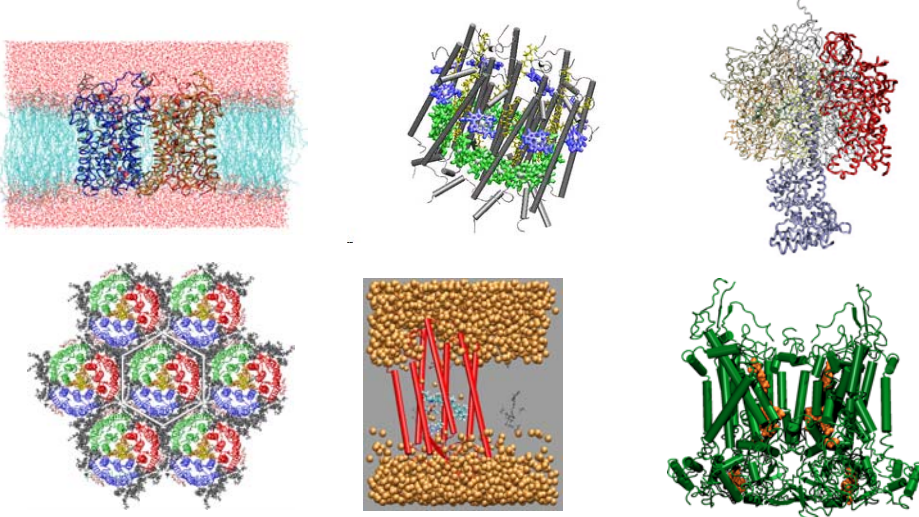


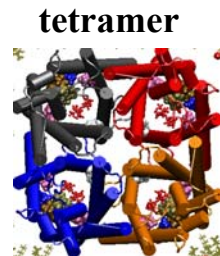
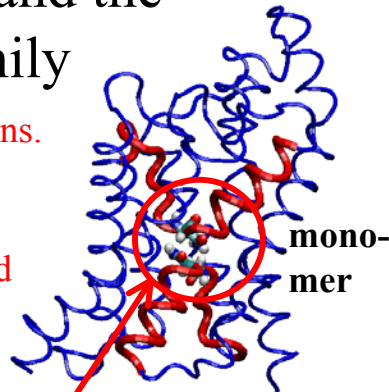
Case Study: Membrane Proteins

Glycerol channel Light harvesting complex ATPase
 Purple Membrane Bacteriorhodopsin bc1 complex



Glycerol Channel and the Aquaporin Family

- Water transport in cells: aquaporins.
- Water and glycerol transport: aquaglyceroporins
- Ions and charged solutes excluded from transport.
- Tetrameric architecture
- Gene duplication; internal repeat with characteristic half-membrane spanning structure.
- Conserved asparagine-proline-alanine residues (NPA motif)

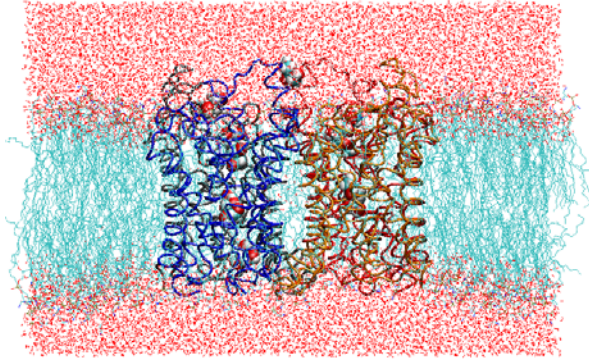


Simulation Scheme

NAMD with full electrostatics (PME), periodic boundary cond. NpT ensemble at 310 K, 1ns equilibration

protein ~ 15,000 atoms
lipids ~ 40,000 atoms
water ~ 51,000 atoms
all ~ 106,000 atoms

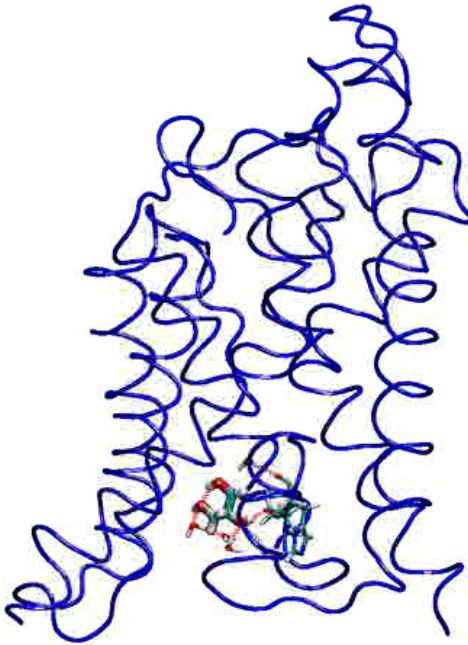
12 days / ns - 64 T3E CPUs



Equilibrated structure after 1ns; note the curved adjustment between lipids-protein

Morten Jensen, Emad Tajkhorshid

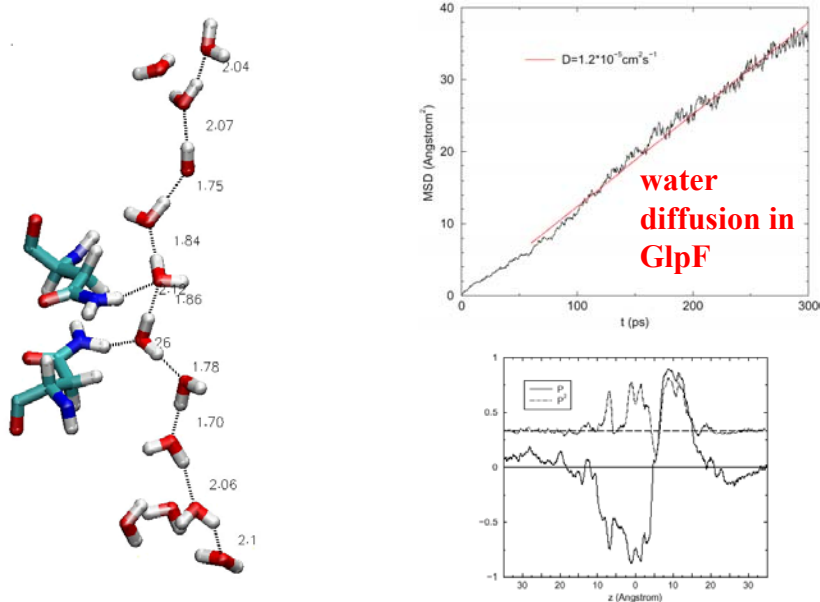
Glycerol Conduction



- Spontaneous glycerol conduction on ns time scale;
- Conduction occurs independently in each monomer;
- Exposed backbone carbonyl oxygen atoms dictates glycerol and water pathway; this explains the non-helical secondary structure in the aquaporin family;
- Glycerol resides at the position of conserved motif for the longest time during simulation = minimum energy site;
- Water molecules are essential for the glycerol transport.

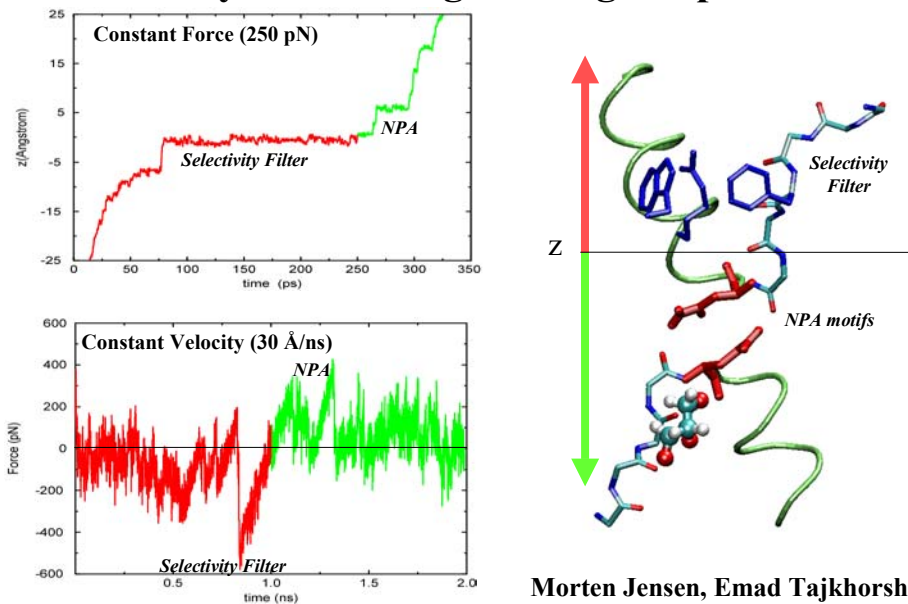
Morten Jensen, Emad Tajkhorshid

Anti-parallel Orientation and Diffusion of Water in GlpF



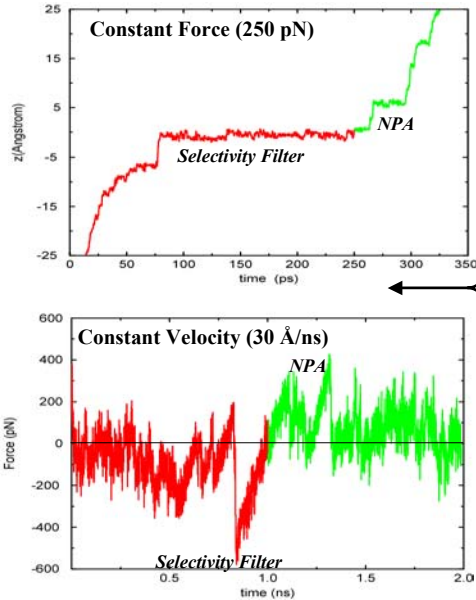
Nollert, Stroud, Jensen, Takshorshid, and Schulten, in preparation

Steered Molecular Dynamics Simulation of Glycerol Passage through GlpF



Morten Jensen, Emad Tajkhorshid

Quantitative Analysis of SMD – Grand Challenge



NIH Resource for Macromolecular Modeling and Bioinformatics
Theoretical Biophysics Group, Beckman Institute, UIUC

- The potential of mean force (PMF) is reconstructed from time series of applied force and displacement

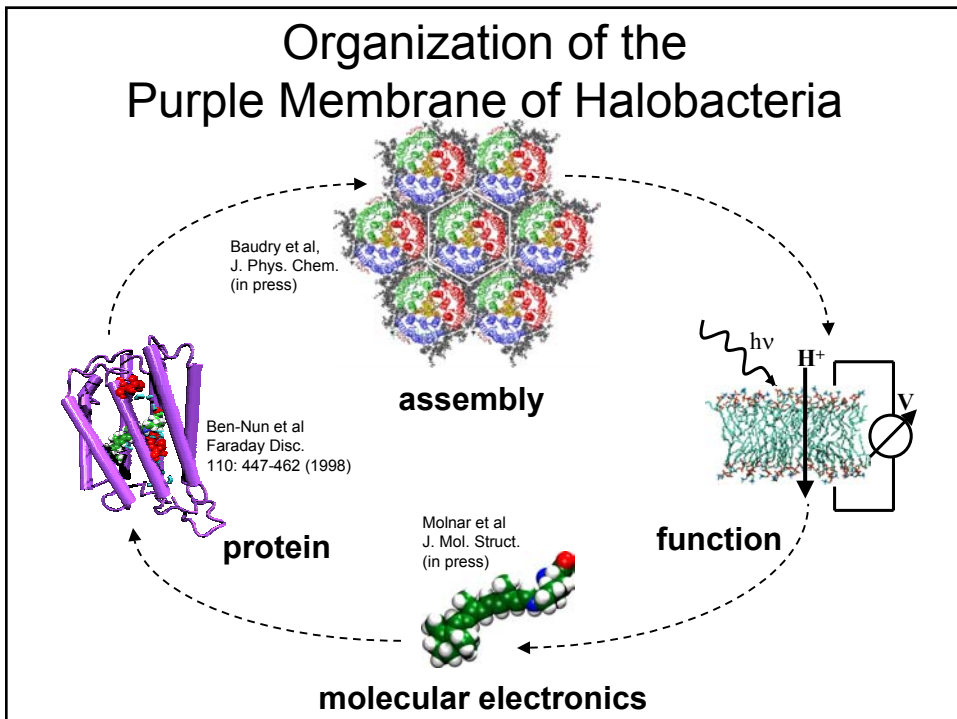
- Non-equilibrium analysis based on the Langevin equation:

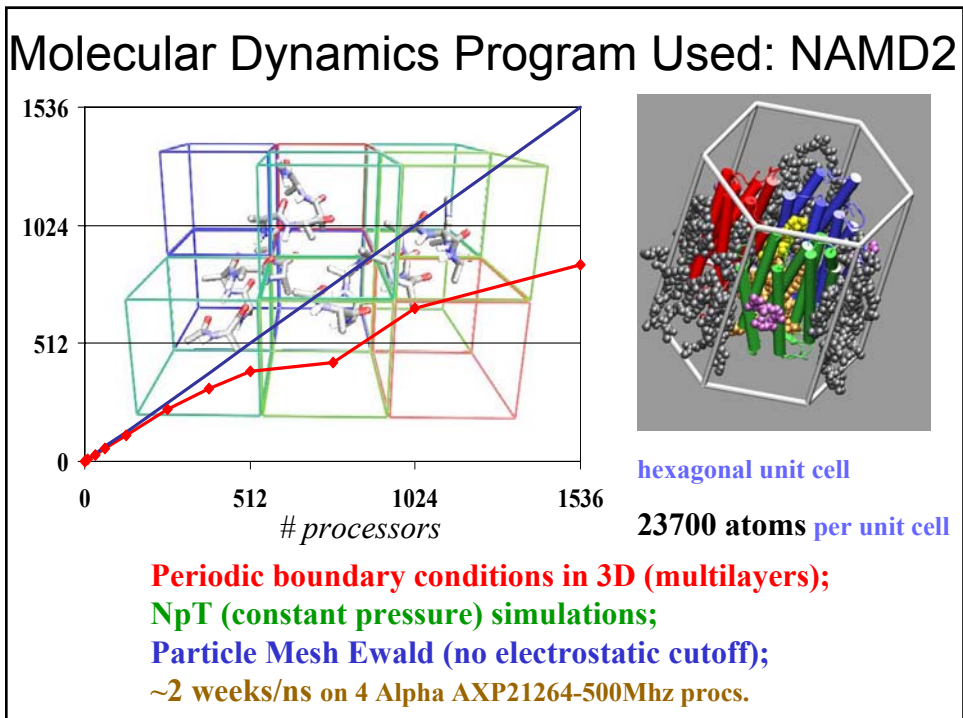
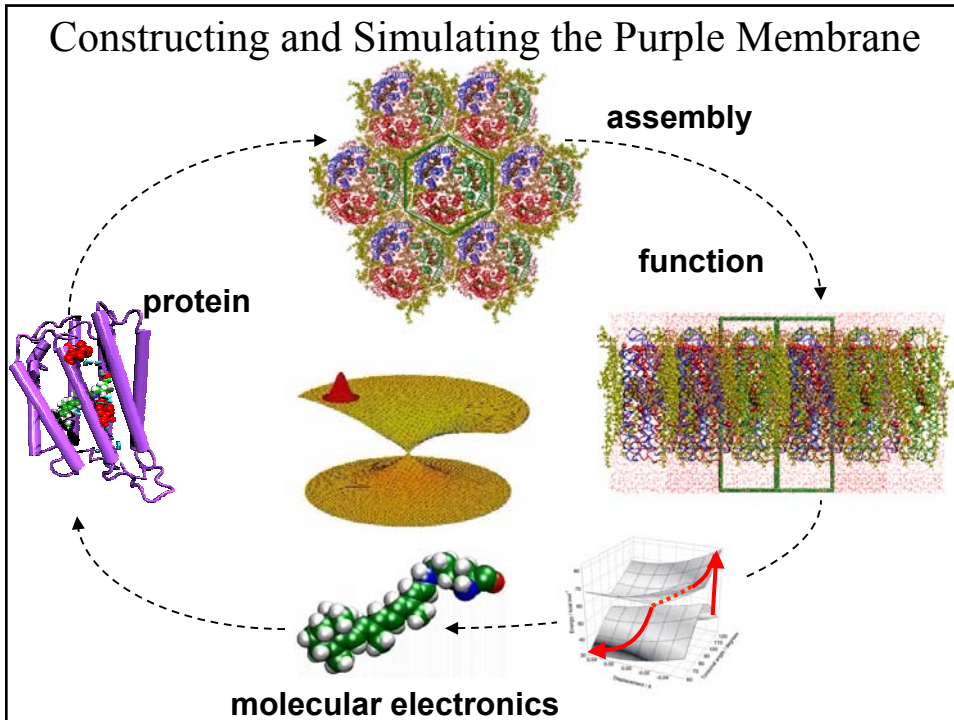
$$\gamma \dot{x} = -dU/dx + k(vt-x) + \sigma \xi(t)$$

- Multiple trajectories can be combined to yield statistically significant results

Morten Jensen, Emad Tajkhorshid

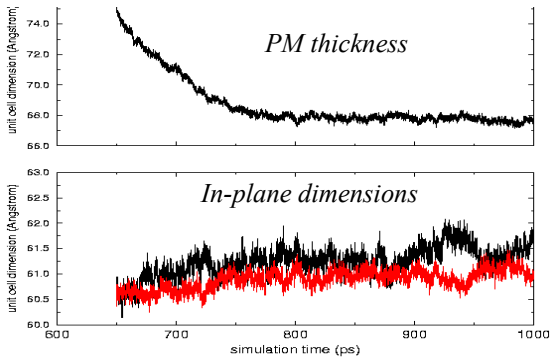
Organization of the Purple Membrane of Halobacteria



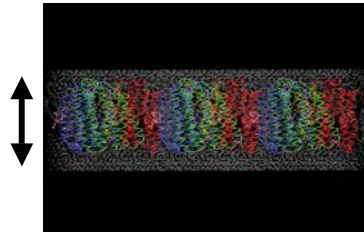


Thermodynamics of the Purple Membrane

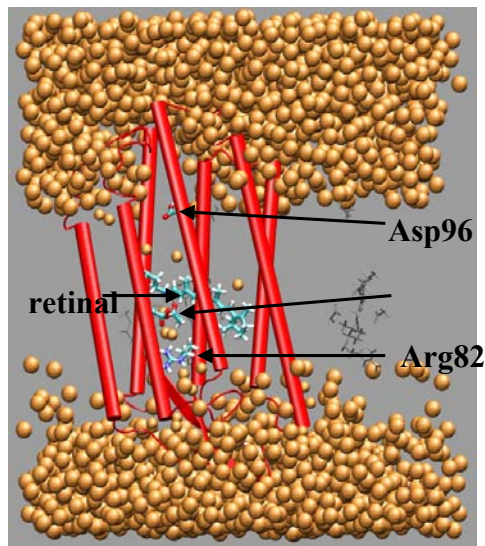
*NpT simulation:
constant temperature,
variable volume*



*Reduction of PM
thickness during
NpT simulation*

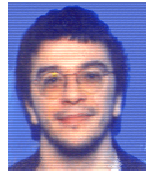


Structure of the Purple Membrane



Knowing now every atom of the integral purple membrane - water system one can describe proton pumping from bulk phase to bulk phase.

Acknowledgements



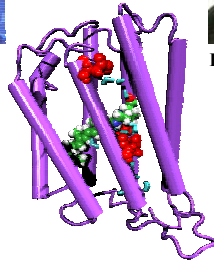
Jerome Baudry



Michal Ben-nun



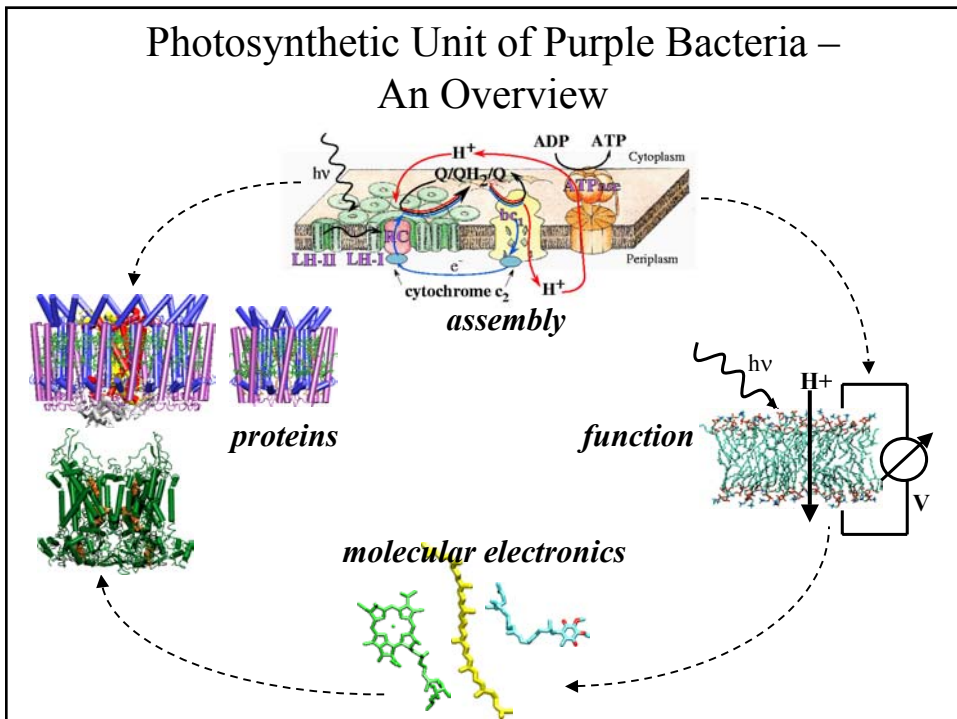
Emad Tajkhorshid



\$\$: Beckman Institute, NSF, HFSP, NIH-NCRR

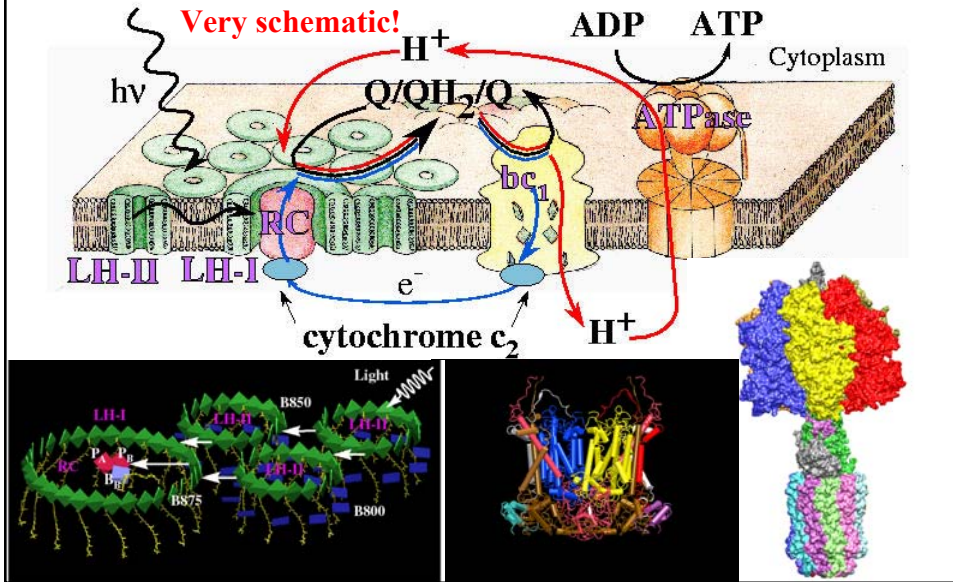


Photosynthetic Unit of Purple Bacteria – An Overview



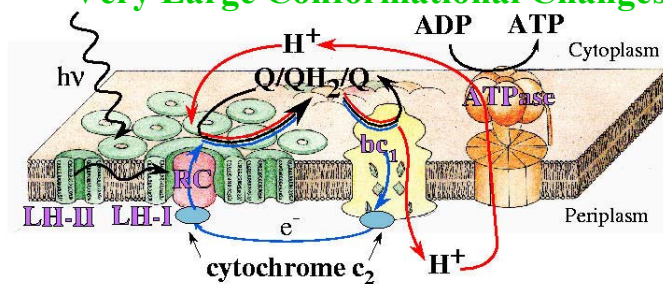
Photosynthetic Apparatus of Purple Bacteria

Function Achieved Through Very Large Structures

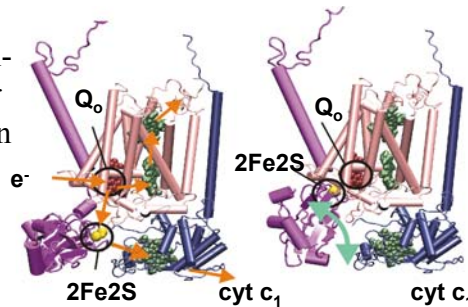


Photosynthetic Apparatus of Purple Bacteria

Very Large Conformational Changes



two pathways for oxidation of Q_o site



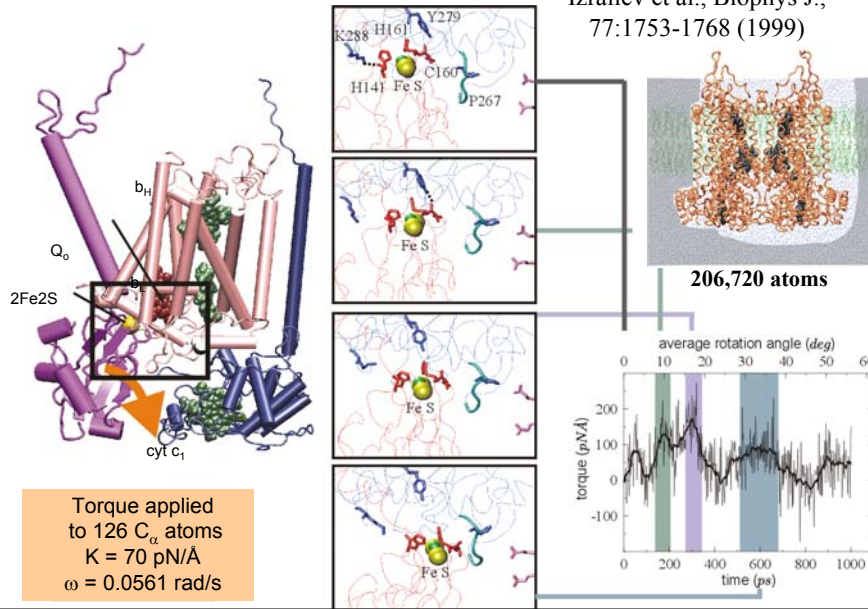
Iron Sulfur Protein head rotation can redirect 2nd electron

Sergei Izrailev

Enforcing domain rotation in the bc₁ complex (3)

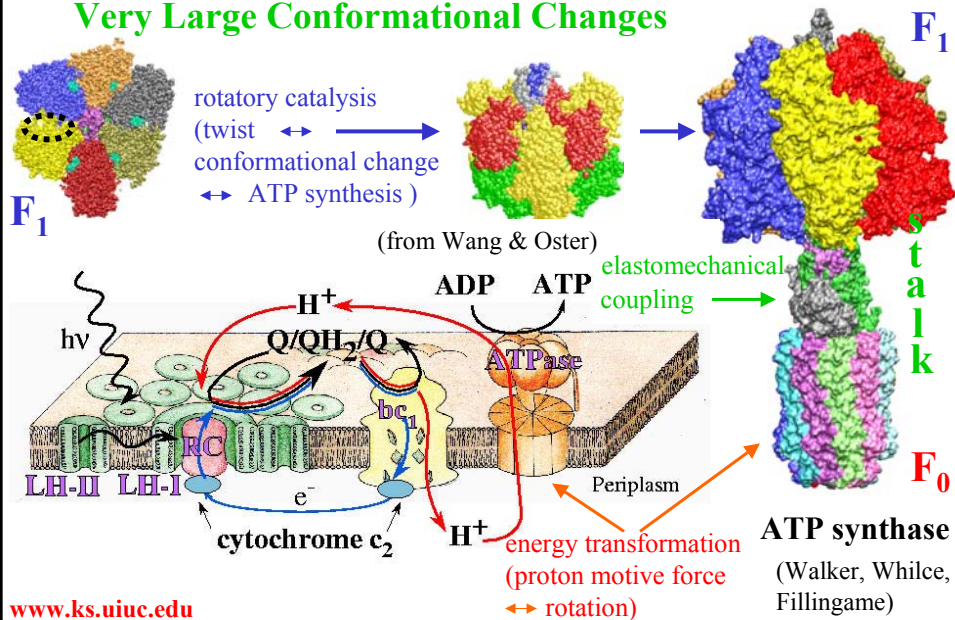
Events during torque application to ISP head

Izrailev et al., Biophys J., 77:1753-1768 (1999)

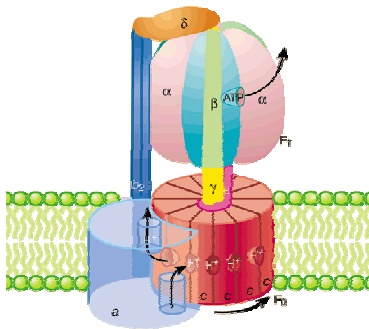


Photosynthetic Apparatus of Purple Bacteria

Very Large Conformational Changes



F₁F₀ ATP Synthase - The Ultimate Power Plant

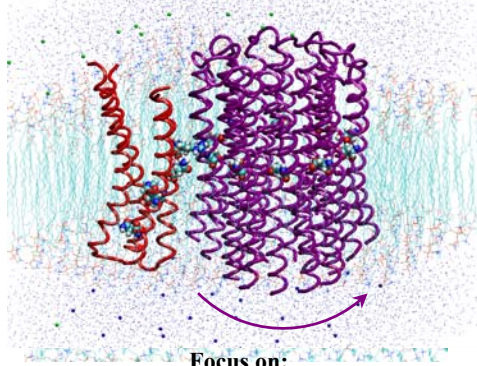


Why ATP synthase?

- Converts the electrochemical energy of the transmembrane proton gradient into the mechanical energy of the central stalk rotation, driving ATP synthesis ($\Delta G = 7.7$ kcal/mol).
- Reversible: can pump protons using ATP energy.
- Nearly 100% efficient.
- Remarkably symmetric structure of the both transmembrane F₀ unit (ab₂c₁₂) and solvent exposed F₁ unit ($\alpha_3\beta_3\gamma\delta\epsilon$).

Steered Molecular Dynamics (SMD) of F₀ unit:

- ~**100k atoms** (17k protein, 39k membrane, 42k solvent)
- System size ~100x100x100Å. PBC, const T, const p.
- Applying constant torque to the central stalk (γ subunit).



Focus on:

- The central stalk connection with the c subunit assembly;
- Rotation of the c subunit assembly in the membrane;
- Dynamics of protein residues involved in proton transfer.

Ilya Balabin