : standard chemical potential of water

X_w : molar fraction of water

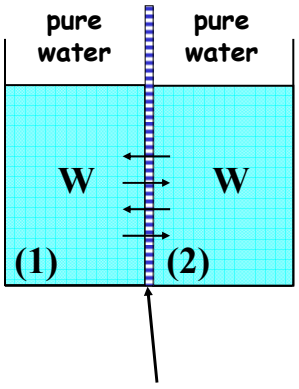
R : the gas constant

T : temperature

P : pressure

V_w : molar volume of water

$X_w = 1 \Rightarrow \ln X_w = 0$



Water flow in either direction is the same, i.e., no net flow of water.

Solutes Decrease the Chemical Potential of Water

$$\mu_w = \mu_w^o + RT \ln X_w + PV_w$$

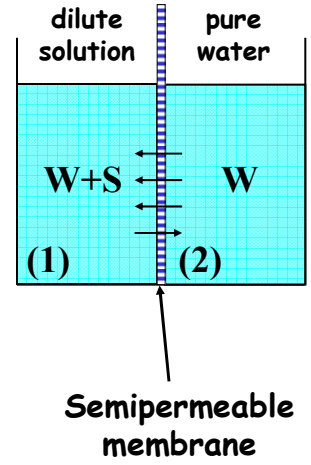
Addition of an impermeable solute to one compartment drives the system out of equilibrium.

$$RT \ln X_w(1) < RT \ln X_w(2)$$

$$\Rightarrow \mu_w(1) < \mu_w(2)$$

Water establishes a net flow from compartment (2) to compartment (1).

$X_w(1) < 1 \quad X_w(2) = 1$



Establishment of Osmotic Equilibrium

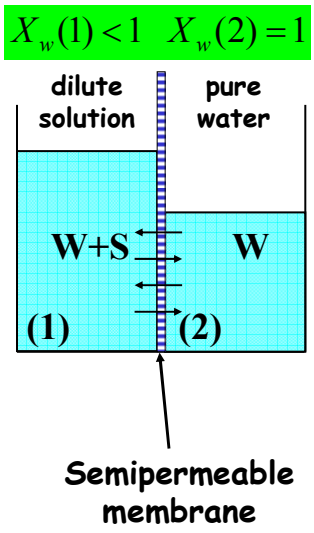
$$@\text{equilibrium}: \mu_w(1) = \mu_w(2)$$

At equilibrium, the chemical potential of any species is the same at every point in the system to which it has access.

$$\mu_w^o(1) + RT \ln X_w(1) + P(1)V_w =$$
$$\mu_w^o(2) + RT \ln X_w(2) + P(2)V_w$$

$$RT \ln X_w(1) + P(1)V_w = P(2)V_w$$

$$\Delta \boldsymbol{PV_w} = -\boldsymbol{RT} \ln \boldsymbol{X_w}(1)$$



Establishment of an Osmotic Equilibrium

$$\Delta \boldsymbol{PV_w} = -\boldsymbol{RT} \ln \boldsymbol{X_w}(1)$$

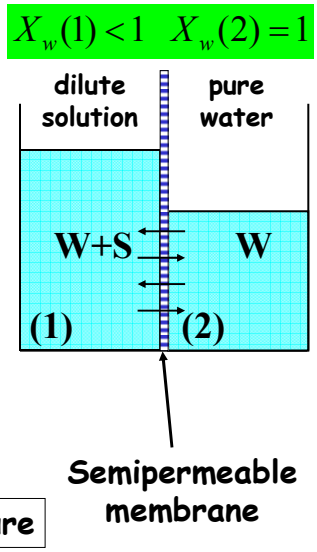
Solute molar fraction in physiological (dilute) solutions is much smaller than water molar fraction.

$$X_w + X_s = 1 \; ; \; X_s << 1$$
$$\Rightarrow \ln X_w = \ln(1 - X_s) \cong -X_s$$

$$\Delta \boldsymbol{PV_w} = \boldsymbol{RTX_s}$$

$$\Rightarrow \prod = \Delta P = \frac{RT}{V_w} X_s$$

Osmotic pressure

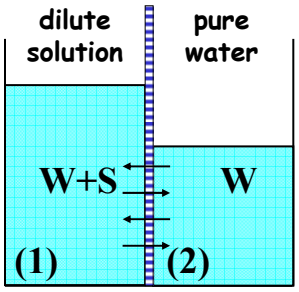


Establishment of an Osmotic Equilibrium

$$\Pi = \Delta P = \frac{RT}{V_w} X_s$$

$X_w(1) < 1 \quad X_w(2) = 1$

Solute concentration (~0.1M) in physiological (dilute) solutions is much smaller than water concentration (55M).



$$X_s = \frac{n_s}{n_s + n_w} \approx \frac{n_s}{n_w} = \frac{n_s}{n_w}\frac{V_w}{V_w}$$

$n_s << n_w$

$$= \frac{n_s}{V_{tot}} V_w = C_s V_w$$

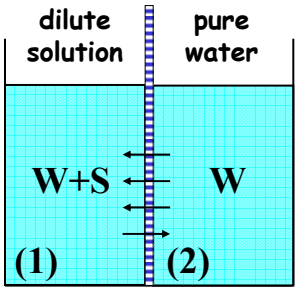
$$\Pi = \Delta P = \frac{RT}{V_w} C_s V_w = RTC_s$$

$$\Delta\Pi = \Delta P = RT\Delta C_s$$

Osmotic Flow of Water

$@\text{equilibrium: } \Delta P - \Delta\Pi = 0$

Net flow is zero



$$J_v \propto \Delta P - \Delta\Pi$$

$$J_v = L_p(\Delta P - \Delta\Pi)$$

Volume flux of water

Hydraulic permeability

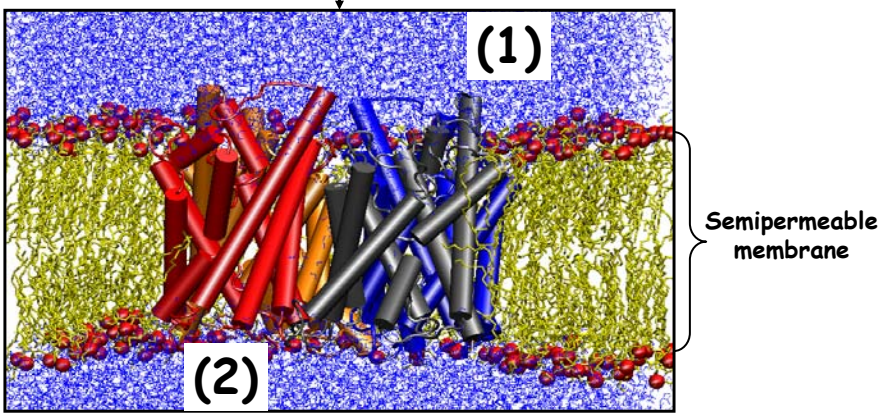
Osmotic permeability

Molar flux of water

$$\Phi_w = \frac{J_v}{V_w} = P_f A\left(\frac{\Delta P}{RT} - \Delta C_s\right)$$

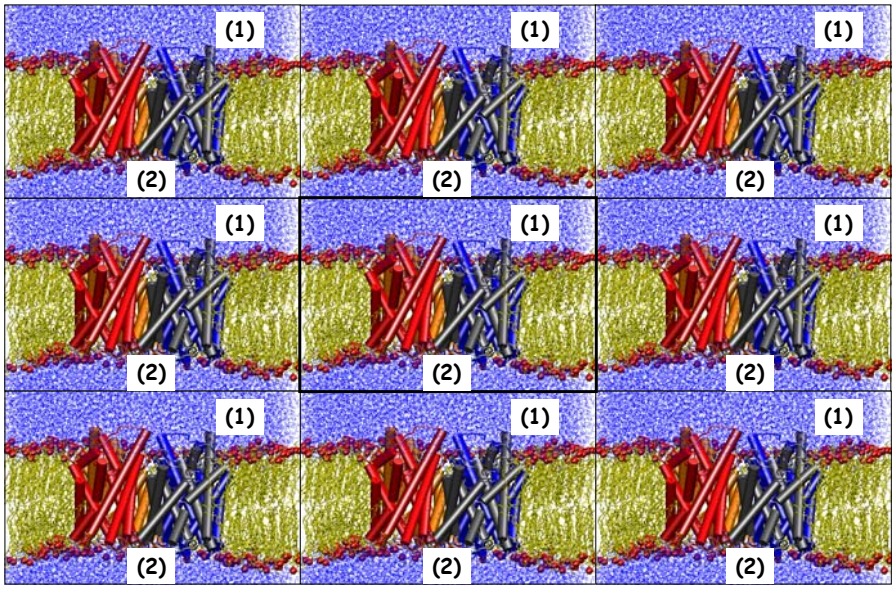
Simulation of osmotic pressure induced water transport may be done by adding salt to one side of the membrane.

$NaCl \rightarrow Na^{+} + Cl^{-}$

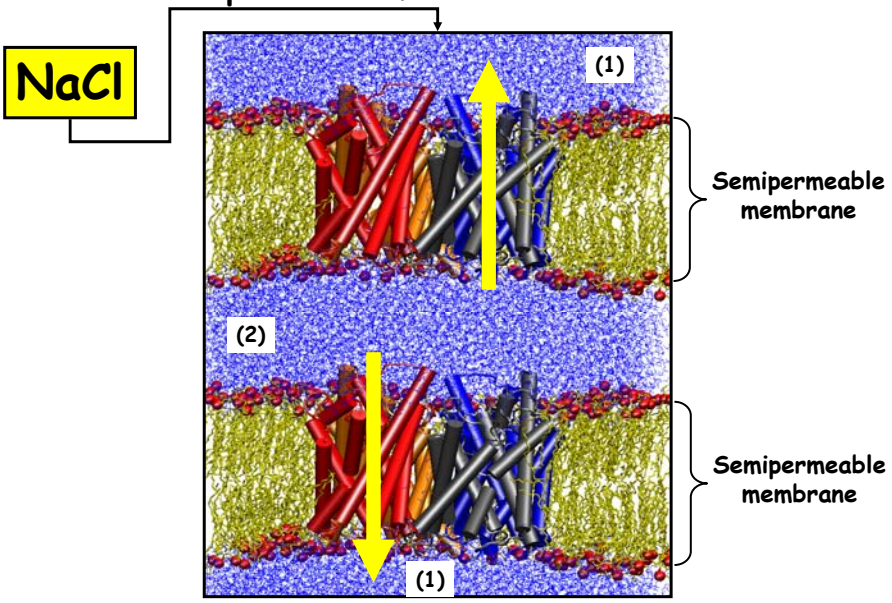


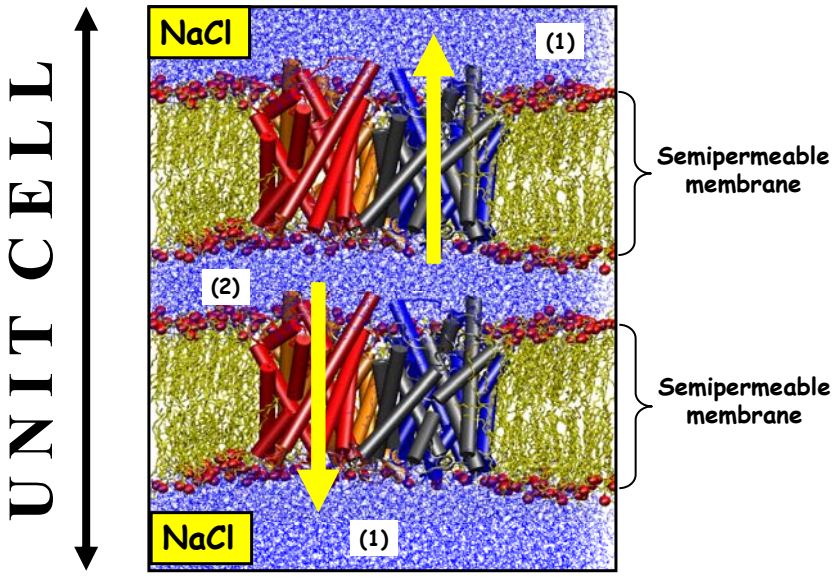
There is a small problem with this setup!

Problem: The solvents on the two sides of a membrane in a conventional periodic system are connected.



We can include more layers of membrane and water to create two compartment of water that are not in contact





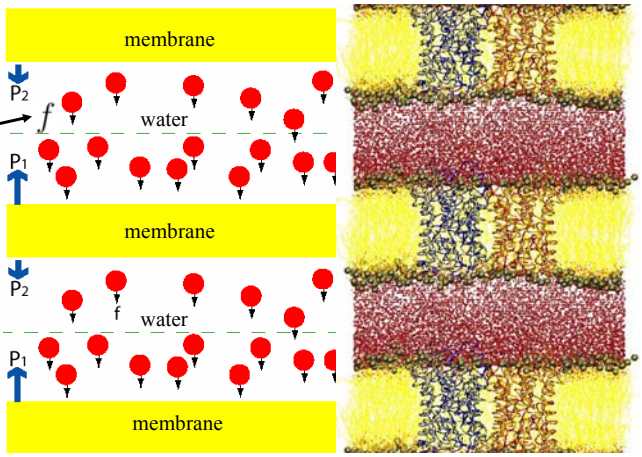
Realizing a Pressure Difference in a Periodic System

$$P_1 = P_2 + nf \Rightarrow \Delta P = nf / A$$

Fangqiang Zhu

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

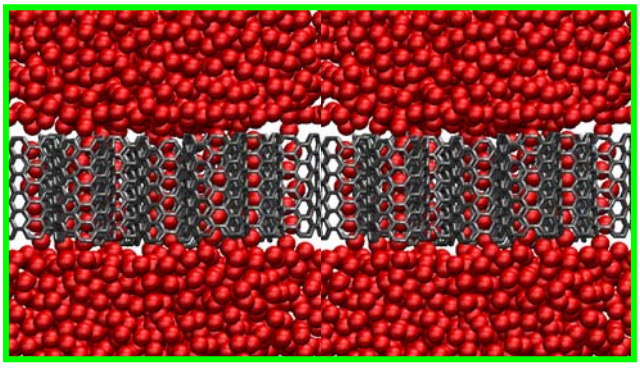
The overall translation of the system is prevented by applying constraints or counter forces to the membrane.



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

Applying a Pressure Difference Across the Membrane

$$\Delta P = nf / A$$

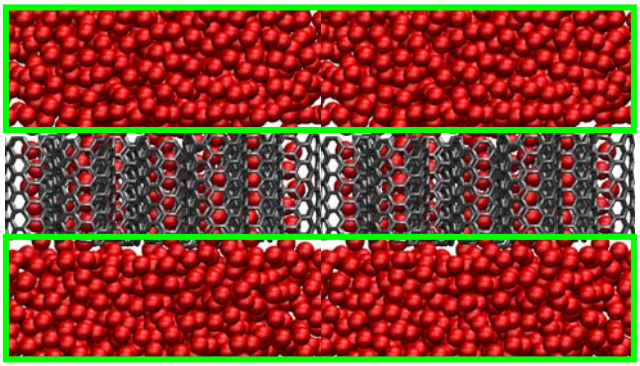


Applying force on all water molecules.

Not a good idea!

Applying a Pressure Difference Across the Membrane

$$\Delta P = nf / A$$

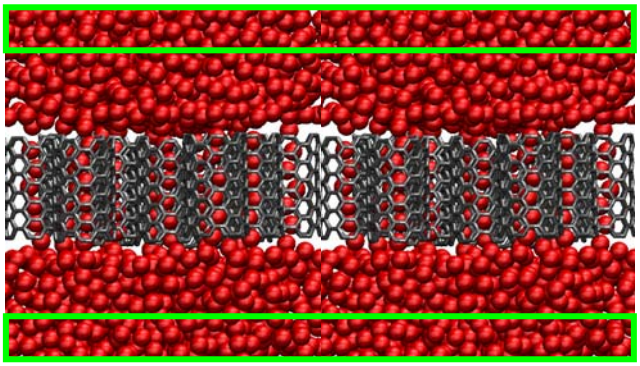


Applying force on bulk water only.

Very good

Applying a Pressure Difference Across the Membrane

$$\Delta P = nf / A$$



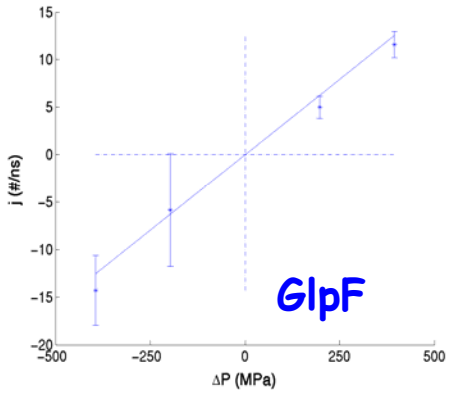
Applying force only on a slab of water in bulk.

Excellent

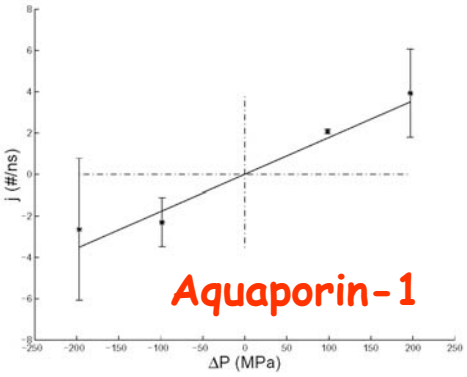
P_f can be calculated from these simulations

$$\Phi_w = P_f A(\frac{\Delta P}{RT} - \Delta C_s)$$

Calculation of osmotic permeability of water channels

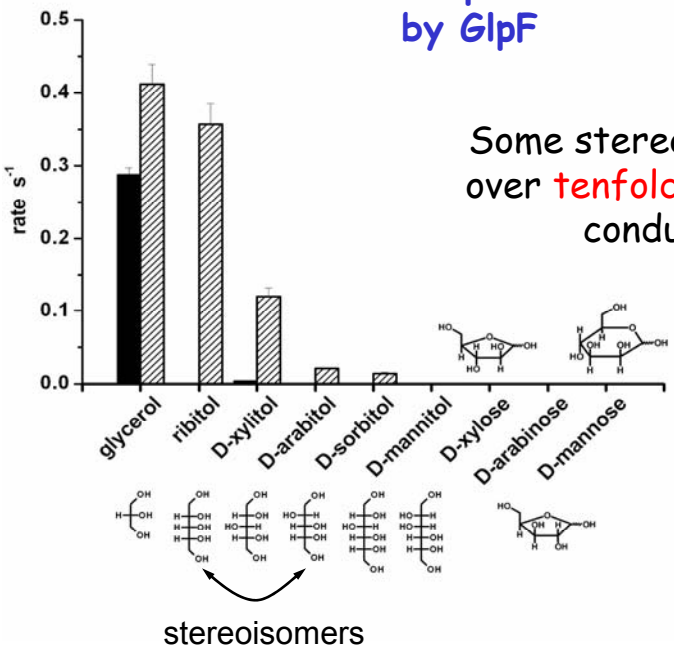


p_f: 1.4×10^{-13} cm^3/s



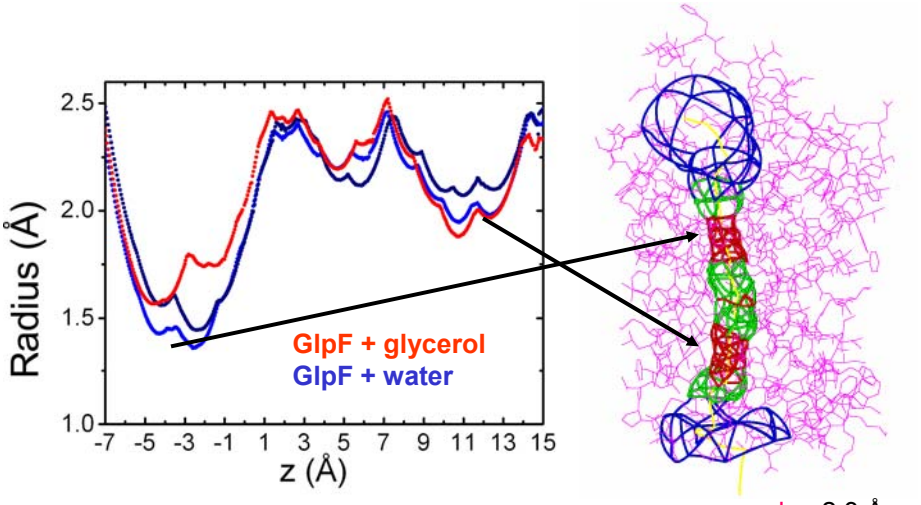
p_f: 7.0 ± 0.9 × 10^{-14} cm^3/s
Exp: 5.4 – 11.7 × 10^{-14} cm^3/s

Stereoselective Transport of Carbohydrates by GlpF



Some stereoisomers show over tenfold difference in conductivity.

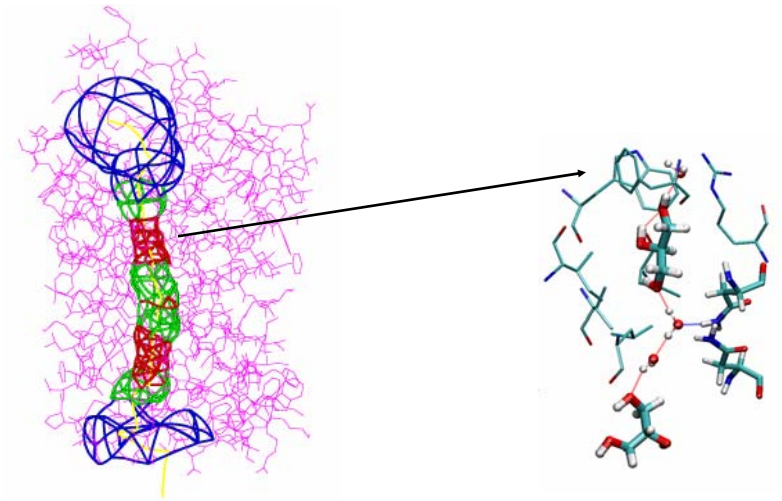
Channel Constriction



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

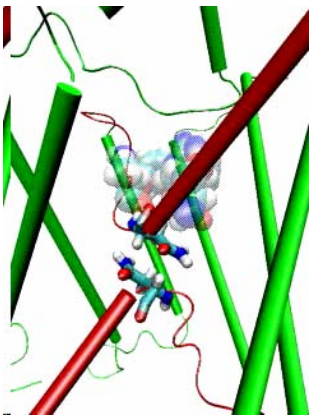
HOLE2: O. Smart et al., 1995

Selectivity filter

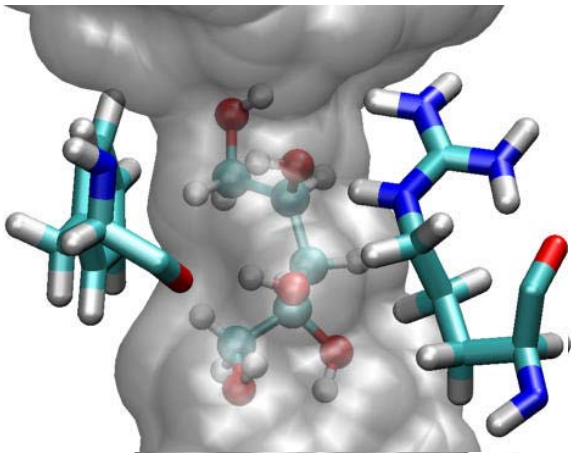


Interactive Molecular Dynamics

VMD ⟷ NAMD

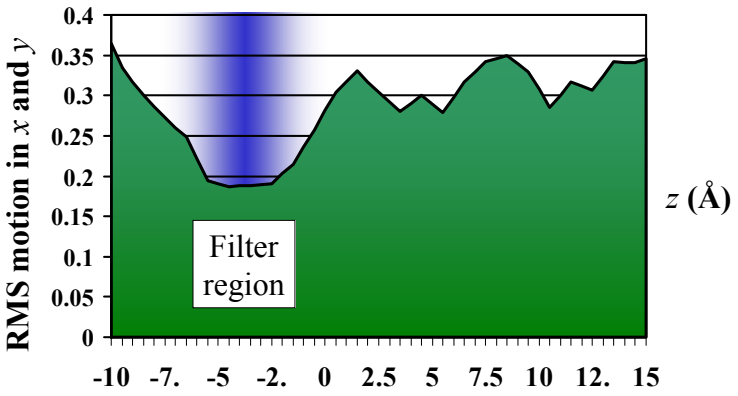


Observed Induced Fit in Filter



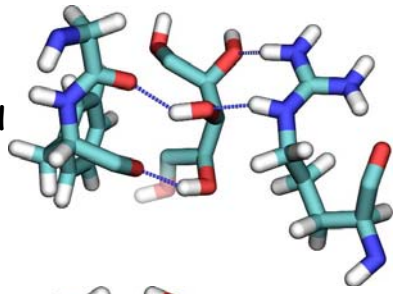
Confinement in Filter

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

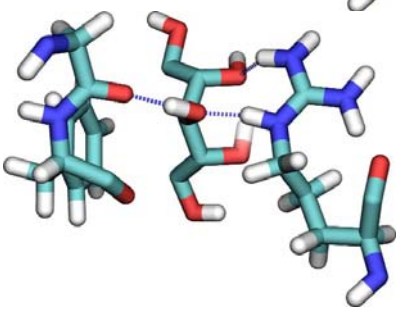


Evidence for Stereoselectivity

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.