

Protein Modeling Division C 2012
San Diego Science Olympiad

Nov. 12, 2011

Bernardo Heights Middle School

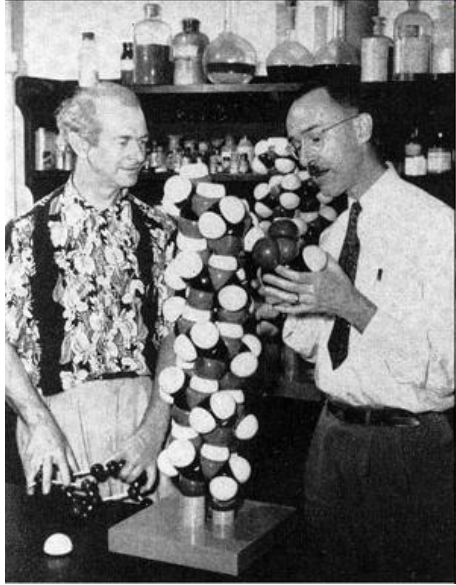
3:20 - 4:00 pm

What is Protein Modeling?



- Learn how to visualize 3D protein structures
- Build an accurate model of a protein structure using plastic tubes or wires
- Learn about protein structures and how they can be used to understand diseases and develop treatments

First Protein Models



<http://www.pnas.org/site/misc/classics1.shtml>

Pauling & Corey 1951
 α helix model



Nature Reviews | Molecular Cell Biology

http://www.nature.com/nrm/journal/v9/n8/fig_tab/nrm2446_F2.html

Kendrew (right) 1958
first protein crystal structure: myoglobin

Perutz (left) 1960, hemoglobin

Protein Modeling C Event

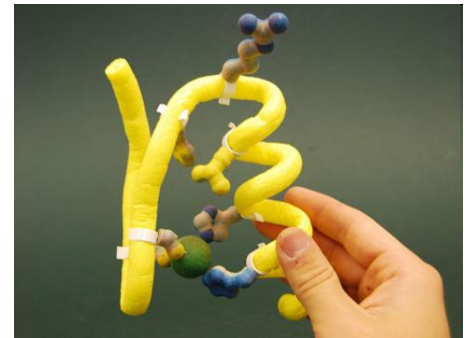
1. Pre-build models

- Build a large protein model
- Will **not** be impounded or scored at SD event!



2. On-site models

- Build a region of a protein
- 50% of score



3. Written test

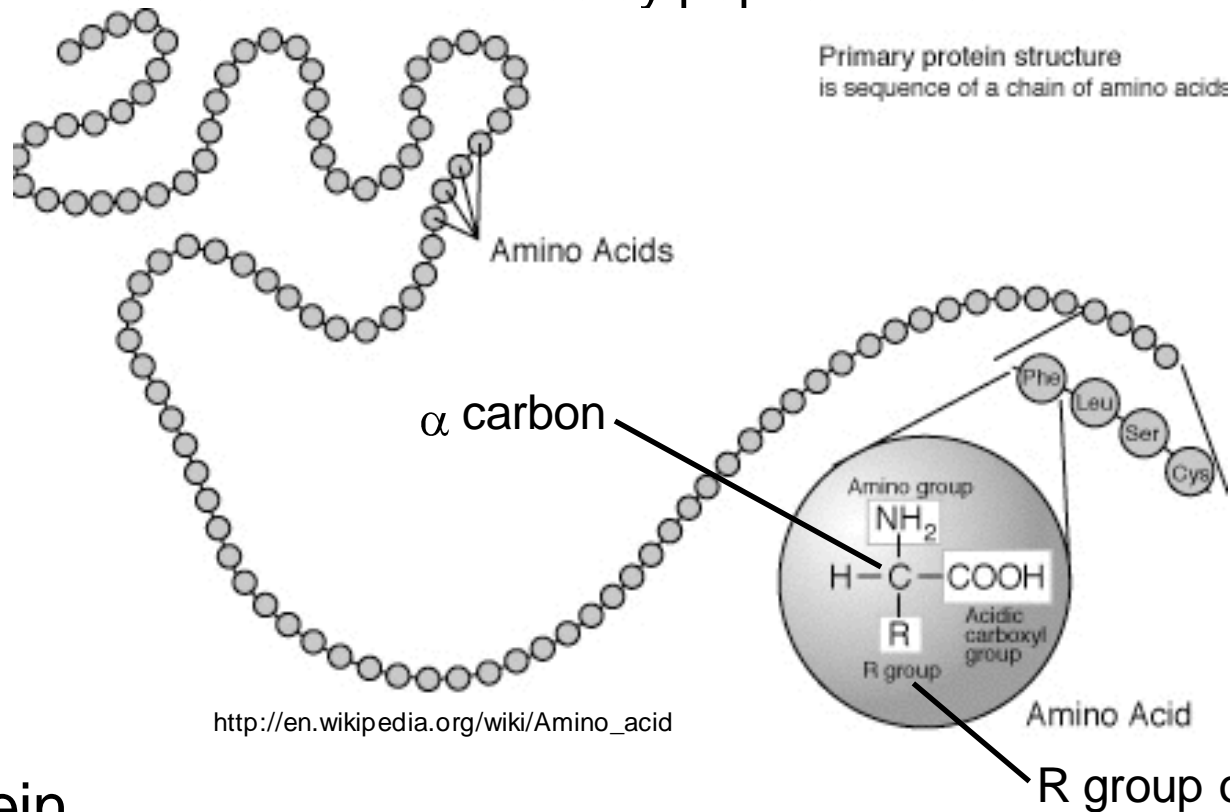
- Multiple choice questions
- 1 written tie-breaker question
- 50% of score

Multiple Choice Questions:

- A** 1. Which of the following amino acids is involved in disulfide bonds?
- A. Cysteine
 - B. Histidine
 - C. Tyrosine
 - D. Methionine
- B** 2. Which of the following bonds is the strongest?
- A. Hydrogen bond
 - B. Covalent bond
 - C. Ionic bond
 - D. Electrostatic bond
- D** 3. On your onsite model, you positioned amino acid Asp151. Which of the following statements is an accurate description of the significance of this amino acid?
- A. Asp151 is involved in binding Tamiflu, an antibiotic used to treat influenza.
 - B. Asp151 plays a role in creating the tertiary structure necessary for the function of neuraminidase.
 - C. Asp151 is one of the important amino acids necessary to dock the influenza virus on the host cell.
 - D. Asp151 is an amino acid that is essential to the catalytic activity of the enzyme.

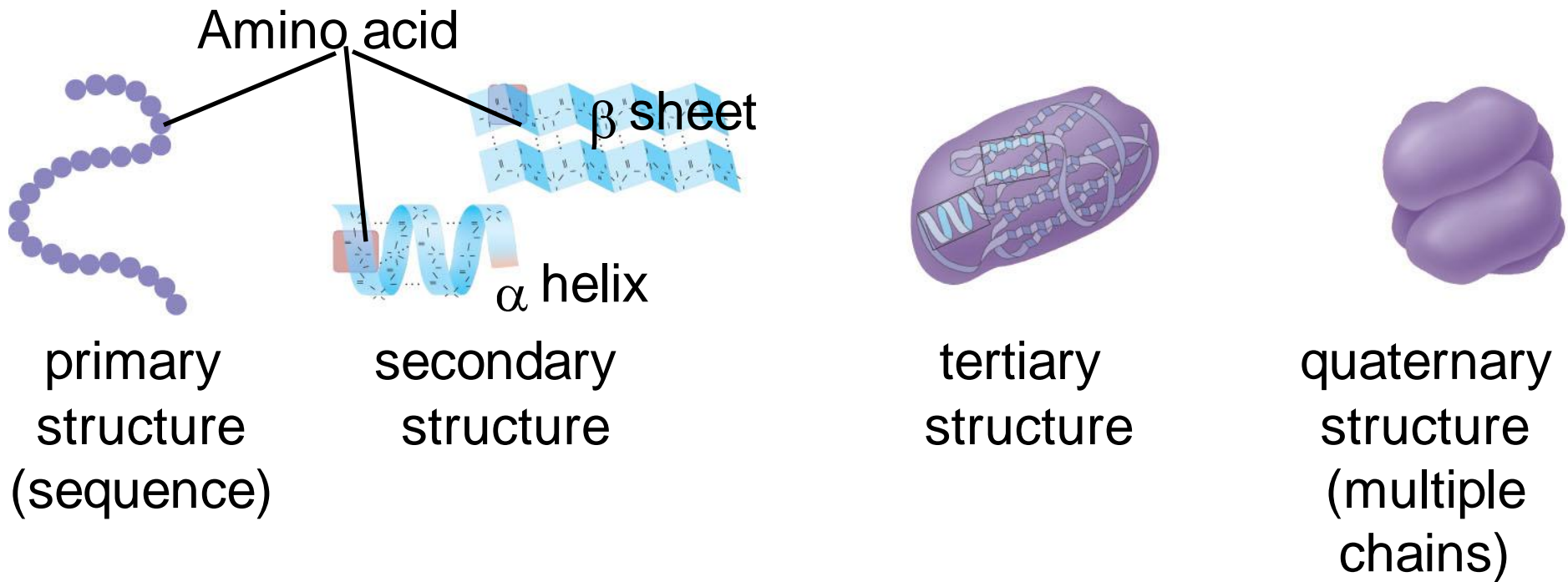
What are Proteins?

- Polypeptides
 - Polymers of amino acids (building blocks or monomers)
 - Amino acids are connected by peptide bonds




- Protein
 - Consists of one or more polypeptides (chains)

4 Levels of Protein Structure

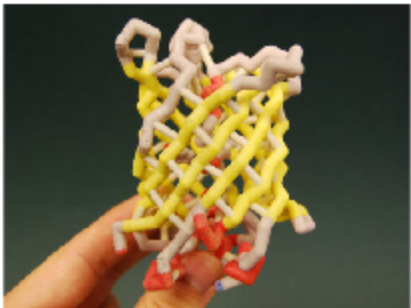


Protein Structure Tutorial



Back to Main Menu	Primary Structure Jmol	Tertiary Structure Jmol
	Secondary Structure Jmol	Quaternary Structure Jmol

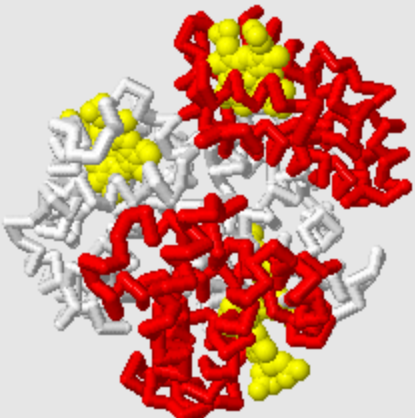
Welcome to the
Protein Structure Online Jmol Collection



Brought to you by the MSOE
Center for BioMolecular Modeling

Click the buttons below or at the top of the screen
to explore each of the four levels of protein structure.

Primary Structure Jmol	Tertiary Structure Jmol
Secondary Structure Jmol	Quaternary Structure Jmol



Copyright - MSOE Center for BioMolecular Modeling

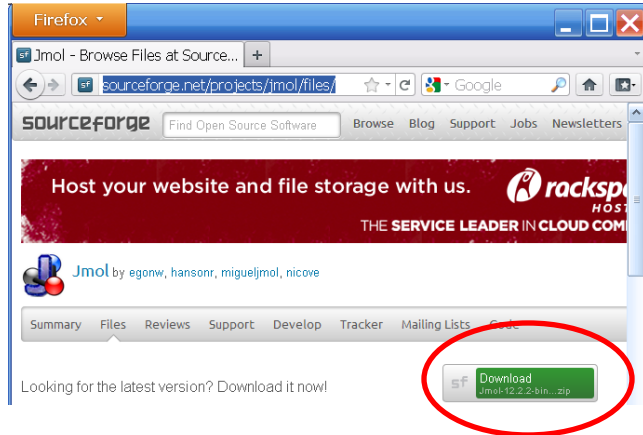
<http://cbm.msoe.edu/includes/jmol/SOJmols/proteinStructureHome.html>

Computer Visualization of Protein Structures

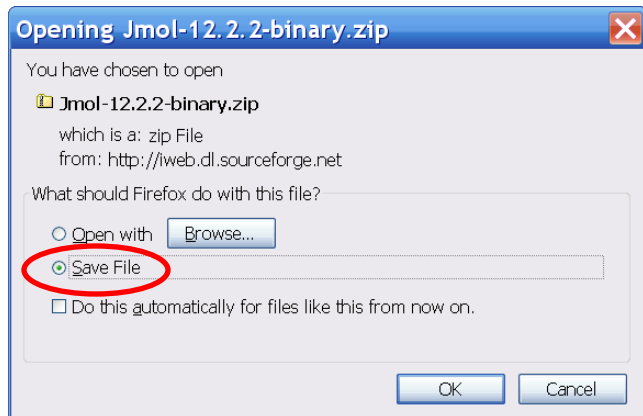
- Jmol, a free open-source program
- Jmol displays protein structures from the Protein Data Bank (<http://www.pdb.org>)
- How do I install Jmol?
- How do I use Jmol?

Installing Jmol

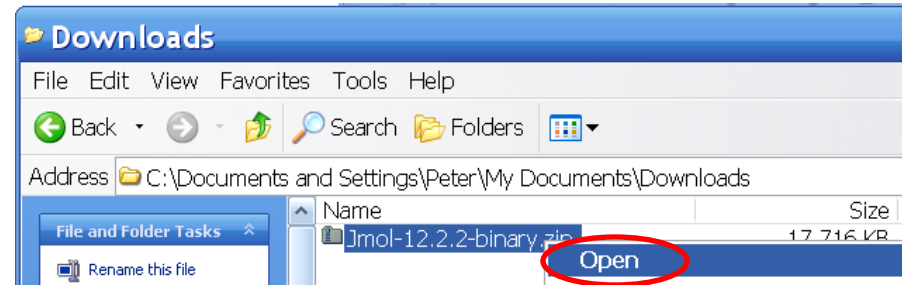
1. Go to <http://sourceforge.net/projects/jmol/files/> and click on the green download button



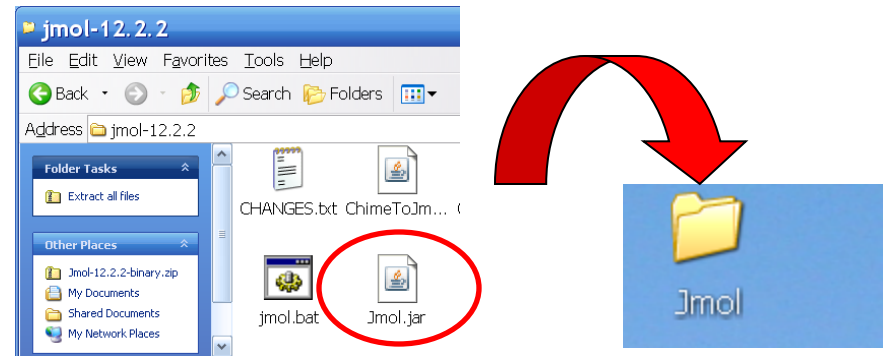
2. Choose Save File and click ok



3. Right click on Jmol-12.2.2-binary.zip file -> Open



4. Copy Jmol.jar file to a new folder



6. Right-click Jmol.jar and select "Send to -> Desktop (create shortcut)"

7. Click on the shortcut to launch Jmol



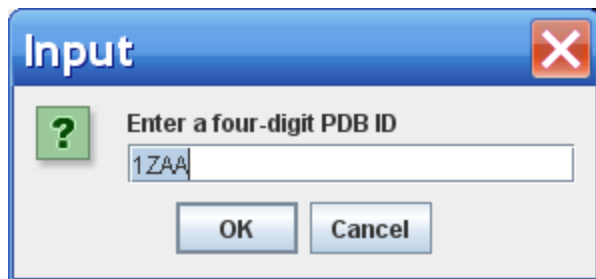
Download a PDB File into Jmol

A Protein Data Bank (PDB) file contains the 3D coordinates of proteins and nucleic acids. Each file has a 4-letter identifier, for example: 1ZAA

To load a PDB file:

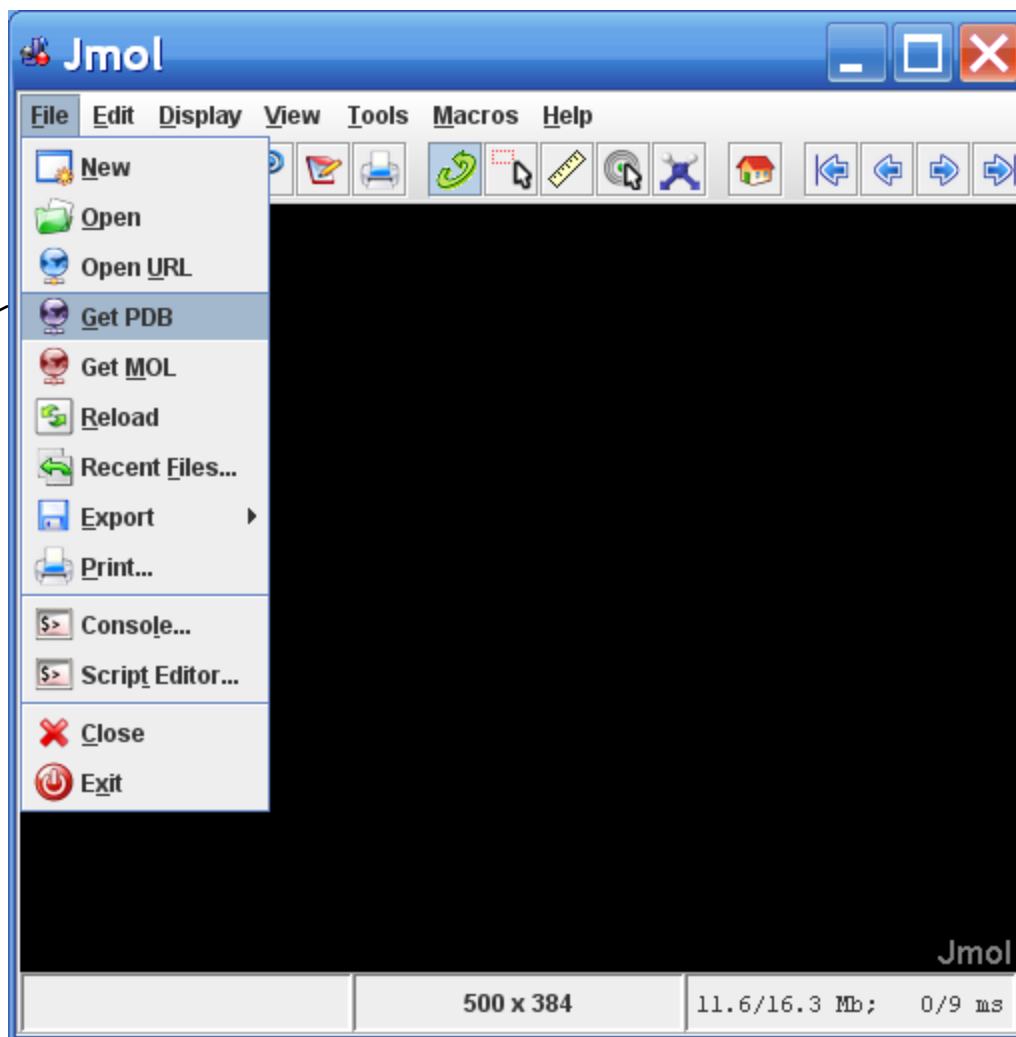
File ->Get PDB

and type in PDB ID

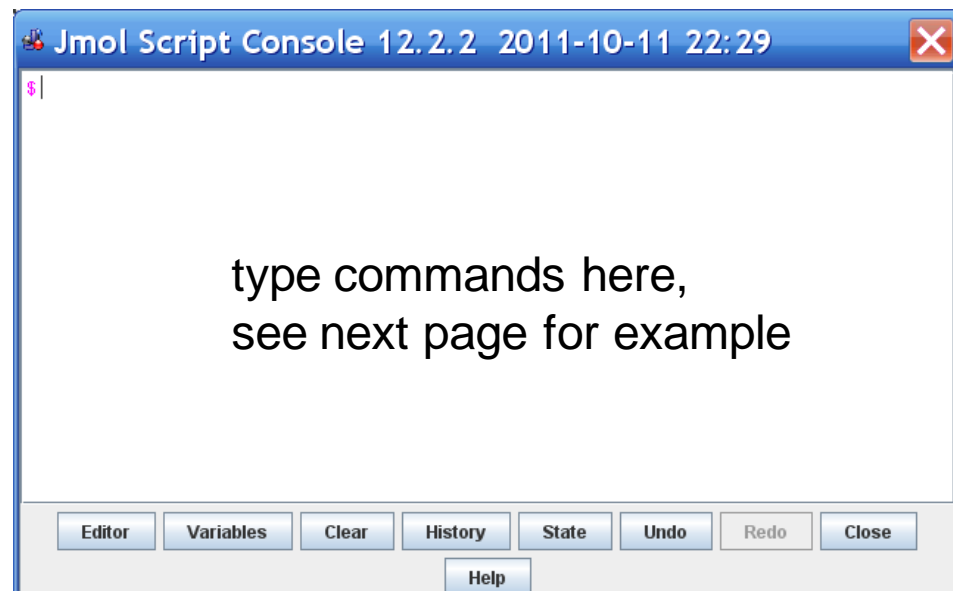
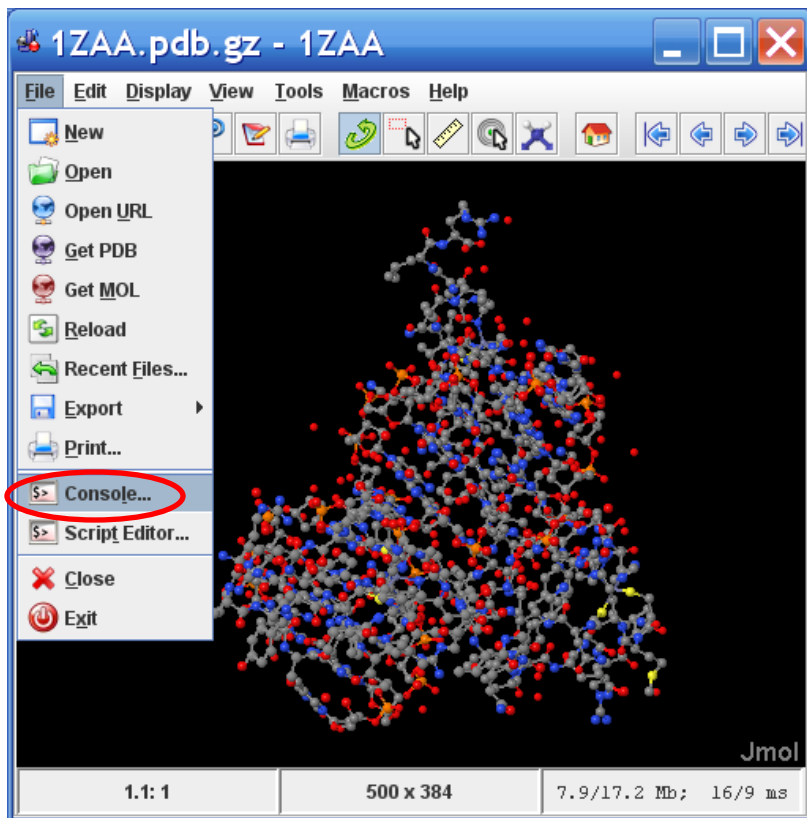


An 'Input' dialog box with a blue title bar and a red 'X' close button. It contains a green question mark icon, the text 'Enter a four-digit PDB ID', a text input field containing '1ZAA', and 'OK' and 'Cancel' buttons.

Note: Internet access required!



Show Jmol Console



Display a Zink Finger Motif in Jmol

For this demo, we only model a region of protein PDB 1ZAA:
chain C amino acids 4 - 31

Turn off the default display:

- `wireframe off`
- `cpk off`

Show backbone for chain c amino acids 4 – 31:

- `restrict *c and 4-31`
- `backbone 300`

Color alpha helix red:

- `select helix`
- `color red`

Color beta sheet yellow:

- `select sheet`
- `color yellow`

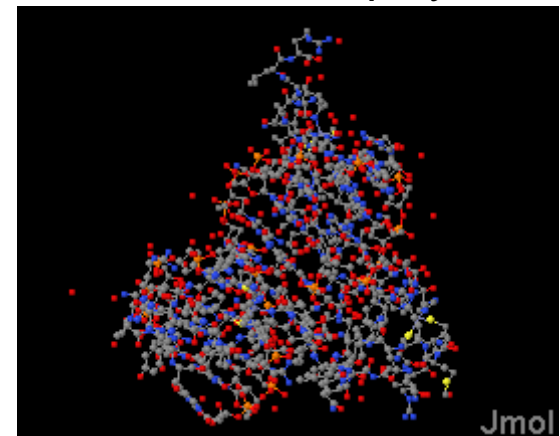
Color the N-terminus blue:

- `select *c and 4`
- `color blue`

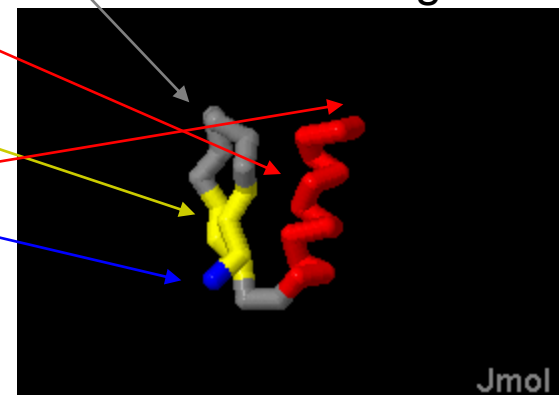
Color the C-terminus red

- `select *c and 31`
- `color red`

Default display



Final display for model building



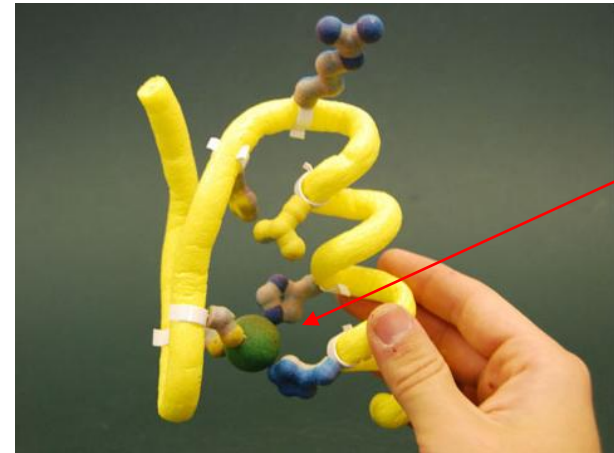
Jmol Tutorials

- Jmol training videos
 - <http://cbm.msoe.edu/teachRes/jmol/trainingguide>
- Jmol quick reference sheet
 - <http://cbm.msoe.edu/includes/jmol/SOJmols/JmolQuickReferenceSheet.pdf>
- Jmol reference guide – if you want to become an expert user
 - <http://chemapps.stolaf.edu/jmol/docs>

Let's build a Zink Finger Motif!

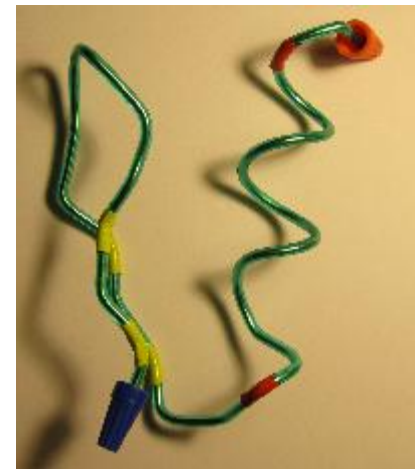
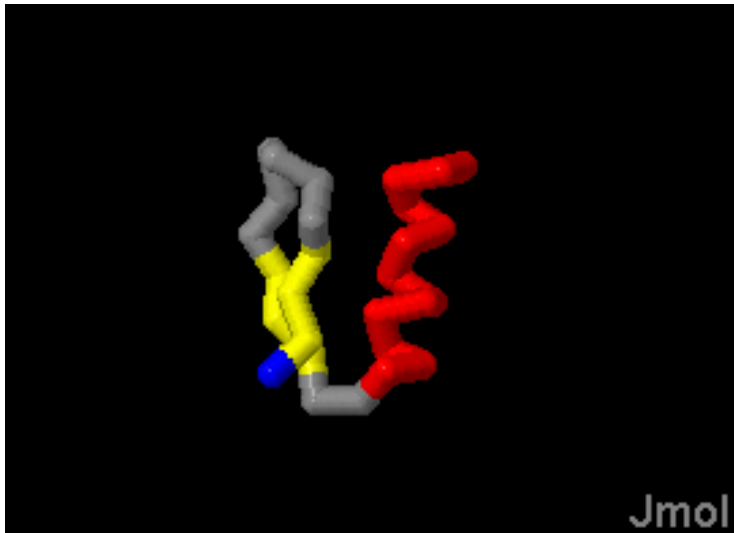
These types of materials will be used at the competition (provided)

Parts List:



zink ion

Alternative materials can be used for the pre-build model and for practicing



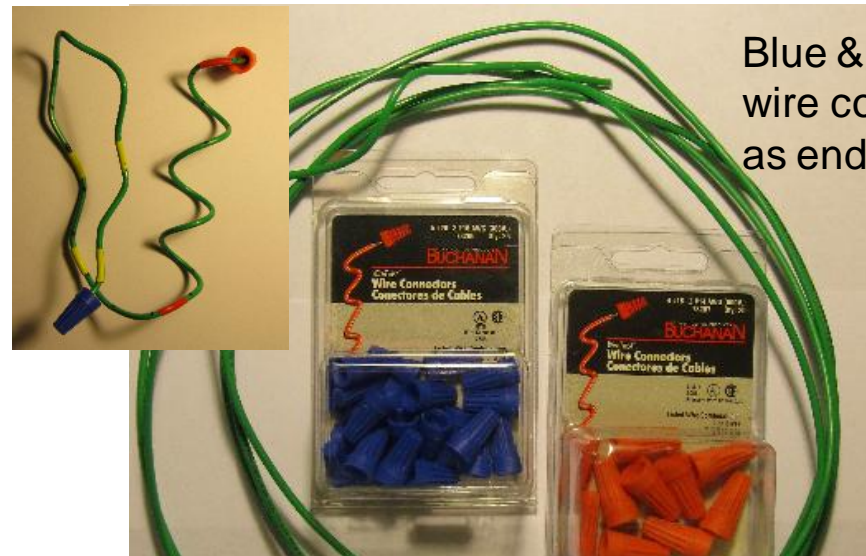
Alternative Materials



14 gauge vinyl-coated steel wire

Pros: cheap (\$3.50/50 ft or \$0.07/feet)
@ Sears, strong and attractive appearance

Cons: need pliers for sharp turns



Blue & red wire connectors as ends

For your safety when handling wire:

- Wear glasses and wash hands
- Protect ends of wire with wire connectors, electrical tape, or twist ends.

12 gauge green nylon-coated **solid** cooper wire

Pros: easy to bend, good for practicing

Cons: loses shape more easily, more expensive (\$0.27/feet @ HomeDepot)

The Story of the 2012 Event



Nick has a mysterious disease that destroys his gut. He has made more than 100 trips to the operating room.

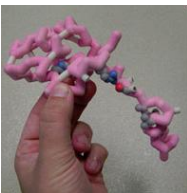
<http://cbm.msoe.edu/stupro/so/module2012/xiapHome.html>

In this event you will learn how modern genetics and structural biology can be used to diagnose and develop treatments for a genetic disease.

You will model two proteins involved in the regulation of programmed cell death that are related to this disease:



Caspase-3 (pre-build model)



XIAP (on-site model)

Pre-build Competition Environment



Important resources

Parts of pre-build set
\$20 + S&H
or use
alternative materials

2012 Science Olympiad
Protein Modeling Event

Pre-Build Competition
Caspase-3 based on 1i3o.pdb.

Directions:
The Pre-Build Model should represent chains A and B of caspase-3 based on the PDB file 1i3o.pdb. This section of the protein has two chains (A and B). Chain A is 143 amino acids long and will require a toober that is 286cm long. Chain B is 101 amino acids long and will require a toober that is 202cm long. (1 amino acid = 2cm)

Resources:
[Pre-Build Amino Acid Numbering Map](#)
[Jmol Quick Reference Sheet](#)

Parts List:

1 Mini-Toober (286cm long)	10 crosslinkers
1 Mini-Toober (202cm long)	2 red end caps
	2 blue end caps

Jmol application pre-loaded with Caspase-3 (PDB file 1i3o.pdb)

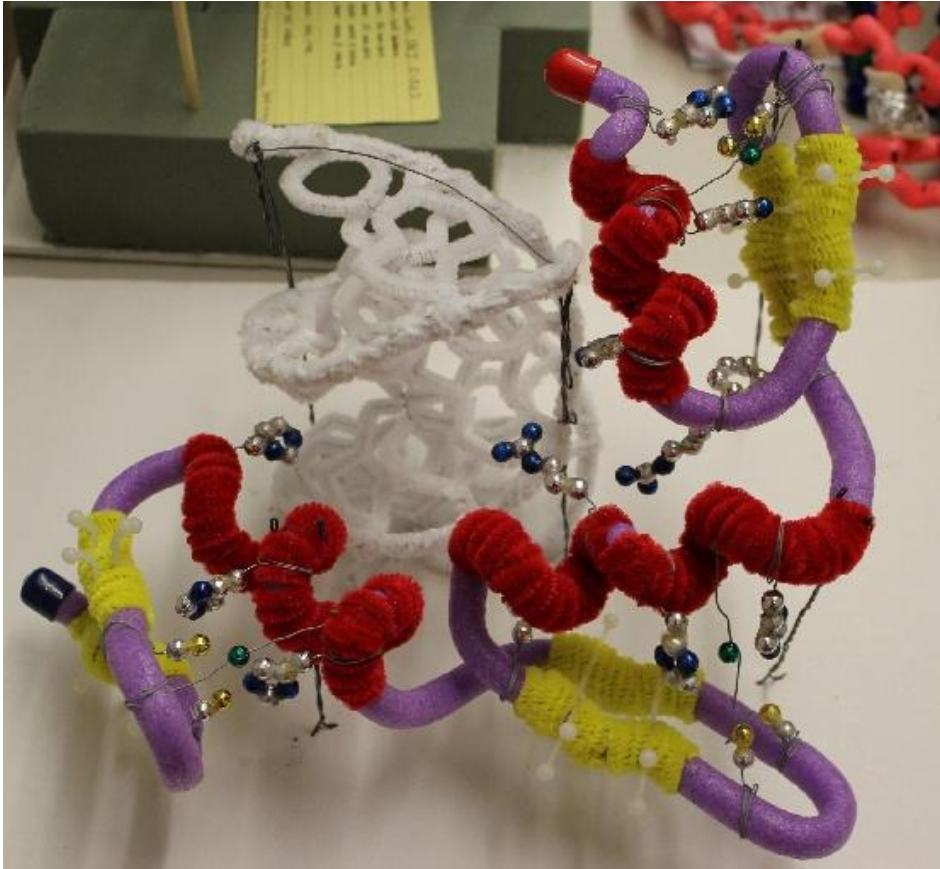
Jmol command window

<http://cbm.msoe.edu/includes/jmol/SOJmols/2012PreBuild.html>

With this environment, you can only work on the pre-build model. The on-site competition will use this environment, so you should become familiar with it.

SD Science Olympiad will not impound or score this model, but it will be scored at the state or national events.

Example of a Pre-Build Model



<http://cbm.msoe.edu/stupro/so/Photos.html>

- Mini-toober model with creative “decorations” that illustrate function of protein
 - Secondary structure
 - Important side chains
 - Additional molecules of importance (here DNA)
 - (cross-linkers or wires to stabilize model)
- Arts & Crafts stores (i.e., Michaels) are a good places to look for “decorations”
- How are pre-build models scored at national tournaments
 - <http://cbm.msoe.edu/stupro/so/SONTEExamRubric.html>

The On-Site Event



2011 Science Olympiad National Tournament

- Two parts
 - Build on-site model of a portion of XIAP (50% of score). The on-site environment will be provided on laptops running the Windows operating system.
 - Multiple choice test (50% of score) plus 1 written question. For example tests from the national tournaments check out: <http://cbm.msoe.edu/stupro/so/SONTEExamRubric.html>
- How much time do you have?
 - 50 minutes for model building and written test
- What can/should you bring to the event?
 - Pencils
 - Up to 5 double-sided 8.5" x 11" pages of notes (anything you think might help you during the event)
- What will the organizers provide?
 - Rulers
 - Sharpies
 - Mini-toobers, foam amino acid sidechains, cross-linkers, blue and red end caps

Parts List:



Written Test

- DNA & RNA
 - Transcription and splicing
 - Translation and genetic code
 - Disease mutations
- Proteins
 - Amino acids: chemical structure, chemical reactions, and properties
 - Primary, secondary, tertiary, and quaternary structure
 - Interactions that hold proteins together, protein folding
 - Protein conformation, geometric features of protein backbones
 - Protein structures determination: X-ray crystallography
 - Protein function, enzymes, enzyme inhibitors
 - Protein visualization in Jmol
- All about the 2012 Story
 - Genome sequencing
 - The cell and its components
 - Regulation of apoptosis (programmed cell death) and connection to genetic disease
 - Immune system
 - Proteins: Caspase-3, XIAP
 - Sequence, structure, function, relationship to disease

Resources

- MSOE Center for BioMolecular Modeling Science Olympiad website
 - This is the most important resource that contains the details about the event
Explore all links on this website! The written test may include any topics from this site.
 - <http://cbm.msoe.edu/stupro/so/index.html>
- Molecular Lending Library for coaches
 - Introduction to Protein Structure Collection (IP)
 - <http://cbm.msoe.edu/teachRes/library/ip.html>
 - Borrow for up to 2 weeks (incl. shipping)
 - Takes several hours to complete all exercises
- RCSB Protein Data Bank (RCSB PDB)
 - Caspases Molecule of the Month:
<http://www.pdb.org/pdb/101/motm.do?momID=56>
 - Educational materials and Molecule of the Month articles: <http://www.pdb.org/pdb-101>
 - Download protein structures: www.pdb.org
 - RCSB PDB tutorials: <http://www.openhelix.com/pdb>
 - New Jersey Science Olympiad: <http://education.pdb.org/olympiad>



Tips

- Go through the interactive protein tutorial
 - <http://cbm.msoe.edu/includes/jmol/SOJmols/proteinStructureHome.html>
- Learn about biomolecules and their function
 - HippoCampus – Biology: <http://www.hippocampus.org>
 - Chapters 1-5: <http://swissmodel.expasy.org/course/course-index.htm>
 - AP Biology books (for example Biology 7th Ed. Campbell and Reece)
- Install Jmol and get familiar with its commands
- Build your first protein model
 - <http://cbm.msoe.edu/includes/jmol/SOJmols/ZincFingerSample.html>
- Coach: borrow Introduction to Protein Structure Collection (IP)
 - <http://cbm.msoe.edu/teachRes/library/ip.html>
- Practice with on-site models from previous Protein Modeling events
 - <http://cbm.msoe.edu/stupro/so/SONTEExamRubric.html>
- Study the 2012 event resources
 - <http://cbm.msoe.edu/stupro/so/2012EventResources.html>
- Attend the workshops in Dec. and Jan.

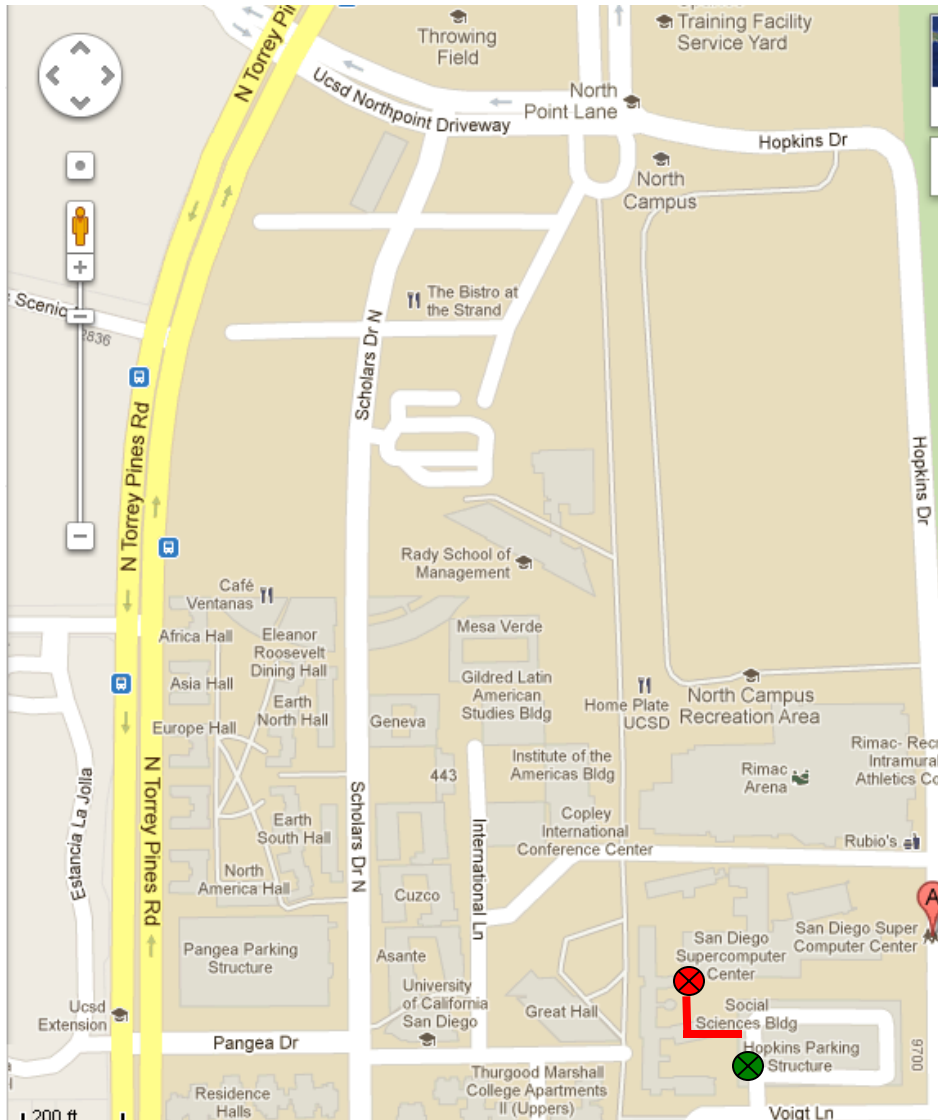
Protein Modeling C Workshops

- Nuts and Bolts of Protein Modeling C – Sat. Dec. 10, 2011
San Diego Supercomputer Center/UCSD, Room 279*, 2:00 – 4:00 pm
 - Introduction to the pre-build model
 - Hands-on protein visualization and model building at computer lab
 - Review of chemistry, biochemistry, and protein structure

- Mastering the Protein Modeling C Event – Sat. Jan. 7, 2012
San Diego Supercomputer Center/UCSD, Room 279*, 2:00 – 4:00 pm
 - Introduction to the on-site model
 - Advanced hands-on protein visualization and model building at computer lab
 - In-depth review of the biological concepts related to this event

* for directions see next page

Workshop Location: San Diego Supercomputer Center, UCSD



- From Torrey Pines Road turn east onto UCSD Northpoint Driveway
- Continue on Hopkins Dr
- Turn right on Voigt Ln and drive up the steep hill. Park in the Hopkins Parking Structure (free on weekends)
- Go to the top of the parking structure (level 7) and cross the pedestrian bridge to the Social Sciences patio.
- Turn right to exit the patio northward along the north-south walkway of the Social Sciences building. The walkway intersects the sidewalk that leads to SDSC.
- Cross this sidewalk and go up the steps. The training room 279 is straight ahead.