Multiscale Structural Visualization with UCSF Chimera

Thomas Ferrin

Resource for Biocomputing, Visualization, and Informatics

University of California, San Francisco

Resource for Biocomputing, Visualization, and Informatics

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

Application areas

Gene characterization and interpretation

Drug design

Variation in drug response due to genetic factors

Protein engineering

Biomaterials design

Prediction of protein function from sequence and structure

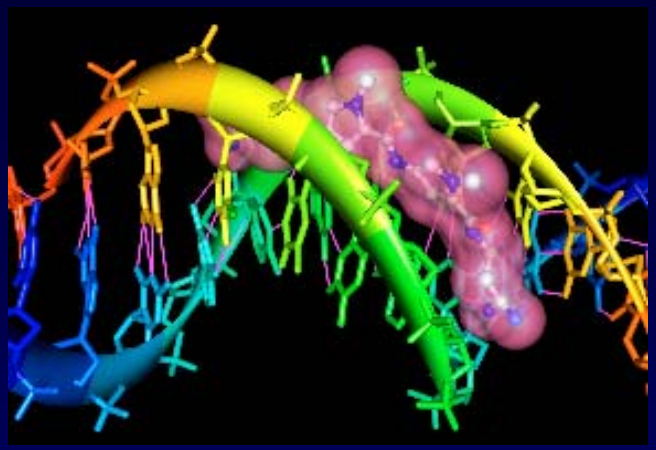
UCSF Chimera - an Extensible Molecular Modeling System

- Chimera is an extensible interactive 3-D modeling system designed to allow developers to quickly incorporate novel visualization algorithms and analysis tools
- Chimera is a standalone program for laptops/desktops that takes maximum advantage of low-cost, state-of-the-art graphics chips
  - $350 today buys you 3-D interactive graphics capabilities that cost $20,000 five years ago
- Chimera comes with extensive documentation for users and developers to enable effective scientific studies to be accomplished rapidly and with a "low entry barrier"

Chimera's Built-in Features

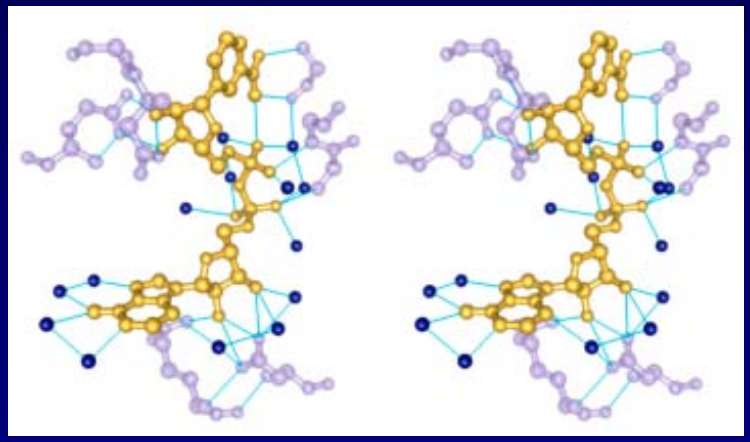
Molecular Graphics:

- 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:

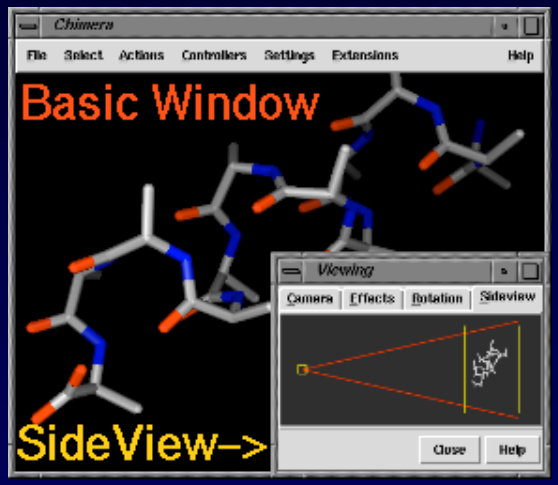
- determination of atom types in arbitrary molecules
- ability to add hydrogen atoms
- high-quality hydrogen bond identification
- selection of atoms/bonds by element, atom type, functional group, and amino acid category
- interactive bond rotation, distance, and angle measurements

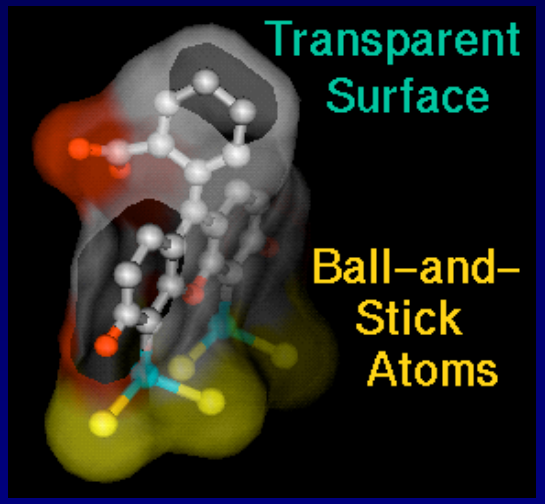


Chimera's Programmability/Extensibility

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

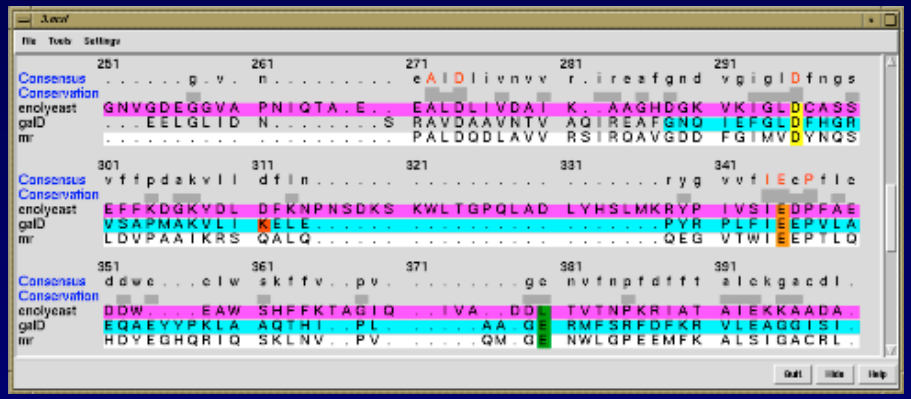




Sample Chimera Extension

Multalign Viewer

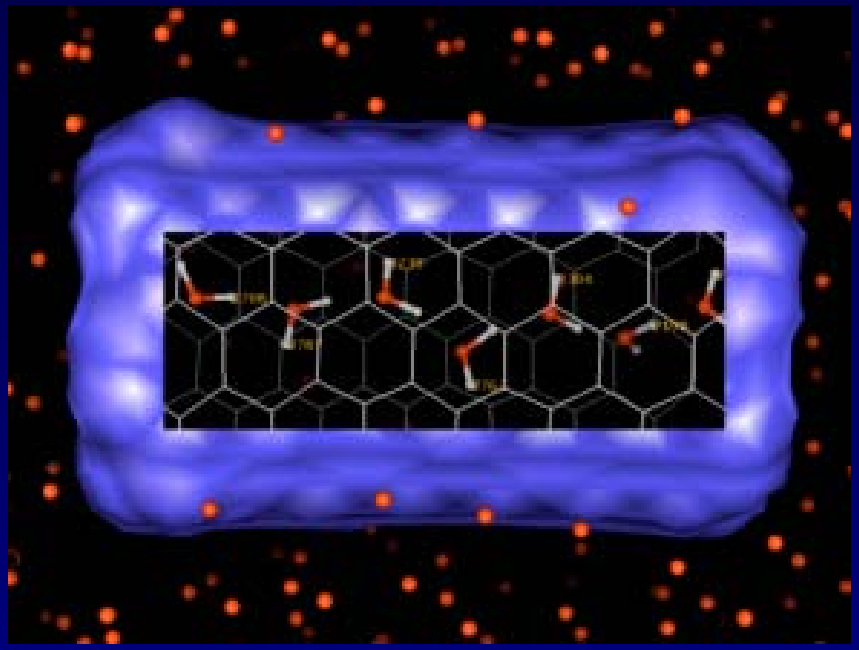
- simultaneously displays multiple protein sequence alignments and corresponding structure superpositions, calculates and displays consensus sequence and conservation histogram, and highlights corresponding regions in both sequence and structure space



Sample Chimera Extension

Molecular Dynamics Trajectories

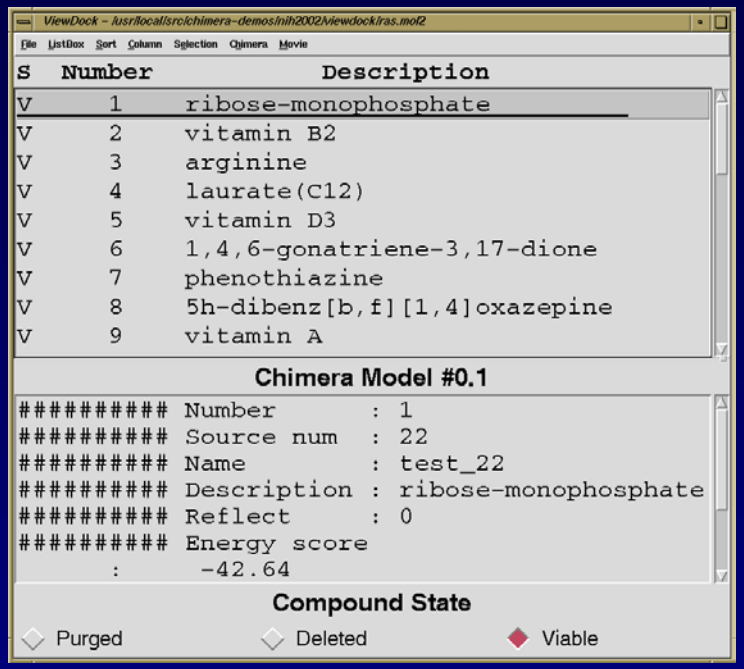
- All built-in Chimera analysis and display capabilities also work with trajectories, including "lens" (rectangular regions containing markedly different display properties)

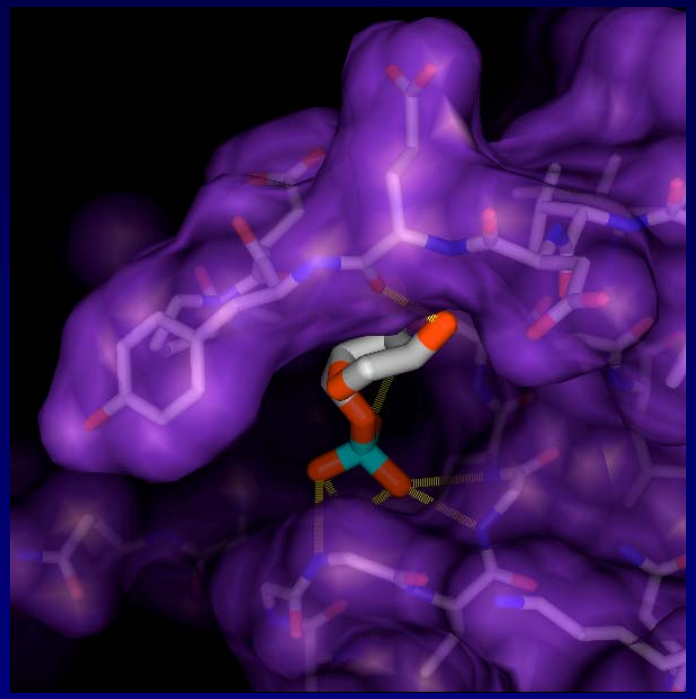


Sample Chimera Extension

ViewDock

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

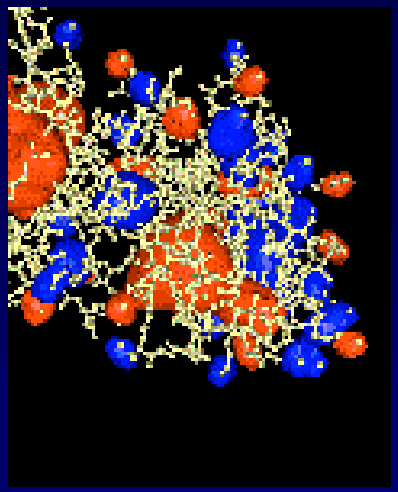




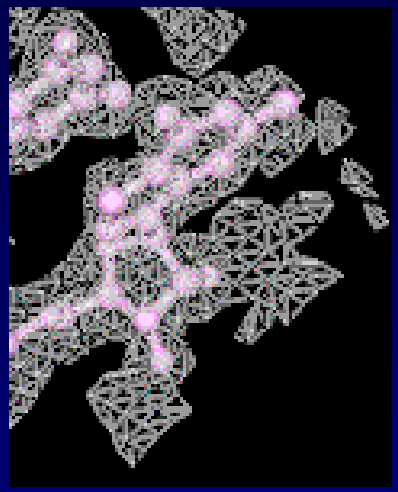
Sample Chimera Extension

Volume Viewer

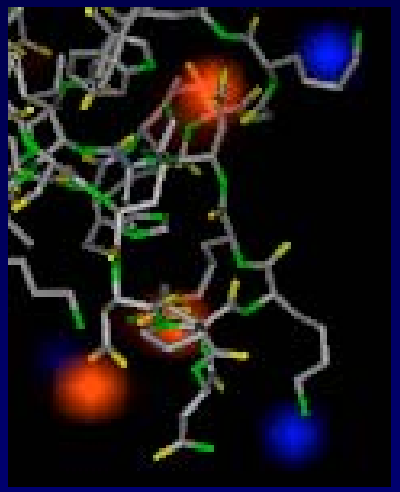
- an extension for visualizing three-dimensional numerical data sets



Electrostatic potential (surfaces)



Electron density (mesh)

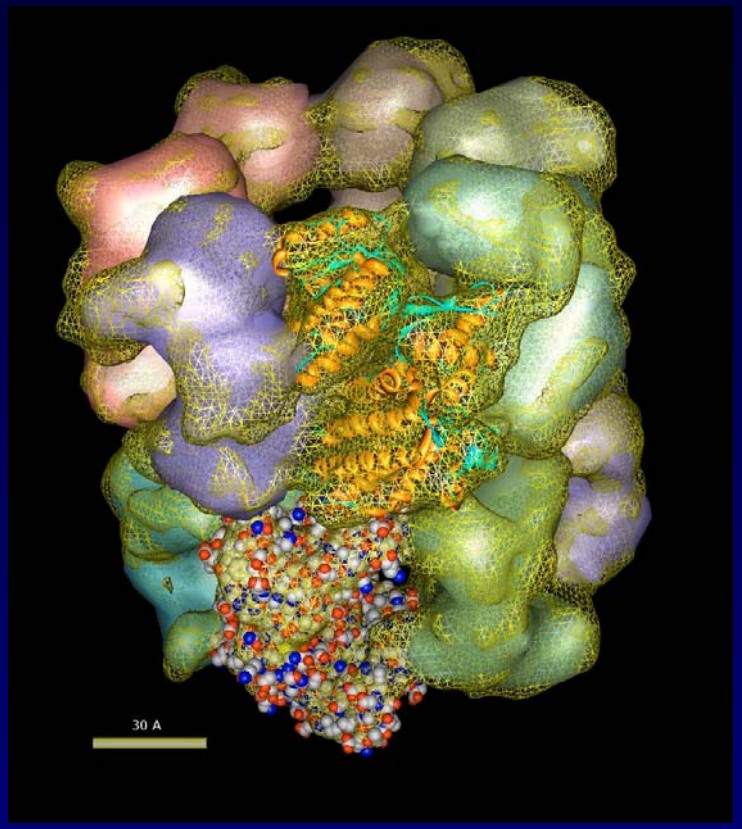


Electrostatic potential (solids)

Sample Chimera Extension

Multiscale Modeling

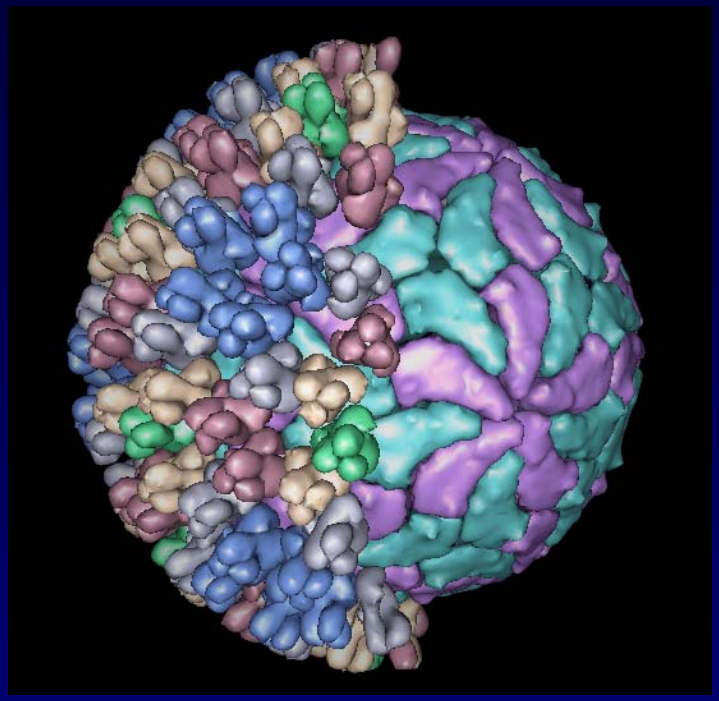
- useful for exploring models of large molecular complexes
- combines volume visualization and atomic resolution capabilities
- example systems include viruses and chromosomes
- GroEL model: 14 copies of the monomeric GroEL crystal structure docked to a 10.3 Å electron microscope map



Live Demo

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 & display



Acknowledgements

Staff:

- Dr. Conrad Huang, Prof. Patricia Babbitt, Tom Goddard, Greg Couch, Eric Pettersen, Dan Greenblatt, Al Conde, Dr. Elaine Meng

Collaborators (partial list):

- **Wah Chiu and Steven Ludtke, Baylor**
- **John Sedat and David Agard, UCSF**
- **David Konerding and Steven Brenner, UCB**

Funding: National Center for Research Resources

- P41-RR01081

Further information:

- www.cgl.ucsf.edu/chimera