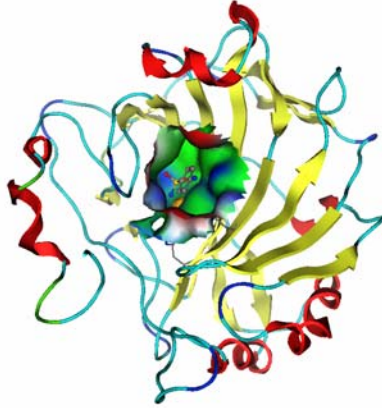


# Molecular Visualization



Jeffrey D. Madura

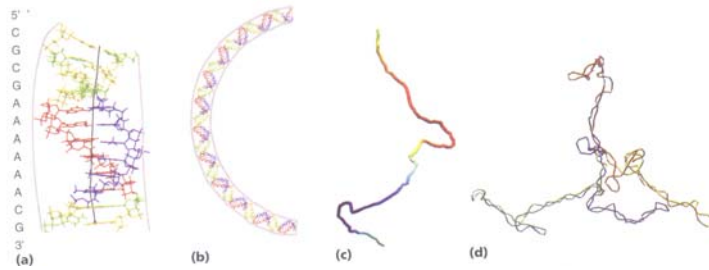
Department of Chemistry & Biochemistry  
Center for Computational Sciences  
Duquesne University

## Introduction

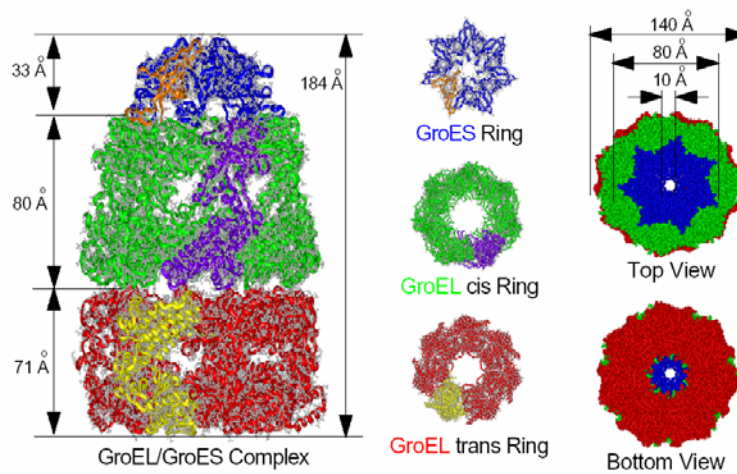
- Assessments of change, dynamics, and cause and effect are at the heart of thinking and explanation. To understand is to know *what cause provokes what effect, by what means, at what rate*. How then is such knowledge to be represented?<sup>1</sup>
- The goal is to design “...proper arrangement in space and time images, words, numbers – for presenting information about motion, process, mechanism, cause, and effect.<sup>1</sup>”
- Therefore visualization, in our case molecular visualization, is extremely important since it is an extremely effective method to convey information.

<sup>1</sup>Tufte, Edward R. “Visual Explanations”, 1997, Graphics Press.

# Examples



# Examples





# History of Visualization of Biological Macromolecules

by [Eric Martz](#) and [Eric Francoeur](#)

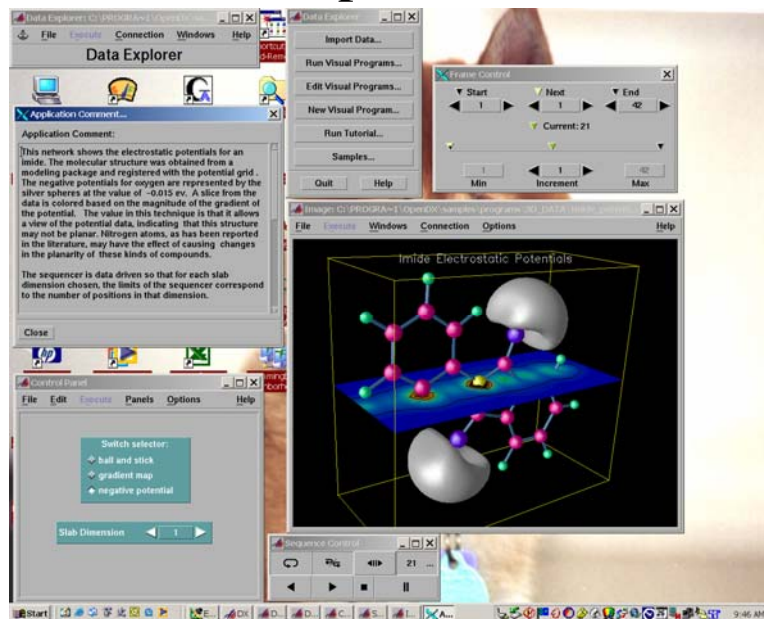
Please send suggestions for improvements to this document to [E.M.](#)  
August 17, 1997; Revised 6/99; 8/00; 8/01; 9/01; 4/02.

## CONTENTS

- [Earliest Macromolecular Crystal Structures](#)
- [Caveat](#)
- Physical Representations
  - [1958: Kendrew's wire models and the Richards Box](#)
  - [1960's: Physical "Ball and Spoke" Models](#)
  - [1970: Byron's Bender](#)
  - [Molecular Sculpture](#)
  - [1990's: Rapid Prototyping](#)
- Computer Representations
  - [1960's - 70's: Earliest Computer Representations](#)
  - [1980: TAMS: Teaching Aids for Macromolecular Structure](#)
  - [1980-1990: Evans & Sutherland Computers](#)
  - [1992: David & Jane Richardson's Kinemage](#)
  - [1993: Roger Sayle's RasMol](#)
  - [1996: MDL's Chime](#)
- [On-Line Museum of the History of Visualization of Biological Macromolecules](#)
- [Bibliography](#)

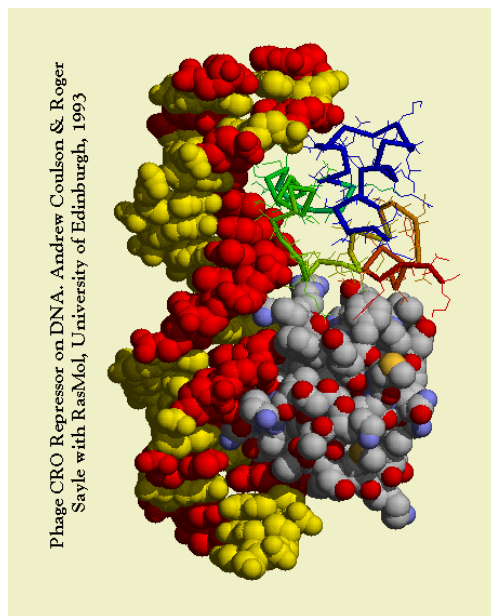
<http://www.umass.edu/microbio/rasmol/history.htm>

# OpenDX



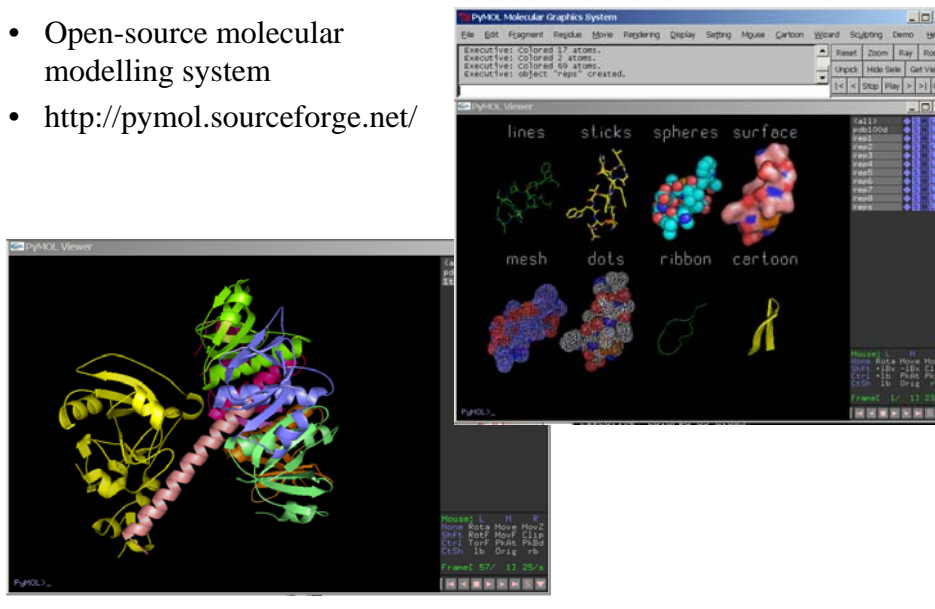
# RasMol

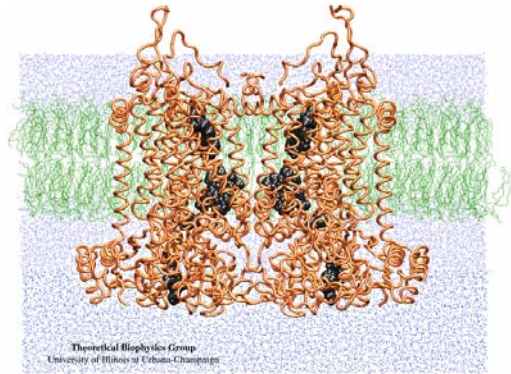
- Created by Roger Sayle
- Easy to use, very basic, and quick to learn.



# PyMol

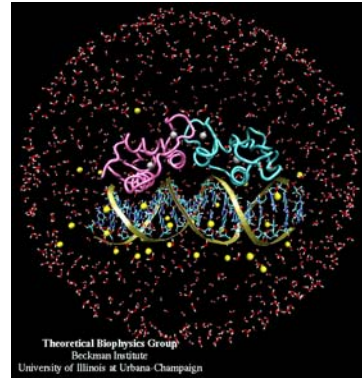
- Open-source molecular modelling system
- <http://pymol.sourceforge.net/>





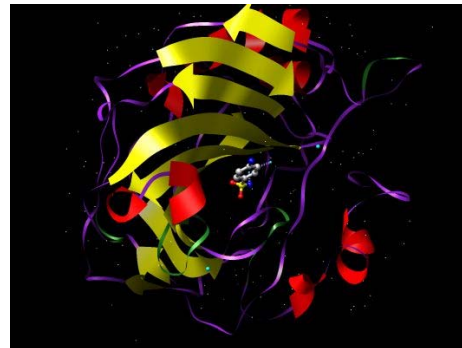
## VMD

- Visual Molecular Dynamics
- It is a molecular visualization program for displaying, animating, and analyzing large biomolecular systems using 3-D graphics and built-in scripting.
- <http://www.ks.uiuc.edu/Research/vmd/>



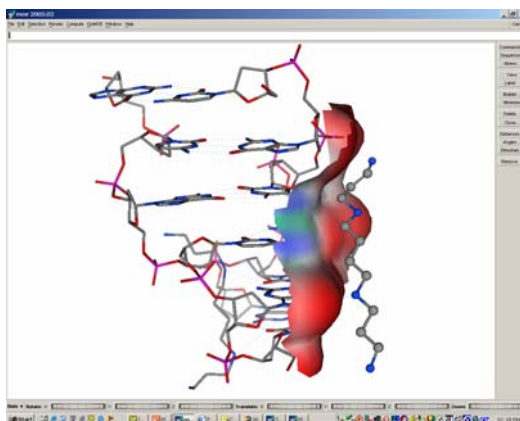
## UCSF Chimera

UCSF Chimera is a highly extensible, interactive molecular graphics program. It is the successor to [UCSF Midas and MidasPlus](#); however, it has been completely [redesigned](#) to maximize extensibility and leverage advances in hardware. UCSF Chimera can be downloaded free of charge for academic, government, non-profit, and personal use. It includes full user documentation and is available for Microsoft Windows, Linux, Apple Mac OS X, SGI IRIX, and HP Tru64 Unix.



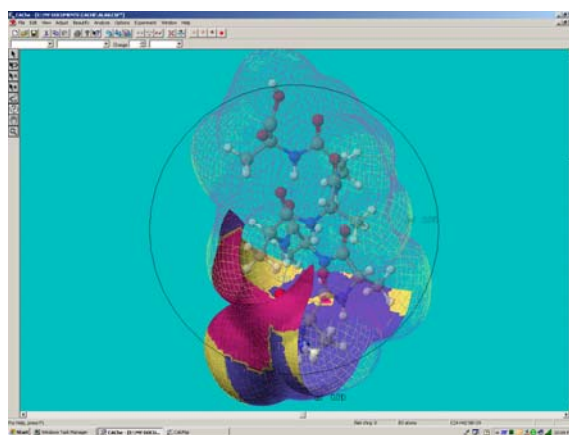
## MOE

- Molecular Operating Environment
- Chemical Computing Group ([www.chemcomp.com](http://www.chemcomp.com))
- Visualization and simulation tool
- Runs on numerous computers and has distributive computing capabilities
- Programmable



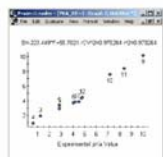
## CAChe

- Computer-Aided Chemistry
  - Visualization and computational tool
  - <http://www.cachesoftware.com>

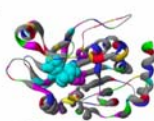




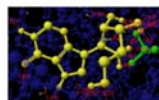
## CAChe



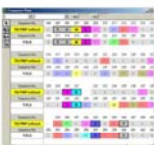
► **New QSAR descriptors** 'automatic' atom properties, e.g. "nitrogen with highest susceptibility to electrophilic attack", "hydrogen with highest partial charge", etc.



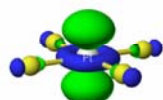
► **Ribbons and curls** rendering simplifies protein visualization and analysis



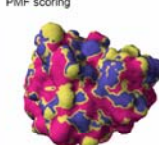
► **ActiveSite™ Automatic Ligand Docking** (optional) docks flexible or rigid ligands into proteins with flexible or rigid side chains, using enhanced PMF scoring



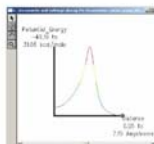
► **Automatic Sequence Alignment** uses the Needleman-Wunsch algorithm to identify conserved residues



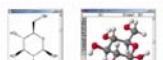
► **Gaussian® Interface** runs Gaussian® jobs from within CAChe, adding powerful *ab initio* capabilities (requires separate Gaussian installation)



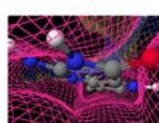
► **Accessible surface** shows hydrophilic areas of H-bond donors and acceptors and lipophilic areas by color



► **Plot reaction paths** automatically, potential energy versus atom displacement



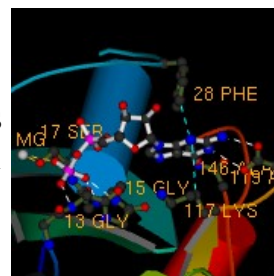
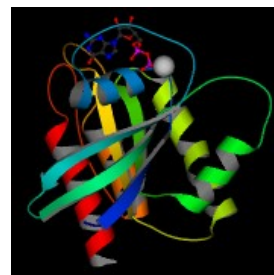
► **Automatic 2D-3D Batch Conversion** while reading MDL SD files into ProjectLeader



► **Ligand pocket surface** showing the chemistry and shape of the protein binding environment simplifies design of new ligands

## Molscript

MolScript is a program for creating schematic or detailed molecular graphics images from molecular 3D coordinates, usually, but not exclusively, protein structures. The user supplies an input file (the script) which specifies the coordinate file, what objects to render and the exact appearance of the objects through the graphics state parameters. There is a helper program [MolAuto](#), which produces a good first-approximation input file from a coordinate file.





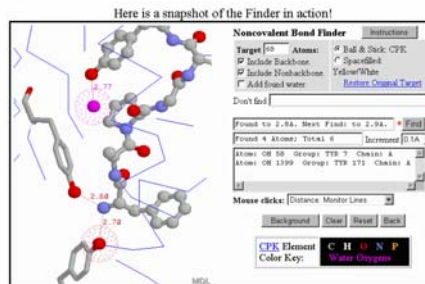
# Others

- Protein Explorer
  - A visualization tool using a web browser
- Chime
  - A browser plugin
- Cn3D
  - From the NCBI and NLM
- For a comprehensive list of Molecular Visualization tools, tutorials, and examples visit [molvisindex.org](http://molvisindex.org)

## Preview: Finding Noncovalent Bonds in Protein Explorer

**Contact Surfaces:** If you want an overview of the noncovalent bonds to a moiety of interest, try the Contact Surfaces capability of Protein Explorer. In addition to the "DISPLAY, Contacts" menu option in QuickViews, **Advanced Explorer** has a *Contact Surfaces* page with much more control over the contact displayed and its rendering.

**Noncovalent Bond Finder:** Use the Noncovalent Bond Finder when you want a more detailed (bond by bond) visualization. The Noncovalent Bond Finder makes it very easy to find and display the atoms closest to any ligand or group of "target atoms" you select. Starting at 2.5 Angstroms, it moves out in steps of 0.1 Angstrom and displays the atoms found. It can be restricted to show only desired categories of atoms, such as carbons in hydrophobic sidechains. It has an introductory tutorial.



# Protein Data Bank

<http://www.rcsb.org>



The screenshot shows the homepage of the RCSB Protein Data Bank. The page features a navigation menu on the left with links to Home, Search, Structures, and Queries. The main content area includes a "Welcome to the RCSB PDB" message, a "NEWS" section with a "RCSB PDB Offers Web Services" article, and a "Molecule of the Month: Glucose Oxidase" section. The page also displays the RCSB PDB logo and the text "An Information Portal to Biological Macromolecular Structures".

## MOE (Molecular Object Environment)

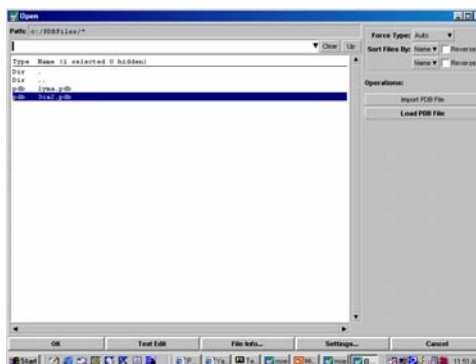
- MOE is a visualization and computational program
- Features include
  - Visualization and manipulation of molecular objects
  - Computation of various molecular properties by a number of methods (e.g. MM/D, Electrostatics, etc.)
  - Database capabilities
  - Programmable using SVL (Scientific Vector Language)
  - Runs on different computational platforms
    - PC, SGI, Sun, HP, and Dec Alpha/NT

## MOE as a Visualization Tool

- MOE is capable of building as well as editing both simple molecules and complex protein structures.
- The next few slides will illustrate MOE's visualization capabilities:
  - The final view will be of carbonic anhydrase (3ca2). The enzyme is represented as a solid ribbon, the zinc atom as a green sphere, the three histidines sticks (blue), and the drug (AMS) as ball and stick (orange).
- We will use this example to show MOE's visualization power by:
  - Editing the display of an existing protein structure.
  - Using the atom builder to modify the drug (AMS) bound to 3ca2.

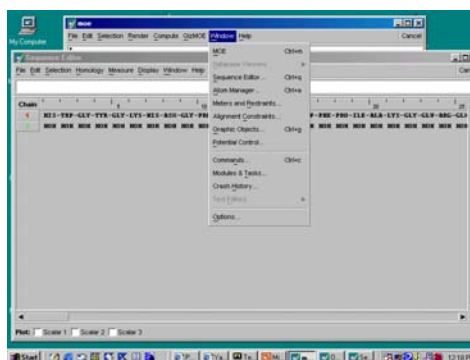
## Creating a View with MOE

- Load the structure file to be viewed (PDB).
  - File, Open. Find the directory that contains the structure. Select the file by choosing either the Load PDB File Operation (mid right) or the Ok button (lower left).



## Creating a View with MOE

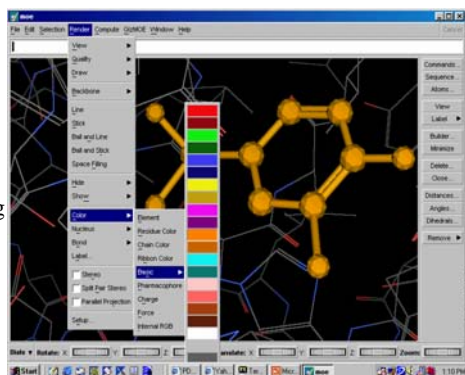
- **Manipulating the protein.**
  - Remove bound water molecules and 2 Hg atoms.
    - Chose Window, Sequence Editor. Select the 2 Hg atoms and “**Split Chain**” to move them to a new chain.
  - **Delete Chains:** Water, 2 Hg atoms.



## Creating a View with MOE

### – Display ligand (ams).

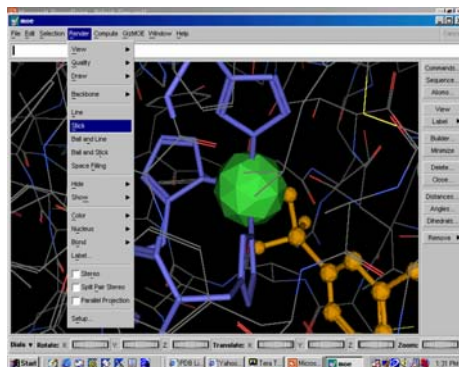
- *Zoom*: Cntrl+Rt/Dial.
- *Translate*: Shift+Rt/Dial.
- *Rotate*: Right/Dial.
- After zooming in on ligand, select it by clicking on any atom while using Cntrl+Lft.
- Under Render, chose Ball and Stick. Then, color the ligand by choosing Color, Basic.



## Creating a View with MOE

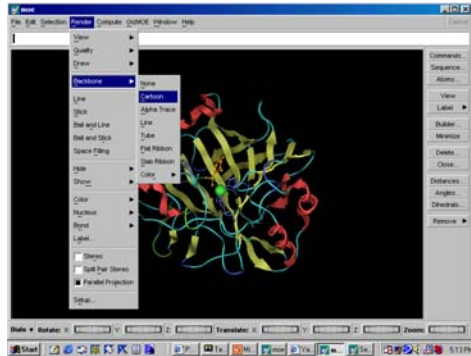
### – Display the Zn atom, highlighting the three bound His residues.

- Select the Zn atom by left clicking once. Under Render, chose Space Filling; then Color, Basic, Green.
- Select the 3 His residues (116, 93, 91) by using Cntrl+left on each. Chose Render, Line; then Color, Basic, Blue.
- Use Builder to remove unbond ligand and Zn atom.



## Creating a View with MOE

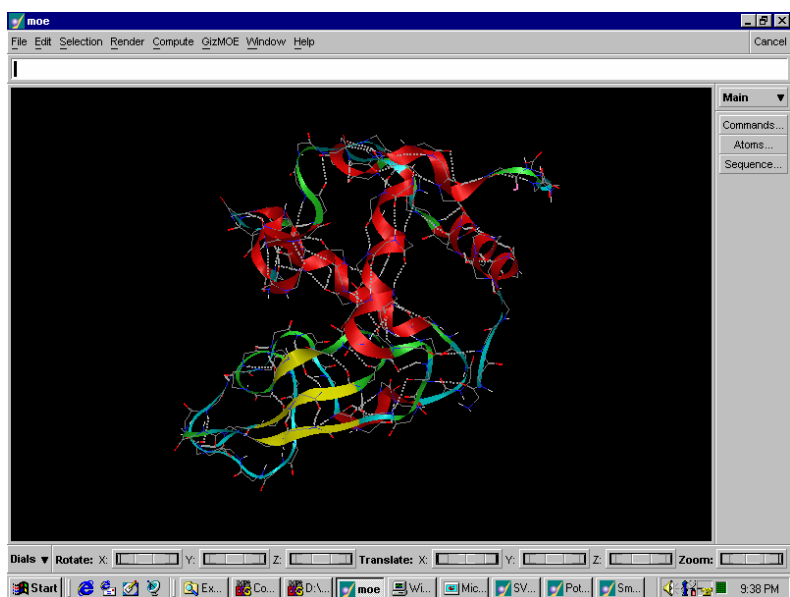
- Change the display of the protein.
  - Use sequence editor to select ligand, Zn, and 3 His residues.
  - Use Selection, Invert to select everything but the original selection.
  - Chose Render, Backbone, Cartoon or Slab Ribbon.



## 3ca2 Visualized with MOE

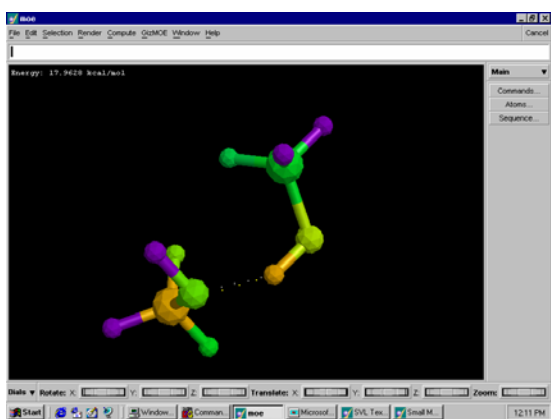


# MOE



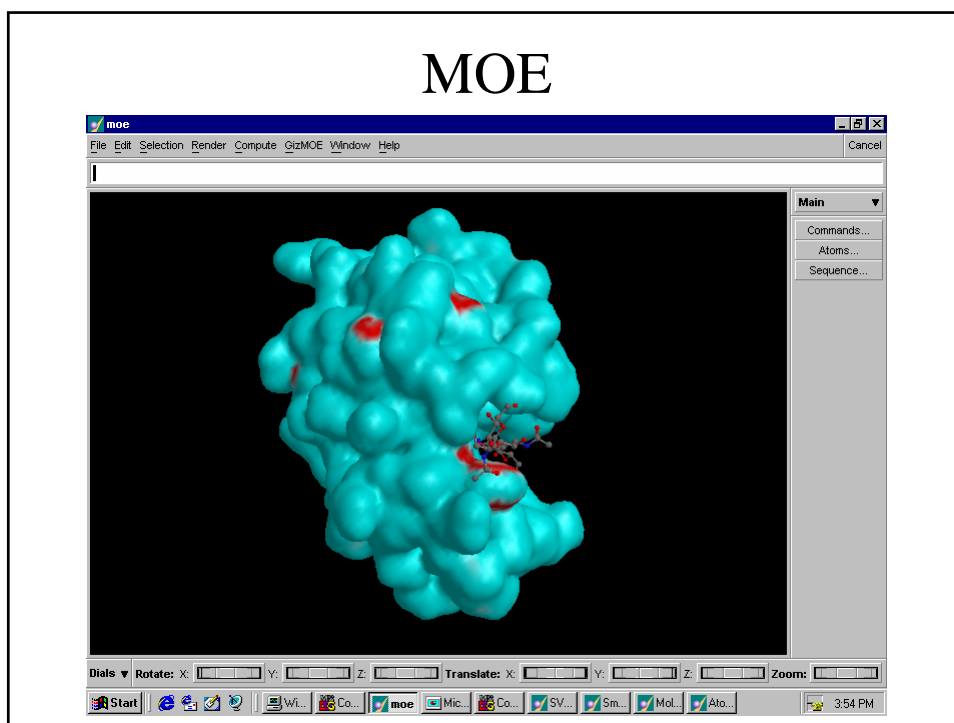
# MOE

- Interactive Modeling
  - Color atoms by force
  - Indicate formation of hydrogen bonds (white dots)
  - Indicate bad van der Waal contacts (yellow dots)
  - Current energy for the system

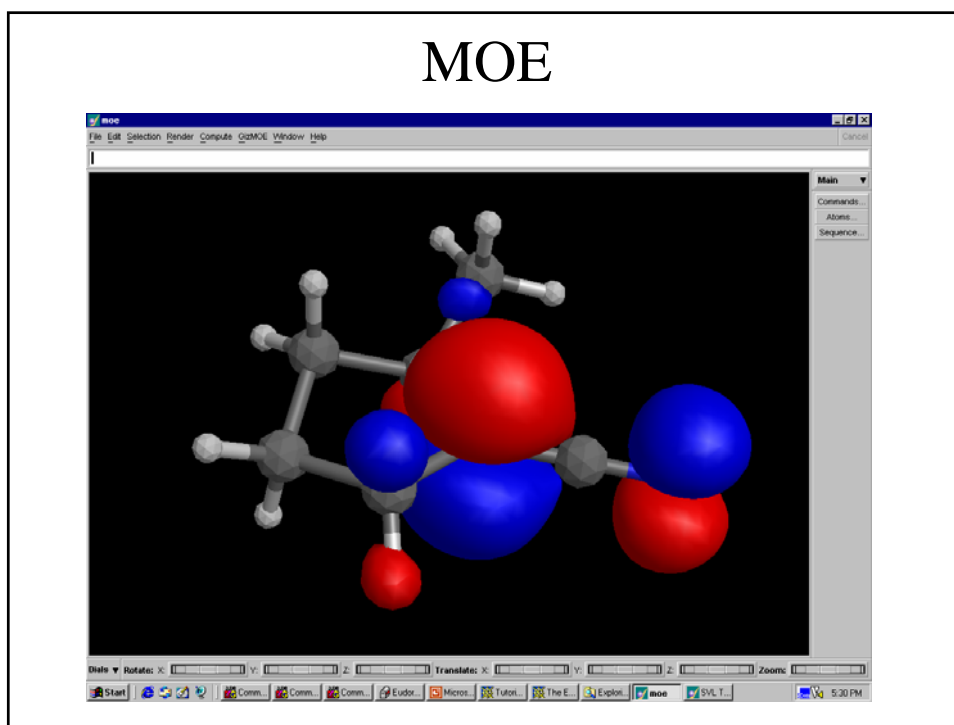




# MOE




# MOE



## Manipulating Molecules:3D Rendering Window

- rotate: **drag middle mouse**
- zoom in/out: **<ctrl>+drag middle mouse**
- shift/pan: **<shift>+drag middle mouse**
- change center of rotation: click the middle mouse button on the desired atom. To reset, **click the middle mouse button away from any atoms.**
- rotate about a bond: select the bonded atoms, then use **<alt>-drag left button.**

## Editing with Molecule Builders

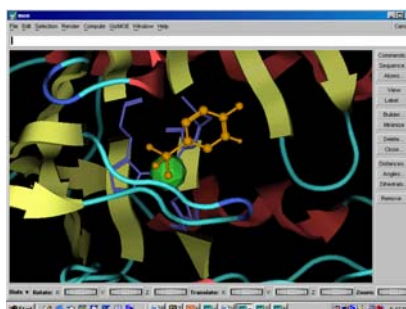
- Tools for Building Molecules in MOE:
  - **Small Molecule Builder** (Edit|Small Molecule Builder) 
  - **Protein Builder** (Edit|Protein Builder)
  - **Carbohydrate Builder** (Edit|Carbohydrate Builder)
    - Creates carbohydrates by linking sugar residues at specific positions. Can invert chiral centers, mutate residues, specify glycosidic torsion angles between residues.
  - **Create Sequence** (SE|Edit|Create Sequence)
- Small Molecule Builder Features:
  - **Build** molecules or add fragments using buttons, SMILES string
  - **Substitutions** can be made by first selecting atom in 3D rendering window
  - **Append** residues to a chain using the name of an existing compound. Or, create a new chain if the name is new.

# Editing with 3D Rendering Window

- 3D Rendering Window:
  - Functions found under Edit menu, or right button bar.
  - Some are on per atom basis, others work on set of selected atoms.

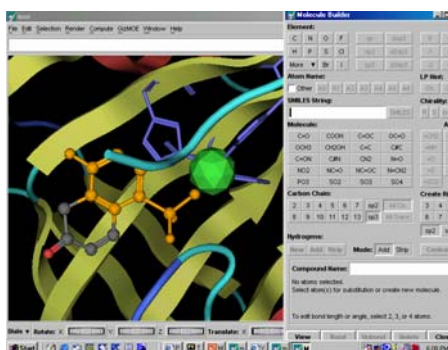
Button Bar for 3D Rendering Window

- Functions include:
  - Adding/Removing H's
  - Change Element
  - Change Ionization
  - Change Geometry
  - Bond/Unbond
  - Delete



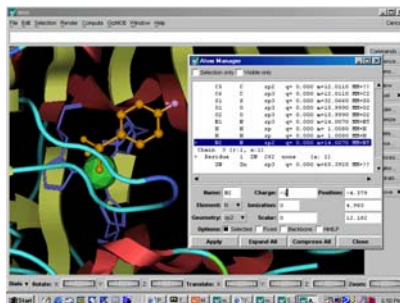
# Editing 3ca2 Ligand

- Delete the Hg atom on the ligand as well as the H that replaces it.
- Fuse a benzene ring to the aromatic already present.
  - Select the 2 Carbons to fuse the ring to. Chose Create Ring (6) with sp<sup>2</sup> geometry
- Replace one of the sp<sup>2</sup> Carbons with a carbonyl functional group.
- Use the Unbond key to release the fused ring from ams and delete it.



## Using the Atom Manager

- Used to view atom attributes.
- Accessed by Edit pulldown in main window or by double clicking on atom of interest.
- Attributes relevant to bonding:
  - Element
  - Ionization: Formal Charge
  - Geometry: hybridization
  - HintLP (toggle to indicate if element has a lone pair not conjugated into aromatic system)
- Use Atom Manager to:
  - Change aromatic ring in ams to cyclohexane
  - Change formal charge of nitrogen
  - Change resonance structure of ams.



## Atom Attributes

- Can be viewed in Atom Manager
- Modified in atom manager or from Edit pulldown in main window
- Attributes relevant to bonding
  - Element
  - Ionization: formal charge
  - Geometry: hybridization
  - HintLP (toggle to indicate if the element has a lone pair not conjugated into an aromatic system)

## Viewing Molecular Data

- MOE has 3 main windows for viewing the molecular data
  - main window
  - atom manager
  - sequence editor
- can be used to view, edit and select molecular data

## Display Options: 3D Rendering Window

- Render|Draw offers options of what to show in the main window
  - Ribbon, Alpha Trace, Hydrogen Bonds, Meters, Constraints, Bond Orders, Coordinate Axes
- these modes are applied to the entire system

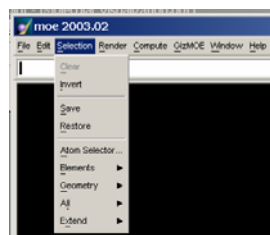
## 3D Rendering Window: Footer



- The footer in the 3D rendering window has 3 pages: Dials, 3D, View
- Dials: rotate and translate the system. Same <ctrl>+middle mouse drag and <shift>+middle mouse drag but the dials may give you more control.
- View: same as Render|View and right button bar View page but with 8 slots instead of 4.
- 3D: controls the Z-axis clipping region and Z-axis depth cue shading parameters.

## Selecting Atoms and Sets of Atoms

- Atom, residue, chain selection sets
- Selection menus provide specialized operations
- most selection operations add to the current selection set





## Selecting Atoms: 3D Rendering Window

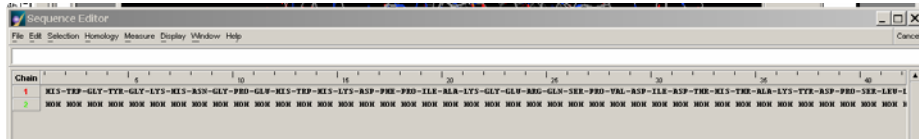
- Left mouse button for selection
- Double click to select and open Atom Manager with the selected atom highlighted
- <Shift>-click to toggle a selection state
- <Ctrl>-click to select entire residue
- <Shift> + <Ctrl>-click to toggle selection of entire residue

## Selecting Atoms: 3D Rendering Window

- Selection Menu used for more advanced types of selections
- Substructure matching and proximity
- Save & Restore selection set



## Selecting Residues: Sequence Editor

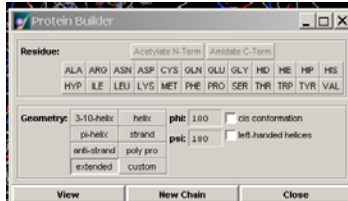


- Left mouse button click to select a residue
- <Shift>-click to extend the selection set to include all residues located in between the previous selection and the current
- <Ctrl>click to toggle a selection state of a residue

## Carbohydrate Builder

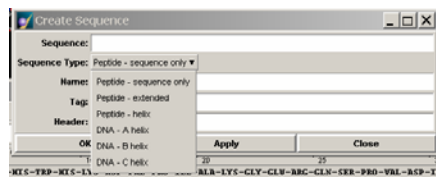
- Creates carbohydrates by linking sugar residues at specific positions
- invert chiral centers or entire residues by first selecting
- mutate residues in existing carbohydrate structures
- specify glycosidic torsion angles between residues

# Protein Builder



- Located under the Edit file menu

# Nucleic Acid Builder



- Hidden in the Sequence Window under Edit|Create sequence

## Problems with Ice/Vacuum Calculations

- Temperature of ice is 0 K!
- Hydrogen bonding over emphasized!
- Energy vs. free energy
- Interacting not Binding

