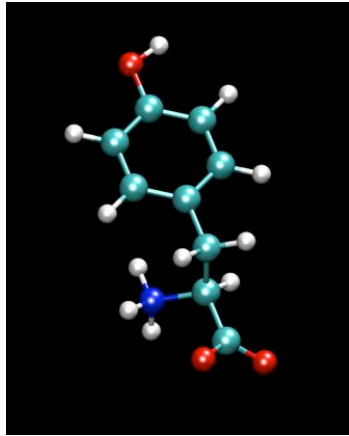
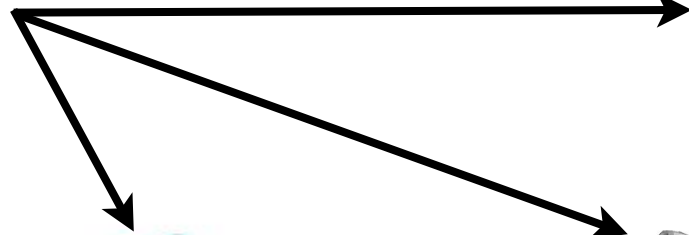


Lecture 1a

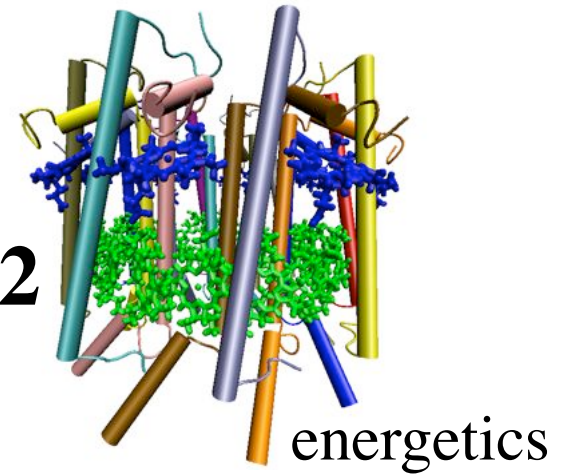
Introduction to Protein Structures - VMD Tool



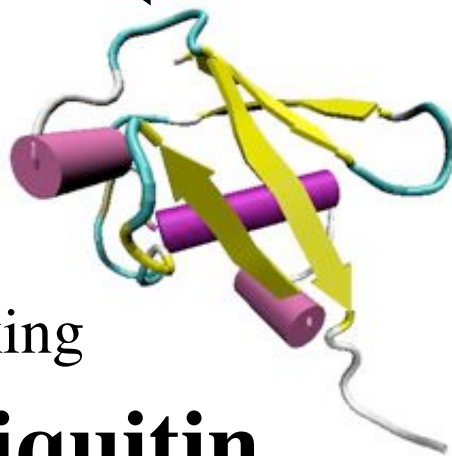
*amino acid
tyrosine*



LH2

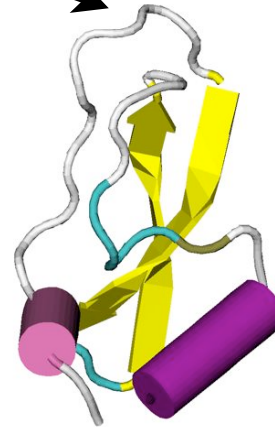


energetics



trafficking

Ubiquitin

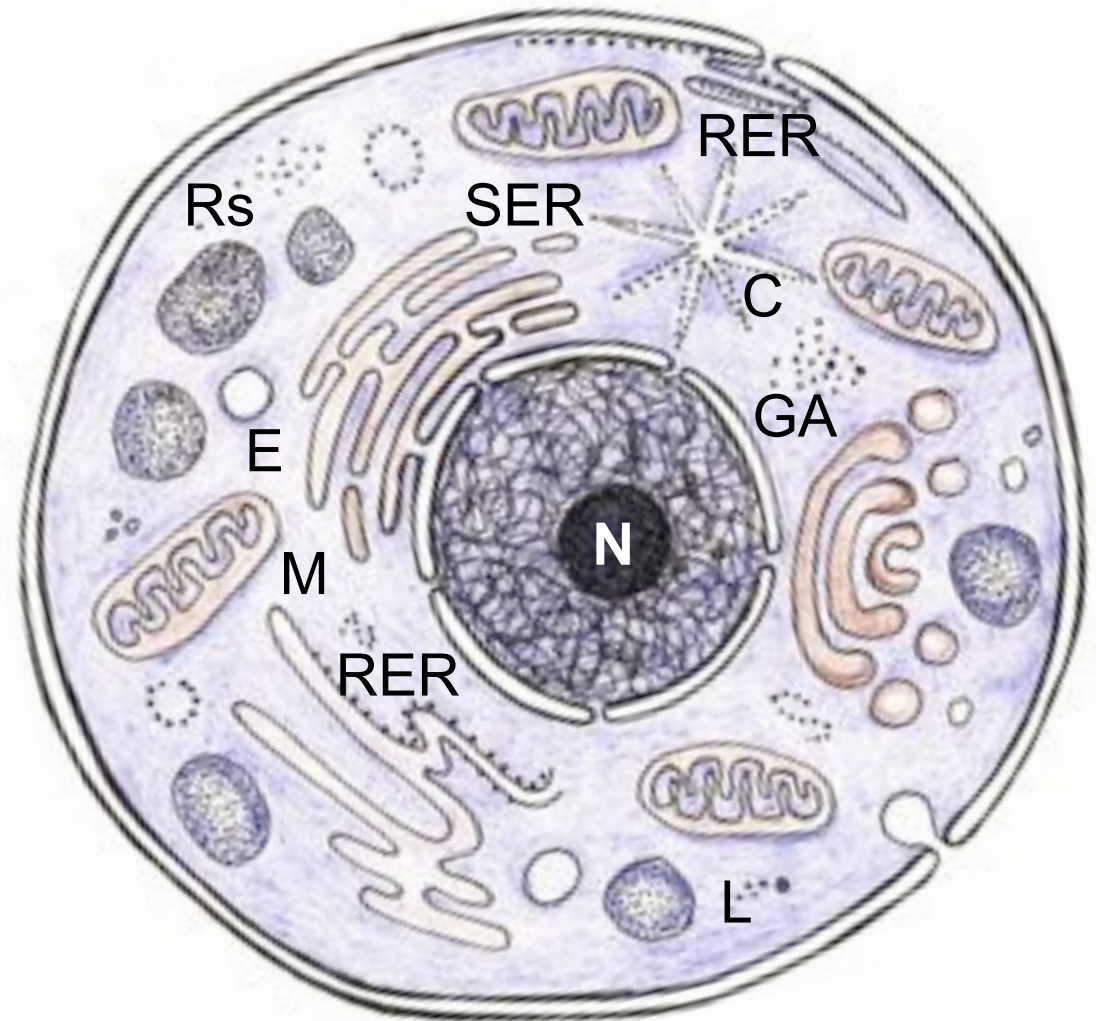


enzymatic control

BPTI

**The
Computational
Microscope**

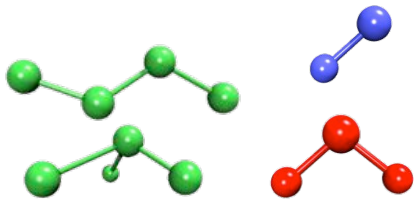
**Computational microscope views
at atomic resolution ...**



**... how living cells maintain
health and battle disease**

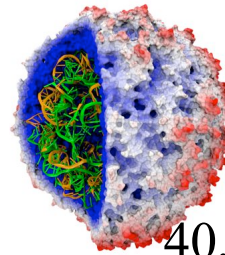
Our Microscope is Made of...

Chemistry



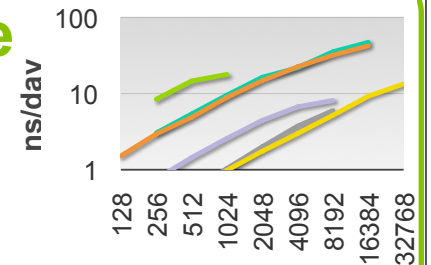
$$U(\vec{R}) = \underbrace{\sum_{\text{bonds}} k_i^{\text{bond}} (r_i - r_0)^2}_{U_{\text{bond}}} + \underbrace{\sum_{\text{angles}} k_i^{\text{angle}} (\theta_i - \theta_0)^2}_{U_{\text{angle}}} + \underbrace{\sum_{\text{dihedrals}} k_i^{\text{dihe}} [1 + \cos(n_i \phi_i + \delta_i)]}_{U_{\text{dihedral}}}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

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

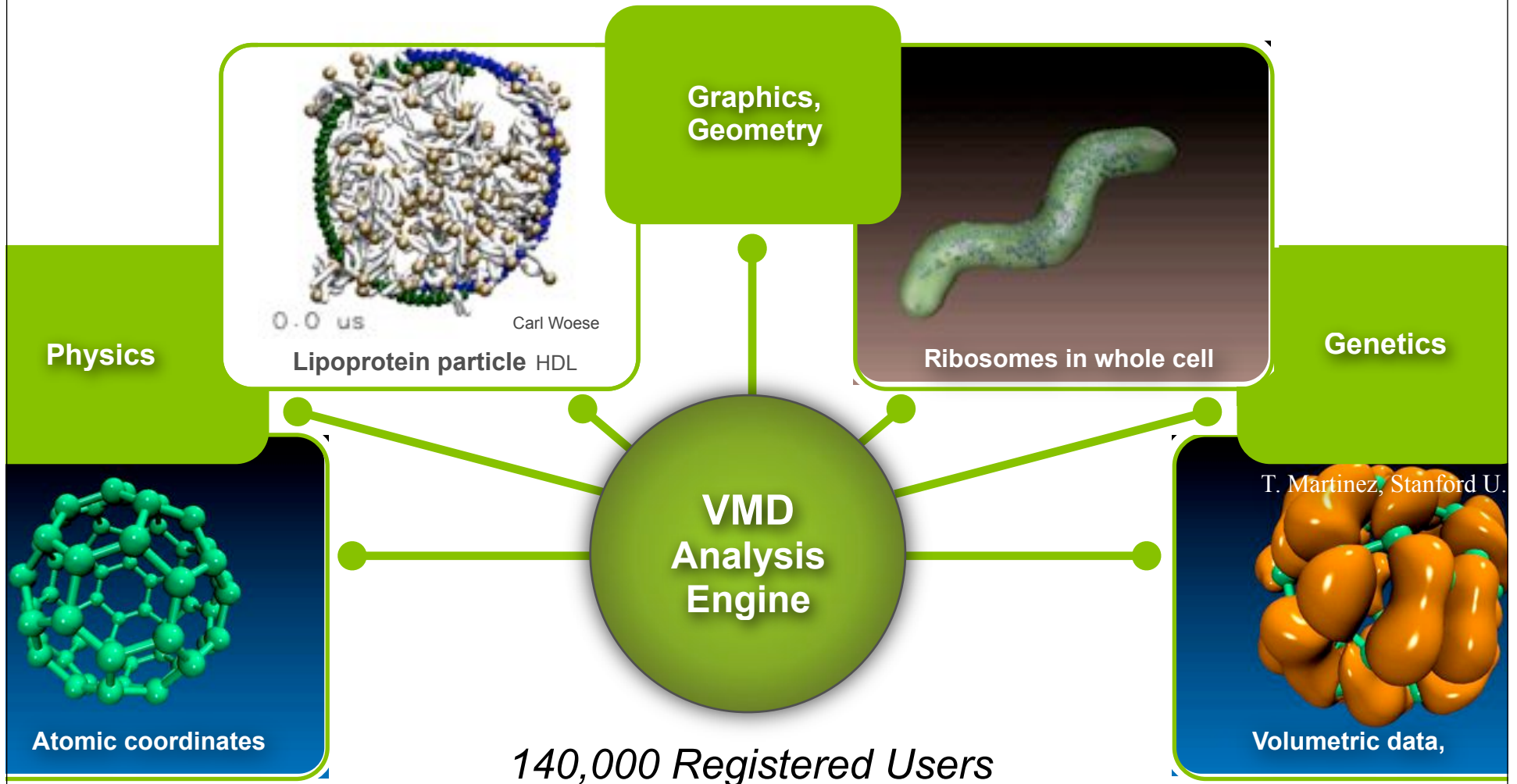
$$\vec{r}_i(t + \Delta t) = 2\vec{r}_i(t) - \vec{r}_i(t - \Delta t) + \frac{\Delta t^2}{m_i} \vec{F}_i(t)$$

(repeat *one billion times* = microsecond)



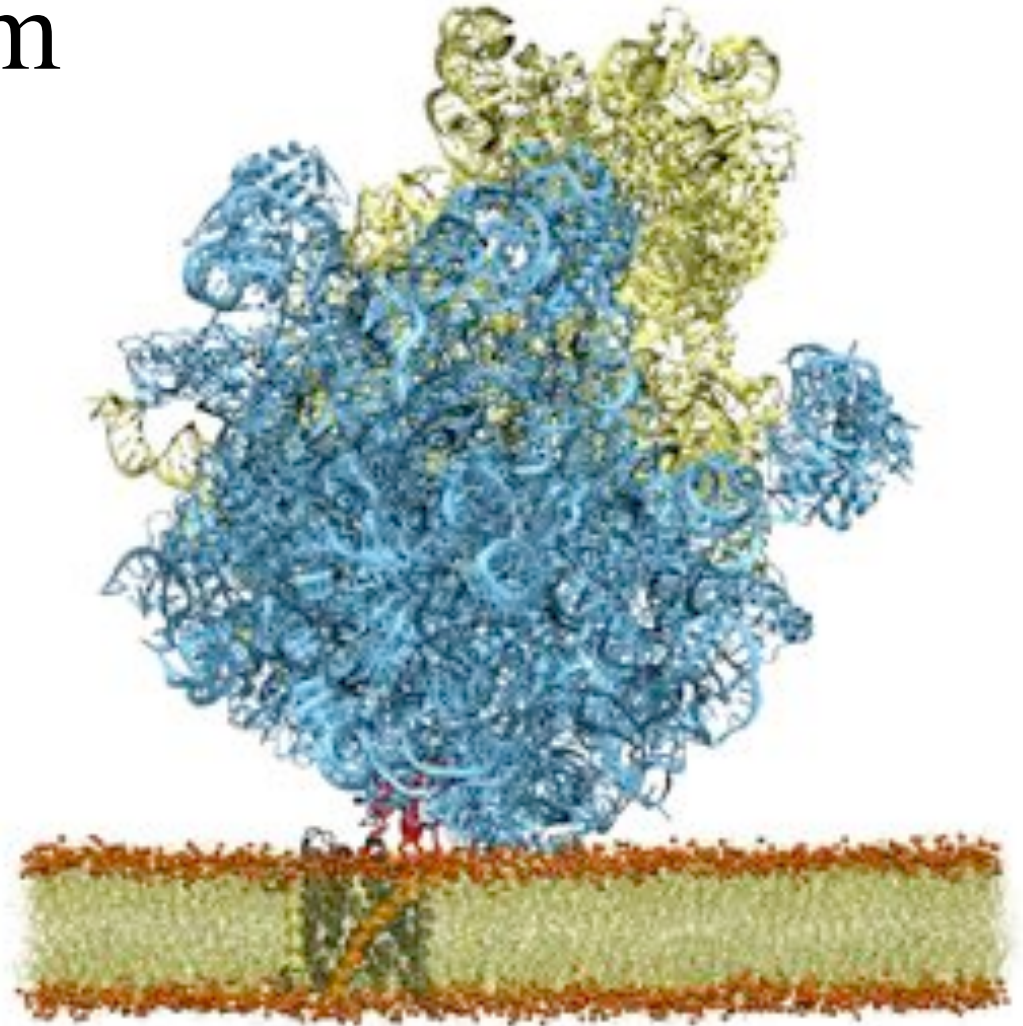
..and Supercomputers

Our Microscope is a “Tool to Think”



Highlights of the VMD Molecular Graphics Program

- > 140,000 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

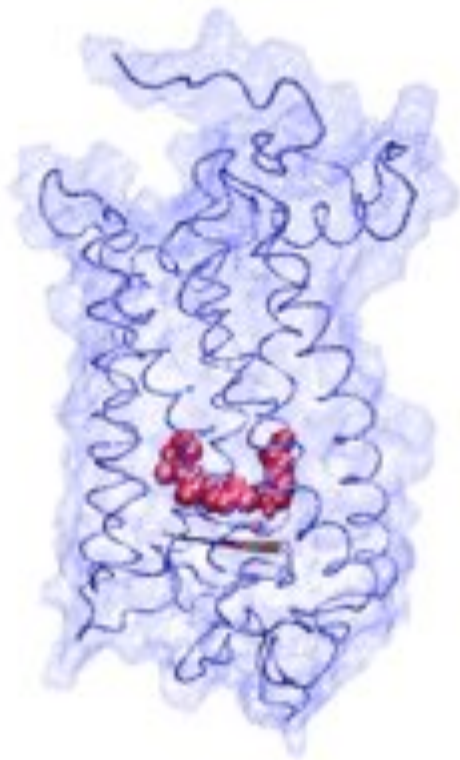


Key Features of VMD

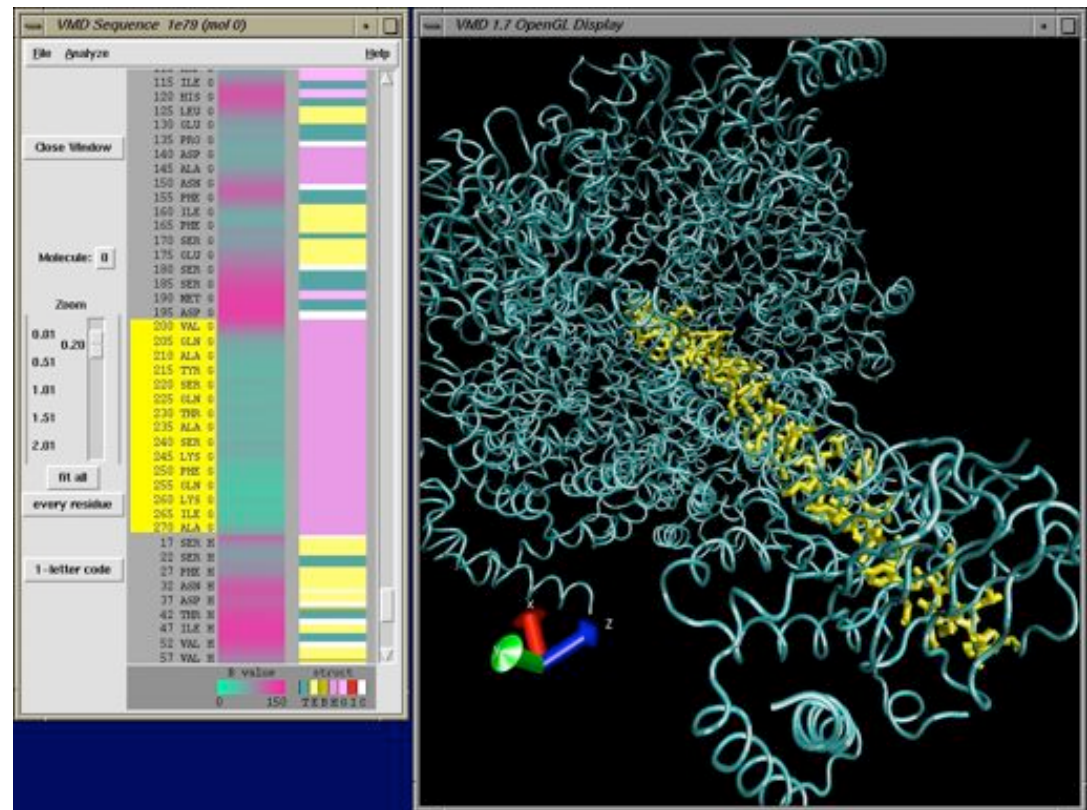
- General 3-D molecular visualization with extensive drawing and coloring methods
- Extensive atom selection syntax for choosing subsets of atoms for display
- Visualization of dynamic molecular data
- Visualization of volumetric data
- No limits on the number of molecules or trajectory frames, except available memory
- Rendering high-resolution, publication-quality molecule images
- Movie making capability
- Extensions to the Tcl/Python scripting languages
- Extensible source code written in C and C++
- Built in GPU acceleration support
- Supports cluster computing for extensive analysis runs
- Building and preparing systems for molecular dynamics simulations
- Interactive molecular dynamics simulations

Molecular Graphics Perspective of Protein Structure and Function

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



animation

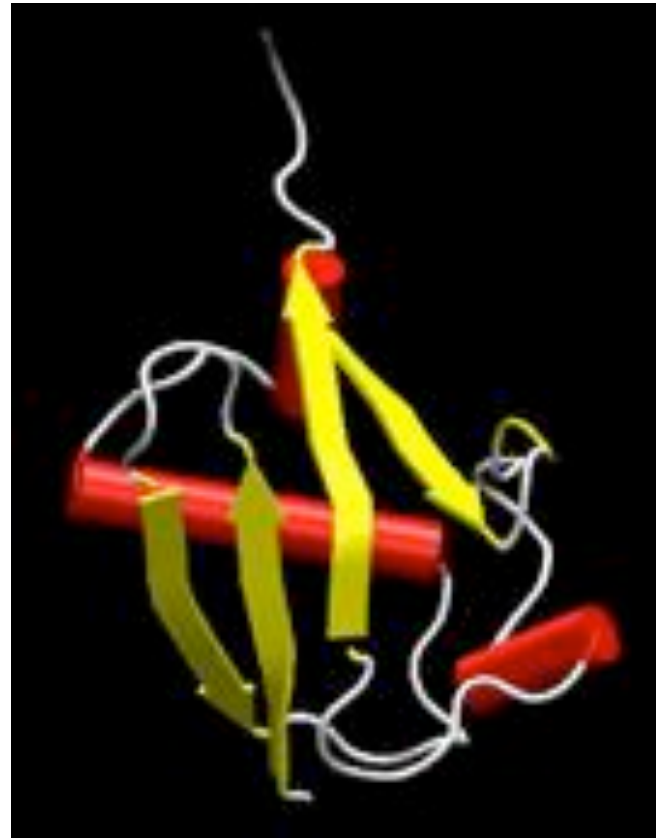


sequence

structure

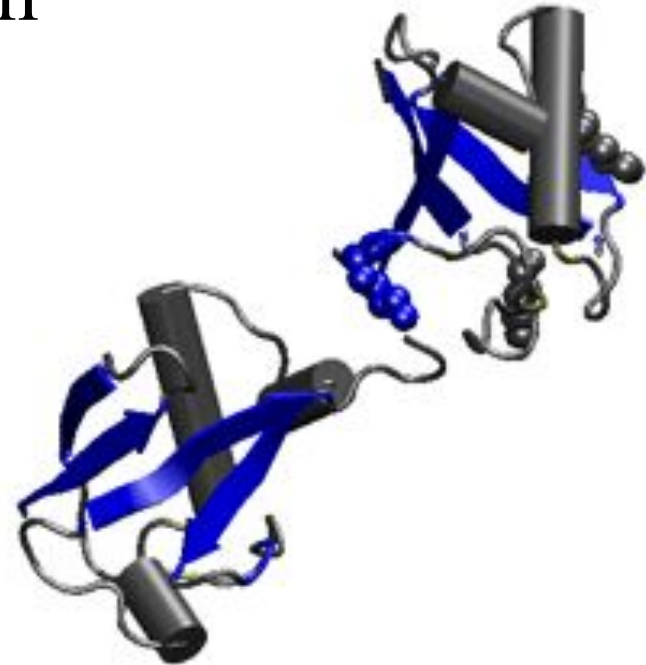
Ubiquitin

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



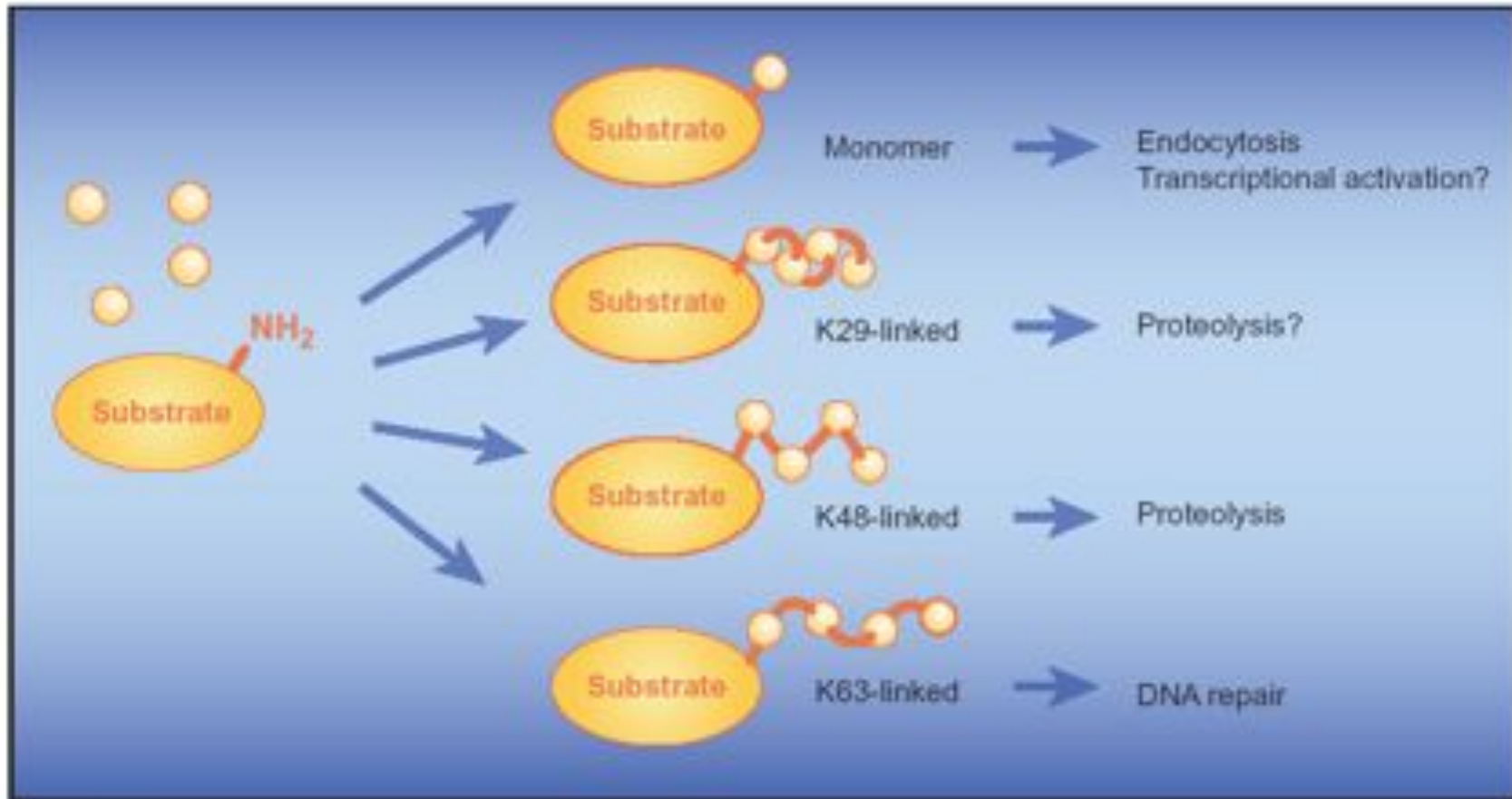
- Glycine at C-terminal attaches to the Lysine on the protein by an isopeptide bond.
- it can attach to other ubiquitin molecules and make a polyubiquitin chain.

There are 7 conserved lysine residues in ubiquitin.



Two ubiquitins attached together through LYS 48. LYS 63 and LYS 29 are also shown there.

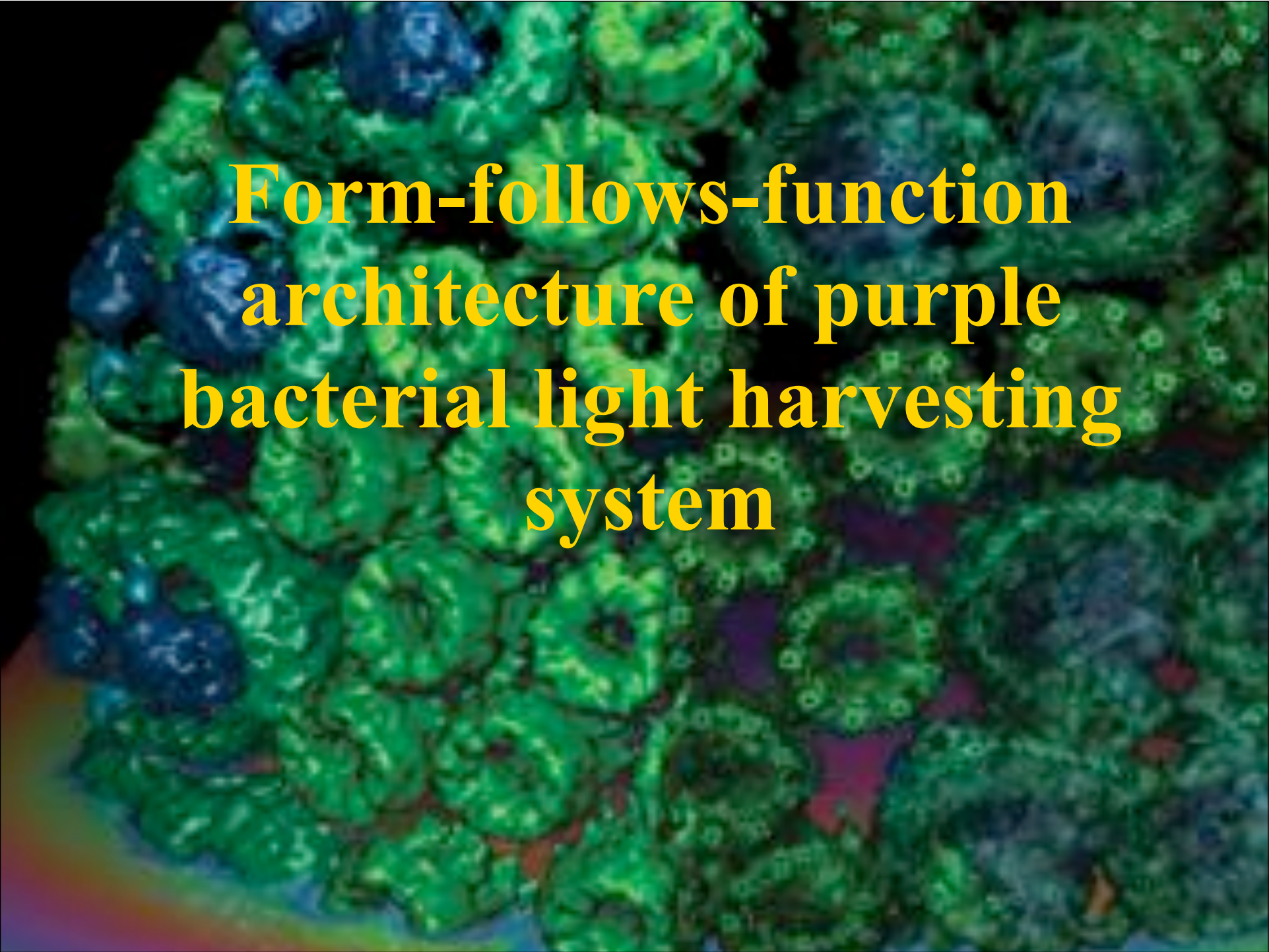
Multi-ubiquitylation targets destination of proteins



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.)

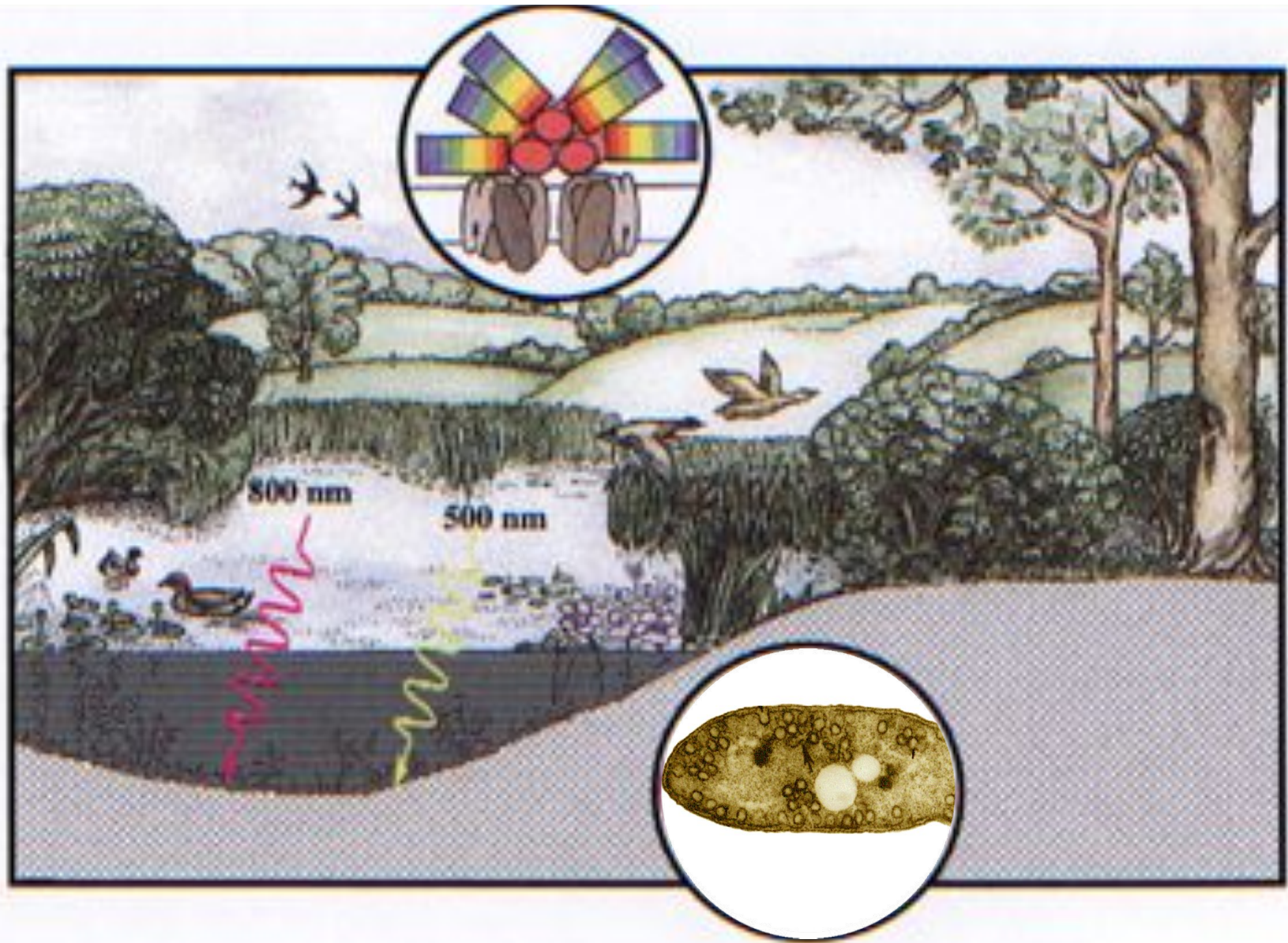
Marx, J., Ubiquitin lives up its name, *Science* 297, 1792-1794 (2002)

VMD session with ubiquitin

A 3D molecular model of a purple bacterial light harvesting system. The structure is composed of numerous green and blue protein subunits arranged in a complex, interconnected network. The green subunits form a dense, interconnected lattice, while the blue subunits are interspersed within this lattice. The overall structure is highly organized and appears to be a large, multi-subunit complex. The background is dark, making the green and blue colors stand out.

**Form-follows-function
architecture of purple
bacterial light harvesting
system**

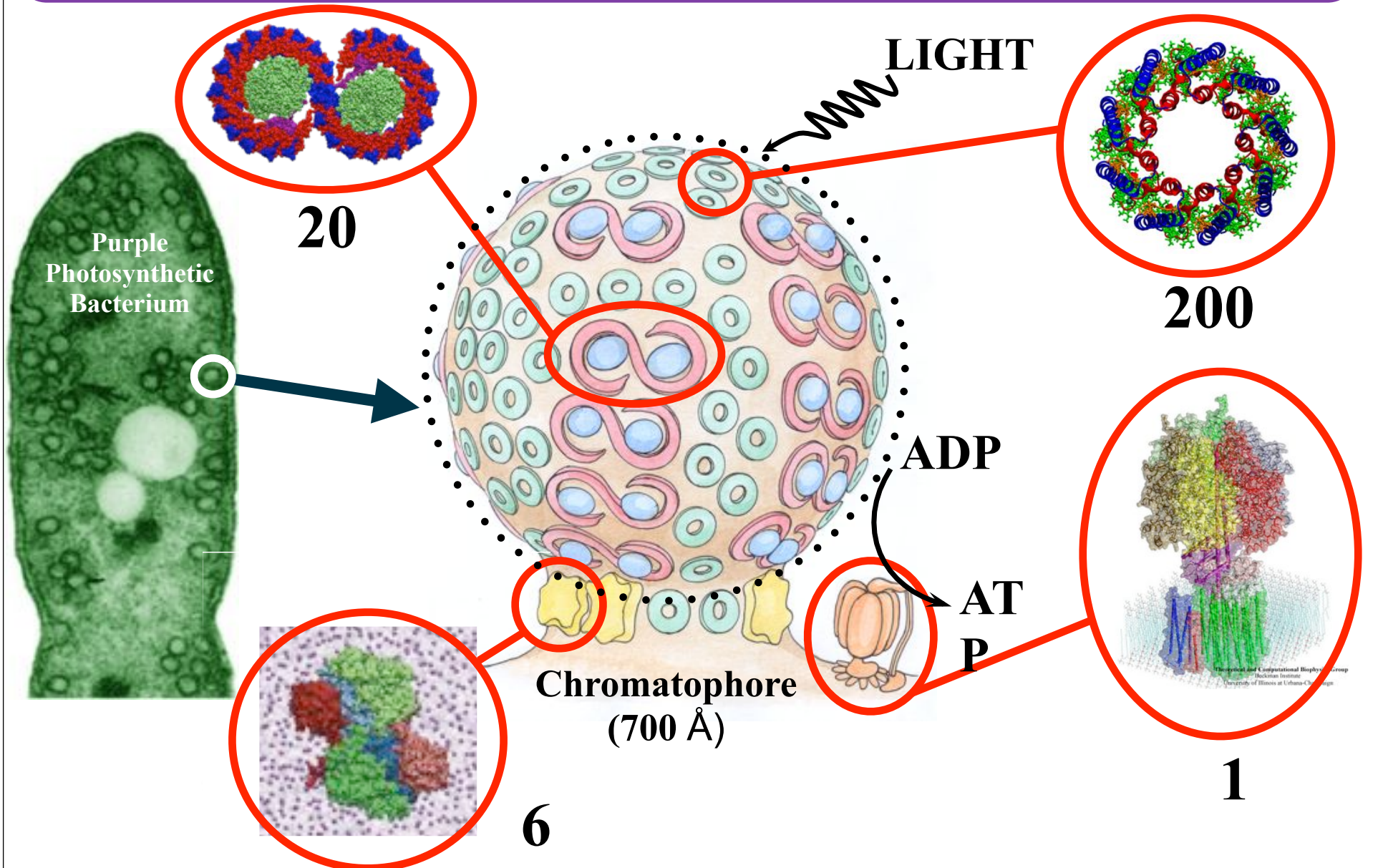
Habitats of Photosynthetic Life Forms



purple bacterium

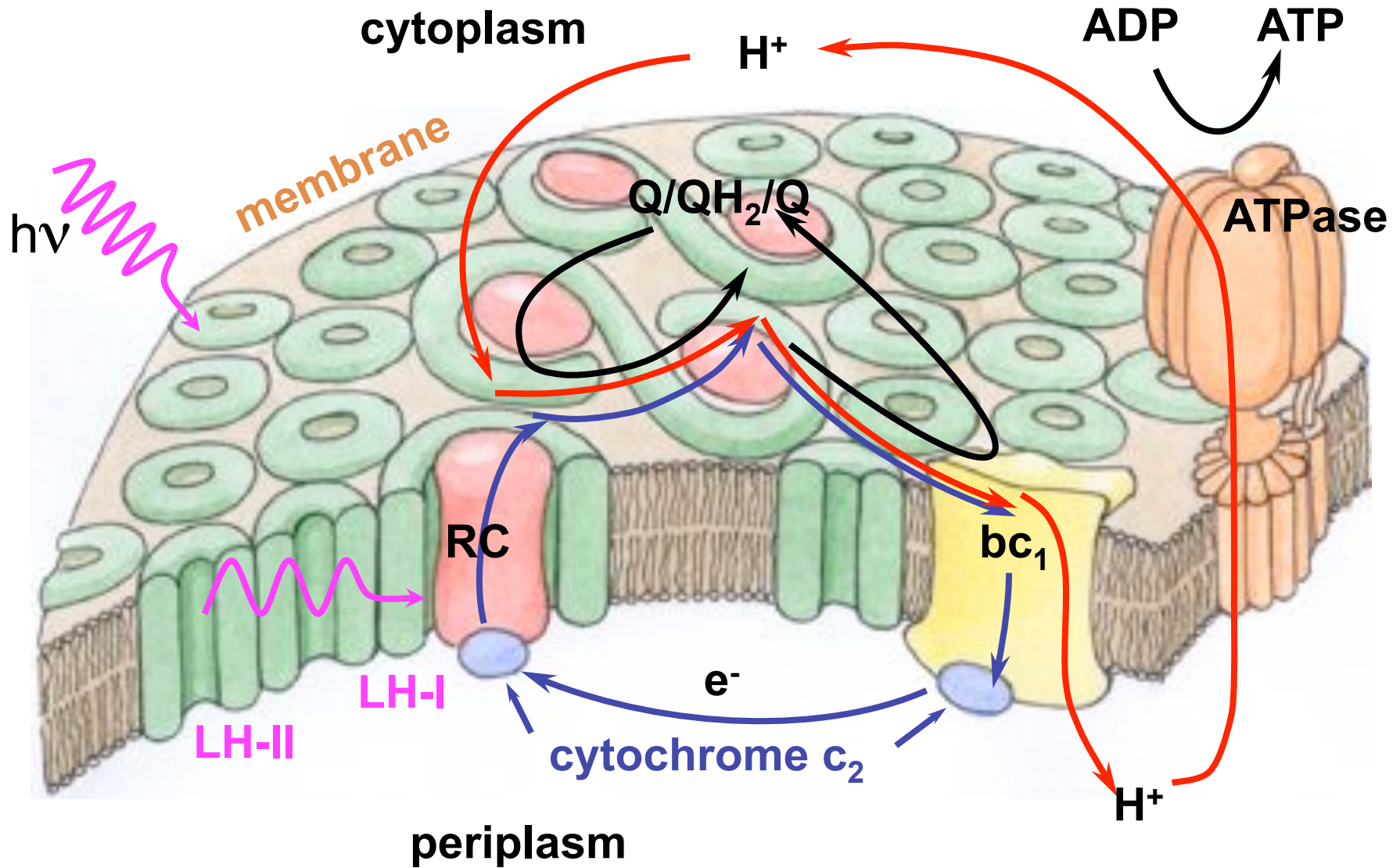
Science 2: How Nature Harvests Sun Light

95% of the energy in the biosphere comes from this energy source

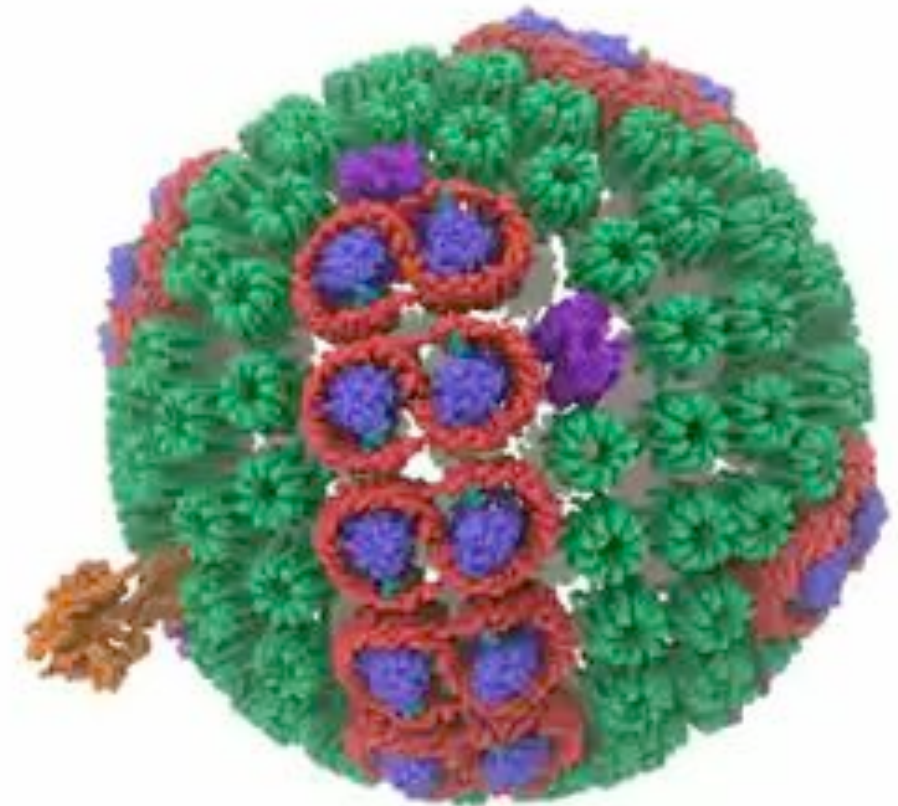
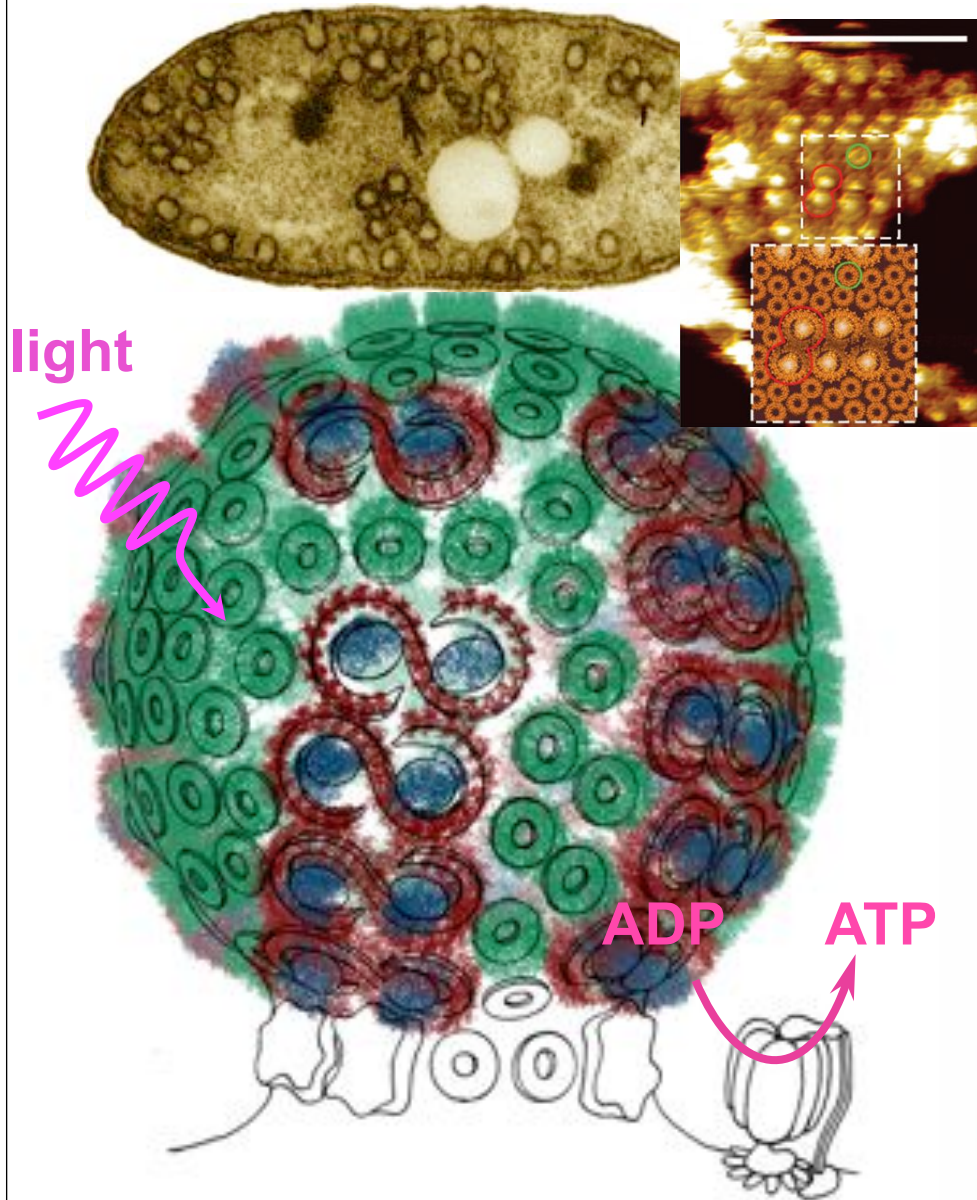


Chromatophore of Purple Bacteria

(section of the chromatophore membrane)

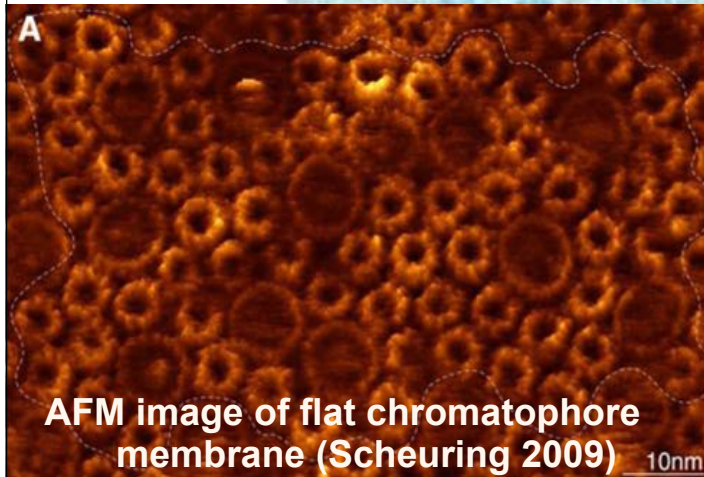
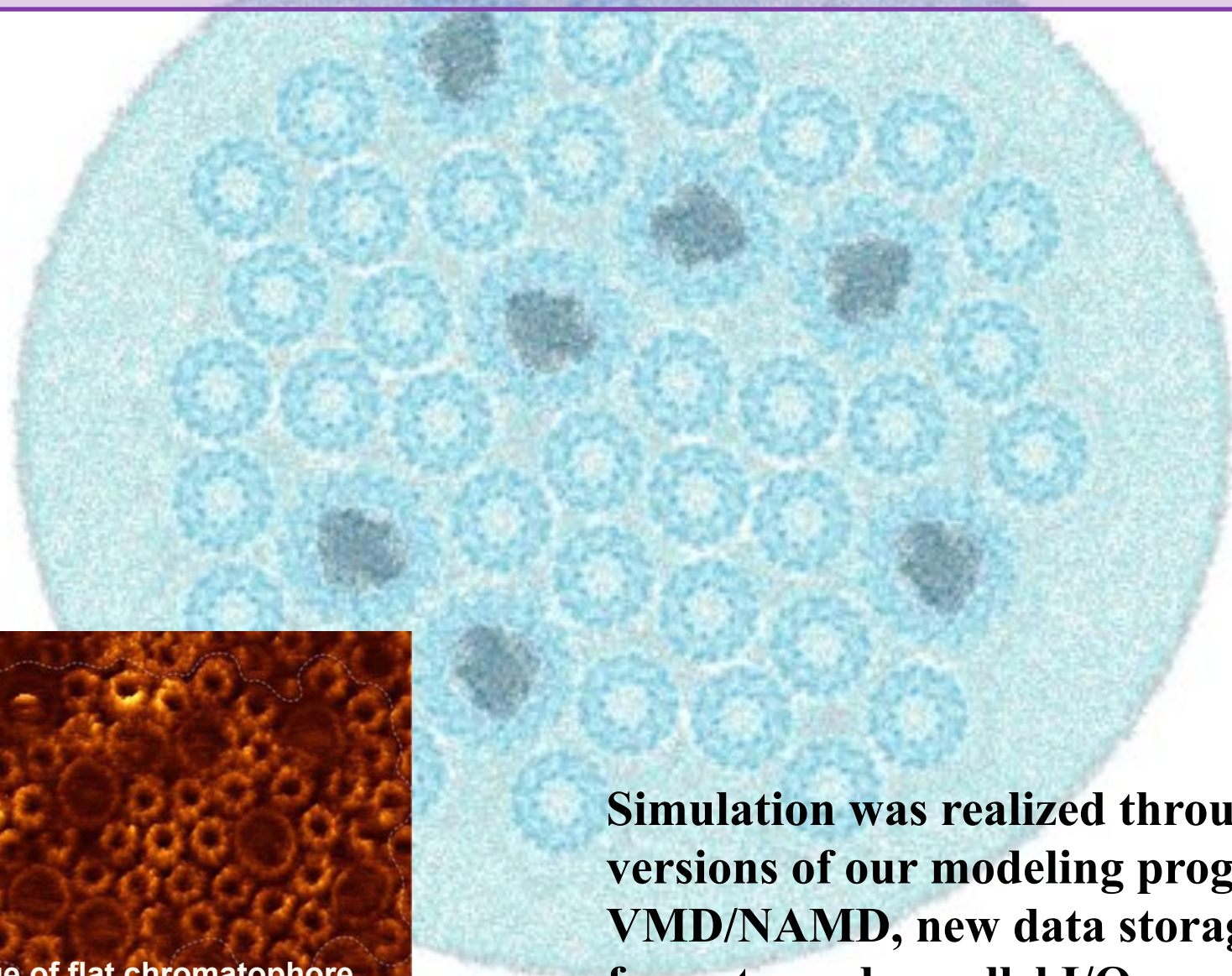


Knowing the Atomic Level Structure of the chromatophore, one can systematically describe its physical mechanism



How Nature Harvests Sun Light

First 23 million atom molecular dynamics simulation

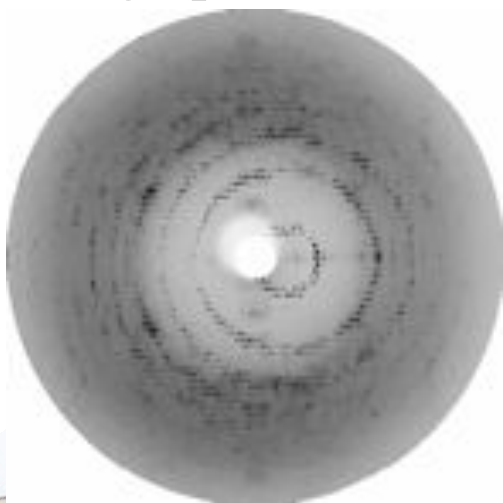


AFM image of flat chromatophore membrane (Scheuring 2009)

Simulation was realized through new versions of our modeling programs VMD/NAMD, new data storage formats, and parallel I/O.

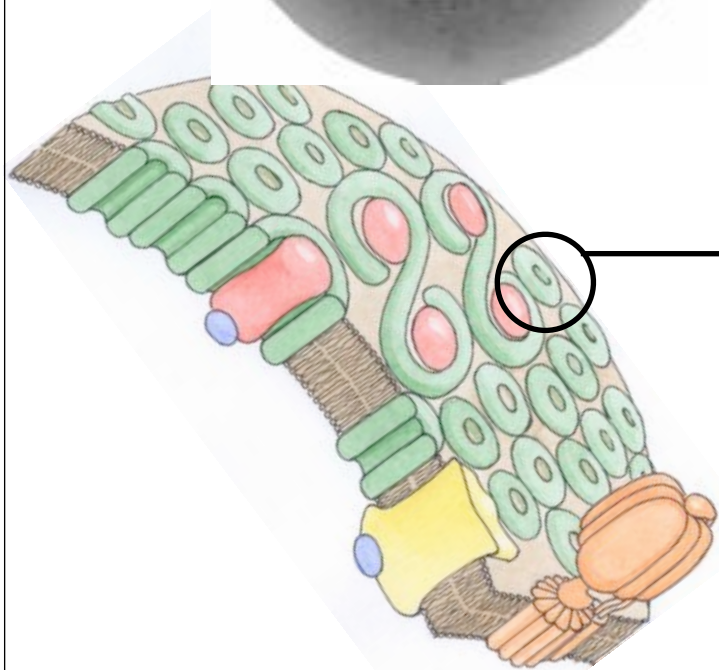
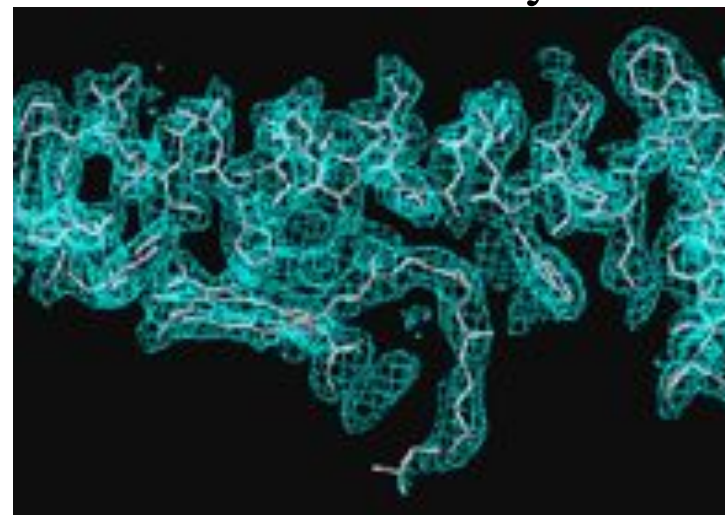
Structure of LH 2 of *Rs. molischianum*

crystallographic diffraction pattern



molecular
replacement →
through
modeling

electron density

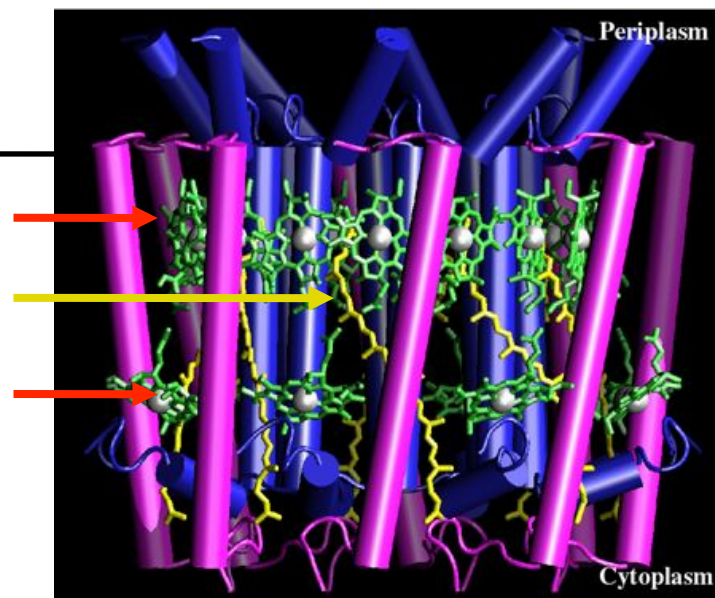


B850 band

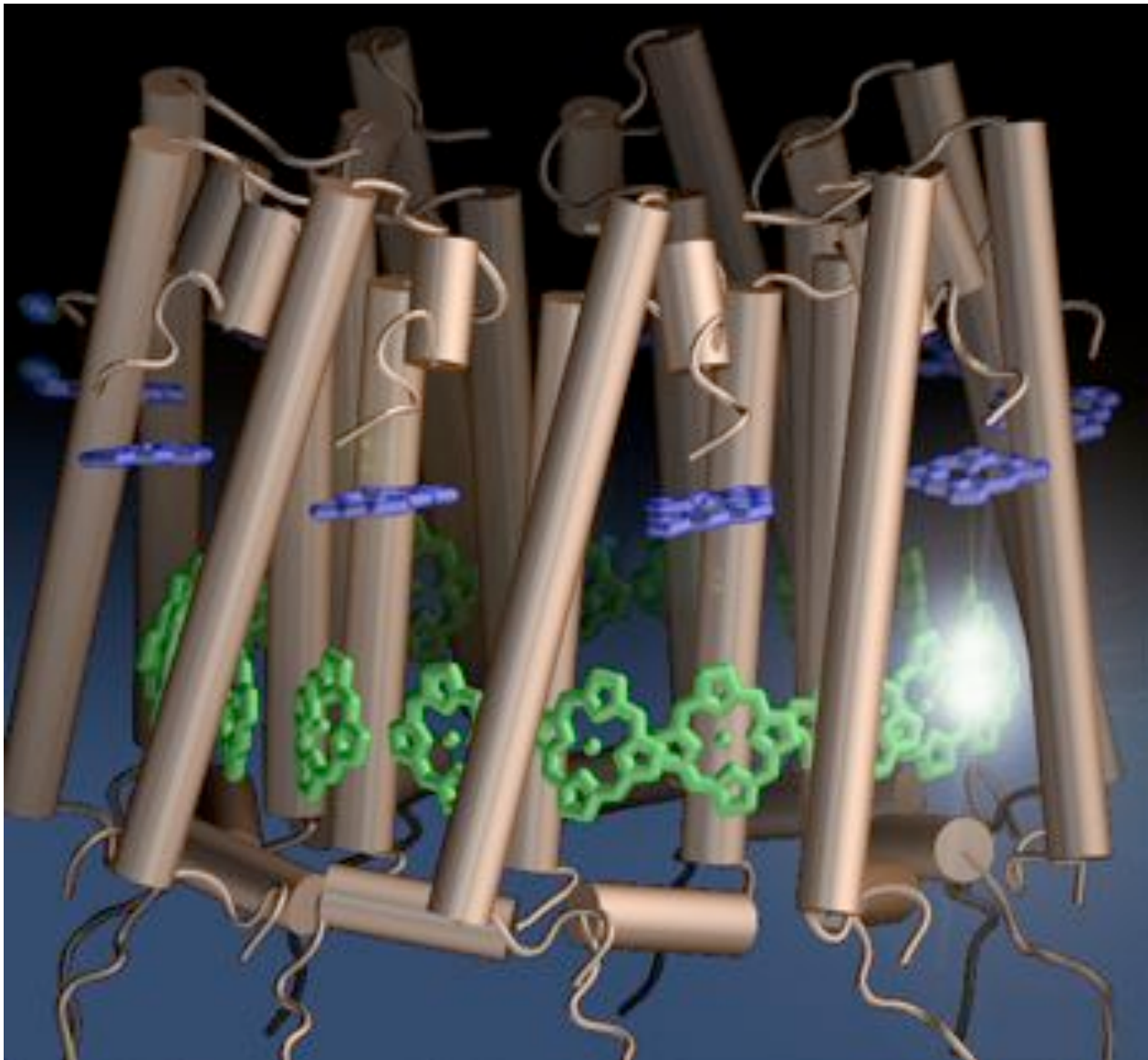
B500 band

B800 band

**optical
spectrum**



Excitonic dynamics in LH2



VMD session with LH2

VMD – “Visual Molecular Dynamics”

<http://www.ks.uiuc.edu/Research/vmd/>

Visualization and analysis of:

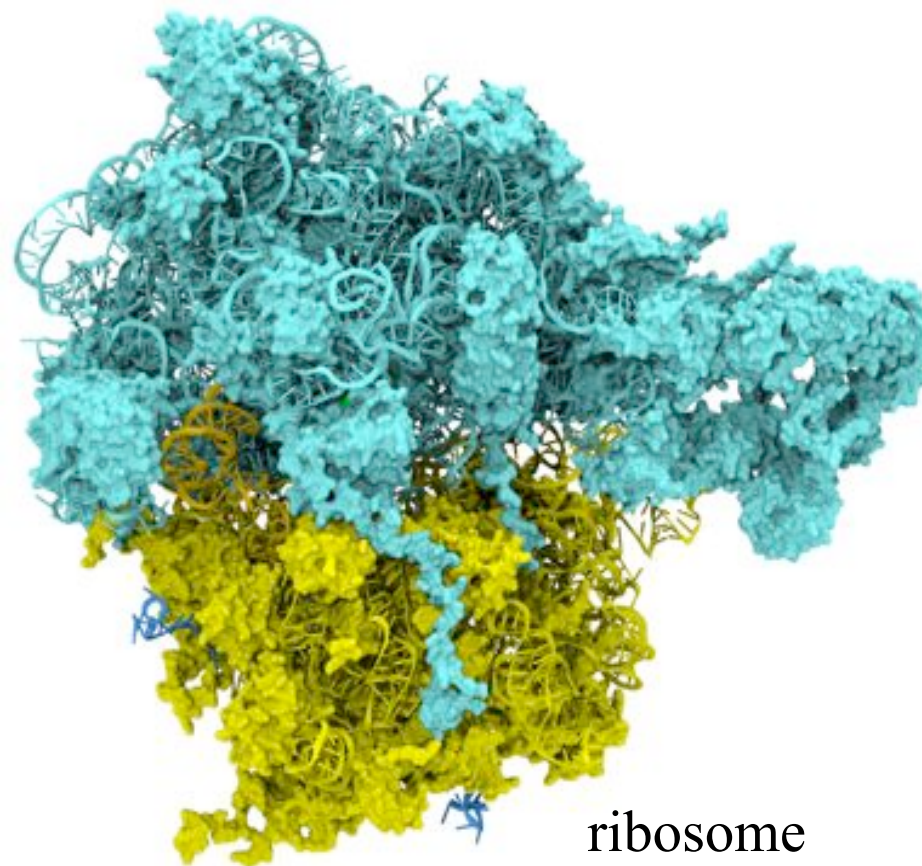
- Molecular dynamics and quantum chemistry simulations
- Sequence data
- Cryo-electron microscopy maps

User-extensible with built-in scripting and many plugins

Supports very large data sets, batch mode analysis on clusters

Takes advantage of advanced technological opportunities:

- High quality interactive display, batch mode rendering, movie making
- Supports multi-core processors, GPUs



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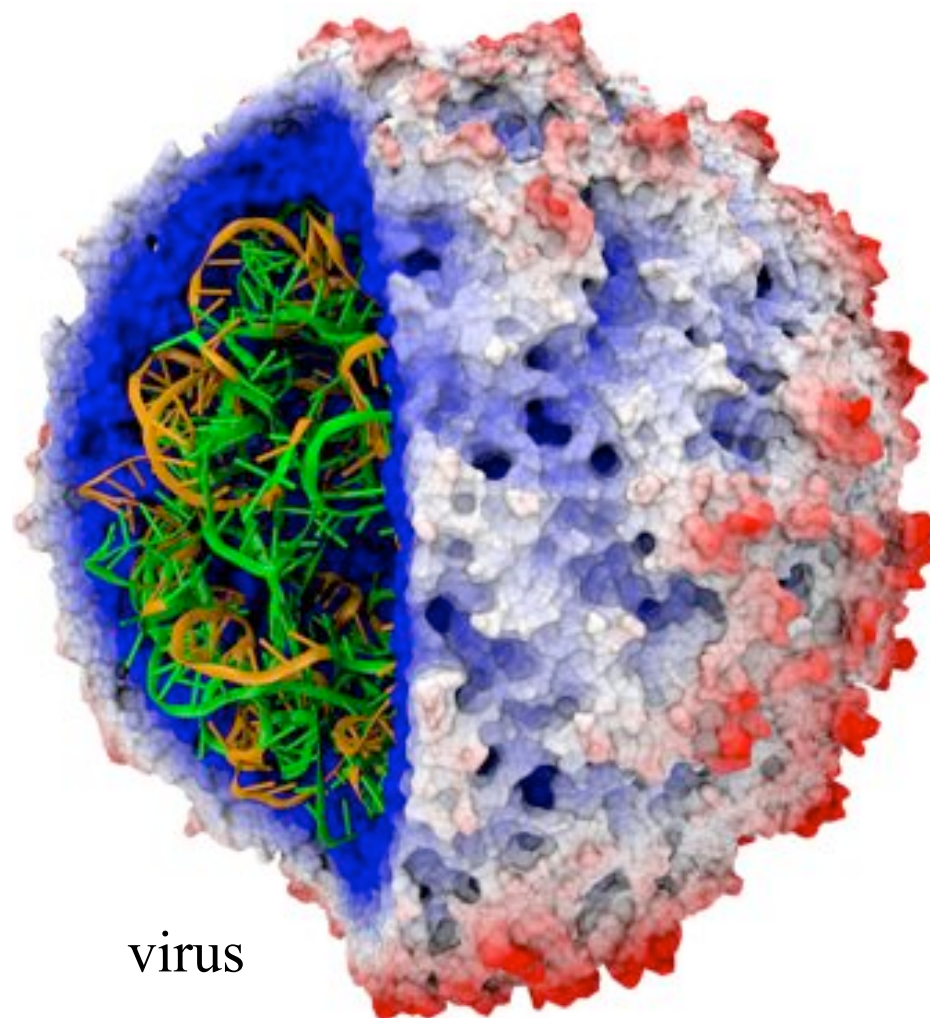
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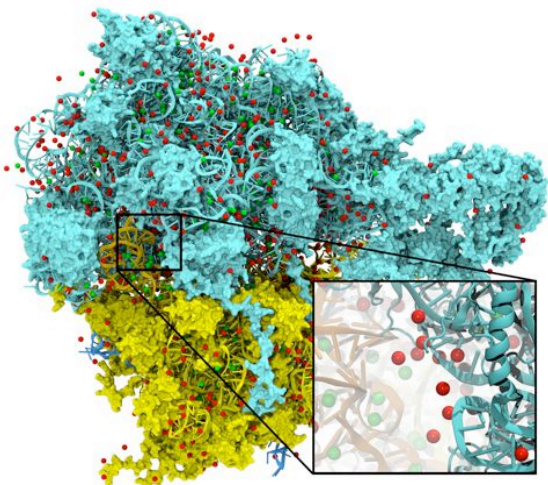
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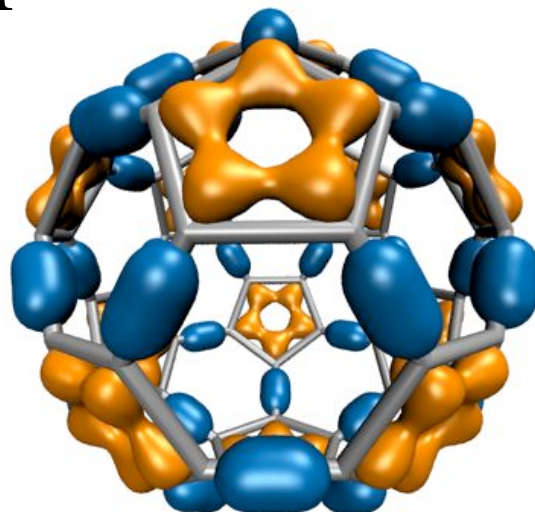


virus

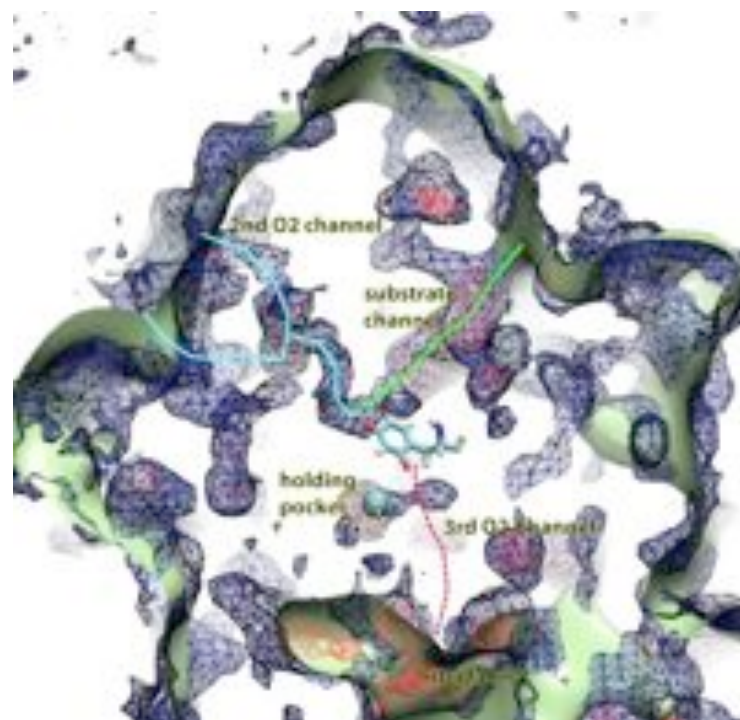
CUDA+OpenCL Acceleration in VMD



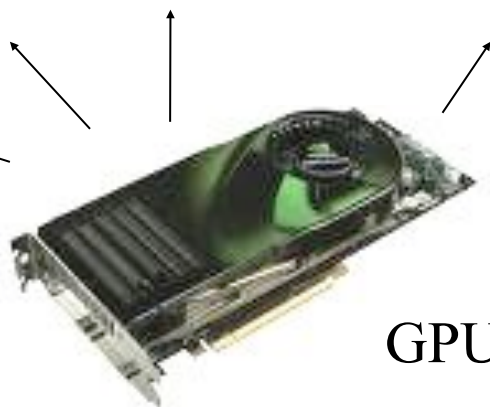
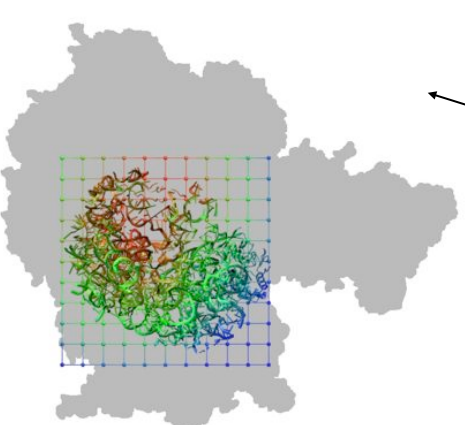
Electrostatic field calculation,
Multilevel Summation Method
20x to 44x faster



Molecular orbital
calculation and display
100x to 120x faster



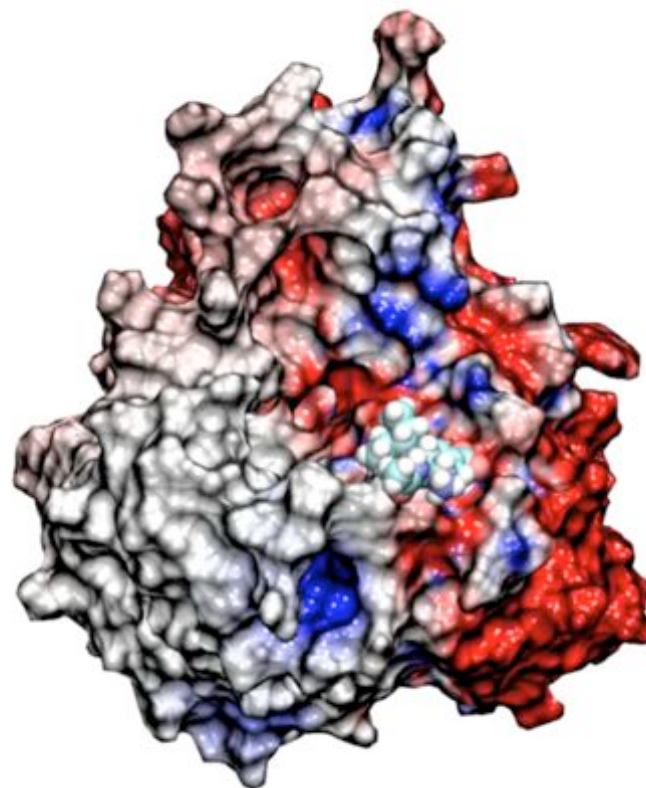
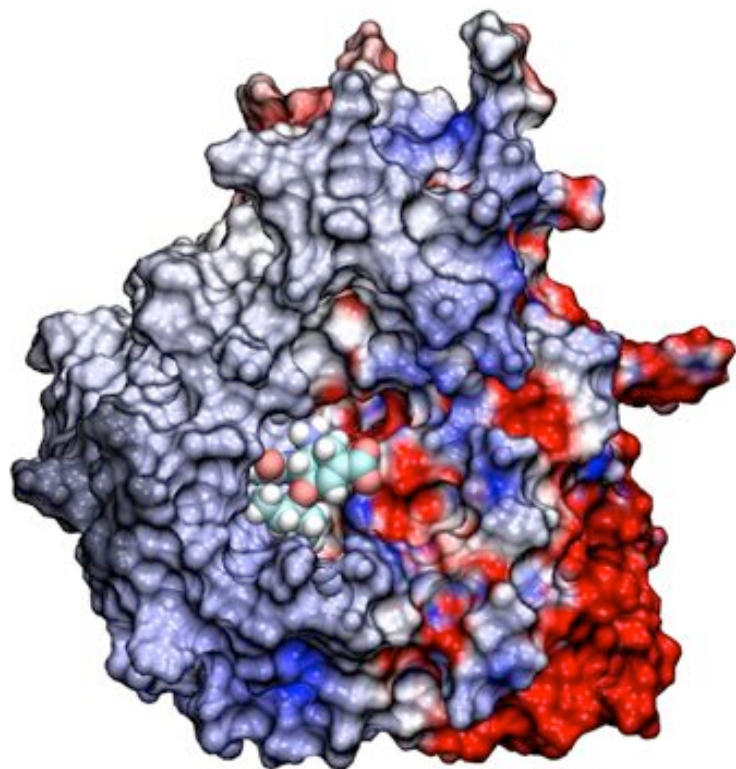
Imaging of gas migration pathways
in proteins with Implicit Ligand
Sampling (ILS) algorithm
20x to 30x faster



GPU

Swine Flu Neuraminidase Electrostatics

Mean electrostatic field needed to identify drug binding pathway



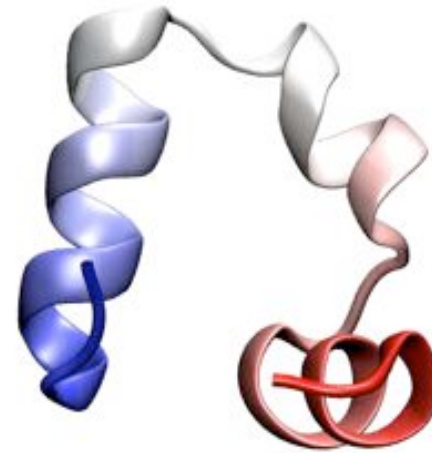
Time-averaged electrostatic field of H1N1 neuraminidase
calculated from VMD Multilevel Summation Tool:

**Computation with NVIDIA Tesla C1060 is 20x faster than
computation on a single CPU core**

Movie of drug (tamiflu) binding

Timeline Tool: identify events in an MD trajectory

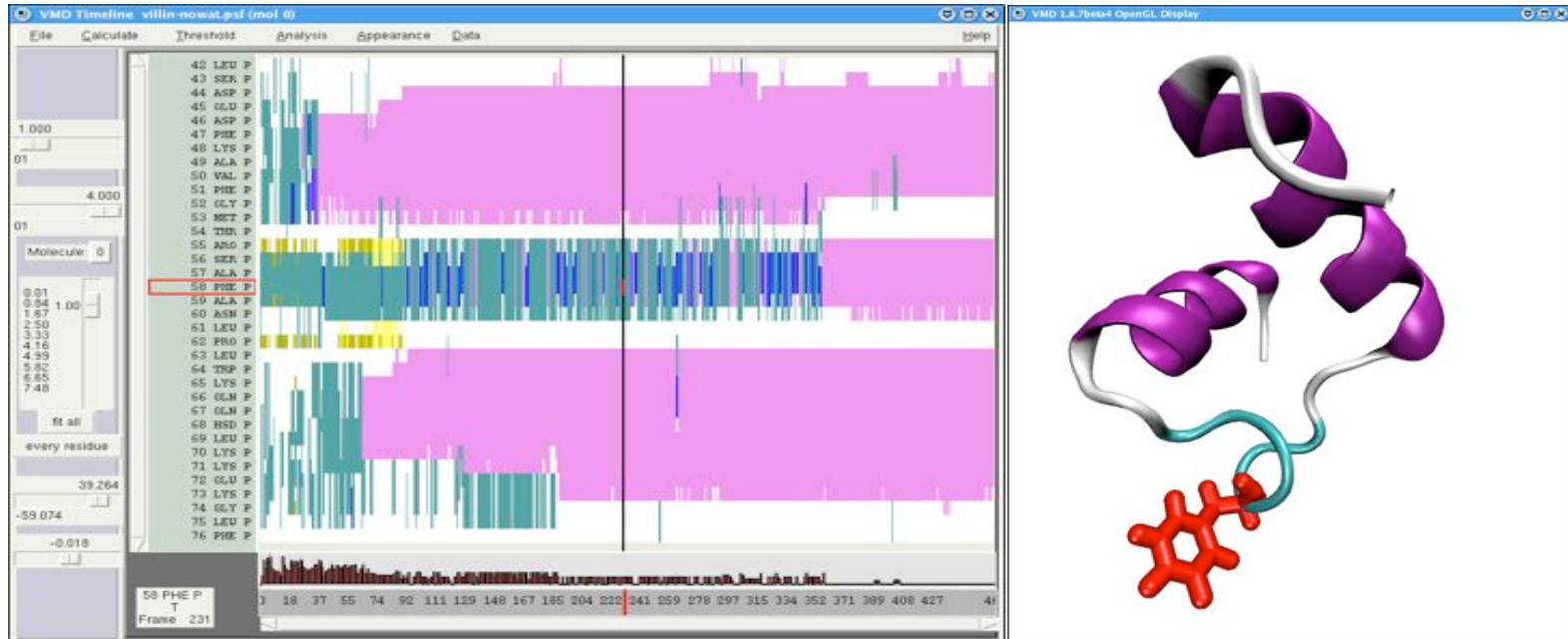
- We have MD trajectories:



- We want to identify events in a trajectory:
 - 7.1 μ s, 600 GB of trajectory data
 - events: 0.5 μ s, *helix 3 forms*; 3.0 μ s, *helix 1 forms*; etc.
 - How long would it take an expert user to visually inspect this trajectory to find motional changes of events?
2 days! (plus: tiring task; one is liable to miss much)

Timeline: a graphing and analysis tool to identify events in an MD trajectory

Events during 7 μ s villin headpiece folding



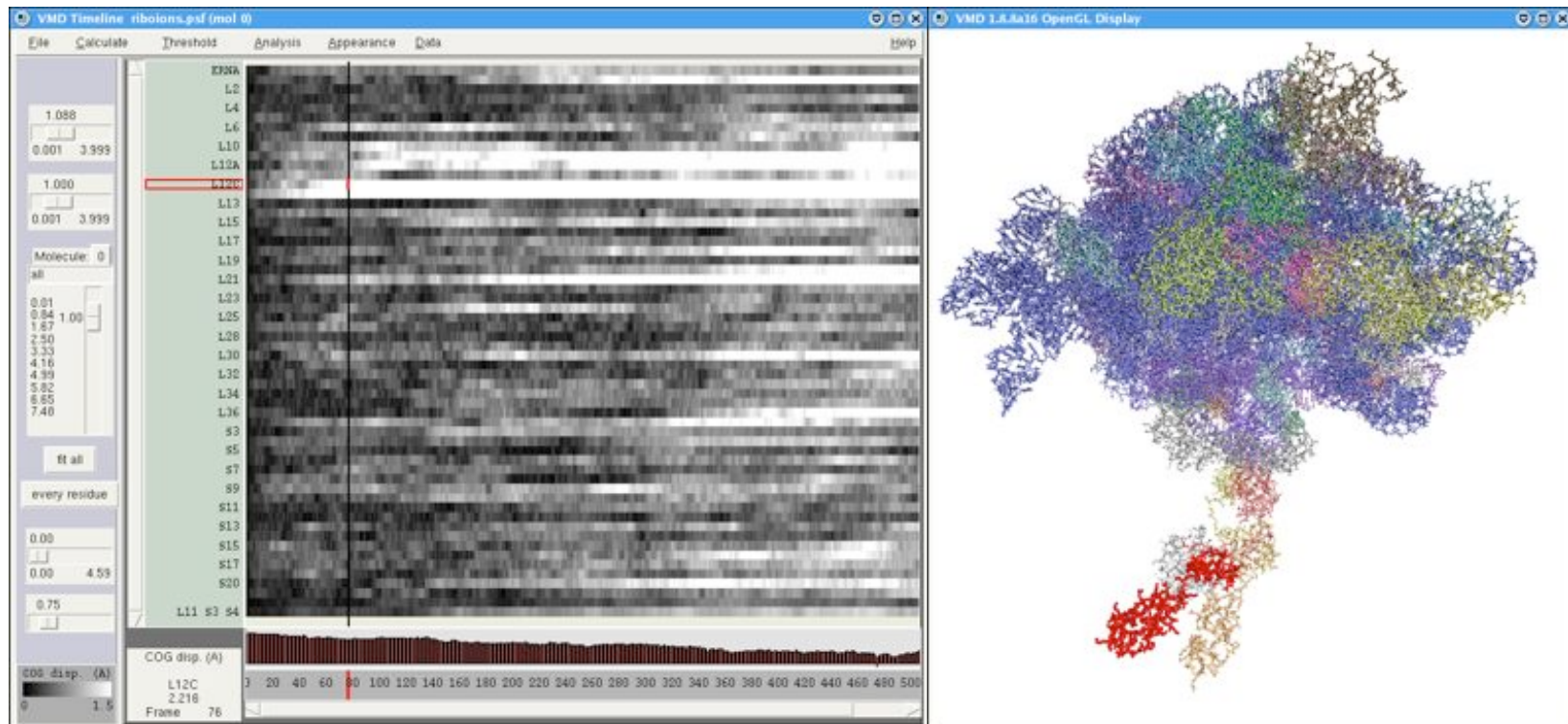
■ Alpha helix ■ Extended beta ■ Isolated bridge ■ 3-10 helix ■ Beta turn □ None (coil)

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

VMD **Timeline plug-in**: live 2D plot linked to 3D structure

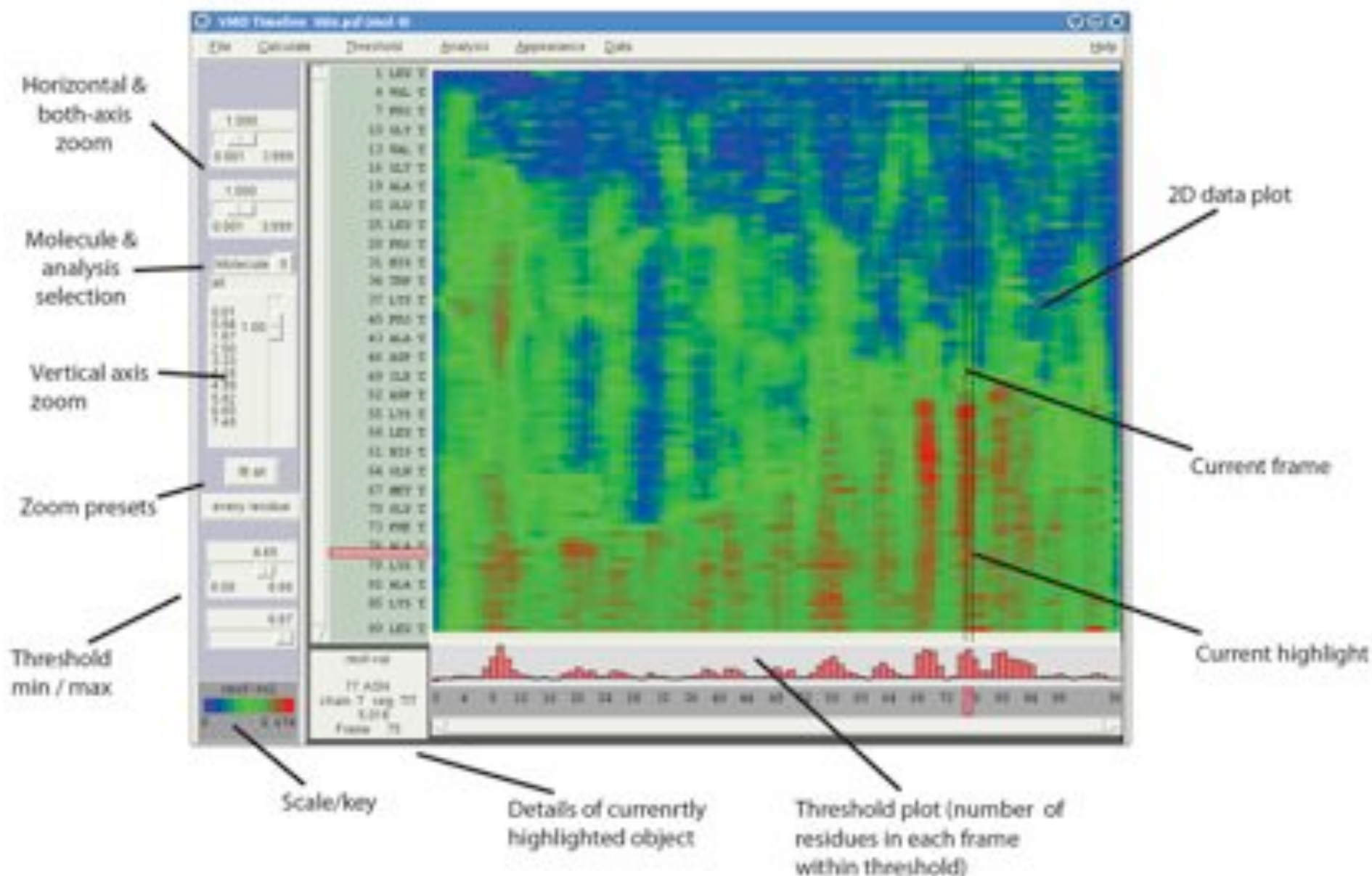
- a single picture shows changing properties across entire structure, entire trajectory.
- explore time vs. attribute (per-residue or per-selection) linked to molecular structure
- many analysis methods available; user-extendable

Timeline and large structures: events during ribosome equilibration



Ribosome equilibration, 17,000+ protein/nucleic residues + ions
Example analysis: displacement (Å) of center-of-geometry of each component protein
(calculation here is per-component-protein, not per-individual-residue)
Finding: peripheral proteins show greater displacement than core proteins

Main Interface Features of Timeline 2D Data Plot





Acknowledgements

VMD team

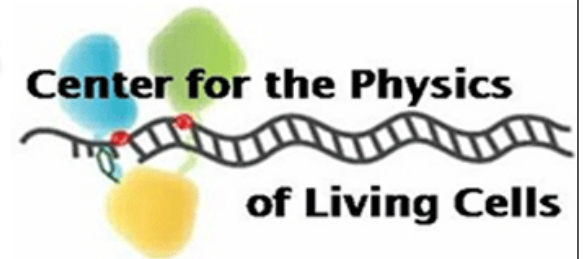
J. Stone (leader)

D. Hardy

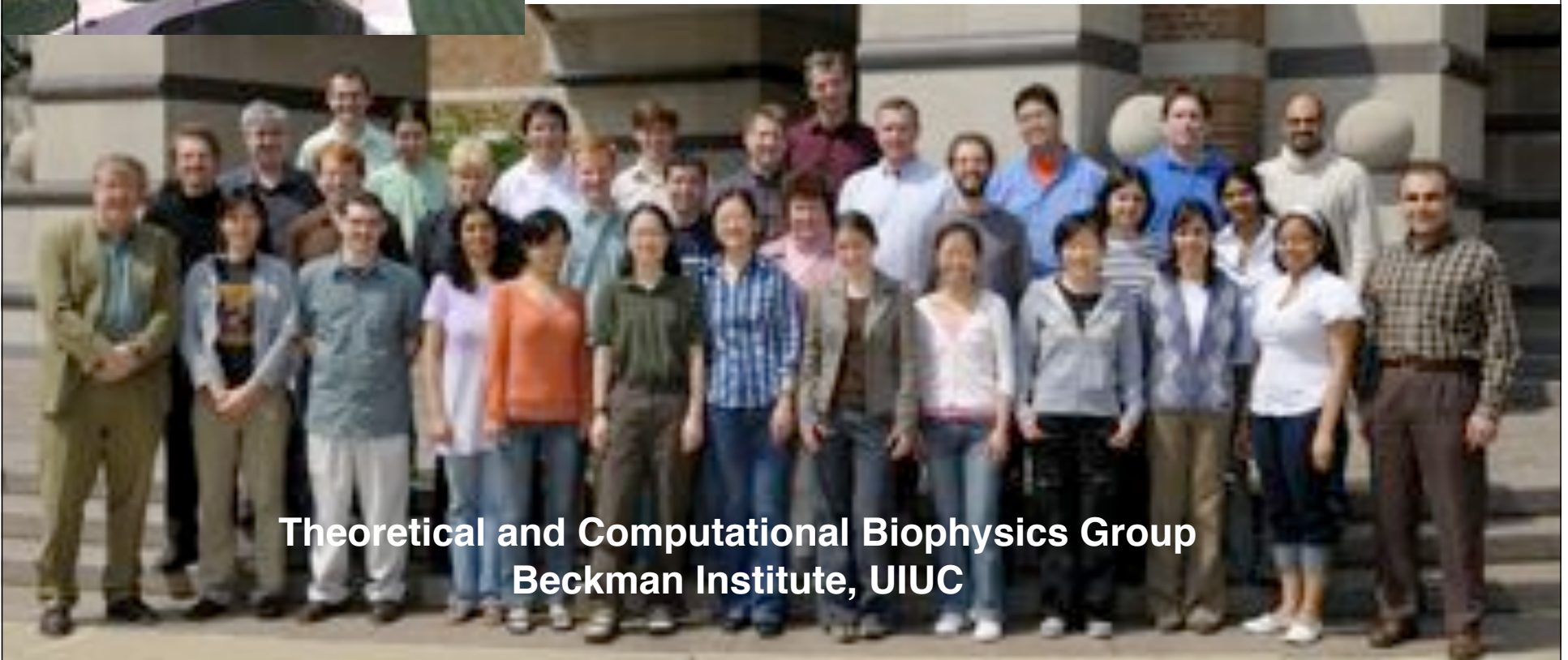
B. Isralewitz

J. Saam

K. Vandivoort



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**Theoretical and Computational Biophysics Group
Beckman Institute, UIUC**