

VMD: Visual Molecular Dynamics

Computational Microscope / Tool to Think

whole cells

1000 nm

cellular subsystems

100 nm

large molecules

10 nm

electrons + small molecules

1 nm

amino acid tyrosine

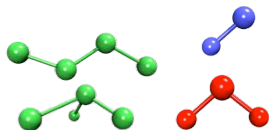
enzymatic control
BPTI
VMD tutorial

trafficking
Ubiquitin
case study

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

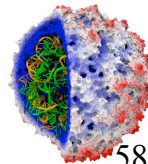
Our Microscope is Made of...

Chemistry



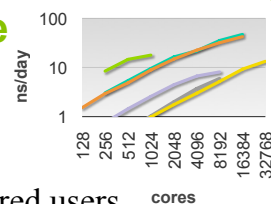
$$U(\vec{R}) = \underbrace{\sum_{bonds} k_i^{bond} (r_i - r_0)^2}_{U_{bond}} + \underbrace{\sum_{angles} k_i^{angle} (\theta_i - \theta_0)^2}_{U_{angle}} + \underbrace{\sum_{dihedrals} k_i^{dih} [1 + \cos(n_i \phi_i + \delta_i)]}_{U_{dihedral}} + \underbrace{\sum_i \sum_{j \neq i} 4 \epsilon_{ij} \left[\left(\frac{\sigma_{ij}}{r_{ij}}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

NAMD Software



Virus

58,000 registered users



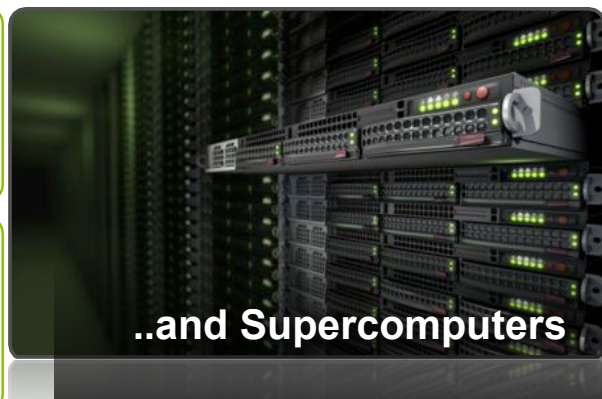
Physics

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

Math

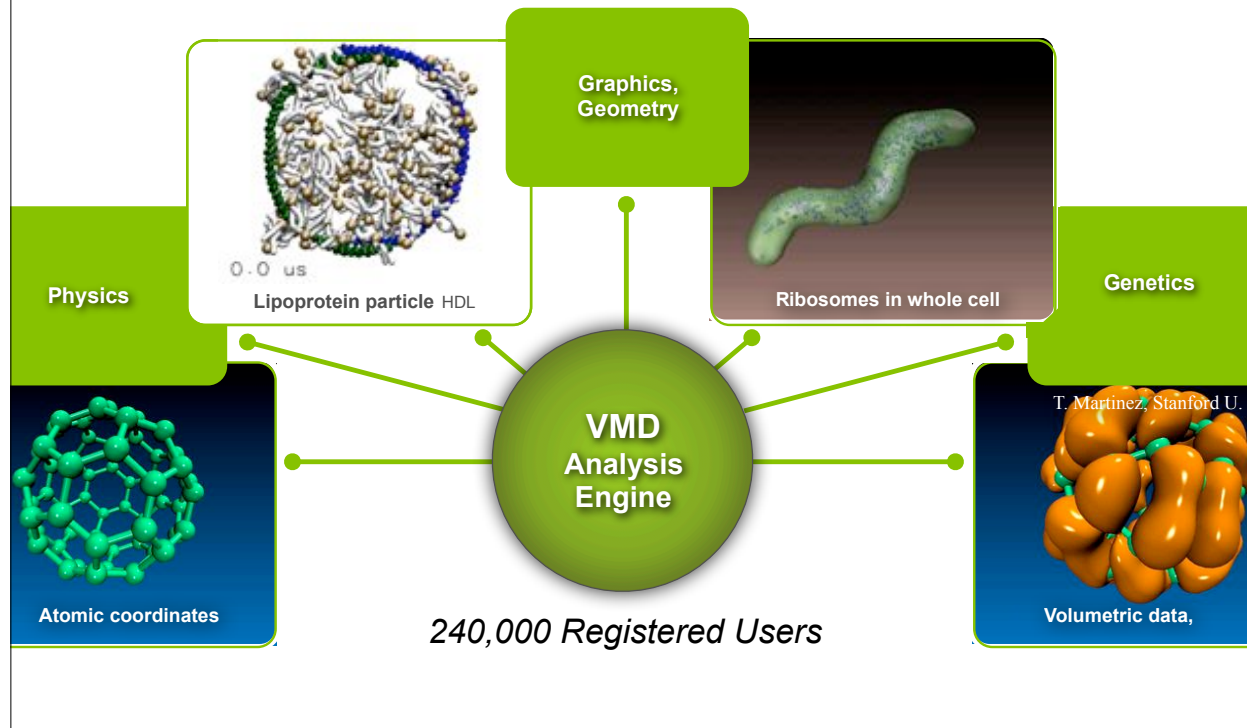
$$\vec{r}_i(t + \Delta t) = 2\vec{r}_i(t) - \vec{r}_i(t - \Delta t) + \frac{\Delta t^2}{m_i} \vec{F}_i(t)$$

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

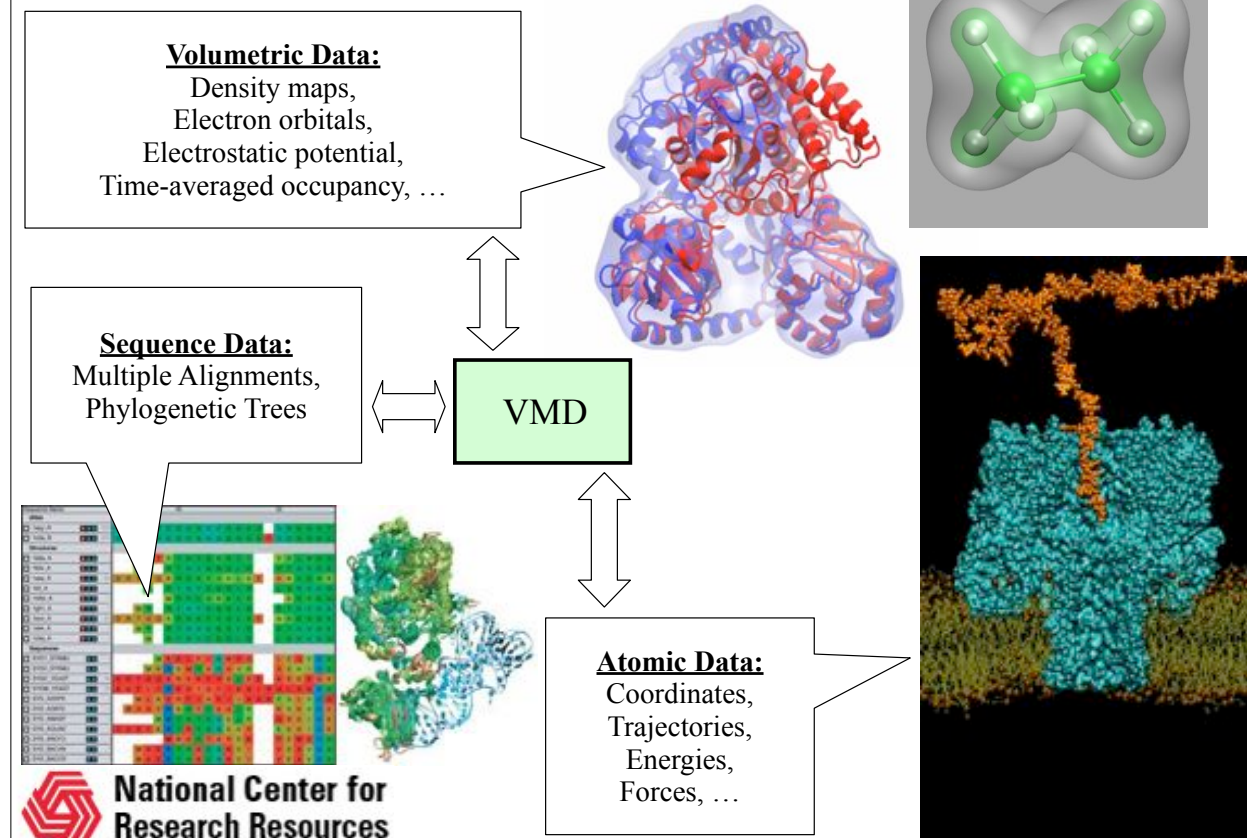


..and Supercomputers

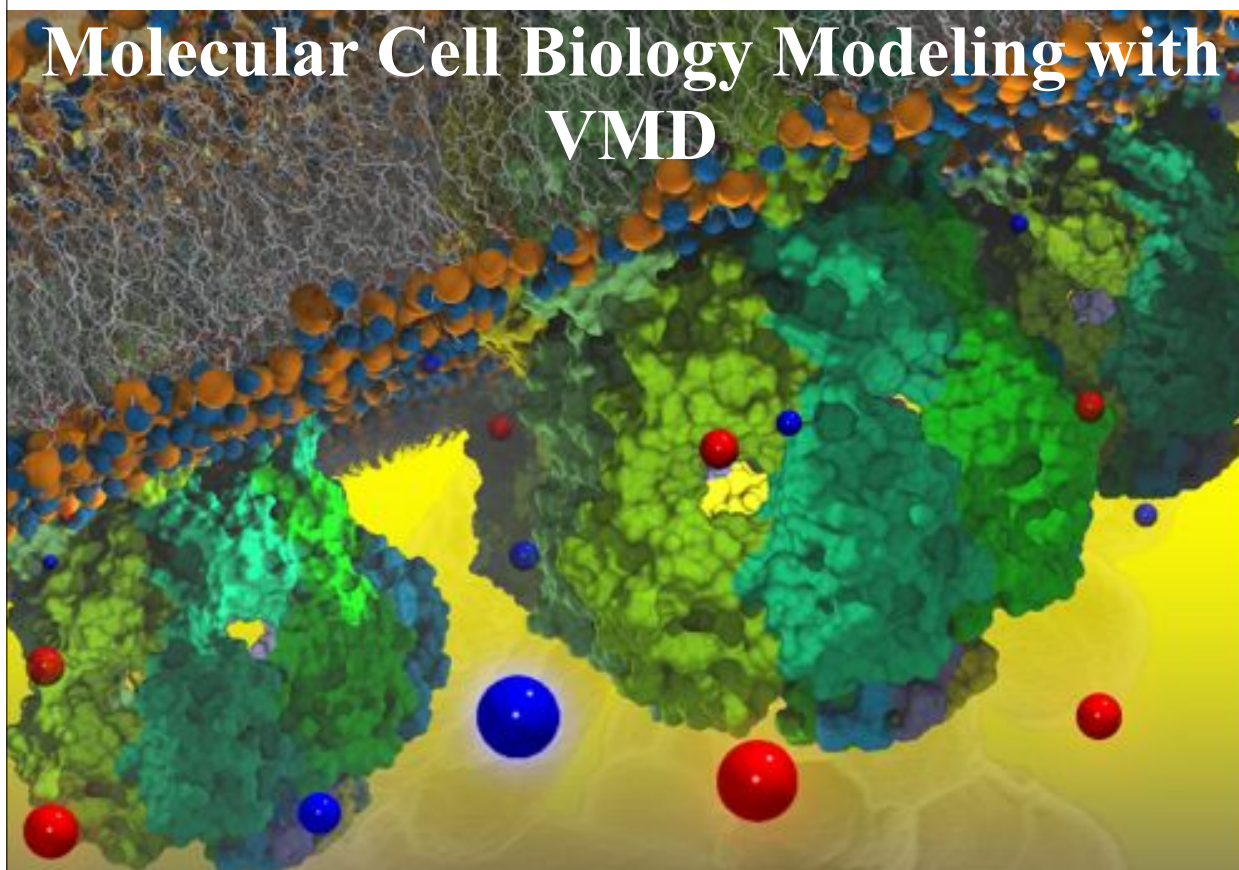
Our Microscope Shows All, from Electrons to Cells



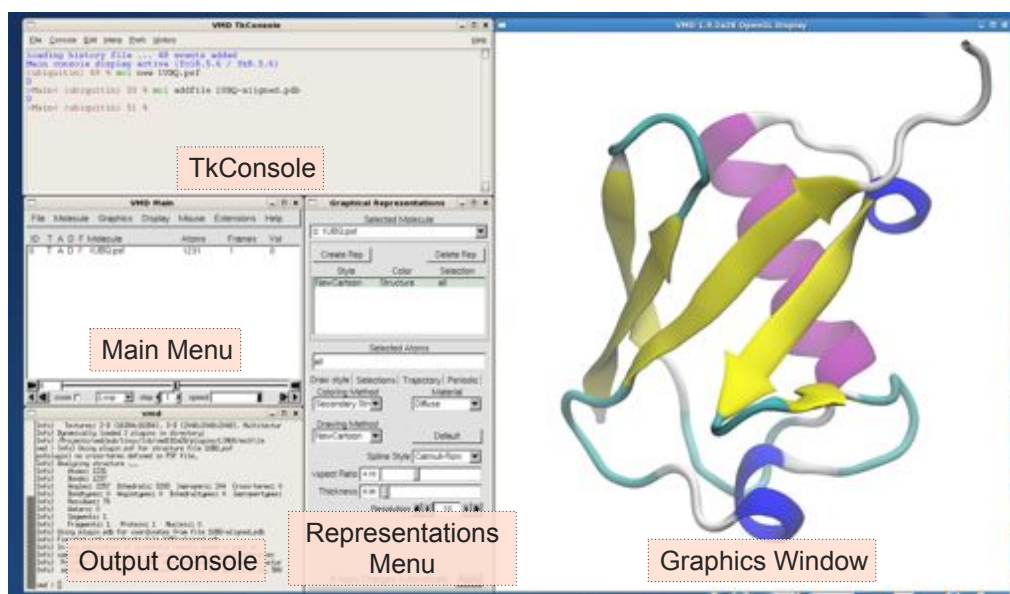
VMD – A Tool to Think Wide



Molecular Cell Biology Modeling with VMD



Molecular Graphics with VMD



typical VMD session

An Example: Ubiquitin and the Proteasome

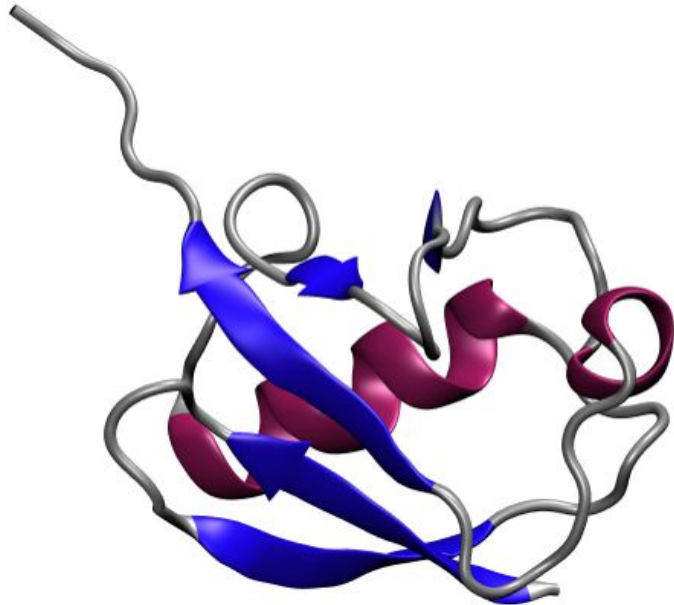
Ubiquitin: a small protein of 76 amino acids

Present in all eukaryotes, and highly conserved

Regulates key cellular processes such as cell division, gene expression, cell trafficking, and protein degradation

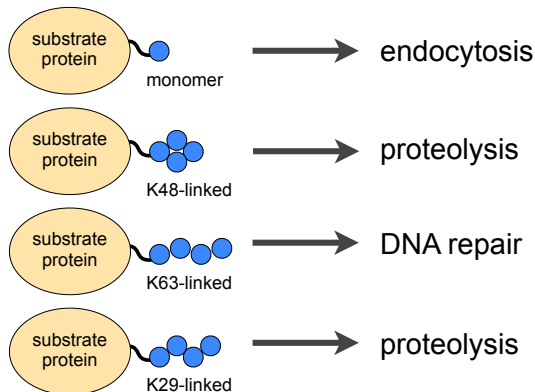
Deficiency in ubiquitin expression can lead to neurodegenerative disorders

Tags misfolded proteins to be degraded in the proteasome (“kiss of death” protein)



Ubiquitin Chains

Ubiquitins monomers attach to others to make a poly-ubiquitin chain



7 conserved lysine residues can form differently shaped chains depending on which lysine is used to connect the monomers

A Glycine at C-terminal attaches to a lysine on the protein by an isopeptide bond

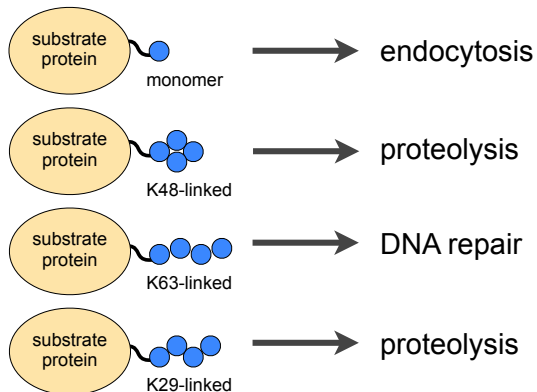
A chain of at least four ubiquitins is needed to be recognized by the proteasome for protein degradation

VMD Session 1:

single ubiquitin

Ubiquitin Chains

Ubiquitins monomers attach to others to make a poly-ubiquitin chain

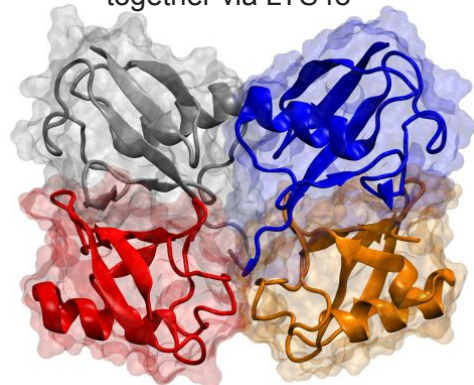


7 conserved lysine residues can form differently shaped chains depending on which lysine is used to connect the monomers

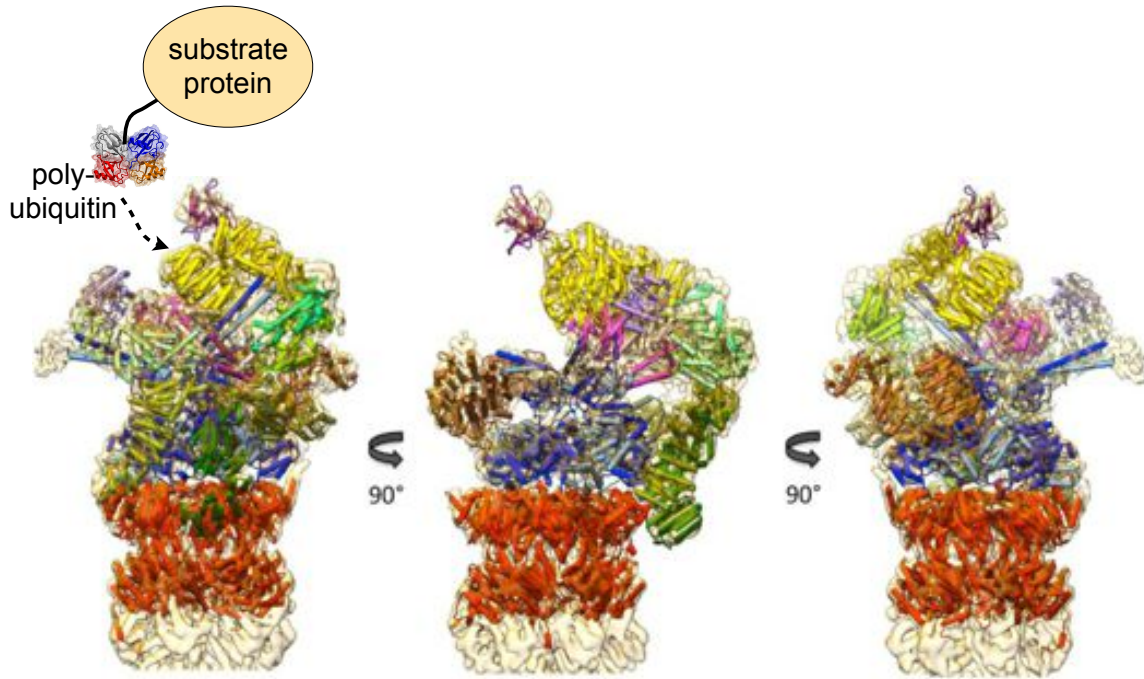
A Glycine at C-terminal attaches to a lysine on the protein by an isopeptide bond

A chain of at least four ubiquitins is needed to be recognized by the proteasome for protein degradation

Four ubiquitins tethered together via LYS48



Structure of the Proteasome



Atomic model of the 26S holocomplex fitted into the cryo-EM map.
Beck F et al. PNAS 2012;109:14870-14875

VMD Session 2: *K48-linked tetra-ubiquitin*

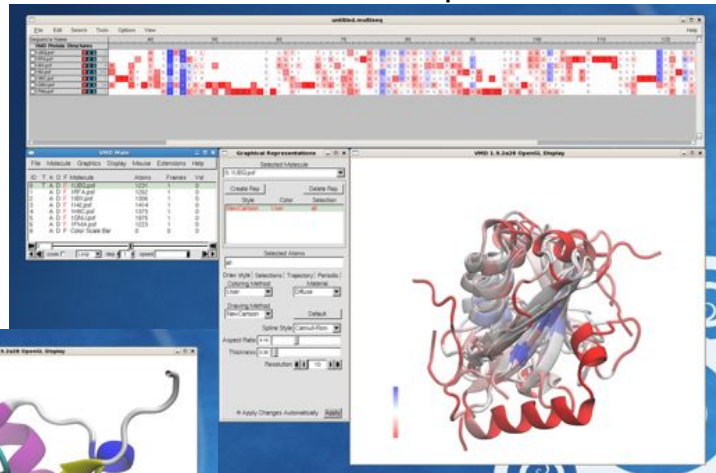
Bioinformatics

MultiSeq

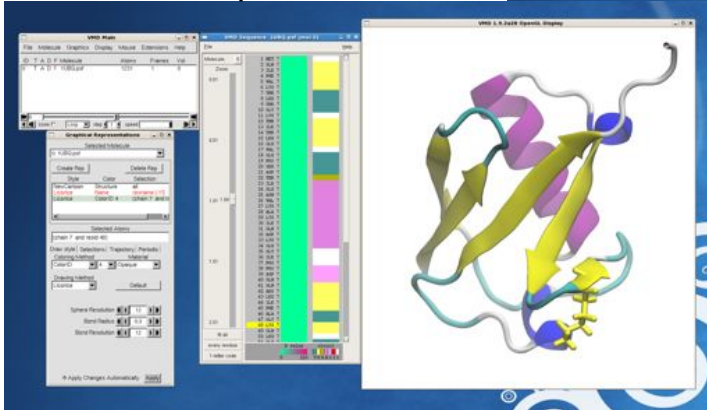
Link sequence to structure

Multiple sequence/
structure alignments

Phylogenetic trees

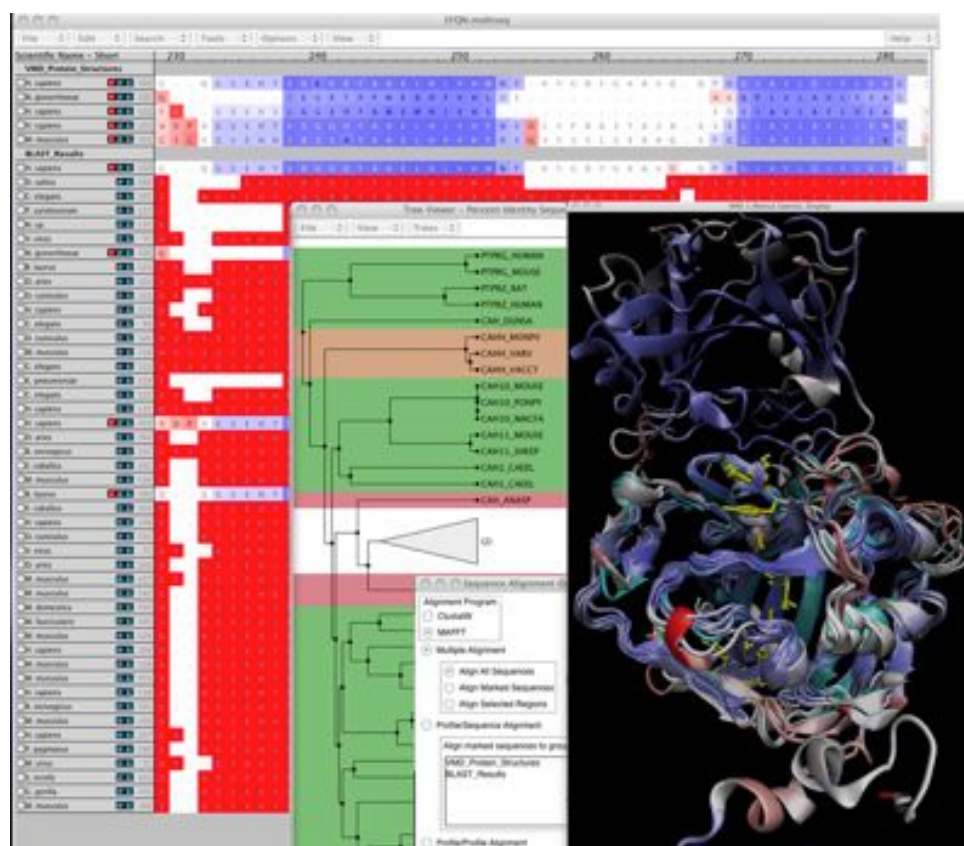


Sequence Viewer



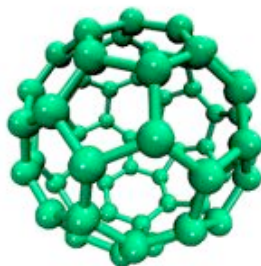
VMD Session 3: *sequences of ubiquitin*

Structure, Sequence and Phylogenetic Analysis with VMD



VMD Handles Volumetric Data

Cryo-EM map of the *E. coli* ribosome at 6.7-Å resolution

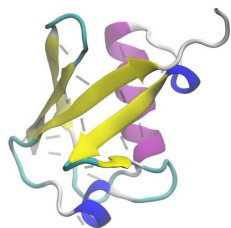


electron density
from QM/MM
calculation
Martinez, Stanford

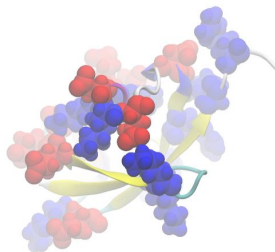


cryo-EM density

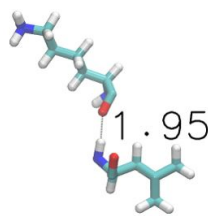
VMD Determines Physical Properties



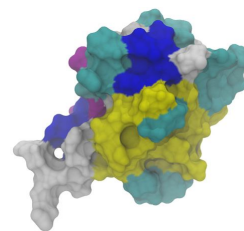
hydrogen bonds



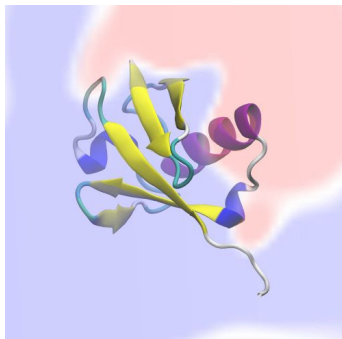
salt bridges



distances



SASA

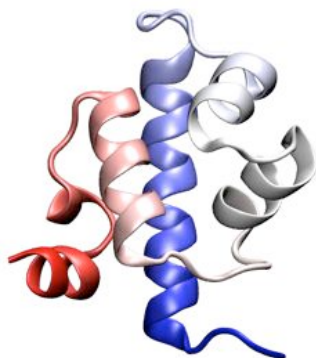


electrostatics

- SASA
- secondary structure
- interaction surfaces
- hydrogen bonds
- salt bridges
- electrostatics
- distances
- angles
- dihedrals
- RMSD
- RMSF
- interaction energies
- forces
- free energy profiles
- normal modes

Trajectory Graphics/Analysis with VMD

Example: protein folding



lambda repressor (2012)
80 amino acids, 100 μ s

Journal of Physical Chemistry Letters, 3:1117-1123, 2012.
Proceedings of the National Academy of Sciences, USA, In press, 2013.

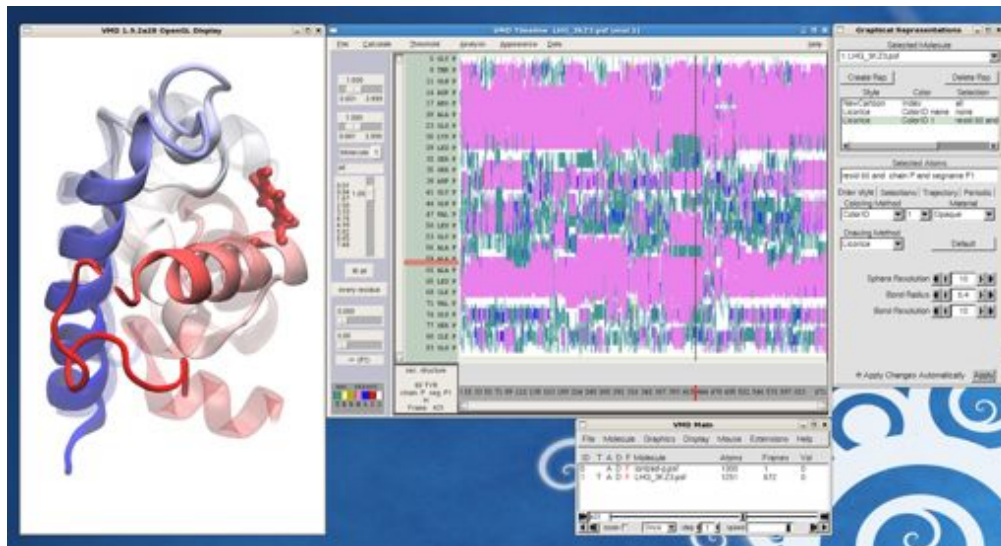
VMD Session 4: *trajectory of villin head piece*

VMD Plugins

Featured example: Timeline

plugin to analyze MD trajectories for events

plot properties, e.g. RMSD, secondary structure, hydrogen bonds, for each residue across a trajectory



VMD Plugins: extensible analysis

Modeling Plugins

- Autonize
- AutoPSF
- Chirality
- Cispeptide
- CGTools
- Dowser
- FFTK
- Inorganic Builder
- MDFF
- Membrane Builder
- MergeStructs
- Molefacture
- Mutator
- Nanotube
- Paratool
- Psfgen
- Solvate
- SSRestrains
- Topotools

Analysis Plugins

- APBSRun
- CatDCD
- Contact Map
- GofRGUI
- HBonds
- ILSTools
- IRSpecGUI
- MultiSeq
- NAMDEnergy
- NAMDPLOT
- NetworkView
- NMWiz
- ParseFEP
- PropKaGUI
- RamaPlot
- RMSD Tool
- RMSD Trajectory Tool
- RMSD Visualizer Tool
- Salt Bridges
- Sequence Viewer
- Symmetry Tool
- Timeline
- VolMap

Visualization Plugins

- Clipping Plane Tool
- Clone Rep
- Dipole Watcher
- Intersurf
- Navigate
- NavFly
- MultiMolAnim
- Color Scale Bar
- Remote
- Palette Tool
- ViewChangeRender
- Viewmaster
- Virtual DNA Viewer
- VMDMovie

Simulation Plugins

- AutoIMD
- IMDMenu
- NAMD GUI
- NAMD Server
- QMTTool

Data Plugins

- Data Import
- Multiplot
- PDBtool
- MultiText

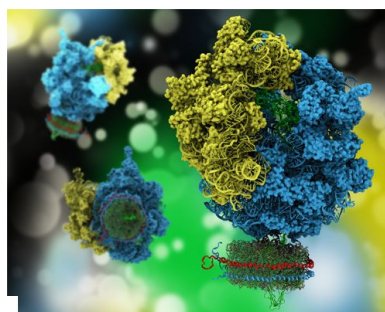
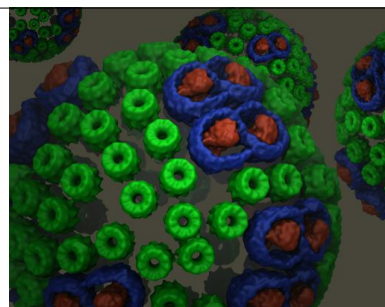
Other Plugins

- AtomEdit
- DemoMaster
- ExecTool
- Hesstrans
- Optimization
- PBCTools
- RESPTool
- RNAview
- SignalProc
- TkCon

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

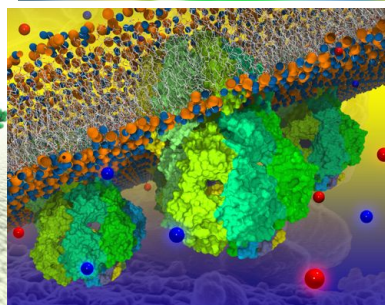
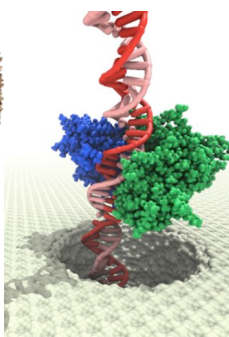
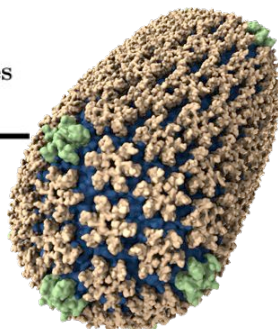
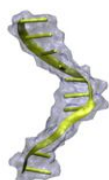
VMD the Artist

Publication-quality images and movies

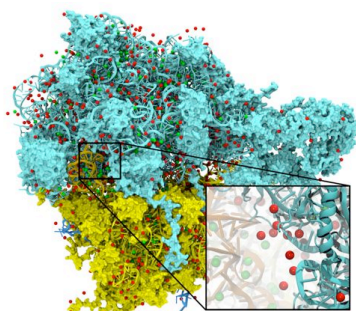


University of Illinois at Urbana-Champaign
Beckmann Institute for Advanced Science and Technology
Theoretical and Computational Biophysics Group
Computational Biophysics Workshop

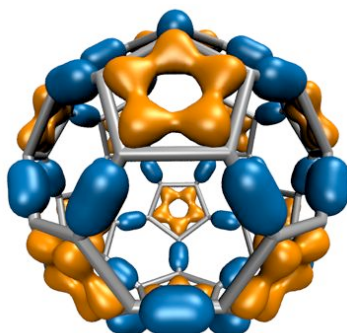
VMD Images and Movies Tutorial



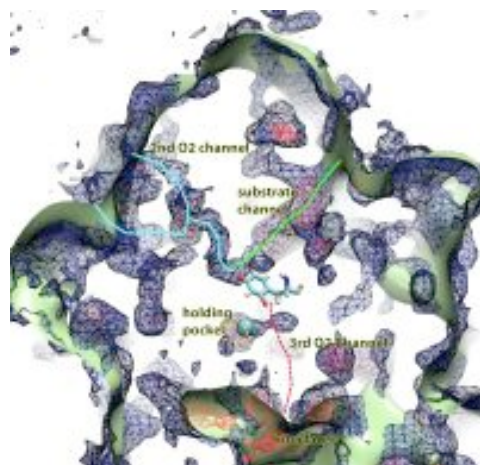
VMD the Compute Engine



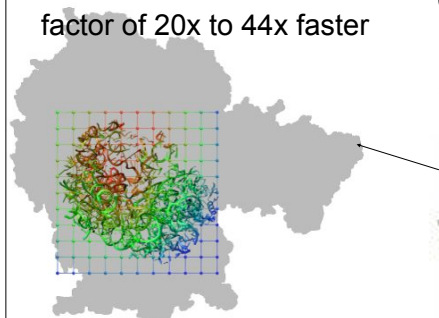
Electrostatic field
calculation, ion placement:
factor of 20x to 44x faster



Molecular orbital
calculation and display:
factor of 120x faster



Imaging of gas migration
pathways in proteins with
implicit ligand sampling:
factor of 20x to 30x faster



Parallel analysis on GPUs

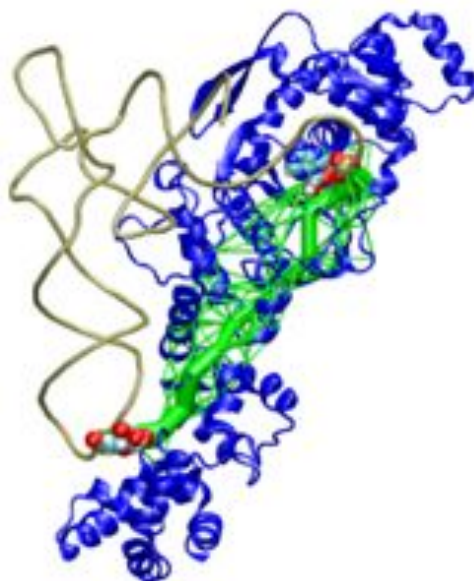
VMD is first bio-software that is optimized for power consumption!

VMD 1.9.1 Released Feb. 4, 2012

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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...

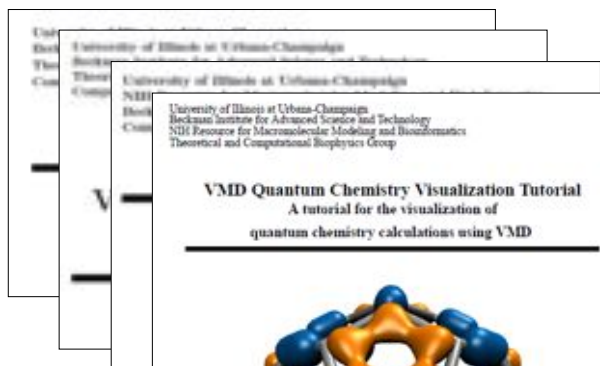


NetworkView: tRNA anti-codon w/
ligand in GluRS active site

VMD and NAMD Work Together



- Over 212,000 registered VMD 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



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.

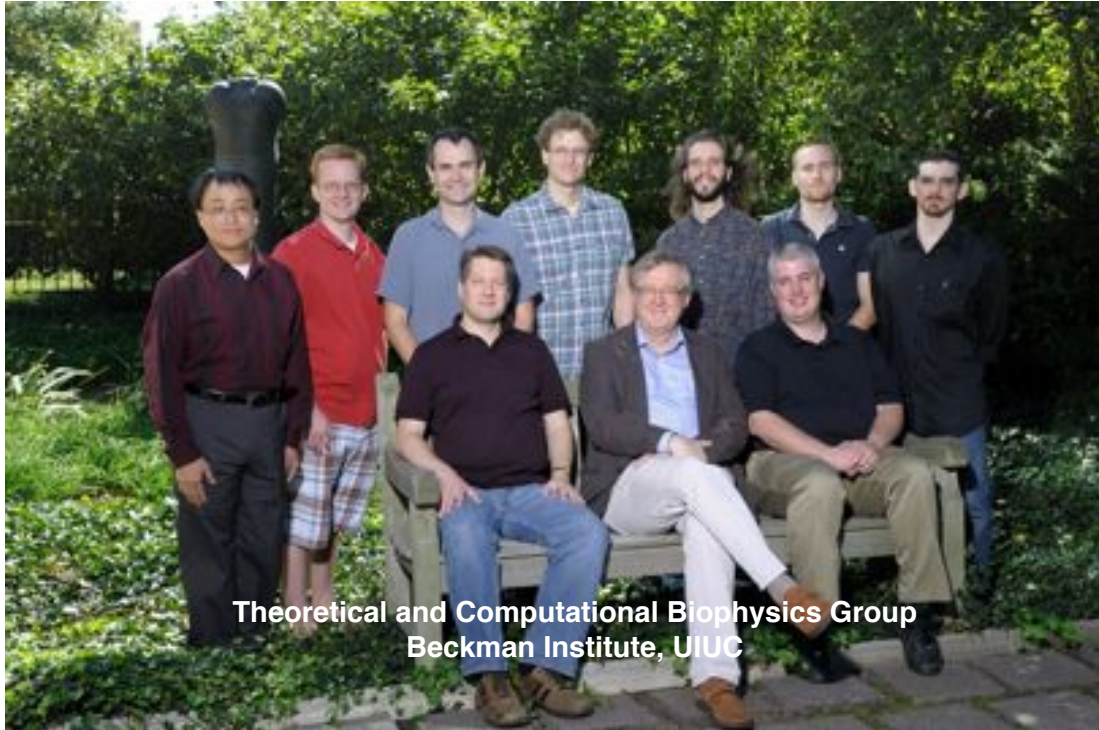


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VMD team
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K. Vandivoort



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