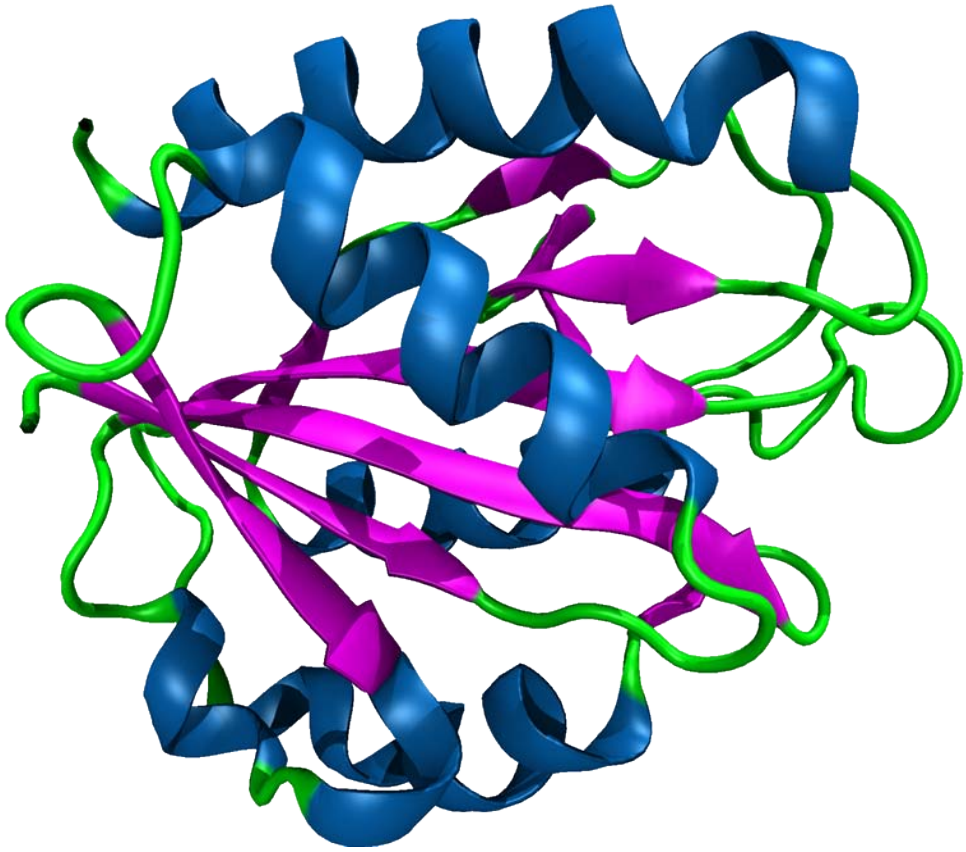
VMD

Visual Molecular Dynamics

User Guide



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Penn
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ITEST-NANO
small things considered

Introduction

VMD (Visual Molecular Dynamics) is a software package for the 3D visualization, modeling and analysis of molecular systems. It is developed and freely distributed by the Theoretical and Computational Biophysics Group at the University of Illinois at Urbana-Champaign. VMD is a powerful instrument used in **real** scientific research. Additionally, it is also a highly effective teaching tool. To increase the usability of this software for high school students, we have developed a simplified graphical user interface (GUI) for ITEST. The ITEST GUI limits the functionality of the program but is more user friendly. This is an abbreviated guide that covers the download, installation and use of VMD and the ITEST GUI. Further questions can be sent to Bob Johnson: bobjohnson1981@gmail.com.

Download and Installation

Download and installation is a two-step process. First, VMD will be downloaded and installed. Then the ITEST GUI files will be downloaded and installed from within VMD.

VMD Installation

1. Go to http://www.ks.uiuc.edu/Research/vmd
2. Click on “Download VMD” on the left side of the screen.
3. Download **VMD Version 1.8.7**

   Windows users should select:
   Windows OpenGL (Microsoft Windows XP/Vista/7 (32-bit) using OpenGL)

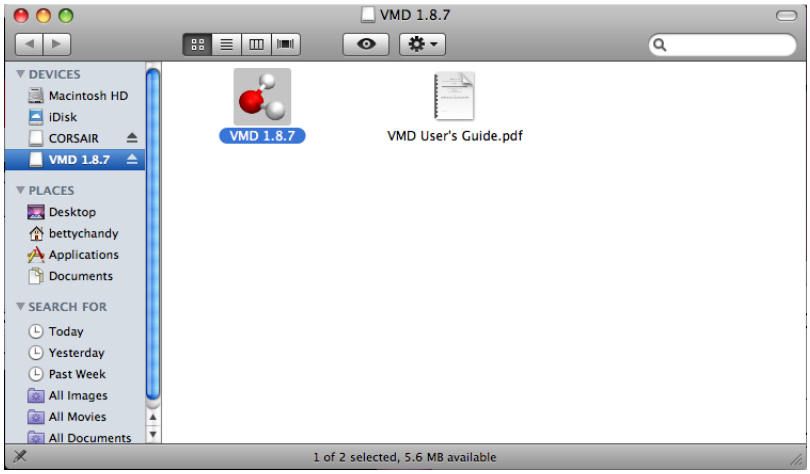
   Mac users with Intel CPUs (newer Macs) should select:
   MacOS X OpenGL (Intel x86) (Apple MacOS-X (10.4.7 or later) with hardware OpenGL (native bundle))

   Mac users with PowerPC CPUs (older Macs) should select:
   MacOS X OpenGL (PowerPC) (Apple MacOS-X (10.4.7 or later) with hardware OpenGL (native bundle))

   To determine what type of CPU is in your Mac, go to the **Finder** and choose **About this Mac** from the **Apple Menu**.
4. Register a username and password
5. Download the file
6. Install VMD

   Windows users:
   To install, double click on vmd187win32.msi and follow the installation instructions

Mac users:
Double click on vmd187macx86104.dmg. The following window will then appear:



Drag the VMD 1.8.7 icon onto your Desktop

7. Run VMD:

   Windows users:
   Go to Start → Programs → University of Illinois → VMD → VMD 1.8.7

   Mac users:
   Double click the VMD 1.8.7 icon on your Desktop

ITEST GUI Installation

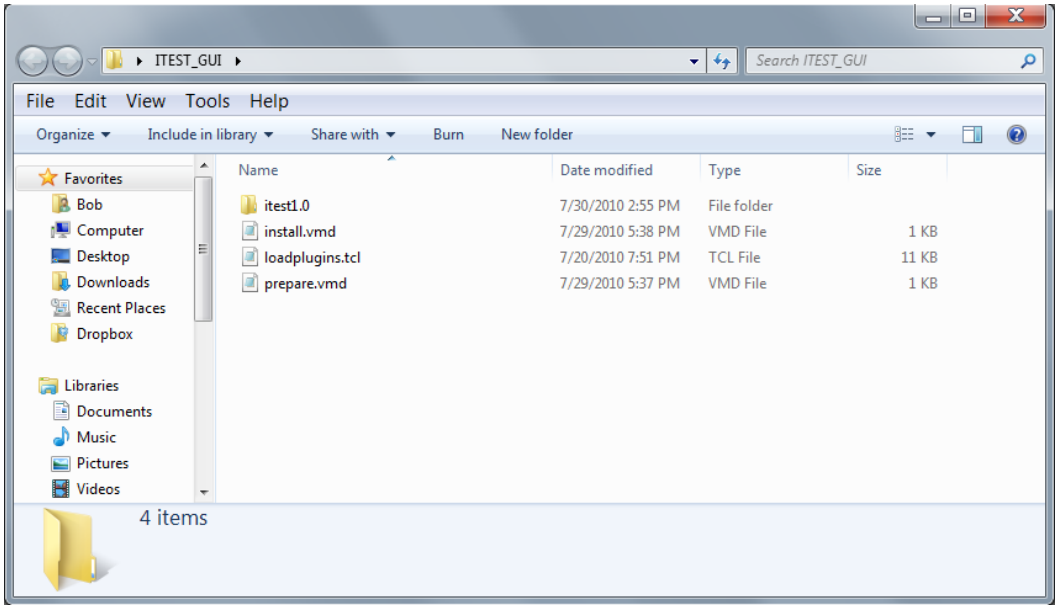
1. Download the file **ITEST_GUI.zip** from the ITEST Google Groups site.

2. Unzip the file

   Windows users:
   Right click on the file and click extract and follow the instructions

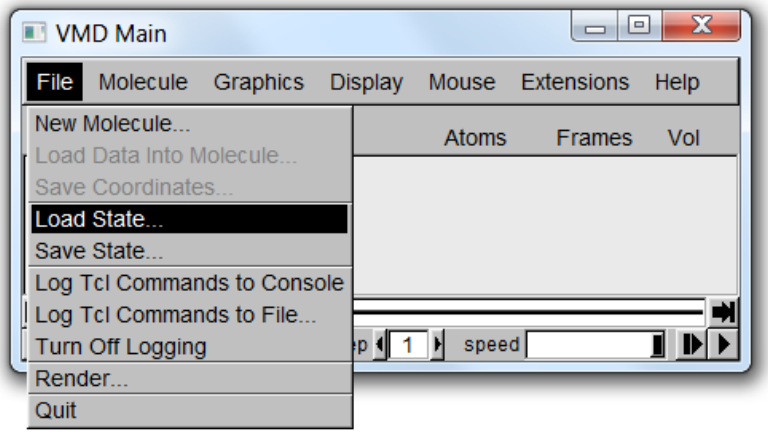
   Mac users:
   Double click on the file

   You will then have a folder called ITEST_GUI that contains the following files:

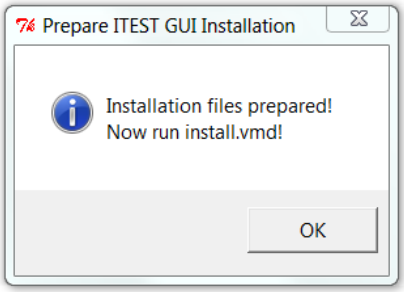


3. Run VMD

4. In the **VMD Main Window** click on **File** and then **Load State...**

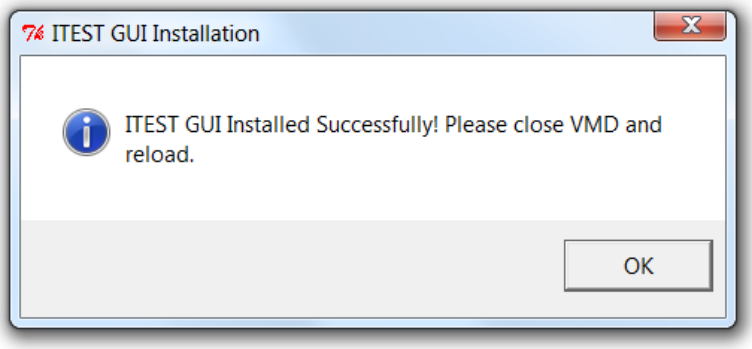


5. Navigate to the ITEST_GUI folder and select **prepare.vmd**. You should then see the following window:



Click OK to continue.

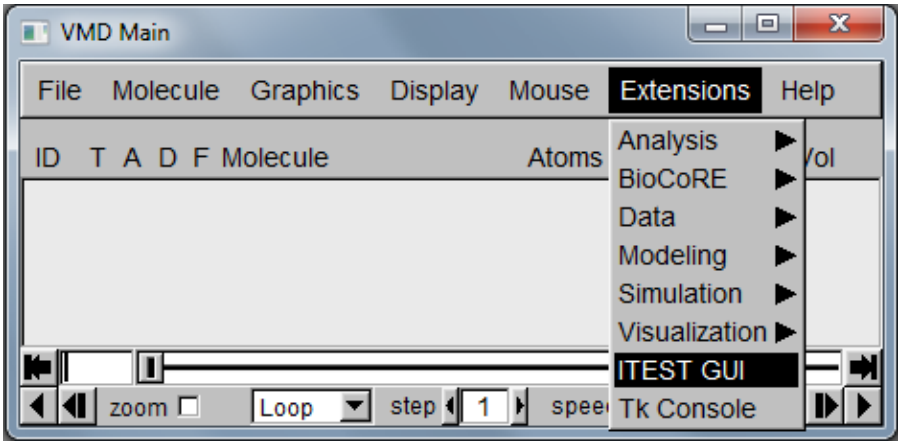
6. Now click on **File** and then **Load State...** again. Navigate to the ITEST_GUI folder and select **install.vmd**. This will install the ITEST GUI files. You should see the following window:



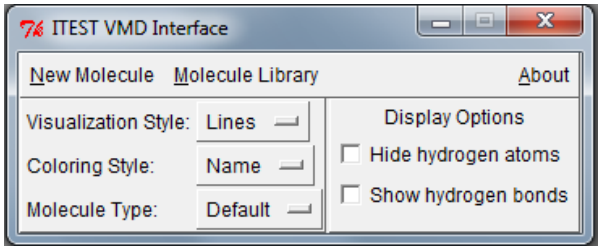
7. Now close the program and then rerun VMD.

ITEST GUI

A simplified interface is made available for ITEST participants. While it is possible to use the normal graphical interface packaged with VMD, it is recommended that those new to VMD use the ITEST GUI (graphical user interface). To access this interface, open VMD and then click on the Extensions menu and then ITEST GUI.

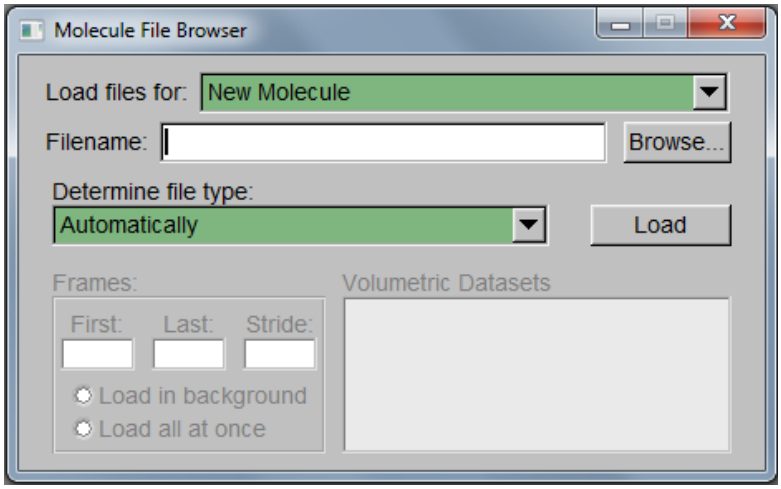


This will open a new window entitled “ITEST VMD Interface”.



Loading Molecules

VMD accepts many types of input files. However, among the most common types are **PDB** (Protein Data Bank) files which have the .pdb file extension. You can find PDB files on the web for many molecules ranging from small organic molecules to large biomolecules like proteins and DNA. Normally, you can simply load these files into VMD without viewing or editing their content. To load a pdb file, click on “New Molecule”. A new window will pop up and you will be able to Browse your computer for the desired pdb file. After you have selected a pdb file with the Browse… button, click Load. The molecule will then appear in the VMD OpenGL Display window.



Changing the Visualization Style

The ITEST GUI enables the user to change the visualization of a loaded molecule. The following visualization styles are available:

Style	Description
Lines	Draws chemical bonds as lines
Stick	Draws chemical bonds as sticks
Ball and Stick	Draws atoms as spheres and chemical bonds as sticks
Space Filling	Draws atoms as spheres with radius given by the actual atomic radius
Surface	Draws the molecule as a 3D surface
Cartoon	Emphasizes the secondary structure of biomolecules
Ribbons	Draws the backbone of proteins or DNA as a ribbon

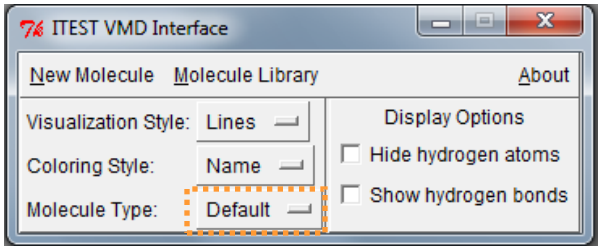
Changing the Coloring Style

The ITEST GUI enables the user to color the molecule according to several styles:

Name	Colors atoms by name. Carbon: Cyan Hydrogen: White Oxygen: Red Nitrogen: Blue Phosphorus: Brown Sulfur: Yellow
Chain	Colors each chain (molecule) of a biomolecular complex a different color
Polarity	Colors amino acids according to polarity Polar: Green Positively Charged: Blue Negatively Charged: Red Hydrophobic: White
Secondary Structure	Colors proteins by secondary structure Alpha Helix: Purple 3-10 Helix: Blue π-helix: Red Beta Sheet: Yellow Turn: Cyan Coil: White
Index	Colors atoms according to index
Throb	Flash different colors
ColorID	User defined color

Select Display Options

The user can select the type of molecule that is currently loaded in VMD via the "Molecule Type" menu. Currently, there are three types of molecules: Default, Nucleic Acids, Protein. Specifying the molecule type will enable additional Display Options that are shown on the right hand side of the GUI.

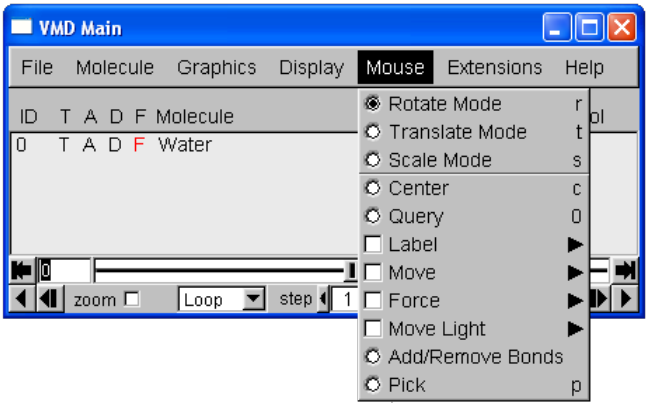


The user can then set additional display options that emphasize properties of the molecule. The display options are given below.

Default	Protein	Nucleic Acids
• Hide hydrogen atoms • Show hydrogen bonds	• Hide hydrogen atoms • Show hydrogen bonds • Show backbone hydrogen bonds • Show bound ligands • Show alpha carbons • Show side chains	• Hide hydrogen atoms • Show hydrogen bonds • Show base hydrogen bonds • Emphasize bases • Emphasize sugars • Emphasize phosphates • Emphasize adenines • Emphasize cytosines • Emphasize guanines • Emphasize thymines • Emphasize uracils

Interaction Modes

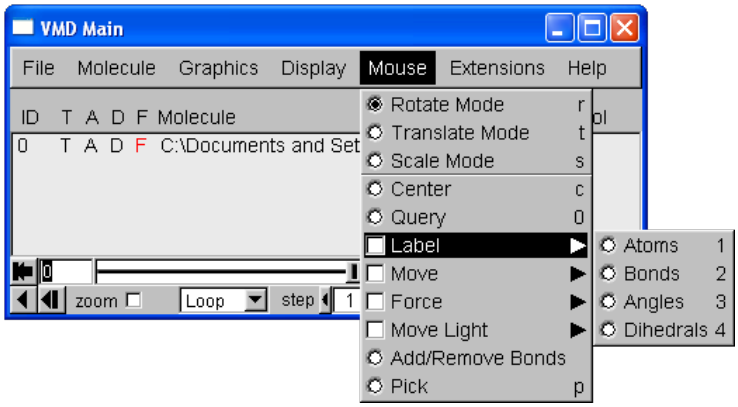
The user can interact with the molecule in a variety of ways. The user can rotate, translate and scale (zoom) the molecule. Each of these interactions modes can be accessed via the **Mouse** menu in the **VMD Main** window or using a shortcut key listed below. After the interaction mode has been selected, click on the **OpenGL** window with the left mouse button and drag the mouse. By default, VMD starts in **Rotate Mode**.



Mode	Shortcut Key	Description
Rotate	r	Rotates the molecule
Translate	t	Translates the molecule
Scale	s	Scales the molecule (zoom)
Center	c	Centers on an atom

Measuring Structural Features

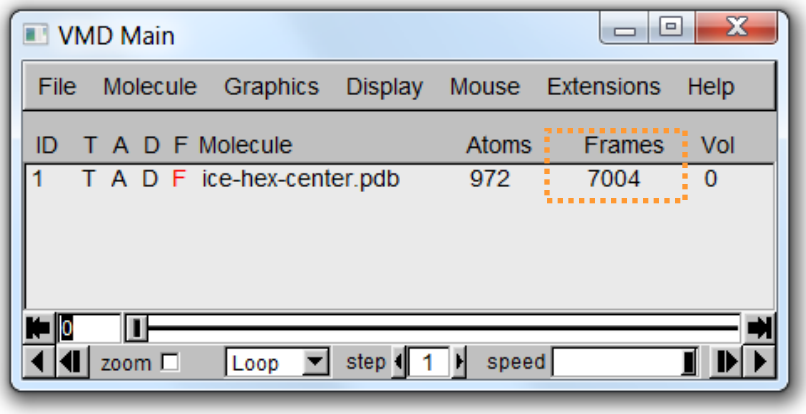
You can place labels that specify the distance between two atoms, the angle formed by three atoms and the dihedral angle formed by four atoms. To do so, select the particular feature you would like to label from the Mouse menu in the VMD Main window or using a shortcut key listed below. Then click on the atoms you would like to measure.



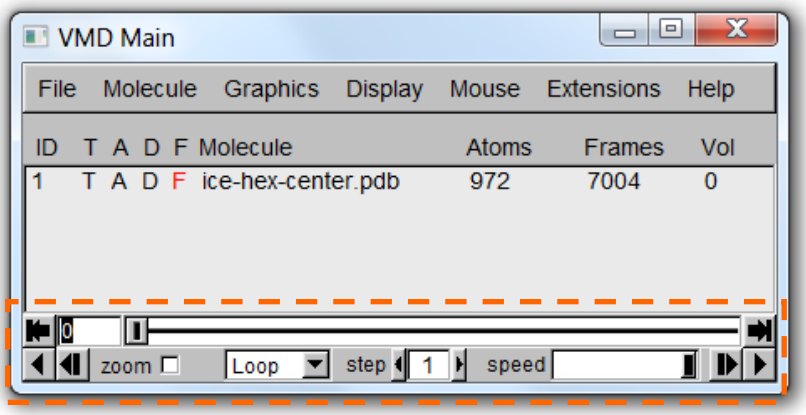
Feature	Shortcut Key	Description
Bond length	2	Distance between two atoms
Angle	3	Angle between three atoms
Dihedral Angle	4	Dihedral angle between four atoms

Playing a Trajectory

VMD can play an animation of a molecule if provided with a trajectory file. Like PDB files, trajectory files come in many different formats. There are a few molecules in the ITEST GUI Molecule Library that contain trajectories. The number of frames in the trajectory is listed in the **VMD Main** Window:



The trajectory can be played using the arrow buttons at the bottom of the **VMD Main** window. The speed can be adjusted with the slider in the bottom right hand corner.



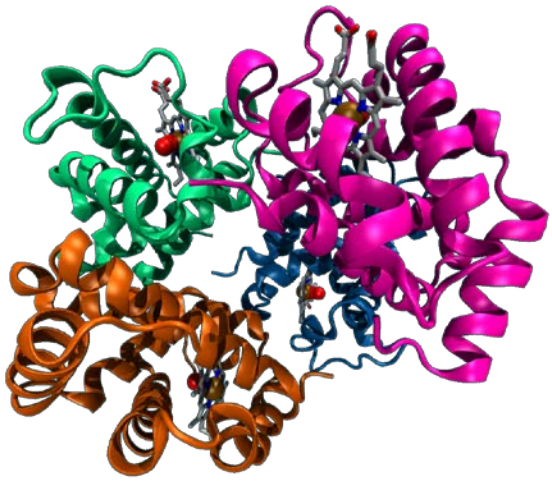
Saving an Image

To save a screenshot of the contents of the **OpenGL** window in the **File** menu of the **VMD Main** window go to: **File → Render → Start Rendering**

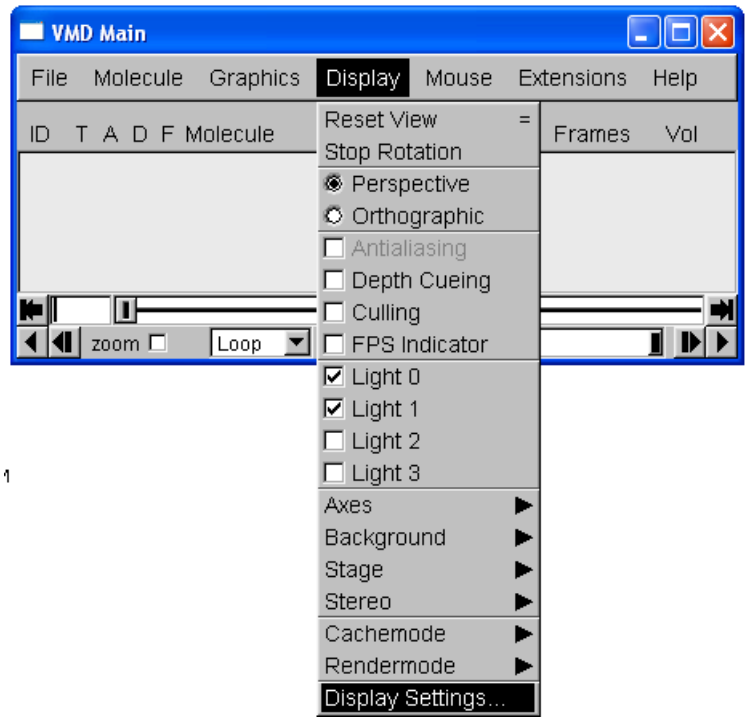
Using the default renderer takes a screen shot of the VMD OpenGL window and saves it as an image.

Saving an Image with Lighting and Shadow Effects

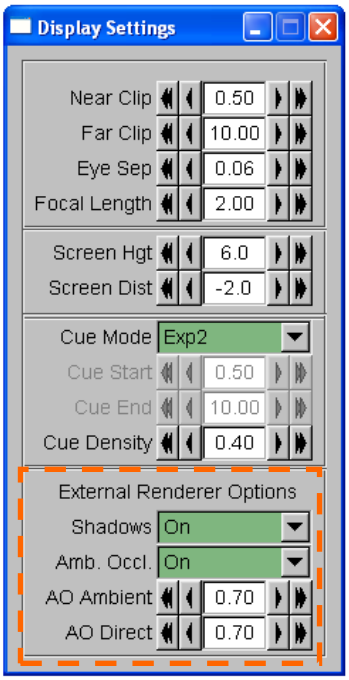
You can also save images that include lighting and shadow effects (see figure below of hemoglobin).



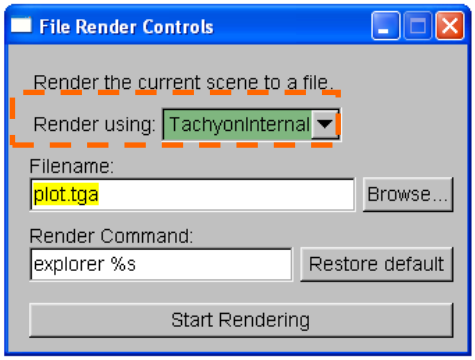
First, specify the strength of the lighting by going to **Display → Display Settings**



Turn **Shadows** and **Ambient Occlusion** on. Adjust **AO Direct** and **AO Direct** to your desired value (values of 0.70 for both usually works pretty well).



Go to **File → Render** and choose **TachyonInternal** as the renderer and click "Start Rendering". It may take a few minutes to render the scene.



Finding PDB Files

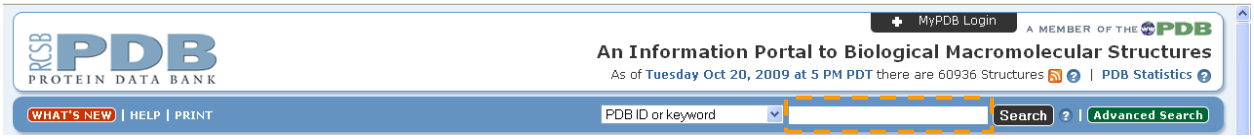
PDB files for many molecules can be found on the web by simply typing "<molecule> pdb" into a search engine. Here, <molecule> is the name of whatever molecule you are interested in. This is usually the best place to start. You can also visit sites such as:

- **Bob Johnson's VMD Resource Page** (www.sas.upenn.edu/~robertjo/pdb)
- **Klotho** (http://www.biocheminfo.org/klotho)
- **Protein Data Bank** (http://www.pdb.org)
- **Nucleic Acids Data Bank** (http://ndbserver.rutgers.edu)
- **European Bioinformatics Institute** (http://www.ebi.ac.uk)

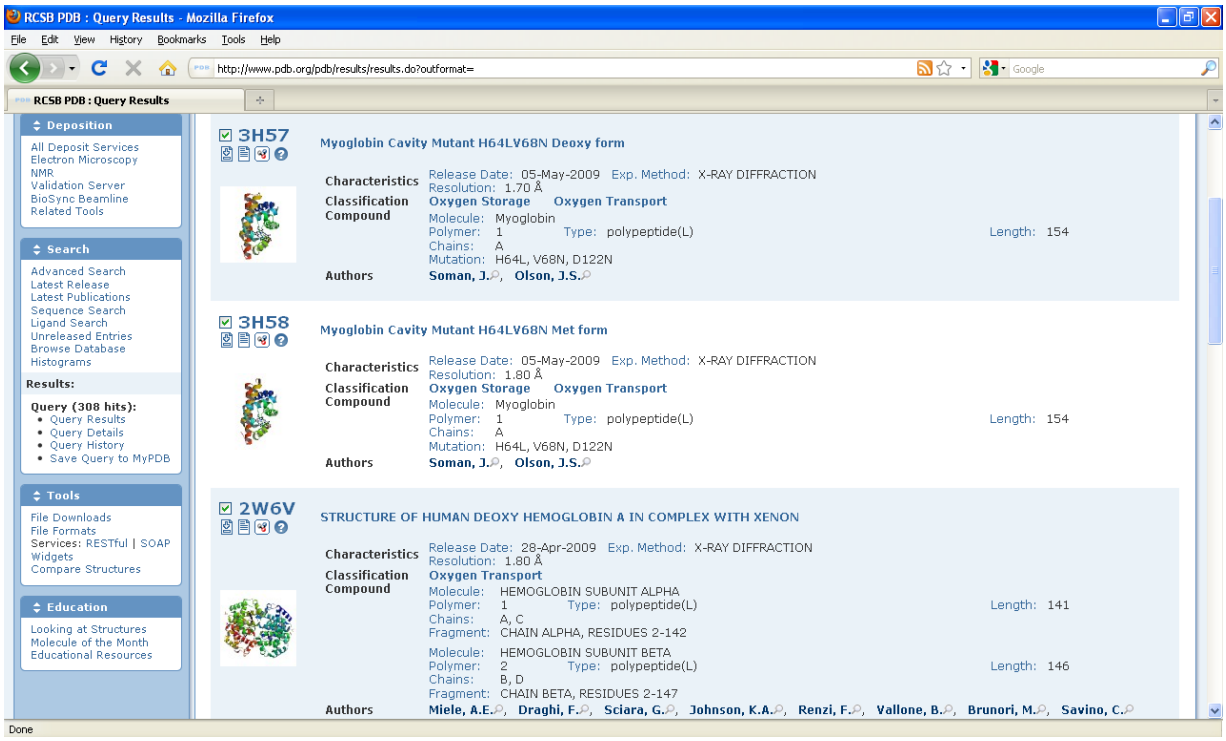
Using the Protein Data Bank

The Protein Data Bank contains PDB files for thousands of proteins whose structure has been resolved experimentally and is an indispensible resource in modern biological research.

Go to www.pdb.org. Type the name of the protein of interest in the search box and click **Search**.

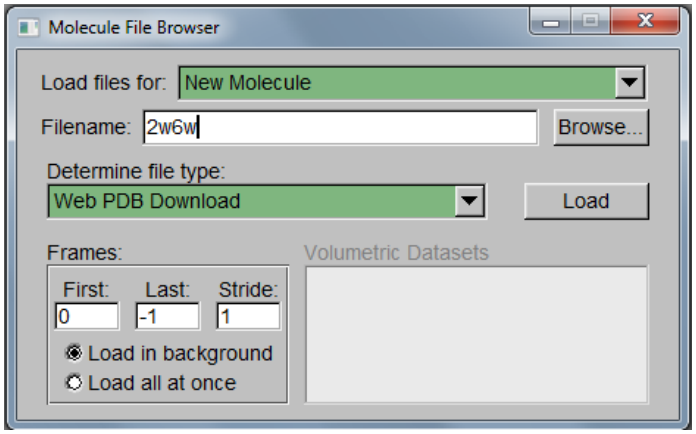


As an example, here are the first few search results for “myoglobin”.



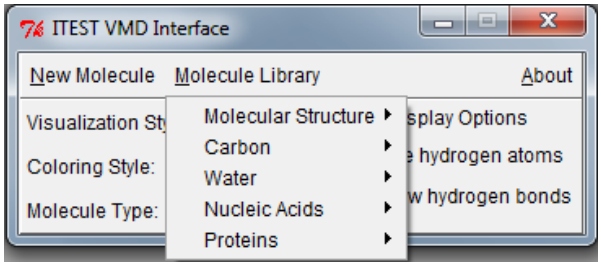
Usually, there are multiple entries for the protein of interest. The entries may differ in the experimental methods or conditions used to resolve the protein’s structure. You may have to browse through several entries before you find the right protein. However, for educational purposes, oftentimes the differences are negligible. Clicking on the title of the entry will transfer you to a page that contains further information about the protein and links to download the PDB file. For example, below is the entry for “CRYSTAL STRUCTURE OF RECOMBINANT SPERM WHALE MYOGLOBIN UNDER 1ATM OF XENON”.

Loading a structure from the Protein Data Bank can be done entirely within VMD. Each entry has a 4 character code (orange box in the image above). To load this structure into VMD, click on New Molecule, enter the 4 character code in the Filename box **and press Enter**. VMD should automatically detect that this is a Protein Data Bank file and "Web PDB Download" should then be displayed under "Determine file type:". You can then load this file by clicking on Load.



Molecule Library

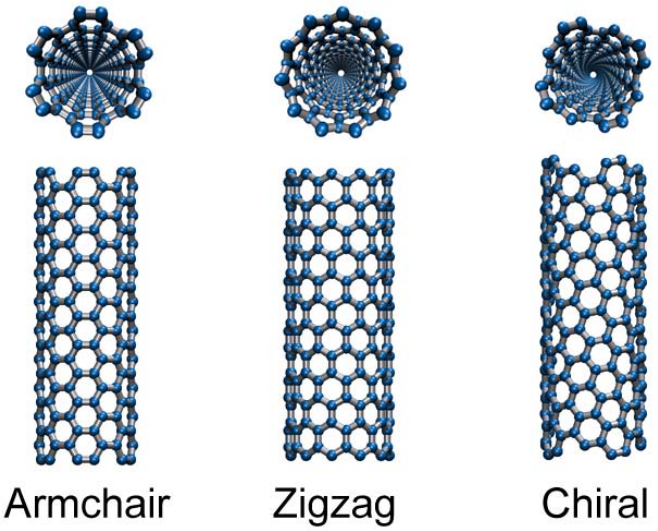
There are a number of molecular structures and animations packaged with the ITEST GUI. They are accessible in the Molecule Library menu at the top.



- **Molecular Structure**
  This menu item contains five geometries (Linear, Trigonal Planar, Tetrahedral, Trigonal Bipyramidal, Octahedral) that depict the basic types of 3D molecular structures predicted by VSEPR.

- **Carbon**
  Allotropes are different structural forms of an element. Allotropes are composed entirely of the same element but differ in the 3D arrangement of the atoms. Even though allotropes are fundamentally composed of the same material, their physical properties can differ greatly. Carbon is one of the best examples of this phenomenon. There are several well-known allotropes of carbon: diamond, graphite, buckyballs, nanotubes. Diamond and graphite have been known for hundreds of years. Even though they are both composed entirely of carbon, their physical properties are virtual opposite of each other. Graphite is soft and brittle, a good conductor of heat and electricity and opaque. Diamond, on the other hand, is one of the hardest naturally occurring materials, is one of the best insulators and transparent.

  Recently, other carbon allotropes were discovered. These include buckyballs (C_{60}) which have the structure of soccer balls and have diameters of about 0.71 nm. Carbon nanotubes are cylindrical tubes of carbon atoms with diameters of about 1 nm. They can assume a variety of atomic structures as shown below. Structures of these allotropes can be accessed from the Carbon menu. Users can even produce their own custom carbon nanotube structure in this menu.



- **Water**
  Water is one of the most important molecules on Earth and behaves very different from many other liquids. Many of water's anomalous properties can be attributed to how water molecules interact with one another. These interactions can be explored in the Water menu of the Molecule Library. The user can select to view the structures of water molecules in a variety of arrangements (monomer, dimer, pentamer). The user can also view a simulation of the transformation of water from solid to liquid to gas phase in the Phases of Water Animation. This animation is a 10.5 ps (10^{-12} s) simulation of solid water (ice) undergoing heating from 100 K to 900 K.

  For the first 1000 frames (1.5 ps), the temperature, and thus thermal fluctuations, are too small to break hydrogen bonds and the water remains in the solid phase (i.e. ice). As a solid, each water molecule is hydrogen bonded to four neighbors. Additionally, water in the solid phase is arranged in a hexagonal crystal lattice.

  In the next 3000 frames (4.5 ps) the water is heated to 370 K. The thermal fluctuations at this temperature cause the ice to melt into a liquid. In the liquid phase, thermal fluctuations cause hydrogen bonds to constantly break and reform. As a result, each water molecule in a liquid is hydrogen bonded to only 2-3 neighboring molecules. Additionally, as the hexagonal crystal melts, the water molecules adopt a more compact arrangement. Thus, liquid water is more dense than solid water which enables ice to float. As the liquid water droplet evolves it gradually becomes more spherical in shape. This is due to surface tension: water molecules on the surface of the droplet feel a constant force towards the center.

  For the last 3000 frames (4.5 ps) the water is heated to 900 K. The high temperature enables water to overcome the attractive hydrogen bond interactions and causes the liquid to evaporate into gas. Water gas (steam) is largely free space.

- **Nucleic Acids**
  Nucleic acids, which includes both DNA and RNA, can form double-stranded structures by forming base pairs between complementary nucleotides. In the Watson-Crick base pairing scheme, which is the most common scheme in biology, adenine pairs with thymine (or uracil in RNA) and guanine pairs with cytosine. Double-stranded structures usually assume a helical configuration. However, the structure of the helix is very sensitive to the nucleotide sequence and environmental factors such as temperature, salt concentration and presence of metal ions. In this menu, the user can explore several possible helical structures of DNA.

  A-DNA: This is a more compact form of B-DNA. A-DNA is a right-handed helical structure that occurs in dehydrated environments or in RNA-DNA hybrids.

  B-DNA: This is the most common structure of DNA in biology. B-DNA is a right-handed helix that contains about 10 base pairs per helical turn.

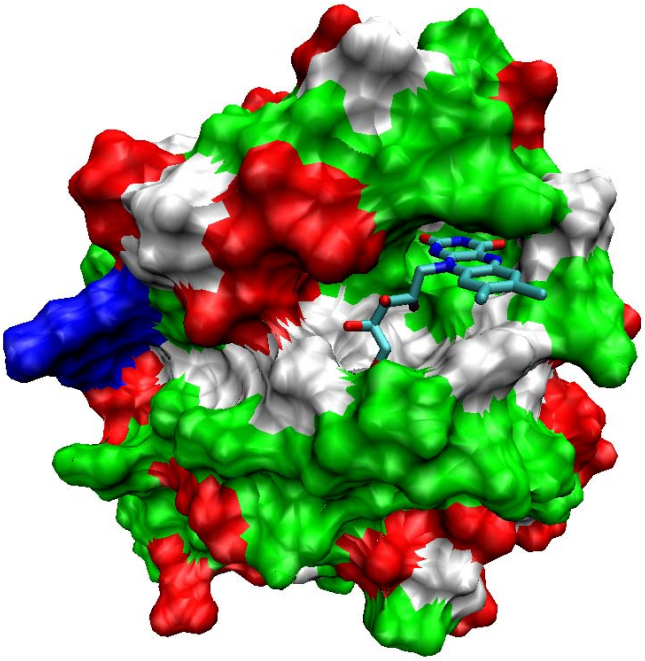
  Z-DNA: This structure can occur in low salt conditions for segments of the DNA that have repeating sequences of G-C/C-G base pairs. Z-DNA is a left-handed helix with the backbone having a zigzag shape..

  Hairpin: If portions of a single strand of DNA are complementary, the DNA can form a hairpin structure.

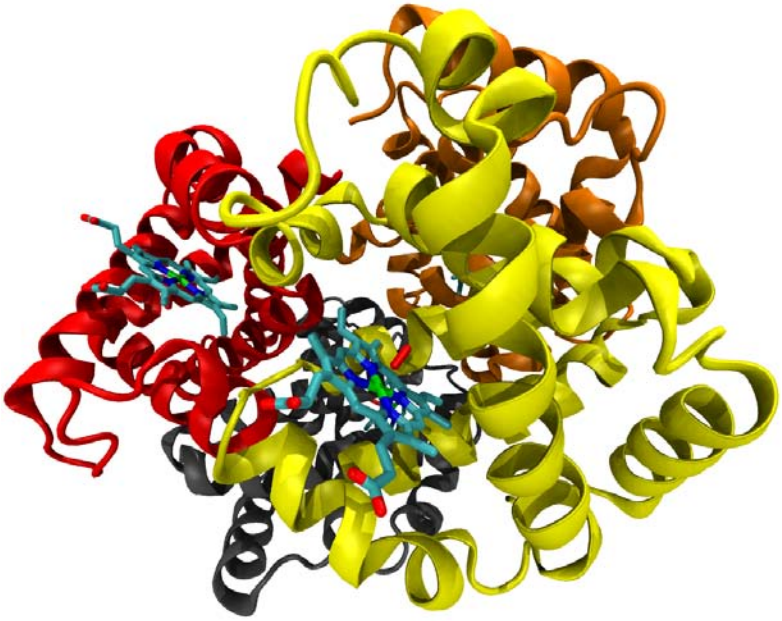
  Additionally, the Display Options menu enables the user to learn about the various structural features of DNA. For example, the user can visualize the three basic units that compose DNA: bases, sugars and phosphates. The user can visualize the different bases (adenine, cytosine, guanine, thymine, uracil) and which ones are complementary. Intra-base pair hydrogen bonds can be displayed as well. This feature can be used to learn about the relative binding strengths of A-T and G-C base pairs, which are held together by two and three hydrogen bonds, respectively.

- **Protein**
  Proteins are biopolymers composed of chains of amino acids. There are 21 naturally occurring amino acids that vary in size, structure and polarity. The Protein menu enables the user to explore the various structural features of proteins.

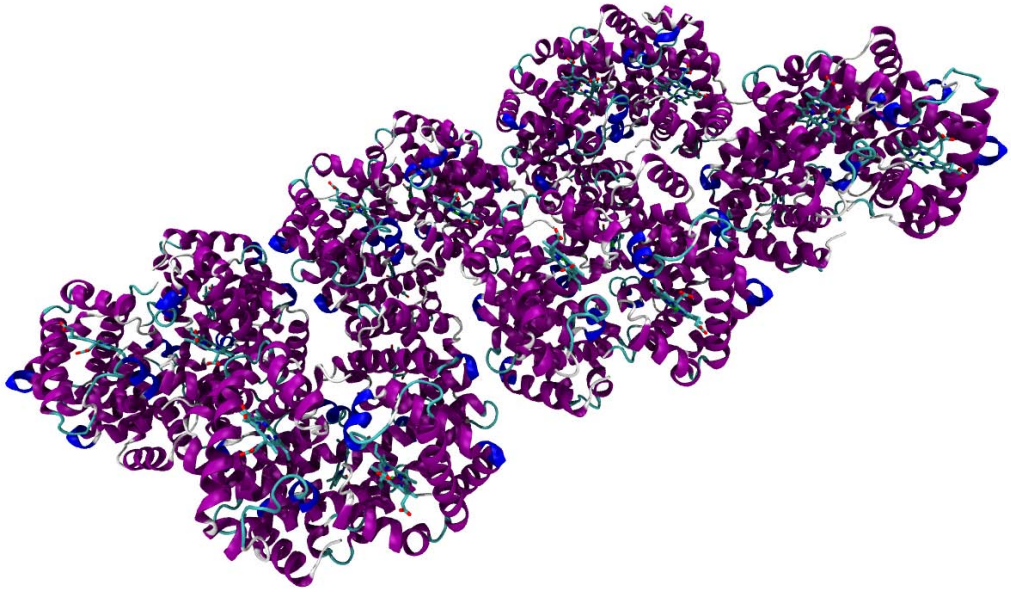
  Flavodoxin: A bacterial protein involved in basic metabolic processes. Flavodoxin binds flavin-mononucleotide. Many proteins bind small molecules (ligands) in order to carry out their functions. The shape of the ligand is complementary to the binding doman of the protein. An example of this is shown in the image below which depicts the flavin-mononucleotide resting in the binding domain of flavodoxin. One way to inhibit a protein's function is to synthesize a molecule (drug) that has a high affinity for the protein's binding domain (often called the active site).



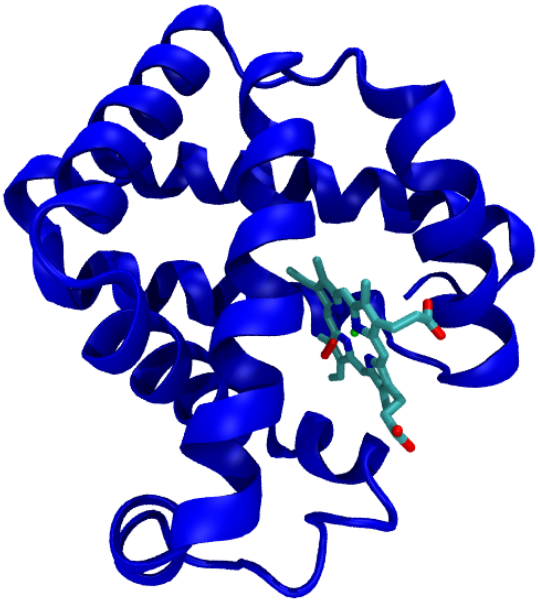
Hemoglobin: Hemoglobin is the protein responsible for binding oxygen molecules within red blood cells. Hemoglobin is composed of a complex of four separate proteins (colored red, yellow, orange and gray below). Each protein within hemoglobin contains a heme group. An oxygen molecule (O_2) can bind to the central iron atom (green atom in below image) in the heme group. Hemoglobin has two forms: oxy- and deoxy-hemoglobin. In oxy-hemoglobin, an oxygen molecule is bound to each of the four heme groups. The binding of oxygen to a heme group triggers a conformational change in hemoglobin that enables oxygen molecules to bind to the remaining heme groups. This conformational change is shown in the Hemoglobin Animation.



Hemoglobin S: Hemoglobin S is a mutated form of hemoglobin that is responsible for sickle cell anemia. Hemoglobin S results when the glutamate in position 6 of each hemoglobin protein is mutated to valine. This mutation causes hemoglobins to congregate and form long fibers. A segment of such a fiber is shown below. These fibers cause red blood cells to become rigid. It is difficult for these rigid red blood cells to pass through narrow capillaries which causes vascular occlusion (blocked blood vessels) and ischemia (restricted blood supply).



Myoglobin: Myoglobin stores oxygen in muscle tissue. Each myoglobin contains a single heme group which binds one oxygen molecule. Myoglobin was the first protein to have its 3D structure determined. High concentrations of myoglobin in muscle tissue enable organisms to hold their breath longer. Whales and seals, for example, contain a high concentration of myoglobin in their muscles.



Ubiquitin: Ubiquitin is a small protein that is found eukaryotic cells. It's main function is to label proteins for degradation. This protein serves as a nice example of protein structure. It is composed of several beta sheets and a single alpha helix. By checking the box "Show backbone hydrogen bonds" reveals that these secondary structural elements are held together by hydrogen bonds within the backbone.