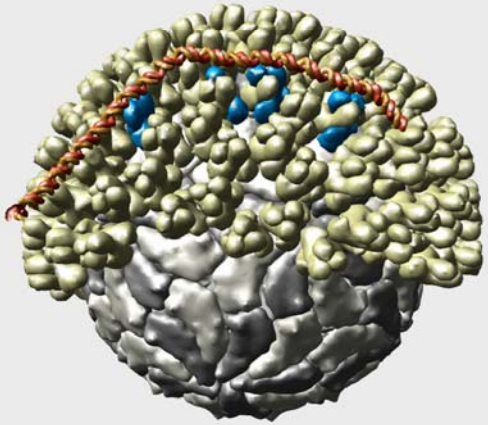
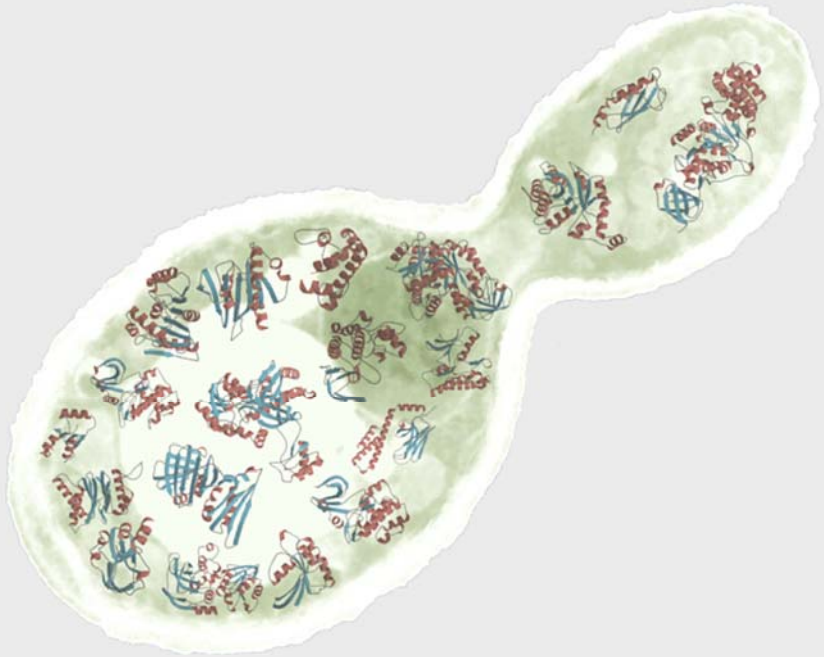
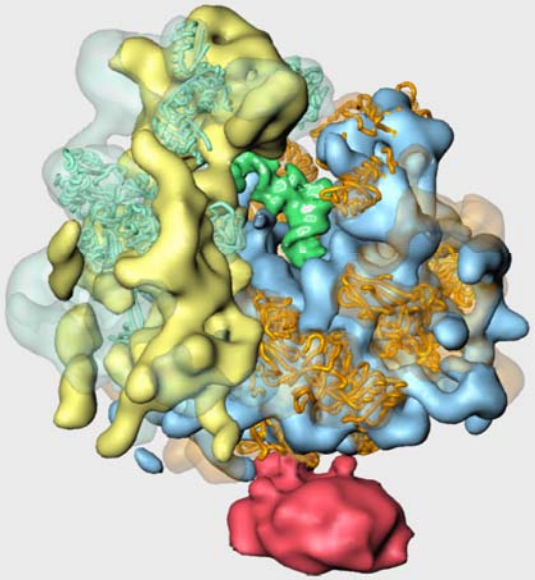
# Multiscale Structural Visualization with UCSF Chimera







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UCSF

# Outline

Today:

- Chimera overview
- Introductory demo
- Bluetongue virus demo

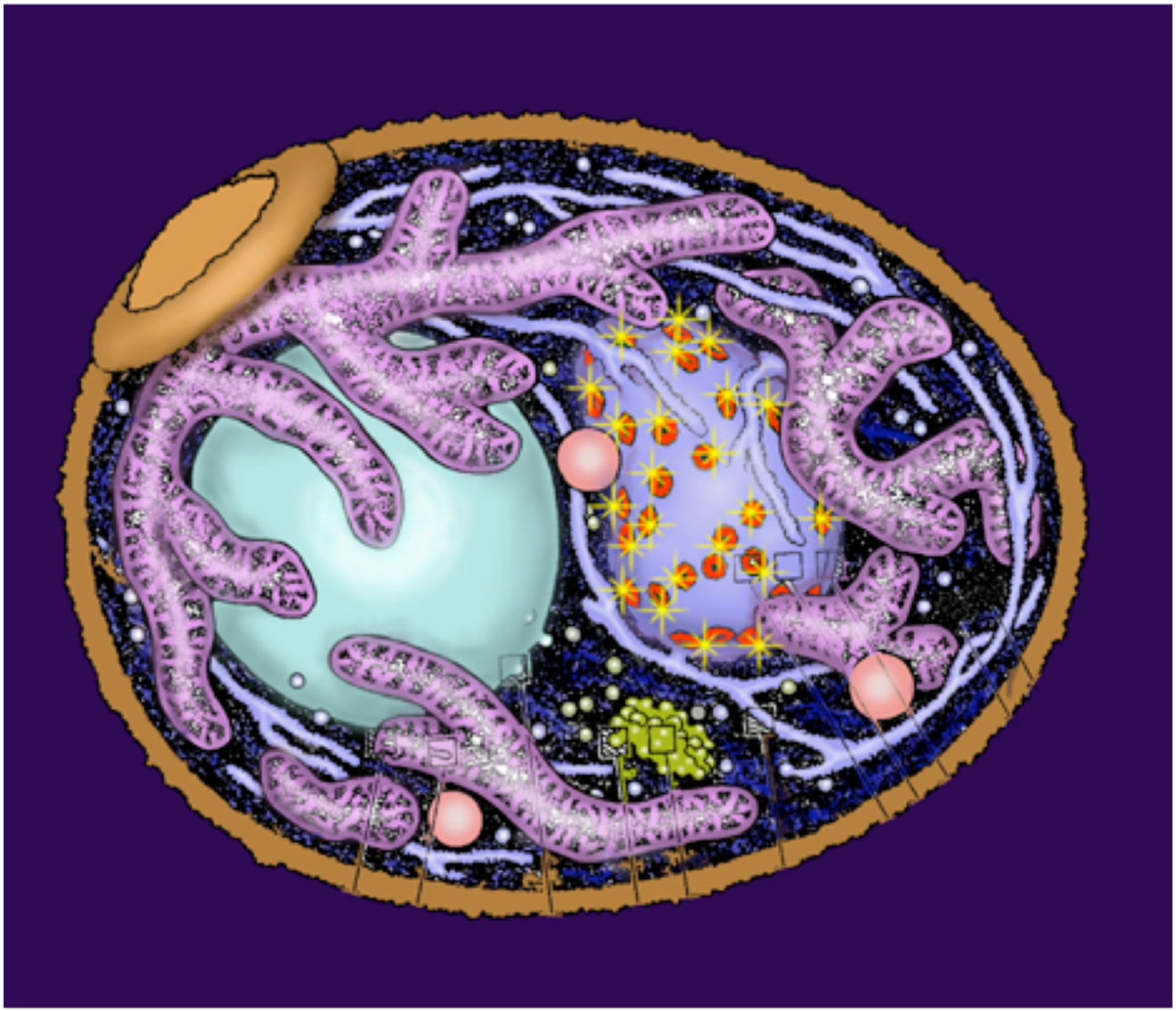
Tomorrow - Tom Goddard "hands-on" exercise:

- Chimera Volume Viewer extension

Copy of this presentation available at:

- www.cgl.ucsf.edu/home/tef/talks/EMANworkshop.pdf

# Cell

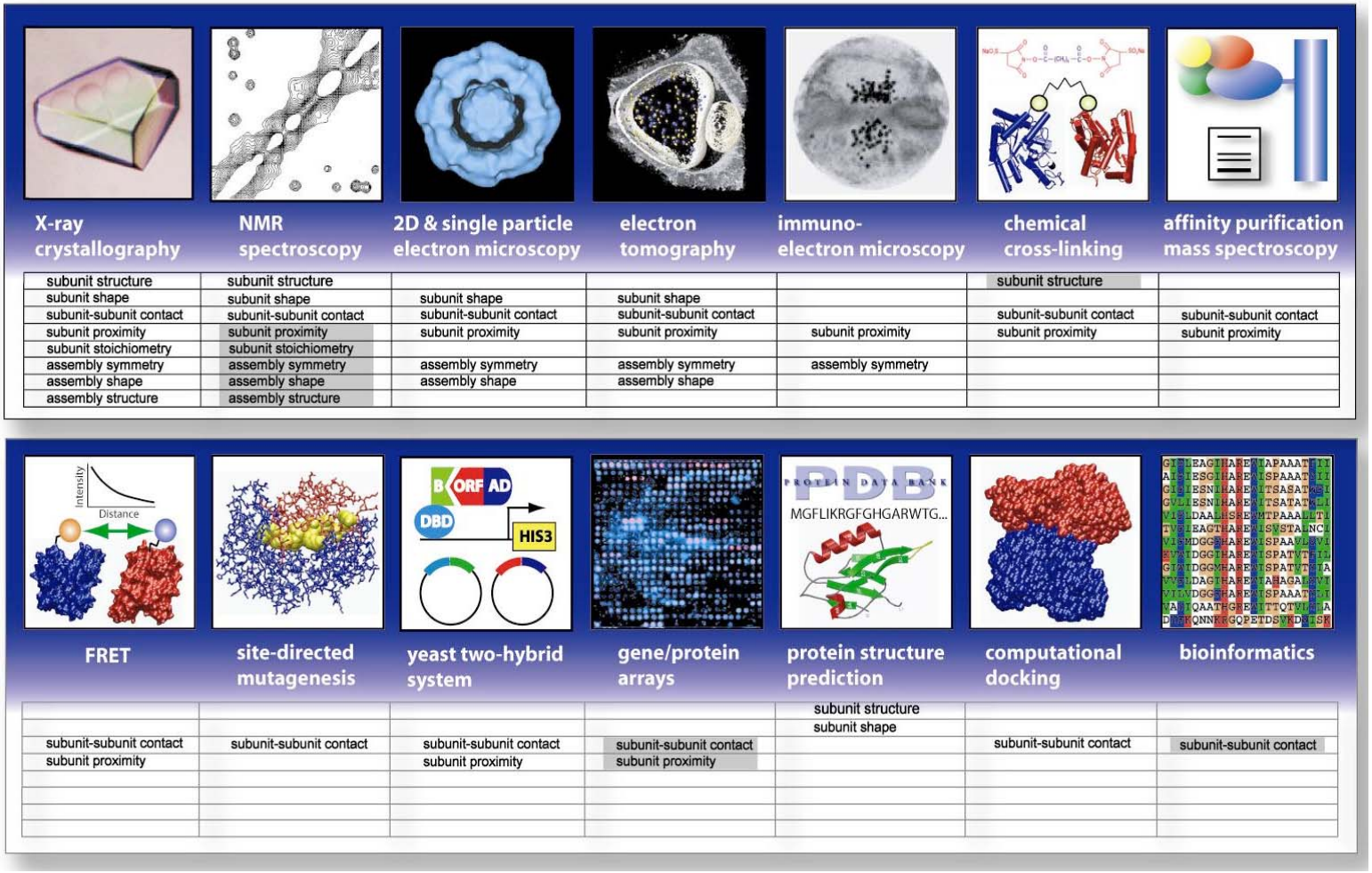


# Determining the Structures of Proteins and Assemblies

Structural information from…

**source**: measurement and models

**resolution**: low or high resolution




| X-ray crystallography | NMR spectroscopy | 2D & single particle electron microscopy | electron tomography | immuno-electron microscopy | chemical cross-linking | affinity purification mass spectroscopy |
|---|---|---|---|---|---|---|
| subunit structure | subunit structure | | | | subunit structure | |
| subunit shape | subunit shape | subunit shape | subunit shape | | | |
| subunit-subunit contact | subunit-subunit contact | subunit-subunit contact | subunit-subunit contact | | subunit-subunit contact | subunit-subunit contact |
| subunit proximity | subunit proximity | subunit proximity | subunit proximity | subunit proximity | subunit proximity | subunit proximity |
| subunit stoichiometry | subunit stoichiometry | | | | | |
| assembly symmetry | assembly symmetry | assembly symmetry | assembly symmetry | assembly symmetry | | |
| assembly shape | assembly shape | assembly shape | assembly shape | | | |
| assembly structure | assembly structure | | | | | |

| FRET | site-directed mutagenesis | yeast two-hybrid system | gene/protein arrays | protein structure prediction | computational docking | bioinformatics |
|---|---|---|---|---|---|---|
| | | | | subunit structure | | |
| | | | | subunit shape | | |
| subunit-subunit contact | subunit-subunit contact | subunit-subunit contact | subunit-subunit contact | | subunit-subunit contact | subunit-subunit contact |
| subunit proximity | | subunit proximity | subunit proximity | | | |

Sali, Earnest, Glaeser, Baumeister. From words to literature in structural proteomics. Nature 422, 216-225, 2003.

# Resource for Biocomputing, Visualization, and Informatics

We are an NIH Biomedical Technology Resource Center, funded by the National Center for Research Resources. We create innovative computational and visualization-based data analysis methods and algorithms, turn these into easy-to-use software tools which we distribute to the scientific community, and apply these tools for solving a wide range of genomic and molecular recognition problems within the complex sequence → structure → function triad.

National Center for Research Resources

# Sample application areas

Insight into molecular structure and function:

- Protein engineering
- Drug design
- Biomaterials design
- Annotation of protein function from sequence and structure

Gene annotation, characterization, and interpretation:

- Pharmacogenetics - understanding and prediction of variation in drug response due to genetic factors
- Mouse gene knock-outs for modeling of human disease

# UCSF Chimera – an Extensible Molecular Modeling System

Chimera is an extensible interactive 3-D modeling system designed to allow developers to quickly incorporate novel visualization algorithms and analysis tools

Chimera runs on laptops/desktops and takes maximum advantage of low-cost, state-of-the-art graphics chips

$500 today buys you 3-D interactive graphics capabilities that cost $20,000 five years ago

Chimera has extensive documentation for users and developers to enable effective scientific studies to be accomplished rapidly and with a "low entry barrier"

# Documentation and Distribution

Documentation

- Extensive User's Guide
- Basic Programmer's Guide

Training

- On-line "Getting Started" tutorial
- Periodic workshops

Platforms

- Windows 98/2000/XP
- Mac OS X
- Linux, SGI, HP Alpha

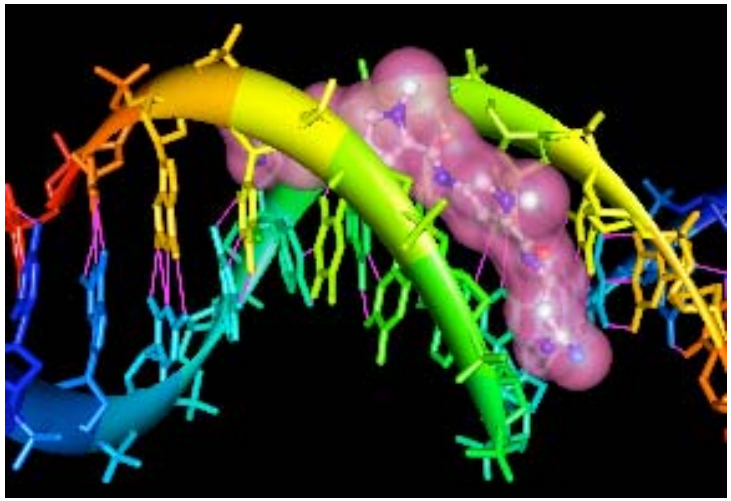
Availability

- Download from our Research Resource Center web site after simple "click to accept" license agreement

# Chimera's Built-in Features

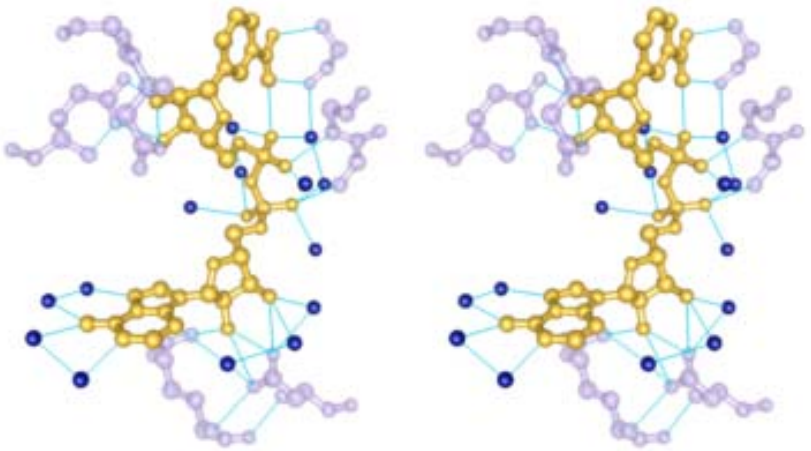
Molecular Graphics:

- interactively manipulate stick, ball-and-stick, CPK, ribbon representations, and molecular surfaces
- highly intuitive model translation, scaling, and rotation
- interactive color editing
- ability to save high resolution images for presentation and publication
- stereo viewing



Chemical Knowledge:

- determination of atom types in arbitrary molecules
- ability to add hydrogen atoms
- high-quality hydrogen bond identification
- selection of atoms/bonds by element, atom type, functional group, and amino acid category
- interactive bond rotation, distance, and angle measurements

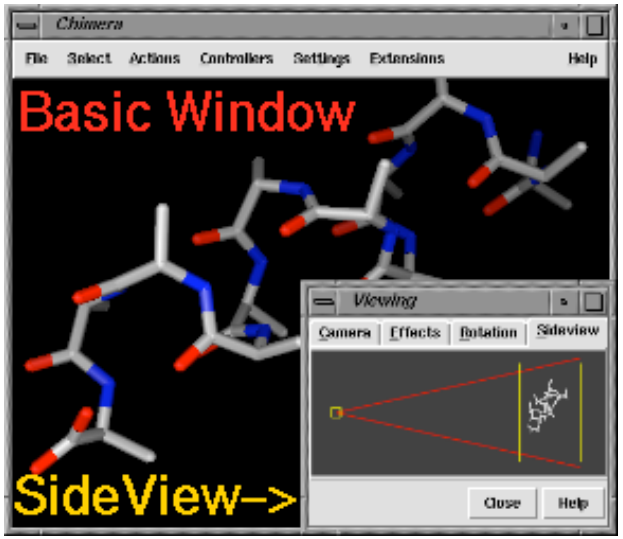


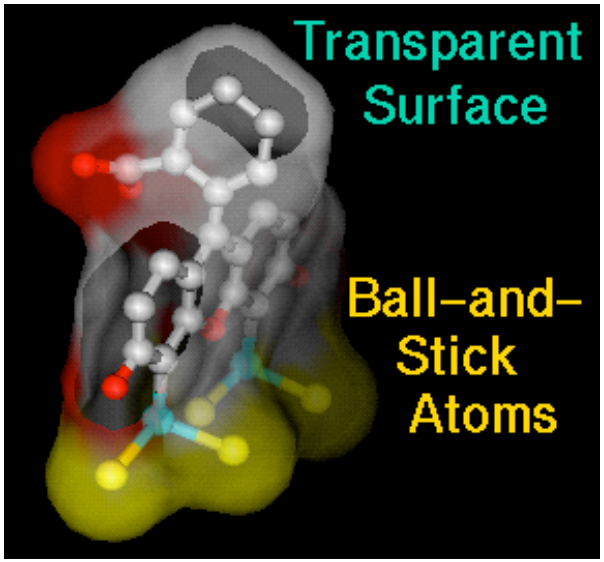
# Chimera's Programmability/Extensibility

Chimera is designed to allow developers to quickly incorporate novel algorithms and analysis tools

- Extensions can control standard Chimera user interface features (e.g. camera, help, menus, toolbar), as well as create their own custom graphical user interfaces

- Extensions are written in the Python programming language
  - Python is easy to learn, even for novice programmers
  - Python is object-oriented and provides features needed for development of complex codes
  - ~30 extensions written to date



# Learn more about Python

Python Web site:

www.python.org

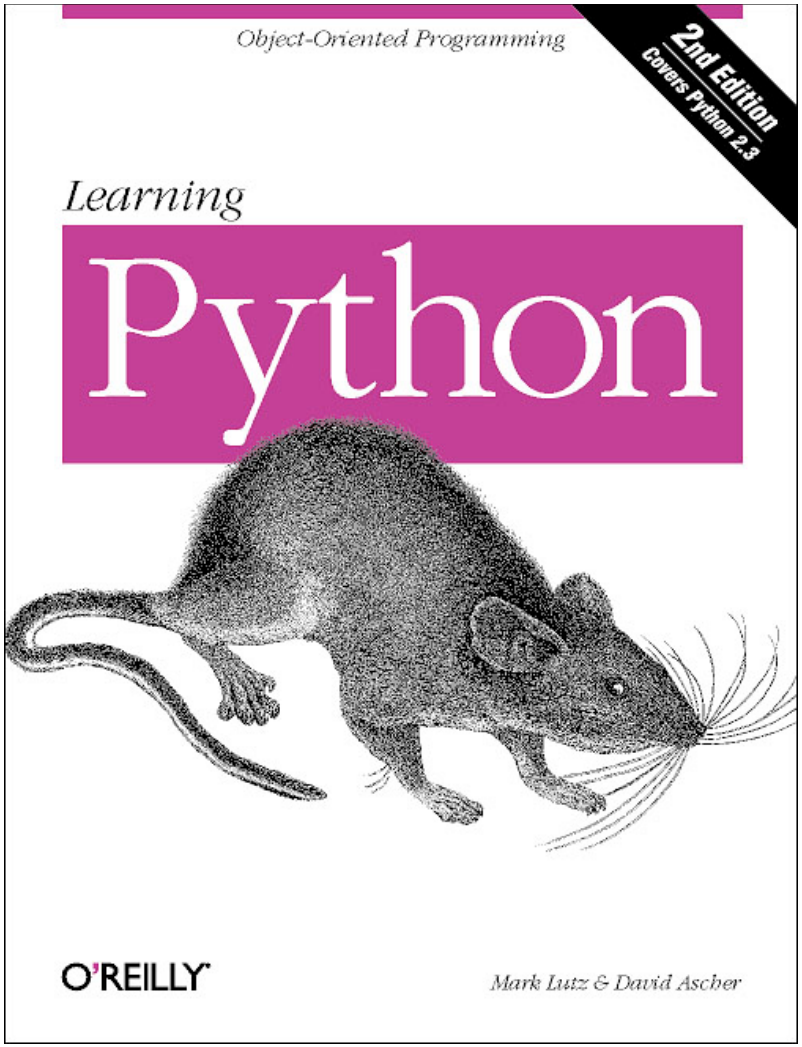
Good book:

"Learning Python"

by Mark Lutz & David Ascher

Available from

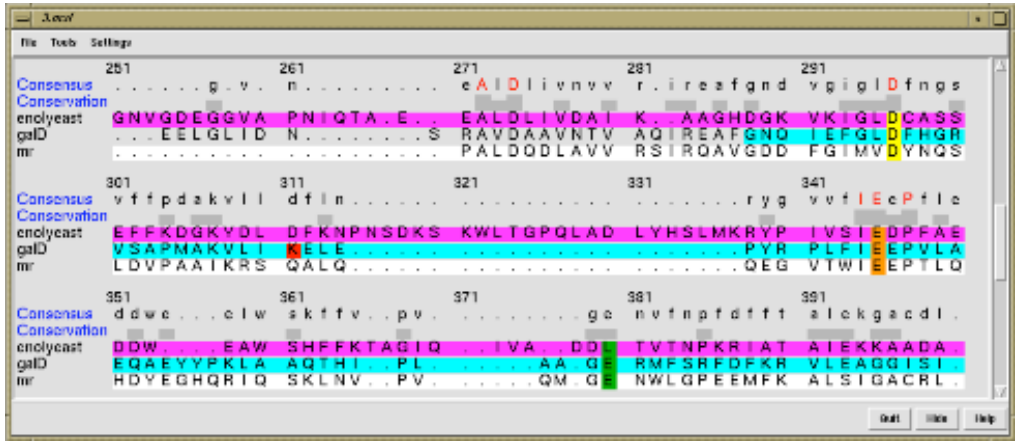
www.oreilly.com/catalog/lpython2



# Sample Chimera Extension

## Multalign Viewer

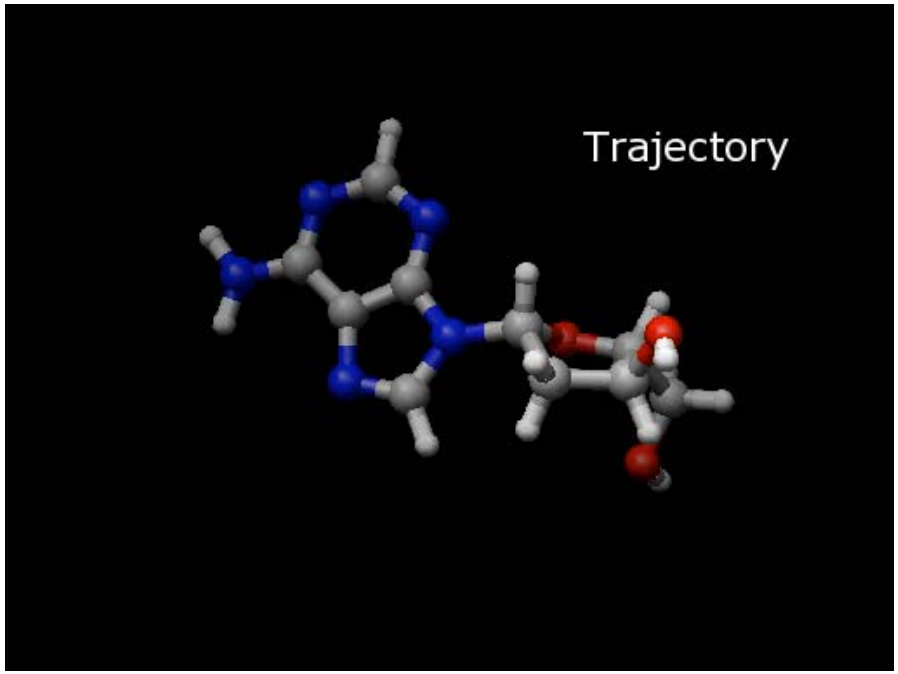
- Simultaneously displays multiple protein sequence alignments and corresponding structure superpositions, calculates and displays consensus sequence and conservation histogram, and highlights corresponding regions in both sequence and structure space



# Sample Chimera Extension

## Molecular Dynamics Trajectories

- All built-in Chimera analysis and display capabilities also work with trajectories. Support is provided for a number of common programs: AMBER, CHARMM, GROMOS, MMTK, NAMD, PDB, and X-PLOR.



# Sample Chimera Extension

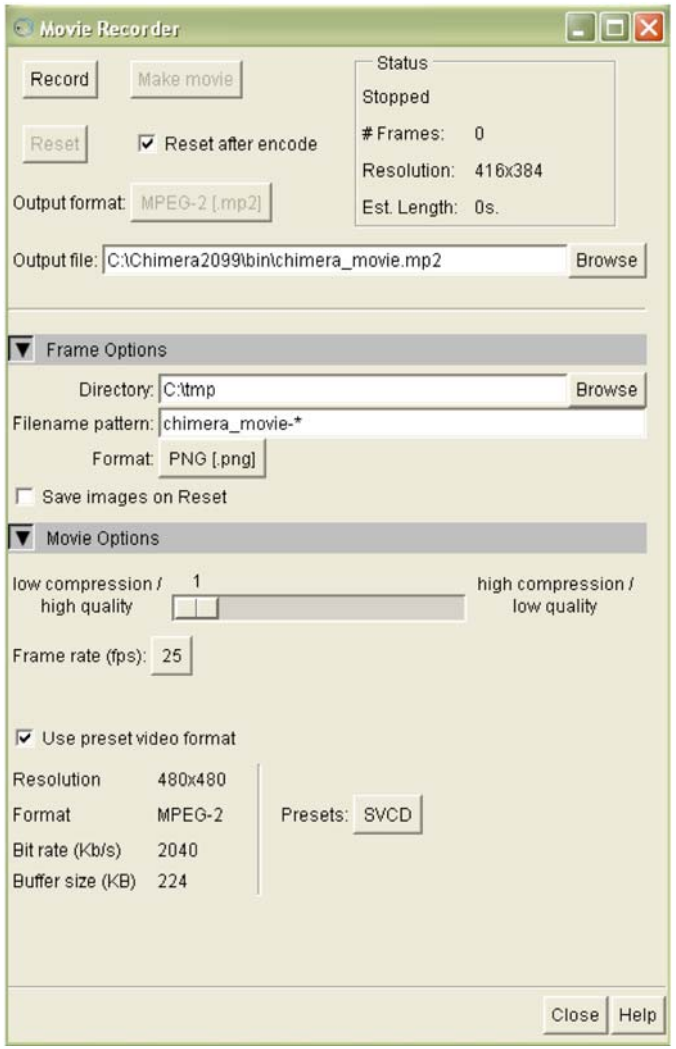
## Movie Recorder

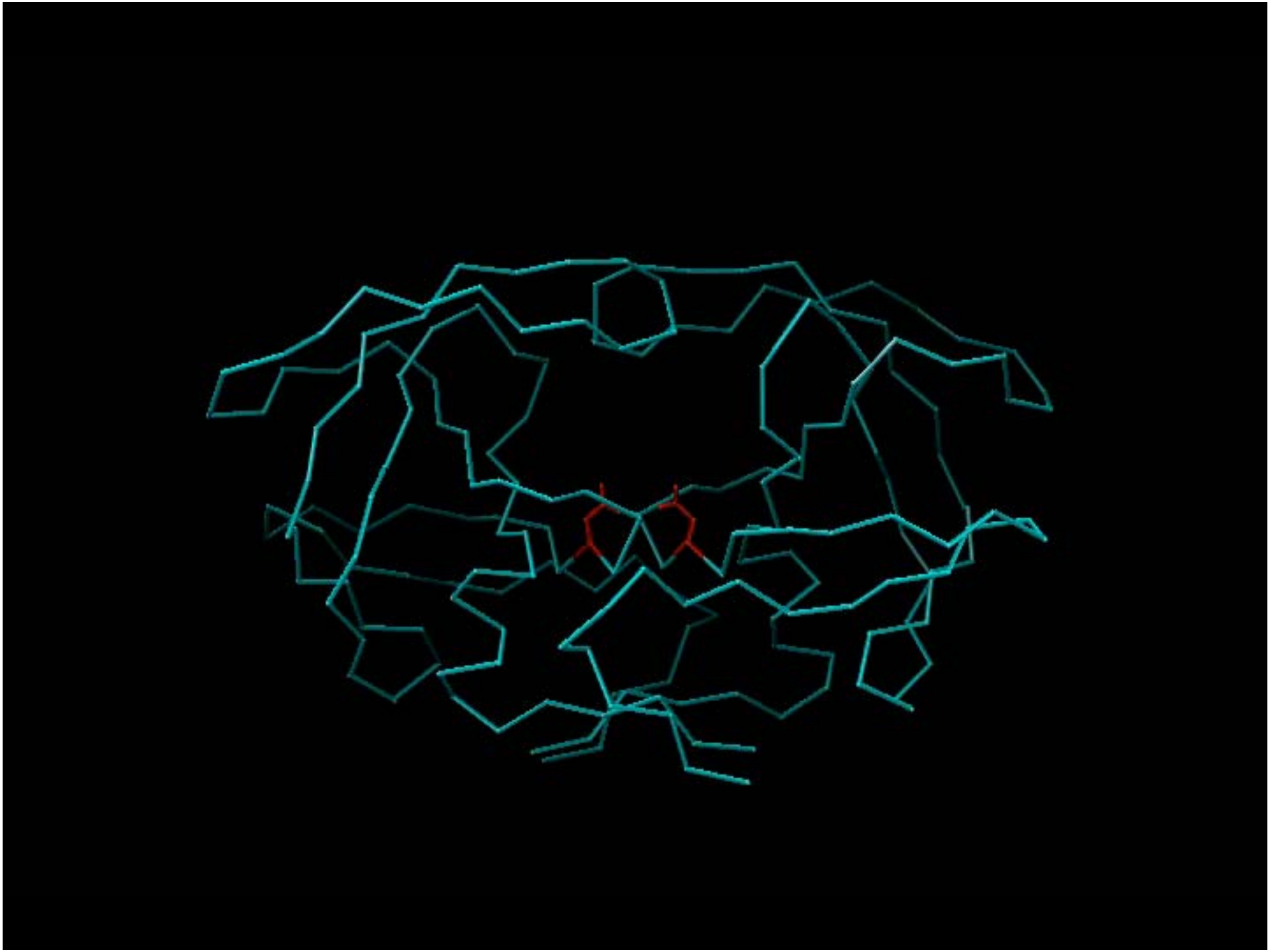
Capture image frames from Chimera and assemble these into a movie file

Formats supported:

- MPEG-1
- MPEG-2
- MPEG-4
- Quicktime

(New feature in release 2104)





# Sample Chimera Extension

## ViewDock

- Rapid screening of promising drug candidates found with the UCSF DOCK program

ViewDock – /usr/local/src/chimera-demos/nih2002/viewdock/ras.mol2

File ListBox Sort Column Selection Chimera Movie

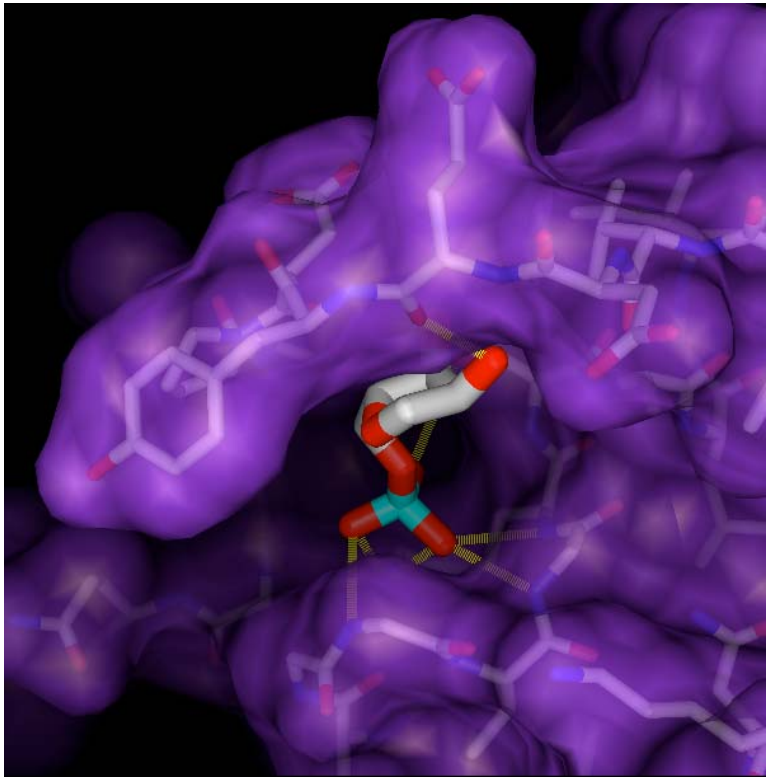
| S | Number | Description |
|---|---|---|
| V | 1 | ribose-monophosphate |
| V | 2 | vitamin B2 |
| V | 3 | arginine |
| V | 4 | laurate(C12) |
| V | 5 | vitamin D3 |
| V | 6 | 1,4,6-gonatriene-3,17-dione |
| V | 7 | phenothiazine |
| V | 8 | 5h-dibenz[b,f][1,4]oxazepine |
| V | 9 | vitamin A |

**Chimera Model #0.1**

```
########## Number       : 1
########## Source num   : 22
########## Name         : test_22
########## Description  : ribose-monophosphate
########## Reflect      : 0
########## Energy score
       :      -42.64
```

**Compound State**

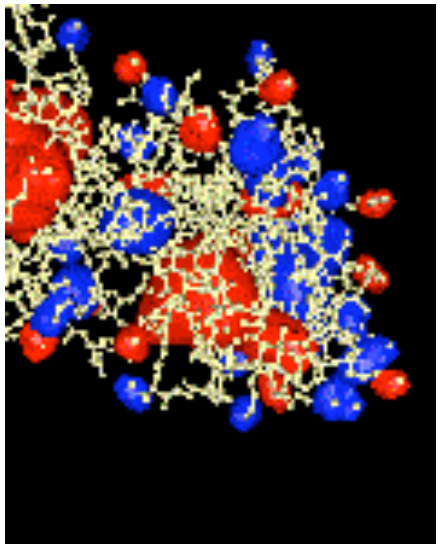
◇ Purged ◇ Deleted ◆ Viable

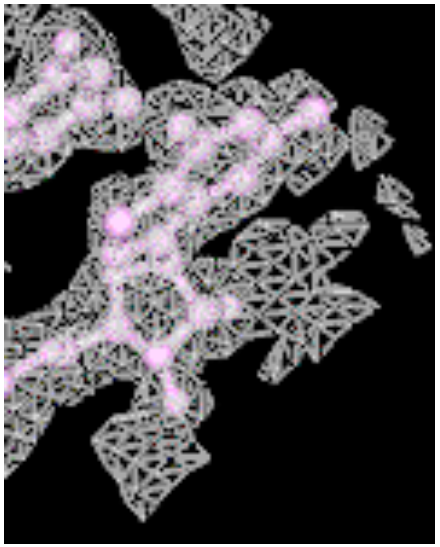


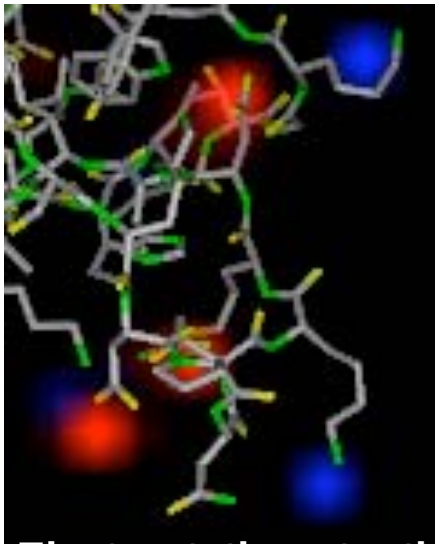
# Sample Chimera Extension

## Volume Viewer

- An extension for visualizing three-dimensional numerical data sets



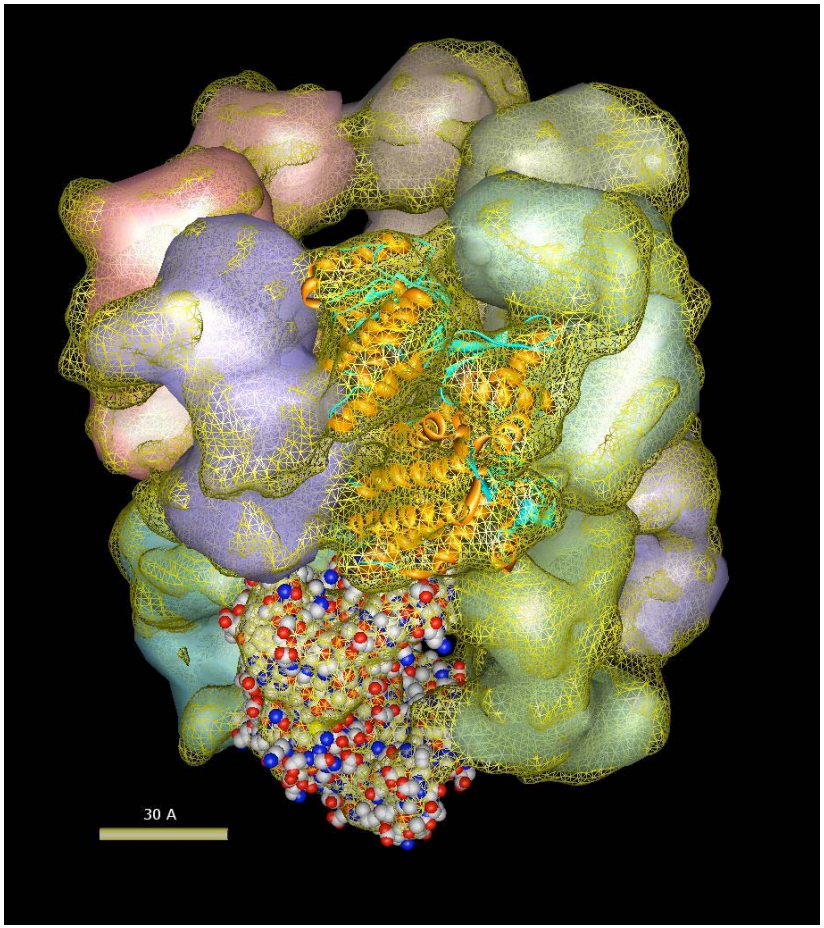




# Sample Chimera Extension

Multiscale Modeling

- useful for exploring models of large molecular complexes
- combines volume visualization and atomic resolution capabilities
- example systems include viruses and chromosomes
- GroEL model: 14 copies of the monomeric GroEL crystal structure docked to a 10.3 Å electron microscope map



# Chimera Demonstration #1

Introduction to molecular representation and basic use

Files used: 2gbp.pdb

Features illustrated:

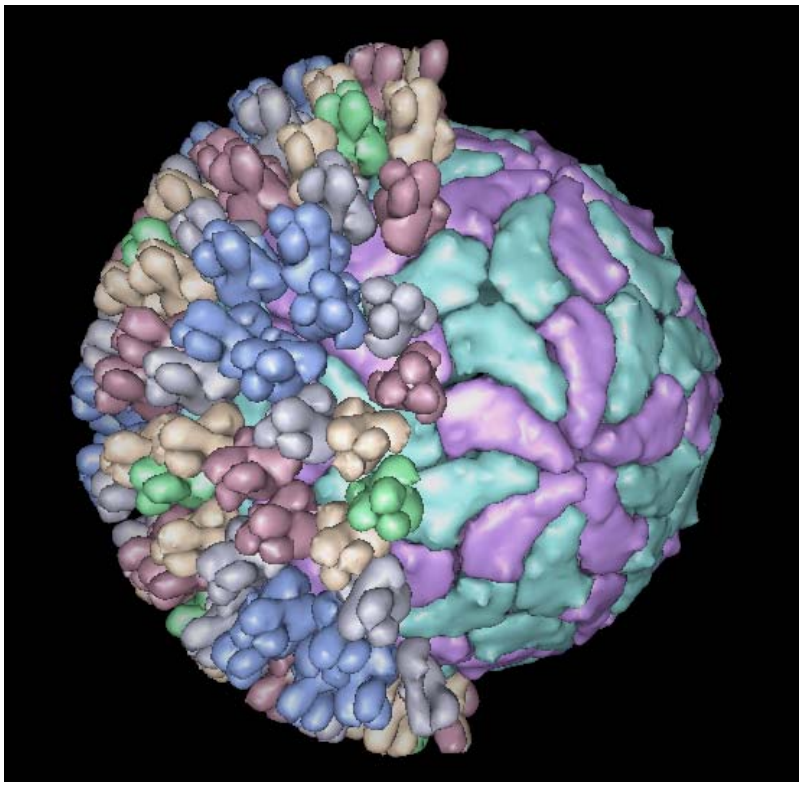
- Opening files
- Selecting and displaying atoms, bonds, and surfaces
- Manipulating models: rotate, translate, scale, clip
- Display styles: wireframe, sticks, balls&sticks, CPK
- Command line

Additional information: UCSF Chimera - A Visualization System for Exploratory Research and Analysis, J. Comp. Chem., 25(13):1605-1612, 2004.

# Chimera Demonstration #2

## Bluetongue Virus Core

- PDB structure 2btv by David Stuart's lab (Nature 395: 470-478, 1998)
- Full particle 700 Å diameter, 3.5 Å resolution, 1000 crystals and $3x10^6$ atoms (no hydrogens)
- Multiscale extension makes 60 copies of unit cell
  - -Outer layer: 260 trimers of VP7 protein in 5 symmetry classes
  - -Inner layer: 60 dimers of VP3
- Extension focuses on hierarchical structure relationships and their selection and display



Additional information: Software Extensions to UCSF Chimera for Interactive Visualization of Large Molecular Assemblies, Structure, 13(3):473-482, 2005.

# Acknowledgements

Staff:

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Further information:

www.cgl.ucsf.edu/chimera