Computational Structural Biology and Molecular Simulation

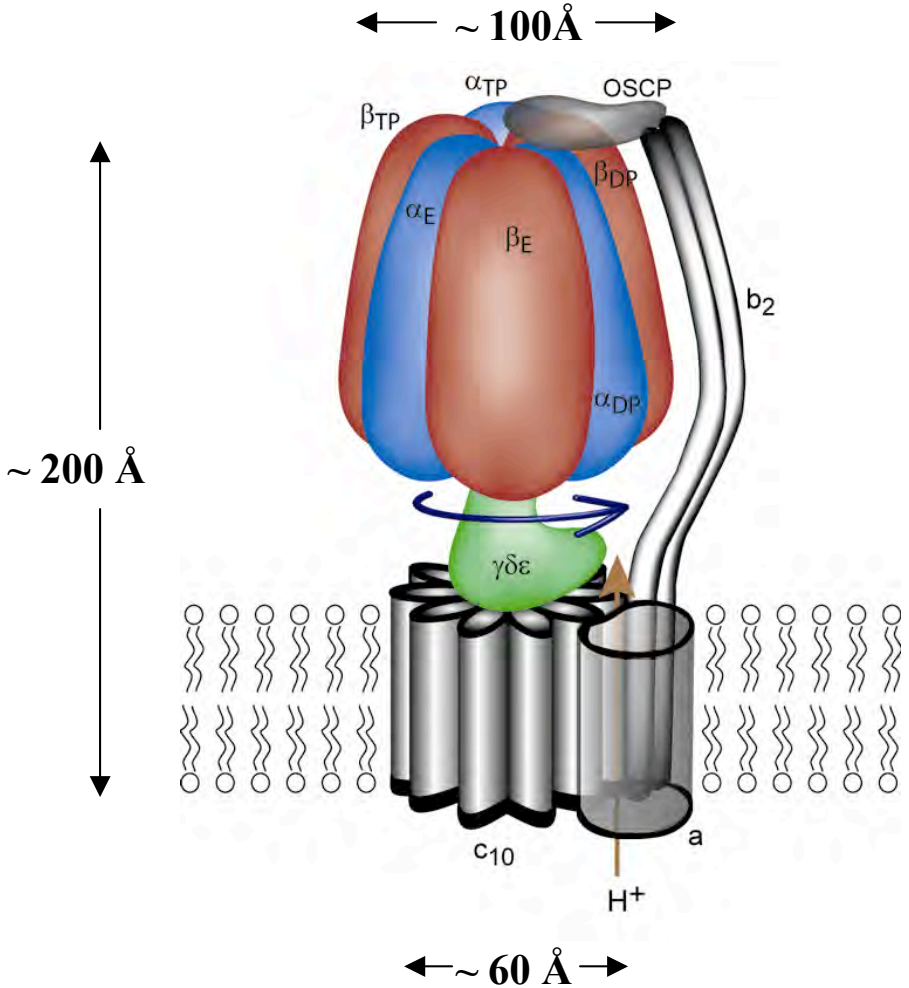
Introduction to VMD Molecular Visualization and Analysis

Emad Tajkhorshid
Department of Biochemistry, Beckman Institute,
Center for Computational Biology and Biophysics
University of Illinois at Urbana-Champaign
Email: emad@life.uiuc.edu

Why do we need to look at proteins in atomic detail?

How can we look at them best and use the information?

ATP-Synthase
One shaft, two motors



~ 80 Å

Soluble part, F_1-ATPase

-Synthesizes ATP when torque is applied to it *(main function of this unit)*

-Produces torque when it hydrolyzes ATP *(not main function)*

~ 60 Å

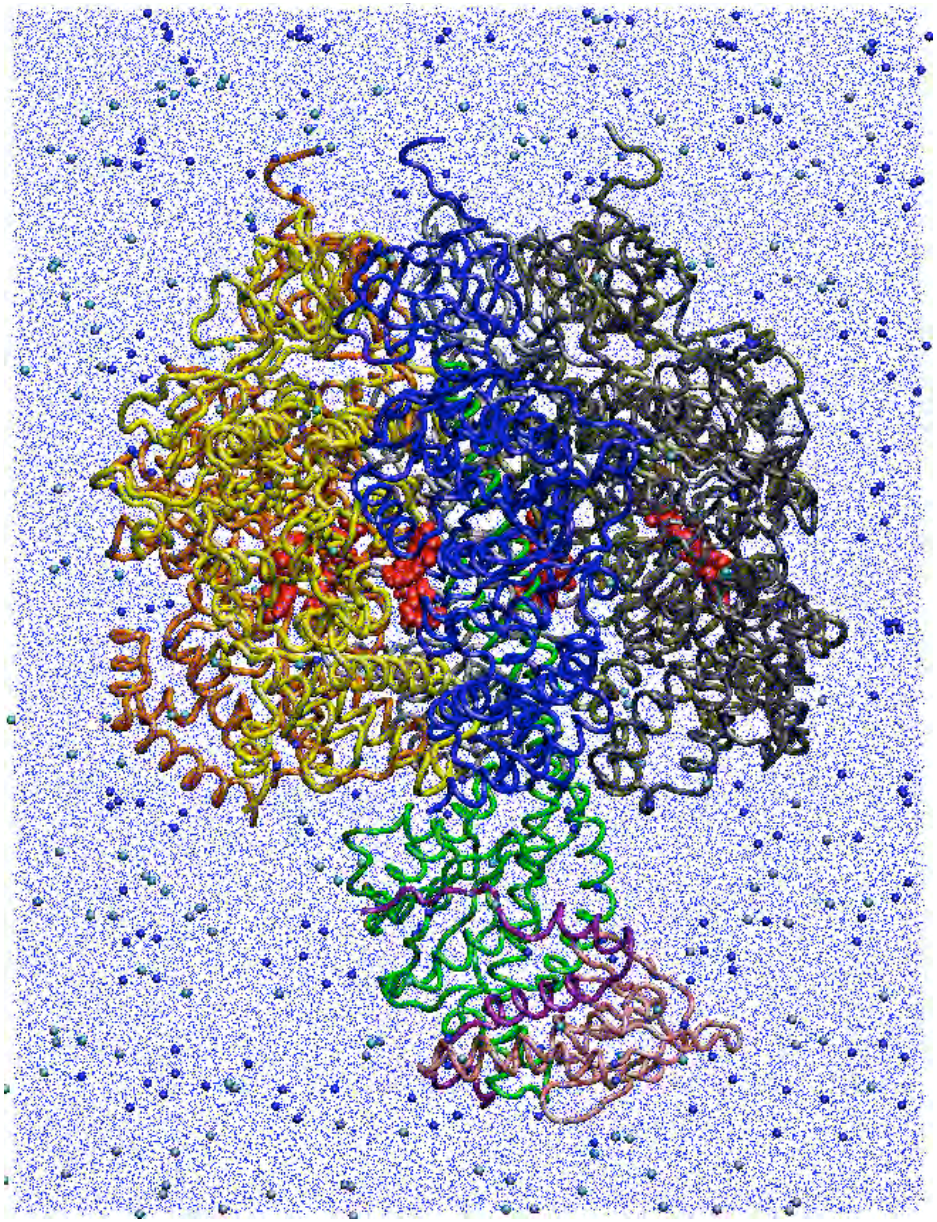
Membrane-bound part, F_0 Complex

- Produces torque when positive proton gradient across membrane*(main function of this unit)*

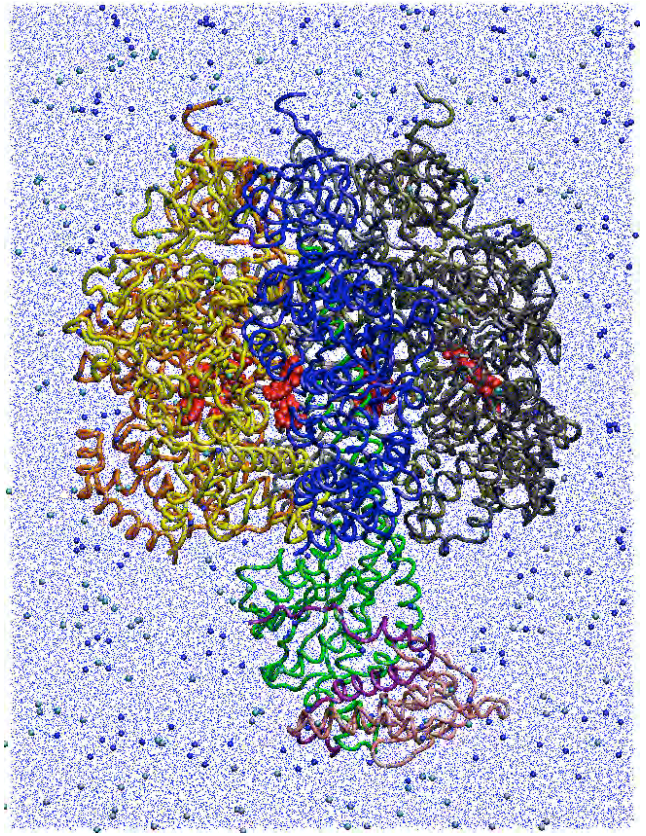
- Pumps protons when torque is applied *(not main function)*

Torque is transmitted between the motors via the central stalk.

Assembling ATP Synthase F_1

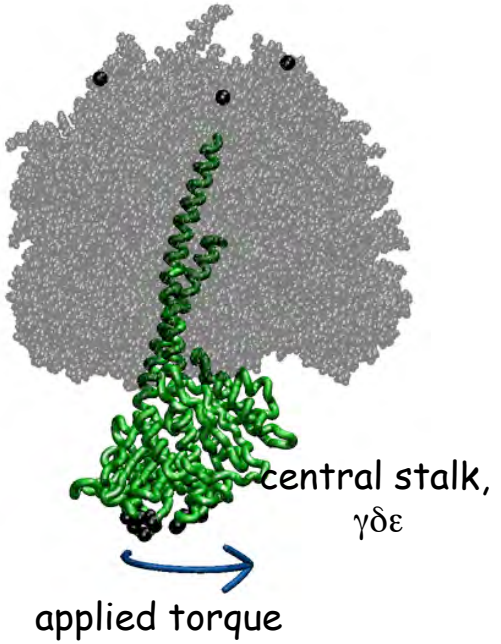


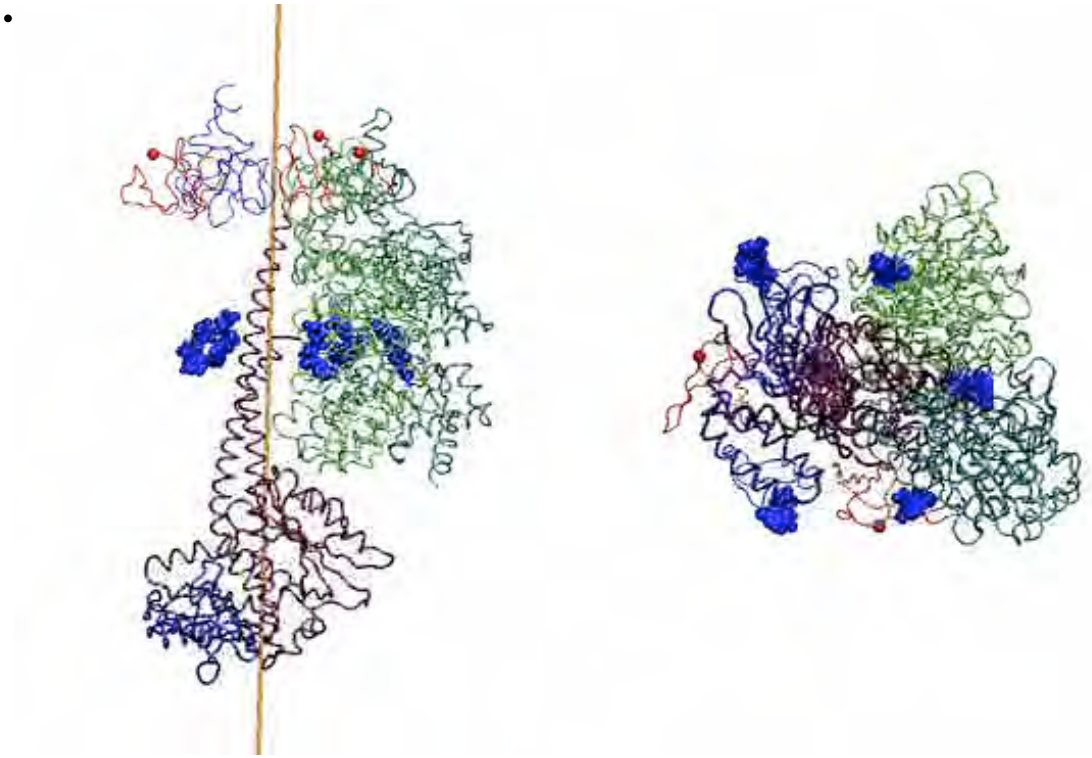
- Start with PDB code 1E79, water, ions, and nucleotides were added (327,000 atoms)
- 1.2 ns equilibration + 10.5 ns torque application



Torque application to F_1

Torque is applied to the central stalk atoms at the F_1-F_o interface to constrain their rotation to constant angular velocity ω = 24 deg/ns.



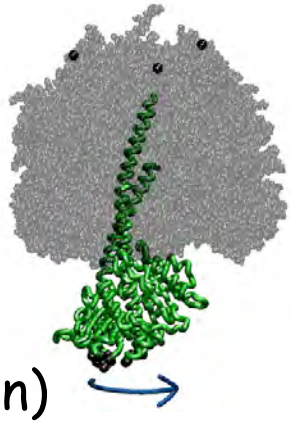


0.0 to 5.0 ns (0 to 120 deg) of torqued F_1 rotation, ω = 24 deg/ns.

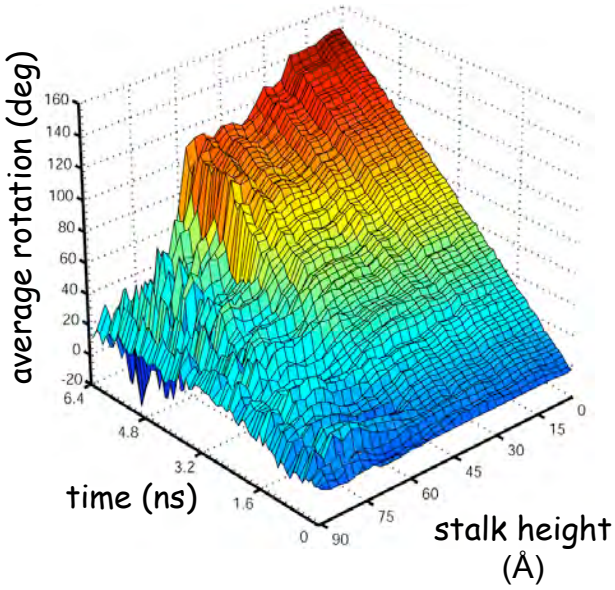
Rotation Produces Synthesis-like events

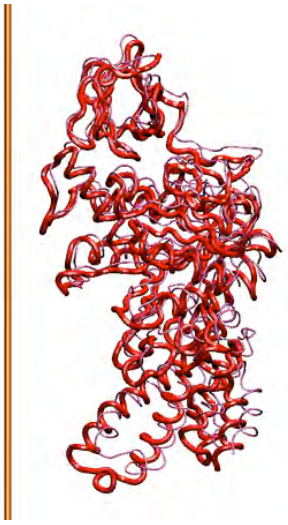
Around 3.0 – 3.5 ns (72 – 84 deg) of rotation, we observe:

- slowed torque transmission along central stalk
- opening and closing motions as expected

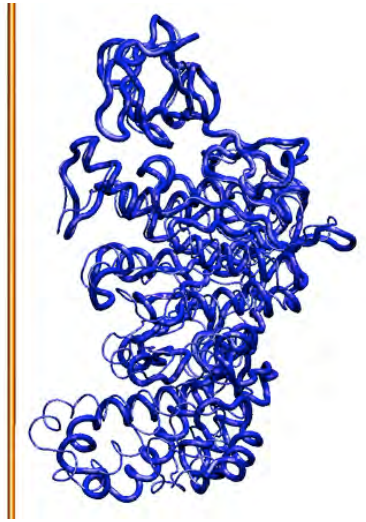


At 3.5 ns (84° rotation)





β_E closes

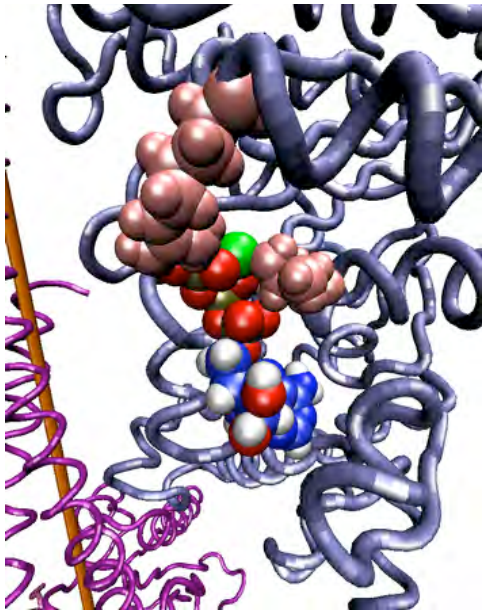


β_{TP} opens

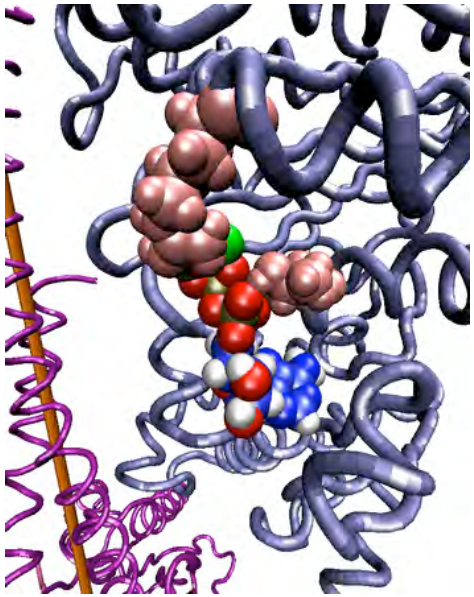
β_{DP} does neither

Rotation Produces Synthesis-like Events

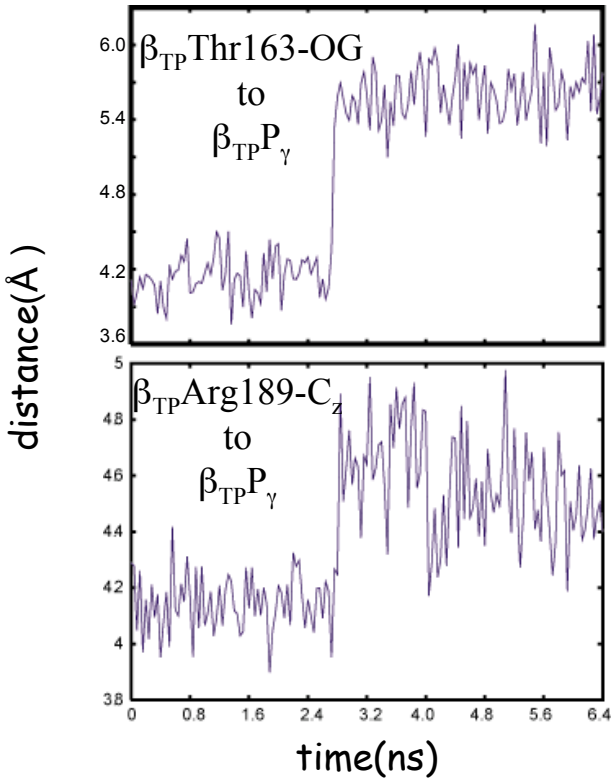
Consistent with unbinding of ATP from the β_{TP} catalytic site



0 ns:
active site closed

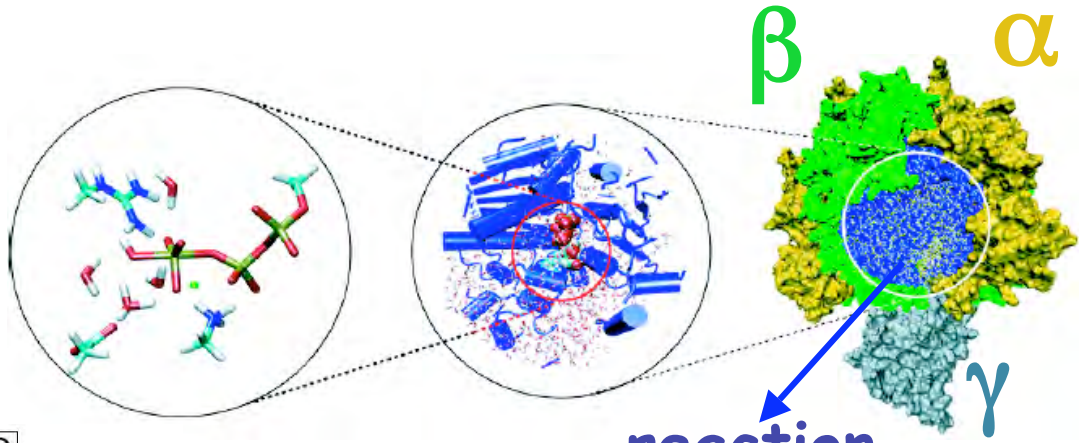


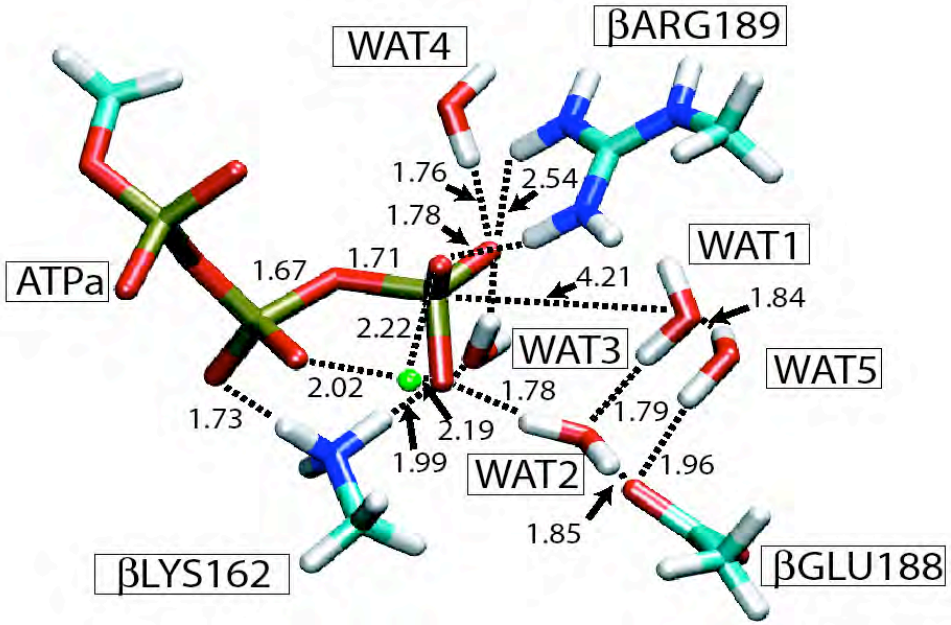
3 ns:
active site open

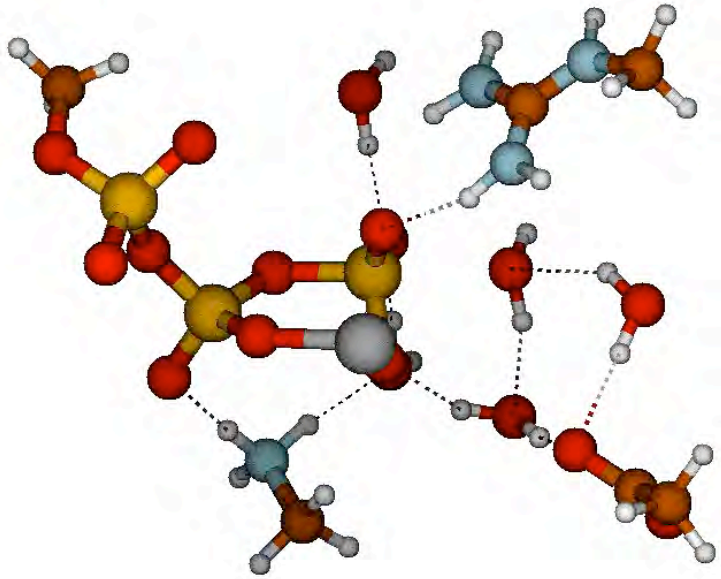


Reaction Mechanism of ATP Hydrolysis

***in situ* quantum (QM/MM) chemistry calculation**

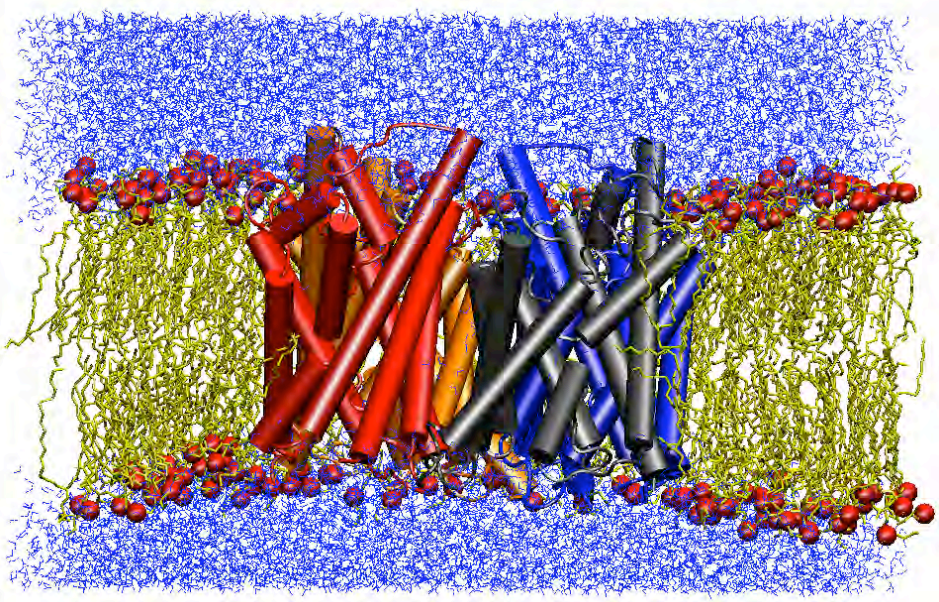


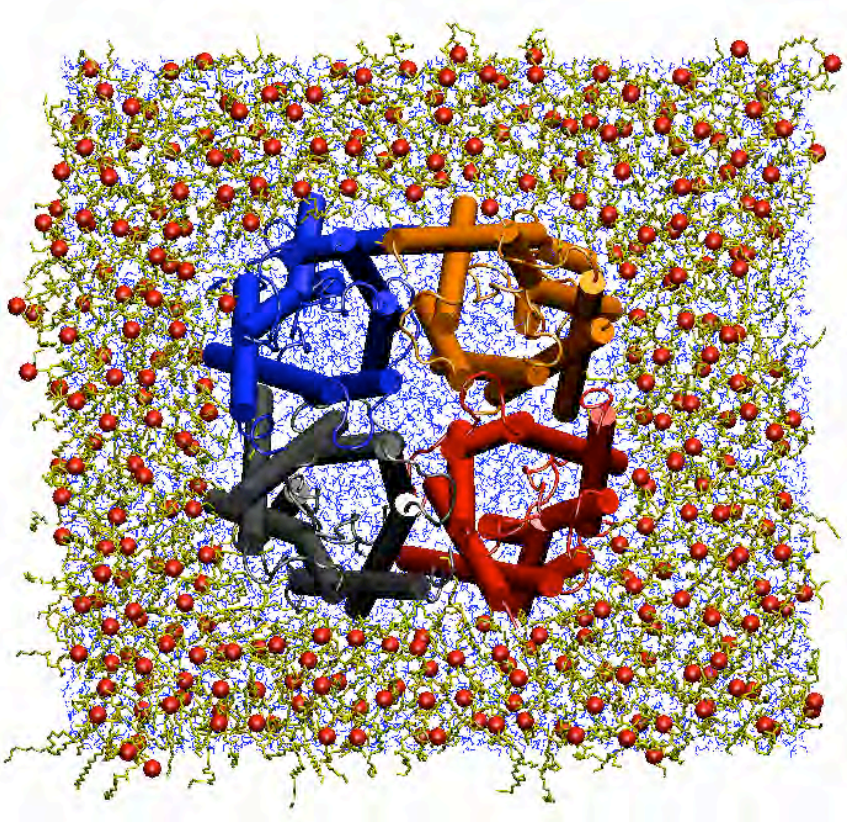




Molecular Dynamics Simulations

Protein:	~	15,000 atoms
Lipids (POPE):	~	40,000 atoms
Water:	~	51,000 atoms
Total:	~	106,000 atoms





NAMD, CHARMM27, PME

NpT ensemble at 310 K

5 ns run of wild-type protein

2 days /ns – 48-proc Linux cluster

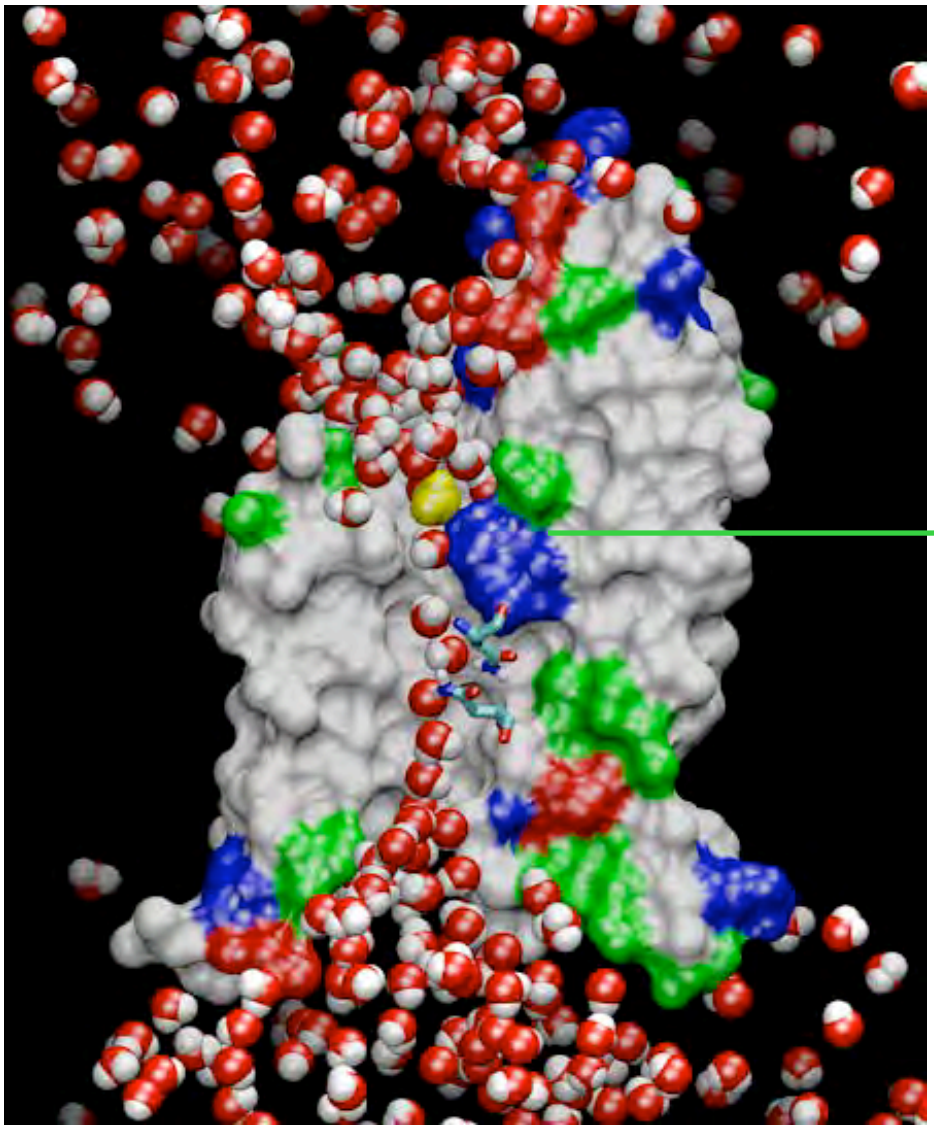
0.35 days /ns – 64 CPUs @ NCSA

Complete description of the conduction pathway

Constriction region

Selectivity filter

Water Permeation in Aquaporins



Hydrophobic channel

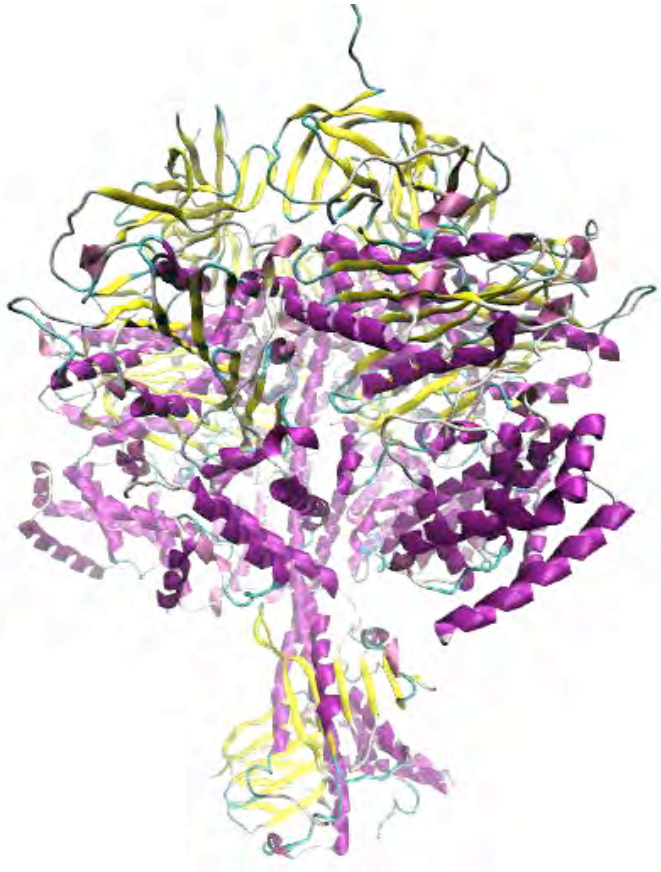
Selectivity filter

106,000 atoms
5 ns simulation

Download the movie from the Nobel Prize web site or from www.ks.uiuc.edu/Research/aquaporins

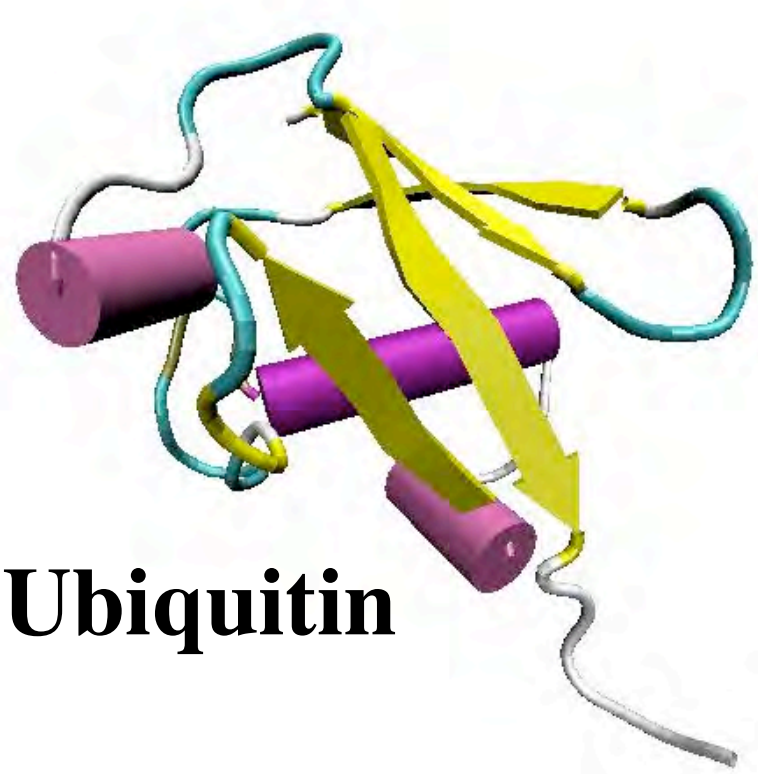
VMD - www.ks.uiuc.edu/Research/vmd

- Platforms:
  - Unix (16 builds)
  - 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

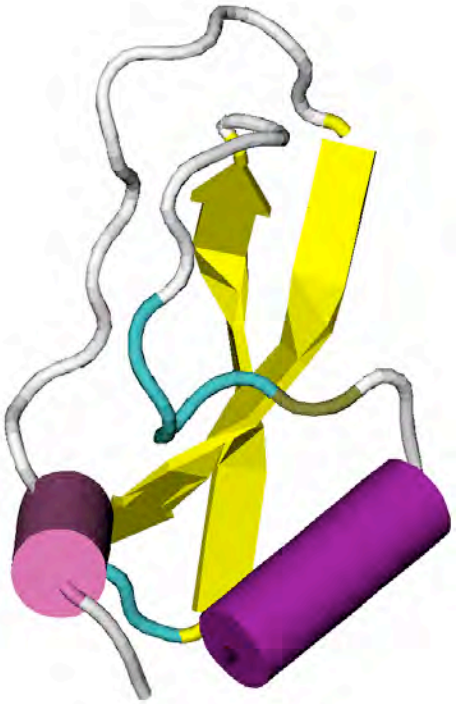


The program is used very frequently for preparation and analysis of simulations

Examples to use with VMD:
Ubiquitin
Bovine Pancreatic Trypsin Inhibitor (BPTI)

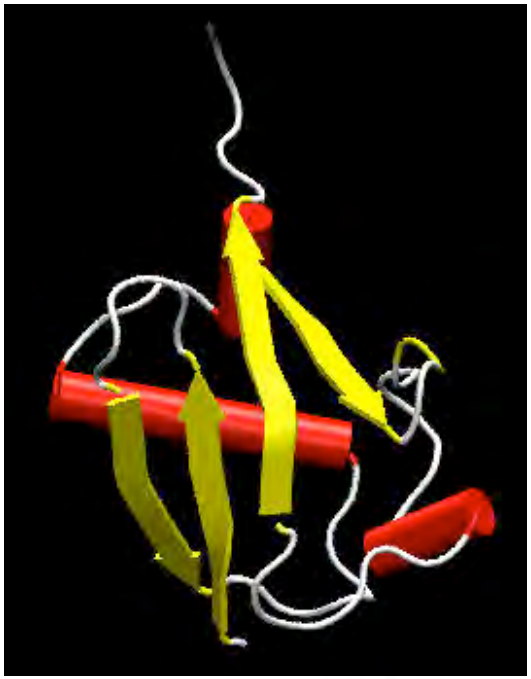


Ubiquitin



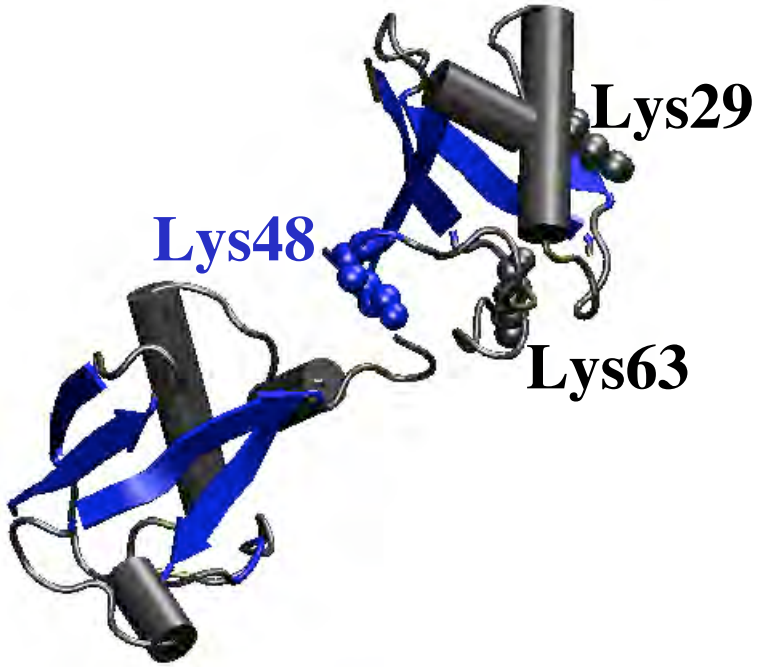
BPTI

Ubiquitin



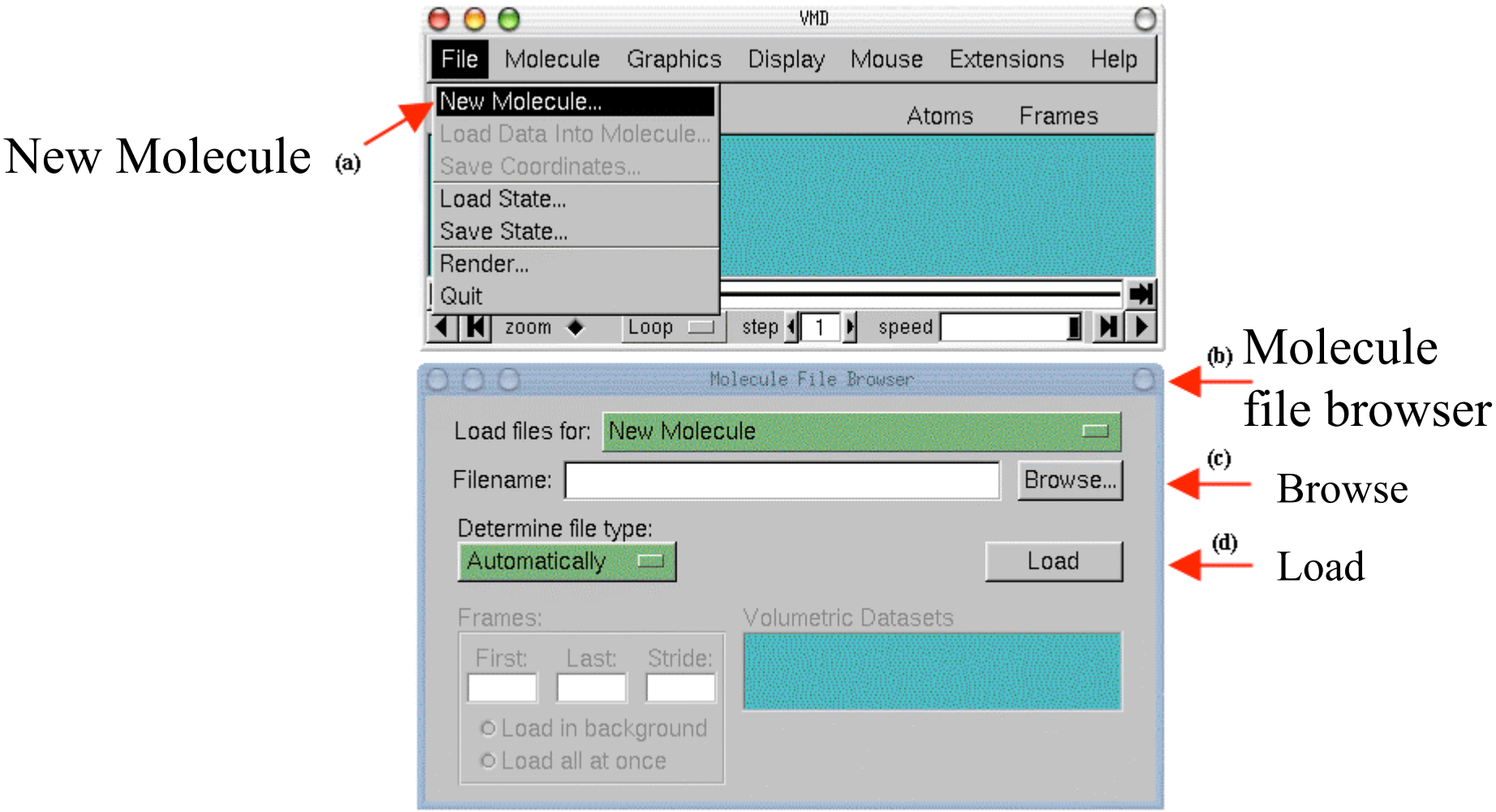
- 76 amino acids
- Highly conserved
- Covalently attaches to proteins and tags them for degradation

- Polymerization at different Lysines results in different signals (7 conserved Lys residues)



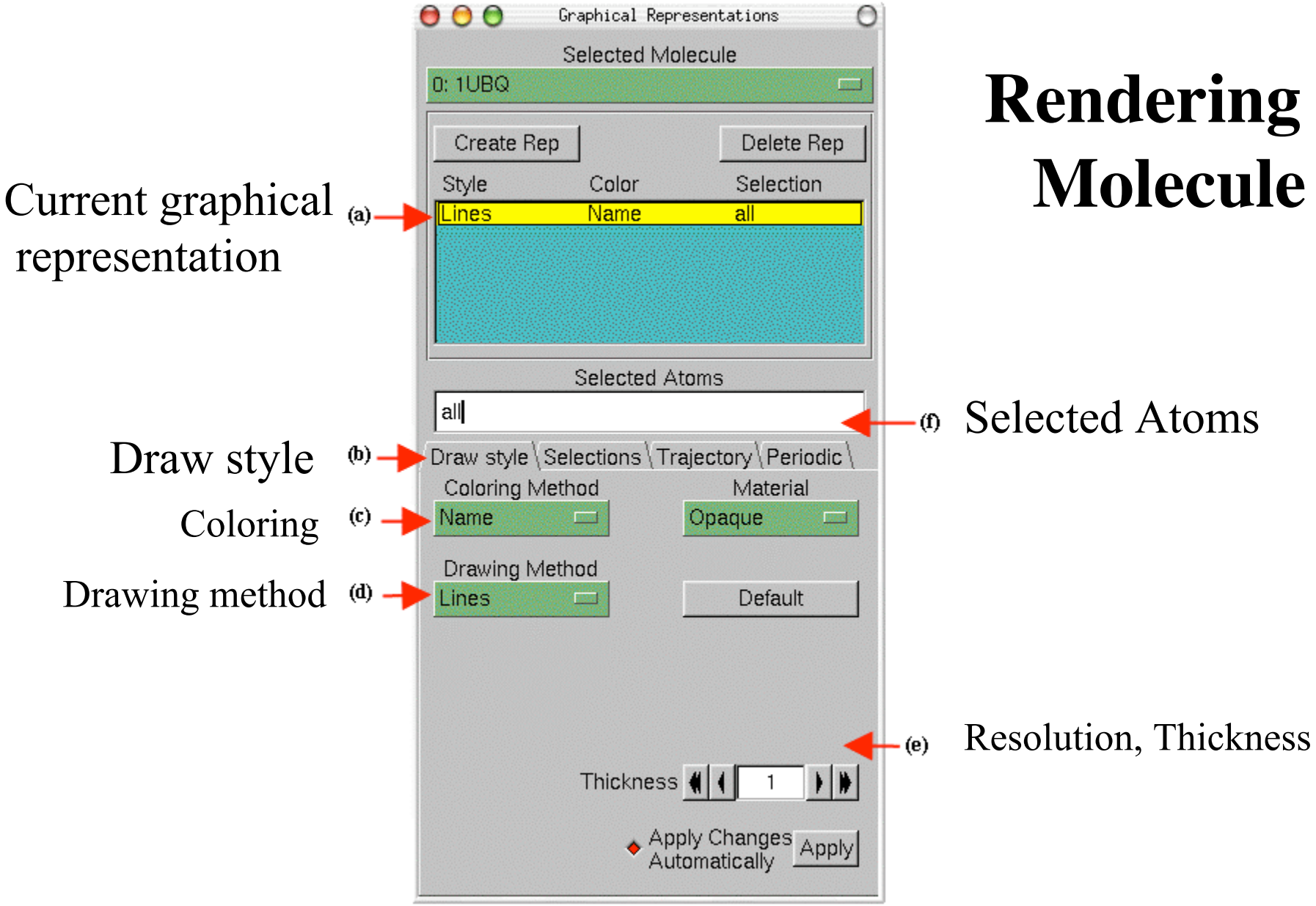
Basics of VMD

Loading a Molecule



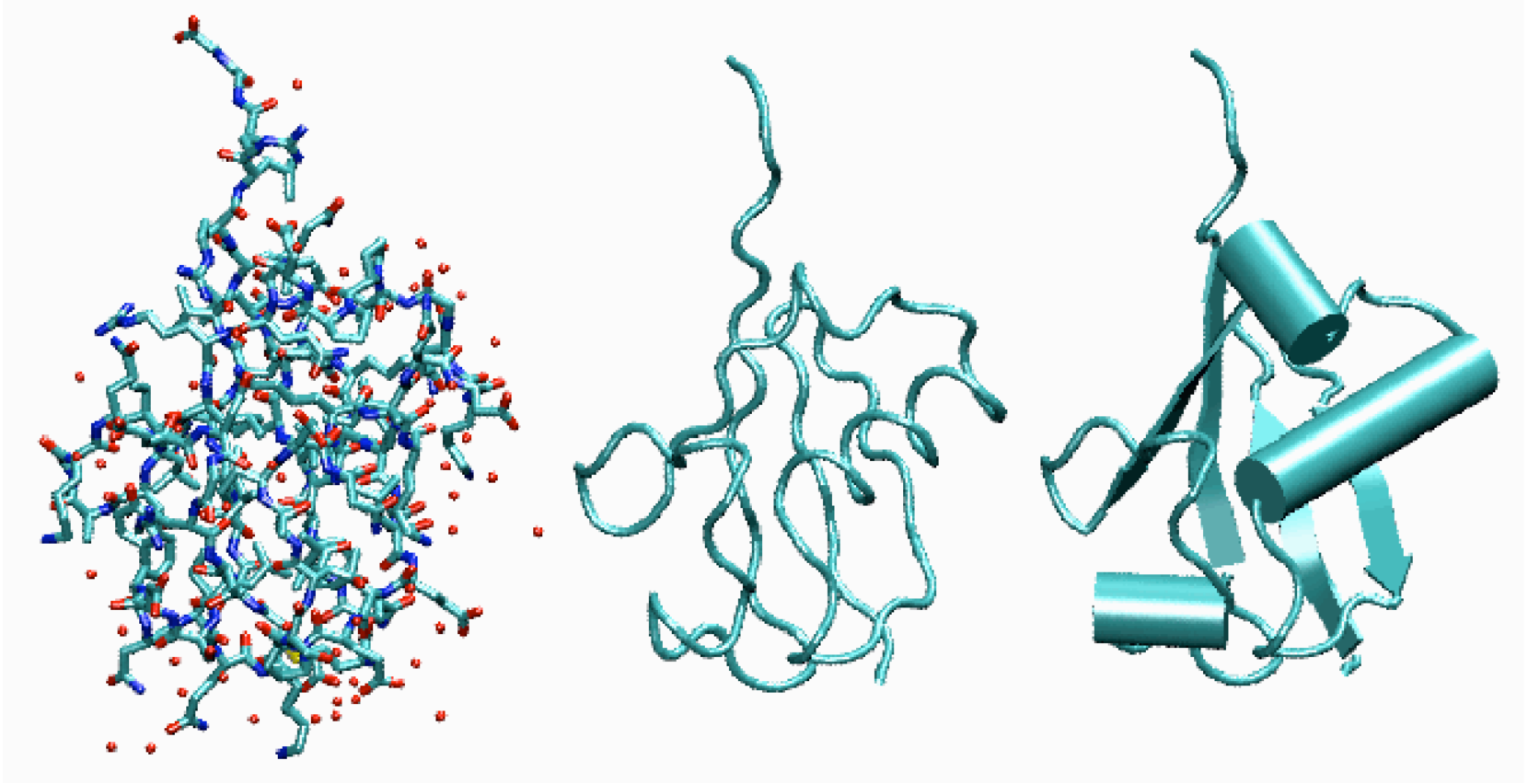
Basics of VMD

Rendering a Molecule



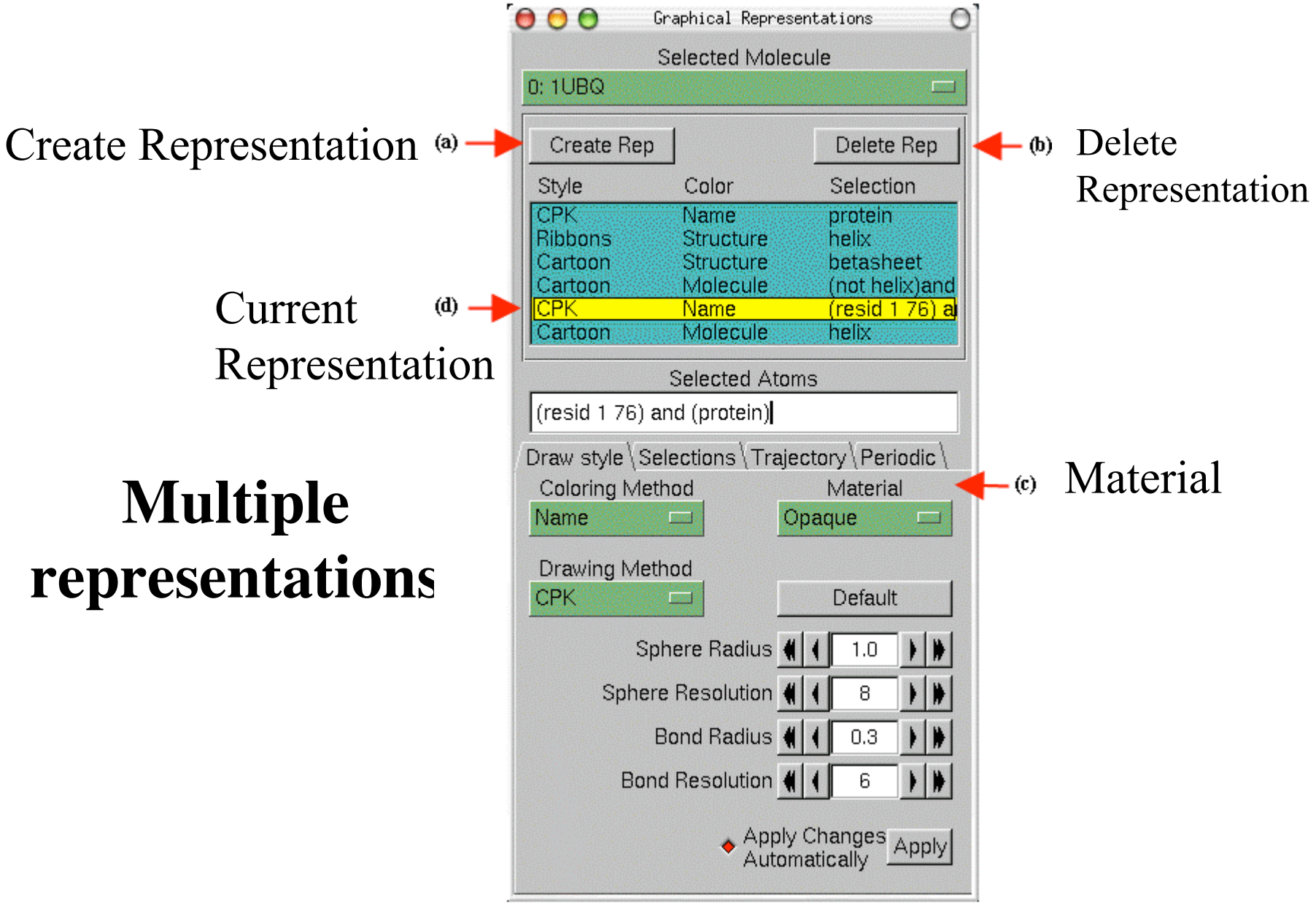
Basics of VMD

Change rendering style



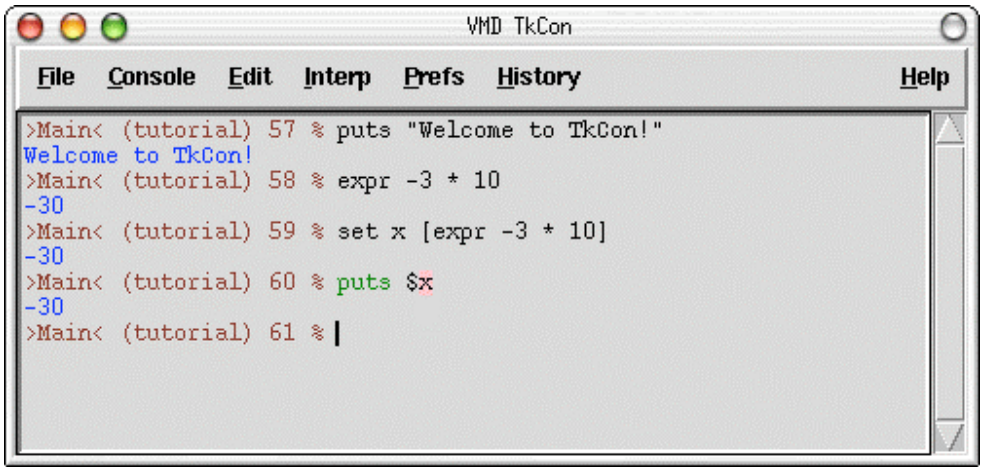
CPK tube cartoon

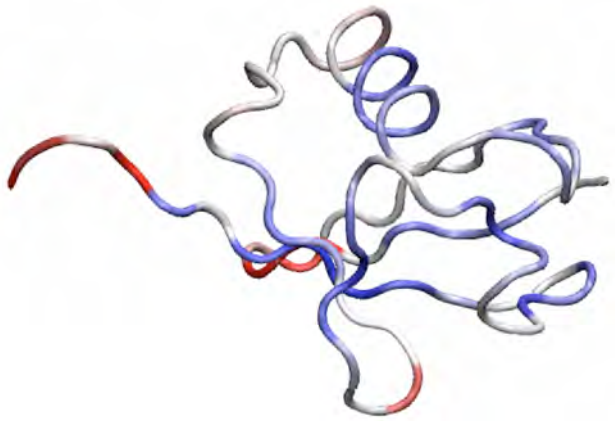
Basics of VMD

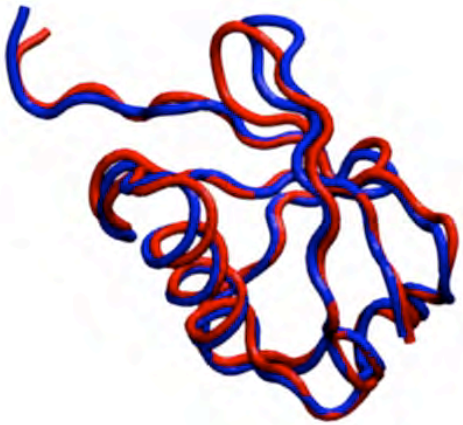


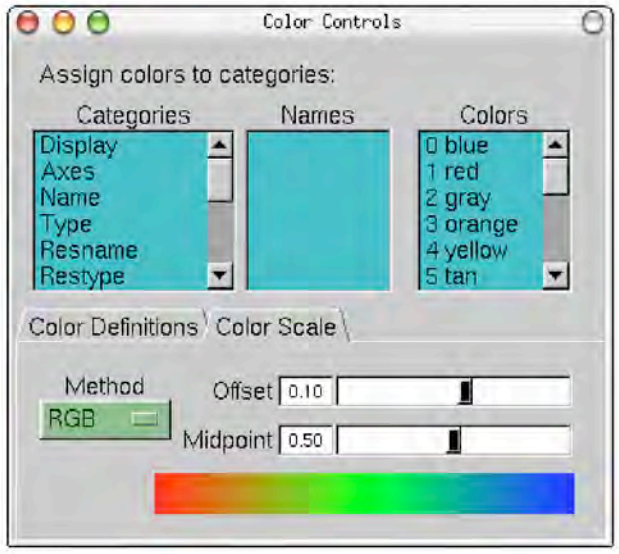
Multiple representations

VMD Scripting





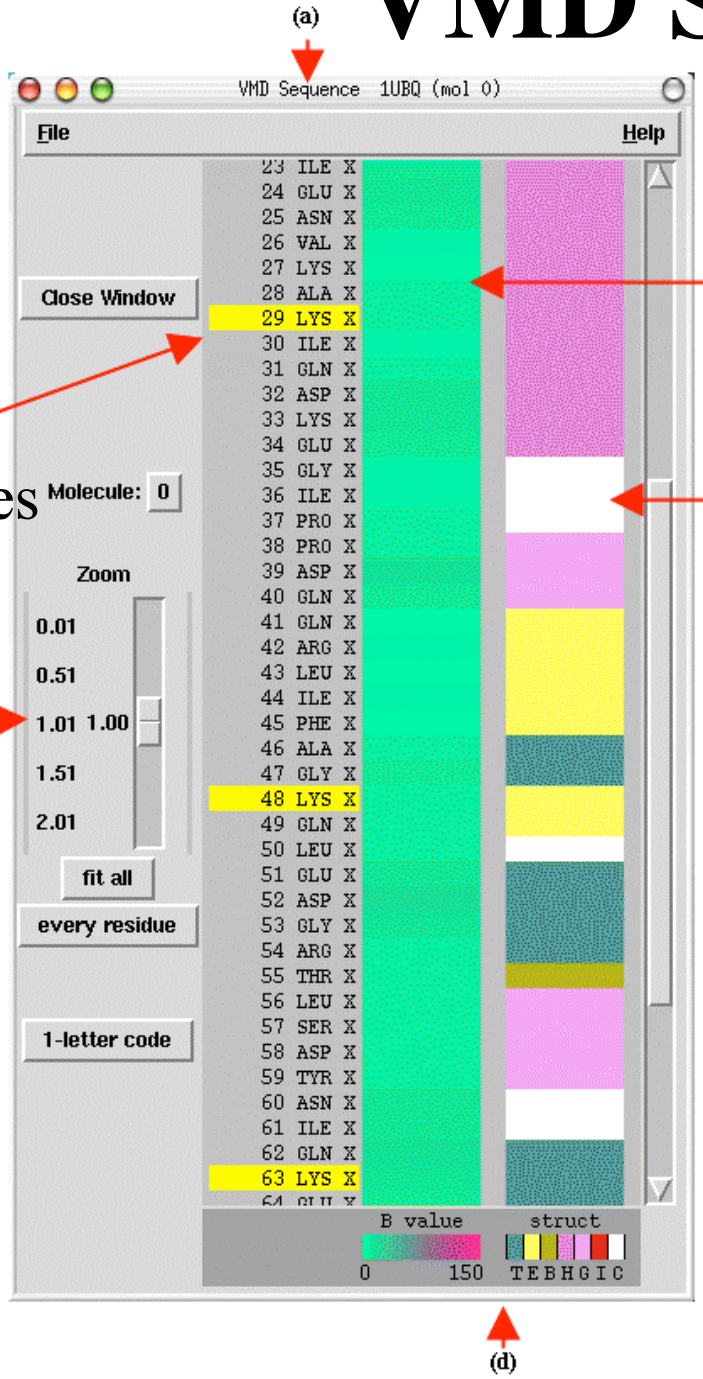




The Color Controls window showing the Color Scale tab.

Left: Initial and final states of ubiquitin after spatial alignment
Right (top): Color coding of deviation between initial and final

VMD Sequence Window

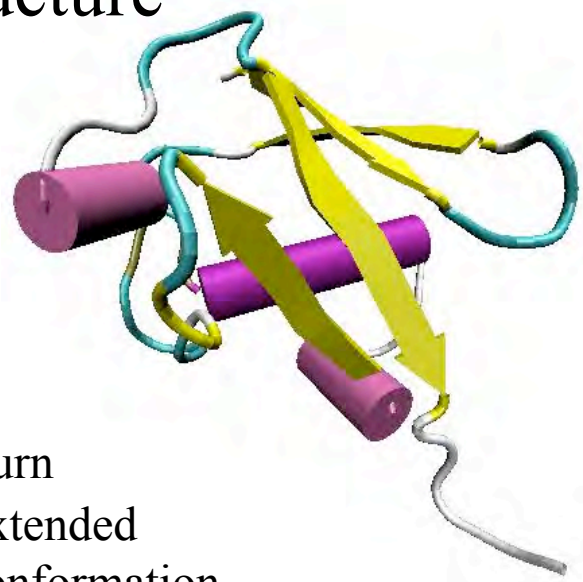


(b) Beta Value

List of the residues (e)

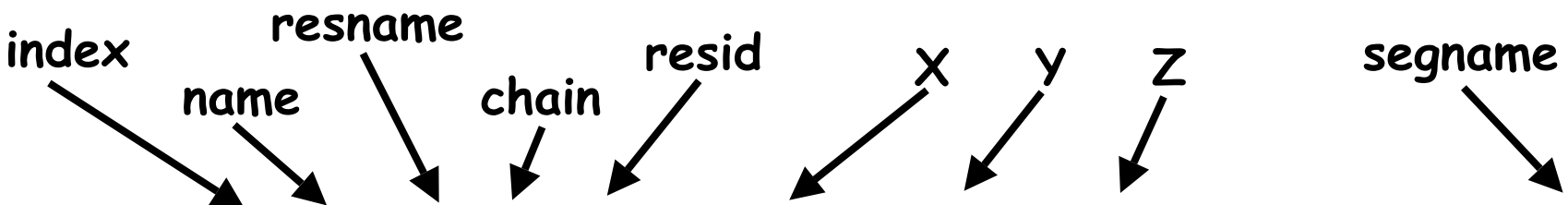
(c) Structure

Zoom (f)



T: Turn
E: Extended conformation
H: Helix
B: Isolated Bridge
G: 3-10 helix
I: Phi helix

Structure of a PDB file

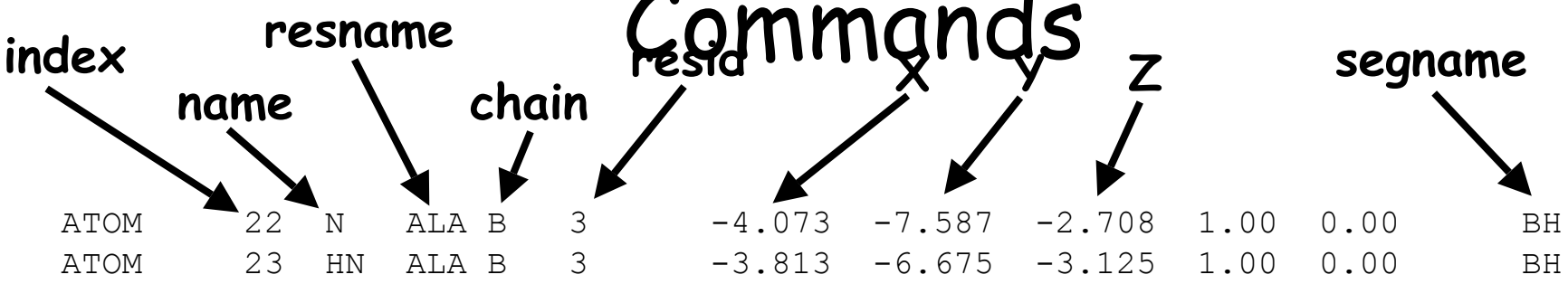



```
ATOM     22  N   ALA B   3      -4.073  -7.587  -2.708  1.00  0.00      BH
ATOM     23  HN  ALA B   3      -3.813  -6.675  -3.125  1.00  0.00      BH
ATOM     24  CA  ALA B   3      -4.615  -7.557  -1.309  1.00  0.00      BH
ATOM     25  HA  ALA B   3      -4.323  -8.453  -0.704  1.00  0.00      BH
ATOM     26  CB  ALA B   3      -4.137  -6.277  -0.676  1.00  0.00      BH
ATOM     27  HB1 ALA B   3      -3.128  -5.950  -0.907  1.00  0.00      BH
ATOM     28  HB2 ALA B   3      -4.724  -5.439  -1.015  1.00  0.00      BH
ATOM     29  HB3 ALA B   3      -4.360  -6.338   0.393  1.00  0.00      BH
ATOM     30  C   ALA B   3      -6.187  -7.538  -1.357  1.00  0.00      BH
ATOM     31  O   ALA B   3      -6.854  -6.553  -1.264  1.00  0.00      BH
ATOM     32  N   ALA B   4      -6.697  -8.715  -1.643  1.00  0.00      BH
ATOM     33  HN  ALA B   4      -6.023  -9.463  -1.751  1.00  0.00      BH
ATOM     34  CA  ALA B   4      -8.105  -9.096  -1.934  1.00  0.00      BH
ATOM     35  HA  ALA B   4      -8.287  -8.878  -3.003  1.00  0.00      BH
ATOM     36  CB  ALA B   4      -8.214 -10.604  -1.704  1.00  0.00      BH
ATOM     37  HB1 ALA B   4      -7.493 -11.205  -2.379  1.00  0.00      BH
ATOM     38  HB2 ALA B   4      -8.016 -10.861  -0.665  1.00  0.00      BH
ATOM     39  HB3 ALA B   4      -9.245 -10.914  -1.986  1.00  0.00      BH
ATOM     40  C   ALA B   4      -9.226  -8.438  -1.091  1.00  0.00      BH
ATOM     41  O   ALA B   4     -10.207  -7.958  -1.667  1.00  0.00      BH
0000000000000000000000000000000000000000000000000000000000000000000000000000
         10        20        30        40        50        60        70
```

>>> It is an ascii, fixed-format file <<<

"No connectivity information"

VMD Atom Selection Commands



(name CA CB) and (resid 1 to 4) and (segname BH)

protein and resname LYS ARG GLU ASP

water and within 5 of (protein and resid 62 and name CA)

water and within 3 of (protein and name O and z < 10)

Protein Data Bank

Format of a PDB file

Inspect ubiquitin with VMD

List of VMD Features

Tcl scripts - example

Structure of a PDB File

Trajectory analysis

Making movies

Making paper quality figures

Autopsf/solvate/ionize

Changing colors

Membrane builder

Atomselect command

webPDB

VMD save state

View master

Trajectories, multiple frame drawing

moving/rotating/saving new pdb

getting command synthax from logfile

RMSD/alignment