Proteins and Mesoscale Data: Visualization of Molecular Dynamics

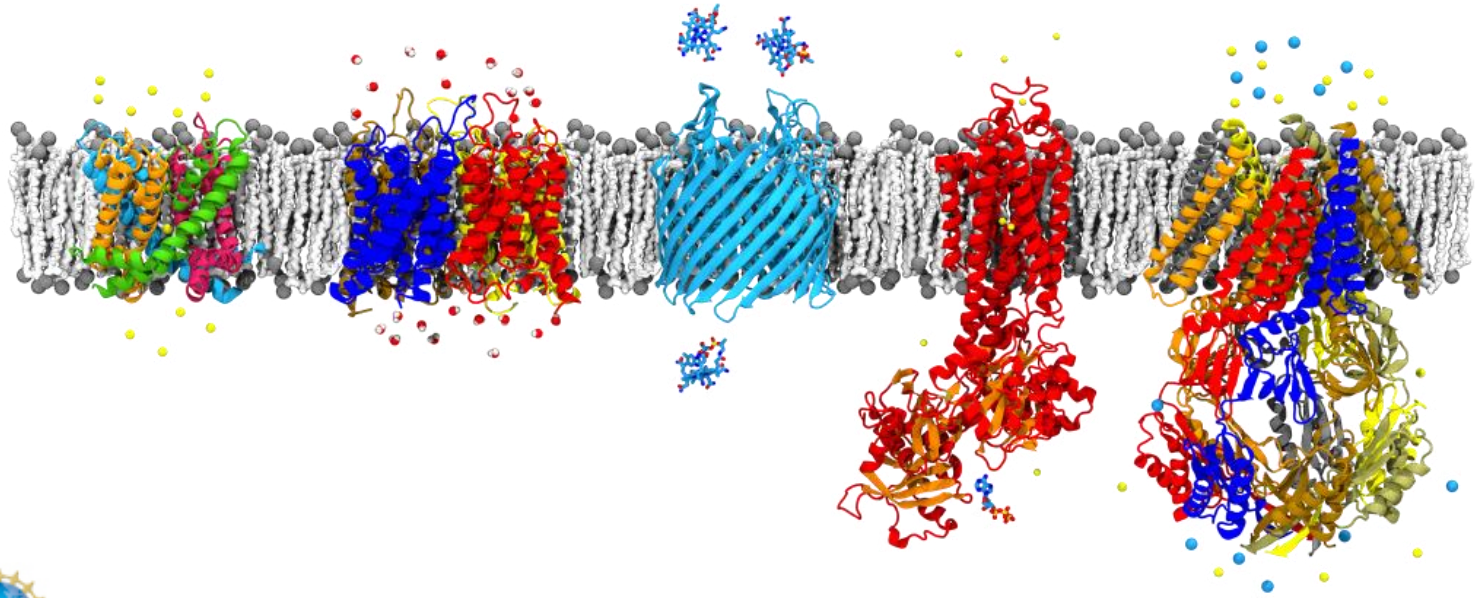
John E. Stone

Theoretical and Computational Biophysics Group

Beckman Institute, University of Illinois at Urbana-Champaign

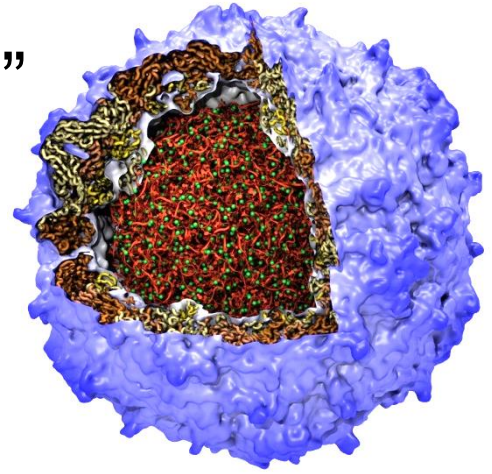
http://www.ks.uiuc.edu/Research/vmd/

VIZBI'15, Broad Institute of MIT and Harvard, Cambridge, MA, Mar 26, 2015

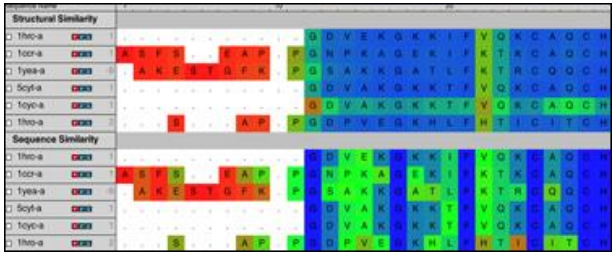


VMD – “Visual Molecular Dynamics”

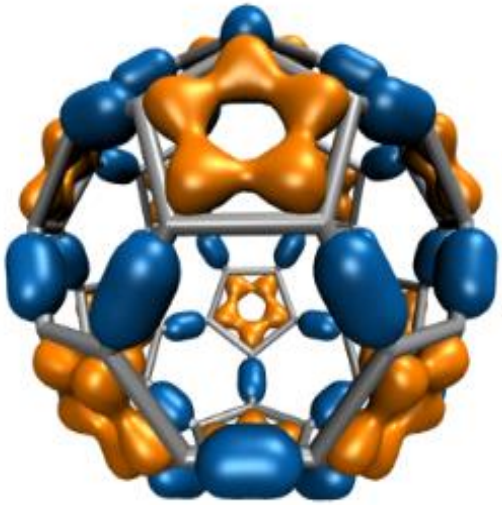
- Visualization and analysis of:
  - molecular dynamics simulations
  - quantum chemistry calculations
  - particle systems and whole cells
  - sequence data
- User extensible w/ scripting and plugins
- http://www.ks.uiuc.edu/Research/vmd/



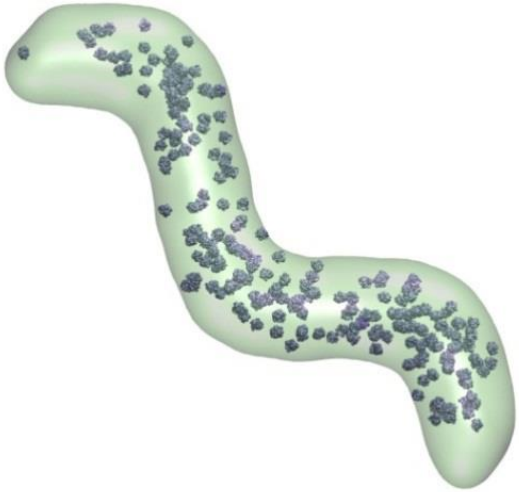
Poliovirus



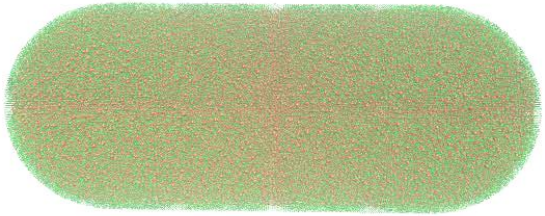
Ribosome Sequences



Electrons in
Vibrating Buckyball



Cellular Tomography
Cryo-electron Microscopy

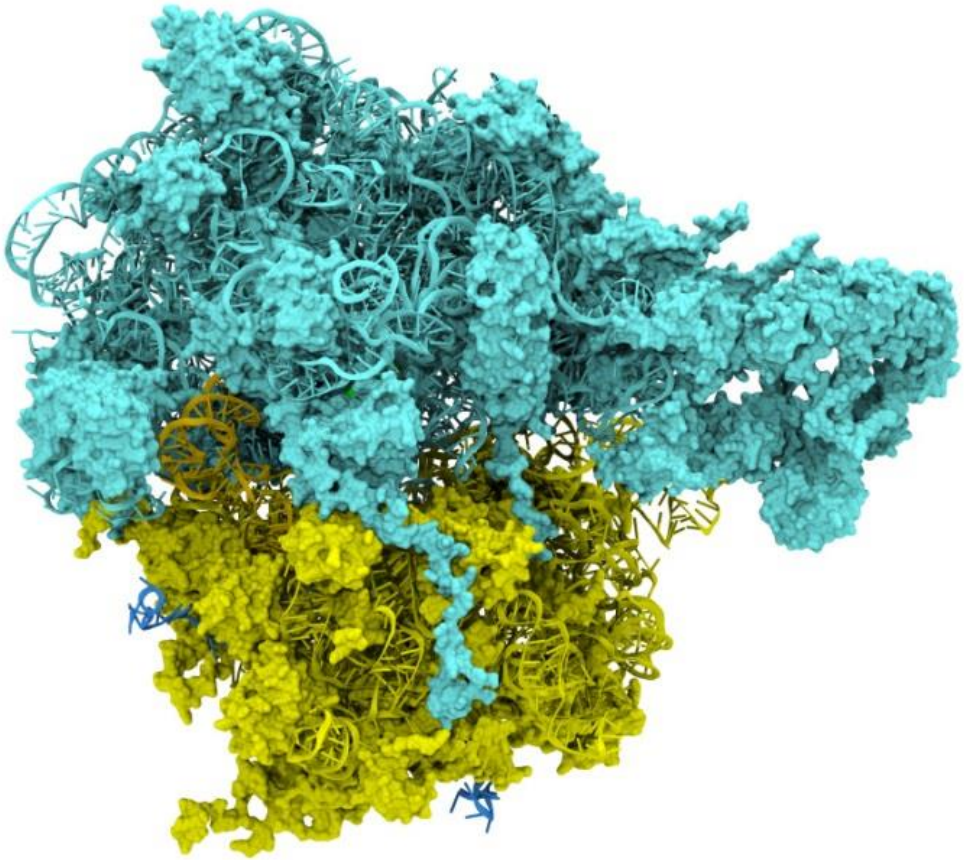


Whole Cell Simulations

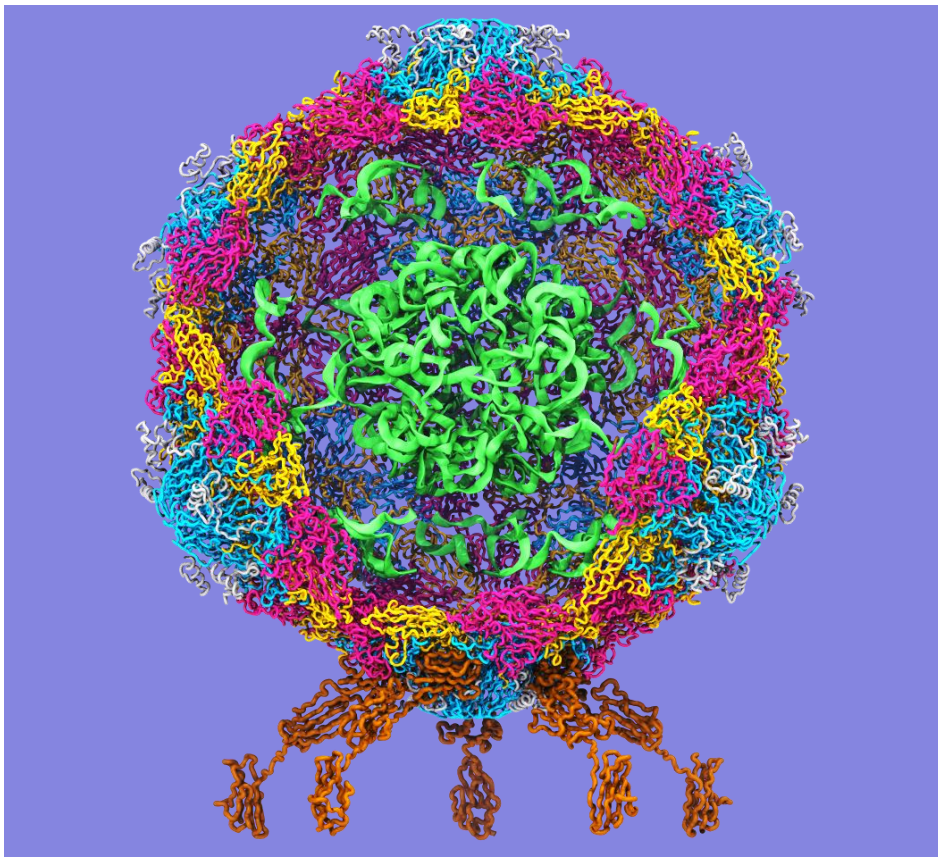
Goal: A Computational Microscope

Study the molecular machines in living cells

Ribosome: target for antibiotics



Poliovirus



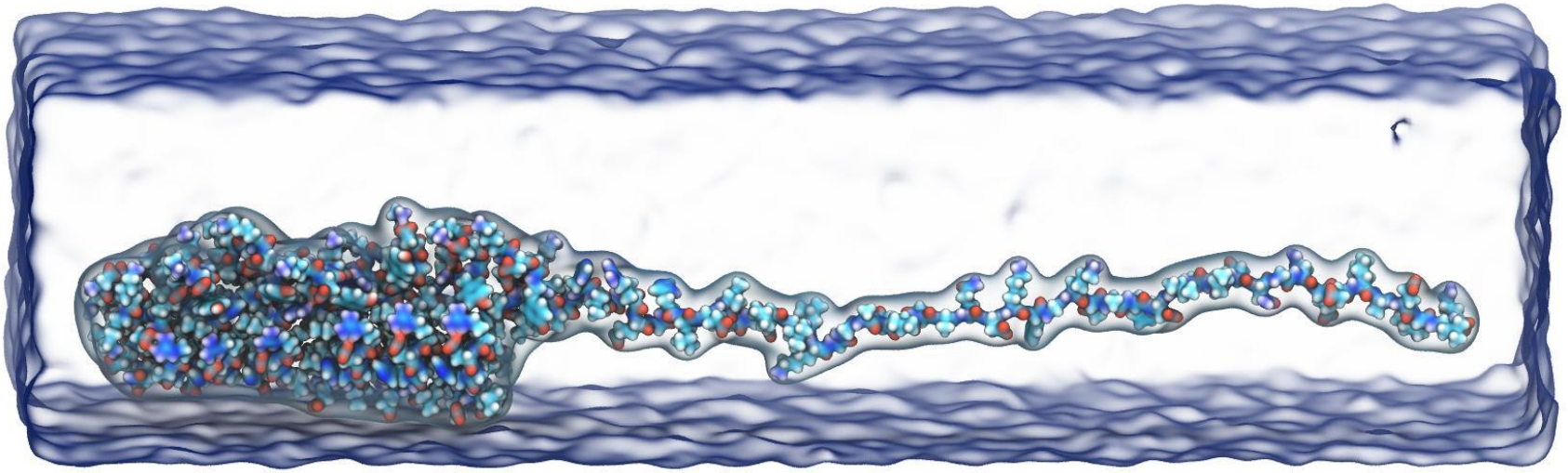
Molecular Visualization Inputs

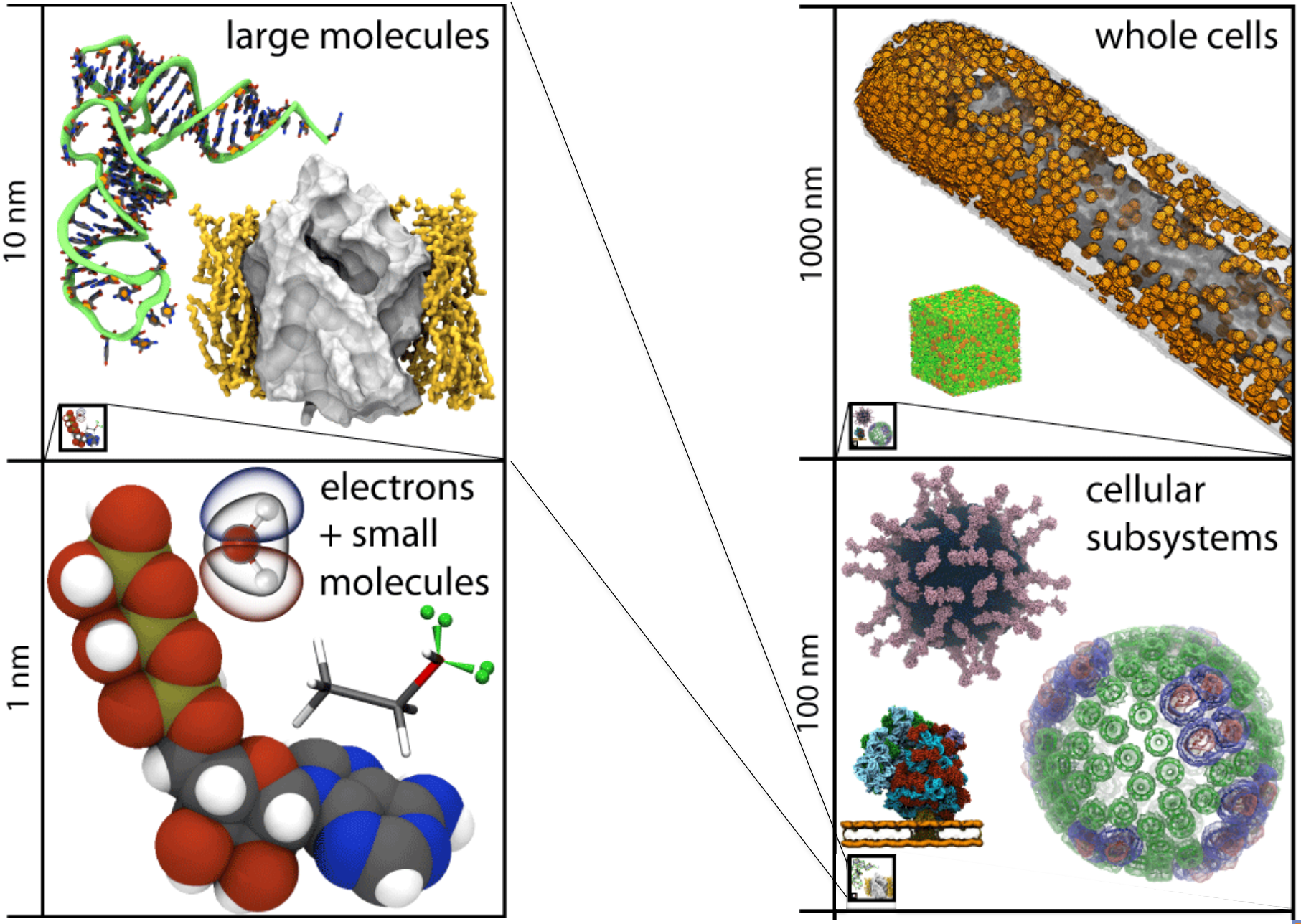
- Molecular structure data
  - Atomic coordinates, atom types, bonds, residues …
- Molecular dynamics data
  - Atom types and force field parameters, electric fields, restraints …
  - Time-varying atomic coordinates
- Experimental imaging data
- Sequence data
- Additional annotations, active sites, etc.

Structure Visualization

Molecular representations provide different levels of abstraction, atomic detail vs. higher level organizational information

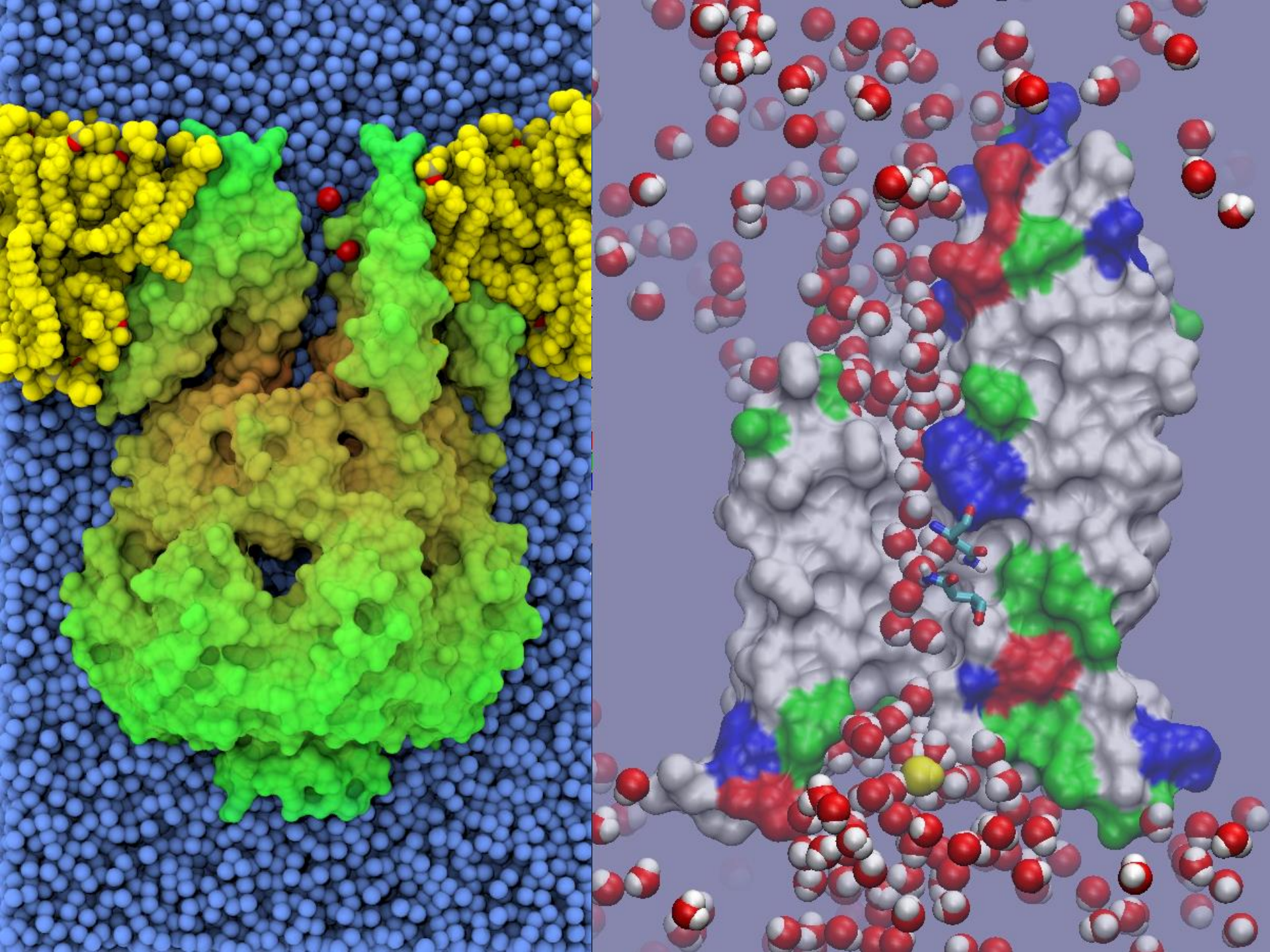
- Atoms, VdW spheres, bonds, ball-stick, …
- Molecular orbitals (quantum chemistry)
- Molecular surfaces
- Coarse-grained “beads”
- Ribbons, secondary structure, “cartoon” reps, RNA/DNA

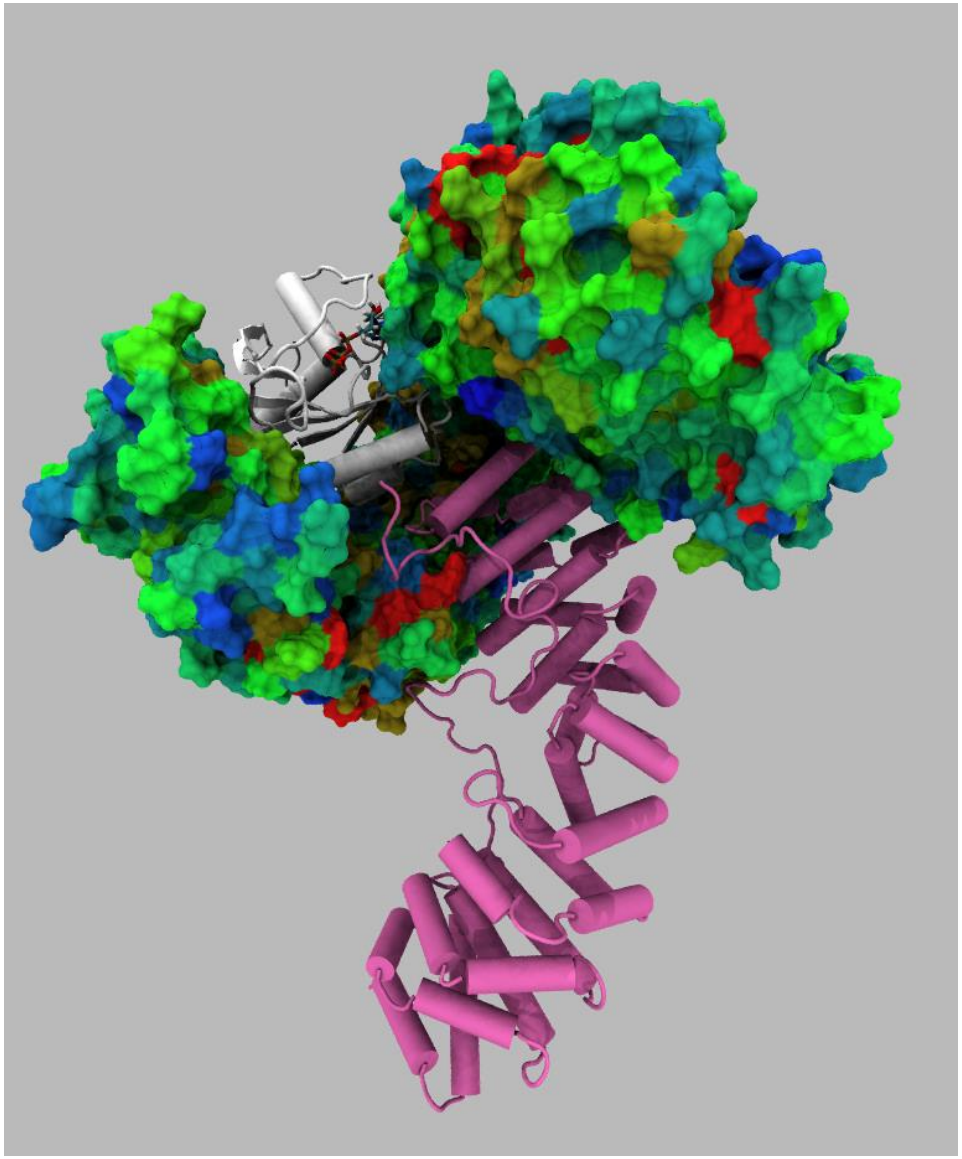



large molecules
10 nm
whole cells
1000 nm
electrons
+ small
molecules
1 nm
cellular
subsystems
100 nm

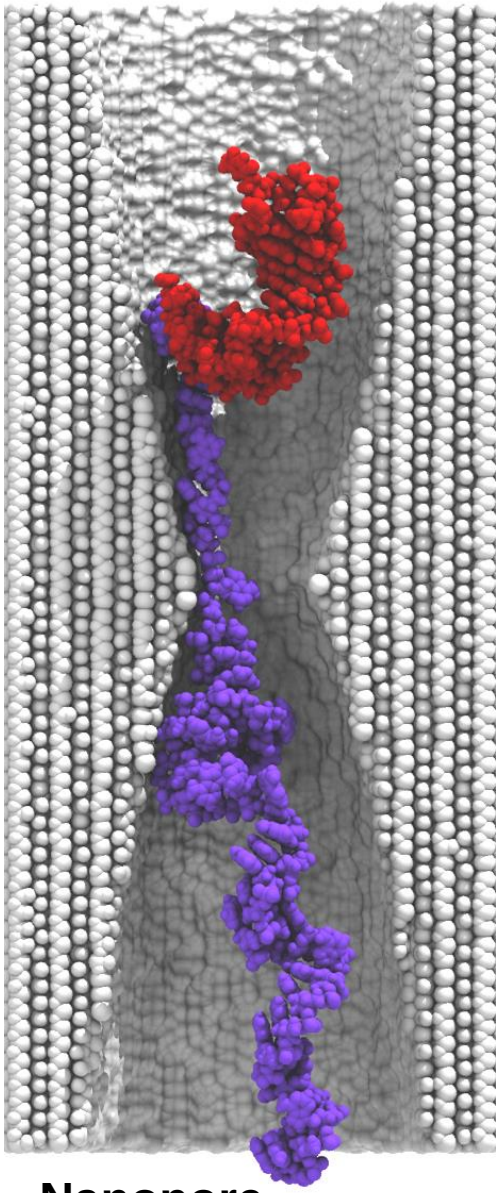
Selection, Filtering

- Most viz tools allow interactive visual picking, menu-driven selections of structure components to display or operate on
- VMD also extensively uses a text-based selection language (think google):
  - “water within 10 of protein and z > 0”
  - Allows selection on user-defined fields
  - Promotes synergy between interactive and scripting interfaces
  - Works very well when dealing with huge time-varying structures

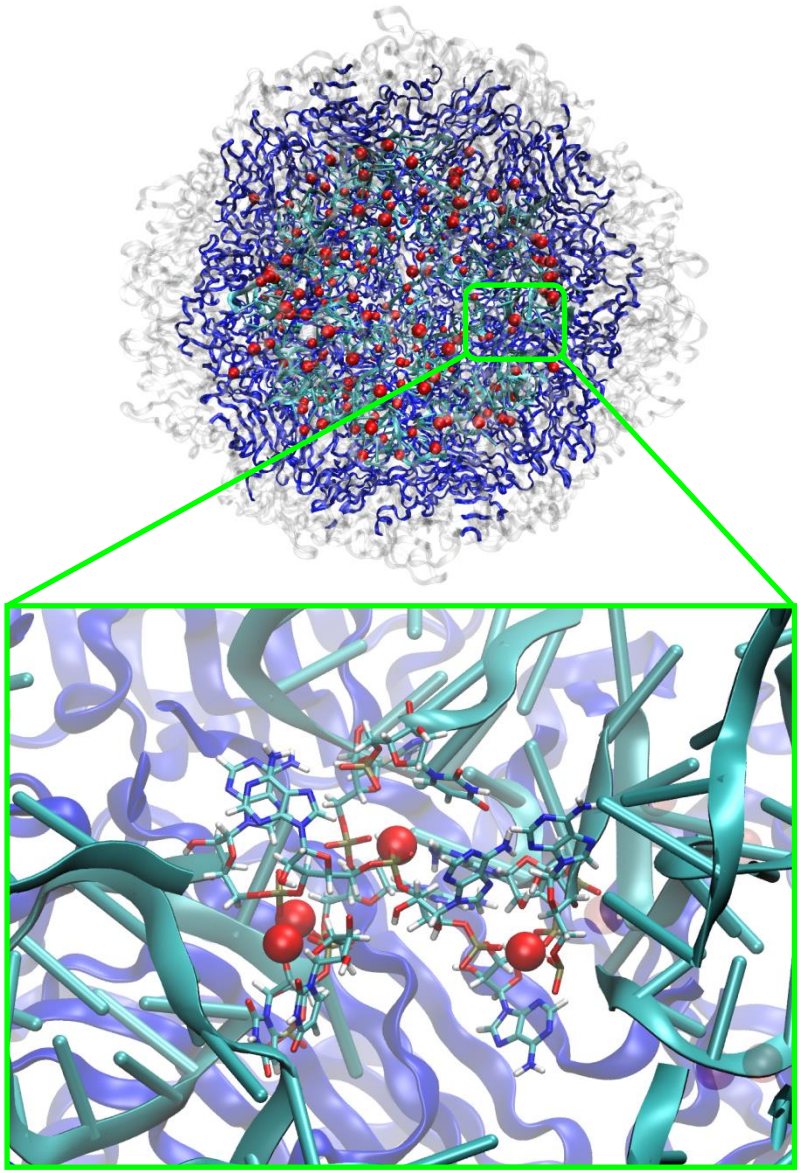


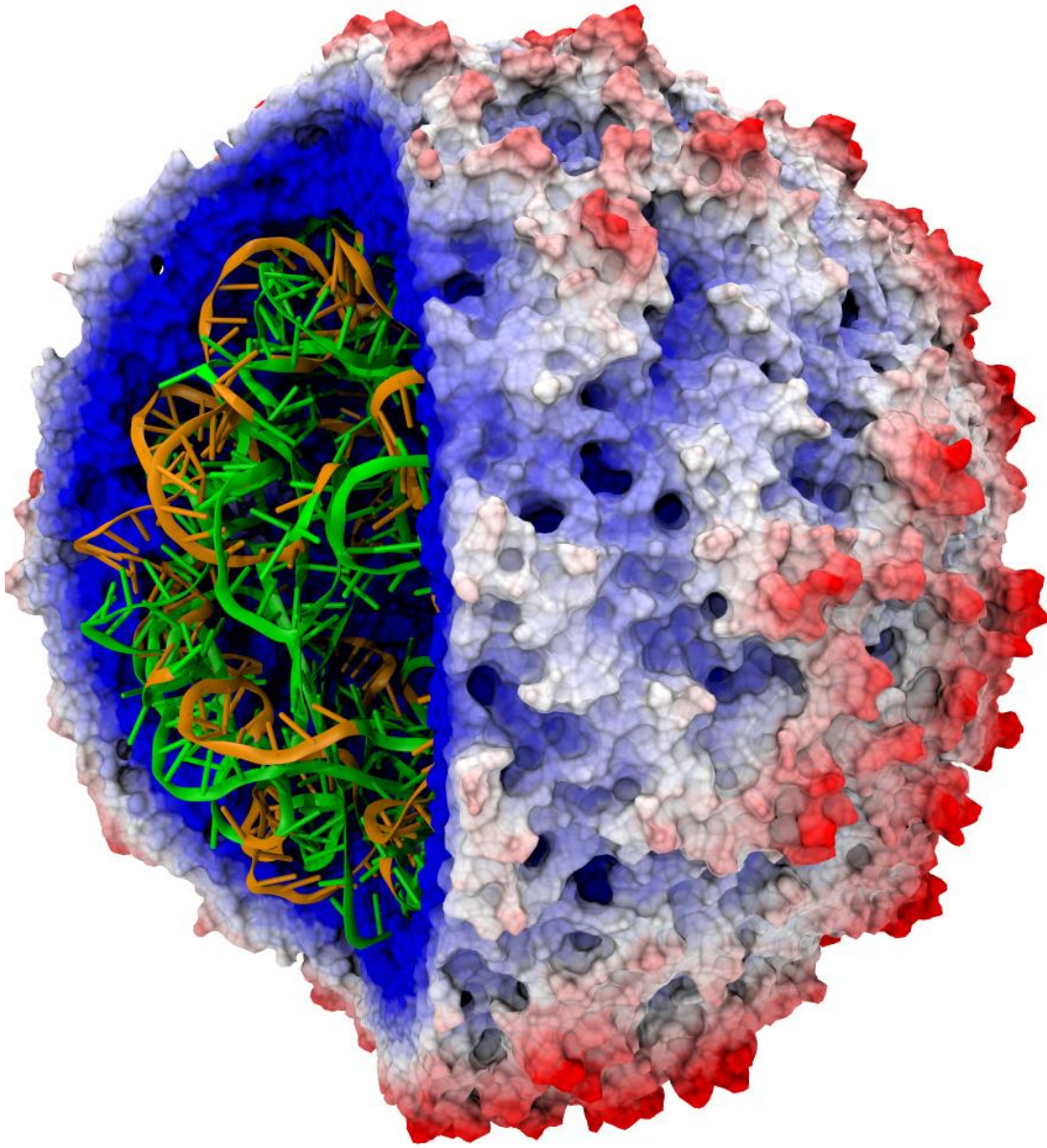


Exportin Cse1p



Nanopore





Satellite Tobacco Mosaic Virus

Biomedical Technology Research Center for Macromolecular Modeling and Bioinformatics
Beckman Institute, University of Illinois at Urbana-Champaign - www.ks.uiuc.edu

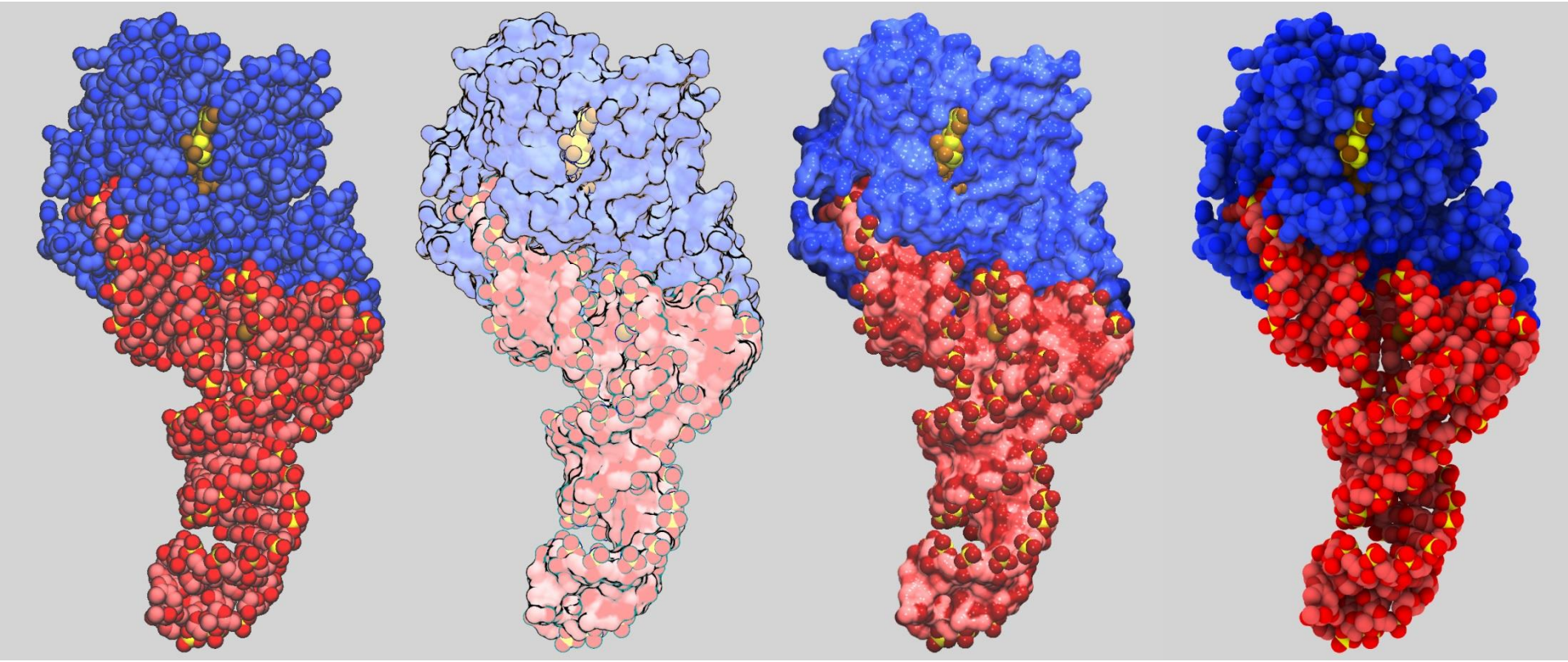
VMD Shading Comparison: EF-Tu

Outline Shader

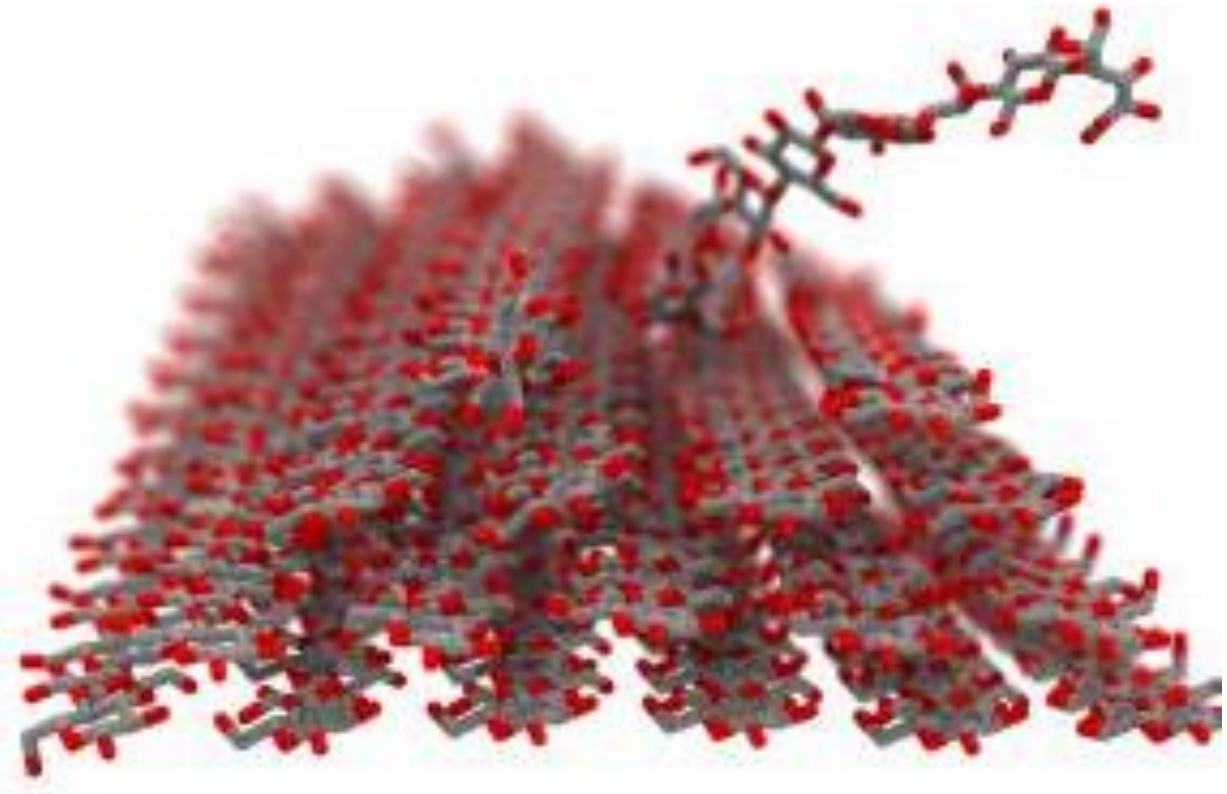
“Goodsell” Shader

Glossy Shader

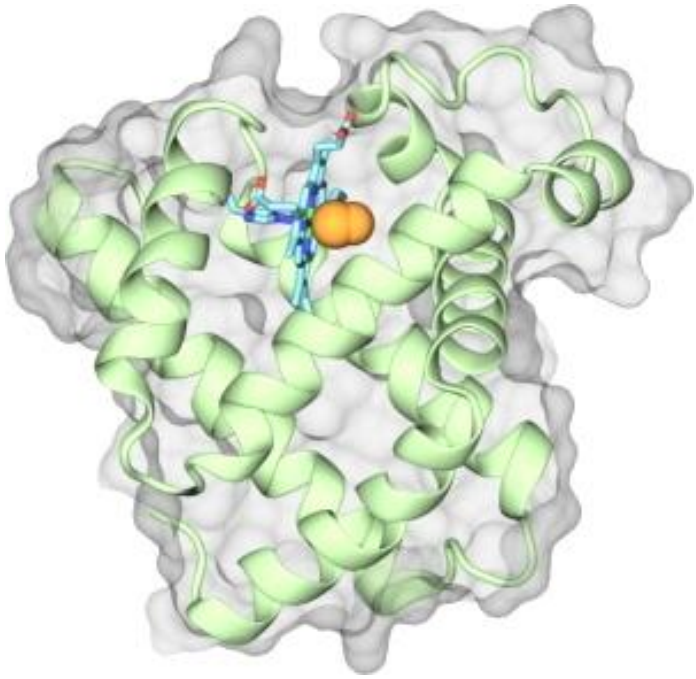
Ambient Occlusion, Shadowing



Diverse Shading and Lighting Approaches



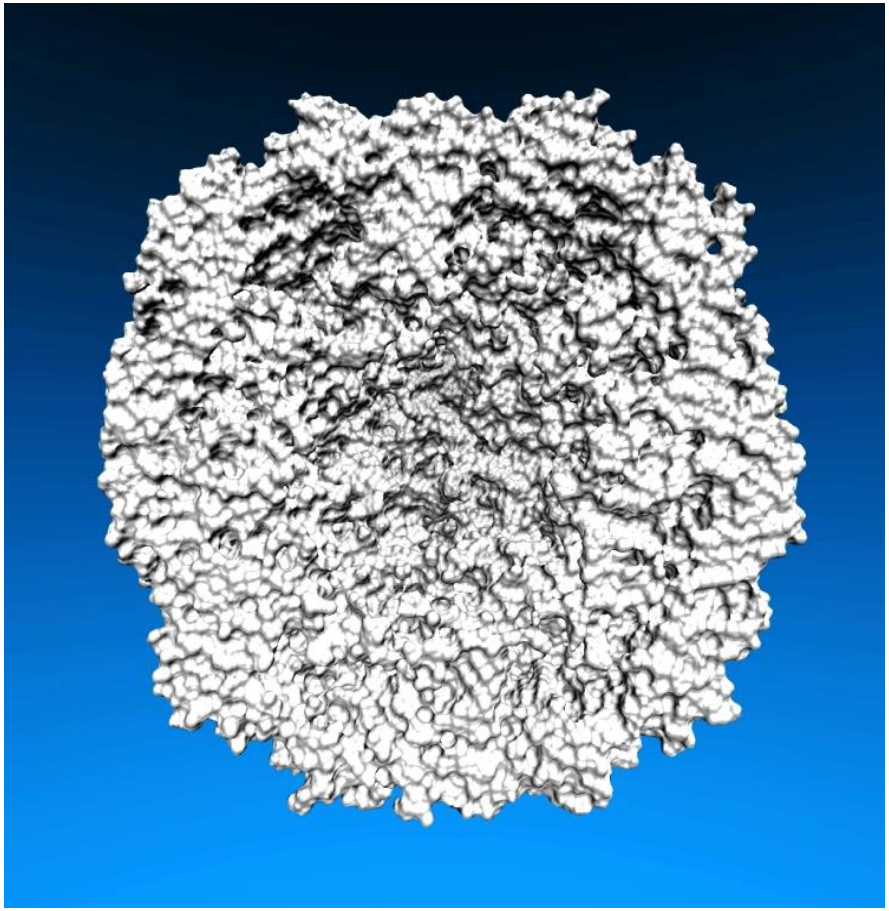
Decrystallization: Interactive Ray Tracing w/ Ambient Occlusion Lighting, Depth of Field Focal Blur



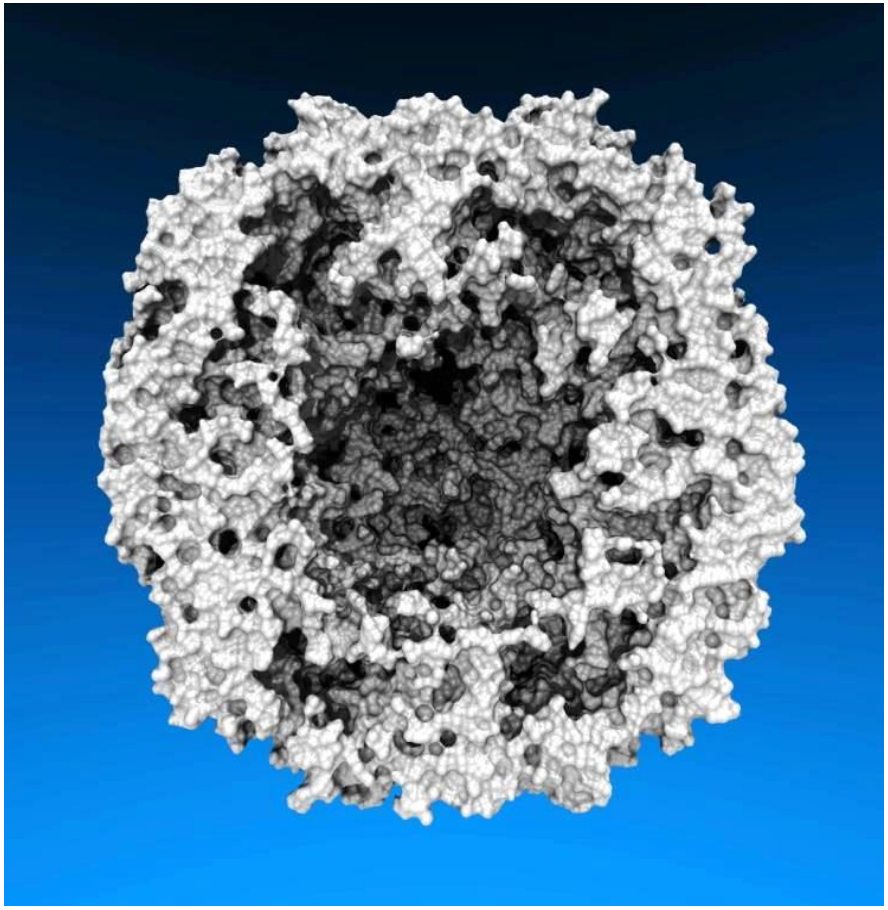
Myoglobin

VMD ***Interactive*** Ray Tracing Lighting Comparison

Two lights, no shadows (typical w/ OpenGL)

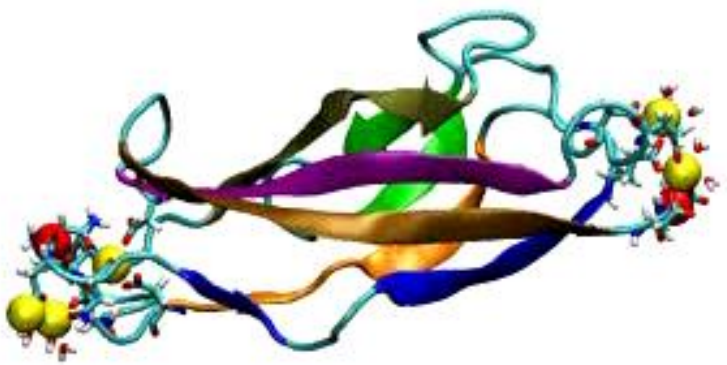


Ambient occlusion lighting + two lights w/ shadows



Visualization of Molecular Dynamics

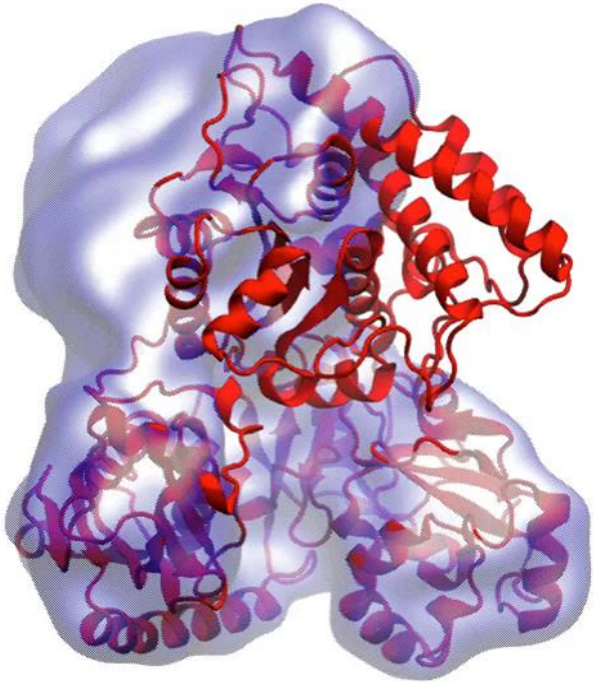
- Classical mechanics simulation of atomic motions (F=ma)
- Molecular dynamics simulations save trajectories of atomic coordinates as simulated time progresses
- Researchers study trajectories by analyzing force profiles, energies, structural changes, etc.
- **Visualization selections, graphics, structure properties recomputed for each trajectory timestep!**



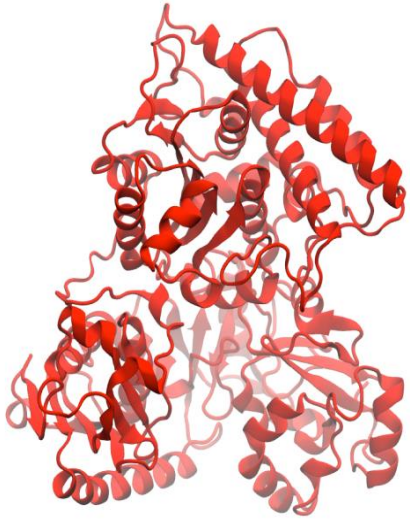
Molecular Dynamics Flexible Fitting (MDFF)

X-ray crystallography → MDFF ← Electron microscopy

APS at Argonne

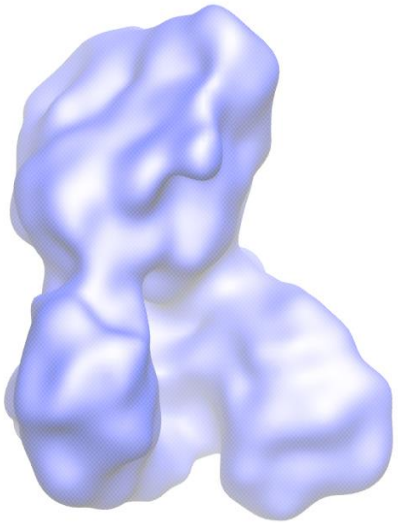


FEI microscope

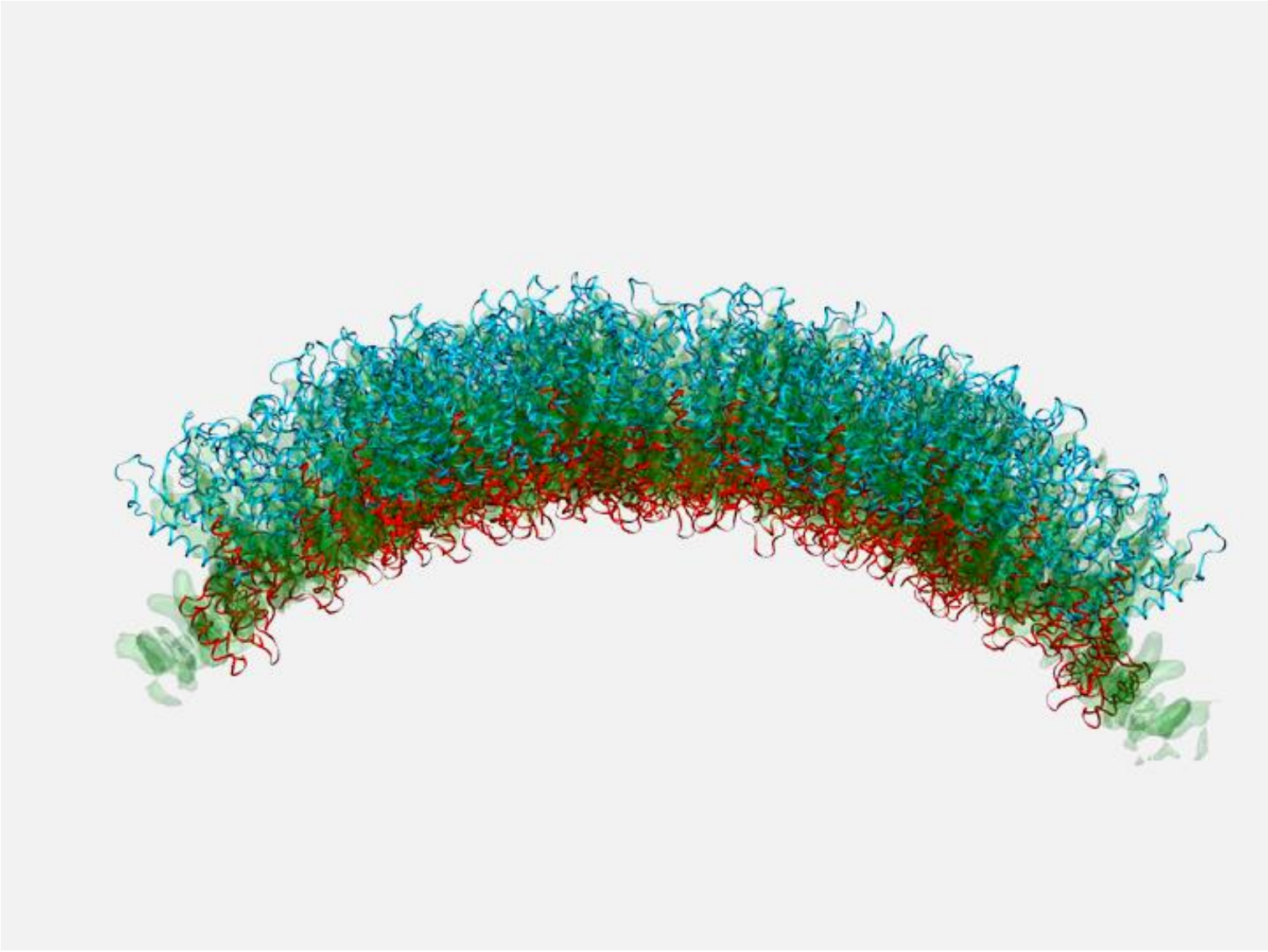


Acetyl - CoA Synthase

ORNL Titan

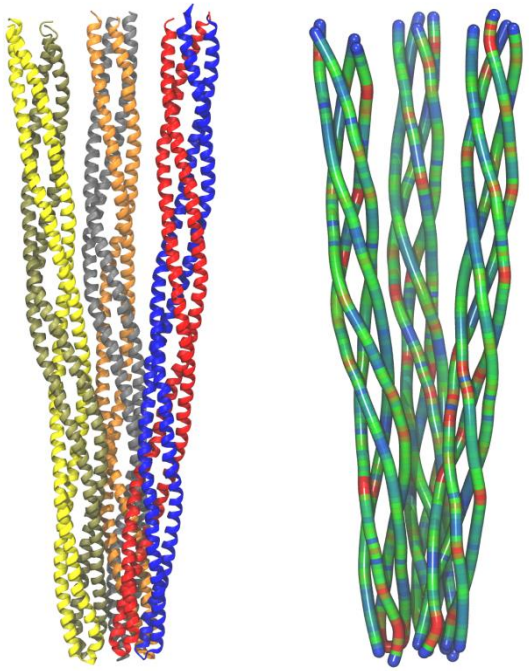


Hexamer of hexamers HIV capsid substructure Molecular Dynamics Flexible Fitting (MDFF) simulation. All-atom structure fitting into cryo-EM density map.



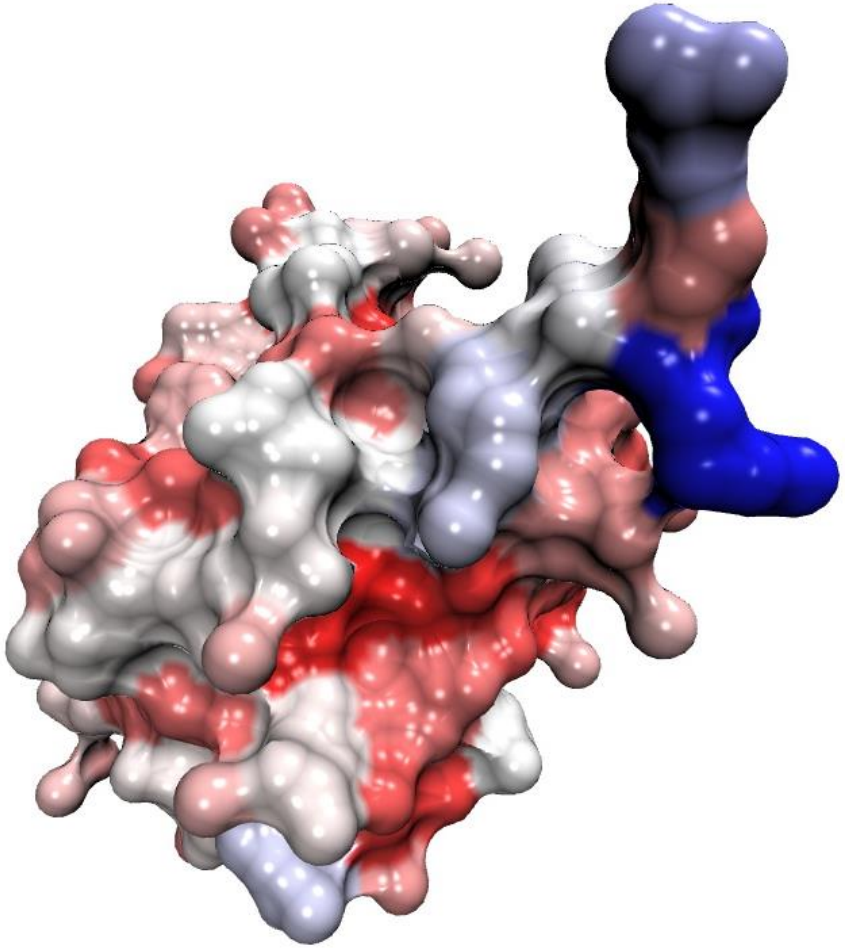
Computed Properties

- Smoothing of thermal noise
- Secondary structure
- Hydrogen bonds, salt bridges
- Forces, energies, stress, strain
- Time averaging of electrostatic fields, occupancy maps
- Quality-of-fit cross correlation with cryo-EM density maps
- Normal modes, principal component analysis, essential dynamics
- Cluster simulation trajectory timesteps by structural similarity

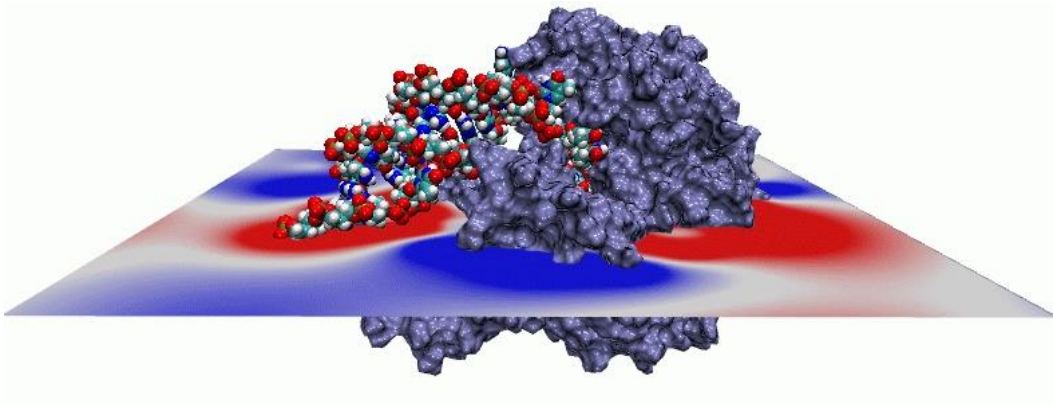


Chemoreceptor trimer-of-dimers analysis with Bendix plugin in VMD

Display of Computed Properties on Structures

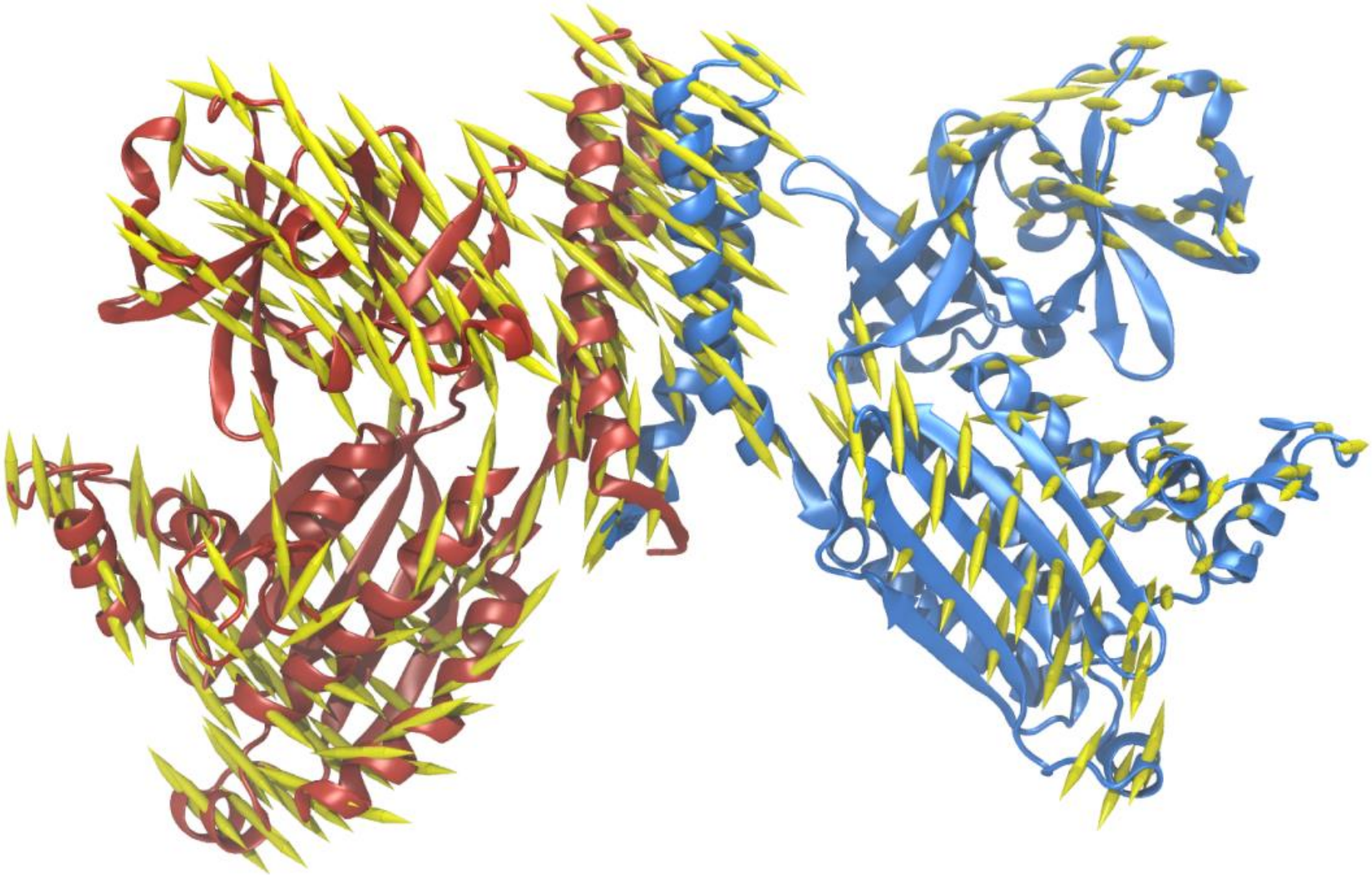


Per-residue solvent-accessible surface area of Ubiquitin

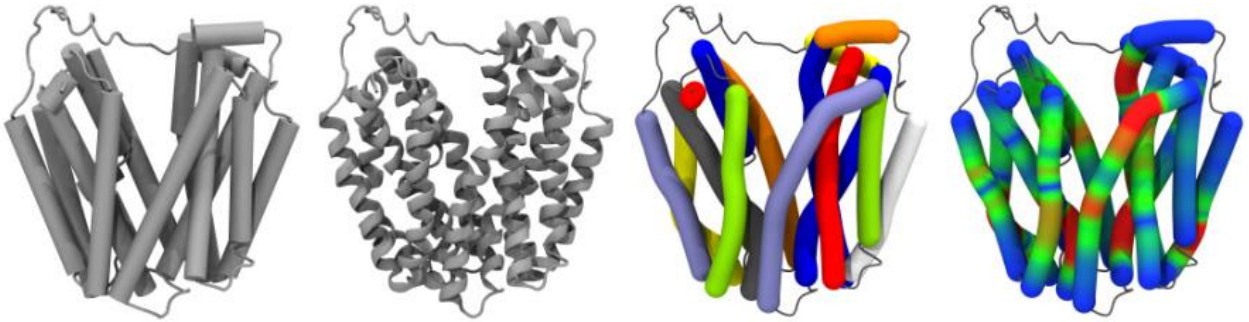


PME electrostatic potential contour for a helicase on a volumetric slice plane

CheA kinase PCA: first principal component porcupine plot

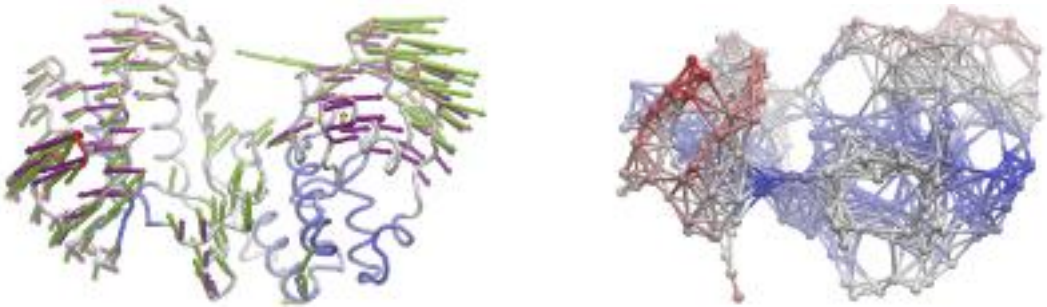


Example VMD Visualization and Analysis Plugins



Bendix

Dahl ACE, Chavent M and Sansom MSP Bendix: intuitive helix geometry analysis and abstraction. *Bioinformatics* 2012 28(16): 2193-2194.



Normal Mode Wizard

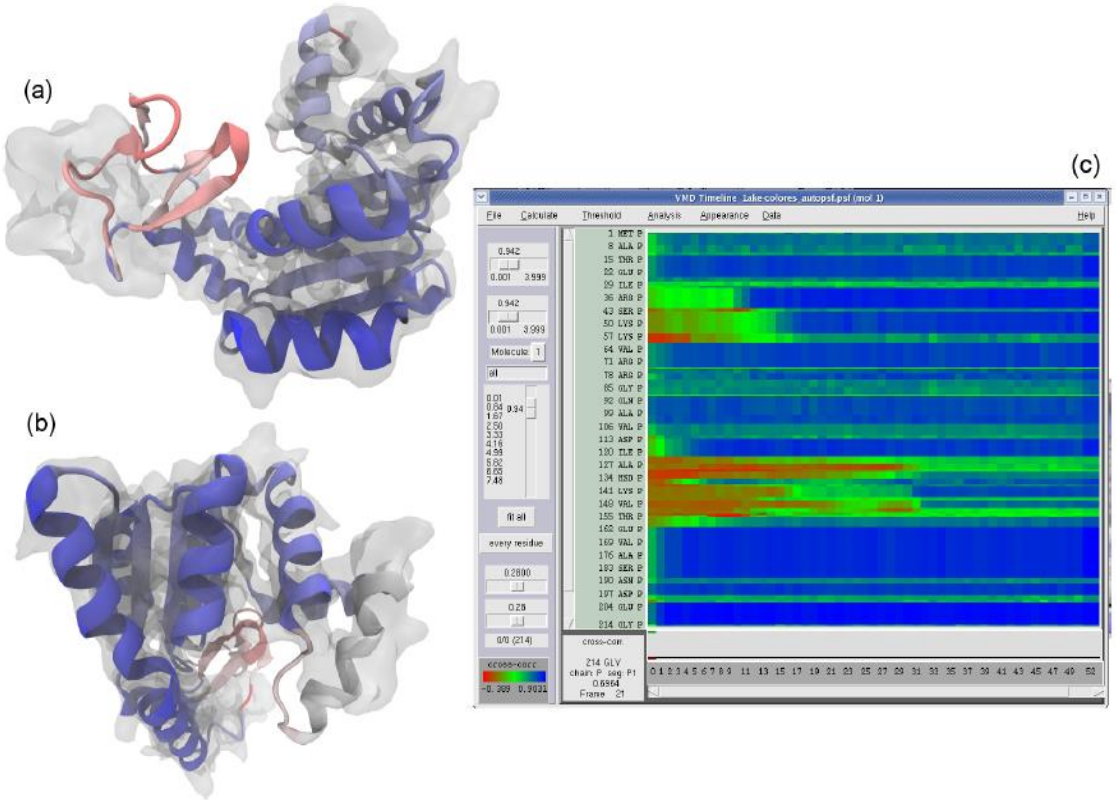
Bakan A, Meireles LM, Bahar I ProDy: Protein Dynamics Inferred from Theory and Experiments. *Bioinformatics* 2011 27(11):1575-1577.

VMD Timeline Plugin: Analyze MD Trajectories for Events

GPU-accelerated MDFF Cross Correlation Timeline

Regions with poor fit

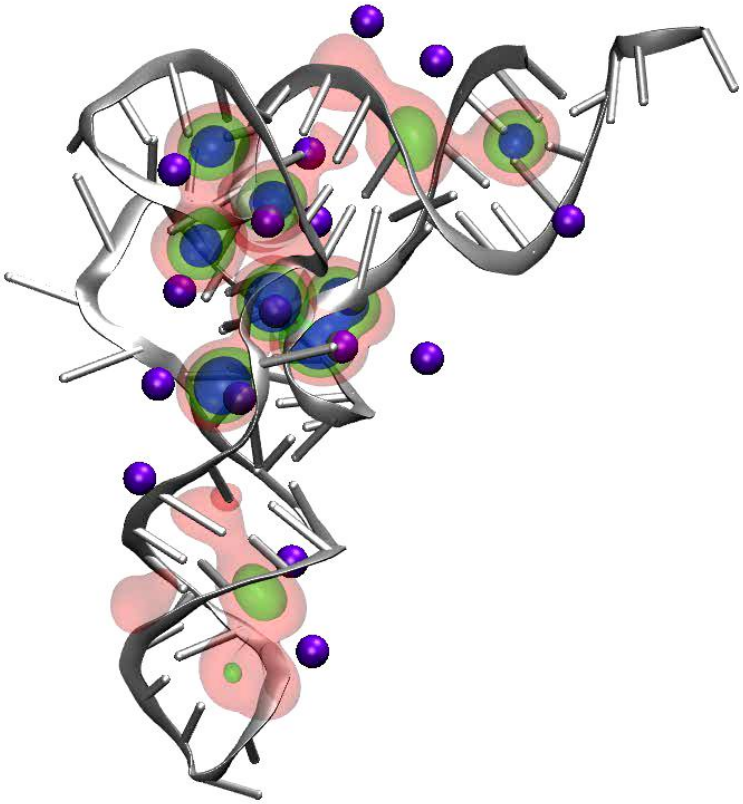
Regions with good fit



- **Interactive** 2-D heatmap plot linked to 3-D structure
- Single picture shows changing properties across structure+trajectory
- Explore time vs. per-selection attribute, linked to molecular structure
- Many analysis methods available; user-extendable

Time-Averaged Volumetric Properties

- Compute density, distance, occupancy, potential maps for a frame or averaged over a trajectory
- Example: display binding sites for diffusively bound ions as probability density isosurfaces

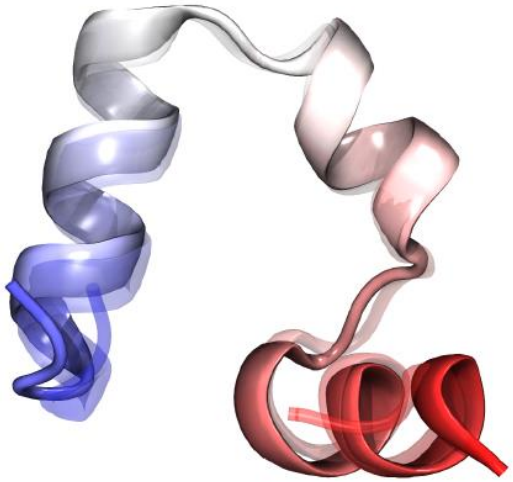


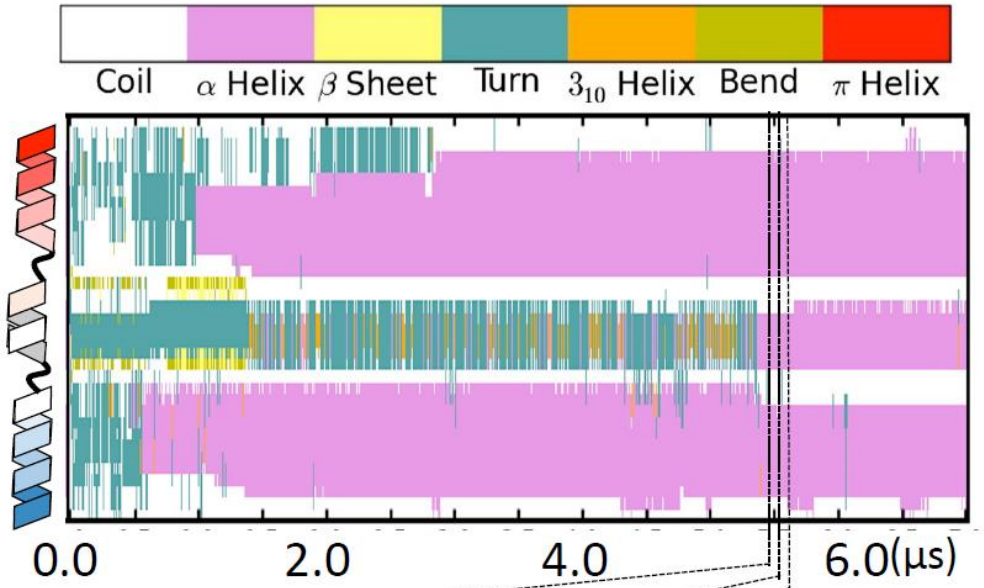
tRNA magnesium ion occupancy: VMD volmap plugin

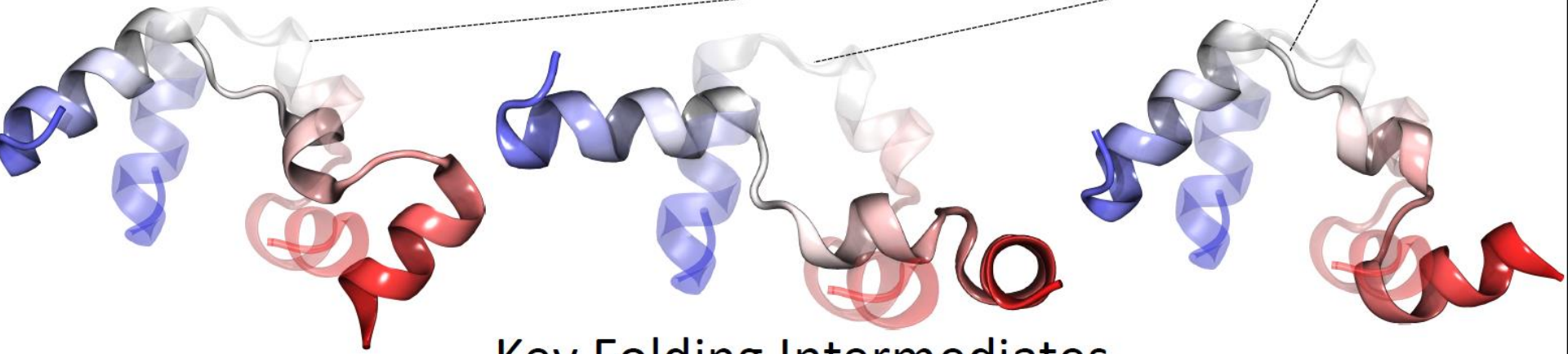
Folding Dynamics of Villin Headpiece Unveiled

6.9μs folding simulation of 30K atoms: 380GB trajectory

Schulten et al. *Biophys J* **94**:**L**75, 2008, **97**: 2009

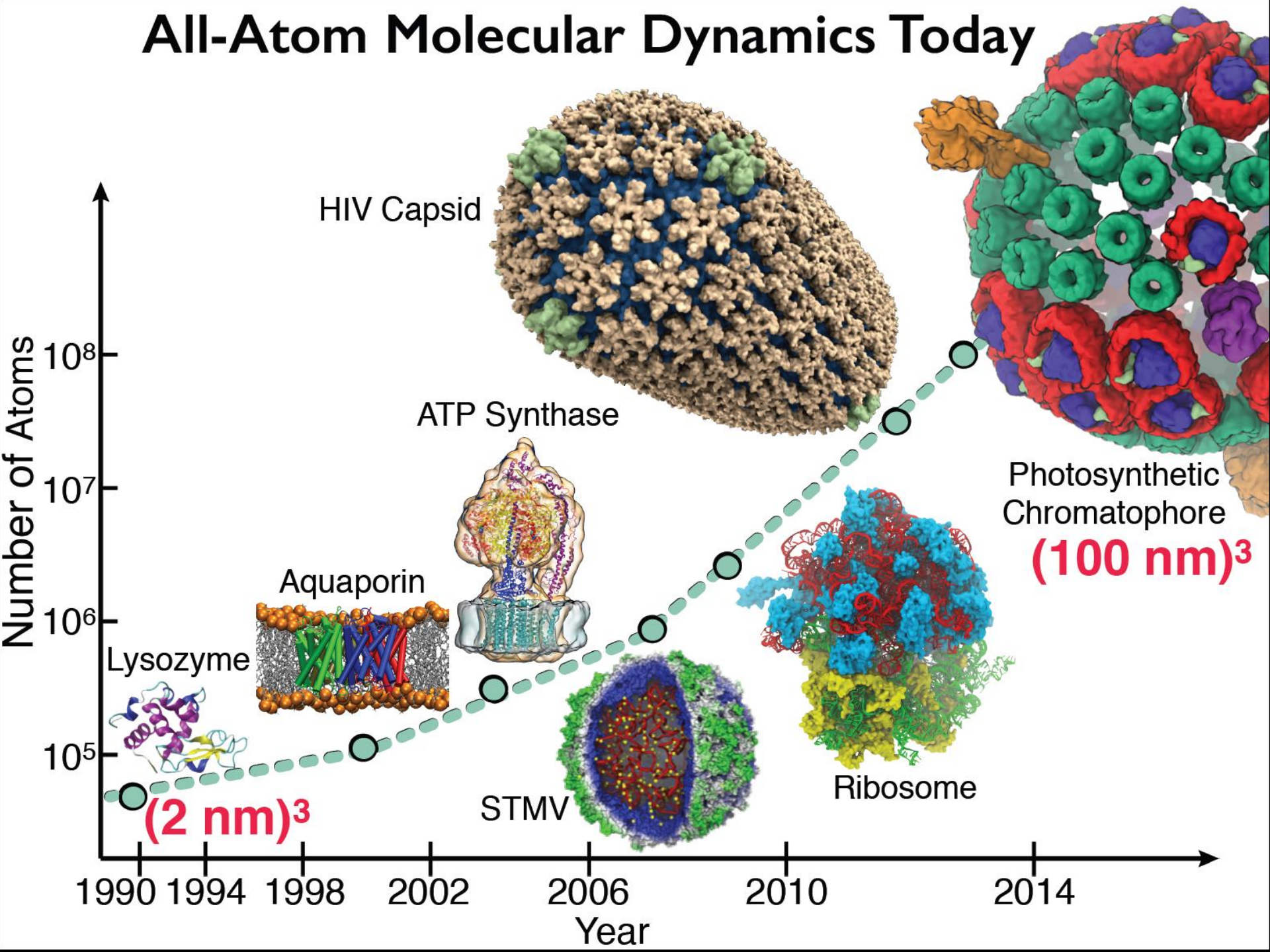




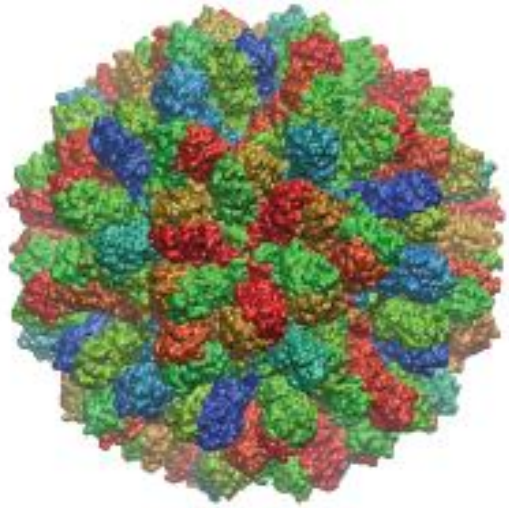


Key Folding Intermediates

All-Atom Molecular Dynamics Today

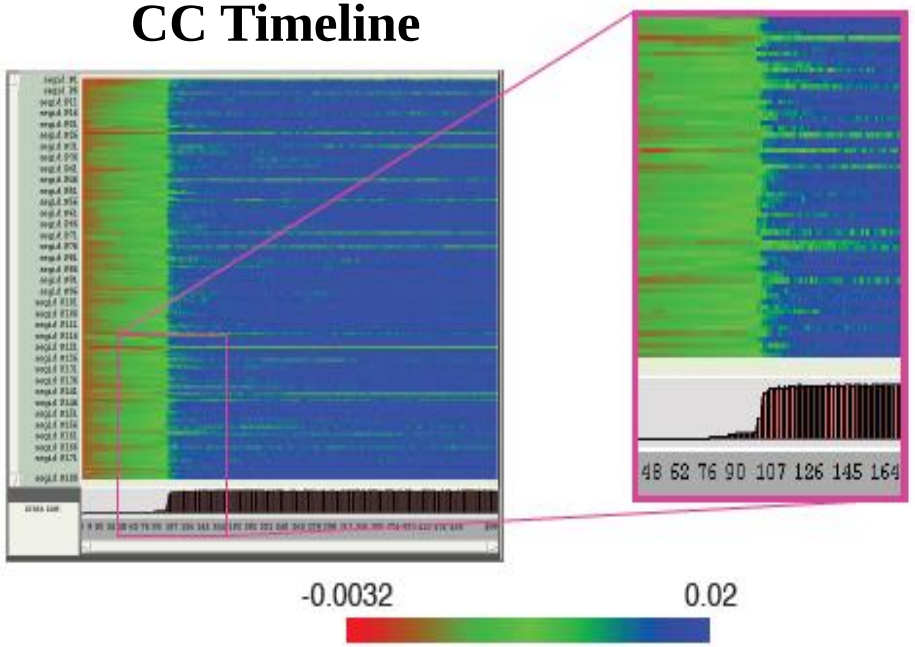


VMD Parallel GPU-accelerated RHDV Cross Correlation Timeline Analysis on Cray XK7



	RHDV
Atoms	**702K**
Traj. Frames	**10,000**
Component Selections	**720**
Single-node XK7 (projected)	**336 hours (14 days)**
128-node XK7	**3.2 hours 105x speedup**
2048-node XK7	**19.5 minutes 1035x speedup**

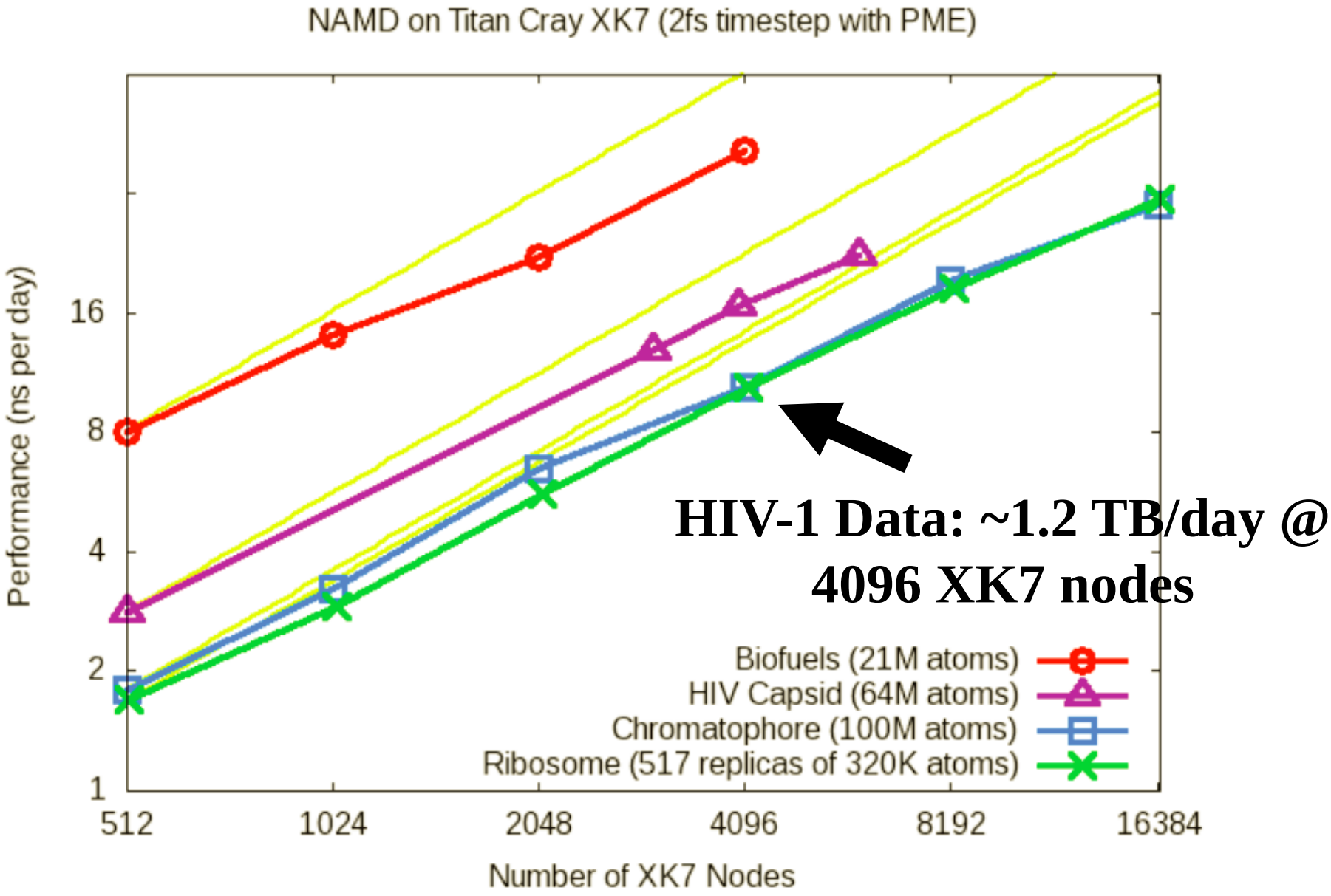
RHDV Group-relative CC Timeline



Calculation would take **5 years** using original serial CC calc. on a desktop workstation!

Stone et al., Faraday Discuss., 169:265-283, 2014.

NAMD Titan XK7 Performance August 2013



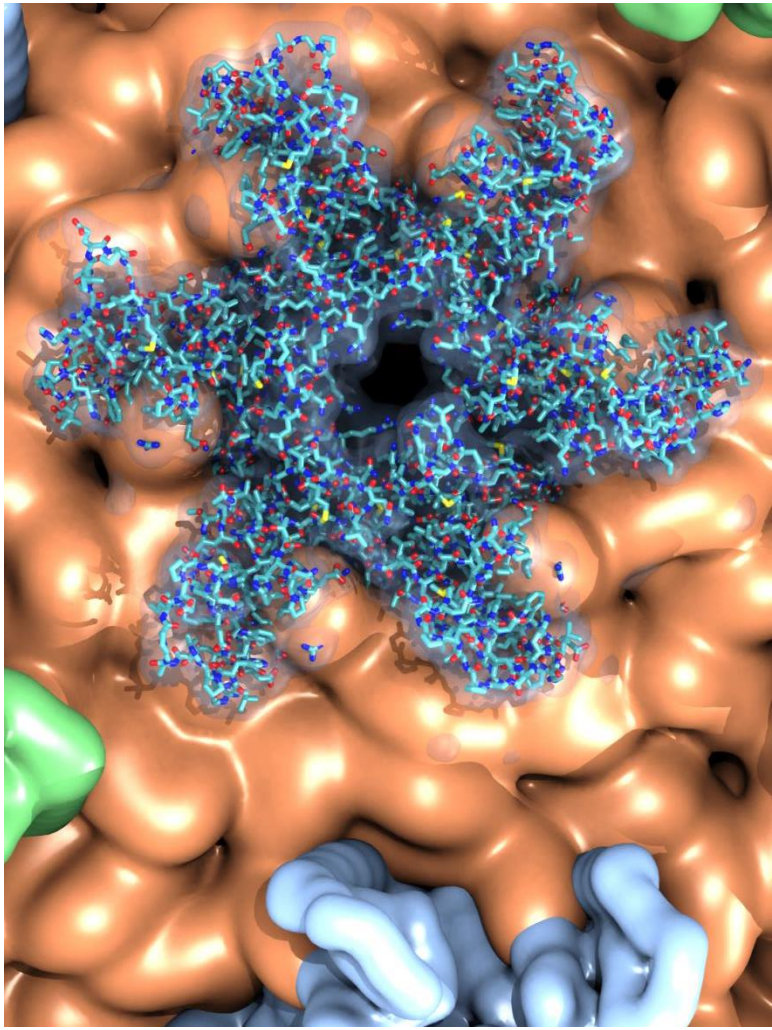
VMD Petascale Visualization and Analysis

- Analyze/visualize large trajectories too large to transfer:
  - Trajectory analysis, e.g. time-averaged electrostatic fields, MDFF quality-of-fit, etc.
  - User-defined parallel analysis operations, data types
  - Parallel rendering, movie making
- Parallel I/O up to **275 GB/sec** on 8192 nodes – read **231 TB in 15 minutes!**
- VMD uses GPU-accelerated Cray XK7 nodes for both visualization and analysis
  - **OpenGL, Ray Tracing**
  - **Future: Remote Interactive Viz!**

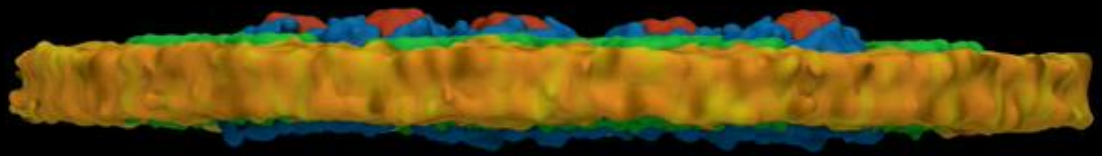
NCSA Blue Waters Hybrid
Cray XE6 / XK7 Supercomputer
22,640 XE6 CPU nodes
4,224 XK7 nodes w/ GPUs

VMD-Next: Coming Soon

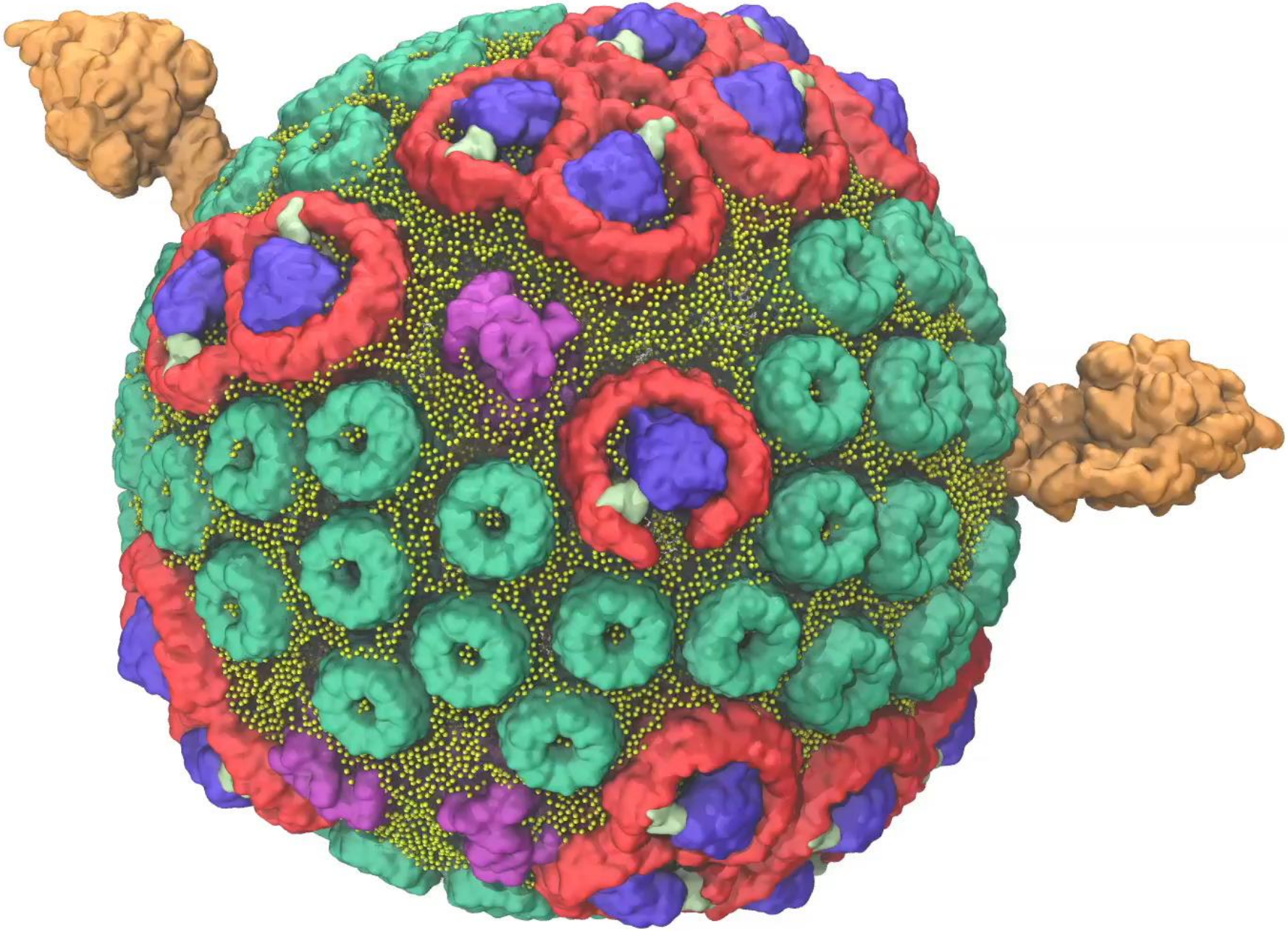
- Improved structure building and analysis tools
- Many new and updated user-contributed plugins:
- Further integration of interactive ray tracing
  - Seamless interactive RT in main VMD display window
  - Support trajectory playback in interactive RT
  - Enable multi-node interactive RT on HPC systems
- Built-in (basic) interactive remote visualization on HPC clusters and supercomputers
- Improved movie making tools, off-screen OpenGL movie rendering, parallel movie rendering:
  - EGL for parallel graphics w/o X11 server



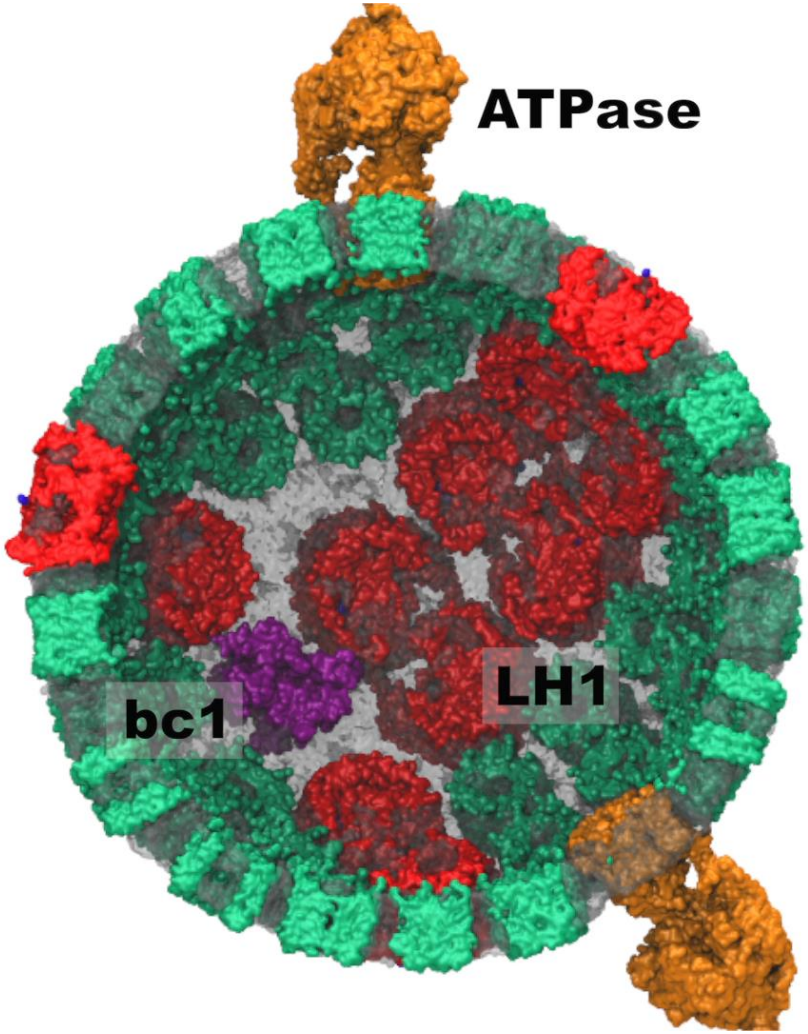
GPU Ray Tracing of
HIV-1 Capsid Detail



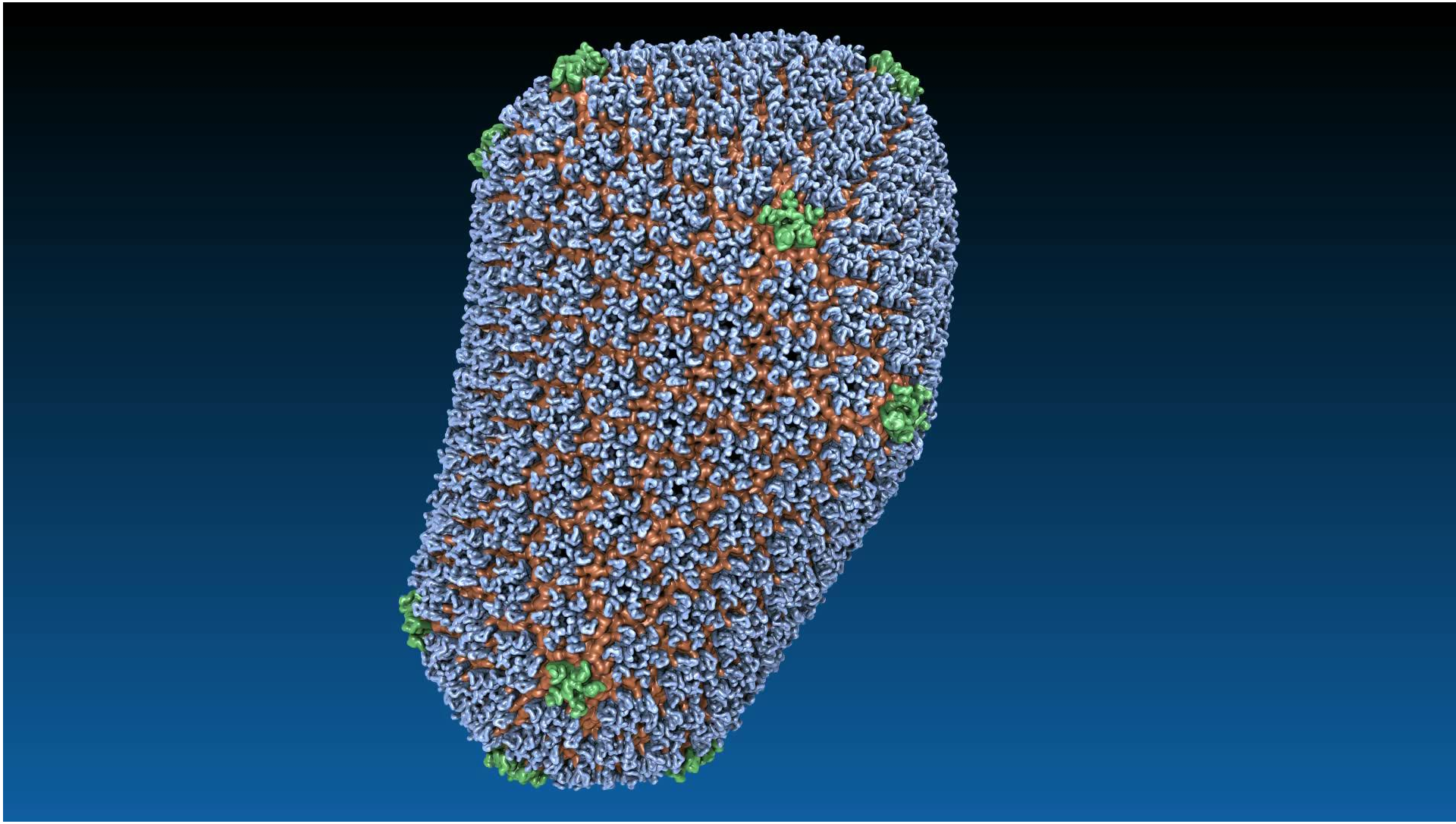
20 M atom chromatophore patch



Chromatophore Electrostatics



HIV-1 Capsid



Acknowledgements

- NIH Center for Macromolecular Modeling and Bioinformatics, and Theoretical and Computational Biophysics Group, University of Illinois at Urbana-Champaign
  - Director: Klaus Schulten
  - Science images created by many current and former group members
- NVIDIA CUDA Center of Excellence, University of Illinois at Urbana-Champaign
- NVIDIA CUDA and OptiX teams
- NCSA Blue Waters Team
- Funding:
  - DOE INCITE, ORNL Titan: DE-AC05-00OR22725
  - NSF Blue Waters:
    NSF OCI 07-25070, PRAC “The Computational Microscope”,
    ACI-1238993, ACI-1440026
  - NIH support: 9P41GM104601, 5R01GM098243-02

Related Publications

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

- **Visualization of Energy Conversion Processes in a Light Harvesting Organelle at Atomic Detail.**
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