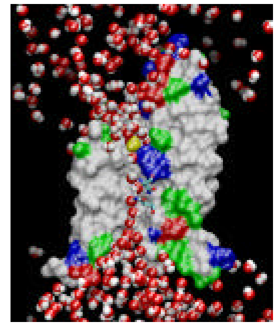
This is a reminder of the Illinois Biophysics Society-sponsored Student Seminar this evening, March 12th.

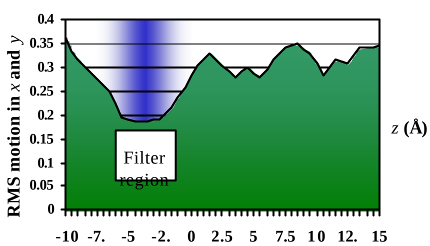
The seminar will be held in the CLSL auditorium, room B102, beginning at 7:00pm.

Food and drinks will be provided.

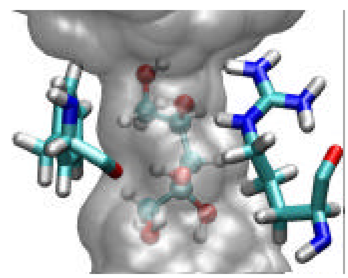


Confinement in Filter

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

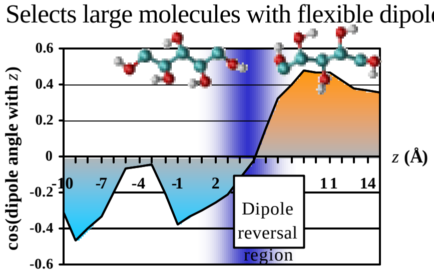


Observed Induced Fit in Filter

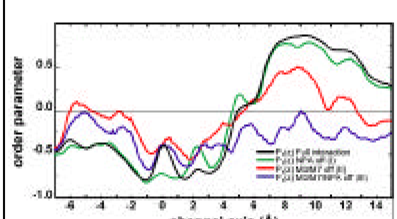


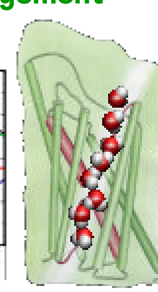
Dipole Reversal in Channel

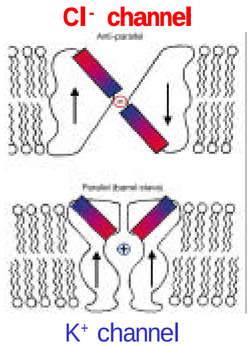
- Dipole reversal pattern matches water.
- Selects large molecules with flexible dipole.

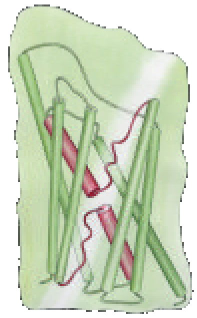


Electrostatic Stabilization of Water Bipolar Arrangement



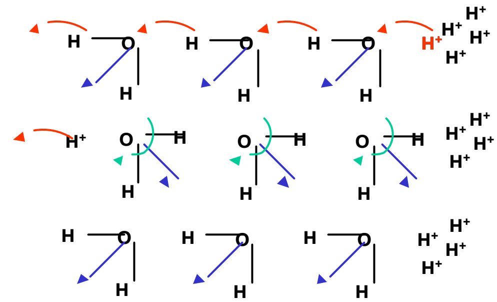




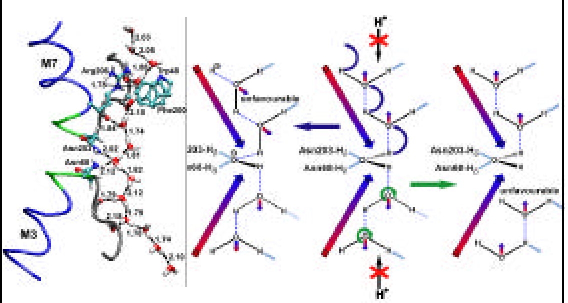


Aquaporins

Proton transfer through water

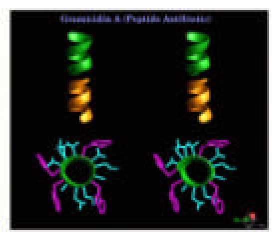


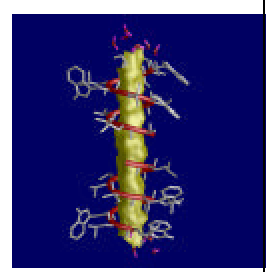
Mechanism of proton Preclusion in Aquaglyceroporins



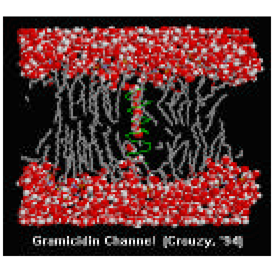
E. Tajkhorshid, P. Nollert, M. Jensen, R. Stroud, K. Schulten, *Science* (submitted)

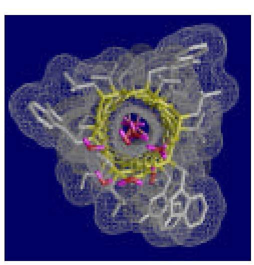
Gramicidin A – forming a membrane leak



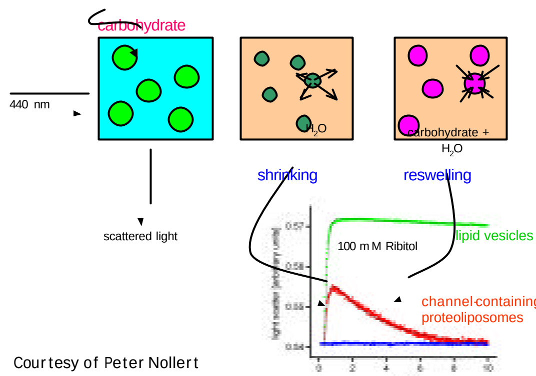


Gramicidin can form a proton wire





Liposome Swelling Assay



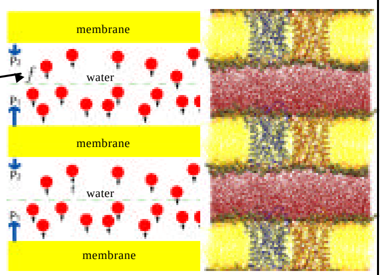
Courtesy of Peter Nollert

Pressure Induced Water Conduction in GlpF

Realizing a pressure difference in a periodic system

$P_1 = P_2 + P_{water} \rightarrow \Delta P = nf / A$

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

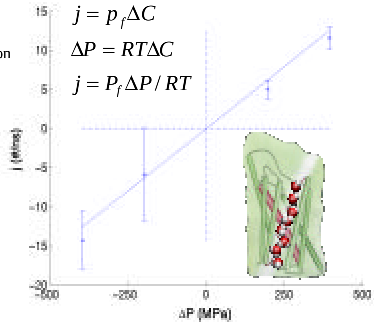


Pressure Induced Water Conduction in GlpF

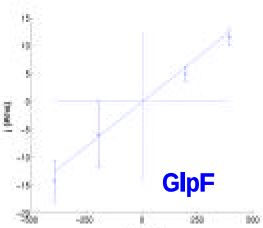
DC: Solute concentration difference

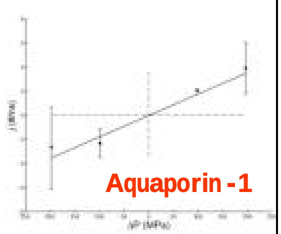
j: water flux through a single channel

$$j = p_f \Delta C$$
$$\Delta P = RT\Delta C$$
$$j = P_f \Delta P / RT$$



Calculation of osmotic permeability of water channels

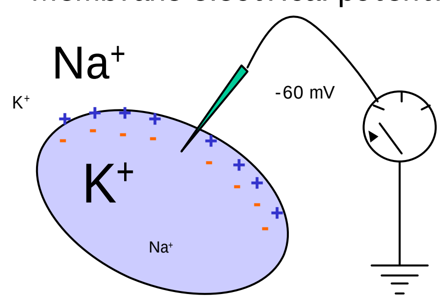




p_f: 1.4×10^{-13} cm³/s

p_f: $7.0 \pm 0.9 \times 10^{-14}$ cm³/s
Exp: 5.4 – 11.7 $\times 10^{-14}$ cm³/s

Membrane electrical potential



The ratio is about 1 to 10

Action potential in excitable cells

Properties of Ion Channels

- Membrane-spanning protein
- Hydrophilic ion conductive pathway
  - Water-filled
  - Traversing ion must lose hydration shell
- Selective
  - charge screening and size
- Gating properties
  - Exist in open and closed states

Substrate is charged and the conduction can be measured very precisely, as opposed to water channels

Control of conduction in ion channels

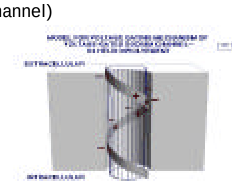
Gating mechanisms (open-closed transition)

Membrane potential change (Voltage gated channels)
- K channels

Binding of a molecule (Ligand-gated channels)
- Acetylcholine nicotinic receptor (Na channel)
- Glutamate receptor (Ca channel)

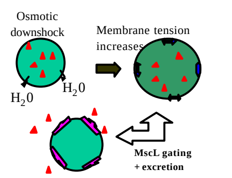
Both voltage and ligand gating

Mechanosensitive channels



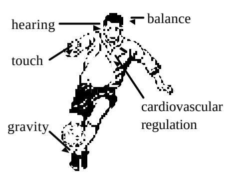
Ubiquitous Mechanosensitive Channels

MscL is a bacterial safety valve



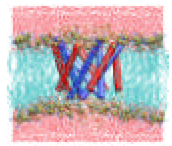
Bacterial MscL is functional in reconstituted lipid bilayers.

Roles in Higher Organisms

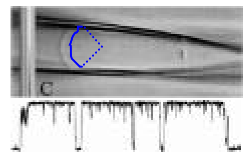


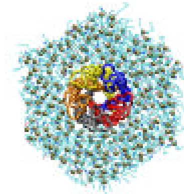
Most eukaryotic MS channels require coupling to the cytoskeleton and/or the extracellular matrix.

Gating Mechanism of a Mechanosensitive Channel



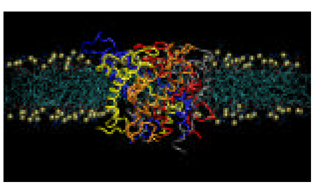
Full helical transmembrane proteins
Sensitive to bilayer thickness
Sensitive to bilayer tension
Non-specific channels





Mechanosensitive Ion Channel

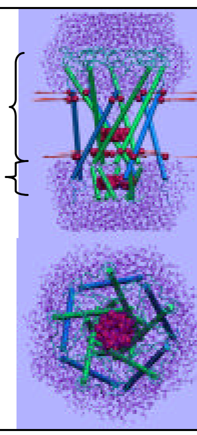
MscL gates by tilting its helices



SMD simulation of MscL

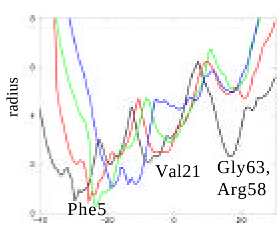
Green: M1
Blue: M2

S1



- Homology model of MscL from *E. coli*
- Constant radial force applied to residues at the ends of M1 and M2.
- 10 ns simulation time.

Helix Tilt During Stretching

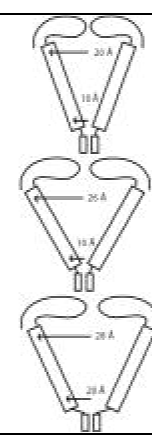


- 10-frame average of coordinates at **10, 1000, 1500, and 2000 ps**

MscL Expanded State

- 0-2 ns: expansion of the periplasmic ends of M1 and M2.
- 2-6 ns: slippage of conserved Ala20 past Ile25 and Phe29.
- 6-10 ns: continued expansion; stretching of linker residues.

Doublemovie.mpg



M1 Helix-helix Contacts

Well-conserved Gly22 and Gly26 mediate packing between neighboring M1 helices.

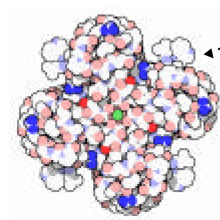
Gly22 contacts are abolished at the onset of pore opening.

Gly26 formed new contacts with Val16, but even these were abolished with continued pore expansion.

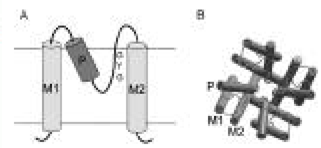
Gly22.mpg

KcsA Potassium Channel

Under physiological conditions, the selectivity filter of the KcsA dehydrates, transfers, and rehydrates a K^+ ion every 10ns.



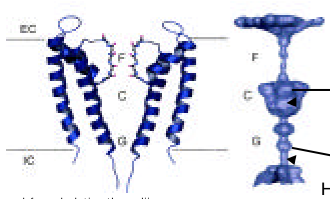
PDB Feb 2003 molecule of the month



KcsA Potassium Channel

Extracellular half is responsible for selectivity

Cytoplasmic half is responsible for gating, through lining of inner helices



The program HOLE is used for calculating the radii

K binding sites in the selectivity filter