An Introduction to Molecular Visualization with UCSF Chimera

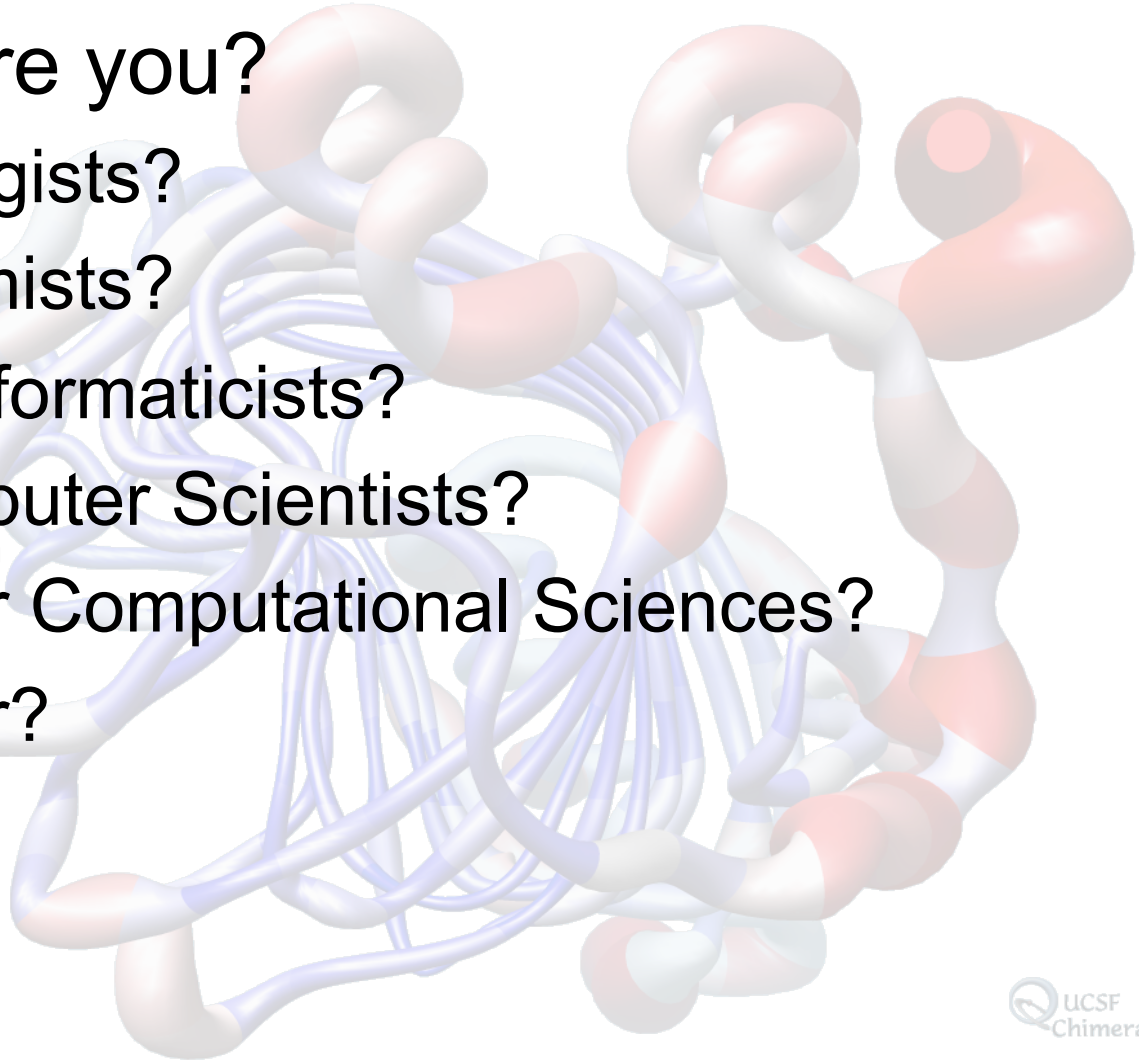
John “Scooter” Morris, Ph.D.
scooter@cgl.ucsf.edu
University of California, San Francisco

Introductions

- About me
  - John “Scooter” Morris:
    - RBVI Executive Director
    - Adjunct Professor, Department of Pharmaceutical Chemistry, UCSF
    - 19 years in pharmaceutical industry (Genentech)
    - 11 years at RBVI

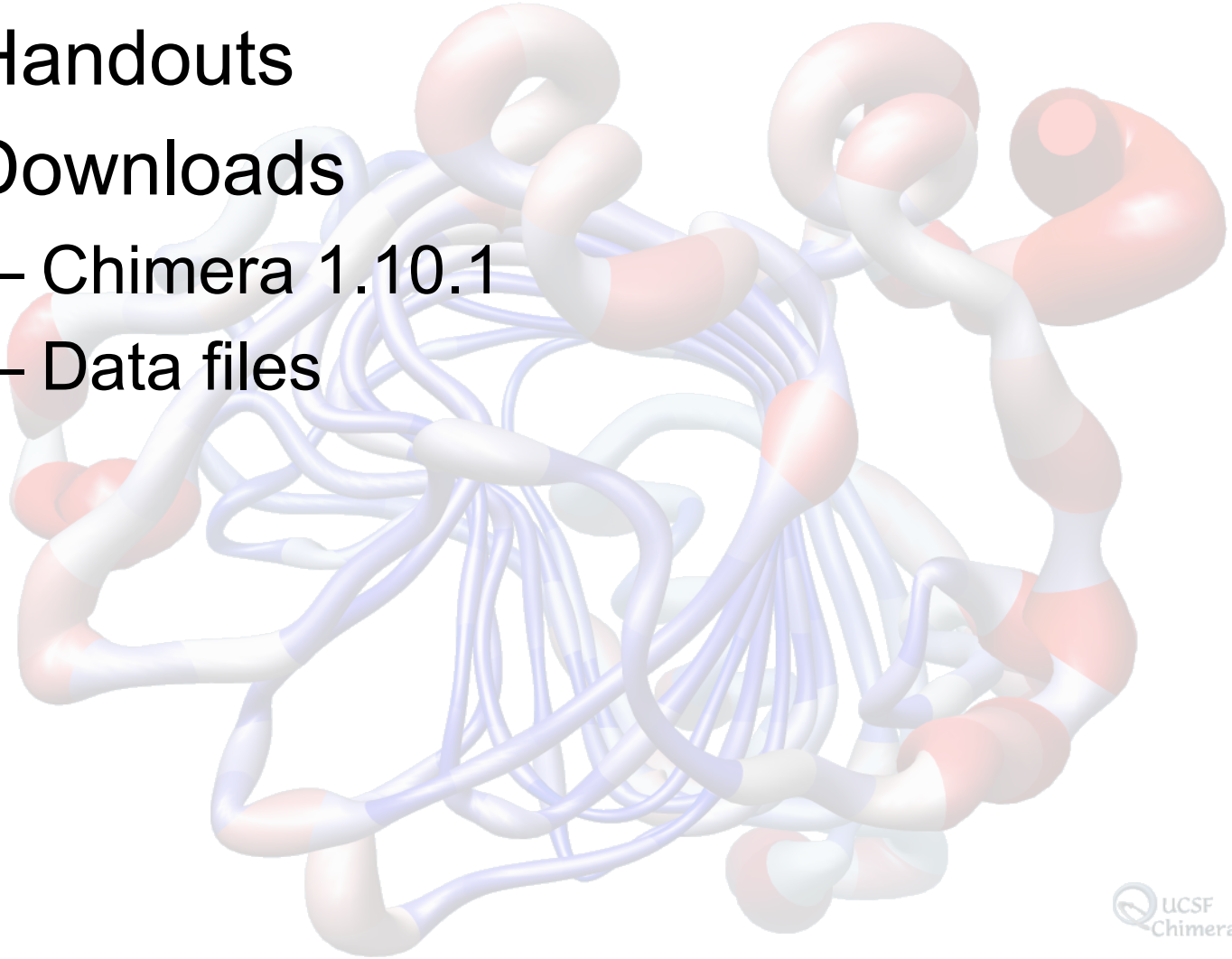
Introductions

- Who are you?
  - Biologists?
  - Chemists?
  - Bioinformaticists?
  - Computer Scientists?
  - Other Computational Sciences?
  - Other?



Materials

- Handouts
- Downloads
  - Chimera 1.10.1
  - Data files

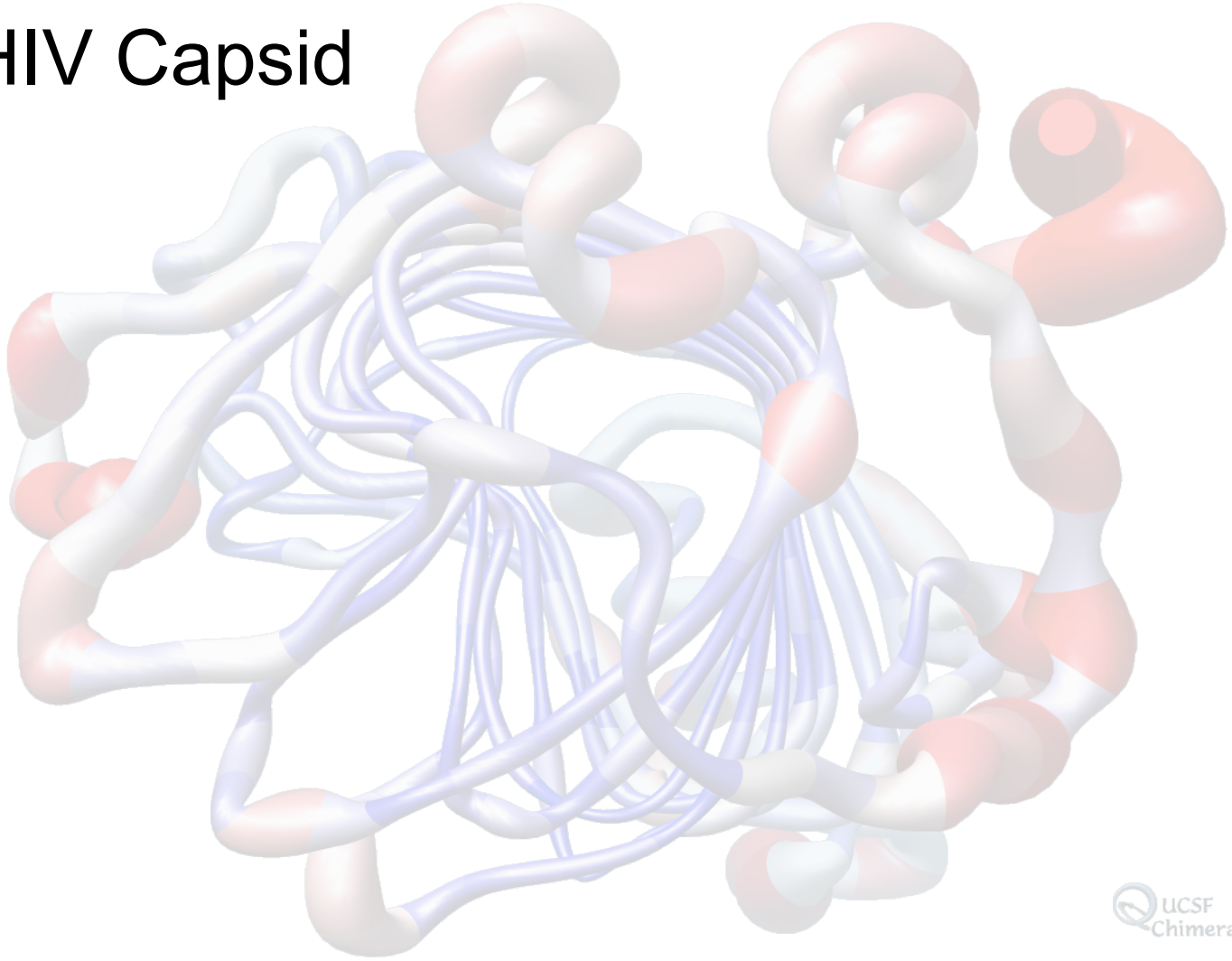


Agenda

- Demo
  - …while Chimera installs.
- Introduction to UCSF Chimera
  - Basic principals
- Hands on Tutorial
- Q&A
- Glimpse of the future (Chimera2)

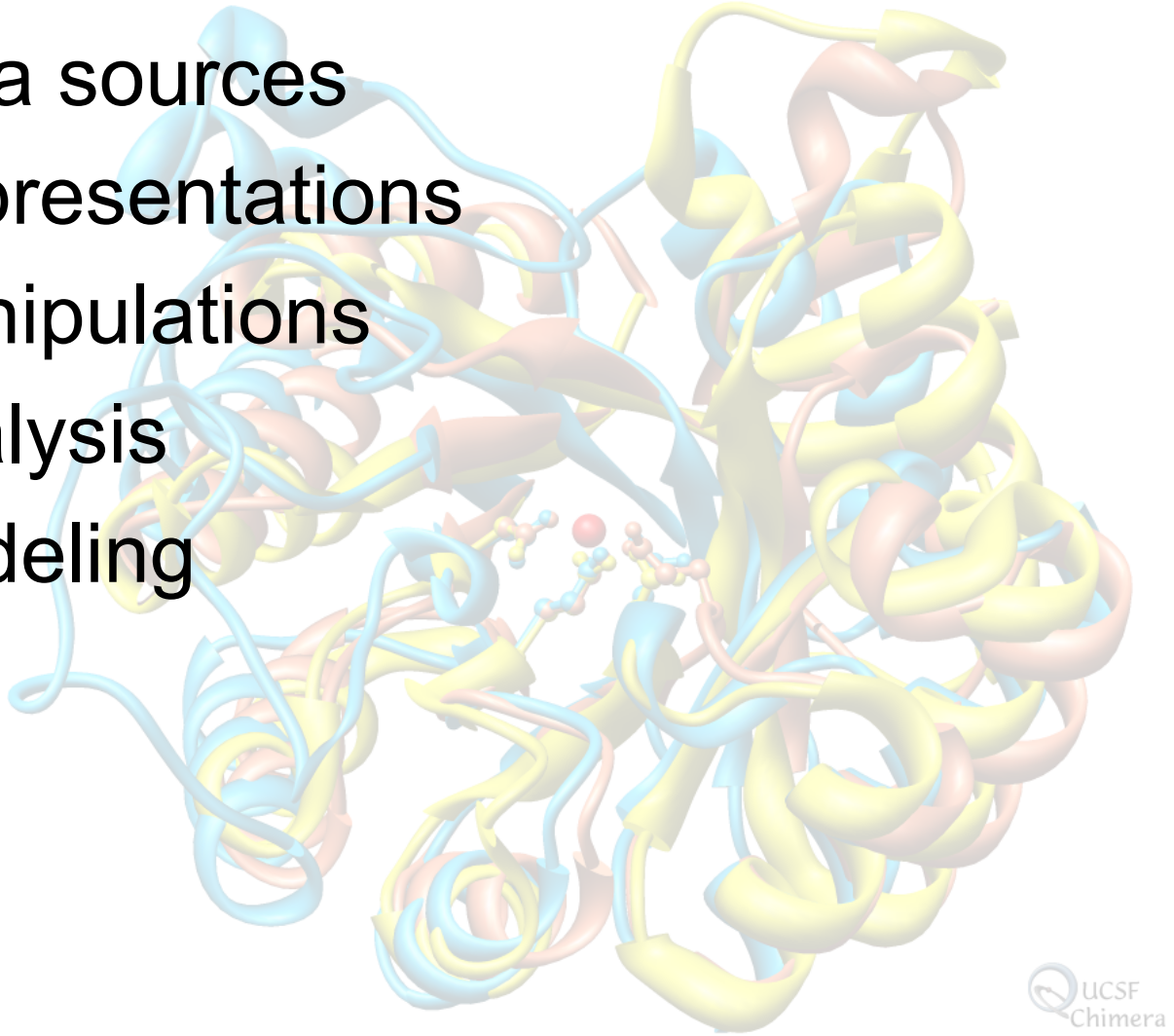
Demo

- HIV Capsid



Molecular Visualization

- Data sources
- Representations
- Manipulations
- Analysis
- Modeling



Definitions

- modeling (model):

  Function: *verb*

  transitive verb

  1 : to plan or form after a pattern **:** SHAPE

  3 b : to produce a representation or simulation of <using a computer to *model* a problem>

  4 : to construct or fashion in imitation of a particular model <*modeled* its constitution on that of the United States>

  intransitive verb

  1 : to design or imitate forms **:** make a pattern <enjoys *modeling* in clay>

- visualization:

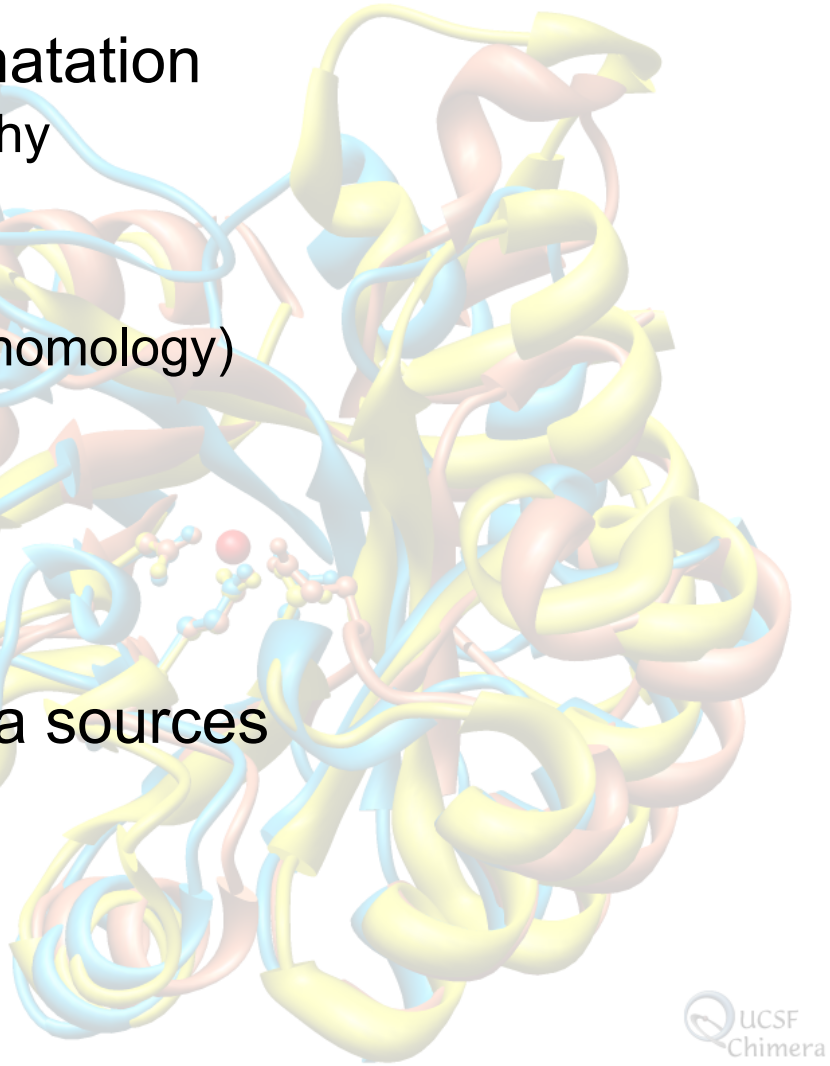
  Function: *noun*

  1 : formation of mental visual images

  2 : the act or process of interpreting in visual terms or of putting into visible form

Data sources

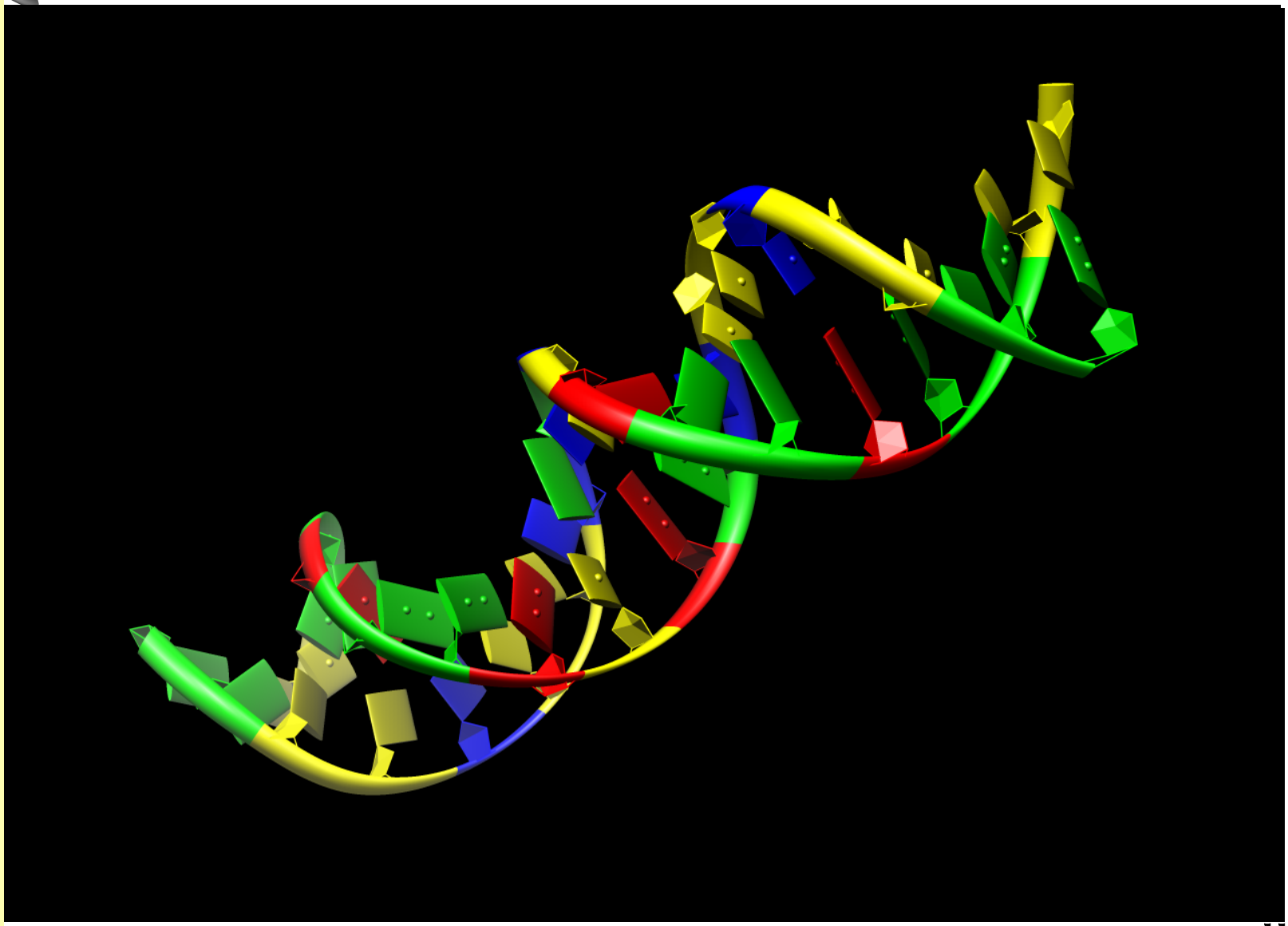
- Structure determinatation
  - Xray crystallography
  - NMR
  - EM/Cryo EM
  - Models (*ab initio*, homology)
- Volumetric data
  - EM/Cryo EM
  - Electron density
  - Light microscopy
- Non-structural data sources
  - Sequence data
  - Pathway data
  - Interaction data
  - Expression data

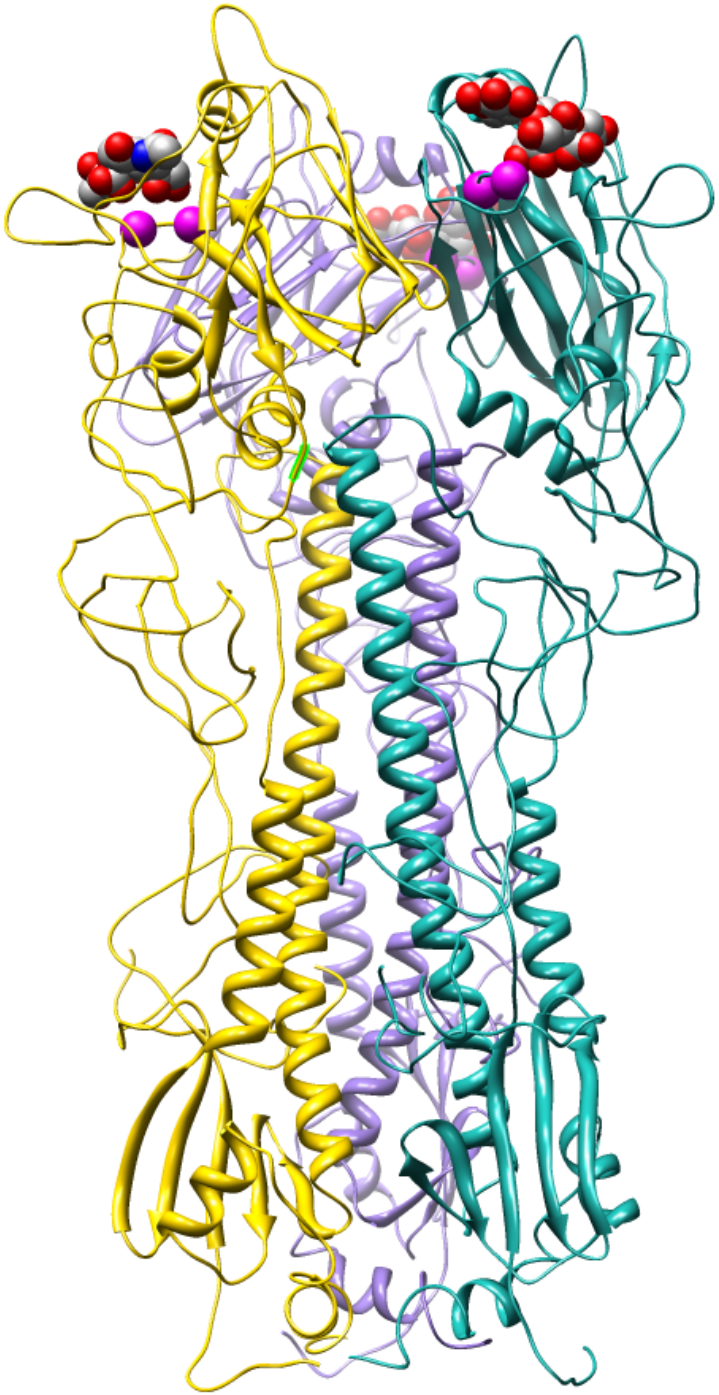


Data sources

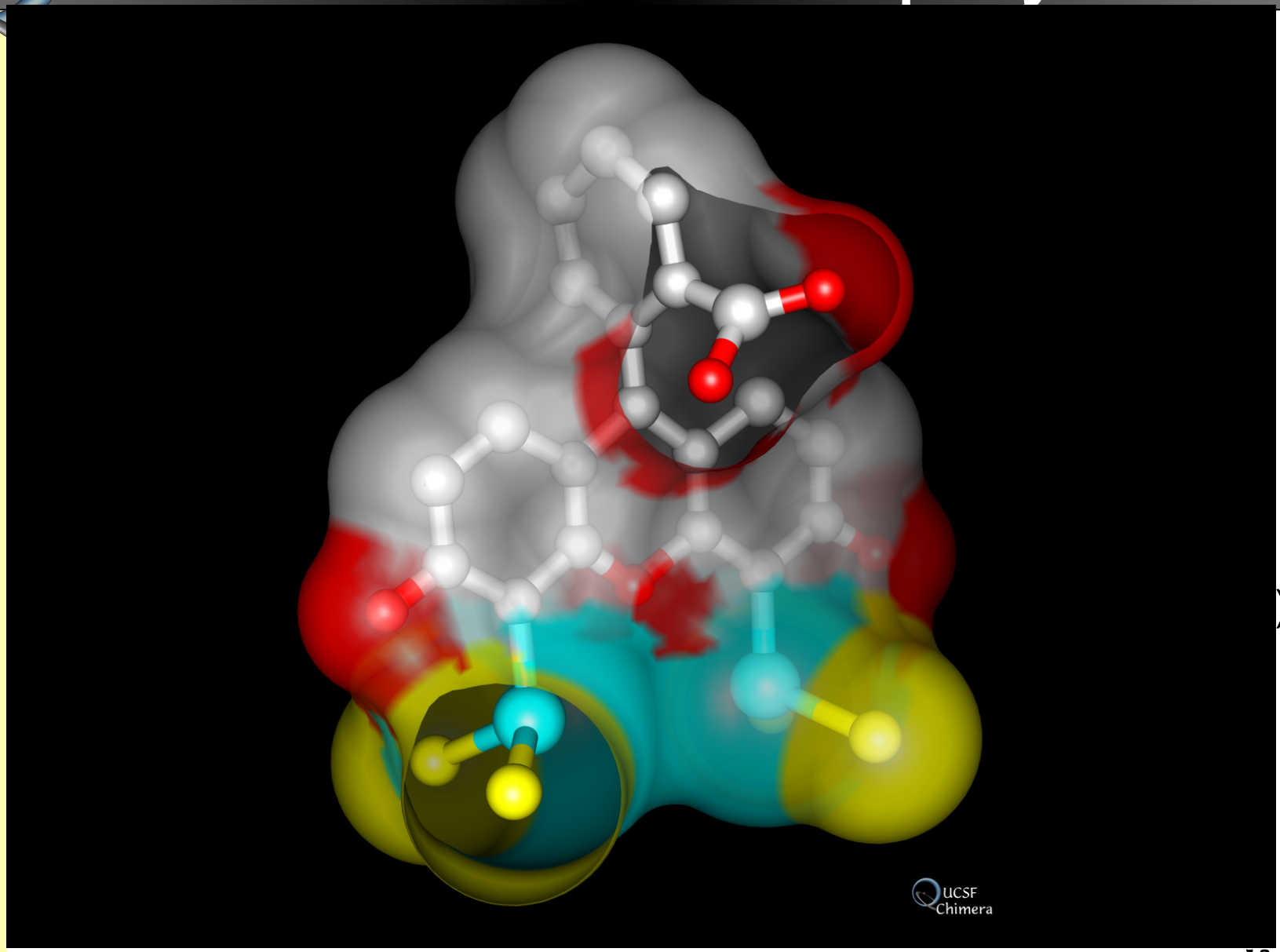
- Structure repositories
  - Protein Databank: http://www.rcsb.org/
  - Nucleic Acid Database (NDB): http://ndbserver.rutgers.edu/
  - Structural Classification of Proteins (SCOP): http://scop.mrc-lmb.cam.ac.uk/scop/
  - ModBase: http://modbase.compbio.ucsf.edu/
  - Cambridge Structural Database (CSD): http://www.ccdc.cam.ac.uk/products/csd/
  - VIPER EM Database: http://mmtsb1.scripps.edu/emdb/
  - EM Database: http://www.ebi.ac.uk/msd-srv/emsearch/index.html
  - Uppsala Electron Density Server: http://eds.bmc.uu.se/eds/

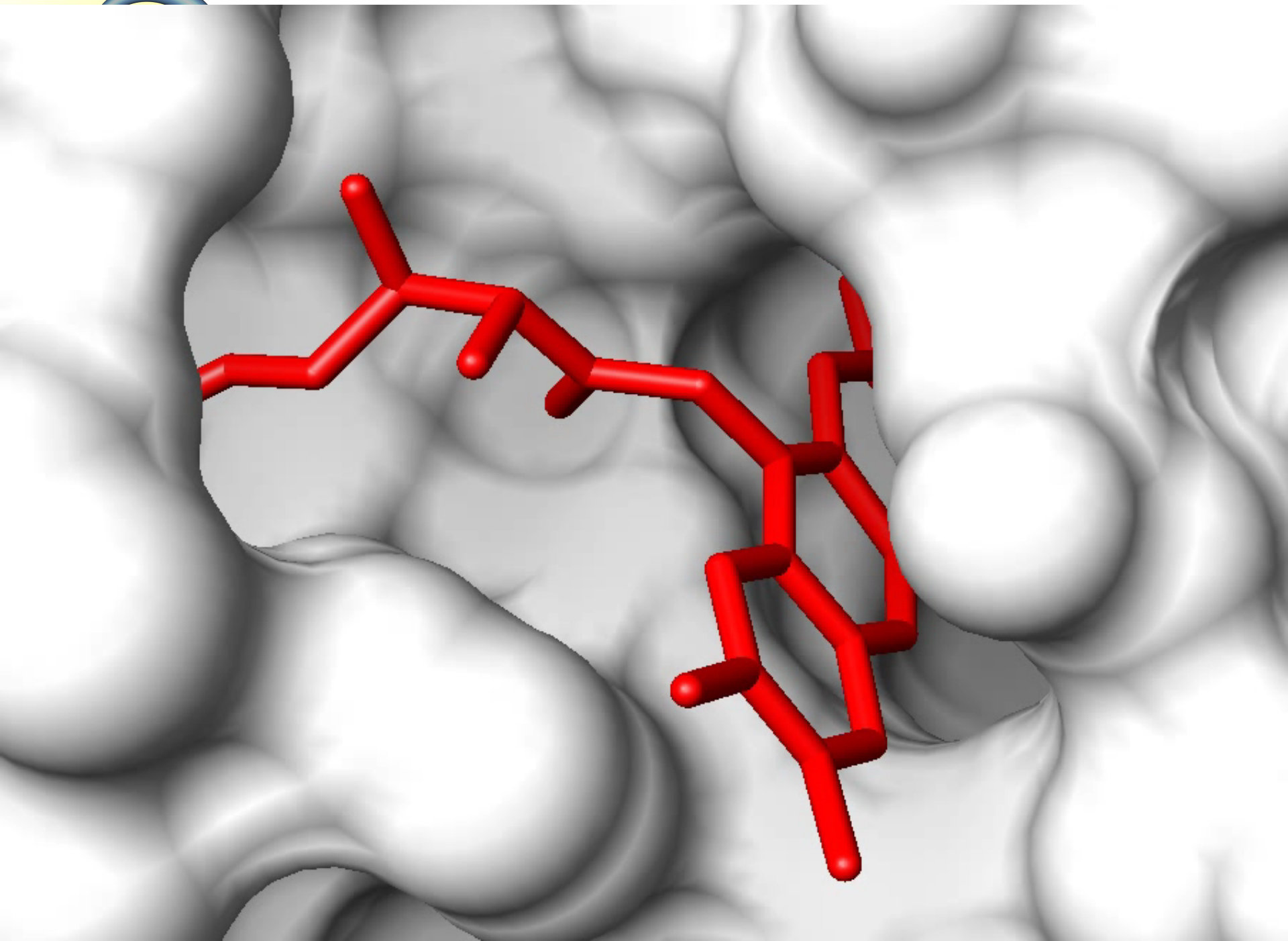
Representations



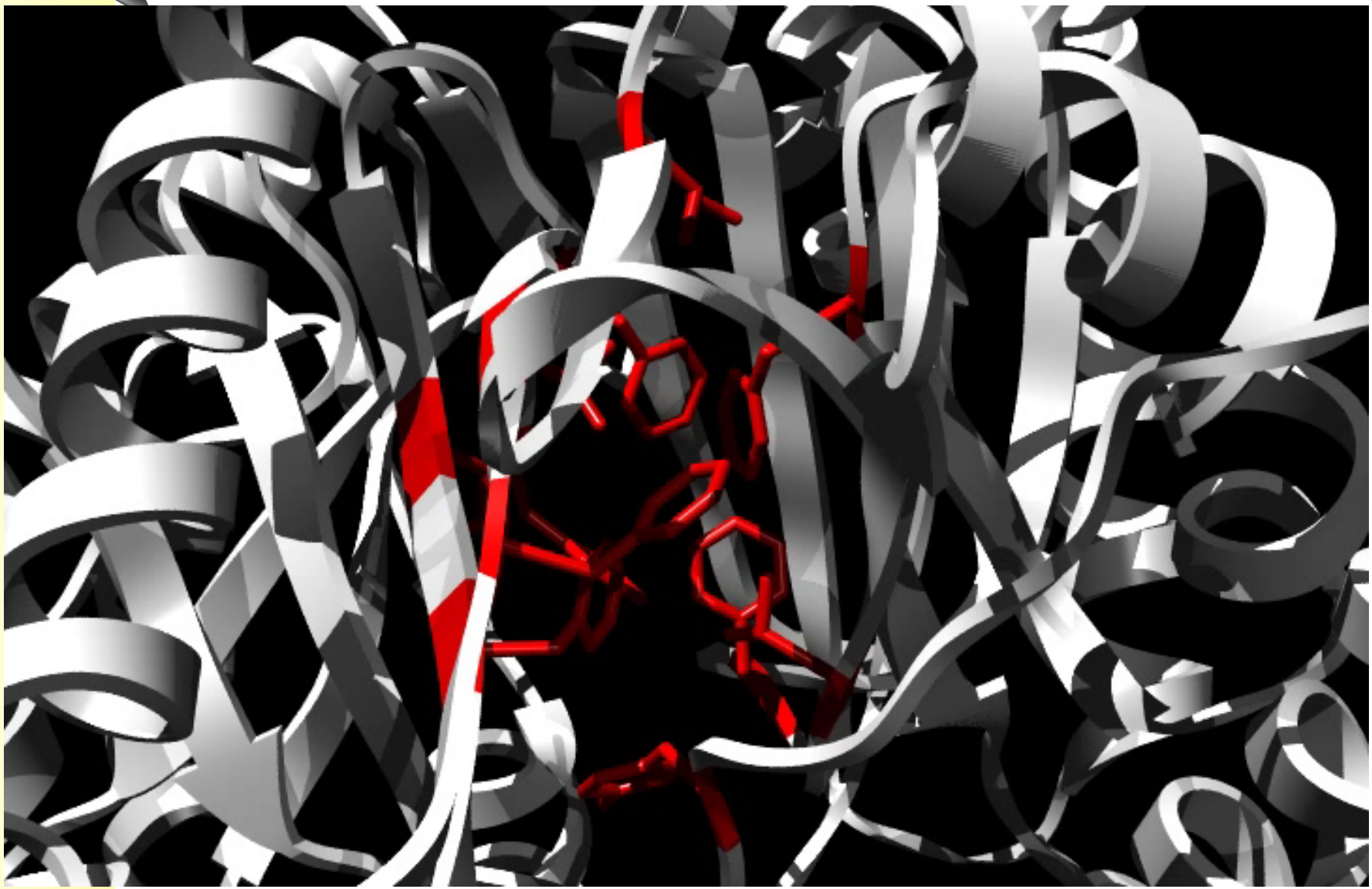


Other Visual Displays



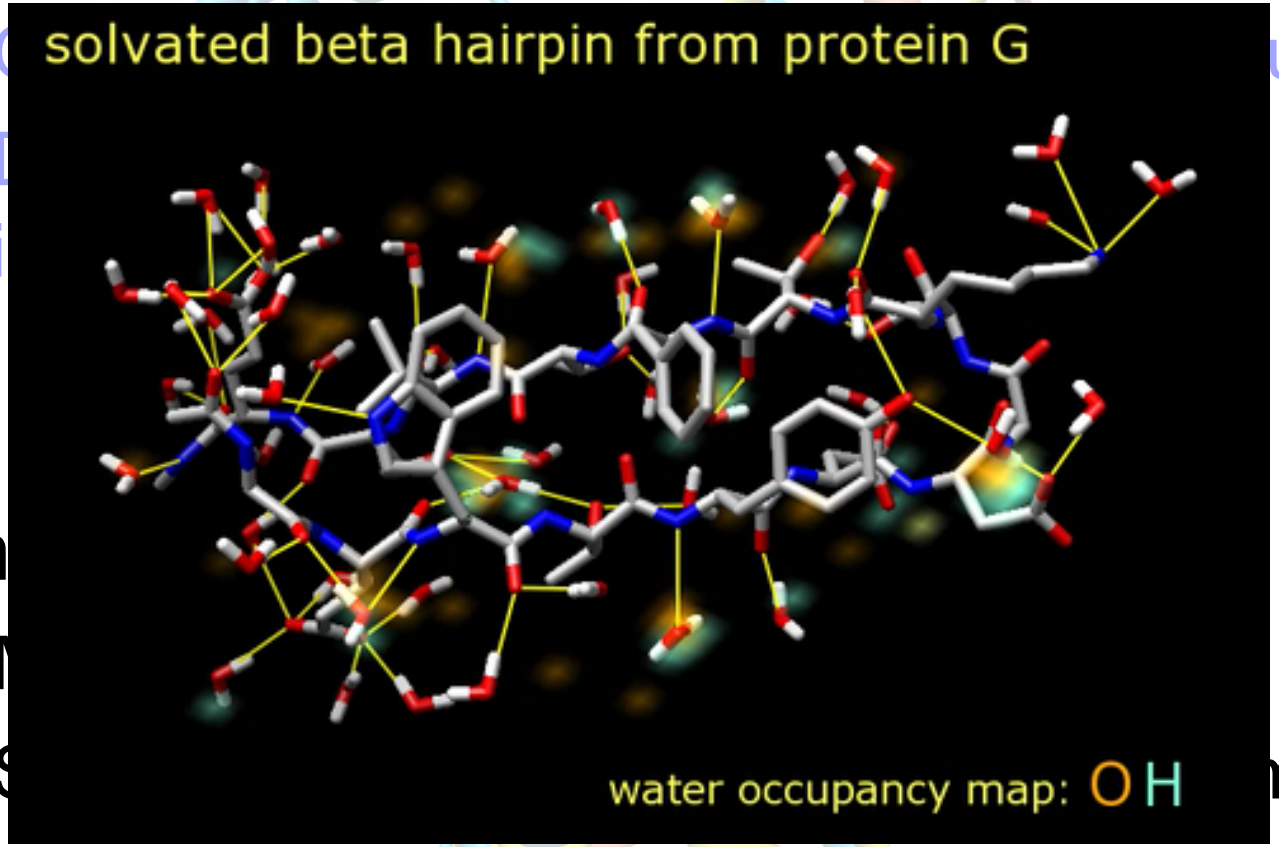


Animation



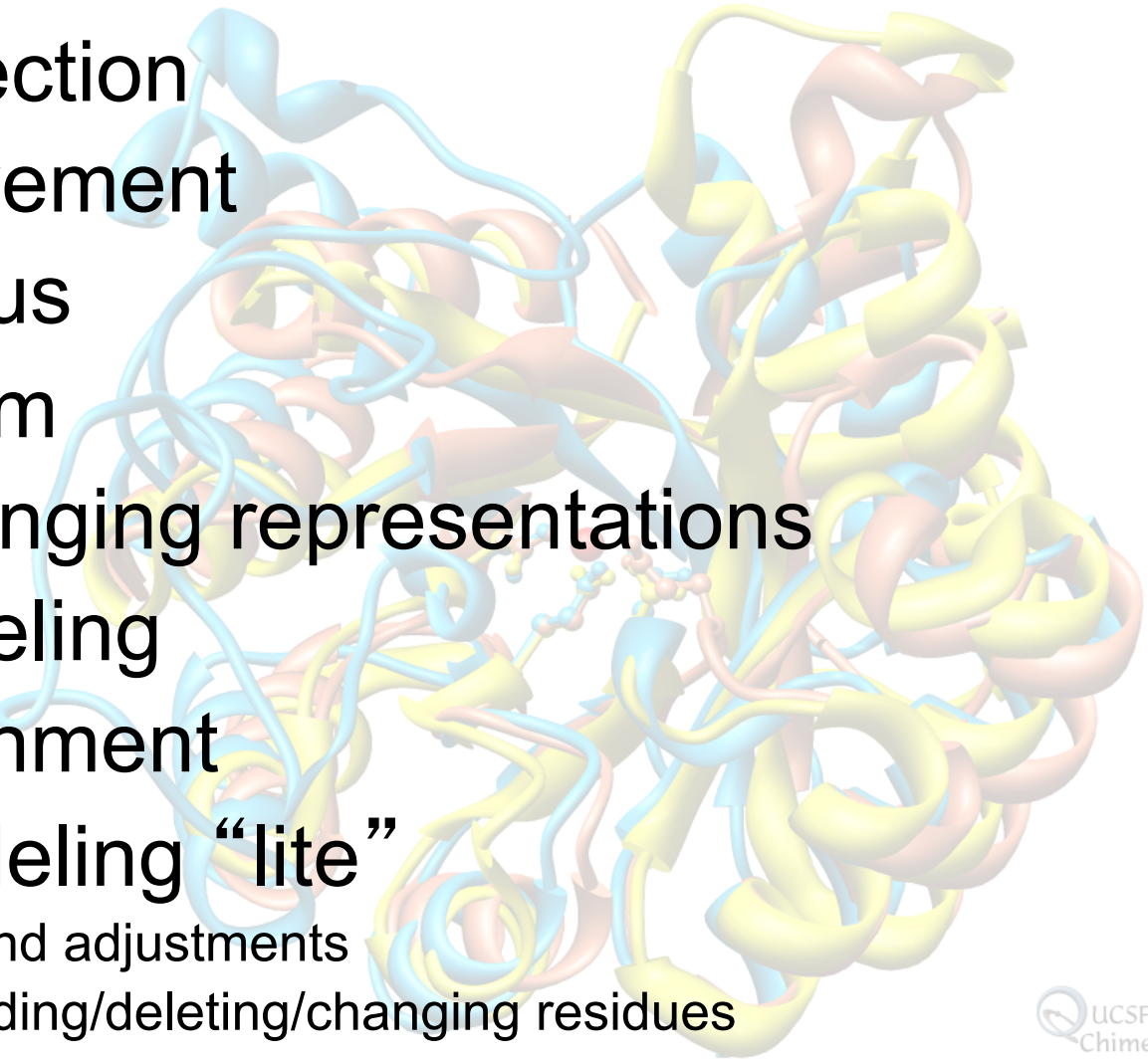
Animation

- Presentation
  - (…ues)
  - D…
    i…
- An…
  - M…
  - S…mations



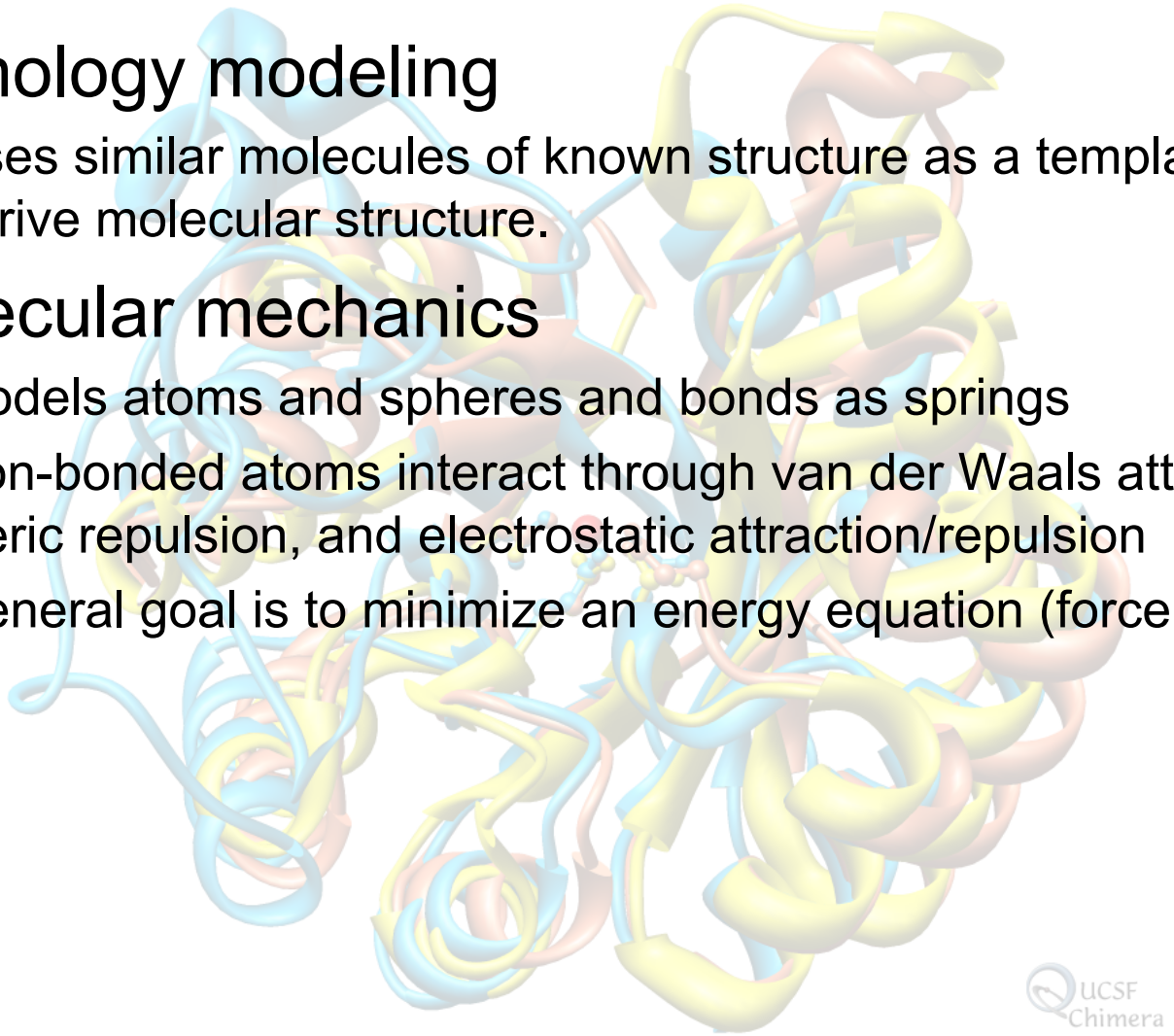
Manipulations

- Selection
- Movement
- Focus
- Zoom
- Changing representations
- Labeling
- Alignment
- Modeling “lite”
  - Bond adjustments
  - Adding/deleting/changing residues



Modeling

- Homology modeling
  - Uses similar molecules of known structure as a template to derive molecular structure.
- Molecular mechanics
  - Models atoms and spheres and bonds as springs
  - Non-bonded atoms interact through van der Waals attraction, steric repulsion, and electrostatic attraction/repulsion
  - General goal is to minimize an energy equation (force field)



Modeling

- Molecular dynamics
  - Models the motions of a molecular system, including conformational transitions and local vibrations, using molecular mechanics force fields
  - Takes into account the thermodynamic environment
  - May be used to compute both thermodynamic and kinetic properties
  - Result is an ensemble (i.e., a movie) of how the molecule moves
- Quantum (*ab initio*) modeling
  - Structures are solved by approximating the Schrödinger equation for all particles (nuclei and electrons) in the system.

(see http://cmm.info.nih.gov)

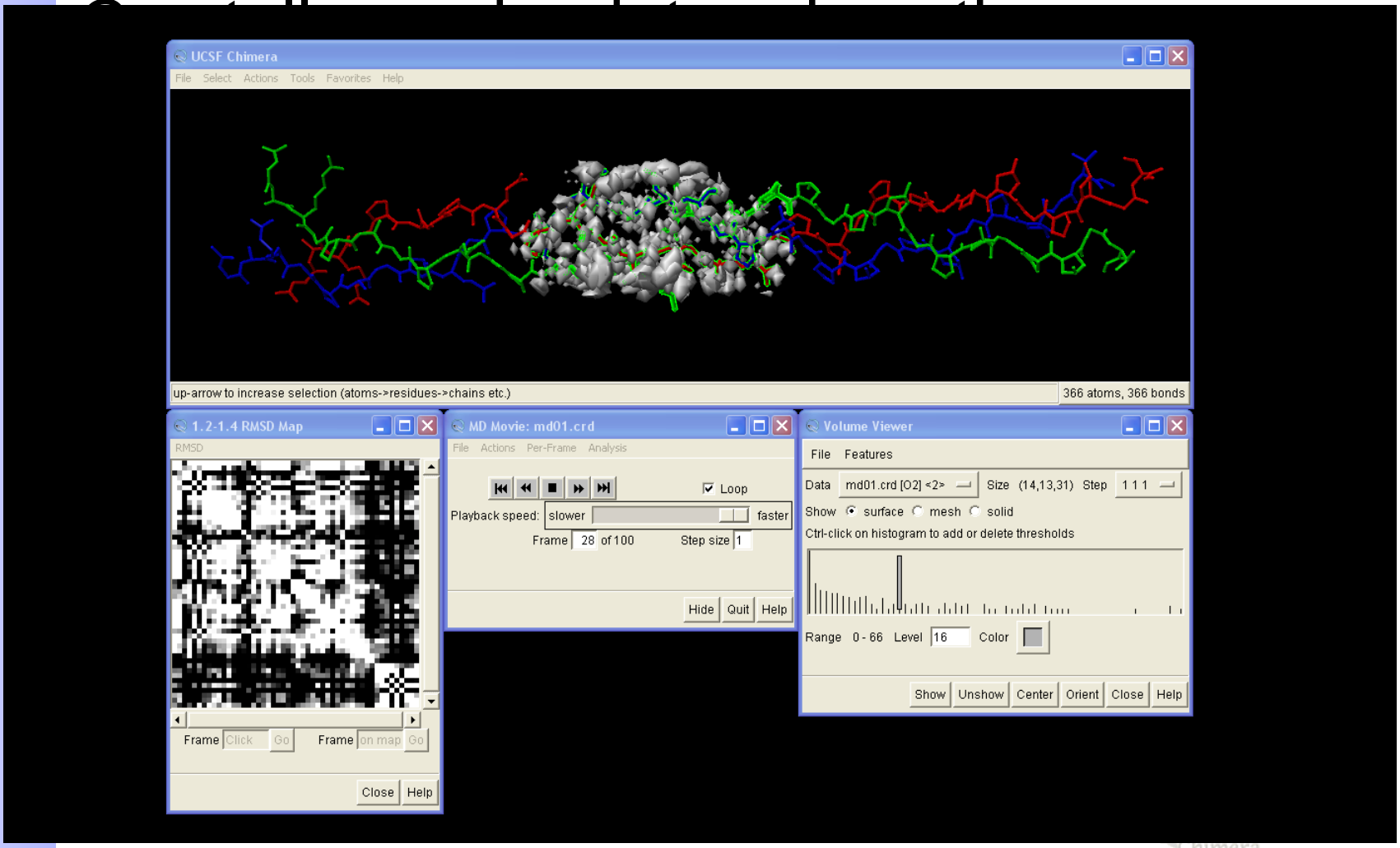
Applications of molecular visualization

- Computational chemistry
  - Dynamic molecules
  - Molecular interactions
- Microscopy
  - Lower resolution, volumetric data
- Genomics
  - Sequence-structure-function relationships
- Systems biology
  - Broad view across variety of data

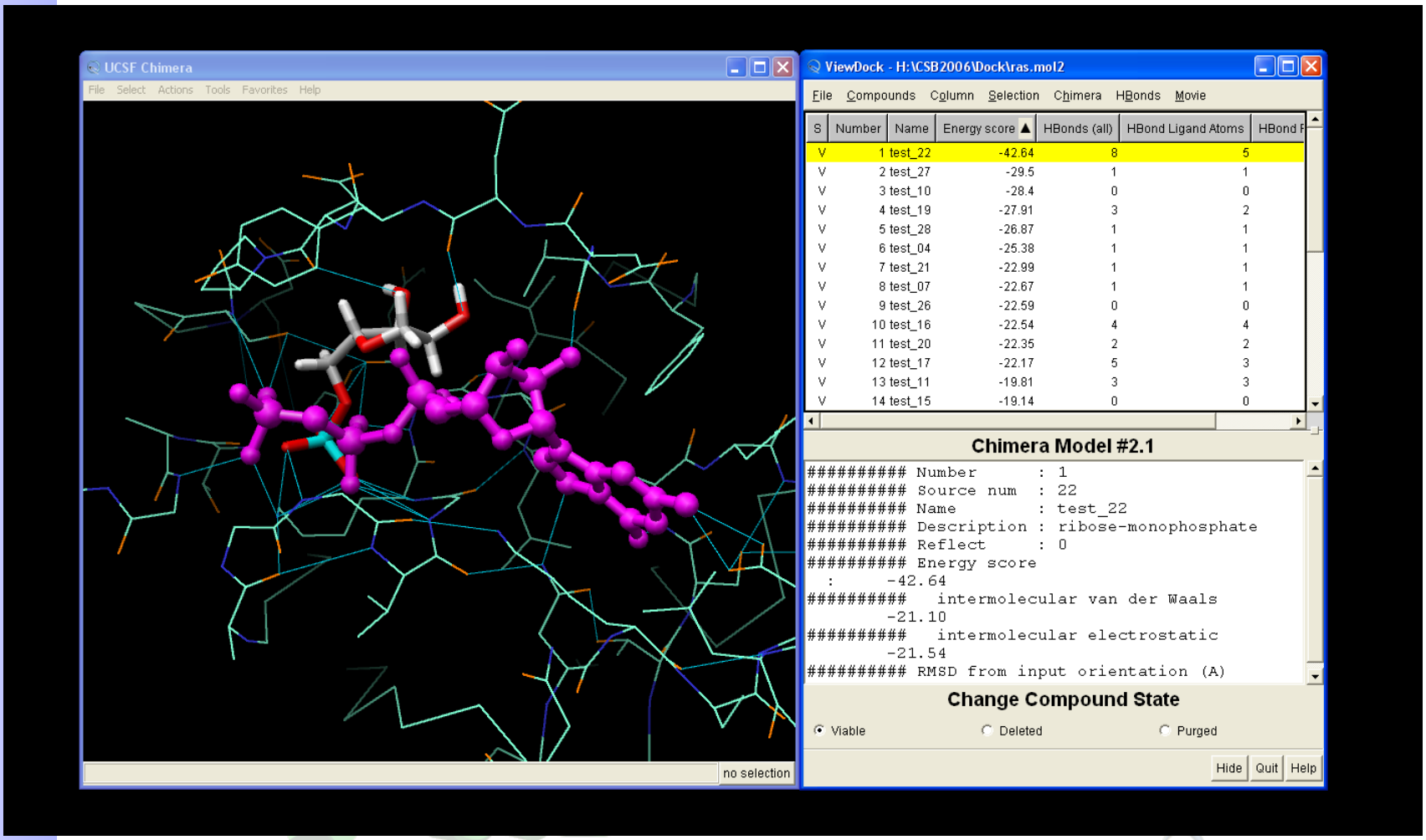
Scenarios of use

- Analysis
  - Molecular dynamics
  - Docking
  - Sequence-structure relationships
  - Low-resolution representations
    - Viruses and large complexes
    - Electron microscopy
  - Structures in context
- Publication
  - High-resolution images
  - Animation

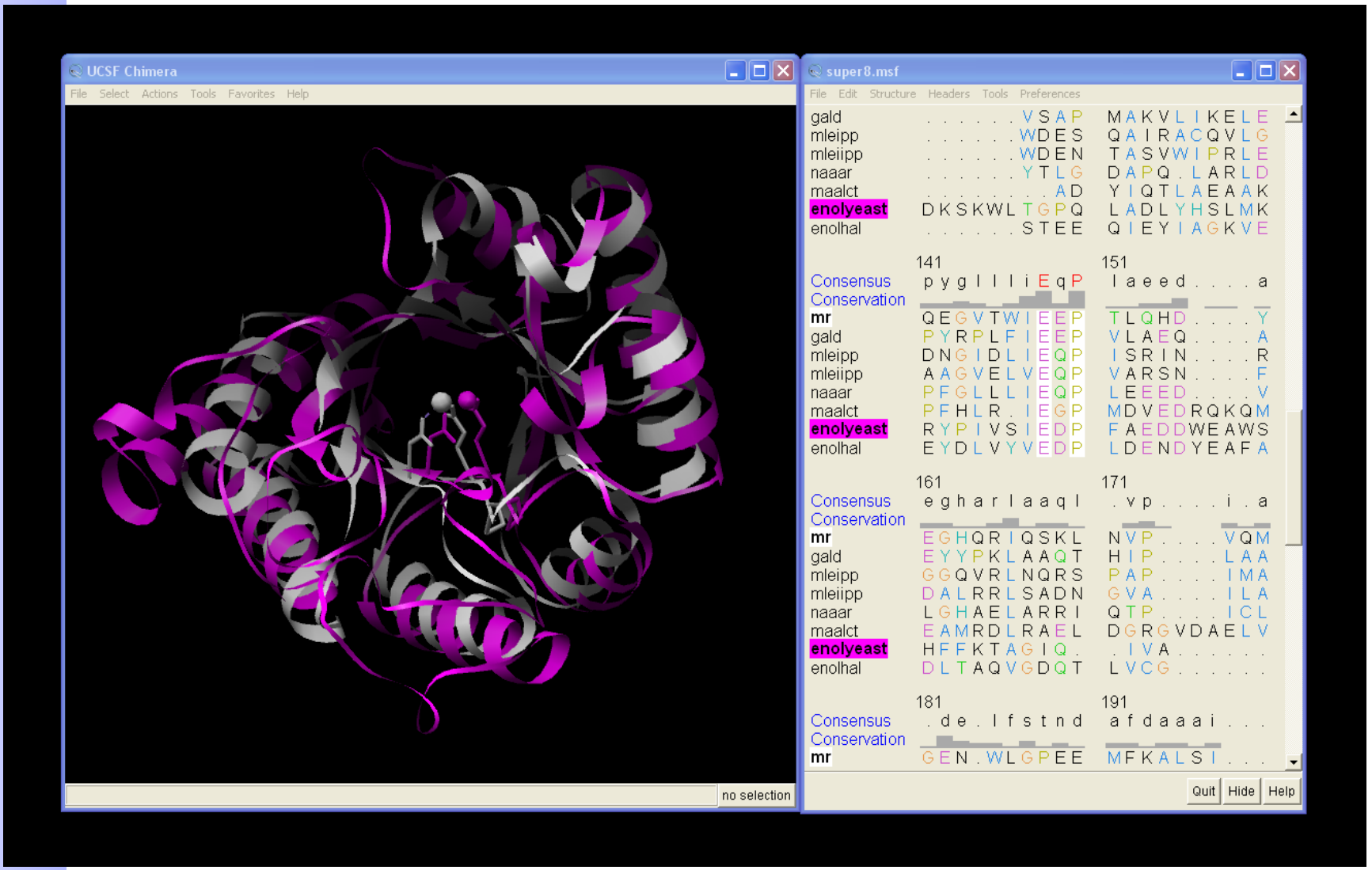
Molecular dynamics

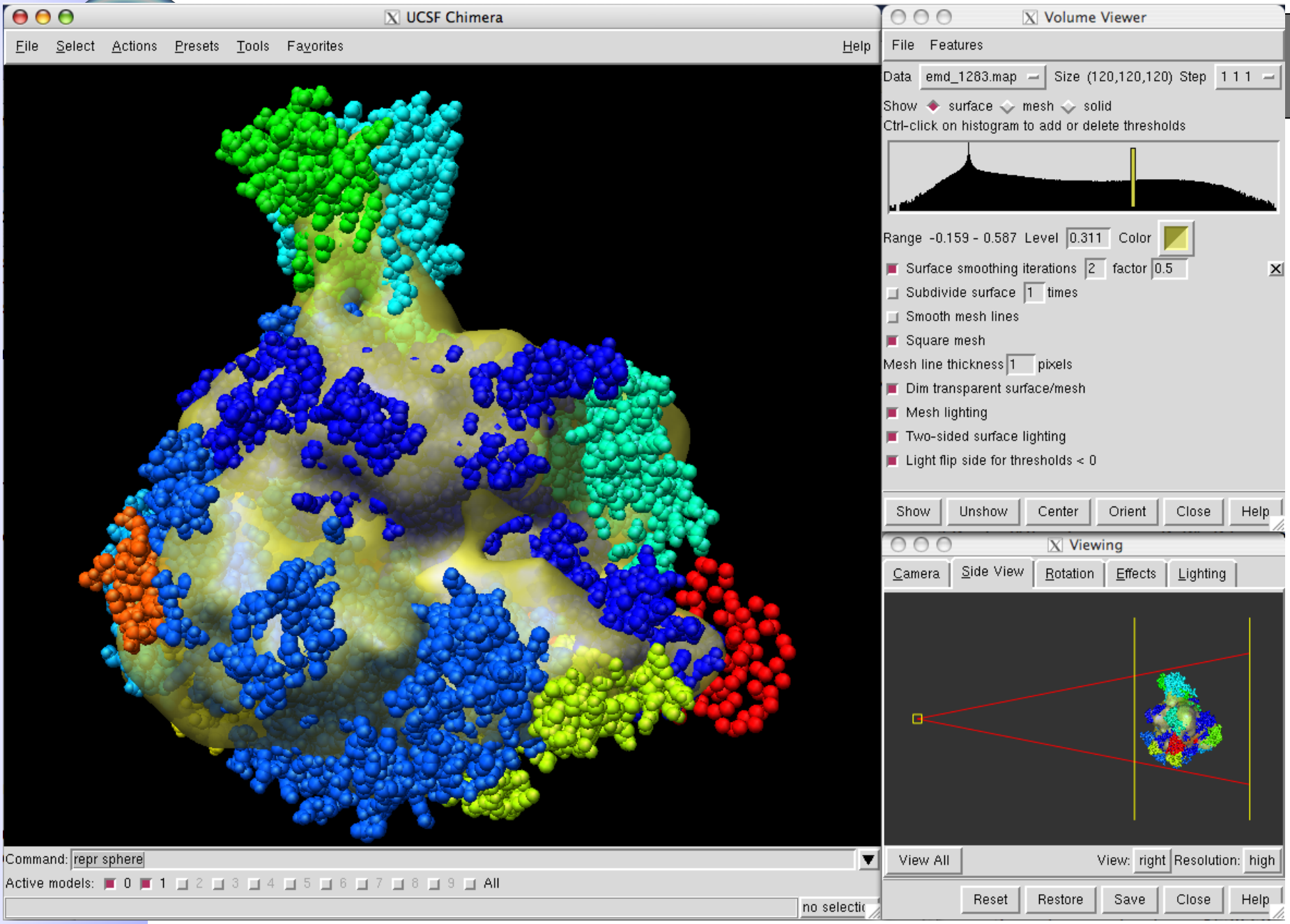


Docking

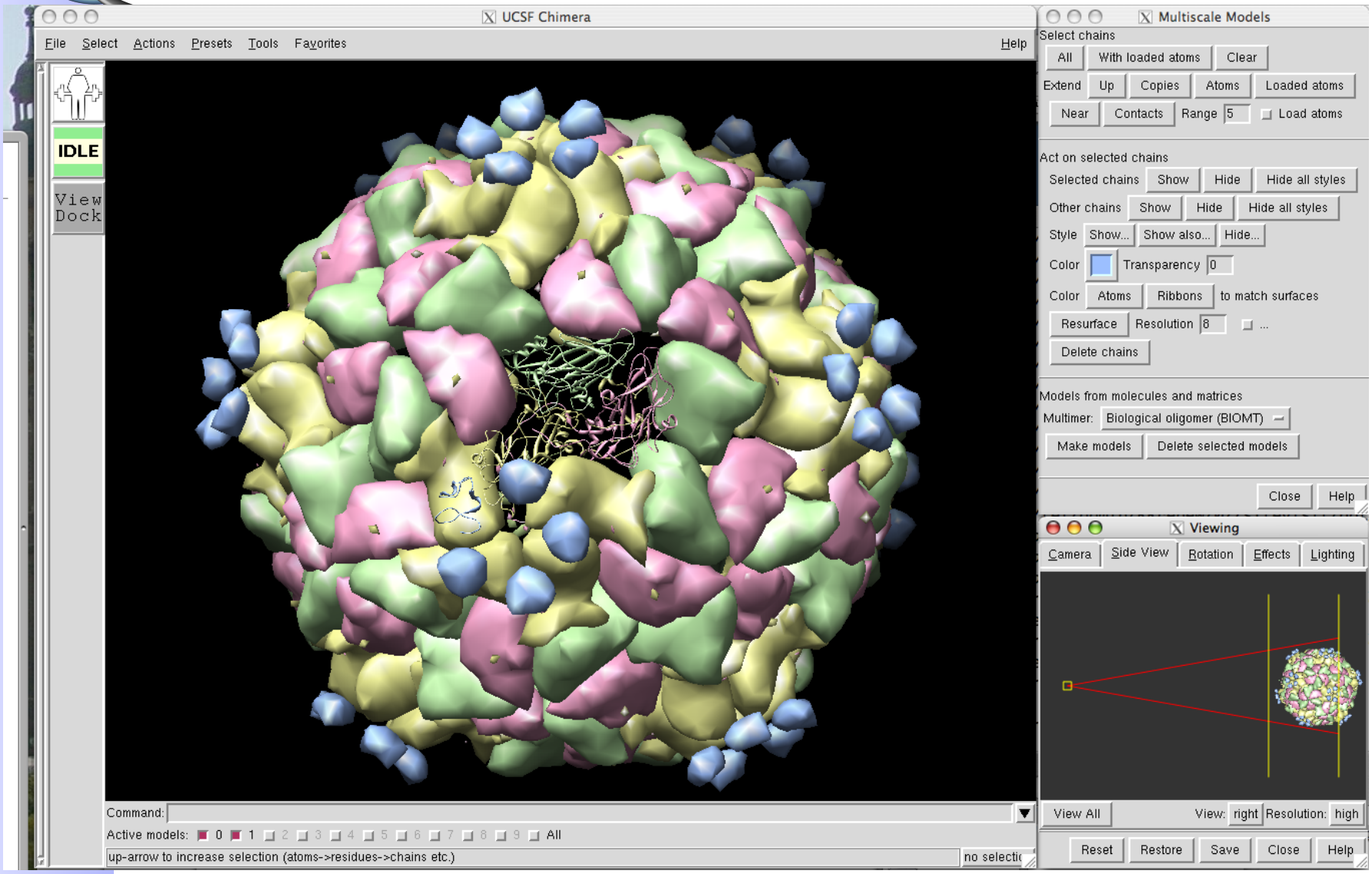

UCSF Chimera
File Select Actions Tools Favorites Help
no selection
ViewDock - H:\CSB2006\Dock\ras.mol2
File Compounds Column Selection Chimera HBonds Movie
S Number Name Energy score HBonds (all) HBond Ligand Atoms HBond F
V 1 test_22 -42.64 8 5
V 2 test_27 -29.5 1 1
V 3 test_10 -28.4 0 0
V 4 test_19 -27.91 3 2
V 5 test_28 -26.87 1 1
V 6 test_04 -25.38 1 1
V 7 test_21 -22.99 1 1
V 8 test_07 -22.67 1 1
V 9 test_26 -22.59 0 0
V 10 test_16 -22.54 4 4
V 11 test_20 -22.35 2 2
V 12 test_17 -22.17 5 3
V 13 test_11 -19.81 3 3
V 14 test_15 -19.14 0 0
Chimera Model #2.1
########## Number : 1
########## Source num : 22
########## Name : test_22
########## Description : ribose-monophosphate
########## Reflect : 0
########## Energy score
: -42.64
########## intermolecular van der Waals
-21.10
########## intermolecular electrostatic
-21.54
########## RMSD from input orientation (A)
Change Compound State
Viable Deleted Purged
Hide Quit Help

Sequence-structure relationships

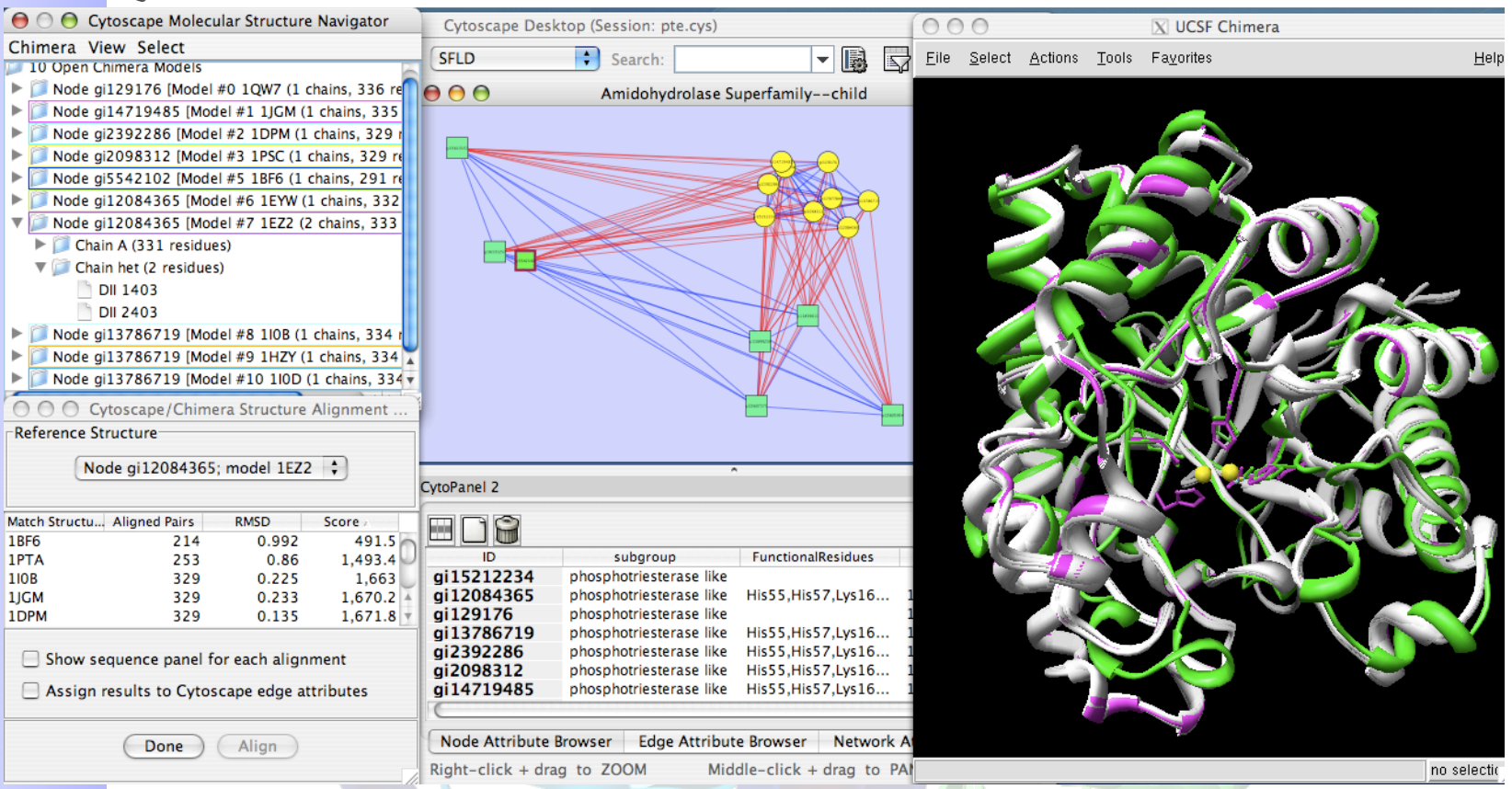



UCSF Chimera
File Select Actions Presets Tools Favorites Help
Command: repr sphere
Active models: 0 1 2 3 4 5 6 7 8 9 All
Volume Viewer
File Features
Data emd_1283.map Size (120,120,120) Step 1 1 1
Show surface mesh solid
Ctrl-click on histogram to add or delete thresholds
Range -0.159 - 0.587 Level 0.311 Color
Surface smoothing iterations 2 factor 0.5
Subdivide surface 1 times
Smooth mesh lines
Square mesh
Mesh line thickness 1 pixels
Dim transparent surface/mesh
Mesh lighting
Two-sided surface lighting
Light flip side for thresholds < 0
Show Unshow Center Orient Close Help
Viewing
Camera Side View Rotation Effects Lighting
View All View: right Resolution: high
Reset Restore Save Close Help

Multiscale representations



Structures in context



Questions?

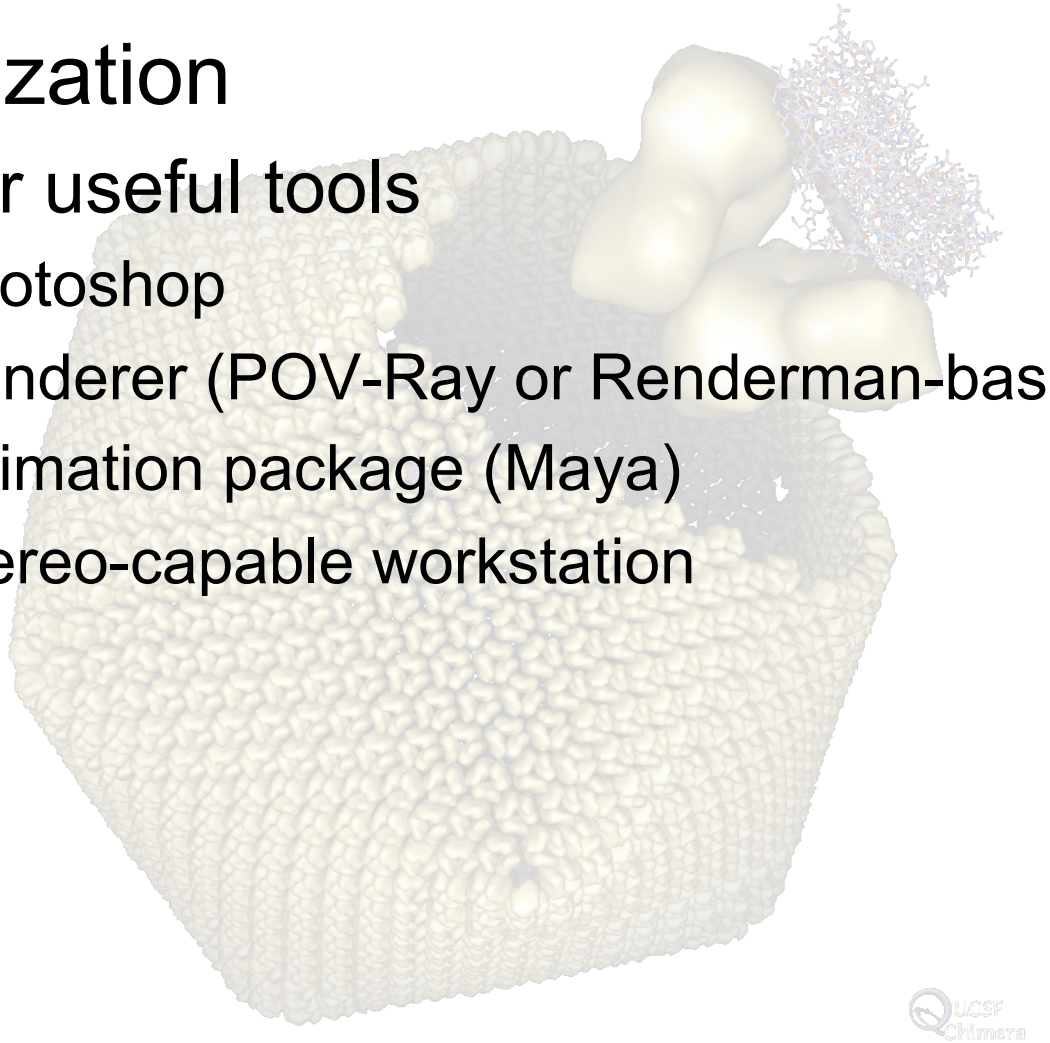
- Any other scenarios of interest?

Available Tools

- Visualization
  - "Full featured" academic packages
    - UCSF Chimera (http://chimera.ucsf.edu/)
    - PyMOL (http://pymol.sourceforge.net/)
    - VMD (http://www.ks.uiuc.edu/Research/vmd/)
  - Viewers
    - Jmol (http://jmol.sourceforge.net/)
    - RasMol/Chime (http://www.openrasmol.org/)
    - SwissProt PDB-Viewer (DeepView) (http://www.expasy.org/spdbv/)
    - RCSB Protein Workshop (http://www.rcsb.org/)

Available Tools

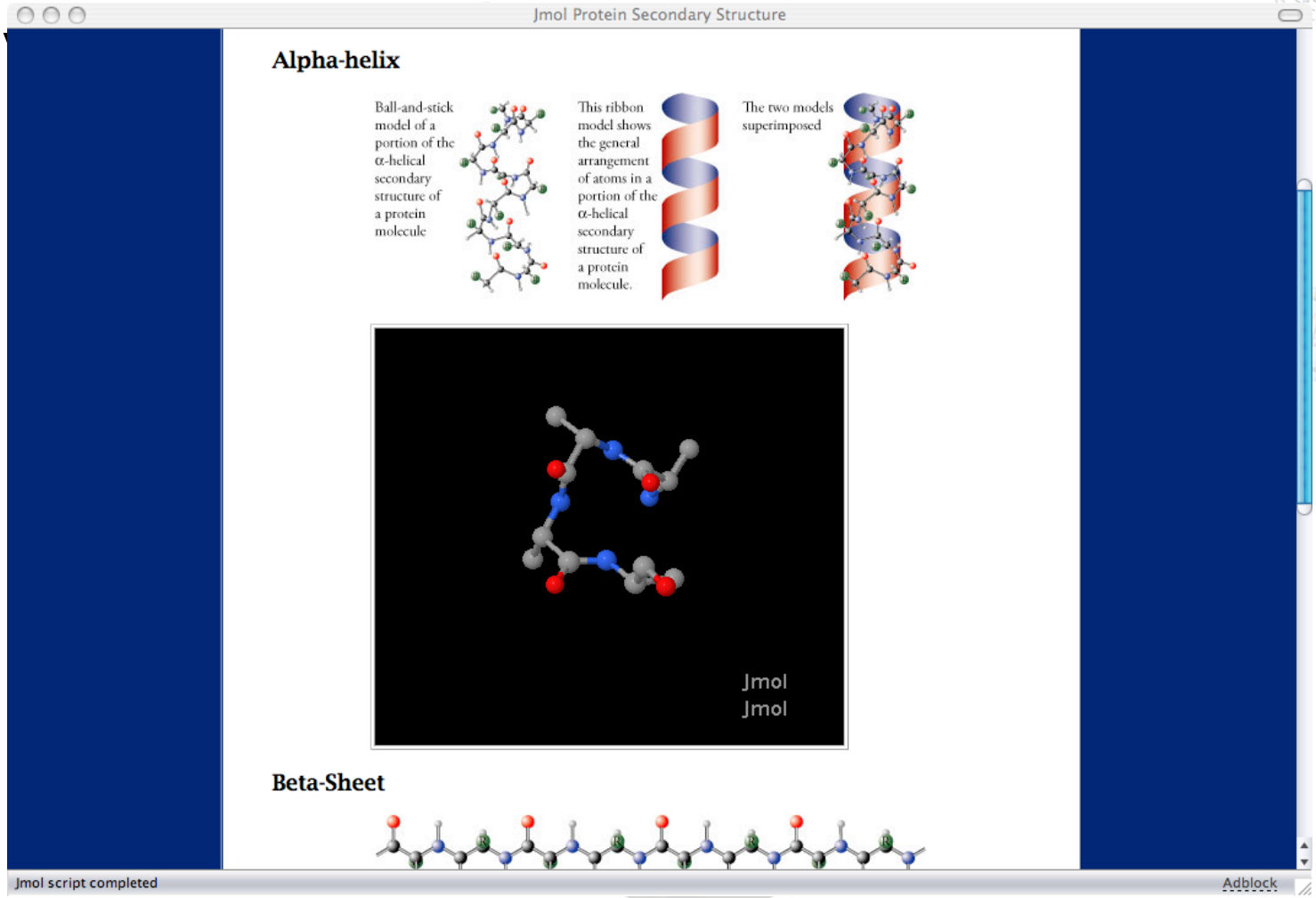
- Visualization
  - Other useful tools
    - Photoshop
    - Renderer (POV-Ray or Renderman-based)
    - Animation package (Maya)
    - Stereo-capable workstation



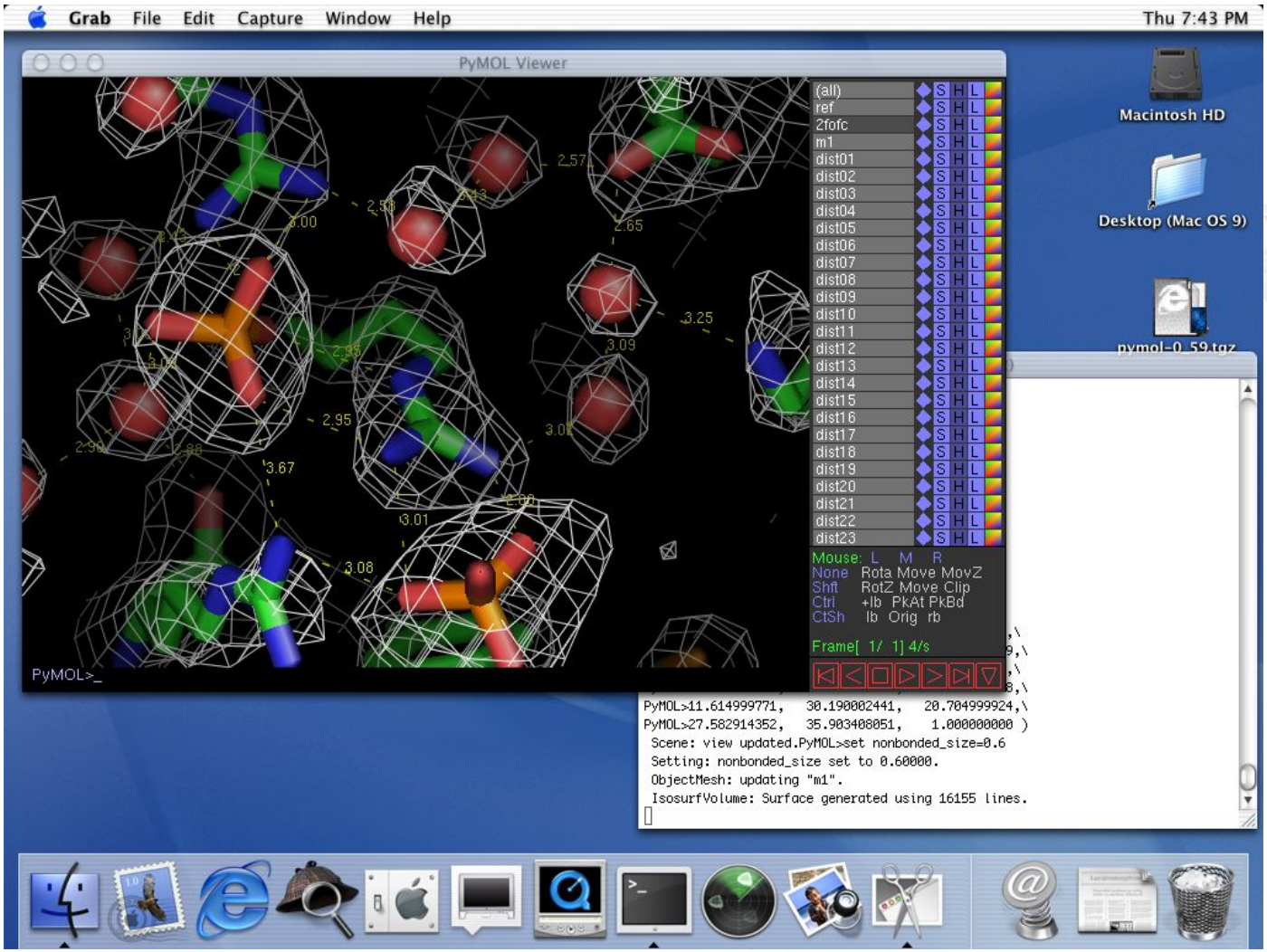
Available Tools

- Analytical tools (partial list)
  - PROCHECK (http://www.biochem.ucl.ac.uk/~roman/procheck/)
  - Structure-Function Linkage Database (http://sfld.rbvi.ucsf.edu/)
  - ExPASy (http://www.expasy.org/)
- Modeling tools
  - Amber (http://amber.scripps.edu/)
  - Charmm (http://www.charmm.org/)
  - NAMD (http://www.ks.uiuc.edu/Research/namd/)
  - Gaussian (http://www.gaussian.com/)
  - ModBase (http://modbase.compbio.ucsf.edu/)
  - Modeller (http://www.salilab.org/modeller/)
  - DOCK (http://dock.compbio.ucsf.edu/)
  - Many, many more (see http://cmm.info.nih.gov/)

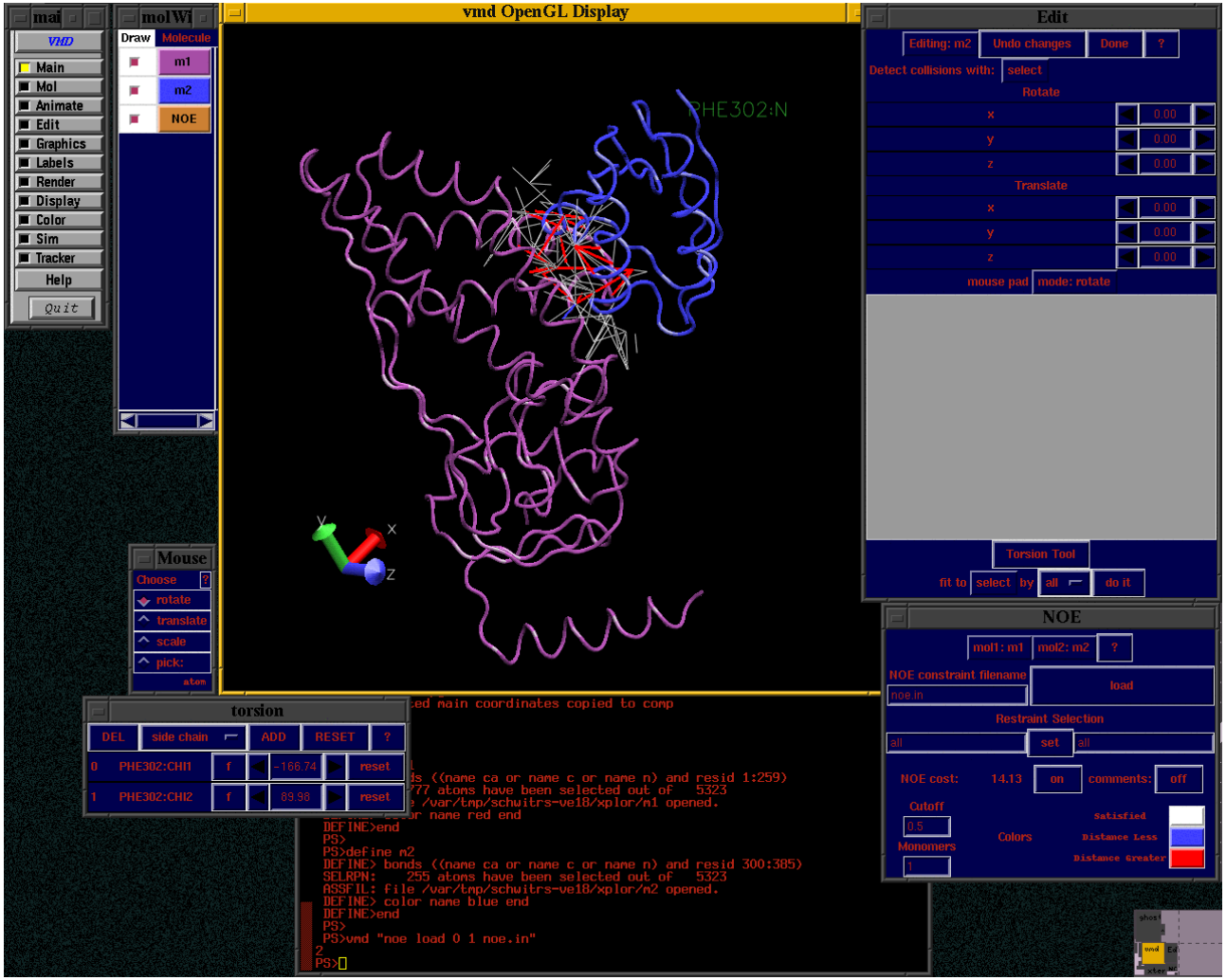
Comparison of Visualization Packages

- 

Comparison of Visualization Packages

- 

Comparison of Visualization Packages



Comparison of Visualization Packages

- Chimera
  - best-in-class for visualizing very large structures
    - multiscale extension
    - volume viewer
  - focus on extensibility, broad functionality
  - primarily analytical interface
  - familiar GUI interface (+command line)
  - scriptable
  - reasonable tools for publication & presentation
  - embedded ray tracer (POV-Ray)
  - excellent sequence/structure capabilities
  - reasonable interface to modeling programs

Comparison of Visualization Packages

- Caveats
  - Our focus is primarily on Chimera
  - We are not users of other packages
  - There is no “best” package for everything (in our opinion)
  - YMMV (Your Mileage May Vary)
    - What we think is easy, you may think is hard
    - What we think is hard, you may think is easy
  - Choosing the best package for you
    - Does what you need
    - Good documentation
    - Good support (either local or from the authors)

UCSF Chimera

- Target audience
  - Scientists who need to analyze and model molecular systems in some detail
  - Scientists who want to develop new analytical methods
  - Scientists or educators who wish to communicate biological concepts visually
- Organization
  - Core features
  - Additional tools

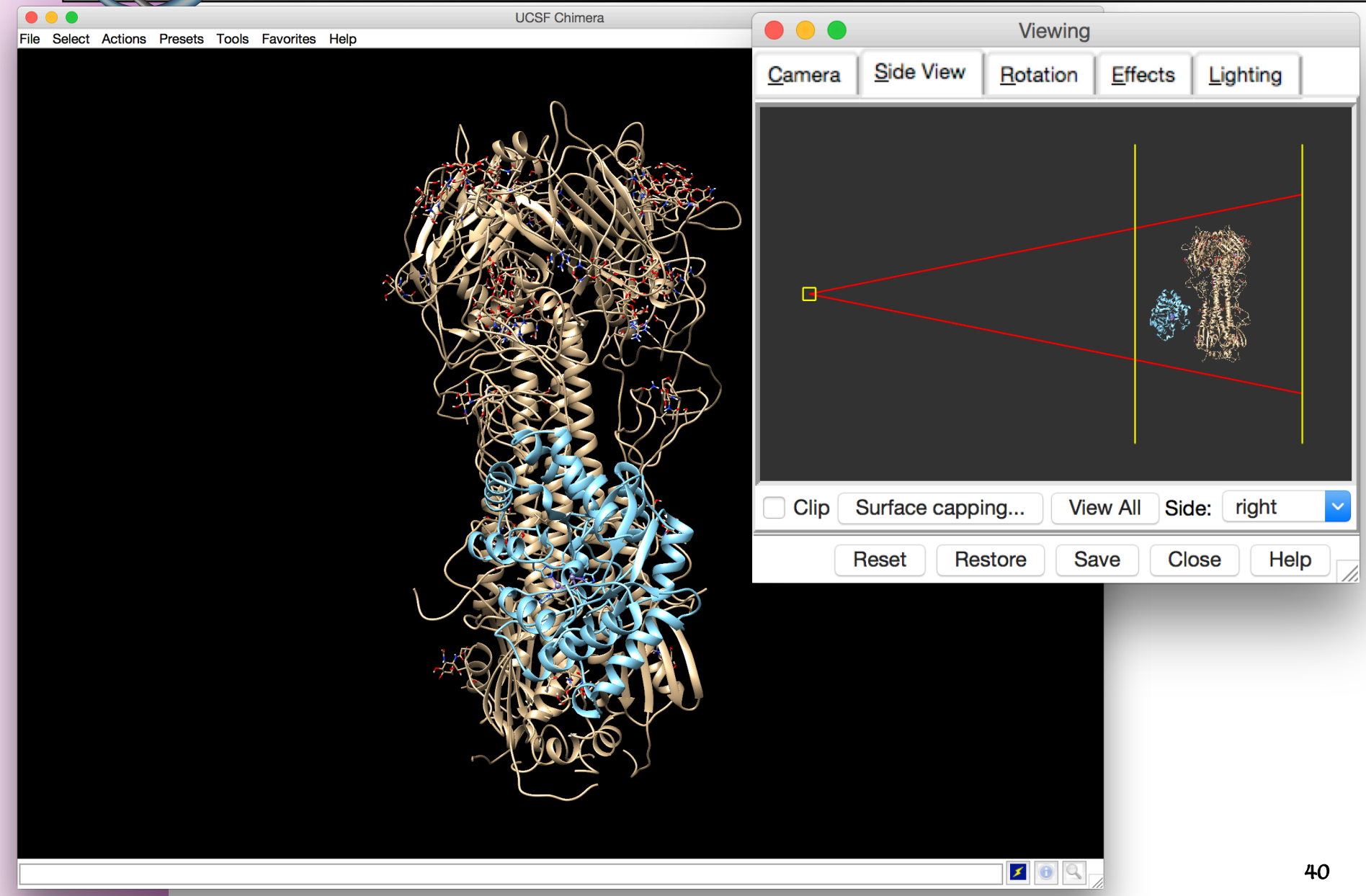
Chimera Core Features

- Concepts
  - Graphical manipulation
  - Chemical knowledge
    - Hierarchy: Model→Chain→Residue→Atom
    - Attributes available at model, residue, and atom levels
  - Selection - Action
  - GUI/Command-line equivalence
    - For core, not necessarily extensions

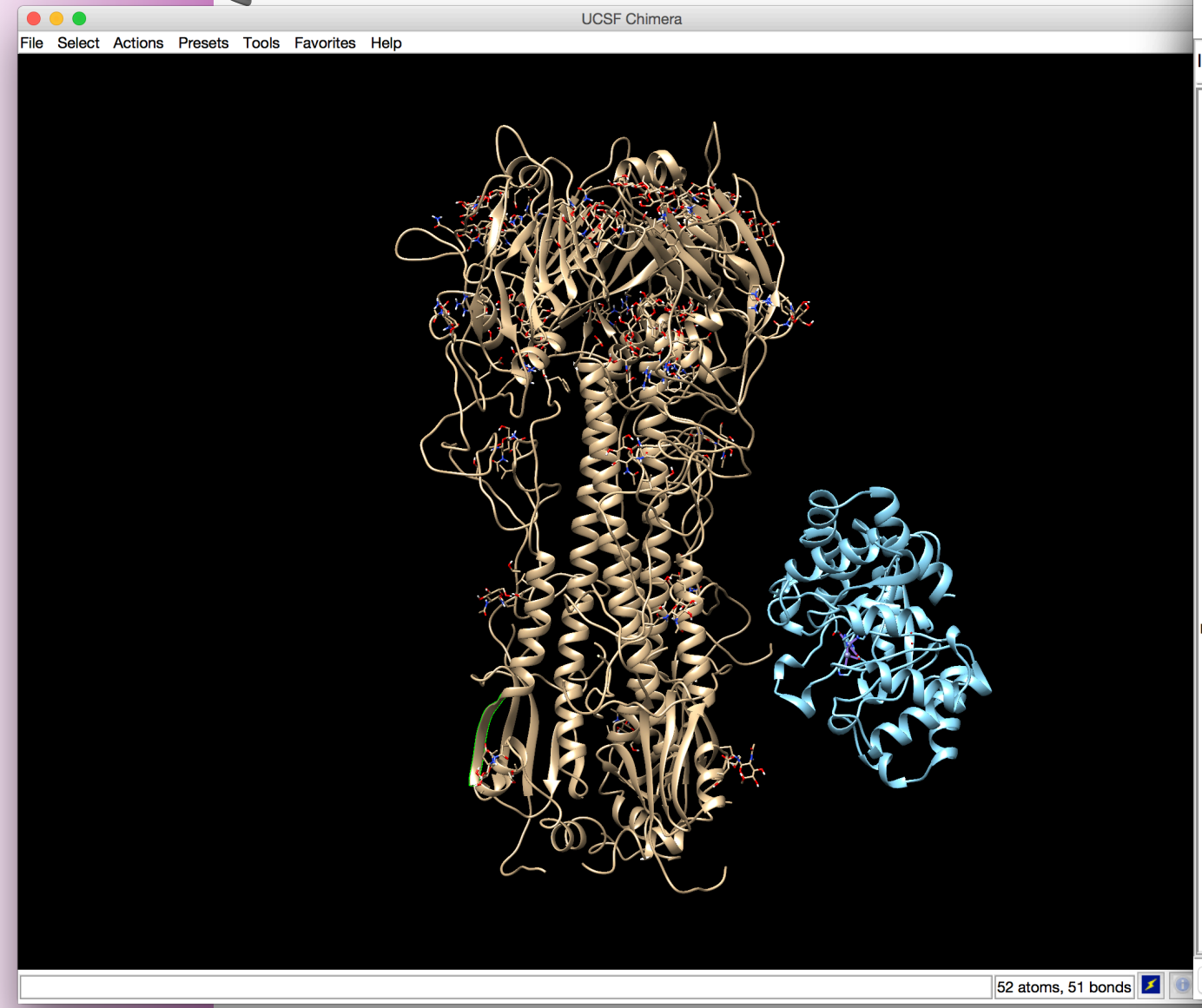
Core Features (cont.)

- Using the mouse
  - Pointer over atom
    - “Tooltip” with atom and residue information
  - Left-button
    - X-Y Rotation (on virtual sphere)
    - Z Rotation (outside of virtual sphere)
  - Middle-button
    - X-Y Translation
  - Right-button
    - Scale
  - Control+
    - Left-button: select (click or drag)
    - Middle-button: Z translation

Core Features (cont.)



Core Features (cont.)



Inspect Selection

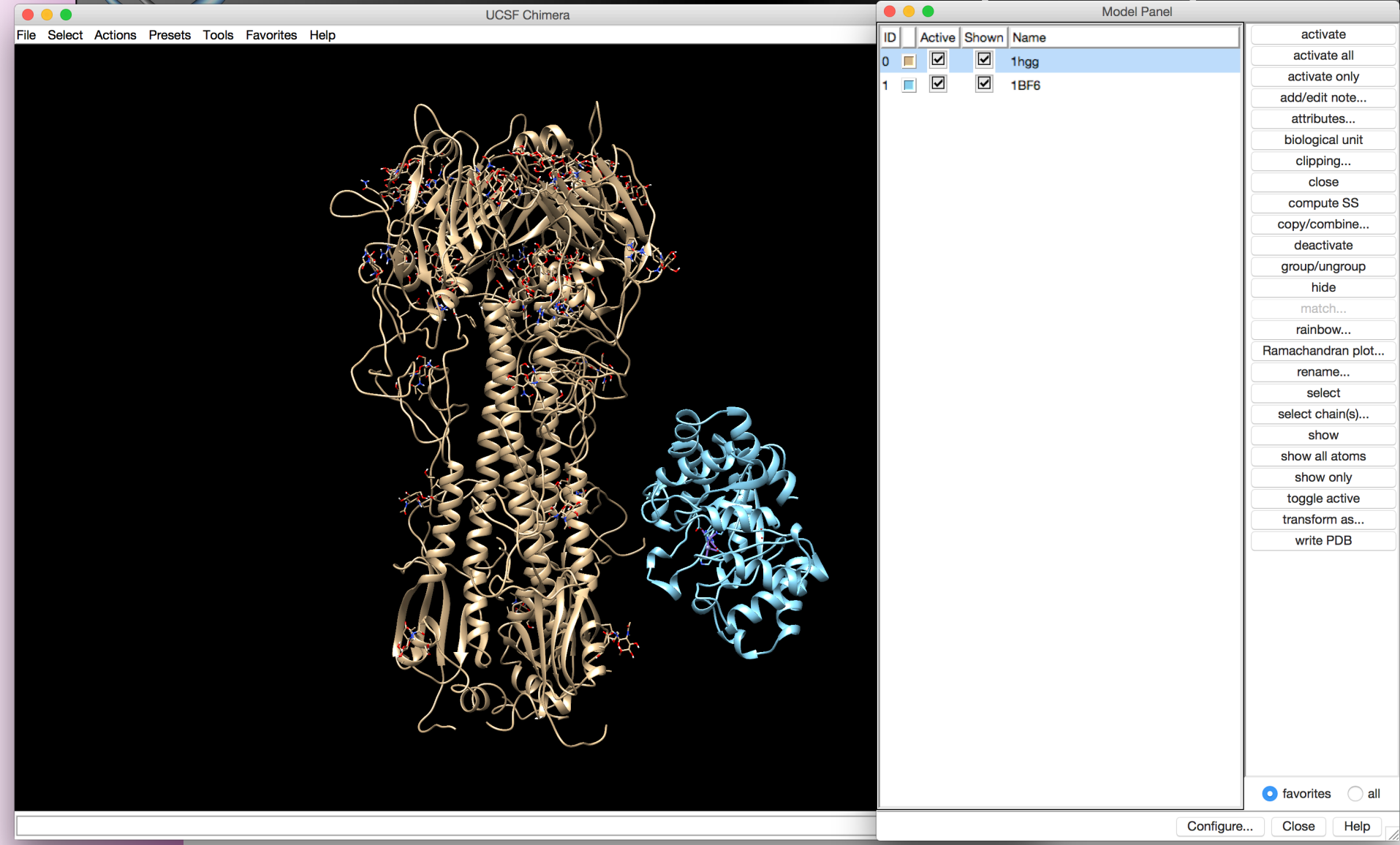
Selected:
1 molecule model
7 residues
52 atoms
51 bonds

Inspect: Molecule model

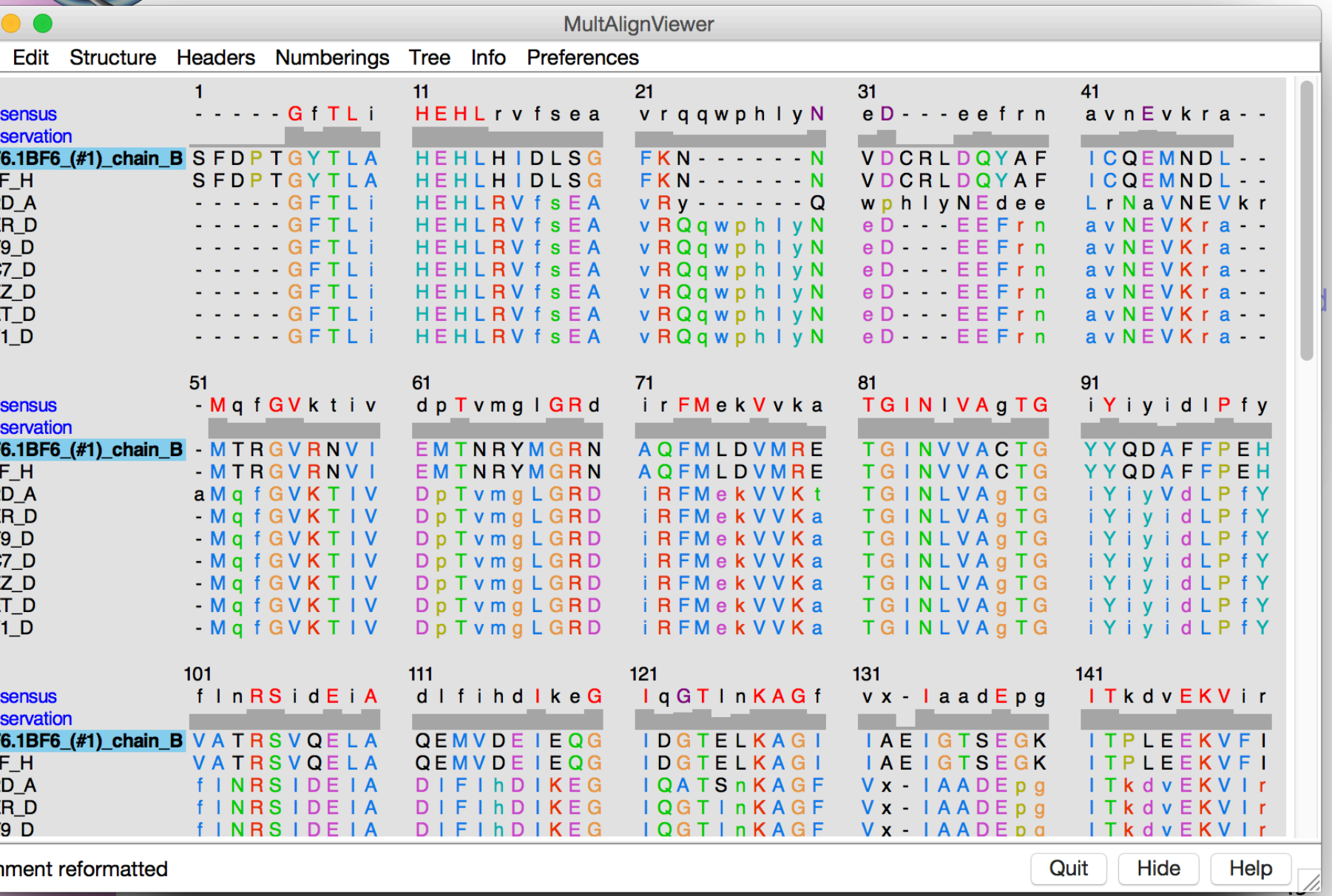
active:	true
aromatic color:	No
aromatic display:	false
aromatic line style:	
aromatic ring style:	disk
auto-chaining:	on
ball scale:	0.25
color:	
displayed:	true
line style:	
line width:	1.0
residue label positioning:	centroid
ribbon (cardinal) smoothing:	none
ribbon (cardinal) stiffness:	0.8
ribbon hides backbone atoms:	true
ribbon inside color:	No
ribbon spline:	B-spline
silhouette:	true
stick scale:	1.0
surface color:	No
surface opacity:	-1.0
vdw density:	5.0
vdw dot size:	1.0

Write List... Write PDB... Close Help

Core Features (cont.)



Core Features (cont.)

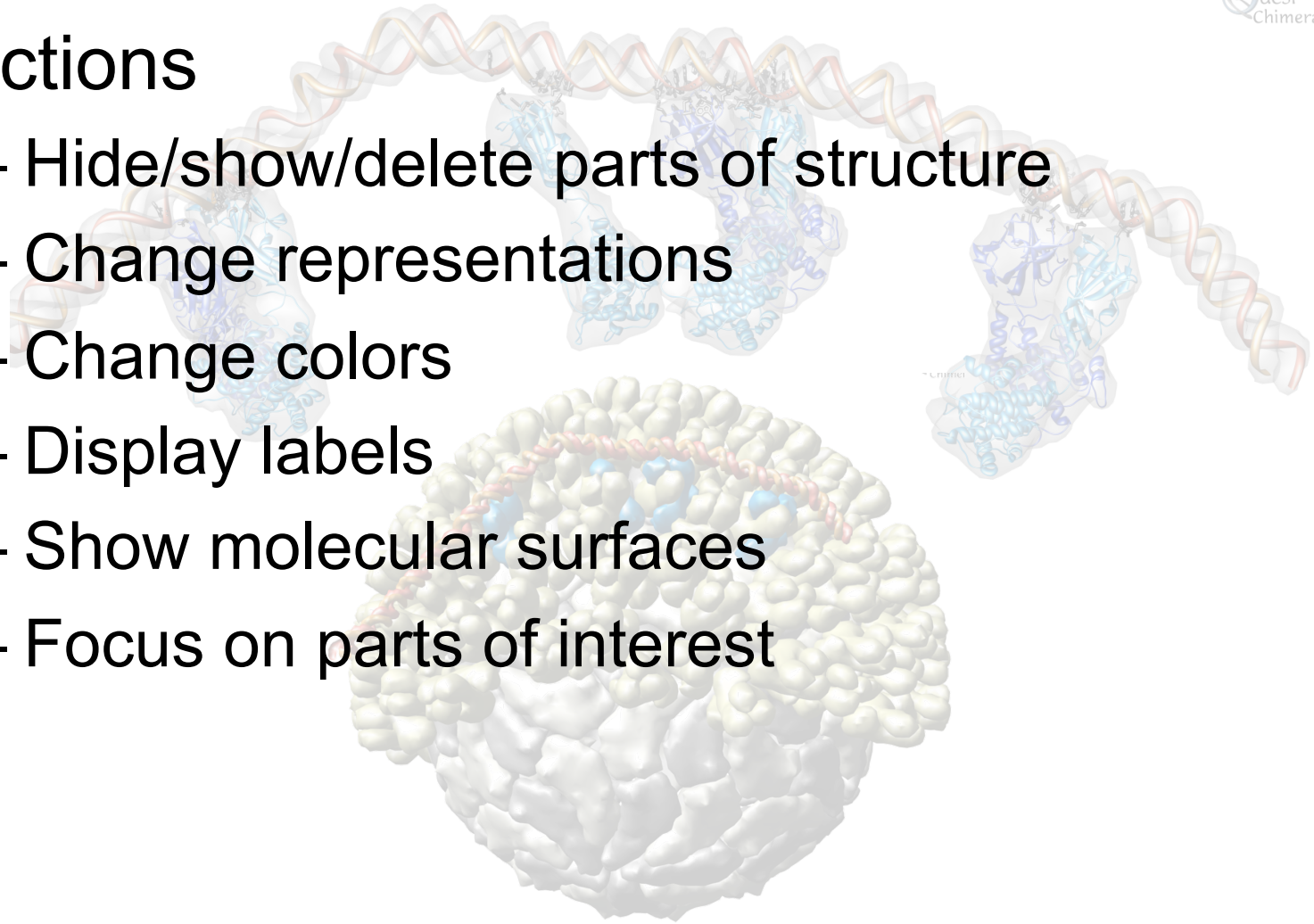


Core Features (cont.)

- Selection methods
  - Using mouse
    - Control-click and control-drag
    - Shift-control-click and shift-control-drag to add to selection
  - By atom and residue names and types
  - By higher order structure
    - e.g., chains, ligands, solvent
  - By spatial location
    - e.g., within some distance of another selection
  - By attribute values
    - e.g., temperature factor, occupancy
  - Can extend any selection with up-arrow: ↑
  - NOTE: by default, if nothing is selected, everything is selected

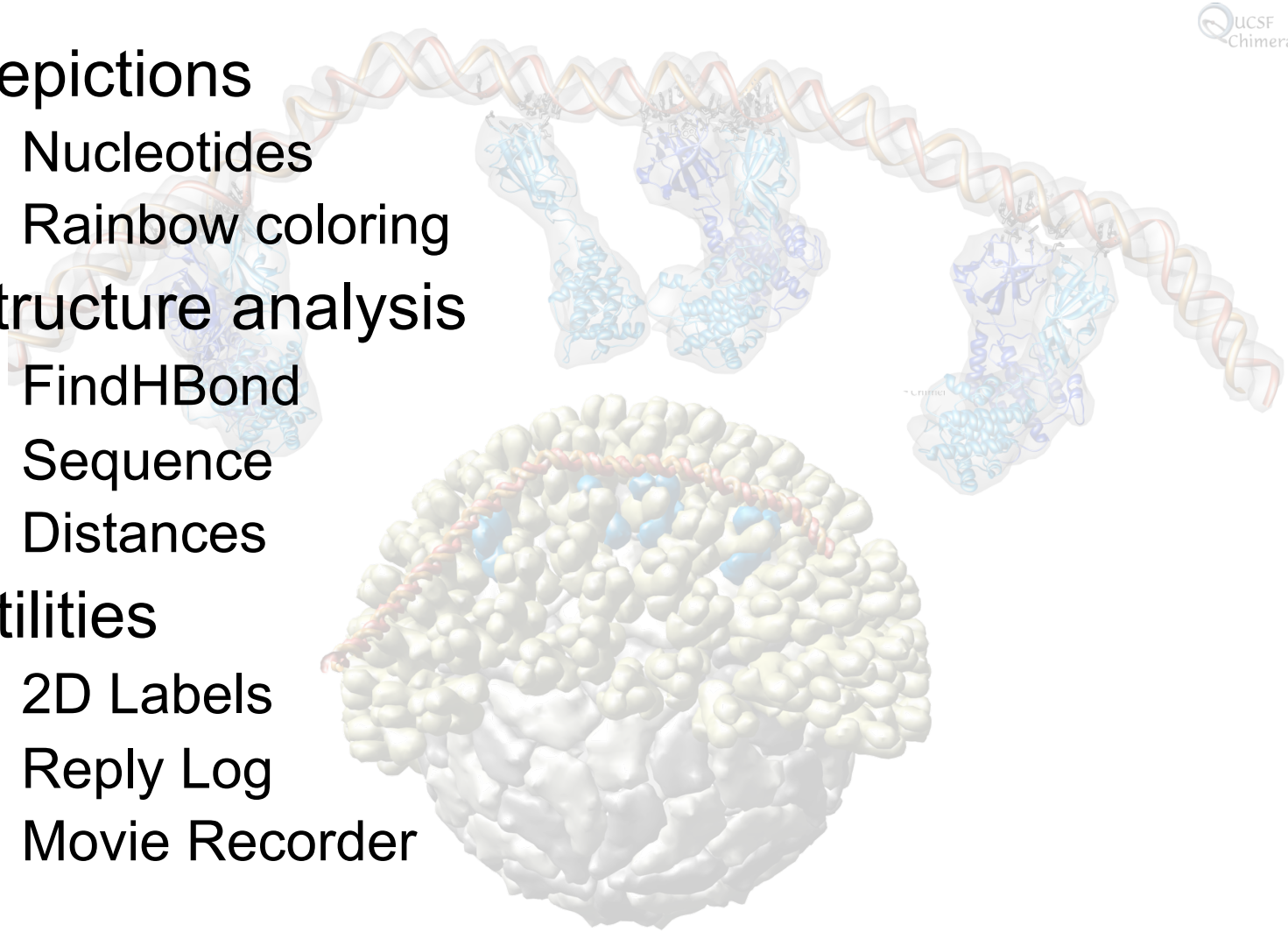
Core Features (cont.)

- Actions
  - Hide/show/delete parts of structure
  - Change representations
  - Change colors
  - Display labels
  - Show molecular surfaces
  - Focus on parts of interest



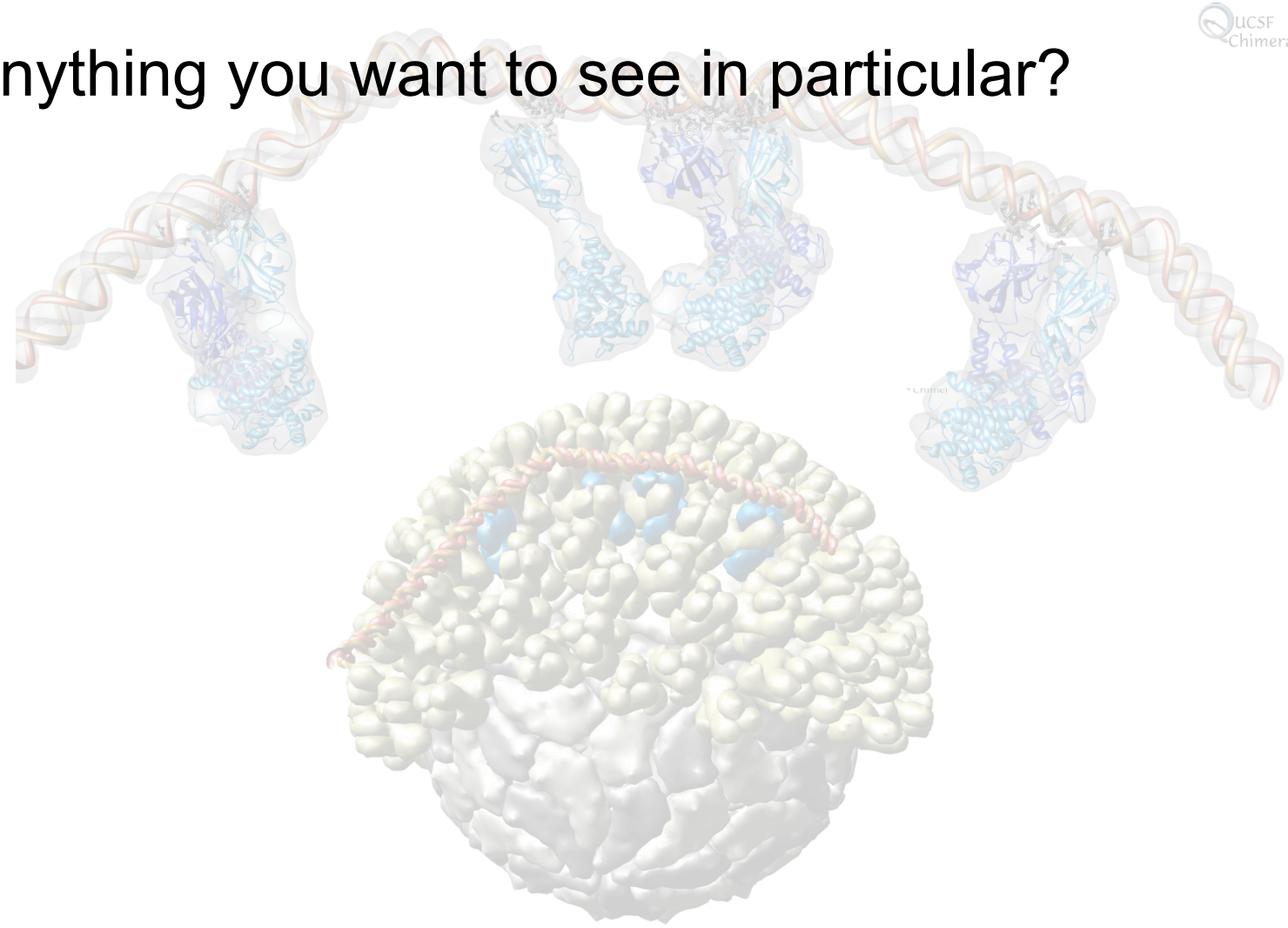
Commonly used tools

- Depictions
  - Nucleotides
  - Rainbow coloring
- Structure analysis
  - FindHBond
  - Sequence
  - Distances
- Utilities
  - 2D Labels
  - Reply Log
  - Movie Recorder



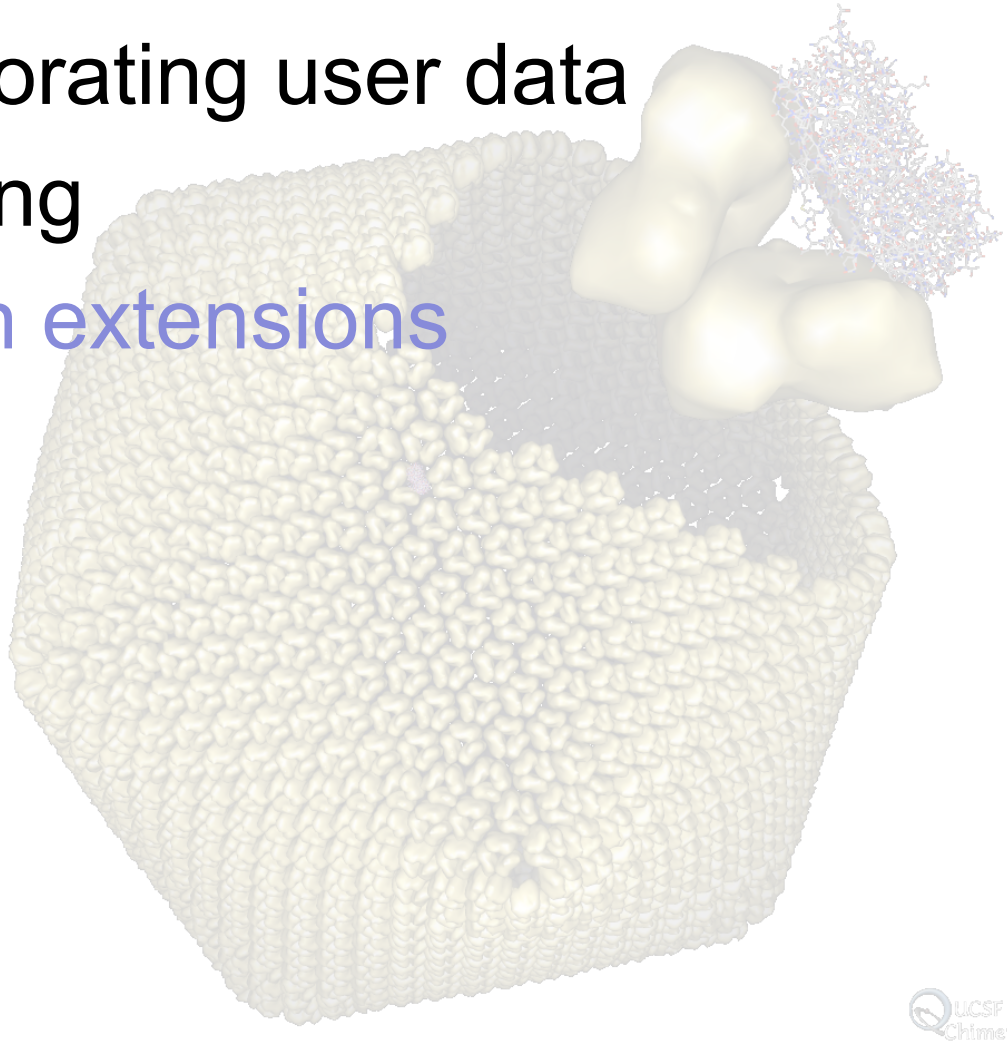
Questions?

- Anything you want to see in particular?

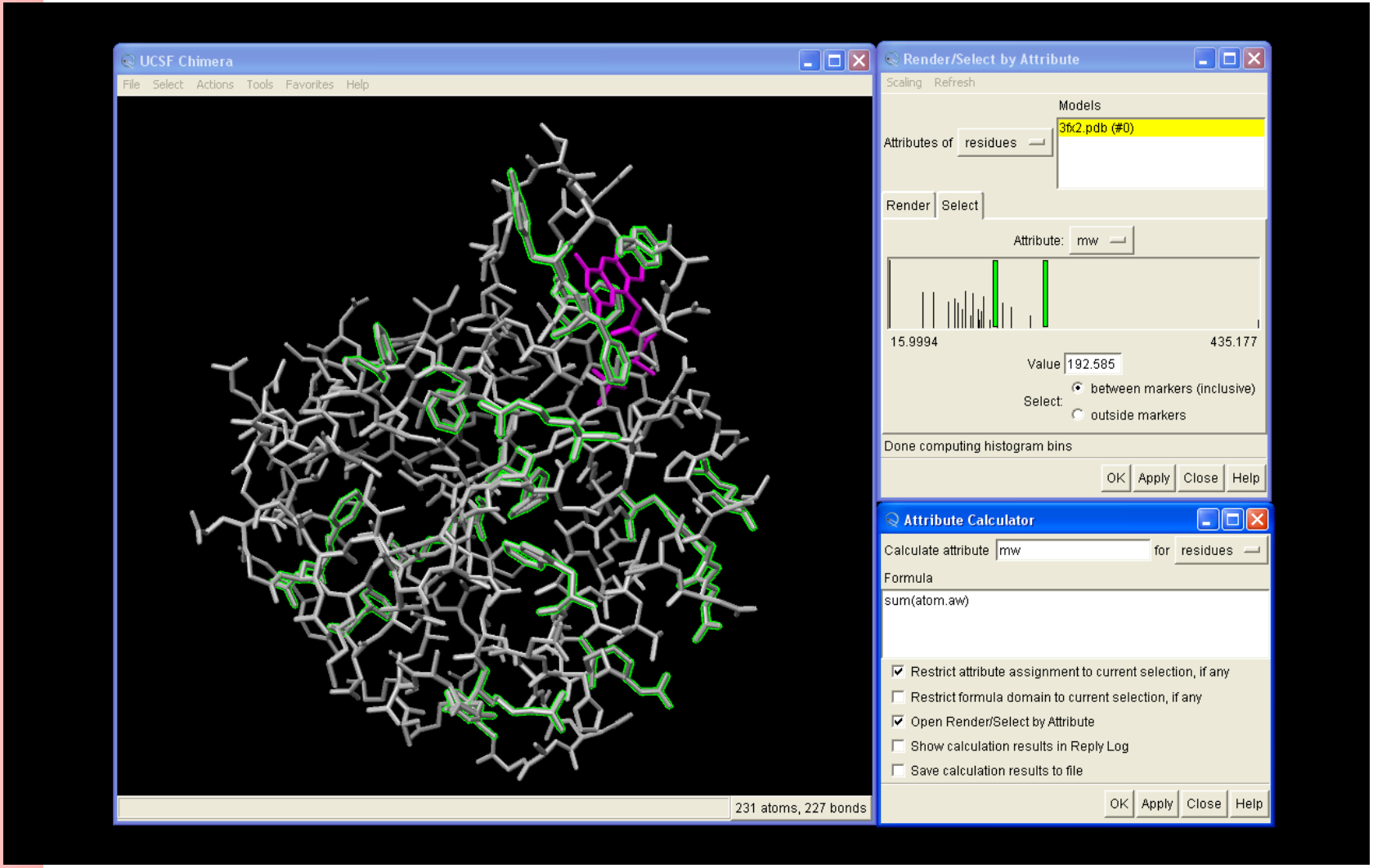


Extending Chimera

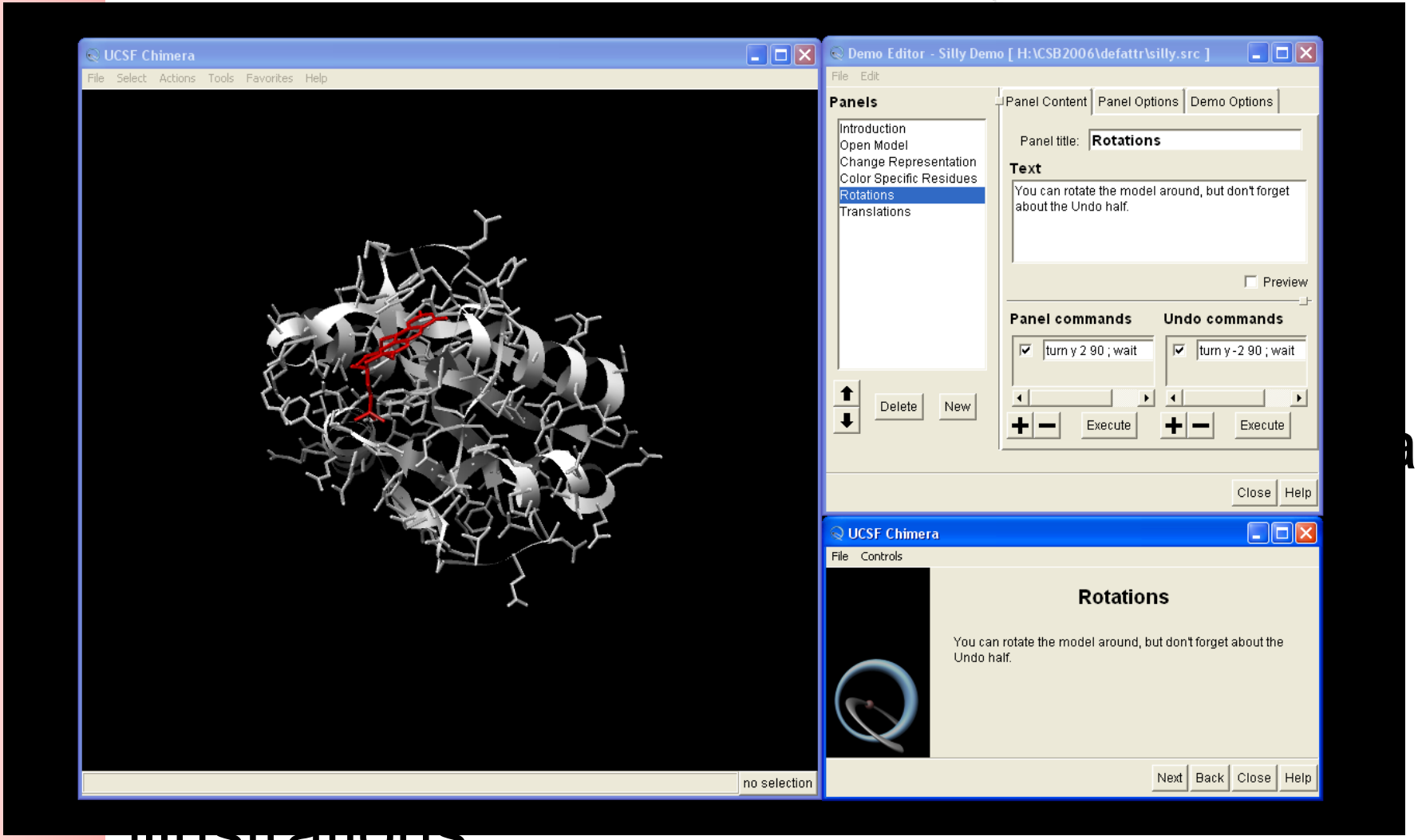
- Incorporating user data
- Scripting
- Python extensions



Incorporating user data



Scripting



illustrations

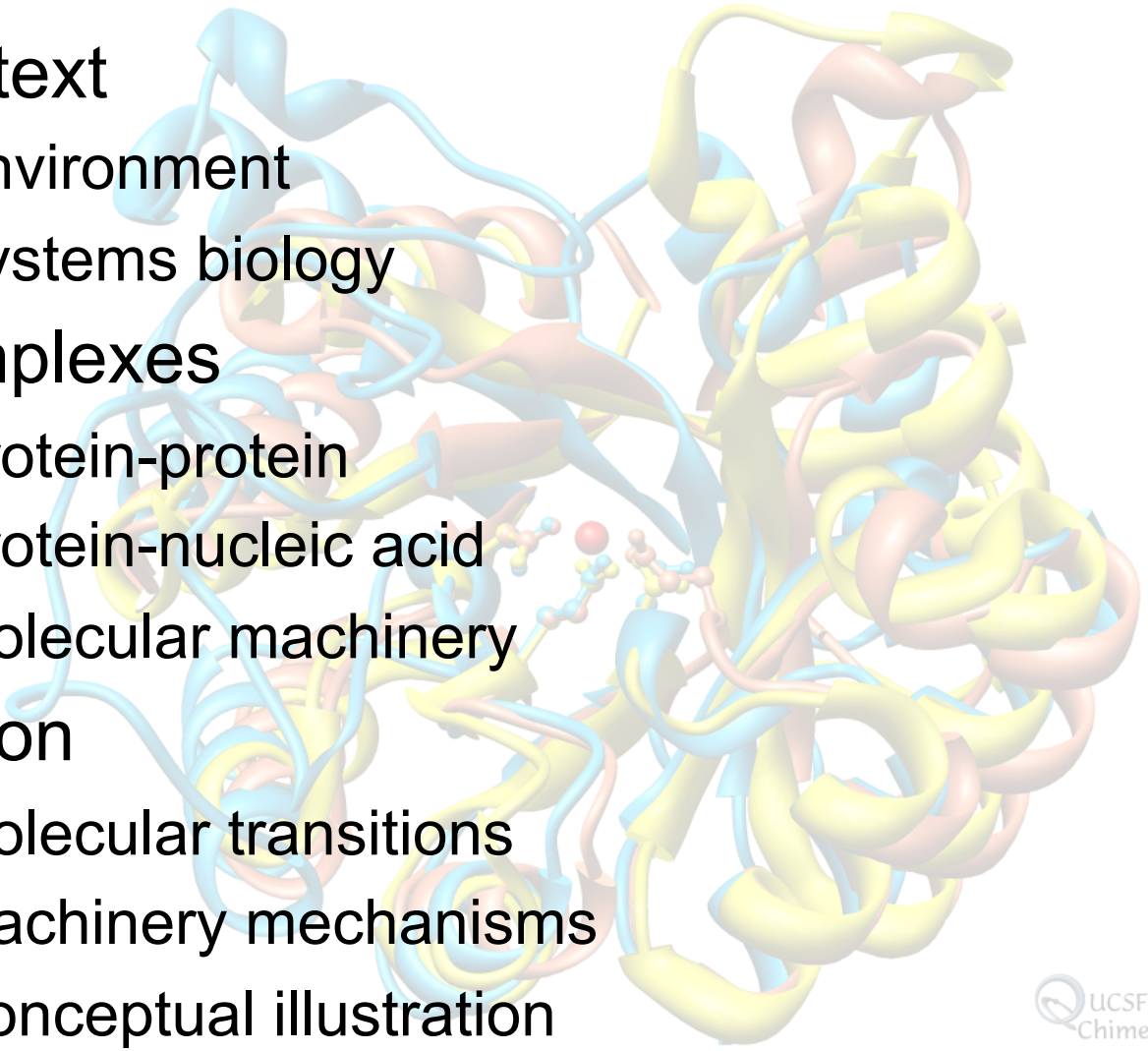
Questions?

Chimera Recent Additions

- Modeling
  - Rotamers
  - Fetch modeled structures from ModBase
  - Web service interface to Modeller and IMP
  - Web service interface to BLAST
- Animation and illustration
  - Movies can now be rendered with POVray
  - Scenes and Storyboards
- Volume visualization
  - New tools for tomographic data
- Systems biology
  - *structureViz:* links Cytoscape to Chimera

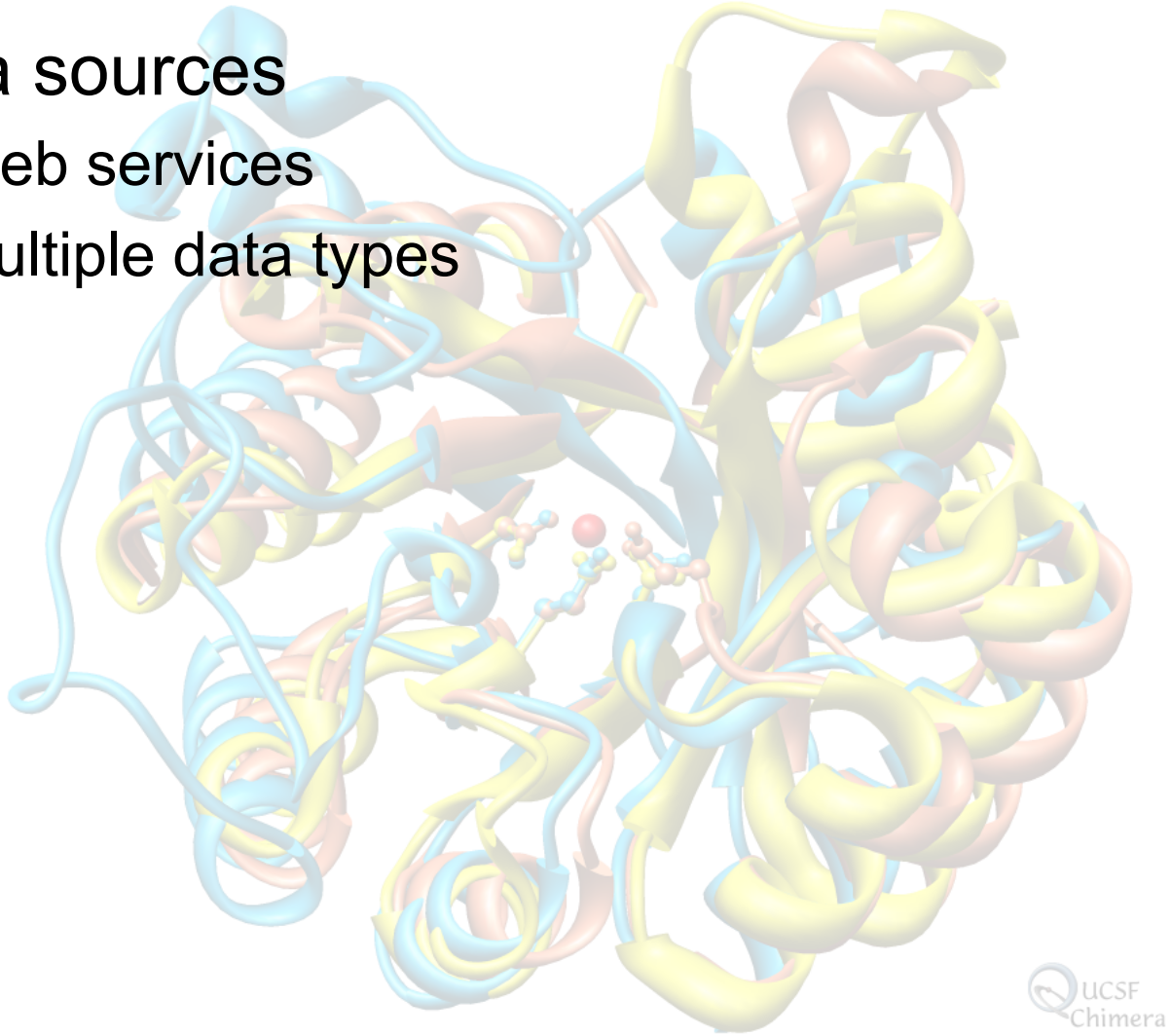
Visualization Directions

- Context
  - Environment
  - Systems biology
- Complexes
  - Protein-protein
  - Protein-nucleic acid
  - Molecular machinery
- Motion
  - Molecular transitions
  - Machinery mechanisms
  - Conceptual illustration



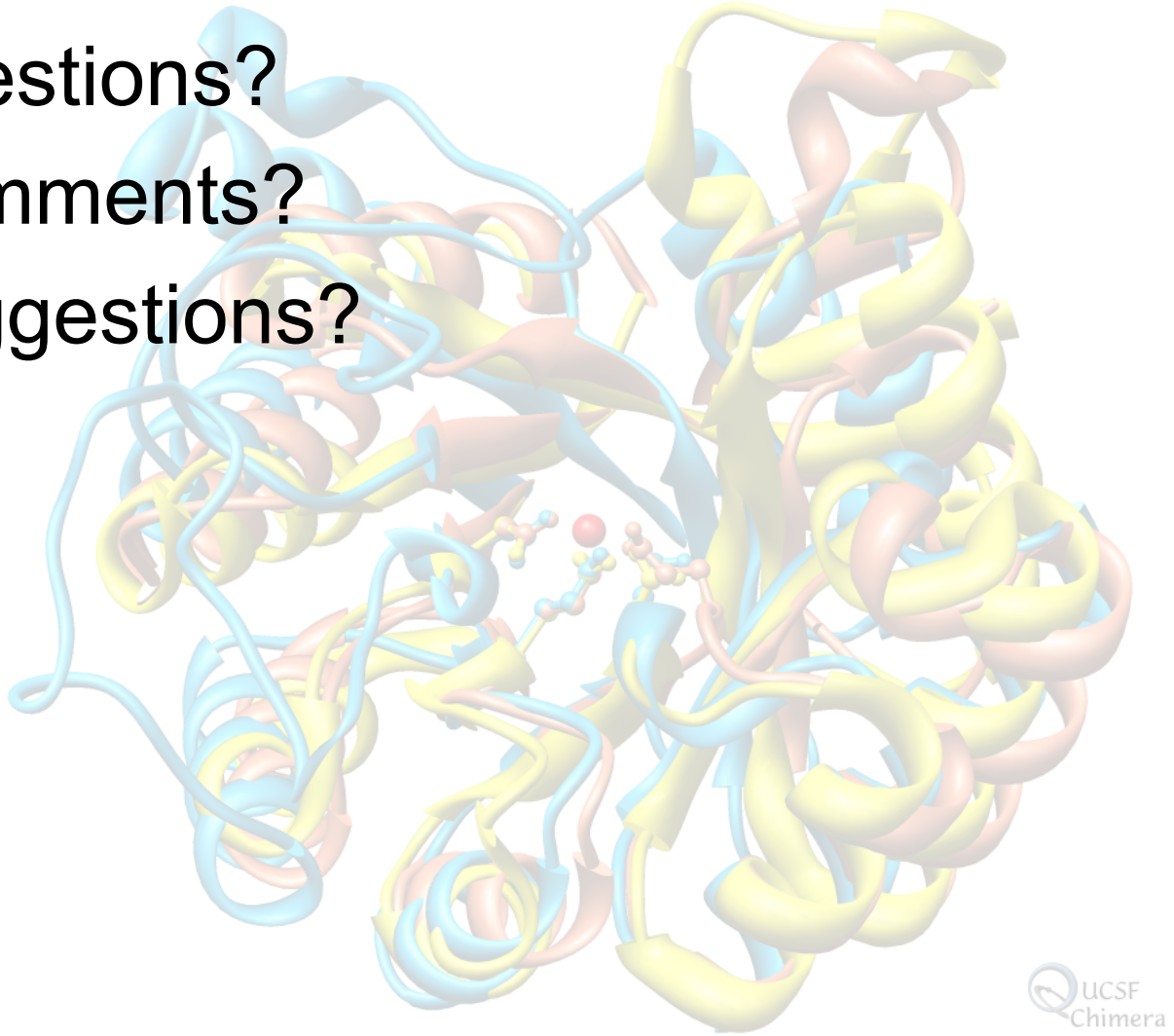
Visualization Directions

- Data sources
  - Web services
  - Multiple data types



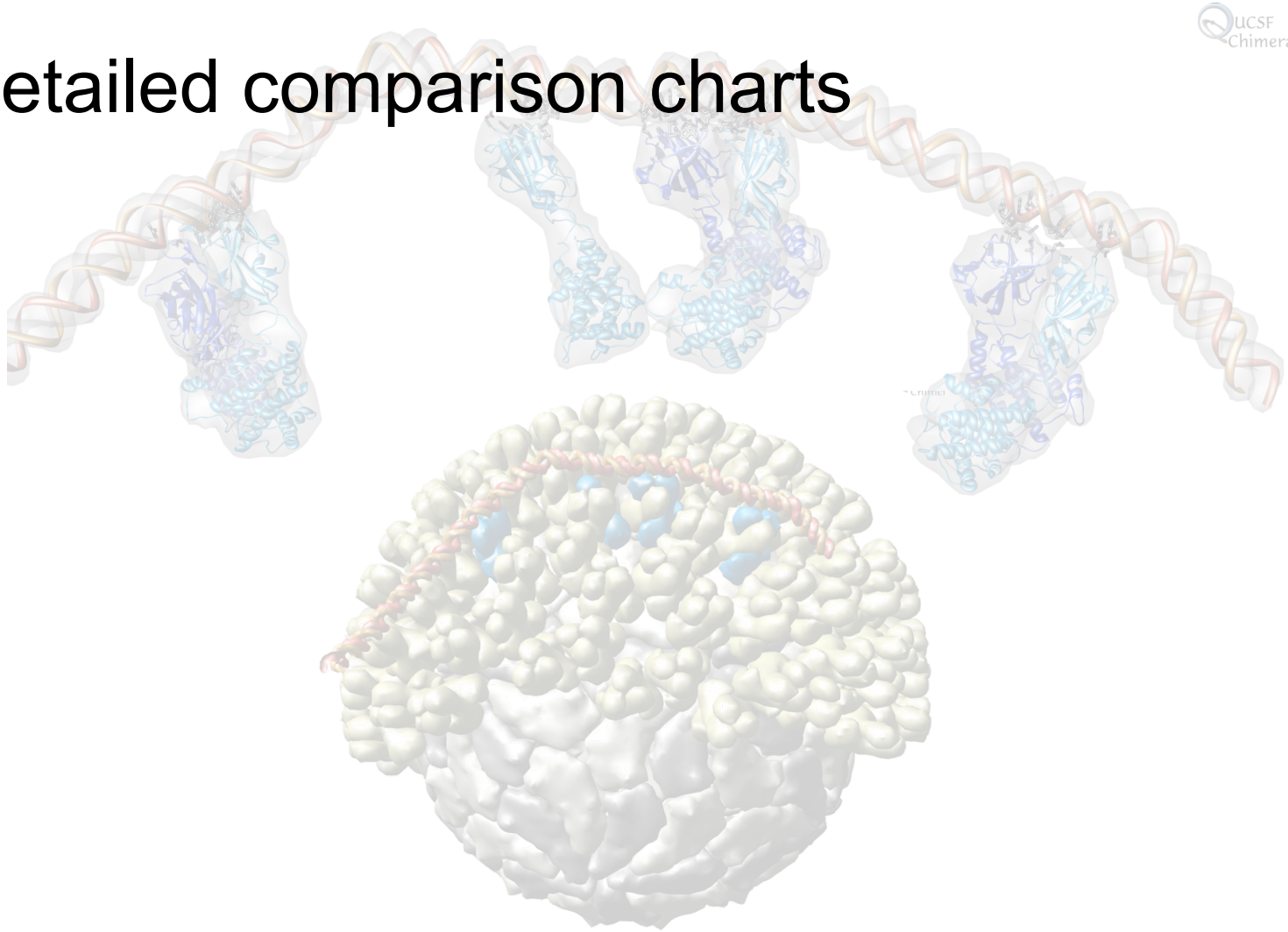
The End

- Questions?
- Comments?
- Suggestions?



Backup Slides

- Detailed comparison charts



feature	Chimera 1.2199	RasMol 2.7.3	Jmol 10.2	PyMol 0.99	Deep View 3.7	VMD 1.8.4	DINO 0.9.1	Molmol 2K.2
PDB	I/O	I/O	I	I/O	I/O	I/O	I/O	I/O
Mol2	I/O	I	-	I	-	I/O	-	I
CIF/mmCIF	-	I	I	-	-	-	-	-
Web app	-	PE	+	-	-	-	-	-
sessions	+	-	-	+	+	+	-	+
color editing	+	-	-	+	+	+	-	+
transparency	+	-	+	+	SG	SD	+	-
molecular surfaces	+	+	+	+	+	+	DR	+
interface surfaces	+	-	-	-	-	+	-	-
solid clipped surface	+	+	-	-	-	PV	+	-
arbitrary clipping	+	-	-	-	-	+	+	-
movable labels	2D	-	-	+	-	-	-	+
special nucleic disp	+	-	-	+	-	+	+	+
geometric objects	+	-	+	+	-	+	-	+
high-quality images	+	-	-	+	-	-	+	+
ray-tracing support	+	+	+	++	+	+	+	+
stereo	+	+	+	+	+	++	+	+
multiscale/low-res	+	-	-	-	-	LR	-	SH
volume isosurfaces	++	-	+	+	+	+	+	+
transparent volumes	+	-	-	-	-	-	-	-
edit/write vol data	+	-	-	-	-	-	-	-
auto fit to density	+	-	-	-	-	-	-	-
measure volume	+	-	-	-	-	-	-	-

feature	Chimera 1.2199	RasMol 2.7.3	Jmol 10.2	PyMol 0.99	Deep View 3.7	VMD 1.8.4	DINO 0.9.1	Molmol 2K.2
atom type ident	+	-	-	-	-	-	-	-
select AA category	+	+	FG/ST	-	+	+	+	-
H addition	+	-	-	SA	SA	SM	-	SR
H-bond ident	++	+	FG	+	+	+	-	+
charge assignment	SR	-	-	SR	SA	SM	-	SR
ESP calculation	ID/DR	CL	-	AP/DR	CL/PB	AP/DR	DR	PB
AA rotamer library	-	-	-	+	+	-	-	-
energy minimization	-	-	-	-	+	NM	-	-
render by attribute (e.g. color bfactor)	++	+	+	+	+	+	+	+
user-defined attribs	+	-	-	-	-	-	-	-
seq align viewer	++	SP	SP/ST(I)	SP	IG	SP/IG	-	-
seq-based match	+	-	-	+	+	-	-	-
struct-based match	+	-	-	SP	+	+	-	-
seq align from match	+	-	-	-	PW	+	-	-
MD playback	+	-	PO	+	-	++	+	PO
view docking results	+	-	-	-	-	-	-	-
context/balloon help	+	-	+	-	-	-	-	+
user docs	++	+	+	OD	+	+	+	++
programming docs	+	-	-	-	+	+	-	-
extensibility	+	-	+	+	-	+	-	-
source distrib	+	+	+	+	-	+	-	+
platforms	W/M/U	W/M/U	W/M/U	W/M/U	W/M/U	W/M/U	M/U	W/U

I input
O output
- feature not present
+ feature present
++ feature present and comparatively extensive or sophisticated
PE Protein Explorer { #52} is a Web application based on RasMol
SG only surfaces and only on Silicon Graphics
SD “screen door” transparency
DR displays results from other programs
PV non-interactive solid-color clip available via POV ray-tracer
2D arbitrary labels can be created and moved in the plane of the screen
SH only certain shapes (rectilinear boxes, spheres, ellipsoids)
FG via FirstGlance in Jmol (http://firstglance.jmol.org)
ST via STING { #56} (http://www.cbi.cnptia.embrapa.br/SMS/); (I) = Windows/Intel Linux only and only alignments from STING-related databases
SA residues with topology files in the distribution (standard amino acids and a few others)
SM small structures only
SR residues in the AMBER 94 library { #77} (used in the ff94-ff99 versions of the force field)
ID interface to DelPhi { #75; #76} (obtained separately)
CL Coulomb’s law calculation
PB Poisson-Boltzmann calculation
AP interface to Adaptive Poisson-Boltzmann Solver { #74} (obtained separately)
NM via input to/output from NAMD { #73}
SP STRAP plug-in { #49}, http://www.charite.de/bioinf/strap/ (Java); according to the author, interfacing to RasMol and VMD may only work on Unix, and only PyMol shows structure superpositions from STRAP (see http://www.charite.de/bioinf/strap/pymol.html)
IG internally generated alignments
PW pairwise comparisons only; adjusts one sequence relative to one other
PO PDB-format input only
OD out-of-date user manual supplemented with mailing list and volunteer-provided tutorials and wiki
platforms: W Windows, M Macintosh, U Unix

Backup

RasMol { #53; #54} : http://www.bernstein-plus-sons.com/software/rasmol/
Jmol { #32}: http://jmol.sourceforge.net/
PyMol { #29}: http://pymol.sourceforge.net/
Deep View (Swiss-Pdb Viewer) { #51}:http://ca.expasy.org/spdbv/
VMD { #24}: http://www.ks.uiuc.edu/Research/vmd/
DINO { #55}: http://www.dino3d.org/
Molmol { #48}: http://hugin.ethz.ch/wuthrich/software/molmol/