NIH Center for Macromolecular Modeling and Bioinformatics
Developer of VMD and NAMD

5 faculty members (2 physics, 1 chemistry,
1 biochemistry, 1 computer science);
8 developers; 1 system admin;
15 post docs; 22 graduate students;
3 administrative staff.

3.8 million website visits (2007–2011);
13 TB data transferred from website (2007–2011);
163 research highlights since 2001.

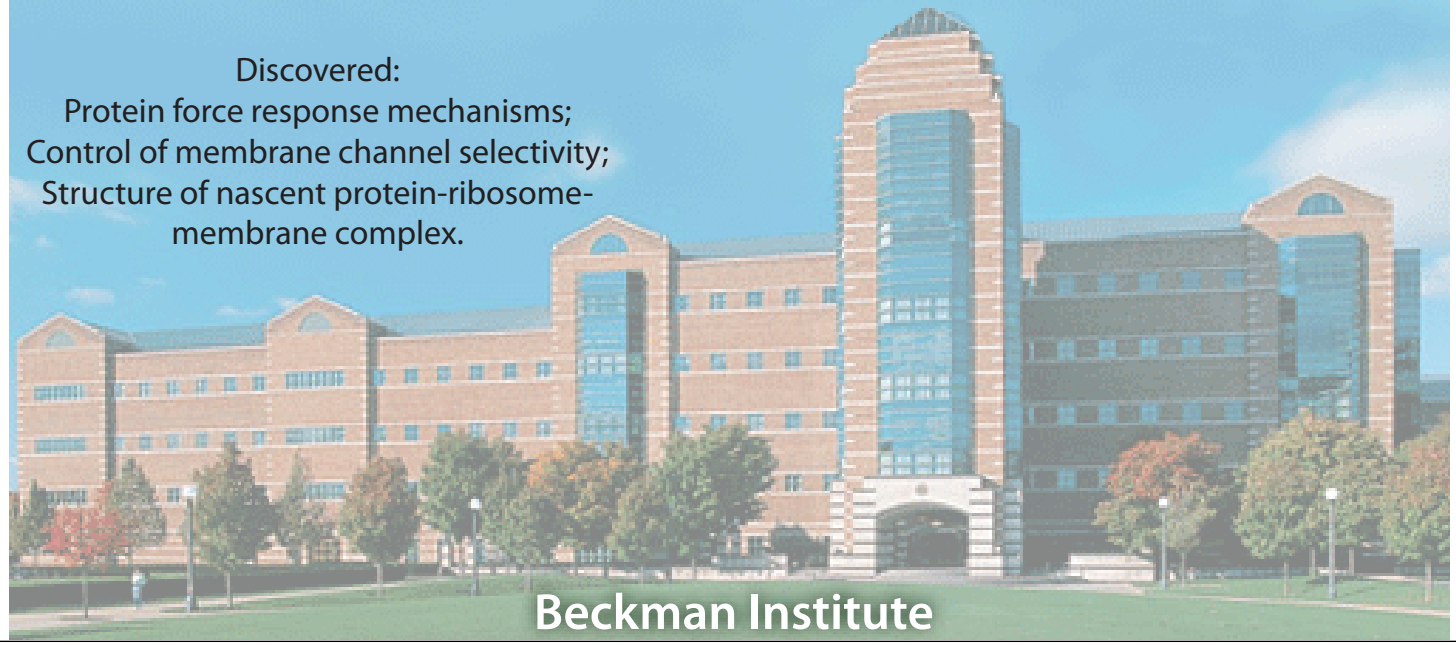
Simulation of integral-protein (aquaporin)-
membrane water system, 2001;
Simulation of whole virus, 2006;
10 μs simulation of protein folding, 2009;
20 million atom simulation of bioenergetic membrane, 2011;
469 Center publications with 26,700 citations;
35 collaborative projects with 59 joint publications (2007–2011).

31 workshops since 2003;
952 researchers trained;
336 lectures given (2007–2011).

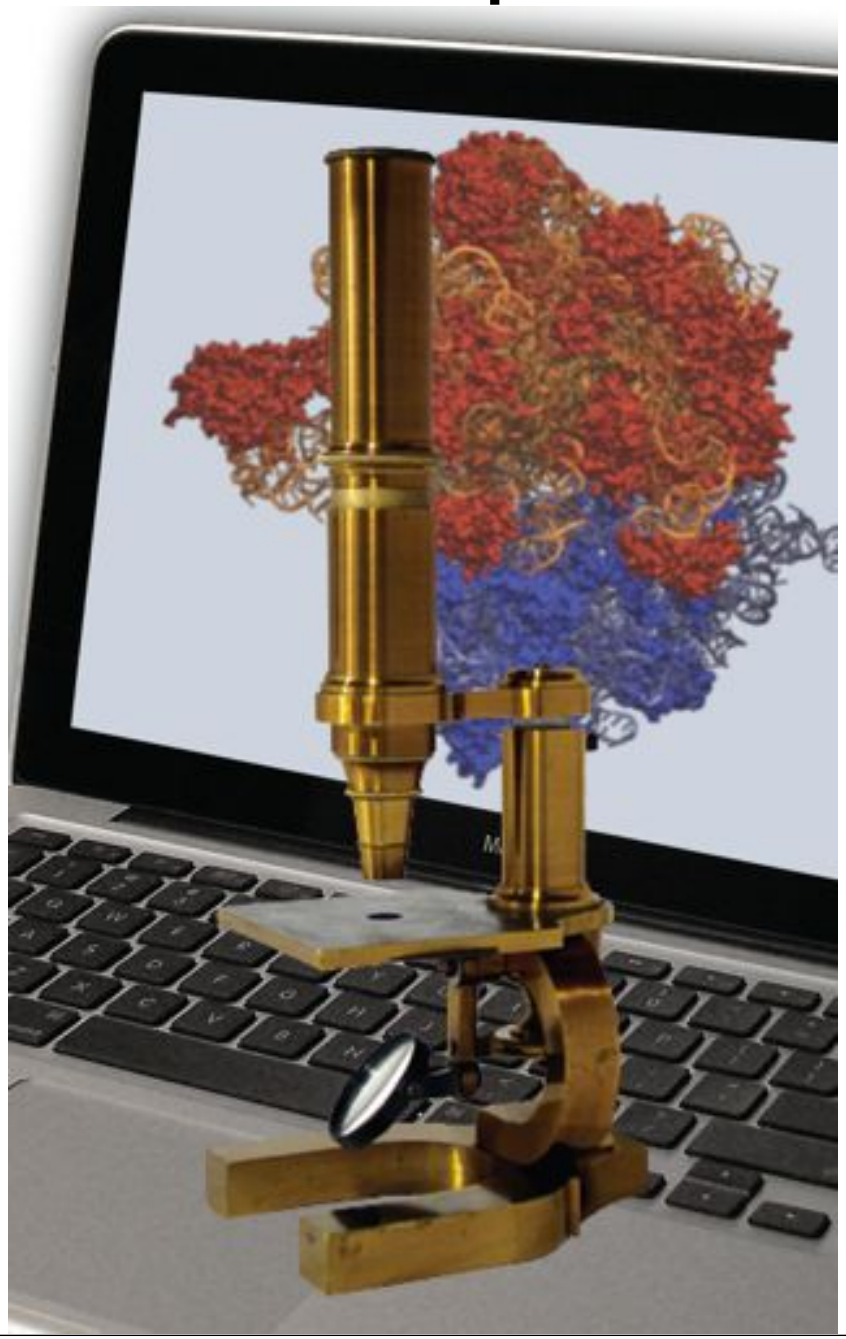
Leader in parallel MD simulation;
Leader in GPU accelerated simulation;
Pioneered use of GPU acceleration for
quantum chemistry visualization.

195,000 VMD users and 47,000 NAMD users;
VMD-L, NAMD-L mailing list received
18,000 and 14,000 emails respectively.

Discovered:
Protein force response mechanisms;
Control of membrane channel selectivity;
Structure of nascent protein-ribosome-
membrane complex.

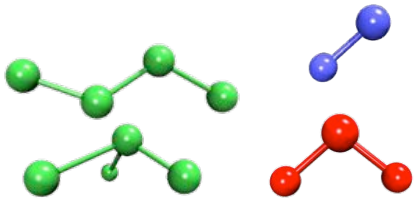


Our Mission: The Computational Microscope



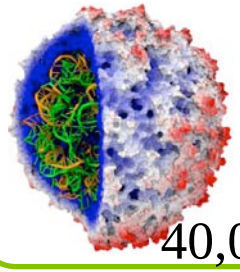
Our Microscope is Made of...

Chemistry



$$U(\vec{R}) = \underbrace{\sum_{bonds} k_i^{bond}(r_i - r_0)^2}_{U_{bond}} + \underbrace{\sum_{angles} k_i^{angle}(\theta_i - \theta_0)^2}_{U_{angle}} +$$
$$\underbrace{\sum_{dihedrals} k_i^{dihe}[1 + \cos(n_i\phi_i + \delta_i)]}_{U_{dihedral}} +$$
$$\underbrace{\sum_i \sum_{j \neq i} 4\epsilon_{ij}\left[\left(\frac{\sigma_{ij}}{r_{ij}}\right)^{12} - \left(\frac{\sigma_{ij}}{r_{ij}}\right)^{6}\right] + \sum_i \sum_{j \neq i} \frac{q_i q_j}{\epsilon r_{ij}}}_{U_{nonbond}}$$

NAMD Software



Virus

40,000 registered users

Physics

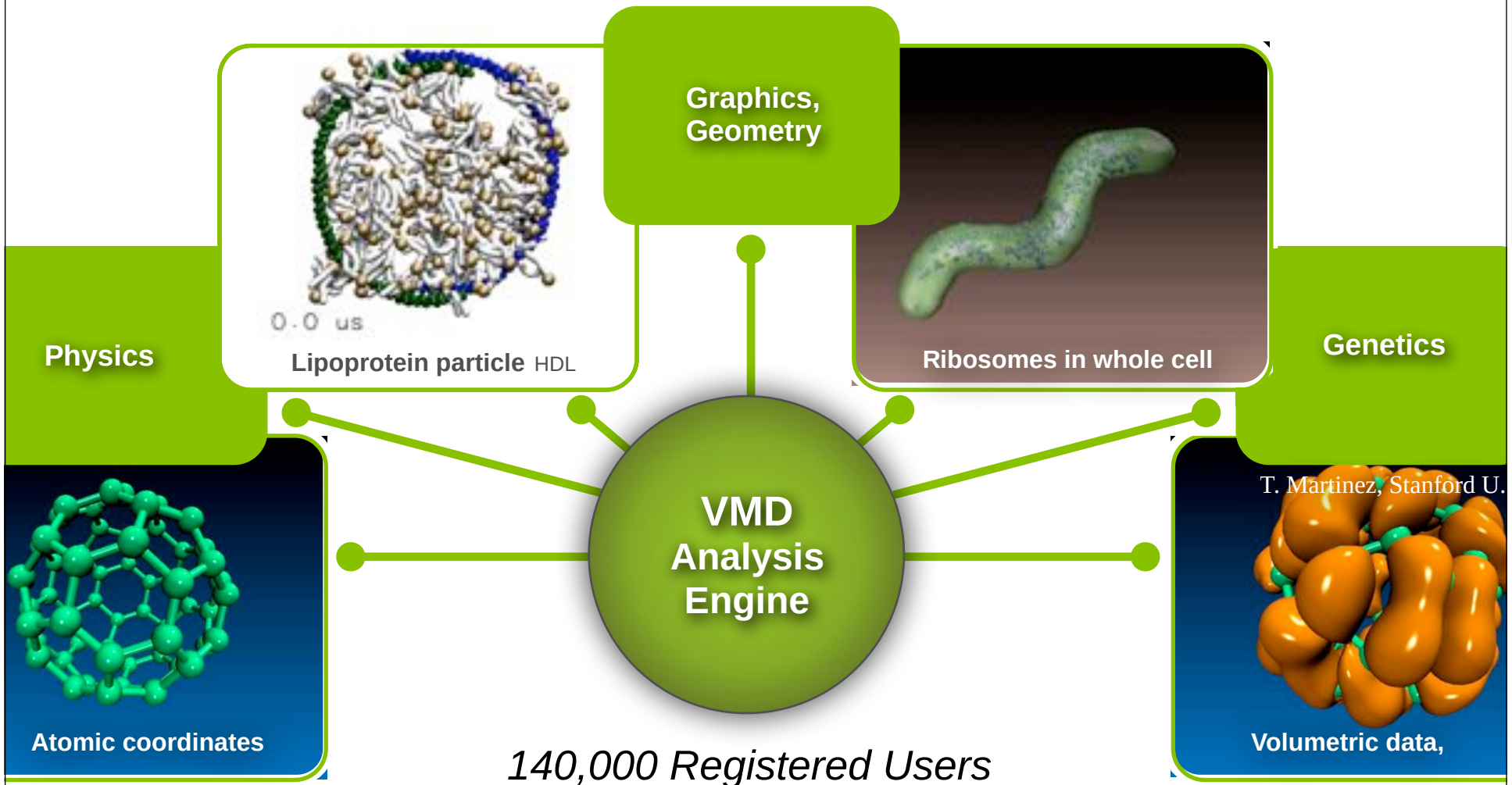
$$m_i \frac{d^2\vec{r}_i}{dt^2} = \vec{F}_i = -\vec{\nabla}U(\vec{R})$$

Math

$$\vec{r}_i(t + \Delta t) = 2\vec{r}_i(t) - \vec{r}_i(t - \Delta t) + \frac{\Delta t^2}{m_i}\vec{F}_i(t)$$

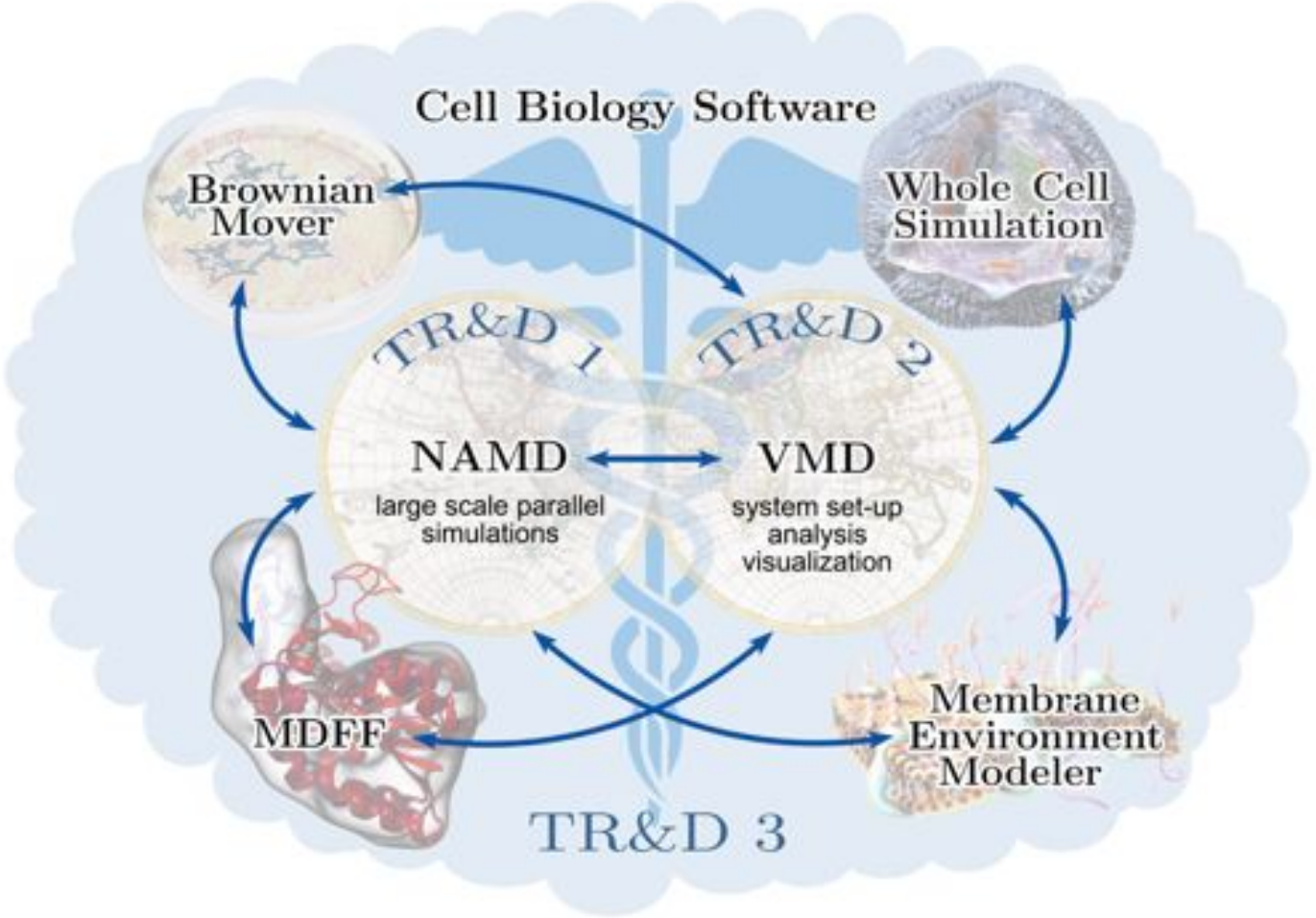
(repeat ***one billion times*** = microsecond)

Our Microscope Shows All, from Electrons to Cells



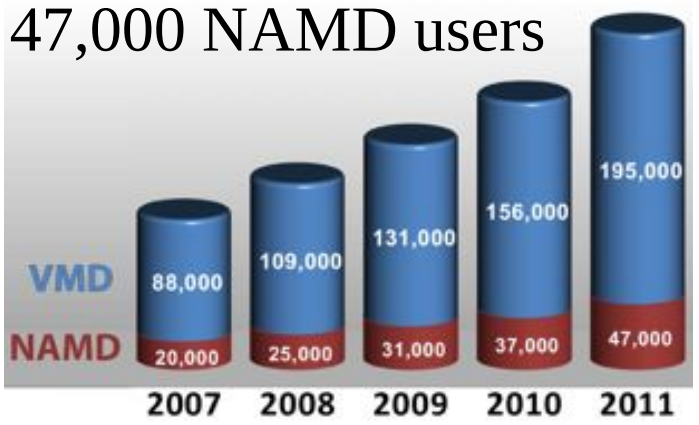
140,000 Registered Users

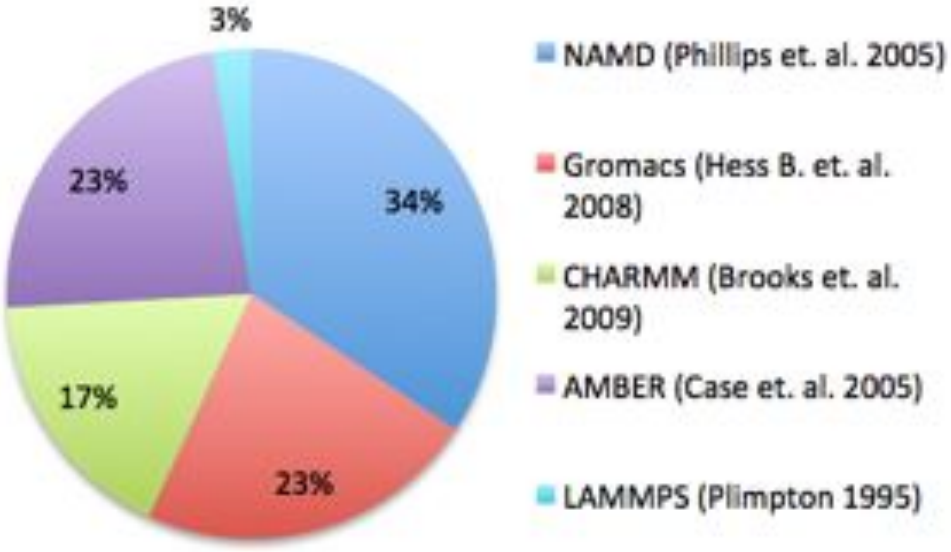
VMD and NAMD Work Together



VMD and NAMD are widely used in life science

195,000 VMD users &
47,000 NAMD users



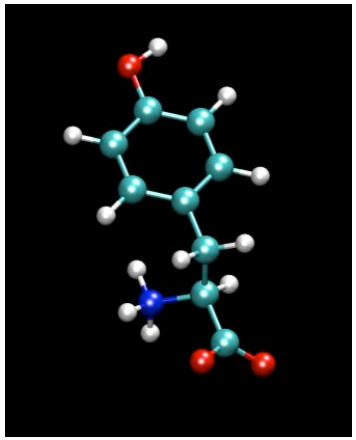


Molecular Dynamics Packages Cited in Biochemistry, Genetics and Molecular Biology Papers in 2011 (source: Scopus; comparing citations for primary publications)

NAMD is the "most used software" in NSF supercomputer centers, representing ~9% of total usage at 150 million SUs per year: nearly half of all biomedical computation at the supercomputing centers!

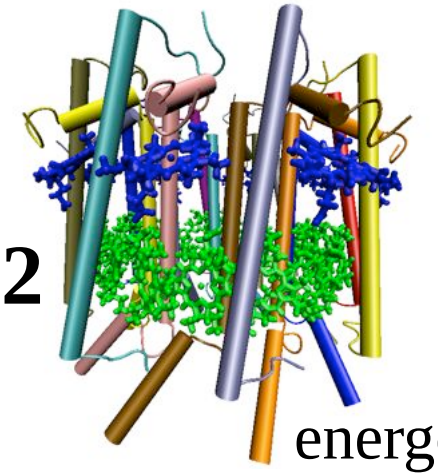
Lecture 1a

Introduction to Protein Structures - Molecular Graphics Tool

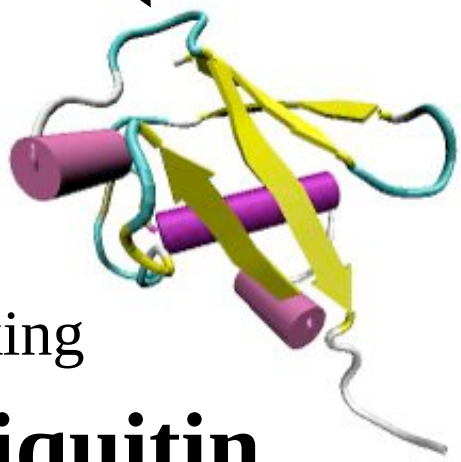


amino acid
tyrosine

LH2

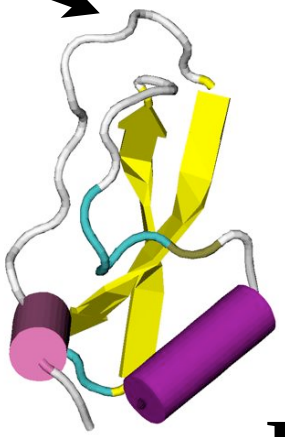


energetics



traficking

Ubiquitin

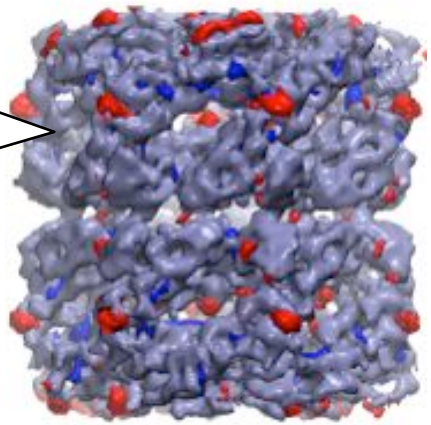


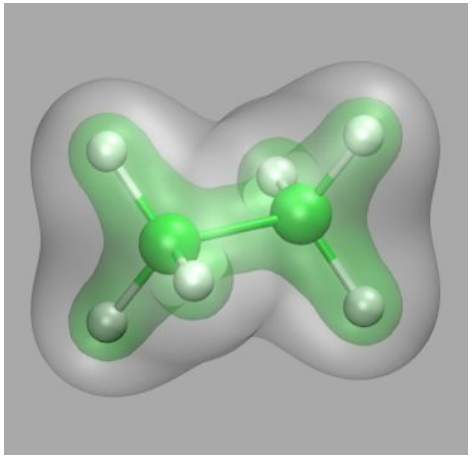
enzymatic control

BPTI

VMD – A Tool to Think

Volumetric Data:
Density maps,
Electron orbitals,
Electrostatic potential,
Time-averaged occupancy, …

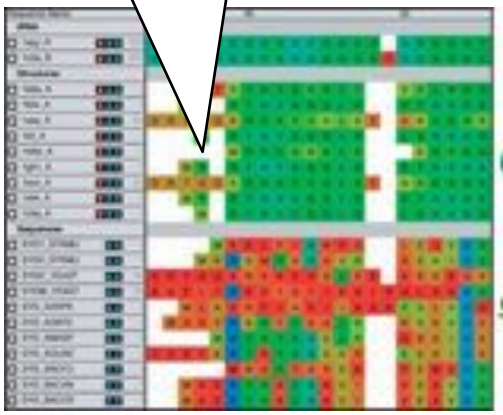




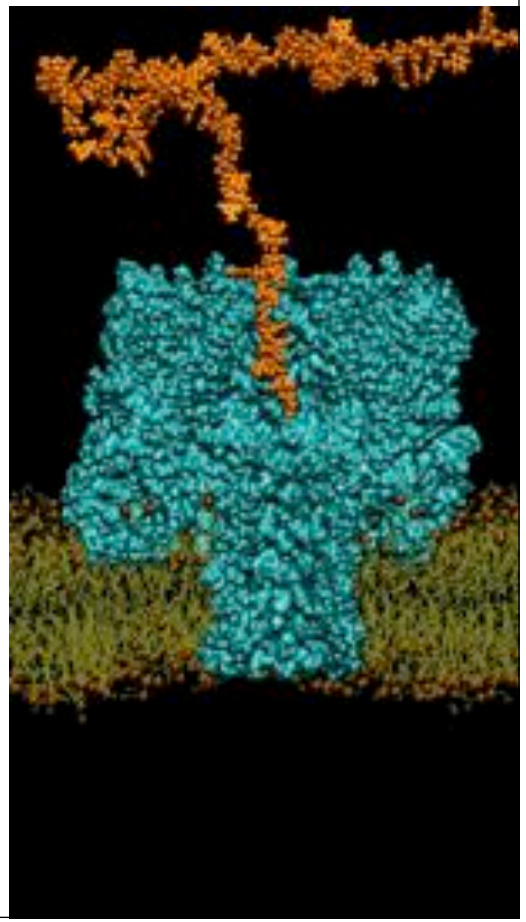
Sequence Data:
Multiple Alignments,
Phylogenetic Trees

VMD

Annotations



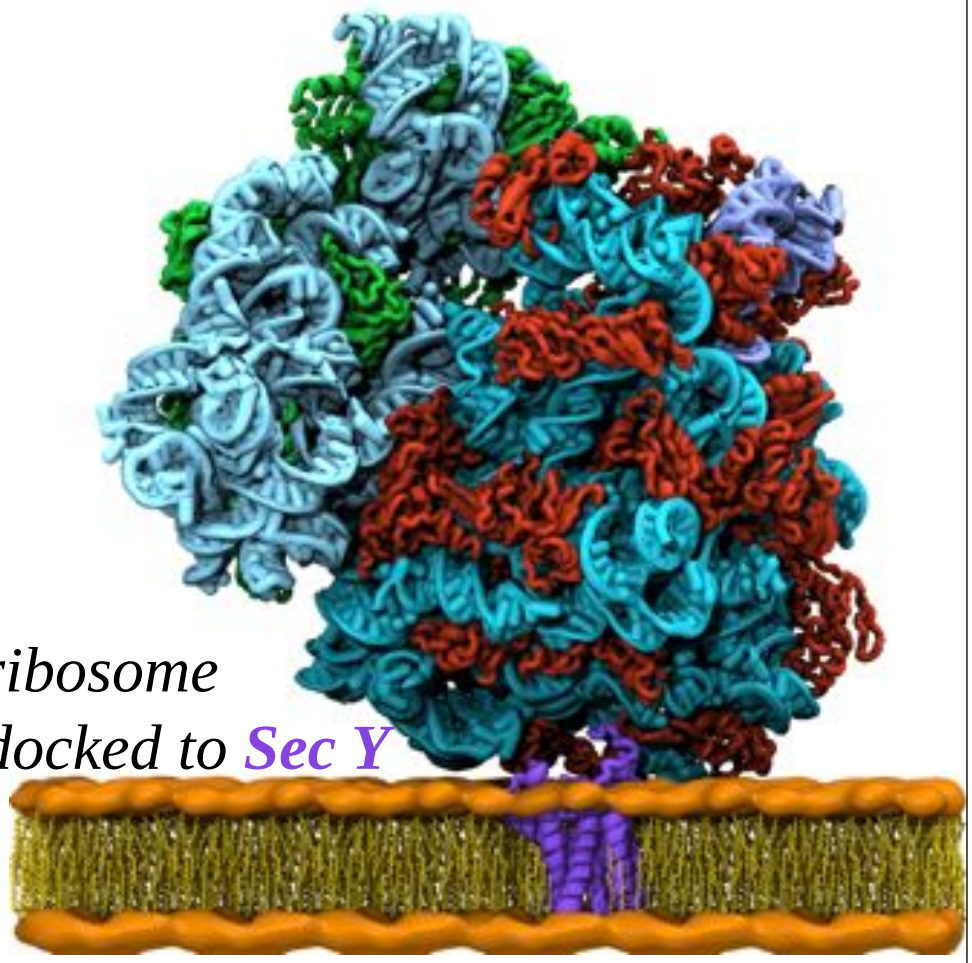
Atomic Data:
Coordinates,
Trajectories,
Energies,
Forces, …



National Center for Research Resources

Highlights of the VMD Molecular Graphics Program

- > 190,000 registered users
- Platforms:
  - Unix / Linux
  - Windows
  - MacOS X
- Display of large biomolecules and simulation trajectories
- Sequence browsing and structure highlighting
- Multiple sequence - structure analysis
- User-extensible scripting interfaces for analysis and customization



ribosome docked to ***Sec Y***

The program is used today more for preparation and analysis of modeling than for graphics

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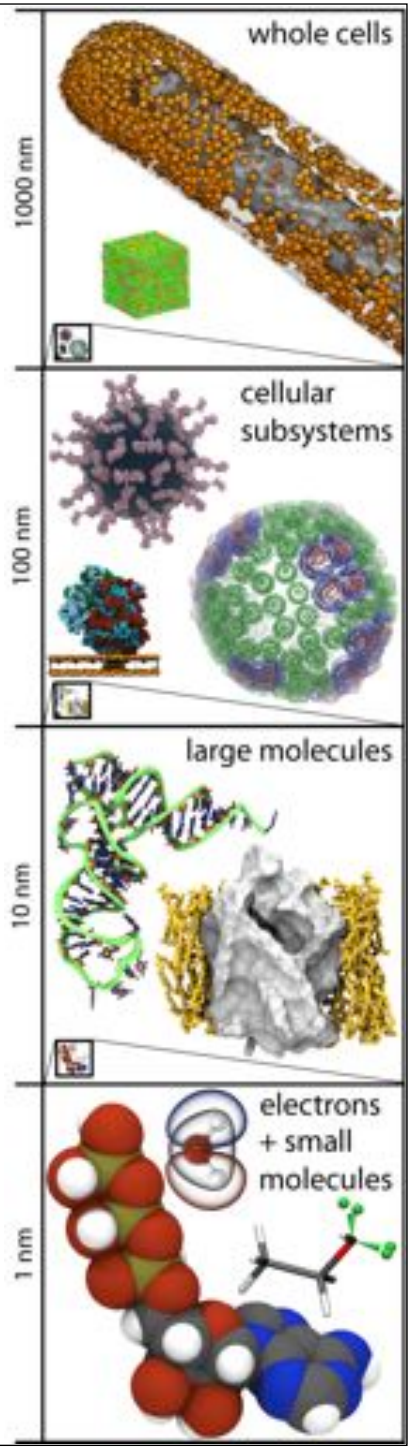
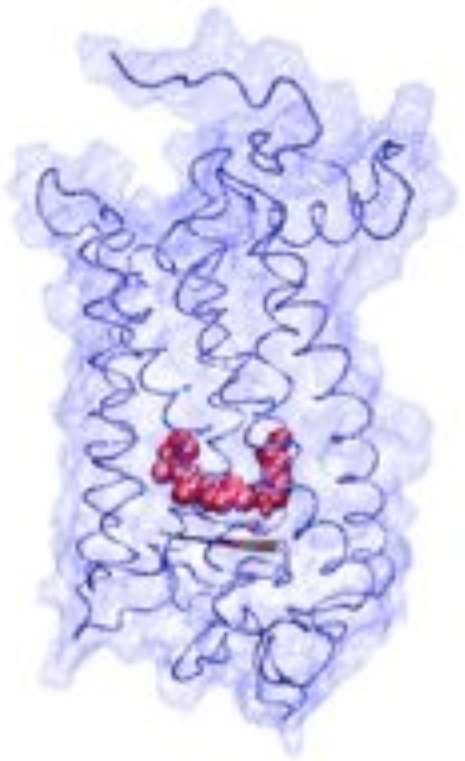
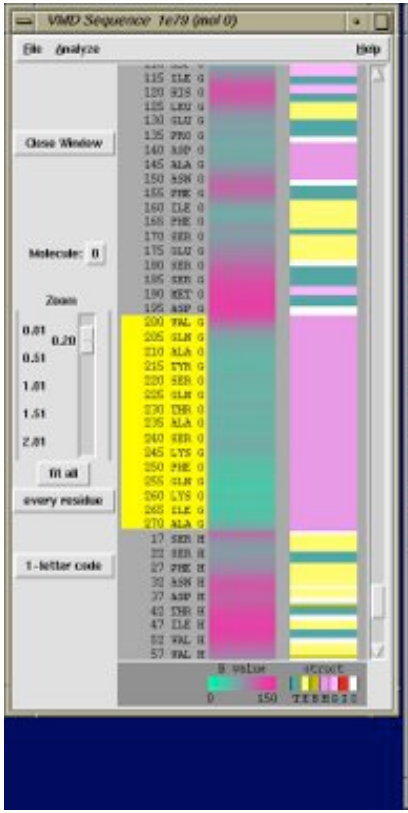
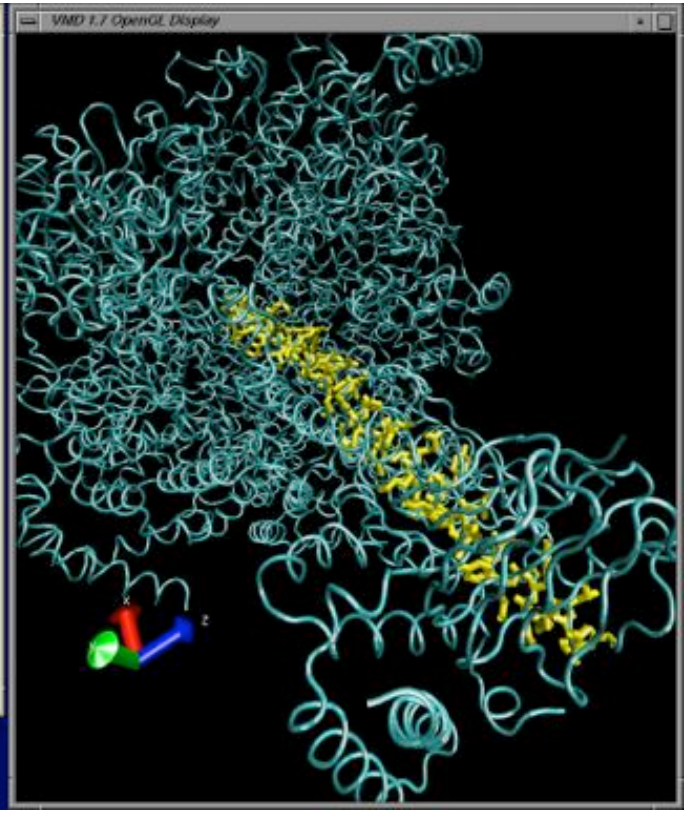


Molecular Graphics Perspective of Protein Structure and Function

see tutorial at http://www.ks.uiuc.edu/Training/Tutorials/



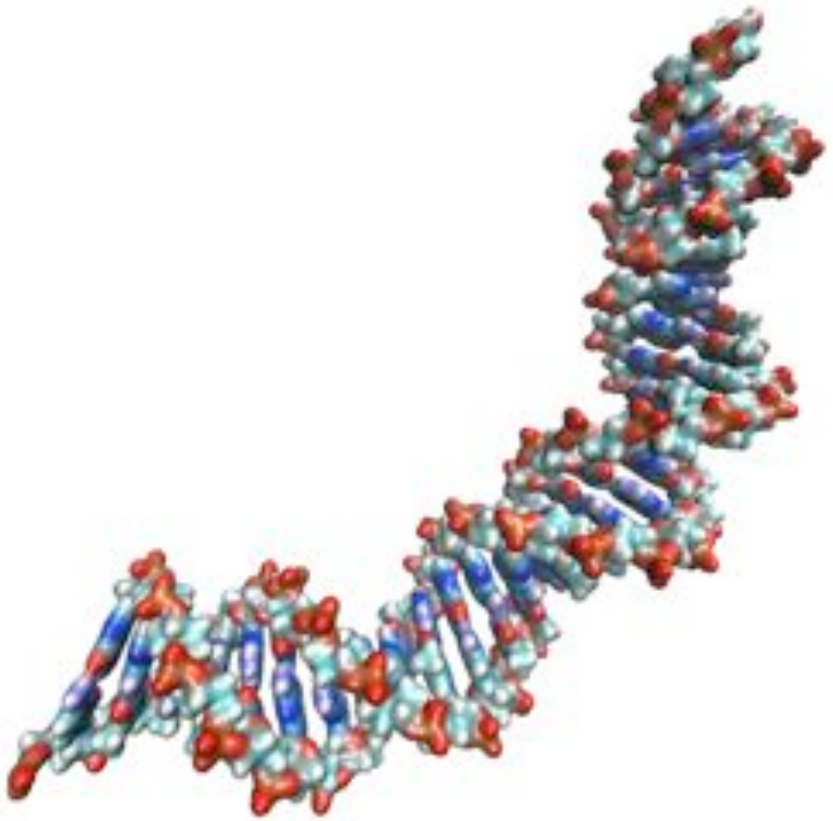




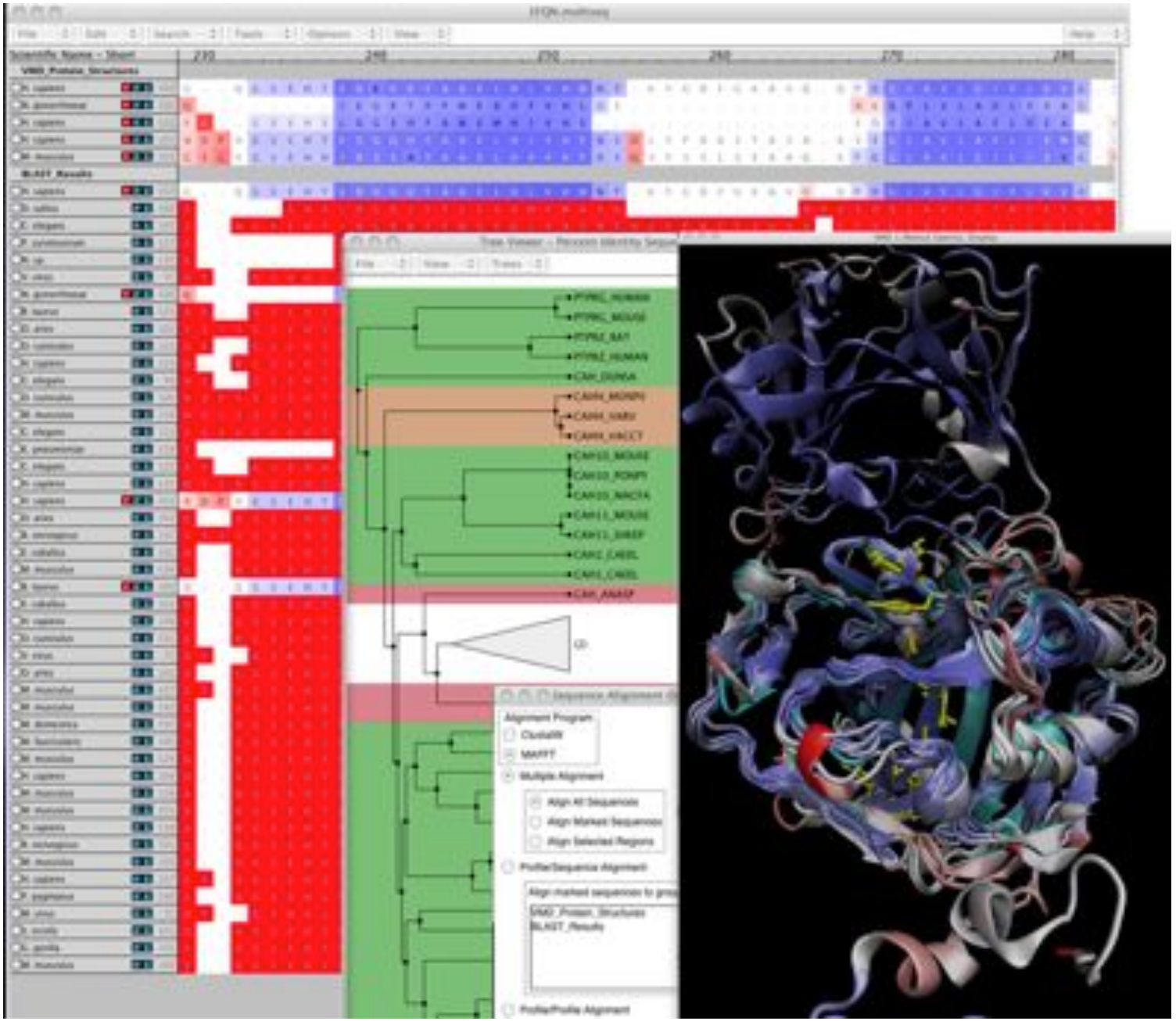
animation sequence structure

Advanced Analysis: "QuickSurf" Molecular Graphics New in VMD 1.9.1

- Supports all-atom, coarse-grained, and cellular scale models
- Displays continuum of structural detail, can be varied dynamically
- Uses multi-core CPUs and GPU acceleration to enable smooth animation of MD trajectories
- Linear-time algorithm, scales to hundreds of millions of particles, limited only by memory capacity



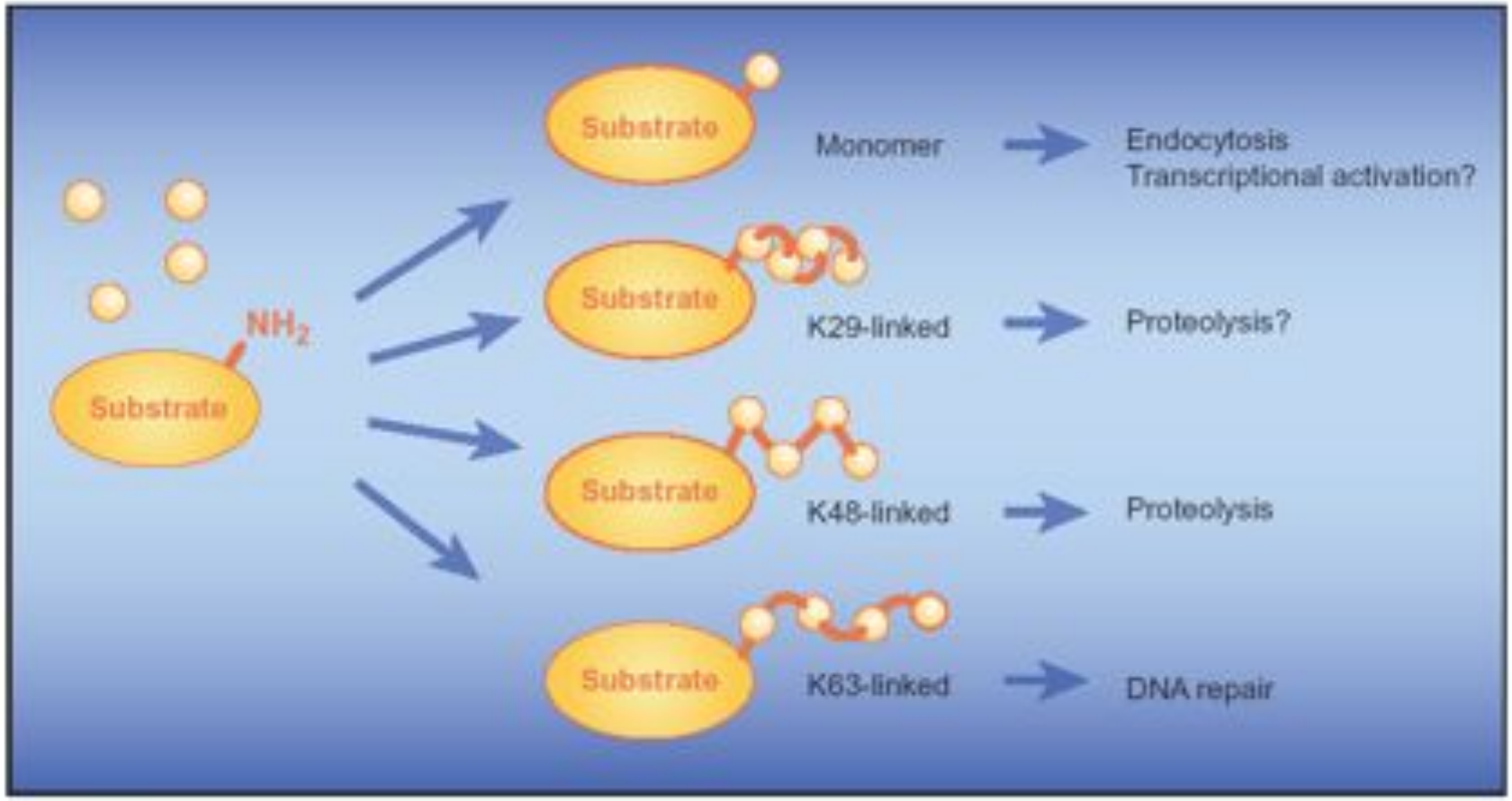
Fast Visualization of Gaussian Density Surfaces for Molecular Dynamics and Particle System Trajectories. M. Krone, J. Stone, T. Ertl, K. Schulten. *EuroVis 2012*, 2012. (*Submitted*)


Scientific_Name - Short
VAST_Protein_Structures
BLAST_Results
Alignment Program
ClustalW
MAFFT
Multiple Alignment
Align All Sequences
Align Marked Sequences
Align Selected Regions
Profile/Sequence Alignment
Profile/Profile Alignment

Ubiquitin

- 76 amino acids
- highly conserved
- covalently attaches to proteins and tags them for degradation
- other cell traficking

Mono-ubiquitylation versus multi-ubiquitylation

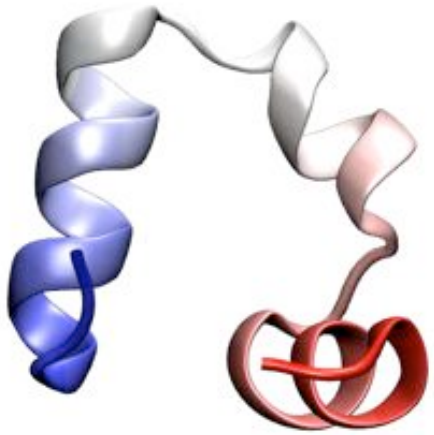


Multifaceted. Ubiquitin can attach to its various substrate proteins, either singly or in chains, and that in turn might determine what effect the ubiquitination has. (K29, K48, and K63 refer to the particular lysine amino acid used to link the ubiquitins to each other.)

Marx, J., Ubiquitin lives up its name, Science 297, 1792-1794 (2002)

VMD Demo

VMD New Timeline plug-in



Alpha helix Extended beta Isolated bridge 3-10 helix Beta turn None (coil)

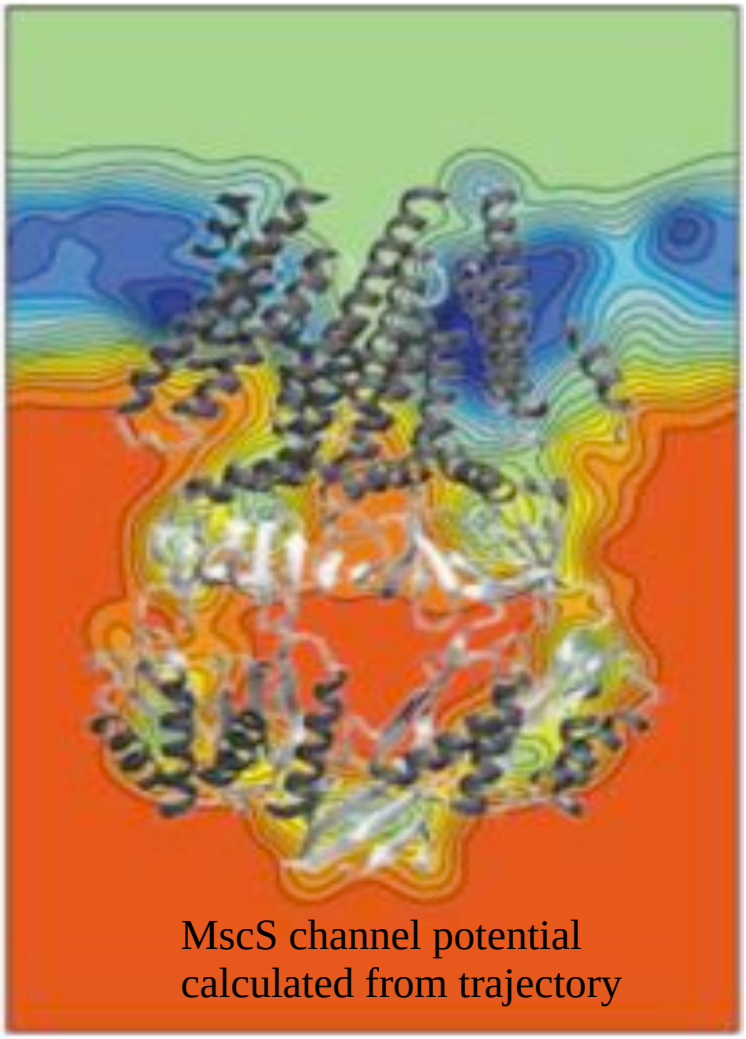
Per-residue secondary structure: villin headpiece folding from a fully denatured state.
7μs simulation; 654 atoms; over 1 million frames to examine

VMD **Timeline plug-in**: graphing and analysis tool to identify events in an MD trajectory
- a single picture shows changing properties across entire structure, entire trajectory.
- explore time vs. attribute (per-residue or per-selection) linked to molecular structure
- many analysis methods available; user-extendable

Electrostatic Potential Maps

New VMD features made possible through GPU computing

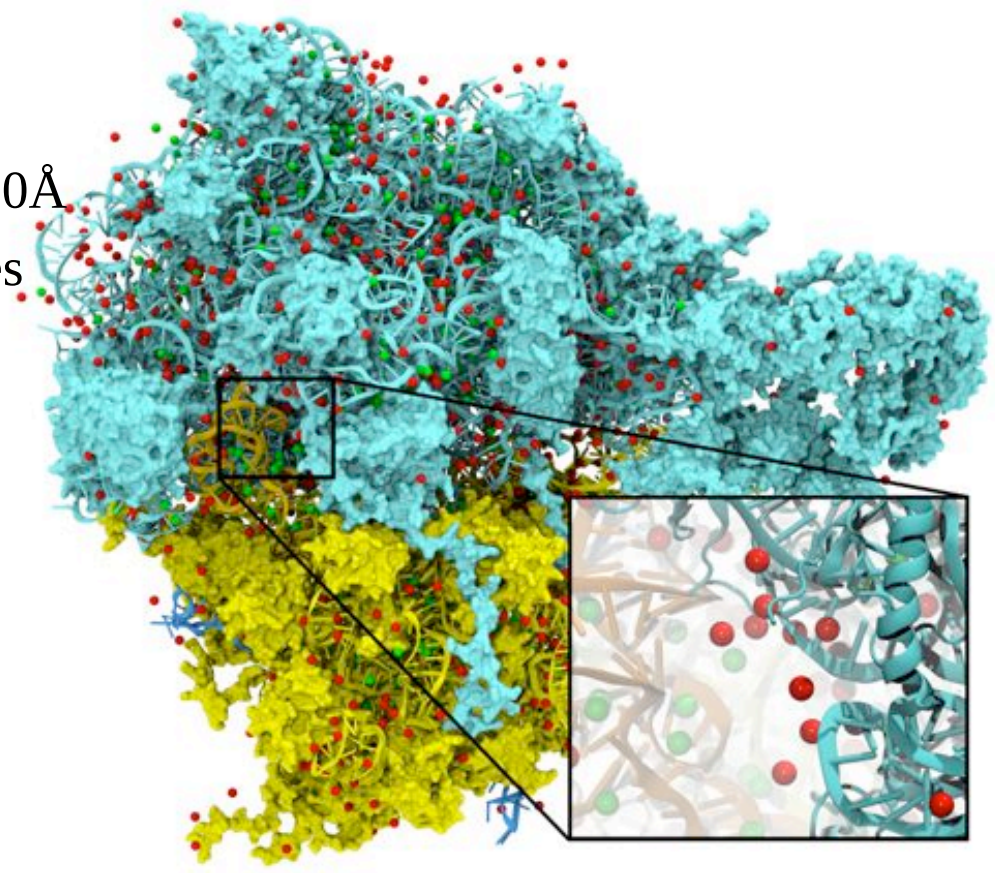
- Electrostatic potentials evaluated on 3-D lattice
- Applications include:
  - Ion placement for structure building
  - Time-averaged potentials for simulation
  - Visualization and analysis



MscS channel potential calculated from trajectory

Time-averaged Electrostatic Potential Calculation for the Ribosome with VMD

- Direct Coulomb summation ~580,000 atoms
  - Lattice spacing 1.0Å, padding 10Å
  - Time-average from 1,000 frames
- 3 GPUs: 49 hours
- 3 CPUs: 0.23 years (est.)

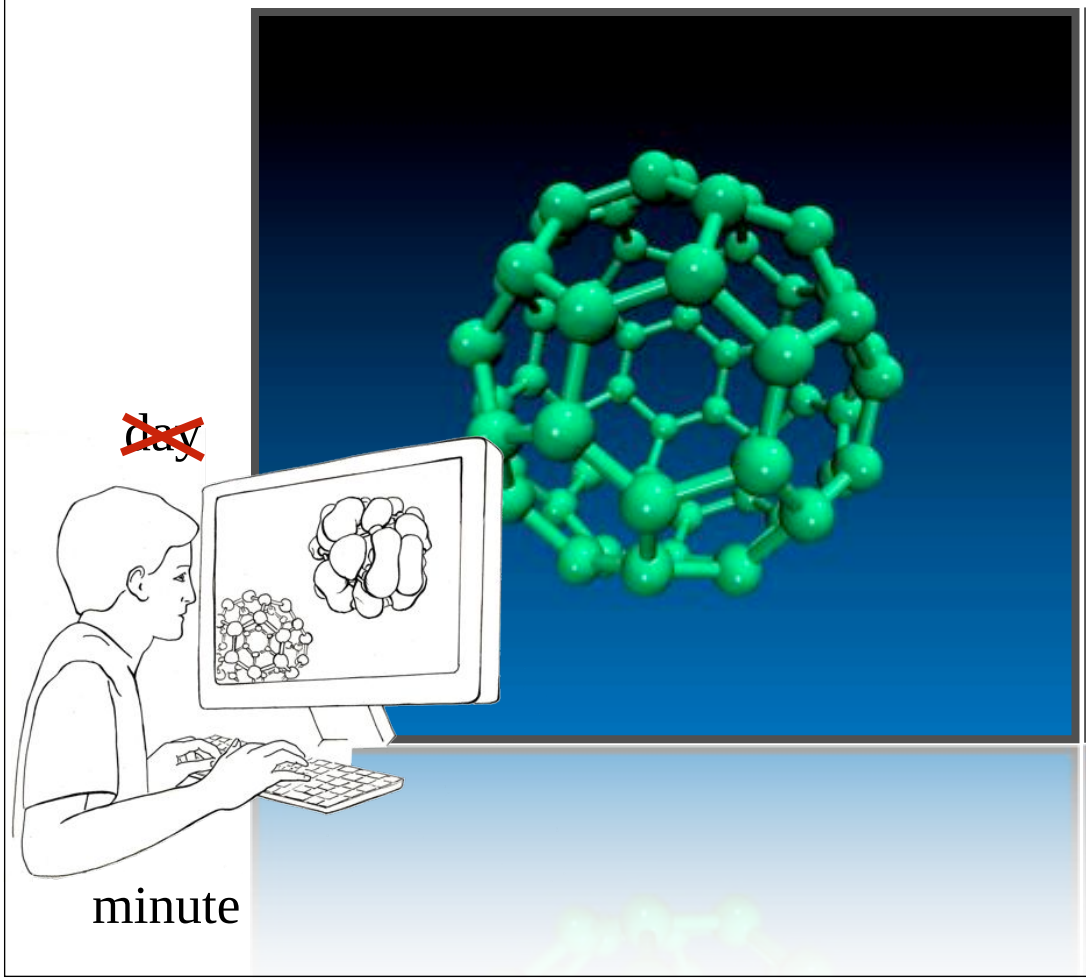


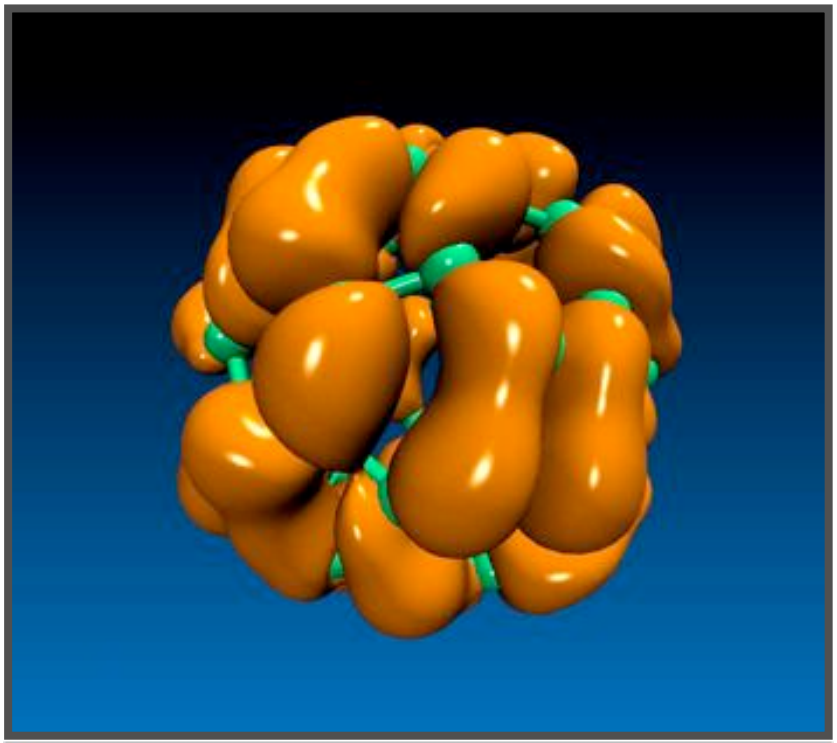
This was one of our early results, using the multi-GPU direct Coulomb summation algorithm, showing the benefit it gave at the time. Now that we have MSM (multilevel summation) we would get much faster performance since it is a linear-time algorithm, but we haven't yet re-run these tests using MSM.

Stone et al. (2007) *J Comp Chem* 28:2618-2640

Quantum Chemistry Visualization

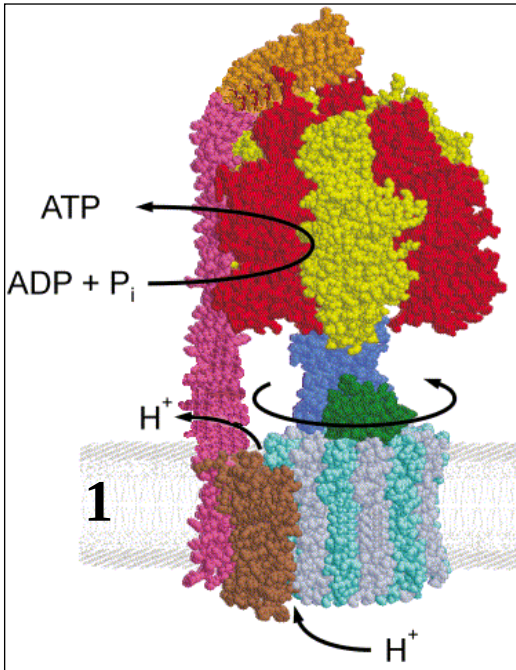
Rendering of electron “clouds” achieved on GPUs as quickly as you see this movie! CPUs: One working day!



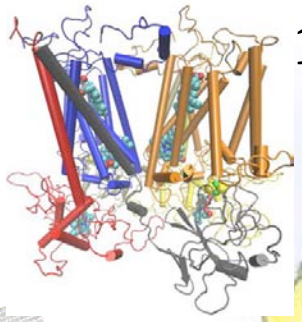


Simulation: Terachem Interactive Visualization: VMD
Courtesy T. Martinez, Stanford

The proteins that make up the chromatophore of photosynthetic bacteria

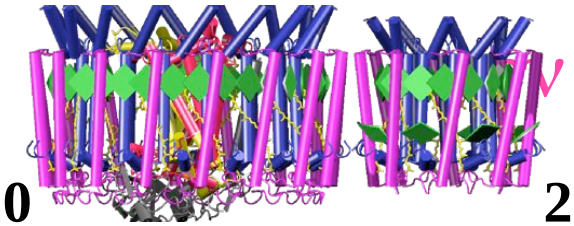


1



10

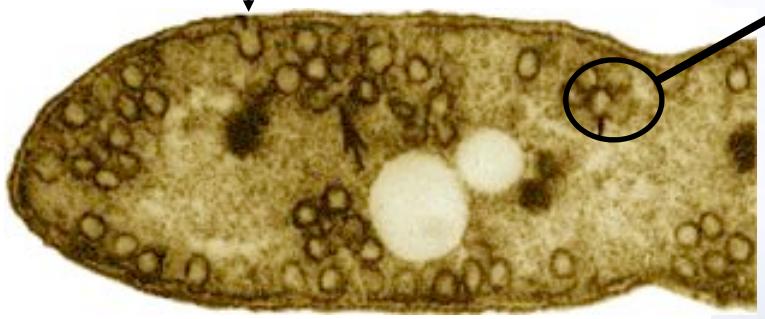
5



20

200

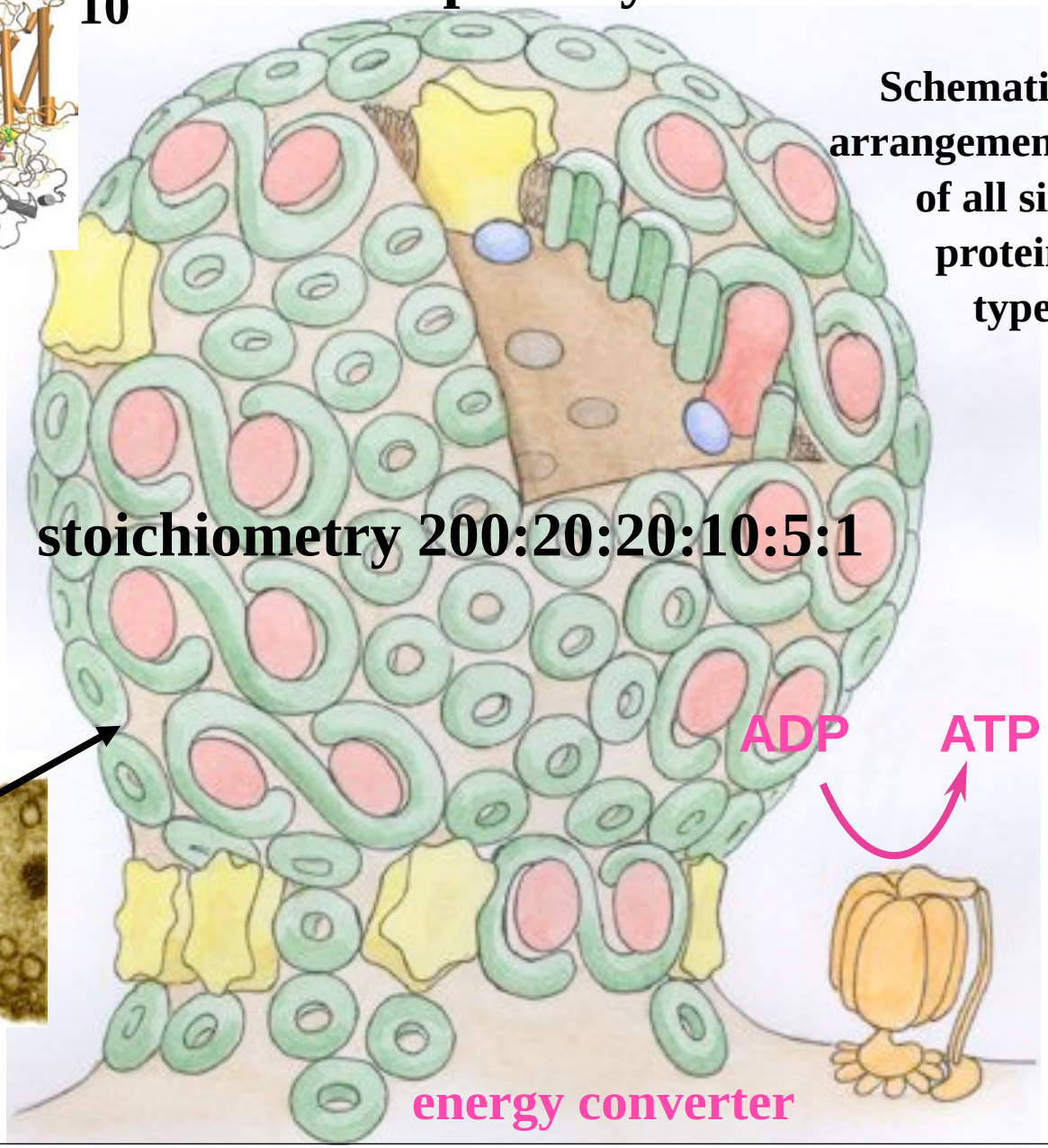
photosynthetic unit



purple bacterium cell

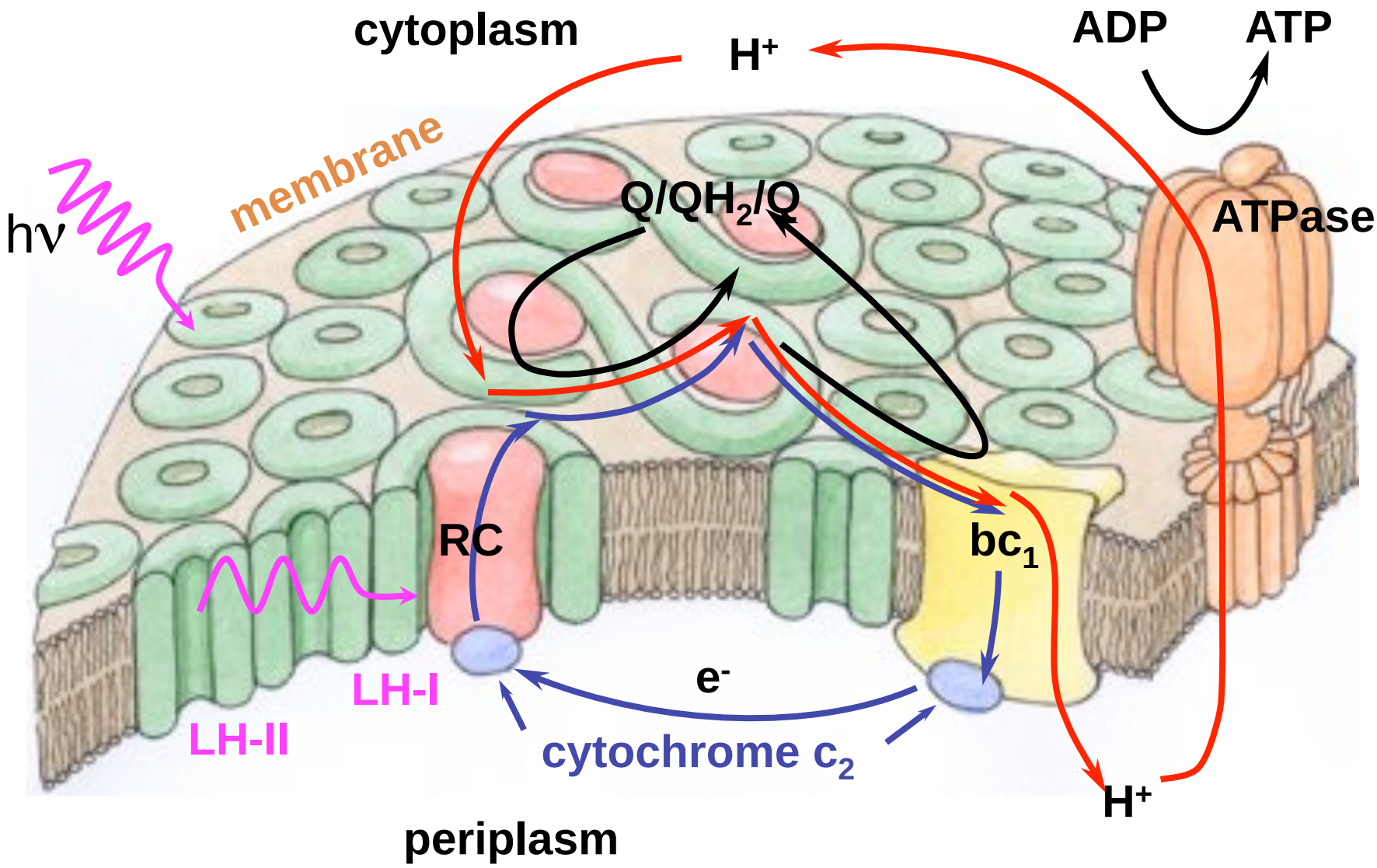
Schematic arrangement of all six protein types

stoichiometry 200:20:20:10:5:1



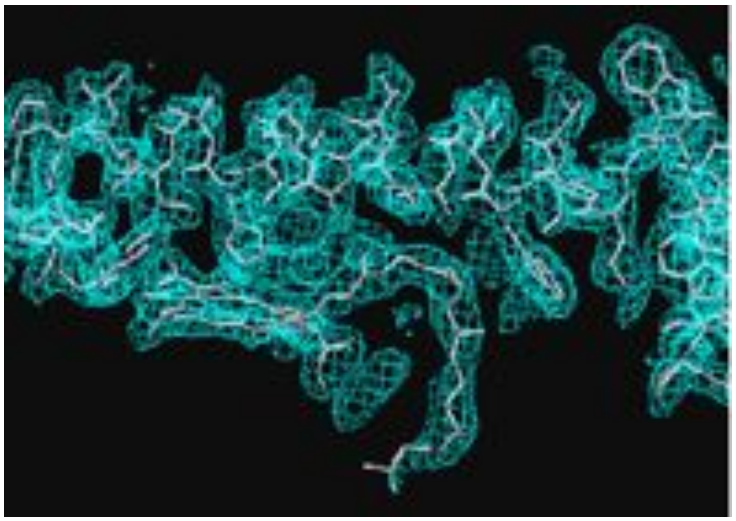
Chromatophore of Purple Bacteria

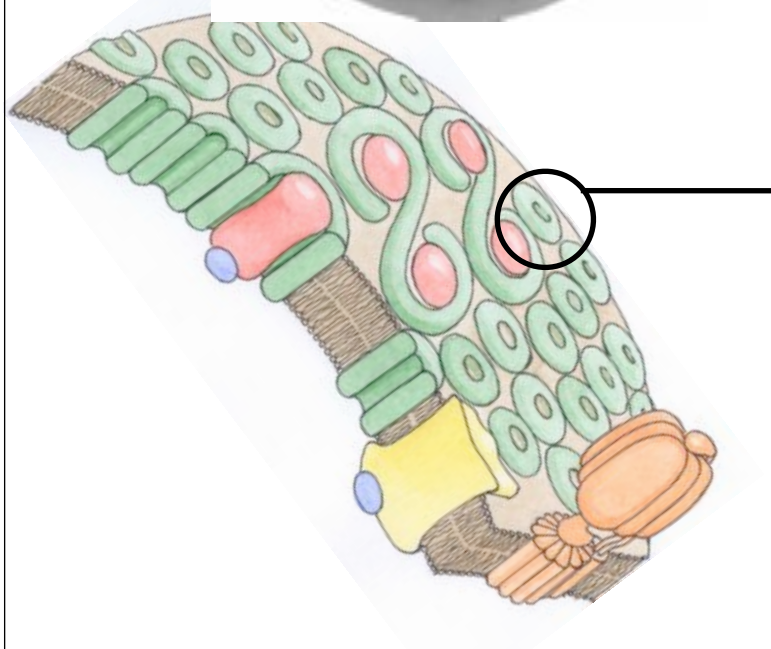
(section of the chromatophore membrane)



Structure of LH 2 of *Rs. molischianum*

molecular replacement



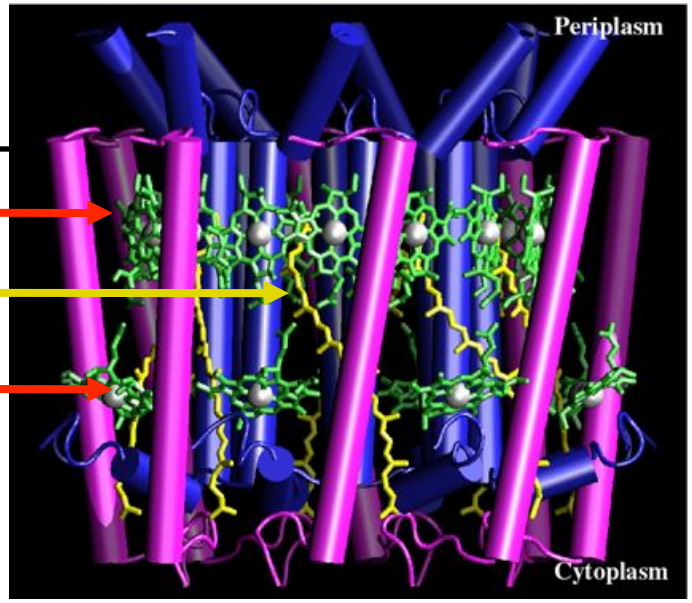


B850 band

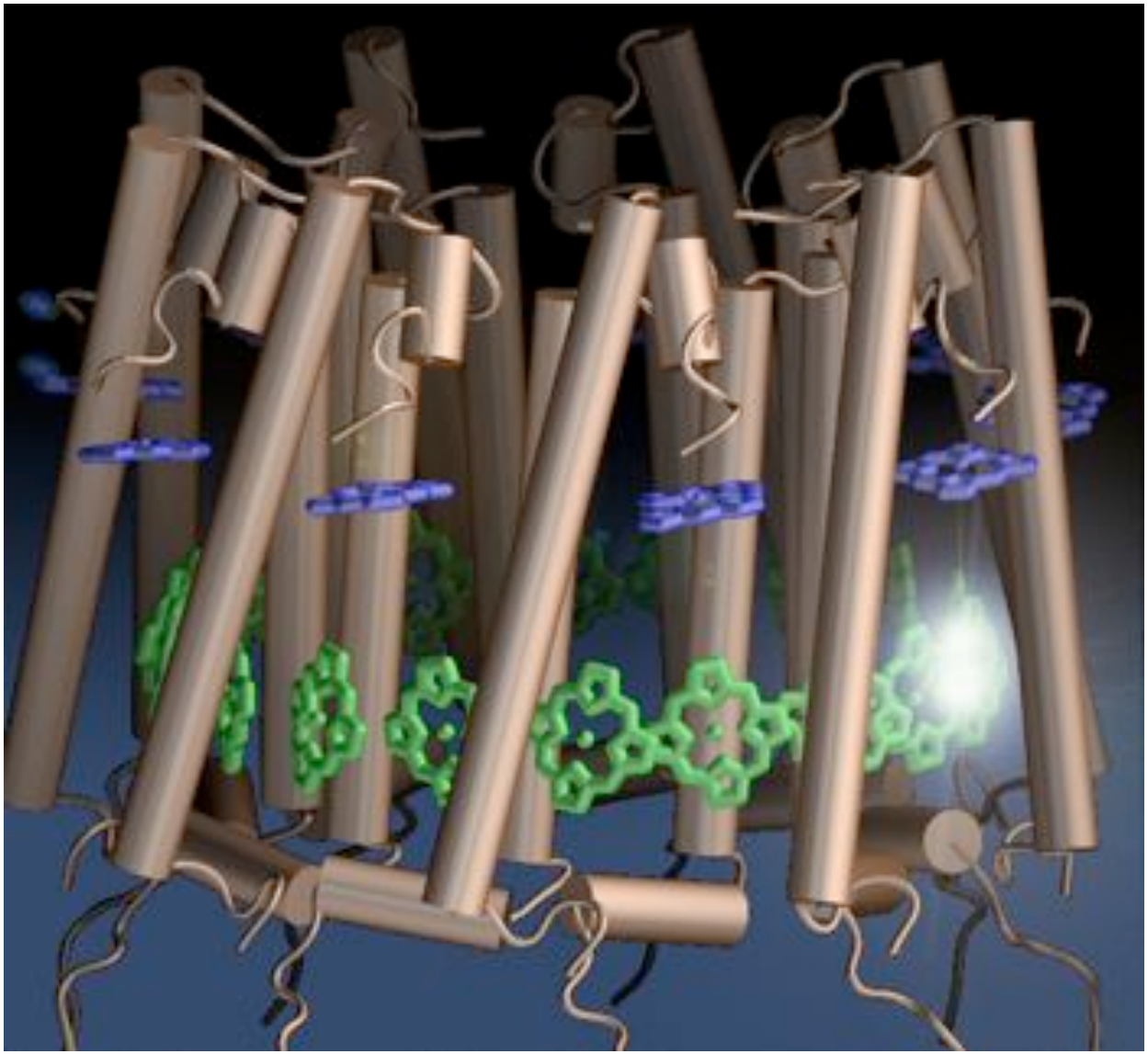
B500 band

B800 band

optical spectrum

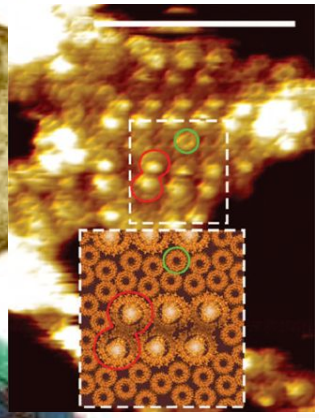


Koepke et al., Structure, **4**, 581 (1996)

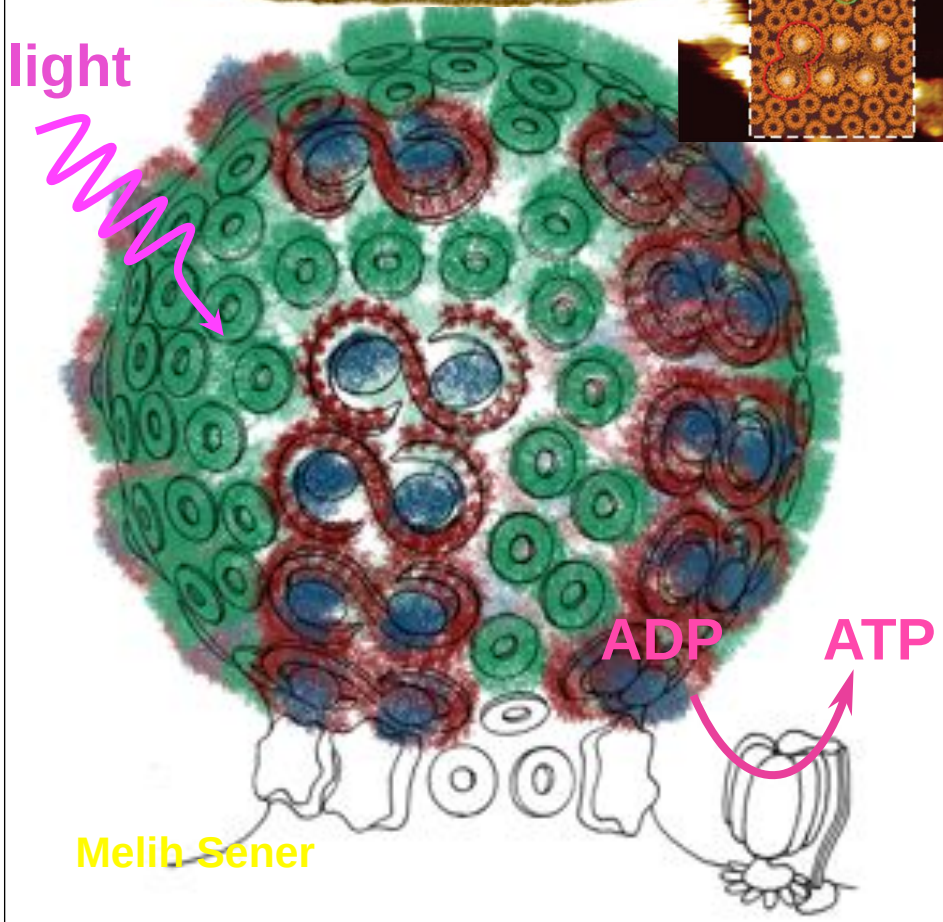


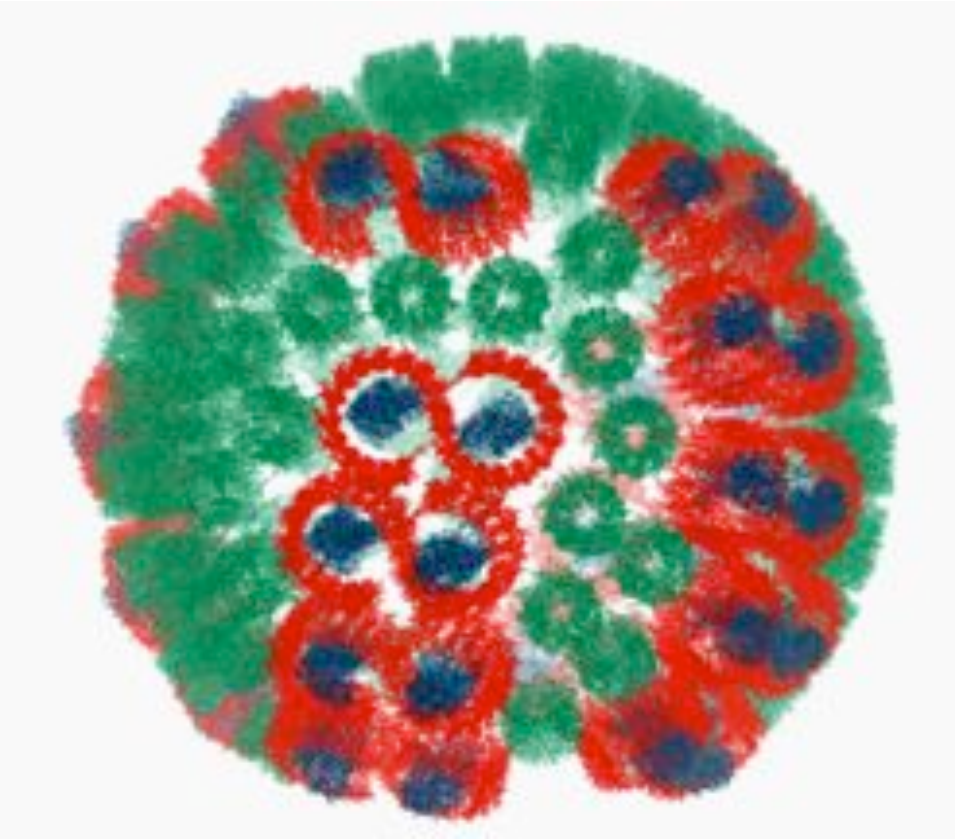
VMD Demo

Knowing the Atomic Level Structure



of the chromatophore, one can systematically describe its physical mechanism



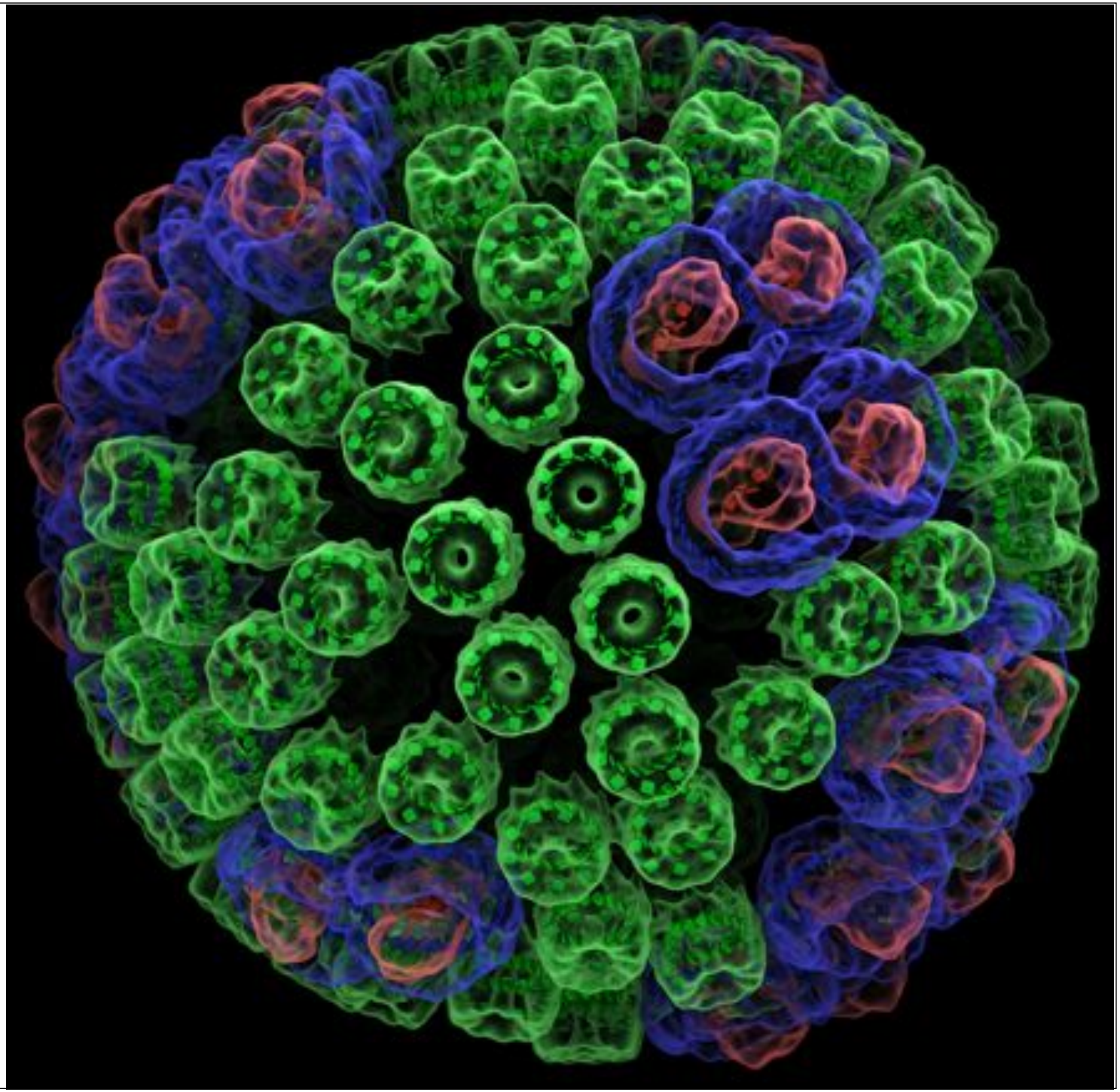


M. Sener, J. Olsen, N. Hunter, and K. Schulten. *PNAS*, **104:** 15723-15728, 2007

VMD Demo

QuickSurf Representation w/ Angle-Modulated Transparency

Chromatophore 10M atoms

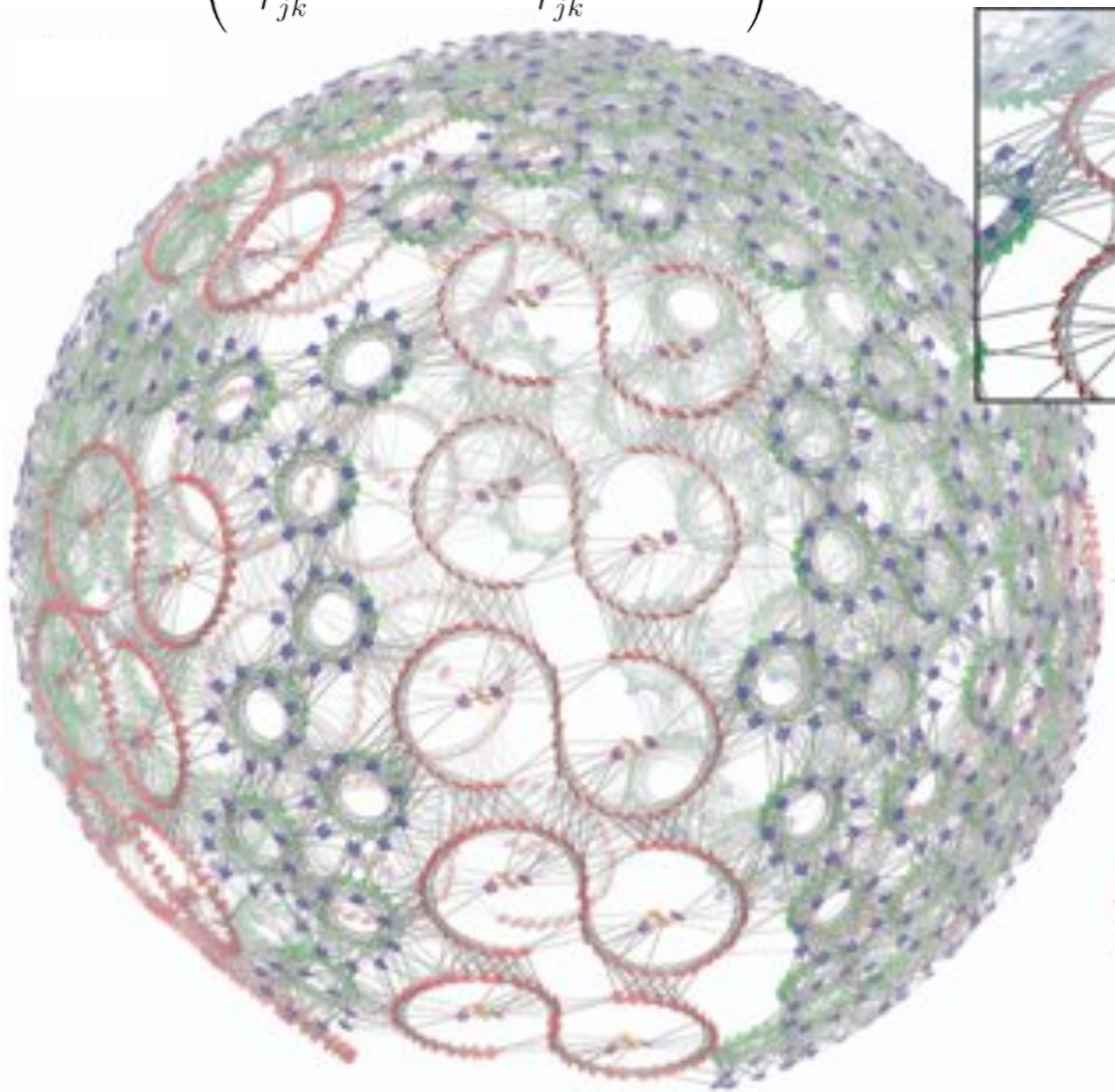


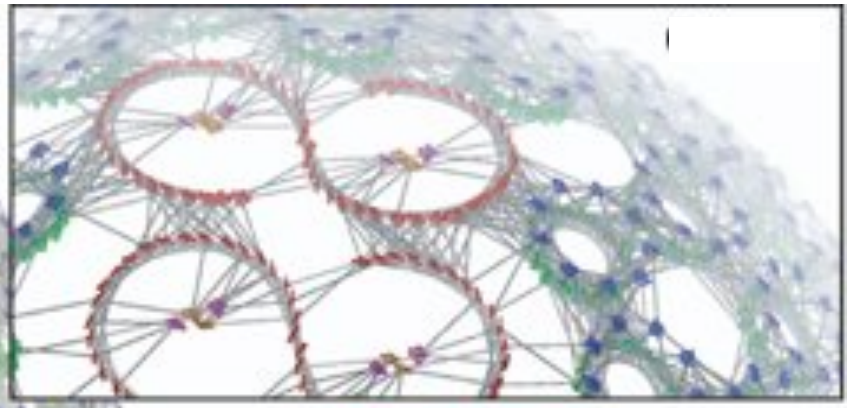
National Center for Research Resources

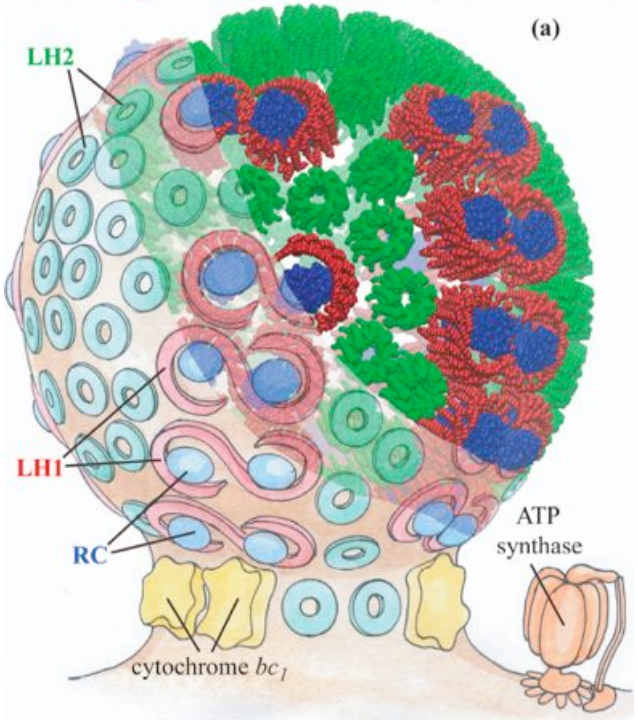
The “Physics” of Light Harvesting in the Chromatophore

Calculated Energy Transfer Rates Determine Optimal Placement of Proteins in Chromatophore

$$W_{jk} = C\left(\frac{\vec{d}_j \cdot \vec{d}_k}{{r_{jk}}^3} - \frac{3(\vec{r}_{jk} \cdot \vec{d}_j)\,(\vec{r}_{jk} \cdot \vec{d}_k)}{{r_{jk}}^5}\right)$$ links: induced dipole - induced dipole interaction







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