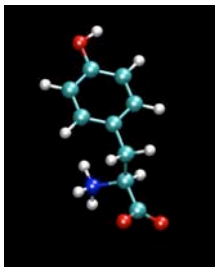
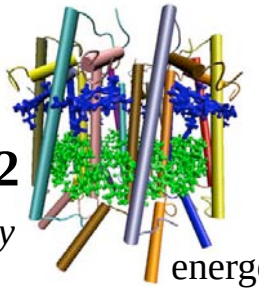
Introduction to Protein Structures - VMD Molecular Graphics Tool



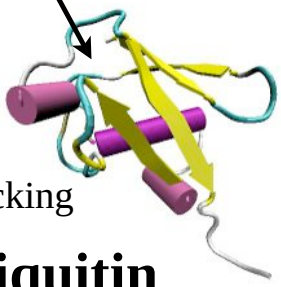
amino acid tyrosine



LH2

case study

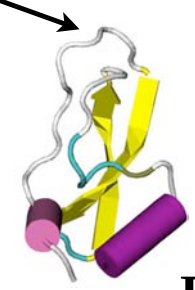
energetics



traficking

Ubiquitin

case study



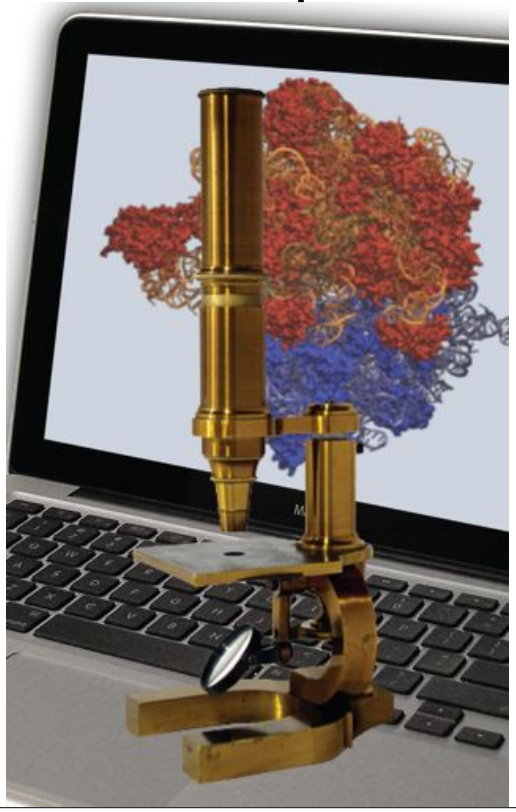
enzymatic control

BPTI

VMD tutorial

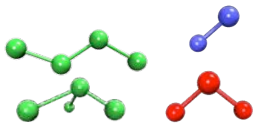
http://www.ks.uiuc.edu/Training/CaseStudies/ http://www.ks.uiuc.edu/Training/Tutorials/

Our Mission: The Computational Microscope



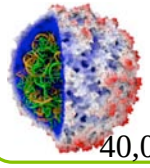
Our Microscope is Made of...

Chemistry

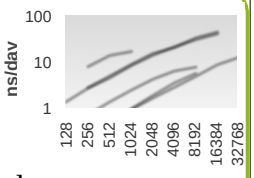


$$U(\vec{R}) = \underbrace{\sum_{bonds} k_i^{bond}(r_i - r_0)^2}_{U_{bond}} + \underbrace{\sum_{angles} k_i^{angle}(\theta_i - \theta_0)^2}_{U_{angle}} + \underbrace{\sum_{dihedrals} k_i^{dihe}[1 + \cos(n_i\phi_i + \delta_i)]}_{U_{dihedral}} + \underbrace{\sum_i \sum_{j \neq i} 4\epsilon_{ij}\left[\left(\frac{\sigma_{ij}}{r_{ij}}\right)^{12}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

NAMD Software



Virus



40,000 registered users

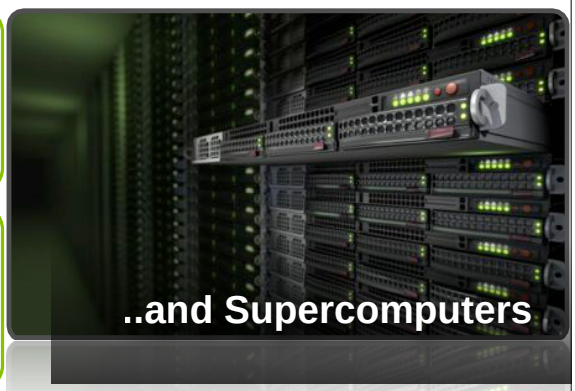
Physics

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

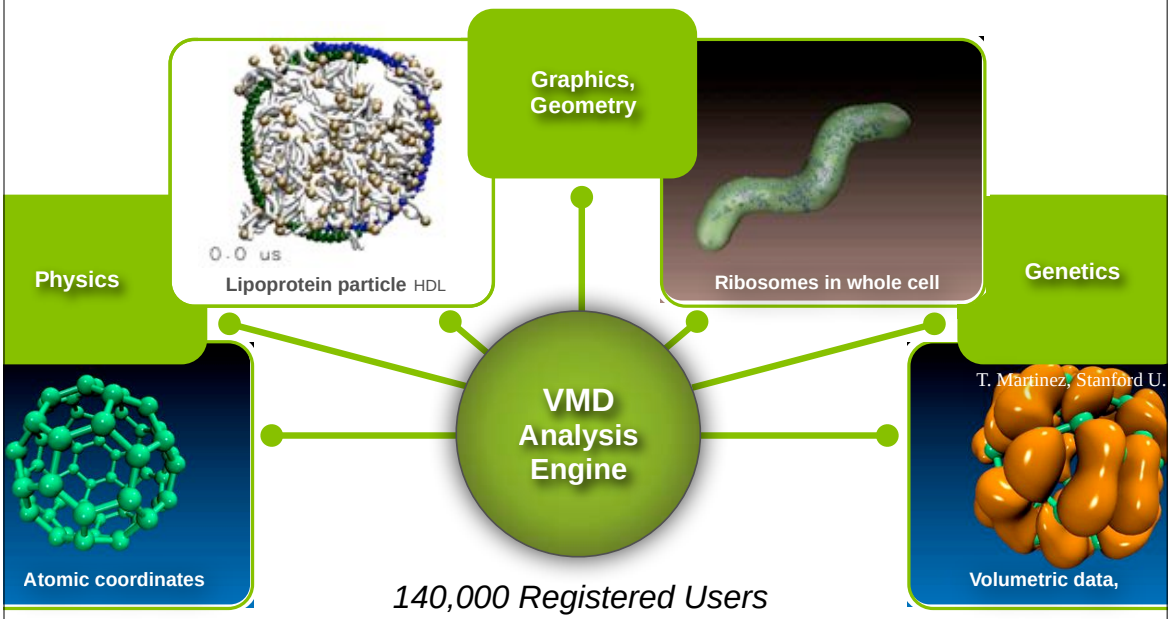
Math

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

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



Our Microscope Shows All, from Electrons to Cells

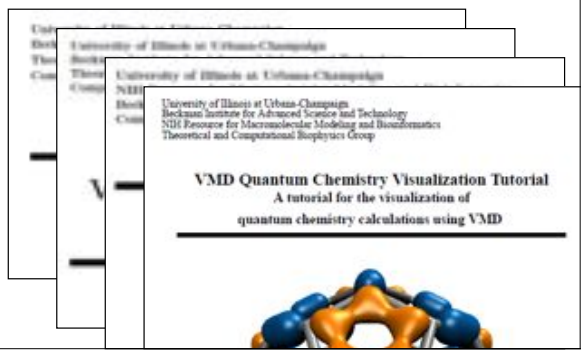


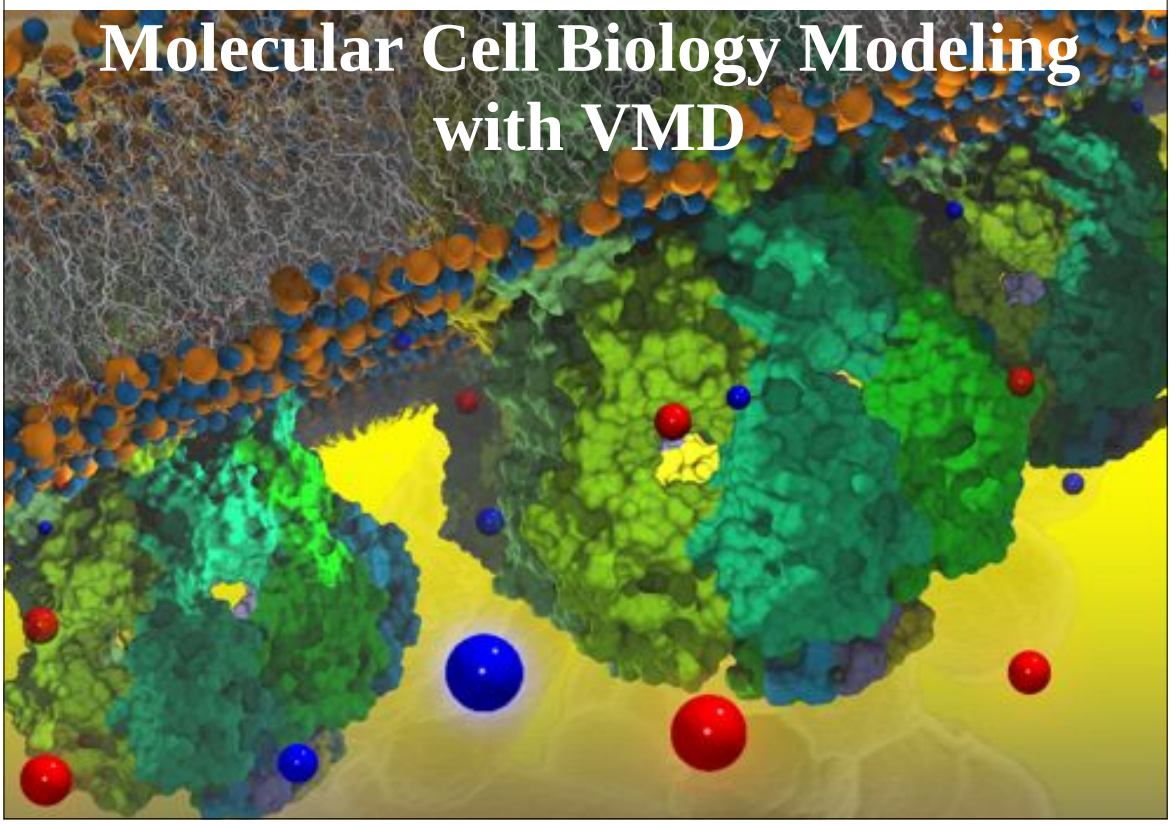
140,000 Registered Users

VMD and NAMD Work Together

- Over 212,000 registered users
  - 18% (39,000) are NIH-funded
  - Over 49,000 have downloaded multiple VMD releases
- Over 8,000 citations
- User community runs VMD on:
  - MacOS X, Unix, Windows operating systems
  - Laptops, desktop workstations
  - Clusters, supercomputers

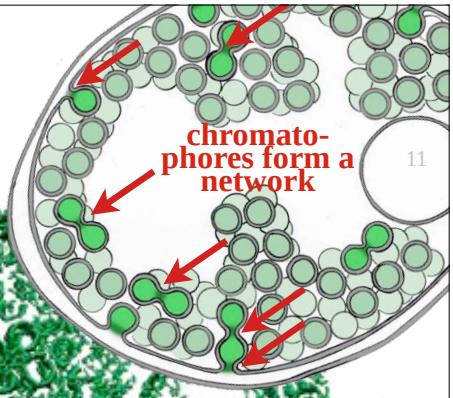
- VMD user support efforts:
  - 20,000 emails, 2007-2011
  - Develop and maintain VMD tutorials and topical mini-tutorials; 11 in total
  - Periodic user surveys

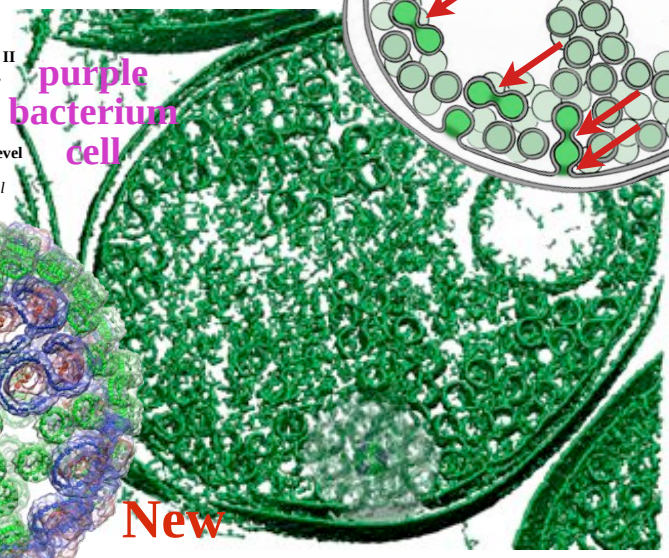




VMD from Electrons to Molecules to Cells

Photosynthetic Organelles in Purple Bacteria

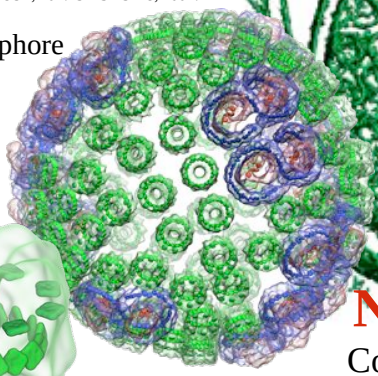




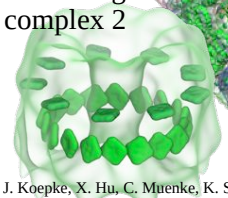
J. Strümpfer and K. Schulten. **Light harvesting complex II B850 excitation dynamics.** *Journal of Chemical Physics*, **131:**225101, 2009.

M. Sener, J. Olsen, C. Hunter, and K. Schulten. **Atomic level structural and functional model of a bacterial photosynthetic membrane vesicle.** *Proceedings National Academy of Sciences, USA*, **104**:15723-15728, 2007.

chromatophore



light harvesting complex 2



J. Koepke, X. Hu, C. Muenke, K. Schulten, and H. Michel. **The crystal structure of the light harvesting complex II (B800-850) from *Rhodospirillum molischianum*.** *Structure*, **4:**581-597, 1996.

New

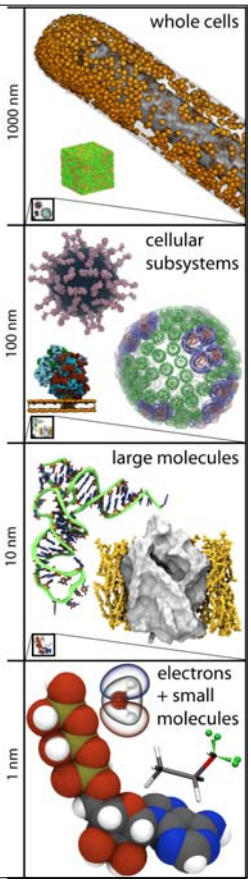
Collaboration with **EM tomography** group of W. Baumeister, MPI Martinsried (with L. Fitting-Kourkoutis, E. Villa)

Show

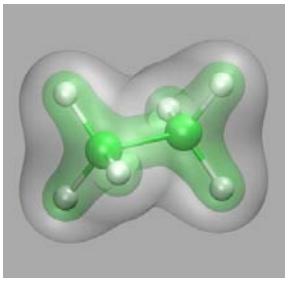
Chromatophore Demo

VMD Interoperability – Linked to Today's Key Research Areas

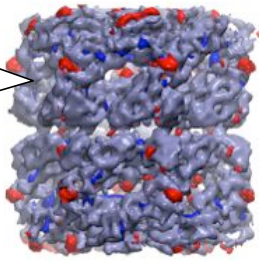
- Unique in its interoperability with a broad range of modeling tools: AMBER, CHARMM, CPMD, DL_POLY, GAMESS, GROMACS, HOOMD, LAMMPS, NAMD, and many more …
- Supports key data types, file formats, and databases, e.g. electron microscopy, quantum chemistry, MD trajectories, sequence alignments, super resolution light microscopy
- Incorporates tools for simulation preparation, visualization, and analysis



VMD – A Broad Tool to Think



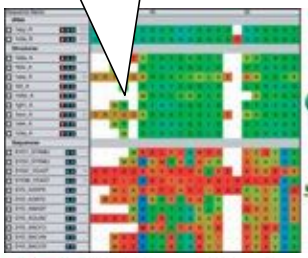
Volumetric Data:
Density maps,
Electron orbitals,
Electrostatic potential,
Time-averaged occupancy, …

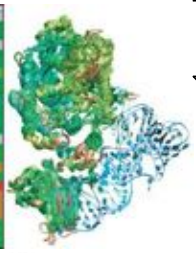


Sequence Data:
Multiple Alignments,
Phylogenetic Trees

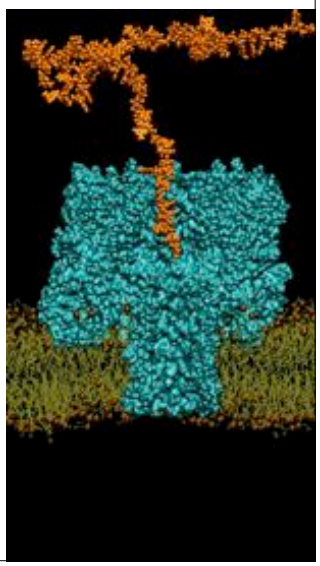
VMD

Annotations





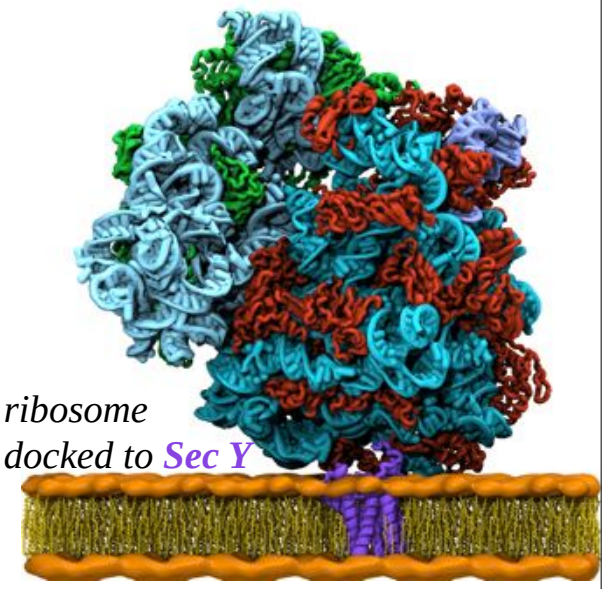
Atomic Data:
Coordinates,
Trajectories,
Energies,
Forces, …



National Center for Research Resources

Highlights of the VMD Molecular Graphics Program

- Display of large biomolecules and simulation trajectories
- Sequence browsing and structure highlighting
- Multiple sequence - structure analysis, phylogenetic analysis
- User-extensible scripting interfaces for analysis and customization

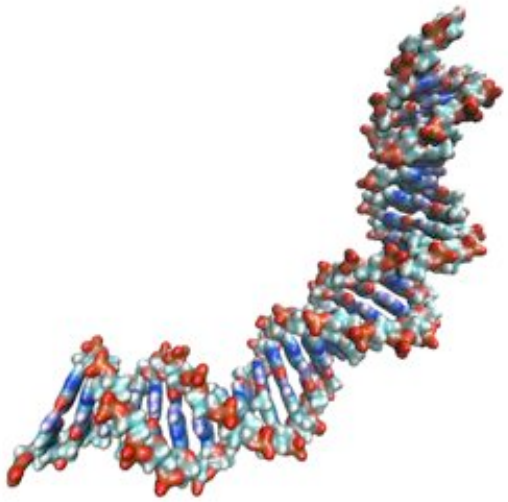


*ribosome docked to **Sec Y***

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

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

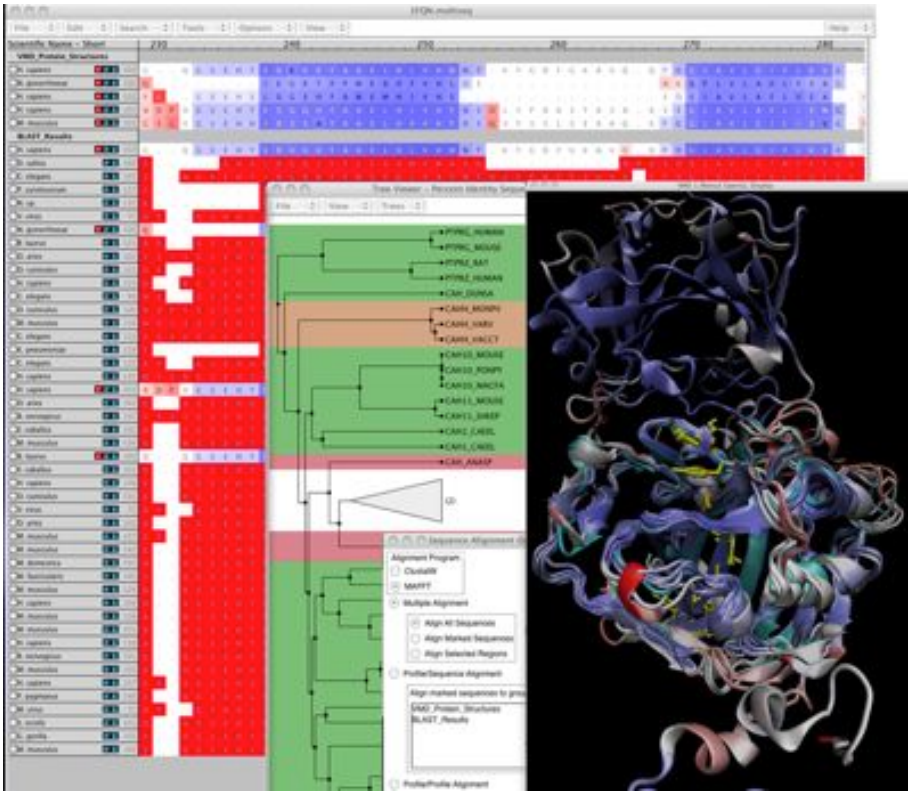


Fast Visualization of Gaussian Density Surfaces for Molecular Dynamics and Particle System Trajectories. M. Krone, J. Stone, T. Ertl, K. Schulten. *EuroVis 2012*, 2012.

Show

Villin Head Piece Folding

Structure, Sequence and Phylogenetic Analysis with VMD



VMD 1.9.1: Force Field Toolkit (*ff*TK) Plugin

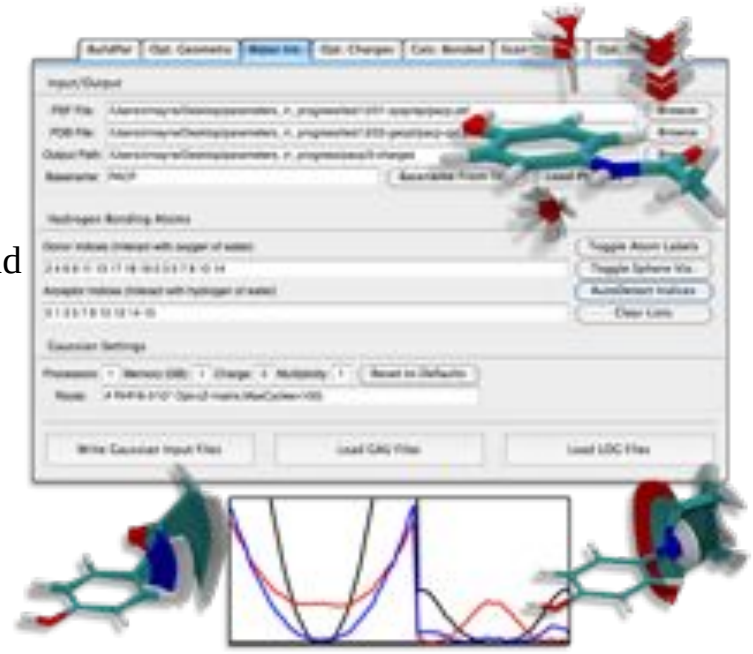
Parameter *development* for small molecules (CHARMM, CGenFF)

GUI-driven

Automates error prone and time consuming steps

Tools for assessing parameter quality

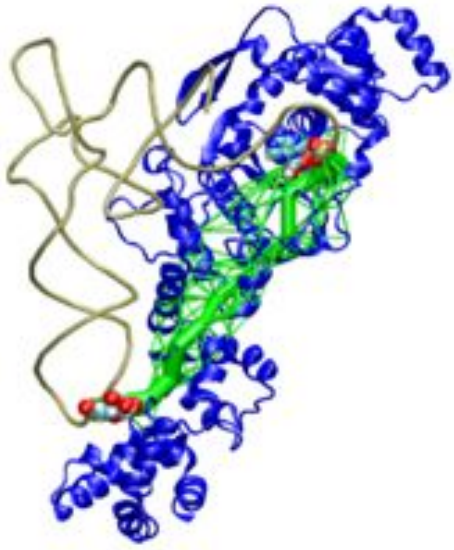
Enables users to become force field developers



VMD 1.9.1 Released Feb. 4, 2012

Key Features

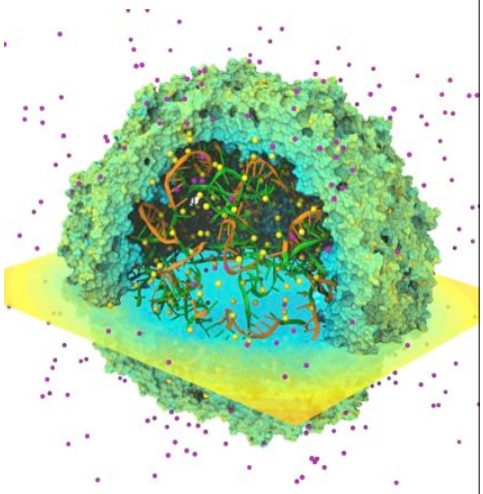
- New **NetworkView** plugin for study of allostery, signaling networks
- New **Force Field Toolkit (ffTK)** assists with CHARMM parameter development
- New "**QuickSurf**" surface representation
- New **user-contributed plugins**:
  - Normal Mode Wizard
  - PropKa interface
  - RMSD Trajectory Tool
  - "Heat map" plotting
  - Many others…



NetworkView: tRNA anti-codon w/ ligand in GluRS active site

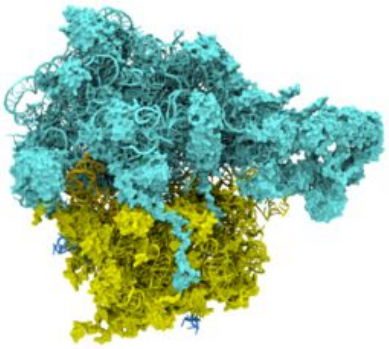
Time-Averaged Electrostatics Analysis on Energy-Efficient GPU Cluster

- **1.5 hour** job (CPUs) reduced to **3 min** (CPUs+GPU)
- Electrostatics of thousands of trajectory frames averaged
- Per-node power consumption on NCSA "AC" GPU cluster:
  - CPUs-only: 299 watts
  - CPUs+GPUs: 742 watts
- GPU Speedup: **25.5x**
- Power efficiency gain: **10.5x**

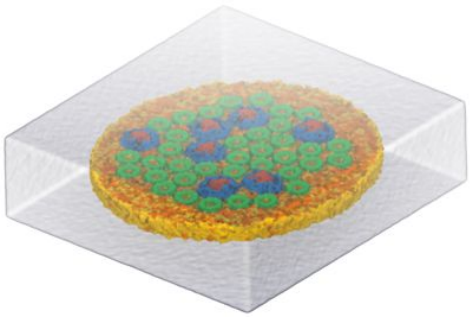


Quantifying the Impact of GPUs on Performance and Energy Efficiency in HPC Clusters. J. Enos, C. Steffen, J. Fullop, M. Showerman, G. Shi, K. Esler, V. Kindratenko, J. Stone, J. Phillips. *The Work in Progress in Green Computing,* pp. 317-324, 2010.

VMD Out-of-Core Trajectory I/O Performance: SSD-Optimized Trajectory Format, 8-SSD RAID



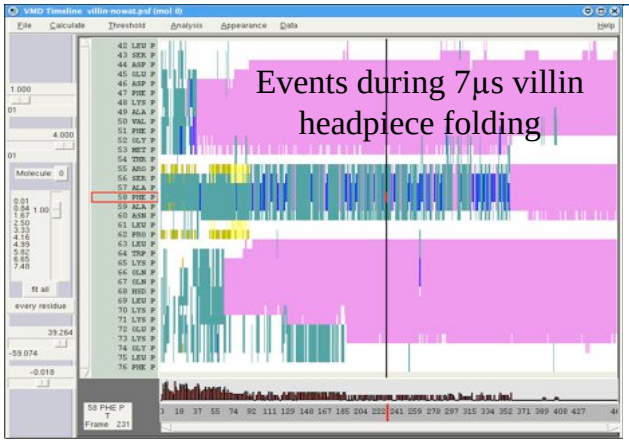
Ribosome w/ solvent
3M atoms
3 frames/sec w/ HD
60 frames/sec w/ SSDs

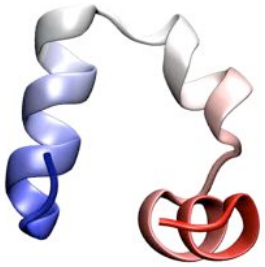


Membrane patch w/ solvent
20M atoms
0.4 frames/sec w/ HD
8 frames/sec w/ SSDs

New SSD Trajectory File Format 2x Faster vs. Existing Formats
VMD I/O rate ~2.1 GB/sec w/ 8 SSDs

VMD New Timeline plug-in





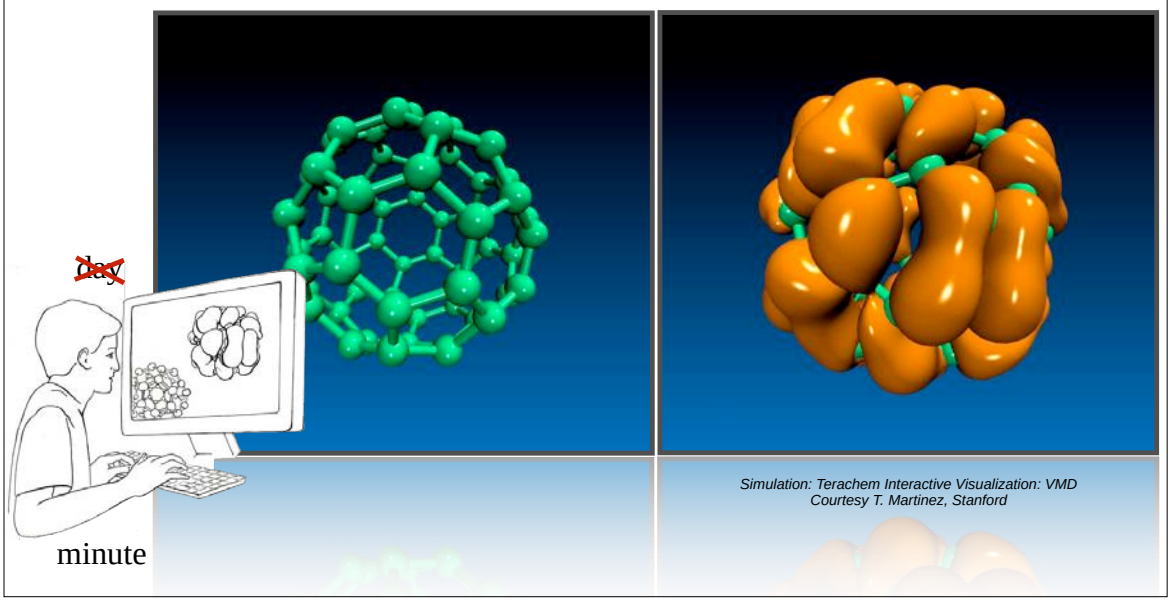
Alpha helix Extended beta Isolated bridge 3-10 helix Beta turn None (coil)

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

Quantum Chemistry Visualization

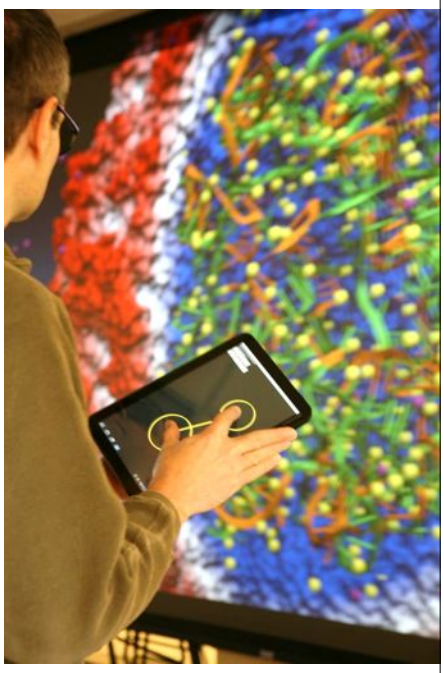
Rendering of electron “clouds” achieved on GPUs as quickly as you see this movie! CPUs: One working day!



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

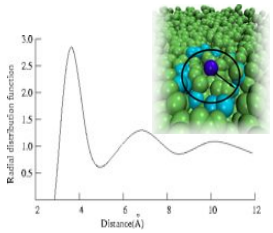
VMD 1.9.1: New Tablet/Phone Interface

- Developed first multi-touch, multi-user, wireless user interface for VMD
  - Early technology development in advance of devices
- New wireless control using VMD remote control app:
  - Multi-touch input and control of VMD session, scripts, plugins
  - Collaborative multi-user interaction
- Recent: tablet display of trajectory timelines, sequence data, plots, and tabular information
- Goal: tablet-native VMD by end of funding period, w/ simplified graphical user interface



GPU Accelerated Trajectory Analysis and Visualization in VMD

GPU-Accelerated Feature	GPU Speedup
Molecular orbital display	120x
Radial distribution function	92x
Electrostatic field calculation	44x
Molecular surface display	40x
Ion placement	26x
MDFF density map synthesis	26x
Implicit ligand sampling	25x
Root mean squared fluctuation	25x
Radius of gyration	21x
Close contact determination	20x
Dipole moment calculation	15x



Selected VMD Plugins: Center Developed, and User Developed

Analysis
- APBSRun
- CatDCD
- Contact Map
- GofRGUI
- HeatMapper
- ILSTools
- IRSpecGUI
- MultiSeq
- NAMD Energy
- NAMD Plot
- NetworkView
- NMWiz
- ParseFEP
- PBCTools
- PMEpot
- PropKa GUI
- RamaPlot
- RMSD Tool
- RMSD Trajectory Tool
- RMSD Visualizer Tool
- Salt Bridges
- Sequence Viewer
- Symmetry Tool
- Timeline
- VolMap

Modeling
- AutoIonize
- AutoPSF
- Chirality
- Cionize
- Cispeptide
- CGTools
- Dowser
- ffTK
- Inorganic Builder
- MDFF
- Membrane
- Merge Structs
- Molefacture
- Mutator
- Nanotube
- Paratool
- Psfgen
- RESPTool
- RNAView
- Solvate
- SSRestraints
- Topotools

Visualization
- Clipping Plane Tool
- Clone Rep
- DemoMaster
- Dipole Watcher
- Intersurf
- Navigate
- NavFly
- MultiMolAnim
- Color Scale Bar
- Remote
- Palette Tool
- ViewChangeRender
- ViewMaster
- Virtual DNA Viewer
- VMD Movie Maker

Simulation
- AutoIMD
- IMDMenu
- NAMD GUI
- NAMD Server
- QMTool

68 MolFile I/O Plugins:
structure, trajectory, sequence, and density map

Collaboration
- BioCoRE Chat
- BioCoRE Login
- BioCoRE VMD Shared Views
- Remote Control

Data Import and Plotting
- Data Import
- Multiplot
- PDBTool
- MultiText

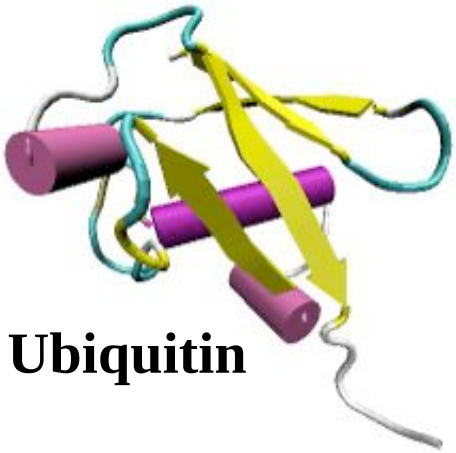
Externally Hosted Plugins and Extensions
- Check sidechains
- MultiMSMS
- Interactive Essential Dynamics
- Mead Ionize
- Clustering Tool
- iTrajComp
- Swap RMSD
- Intervor
- SurfVol
- vmdICE

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

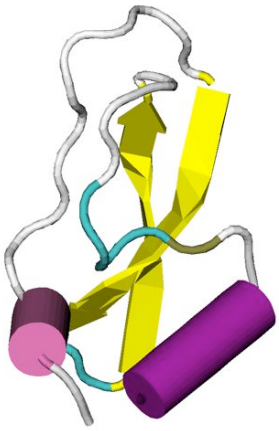
Focus on two proteins

Ubiquitin (used in VMD Tutorial)

Bovine Pancreatic Trypsin Inhibitor (BPTI, available as a case study, www.ks.uiuc.edu)



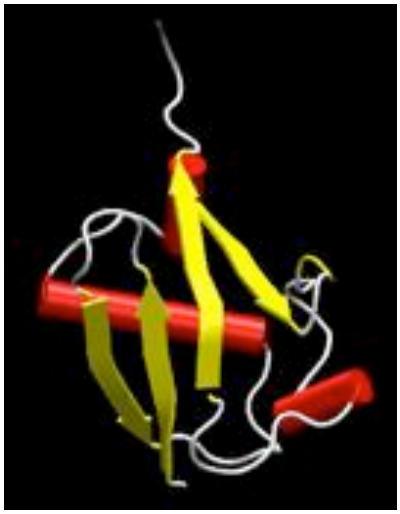
Ubiquitin



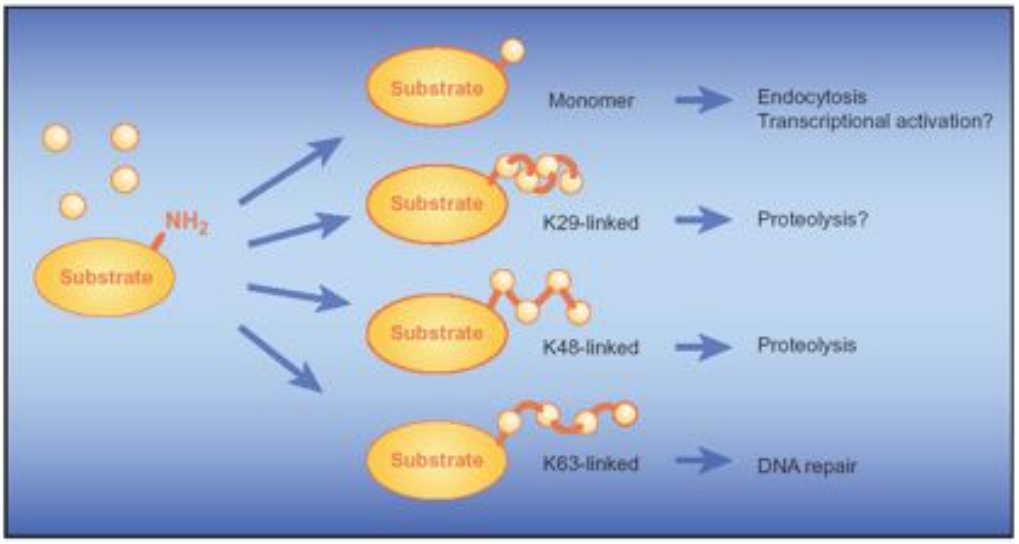
BPTI

Ubiquitin

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



Mono-ubiquitylation versus multi-ubiquitylation



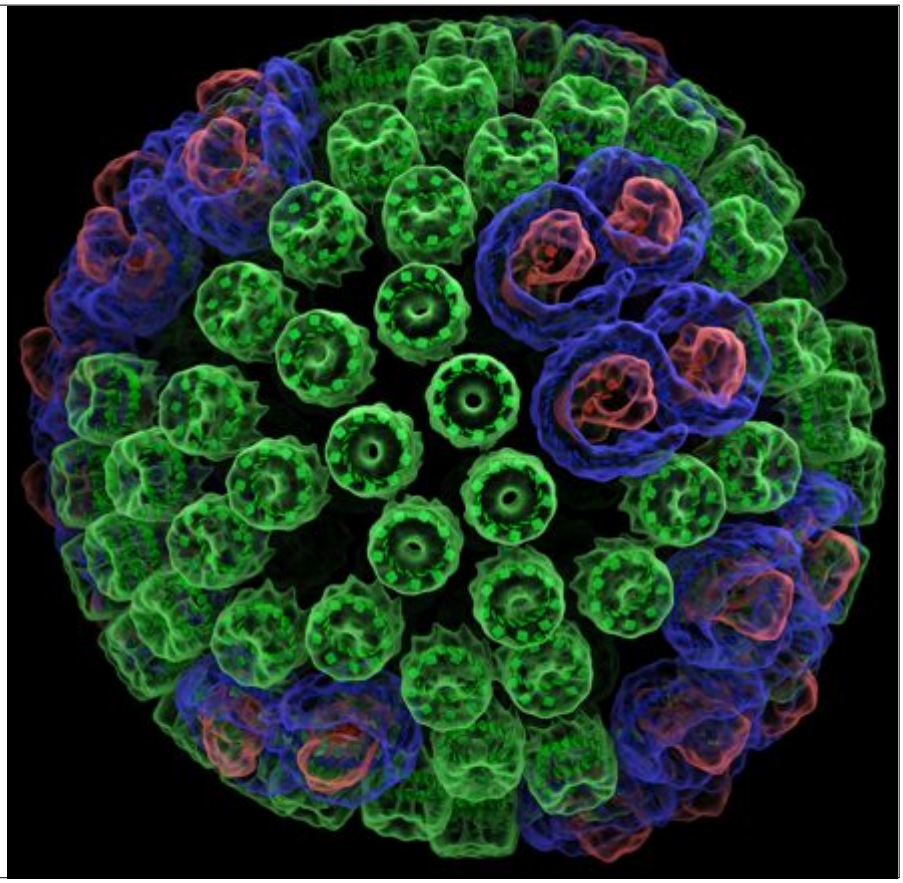
Multifaceted. Ubiquitin can attach to its various substrate proteins, either singly or in chains, and that in turn might determine what effect the ubiquitination has. (K29, K48, and K63 refer to the particular lysine amino acid used to link the ubiquitins to each other.)

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

VMD Demo

QuickSurf Representation w/ Angle-Modulated Transparency

Chromatophore 10M atoms



Summary of VMD Features

- Supports a wide range of scales needed in molecular and cellular biology, and beyond
- Integrates multiple experimental data modalities: sequence, structure, electron microscopy
- Unique support for very large molecular systems, long-timescale trajectories
- Leverages advanced computing technologies to solve challenging computation and analysis problems:
  - GPU computing
  - Parallel visualization and analysis
  - High-throughput data access using SSDs, new file formats

Achievements Built on People

5 faculty members (2 physics, 1 chemistry, 1 biochemistry, 1 computer science);
8 developers; 1 system admin.; 16 post docs; 24 graduate students; 3 administrative staff

33 workshops since 2003; 1044 researchers trained; 347 lectures given (2007–2012).

4.1 million website visits (2007–2011); 15 TB data transferred from website (2007–2011); 184 research highlights since 2001.

212,000 VMD users and 51,000 NAMD users; VMD-L, NAMD-L mailing lists received 20,000 and 16,000 emails, respectively.

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VMD team

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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
- Supports all major molecular data file formats
- No limits on the number of molecules or trajectory frames, except available memory
- Molecular analysis commands
- Rendering high-resolution, publication-quality molecule images
- Movie making capability
- Building and preparing systems for molecular dynamics simulations
- Interactive molecular dynamics simulations
- Extensions to the Tcl/Python scripting languages
- Extensible source code written in C and C++