

Protein Structure, Function and Disease

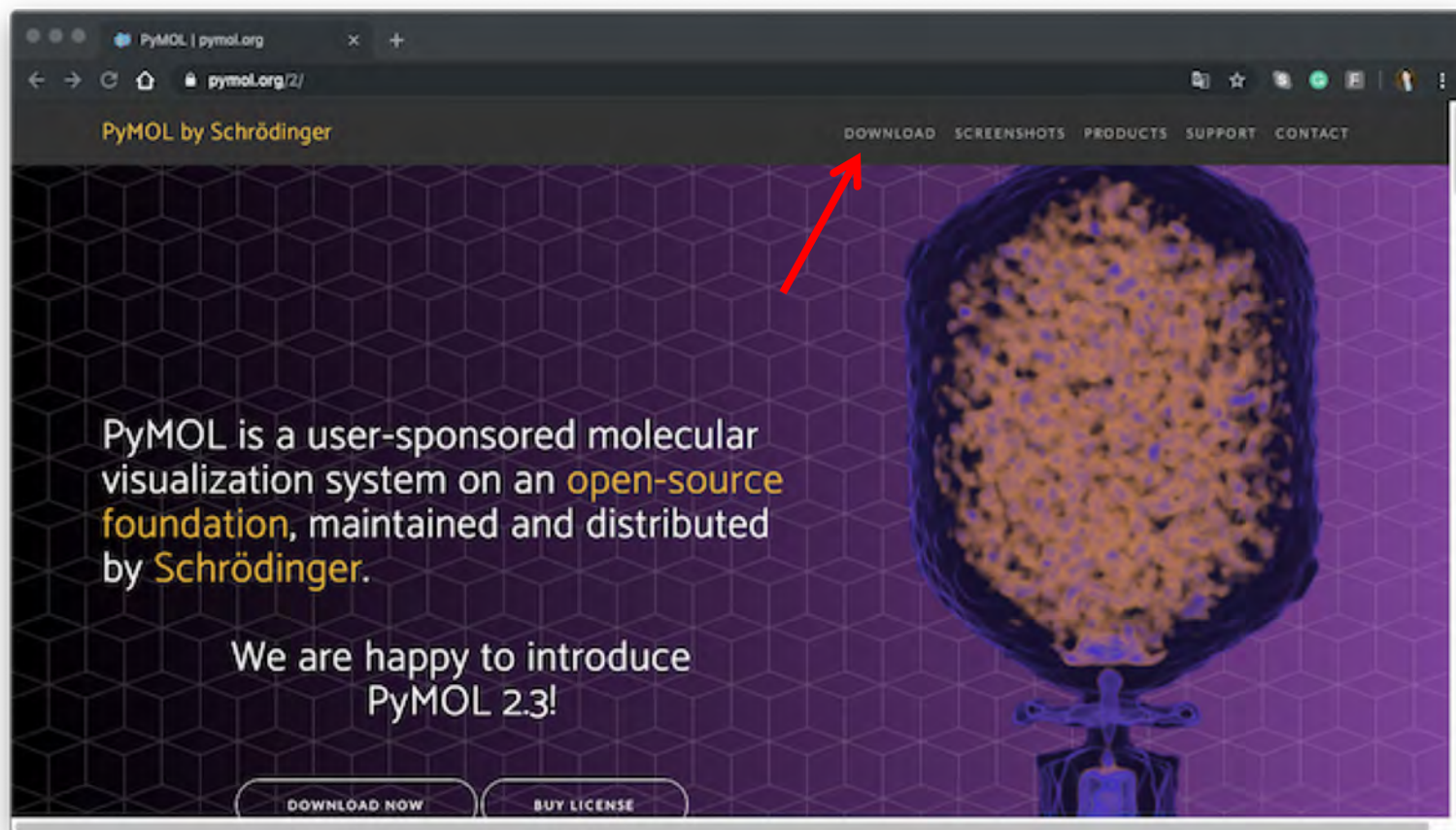
Basic tool(s) to visualize protein structures: PyMOL and UCSF Chimera.

Jyh-Yeuan (Eric) Lee, Assistant Professor, BMI



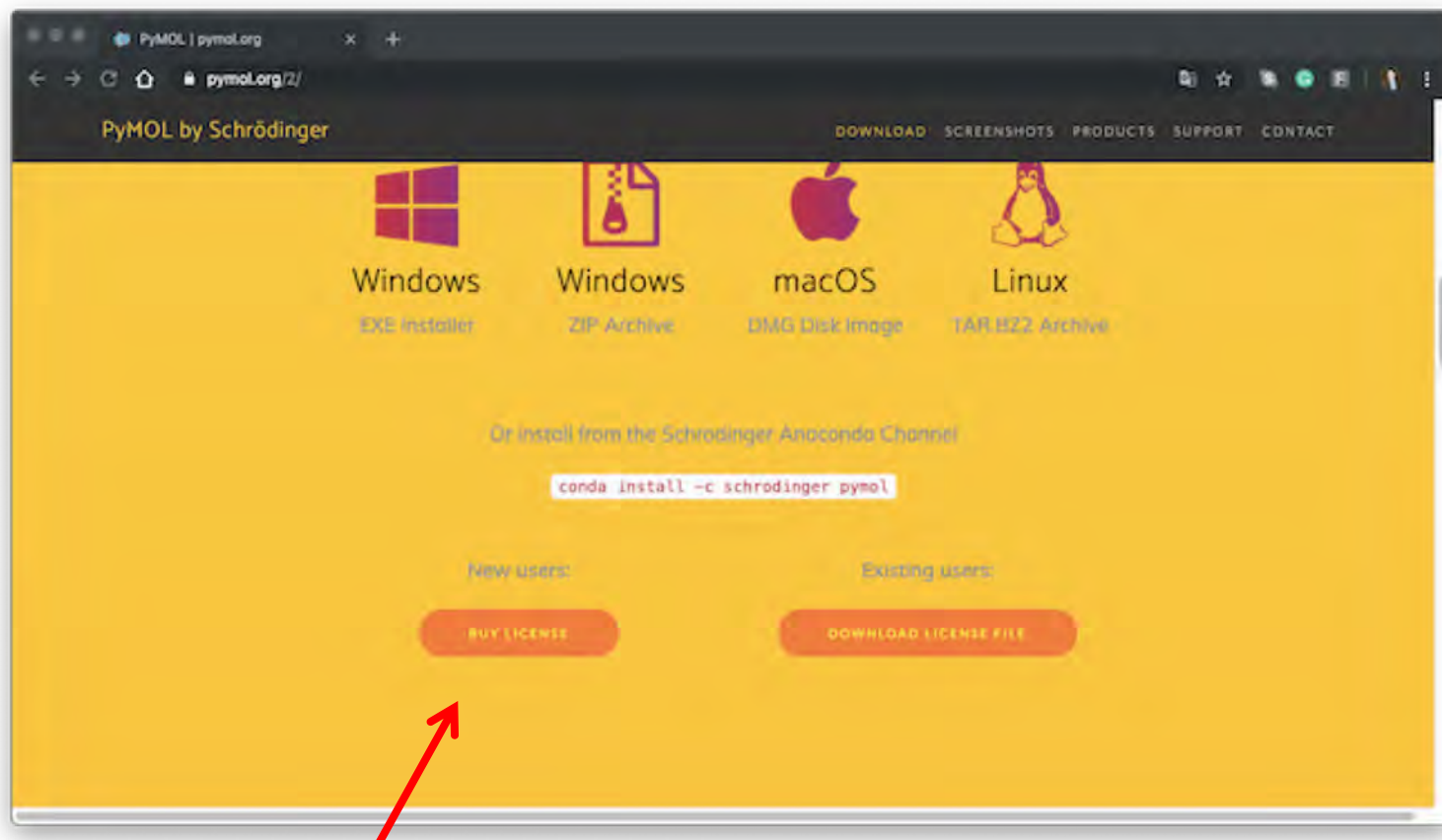
Step-by-step installation: PyMOL

1) Go to <https://pymol.org/>; click on “DOWNLOAD”.



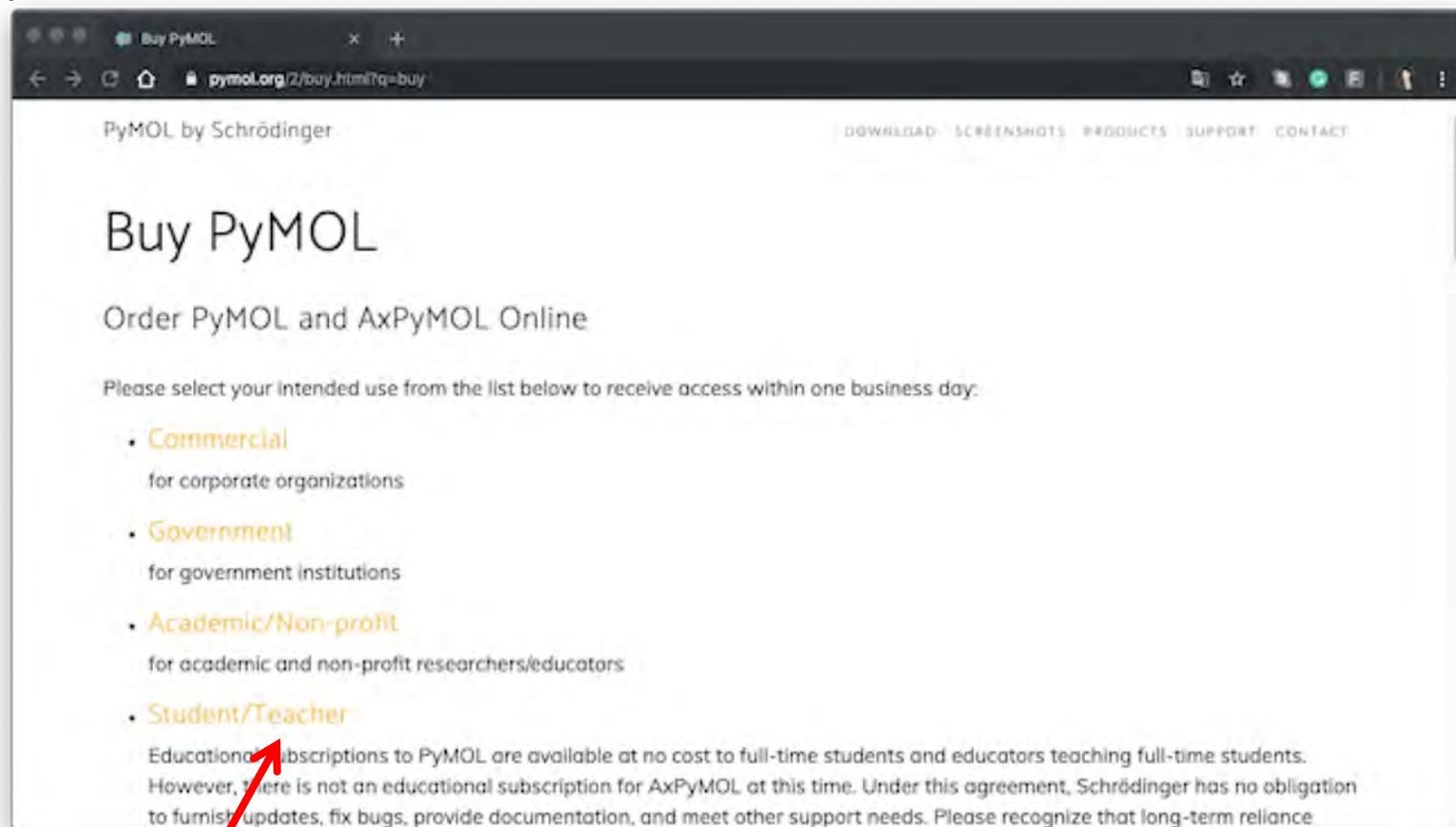
Step-by-step installation: PyMOL

2) Scroll down to “BUY LICENSE”; click on it.



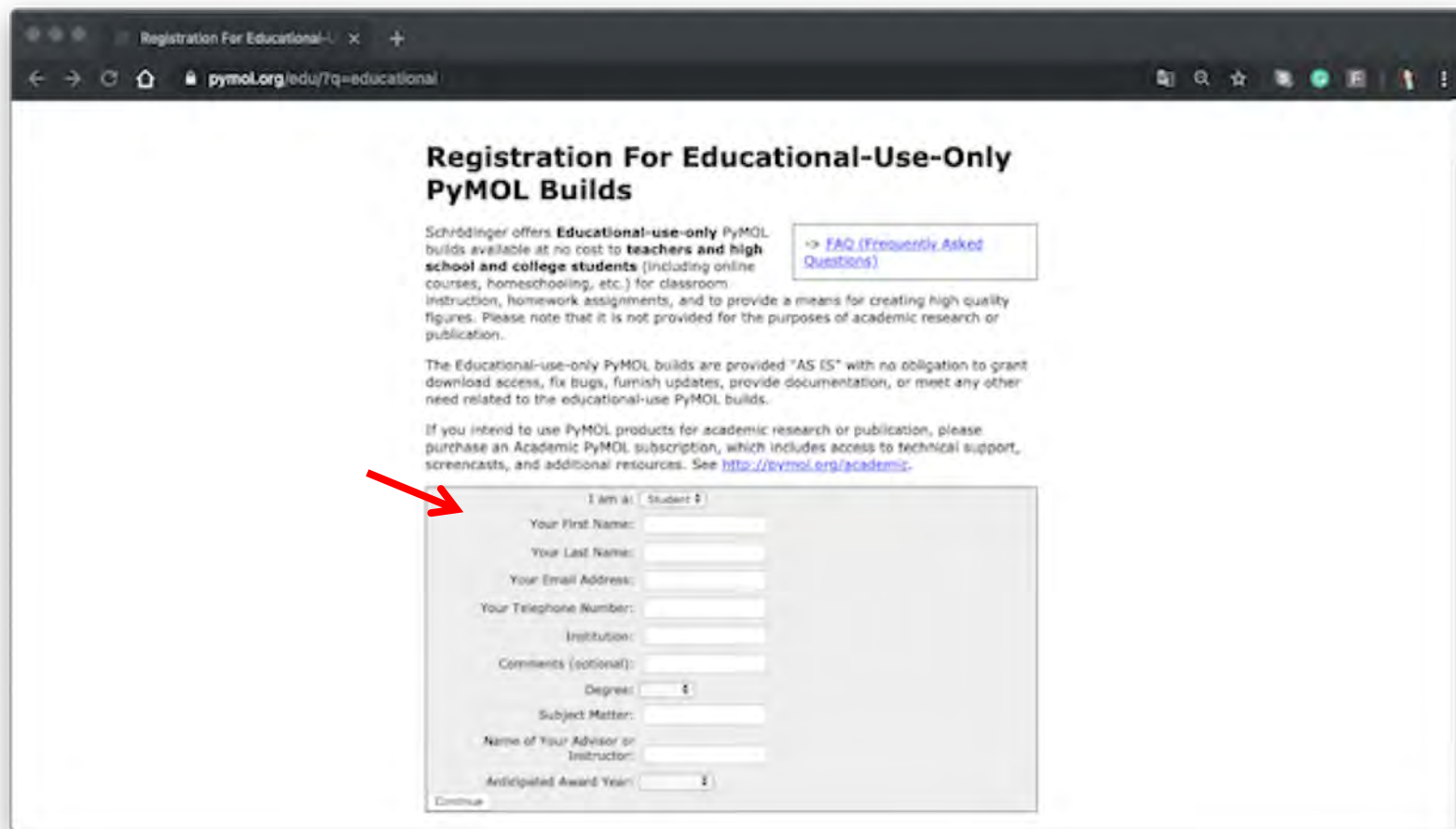
Step-by-step installation: PyMOL

3) Select “Student/Teacher”



Step-by-step installation: PyMOL

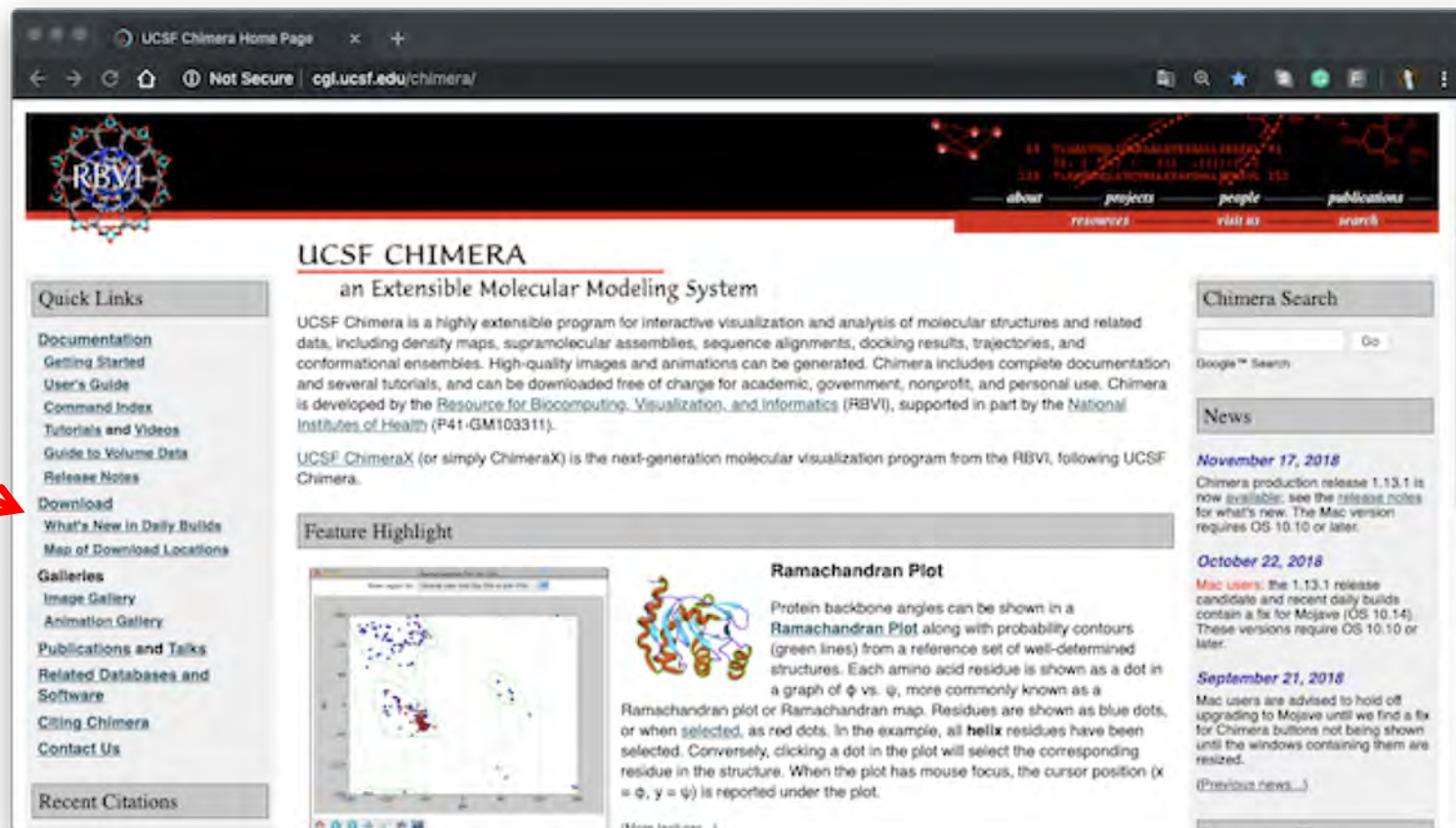
4) Register; then wait for an instruction email.



The screenshot shows a web browser window with the address bar displaying `pymol.org/edu/?q=educational`. The page title is "Registration For Educational-Use-Only PyMOL Builds". The text on the page states: "Schrodinger offers **Educational-use-only** PyMOL builds available at no cost to **teachers and high school and college students** (including online courses, homeschooling, etc.) for classroom instruction, homework assignments, and to provide a means for creating high quality figures. Please note that it is not provided for the purposes of academic research or publication." A link to "FAQ (Frequently Asked Questions)" is provided. Below this, it says: "The Educational-use-only PyMOL builds are provided 'AS IS' with no obligation to grant download access, fix bugs, furnish updates, provide documentation, or meet any other need related to the educational-use PyMOL builds." It also mentions: "If you intend to use PyMOL products for academic research or publication, please purchase an Academic PyMOL subscription, which includes access to technical support, screencasts, and additional resources. See <http://pymol.org/academic>." A red arrow points to the registration form, which includes a dropdown menu for "I am a:" with "Student" selected. The form fields are: "Your First Name:", "Your Last Name:", "Your Email Address:", "Your Telephone Number:", "Institution:", "Comments (optional):", "Degree:" (with a dropdown menu), "Subject Matter:", "Name of Your Advisor or Instructor:", and "Anticipated Award Year:" (with a dropdown menu). A "Continue" button is at the bottom of the form.

Step-by-step installation: Chimera

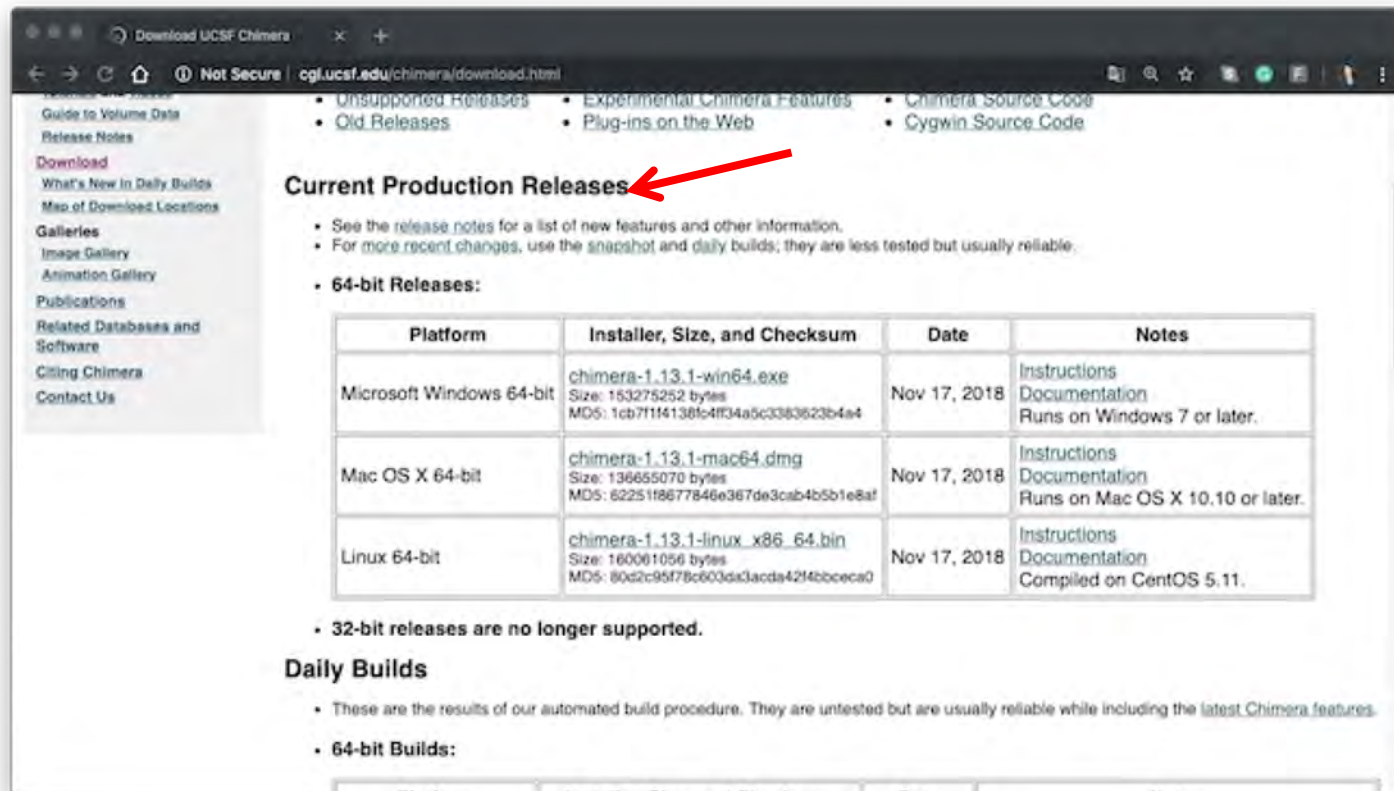
1) Go to <http://www.cgl.ucsf.edu/chimera/>; click on “Download”.



The screenshot shows the UCSF Chimera website. The browser's address bar displays <http://www.cgl.ucsf.edu/chimera/>. The website header features the RBVI logo and navigation links: [about](#), [projects](#), [people](#), [publications](#), [resources](#), [visit us](#), and [search](#). The main heading is "UCSF CHIMERA" with the subtitle "an Extensible Molecular Modeling System". Below this, a paragraph describes Chimera as a highly extensible program for interactive visualization and analysis of molecular structures. A sidebar on the left, titled "Quick Links", contains a "Download" section with links to "What's New in Daily Builds" and "Map of Download Locations". A red arrow points to the "Download" link. Other sidebar links include "Documentation", "Galleries", "Publications and Talks", "Related Databases and Software", "Citing Chimera", and "Contact Us". The main content area includes a "Feature Highlight" section for the "Ramachandran Plot", which shows a plot of protein backbone angles and explains how residues are represented as dots. A "Chimera Search" box and a "News" section with recent updates are also visible on the right.

Step-by-step installation: Chimera

2) Choose the installer suitable for your OS.



The screenshot shows the UCSF Chimera download page. A red arrow points to the 'Current Production Releases' section. The page includes a sidebar with navigation links, a list of links at the top, and a table of 64-bit releases.

Current Production Releases

- See the [release notes](#) for a list of new features and other information.
- For [more recent changes](#), use the [snapshot](#) and [daily builds](#); they are less tested but usually reliable.

64-bit Releases:

Platform	Installer, Size, and Checksum	Date	Notes
Microsoft Windows 64-bit	chimera-1.13.1-win64.exe Size: 153275252 bytes MD5: 1cb7f114136fc4ff34a5c3363623b4a4	Nov 17, 2018	Instructions Documentation Runs on Windows 7 or later.
Mac OS X 64-bit	chimera-1.13.1-mac64.dmg Size: 136655070 bytes MD5: 62251f8677846e367de3cab4b5b1e8af	Nov 17, 2018	Instructions Documentation Runs on Mac OS X 10.10 or later.
Linux 64-bit	chimera-1.13.1-linux_x86_64.bin Size: 160061056 bytes MD5: 80d2c95f78c603d53acd42f4bbeca0	Nov 17, 2018	Instructions Documentation Compiled on CentOS 5.11.

32-bit releases are no longer supported.

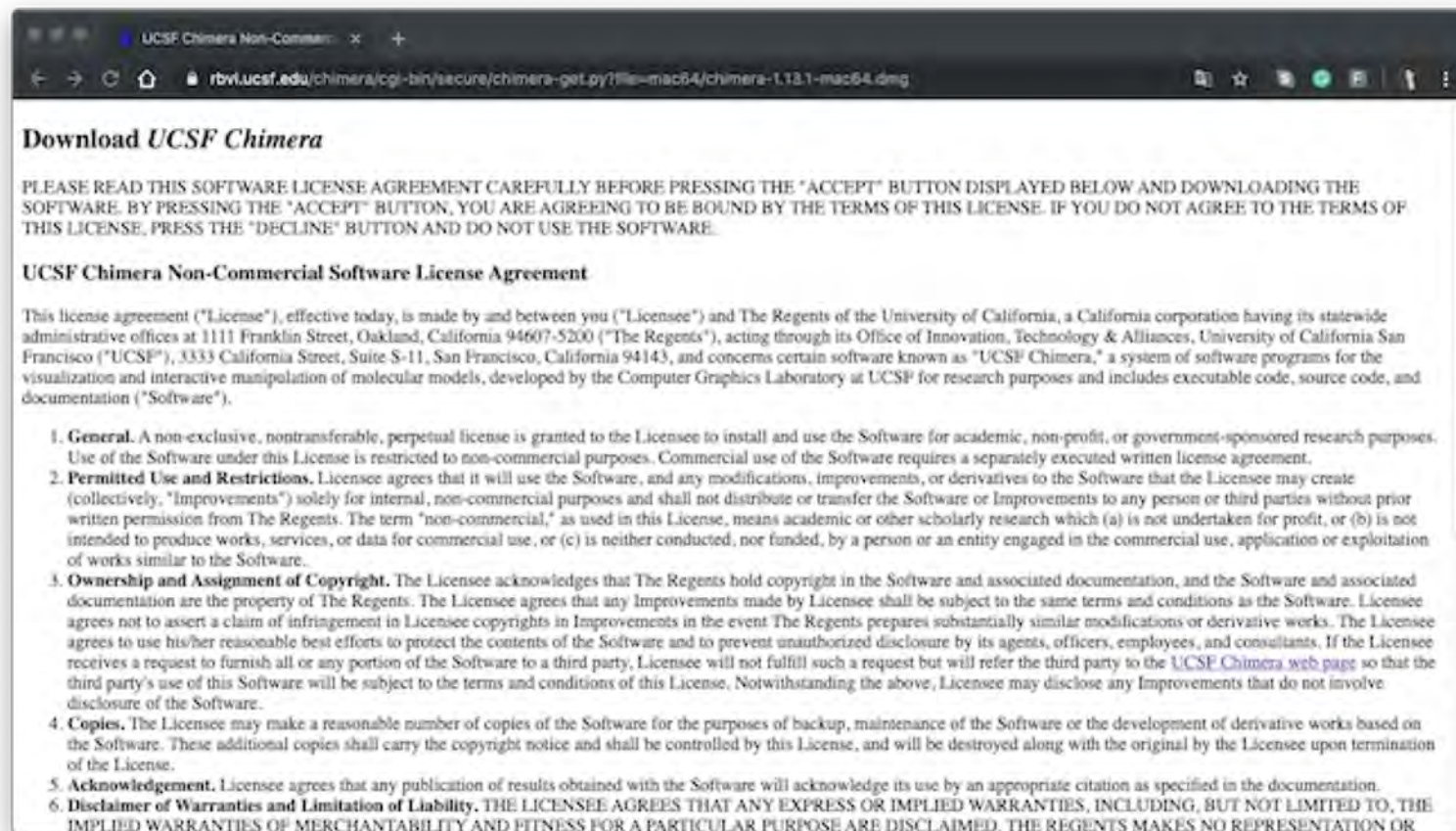
Daily Builds

- These are the results of our automated build procedure. They are untested but are usually reliable while including the latest Chimera features.

64-bit Builds:

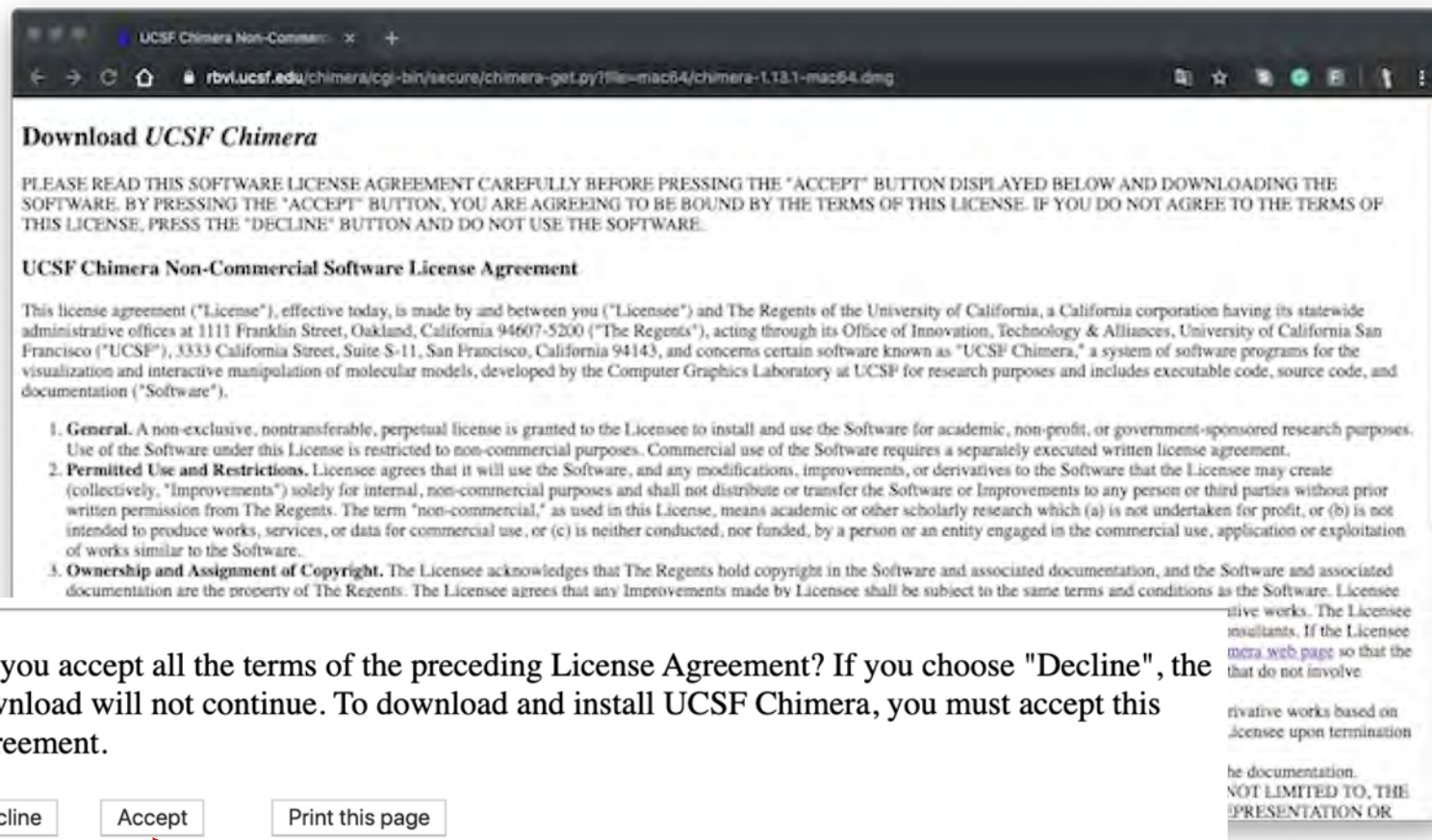
Step-by-step installation: Chimera

3) "Accept" and start downloading.



Step-by-step installation: Chimera

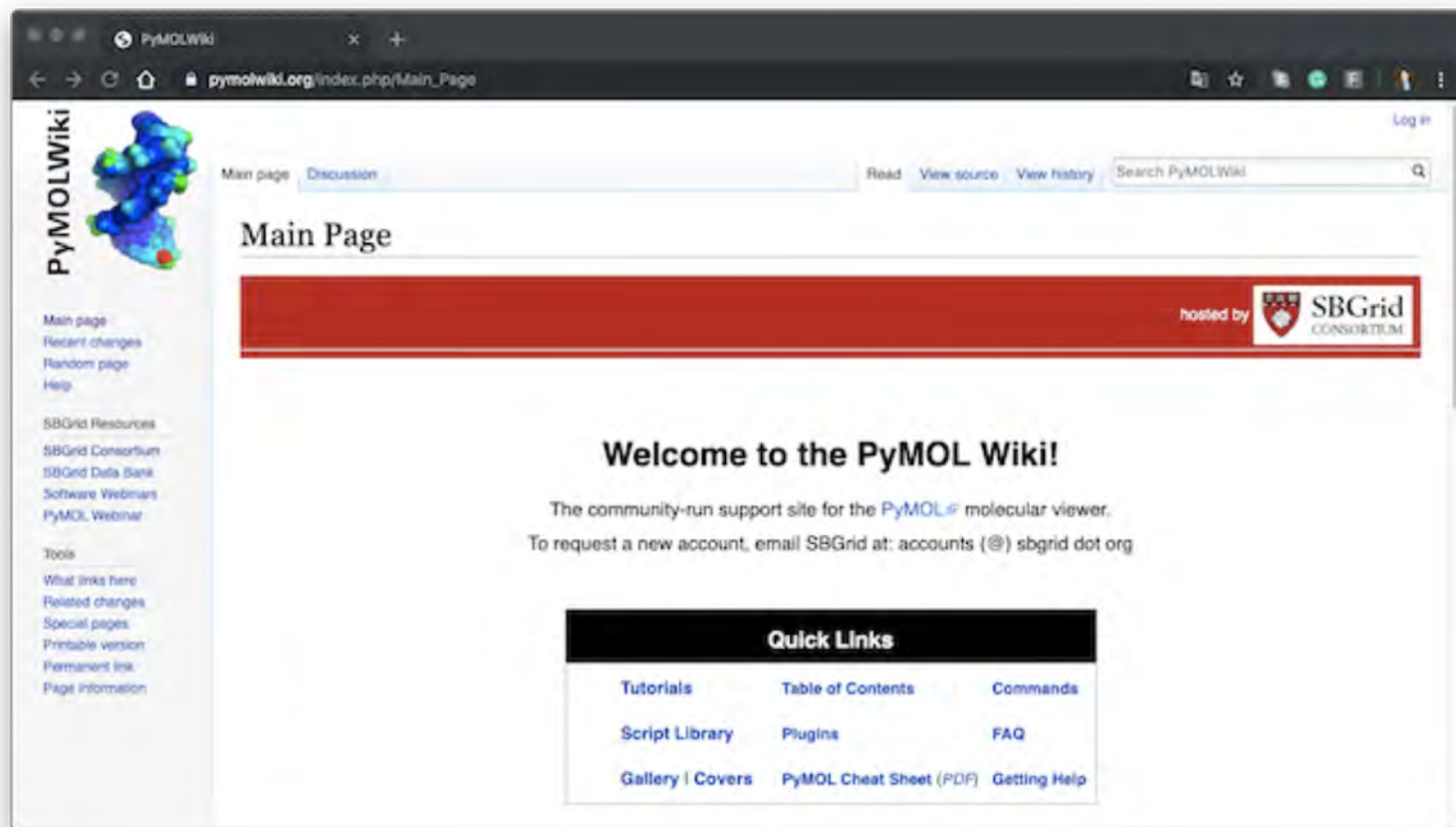
3) "Accept" and start downloading.



Do you accept all the terms of the preceding License Agreement? If you choose "Decline", the download will not continue. To download and install UCSF Chimera, you must accept this Agreement.


PyMOL Wiki

https://pymolwiki.org/index.php/Main_Page



UCSF Chimera tutorials

<http://www.cgl.ucsf.edu/Outreach/Tutorials/GettingStarted.html>



UCSF Chimera - Getting Started

This tutorial provides an overview of basic features in Chimera. You can interact with Chimera using menus and/or commands. The basic features of Chimera are available either way, but not all command functions are available in menus or graphical interfaces, and not all menu or graphical interface functions are available in commands. Thus, it is useful to become familiar with both ways of interacting with Chimera.

The **Working with menus** and **Working with commands** sections are independent of each other and (for the most part) cover identical operations, accomplished in different ways. If you go through both sections, you can skip portions that cover issues you already understand. You can also go back and forth between the sections to see the correspondence between menu and command operations.

Outline:

- [Working with menus - Part 1](#)
 - [Getting started](#)
 - [Opening a structure](#)
 - [Side View](#)
 - [Using the mouse](#)
 - [Selection with the mouse](#)
 - [Selection/Action](#)
 - [Models and model status](#)
- [Working with menus - Part 2](#)
 - [Setup](#)
 - [Representations](#)
 - [Surfaces](#)
- [Front image how-to \(menu\)](#)
- [Working with commands - Part 1](#)
 - [Getting started](#)
 - [Opening a structure](#)

DNA helix with bound netropsin

Typographical Conventions

Item	Example	Description
Keyboard key	Ctrl	The control key
Mouse key	Btn1	Mouse button 1 (left button)
Menu action	File → Open	File menu bar dropdown

Journal club: objectives and guidelines

- **Objectives:**

- To use graphic tools to inspect protein structures.
- To provide a short summary of a scientific discovery.

- **Guidelines:**

- Each team downloads the assigned model from Protein Data Bank (<https://www.rcsb.org/>) and the affiliated research paper from Brightspace.
- Study the background and the significance of the assigned subject and what the structural model shows.
- Prepare ~10-minute presentation (PowerPoint or Keynote) with 2-5 minutes of discussion.

Journal club: teams and models (PDB #)

Team 1	6PXW	Team 6	3GD8
Team 2	4MBS	Team 7	5V9U
Team 3	4XP1	Team 8	4F2A
Team 4	4NTJ	Team 9	3TO3
Team 5	3BPS	Team 10	1DB1

Protein in action at atomic resolution

Demo example: statin and HMG-CoA reductase

The screenshot shows the RCSB PDB homepage in a web browser. The browser's address bar displays 'rscb.org'. The website's navigation bar includes links for 'RCSB PDB', 'Deposit', 'Search', 'Visualize', 'Analyze', 'Download', 'Learn', and 'More'. A 'MyPDB' button is located on the right. The main header features the 'RCSB PDB PROTEIN DATA BANK' logo and the text '155830 Biological Macromolecular Structures Enabling Breakthroughs in Research and Education'. Below this, there are logos for 'PDB-101', 'EMDB Resource', 'RCSB PDB', 'PDBe', 'PDBj', and 'Worldwide Protein Data Bank'. A search bar on the right contains the text '1hw9' and a 'Go' button. A dropdown menu below the search bar shows 'PDB ID' and '1HW9'. The main content area has a 'Welcome' section with a sidebar containing links for 'Deposit', 'Search', 'Visualize', 'Analyze', 'Download', and 'Learn'. The main text area includes a section titled 'A Structural View of Bi...' with a paragraph about the resource's purpose and another paragraph about the RCSB PDB's role. Below this is a section titled 'Job Opportunities for Biocurators and Developers' with a 'JOIN OUR TEAM' button. On the right side of the main content area, there is a 3D molecular model of a protein structure, likely HMG-CoA reductase, with a green surface representation of a ligand (statin) bound to it. A 'Contact Us' button is visible on the far right.

Protein in action at atomic resolution

Demo example: statin and HMG-CoA reductase

The screenshot displays the RCSB PDB website interface. The browser address bar shows rcsb.org/structure/1HW9. The main navigation bar includes links for Deposit, Search, Visualize, Analyze, Download, Learn, and More, along with a MyPDB button. The PDB logo is prominently displayed, accompanied by the text "155830 Biological Macromolecular Structures Enabling Breakthroughs in Research and Education". A search bar is available for PDB ID, author, macromolecule, sequence, or ligands. Below the navigation bar, tabs for Structure Summary, 3D View, Annotations, Sequence, Sequence Similarity, Structure Similarity, and Experiment are visible. The Structure Summary tab is active, showing a 3D ribbon diagram of the protein complex. To the right of the diagram, the entry details for 1HW9 are listed: "COMPLEX OF THE CATALYTIC PORTION OF HUMAN HMG-COA REDUCTASE WITH SIMVASTATIN". Additional information includes the DOI (10.2210/pdb1HW9/pdb), Classification (OXIDOREDUCTASE), Organism(s) (Homo sapiens), Expression System (Escherichia coli), and Mutation(s) (1). The deposition and release dates (2001-01-09 and 2001-05-11) and the deposition author(s) (Istvan, E.S., Delsenhofer, J.) are also provided. At the bottom, there are links for Experimental Data Snapshot, wwPDB Validation, and 3D Report/Full Report.

RCSB PDB - 1HW9: COMPLEX

rcsb.org/structure/1HW9

RCSB PDB Deposit Search Visualize Analyze Download Learn More

155830 Biological Macromolecular Structures Enabling Breakthroughs in Research and Education

Search by PDB ID, author, macromolecule, sequence, or ligands

Go

Advanced Search | Browse by Annotations

PDB-101 PDB EMDB BioResource

Structure Summary 3D View Annotations Sequence Sequence Similarity Structure Similarity Experiment

Biological Assembly 1

1HW9

COMPLEX OF THE CATALYTIC PORTION OF HUMAN HMG-COA REDUCTASE WITH SIMVASTATIN

DOI: 10.2210/pdb1HW9/pdb

Classification: [OXIDOREDUCTASE](#)

Organism(s): [Homo sapiens](#)

Expression System: [Escherichia coli](#)

Mutation(s): 1

Deposited: 2001-01-09 Released: 2001-05-11

Deposition Author(s): [Istvan, E.S.](#), [Delsenhofer, J.](#)

Experimental Data Snapshot

Method: X-RAY DIFFRACTION

wwPDB Validation

3D Report Full Report

Metric Percentile Ranks Value

Protein in action at atomic resolution

Demo example: statin and HMG-CoA reductase

The screenshot displays the RCSB PDB website interface. The browser address bar shows rcsb.org/structure/1HW9. The page header includes navigation links: Deposit, Search, Visualize, Analyze, Download, Learn, and More. The main banner features the PDB logo and the text "155830 Biological Macromolecular Structures Enabling Breakthroughs in Research and Education". A search bar is present with the placeholder text "Search by PDB ID, author, macromolecule, sequence, or ligands". Below the banner, a navigation bar offers tabs for Structure Summary, 3D View, Annotations, Sequence, Sequence Similarity, Structure Similarity, and Experiment. The main content area displays the entry "1HW9" with the title "COMPLEX OF THE CATALYTIC PORTION OF HUMAN HMG SIMVASTATIN". A 3D ribbon diagram of the protein complex is shown on the left. To the right of the diagram, the entry details are listed: DOI: 10.2210/pdb1HW9/pdb, Classification: OXIDOREDUCTASE, Organism(s): Homo sapiens, Expression System: Escherichia coli, Mutation(s): 1, Deposited: 2001-01-09, Released: 2001-05-11, Deposition Author(s): Istvan, E.S., Delsenhofer, J., Experimental Data Snapshot, Method: X-RAY DIFFRACTION, and wwPDB Validation. A dropdown menu on the right side of the page lists various file formats for download, including FASTA Sequence, PDB Format, PDB Format (gz), PDBx/mmCIF Format, PDBx/mmCIF Format (gz), PDBML/XML Format (gz), Biological Assembly 1, Structure Factors (CIF), and Structure Factors (CIF.gz).

Protein in action at atomic resolution

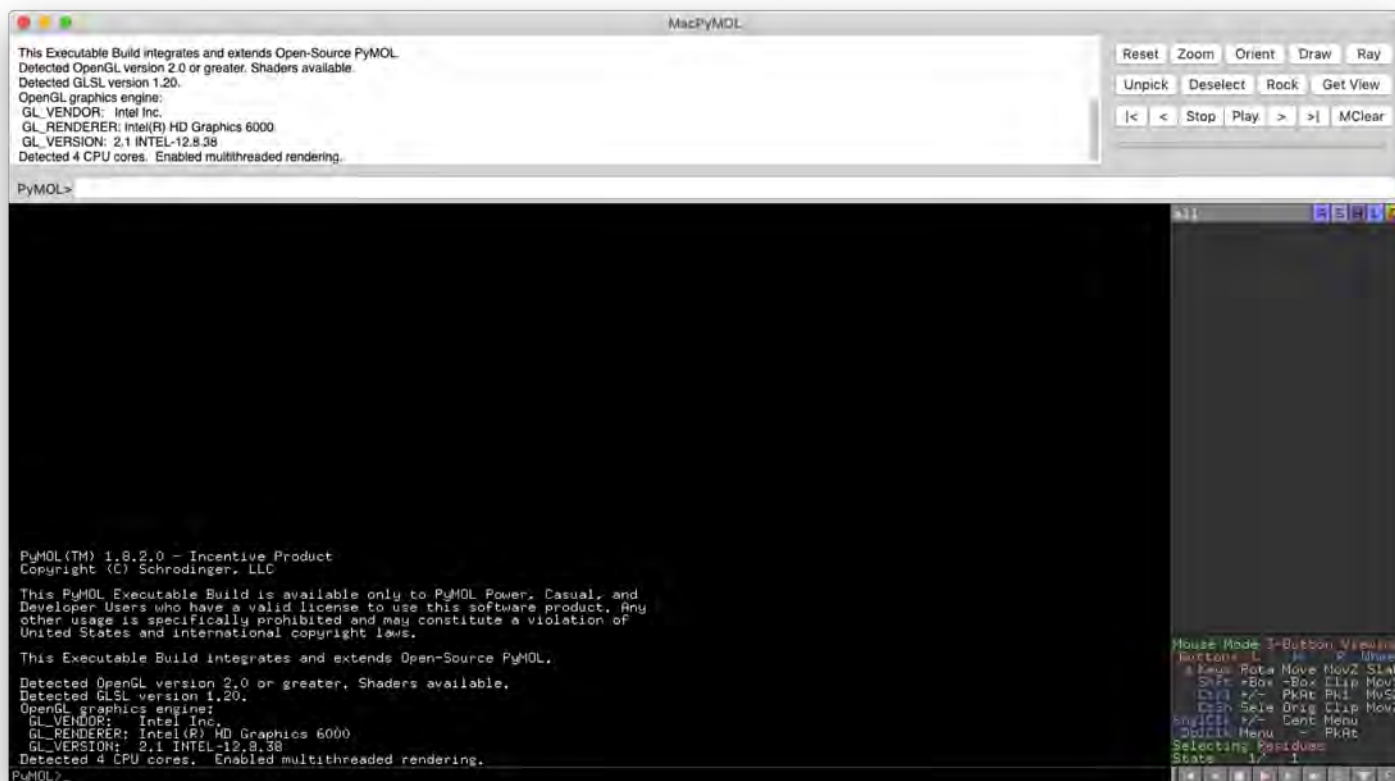
Demo example: statin and HMG-CoA reductase

The screenshot shows the RCSB PDB website for entry 1HW9: COMPLEX. The page is divided into several sections:

- Protein Workshop | Ligand Explorer**:
 - Global Symmetry: Dihedral - D2 (3D View)
 - Global Stoichiometry: Homo 4-mer - A4
 - Biological assembly: 1 assigned by authors and generated by PISA (software)
- Macromolecule Content**:
 - Total Structure Weight: 203968.42
 - Atom Count: 12009
 - Residue Count: 1868
 - Unique protein chains: 1
- Literature**:
 - Download Primary Citation
 - Structural mechanism for statin inhibition of HMG-CoA reductase.
 - Istvan, E.S., Deisenhofer, J. (2001) Science 292: 1160-1164
 - PubMed: 11349148
 - DOI: 10.1126/science.1059344
 - Primary Citation of Related Structures: 1HWL, 1HWK, 1HWJ, 1HWI, 1HWB
 - PubMed Abstract: HMG-CoA (3-hydroxy-3-methylglutaryl-coenzyme A) reductase (HMGR) catalyzes the committed step in cholesterol biosynthesis. Statins are HMGR inhibitors with inhibition constant values in the nanomolar range that effectively lower serum cholesterol lev ...
- Macromolecules**:
 - Find similar proteins by: Sequence | Structure

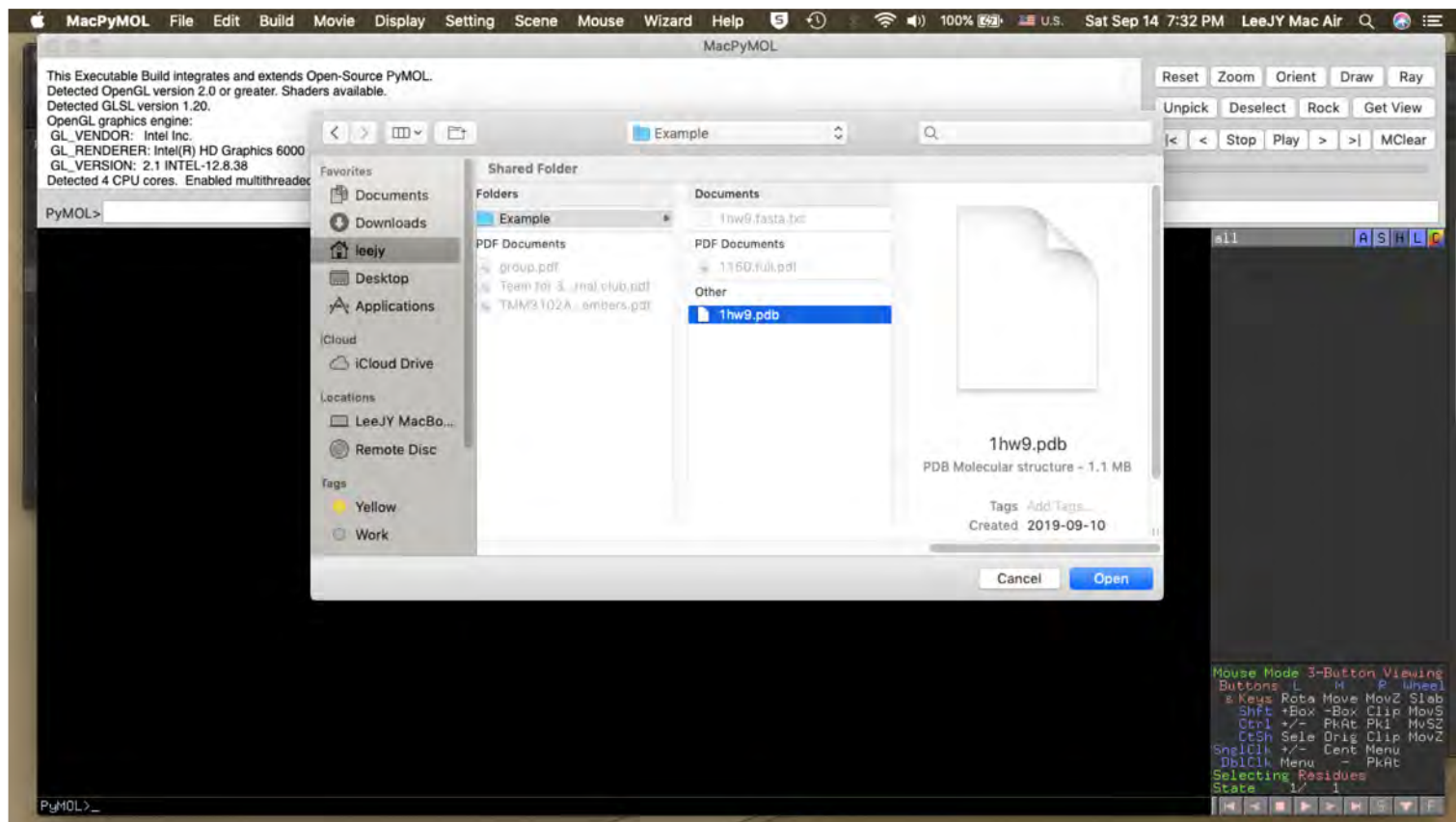
Protein in action at atomic resolution

Demo example: statin and HMG-CoA reductase; PyMOL



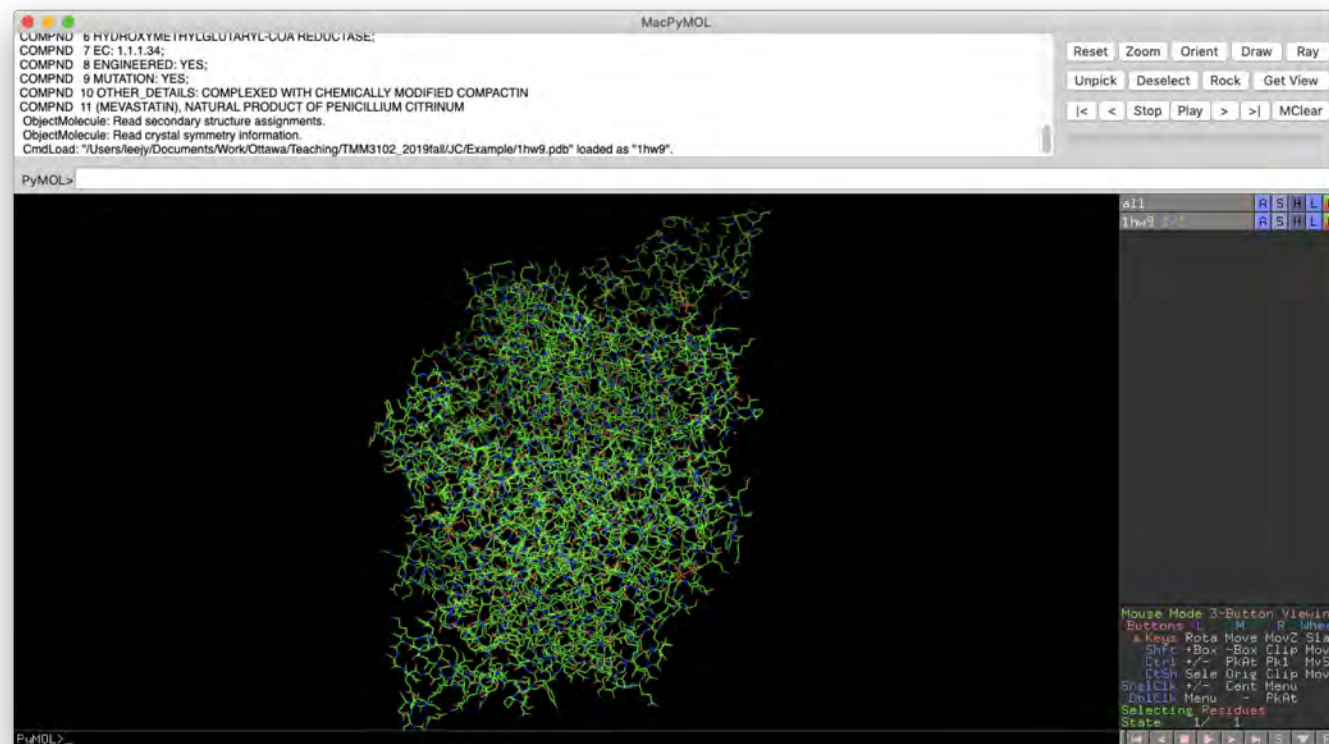
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Demo example: statin and HMG-CoA reductase; PyMOL



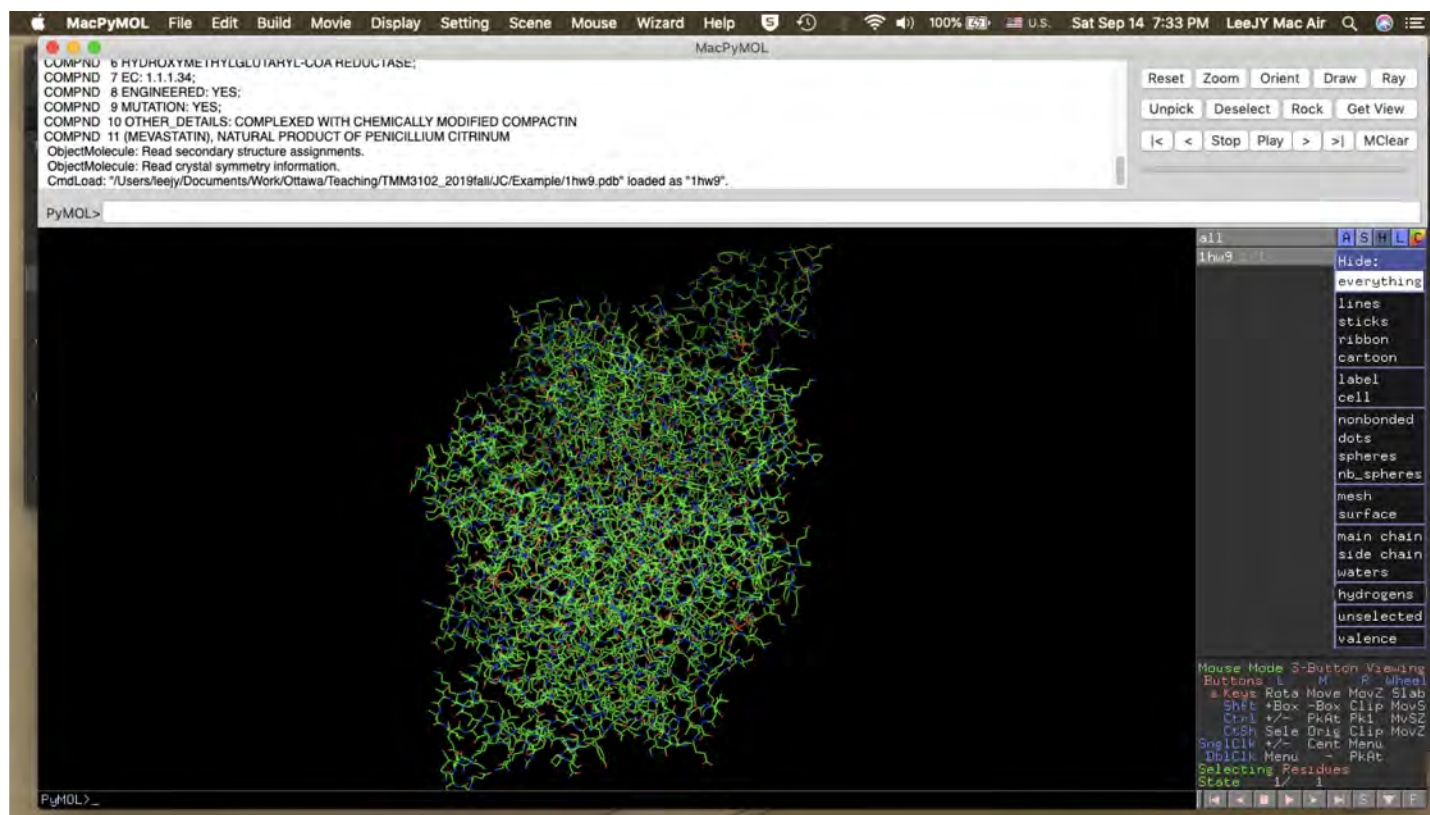
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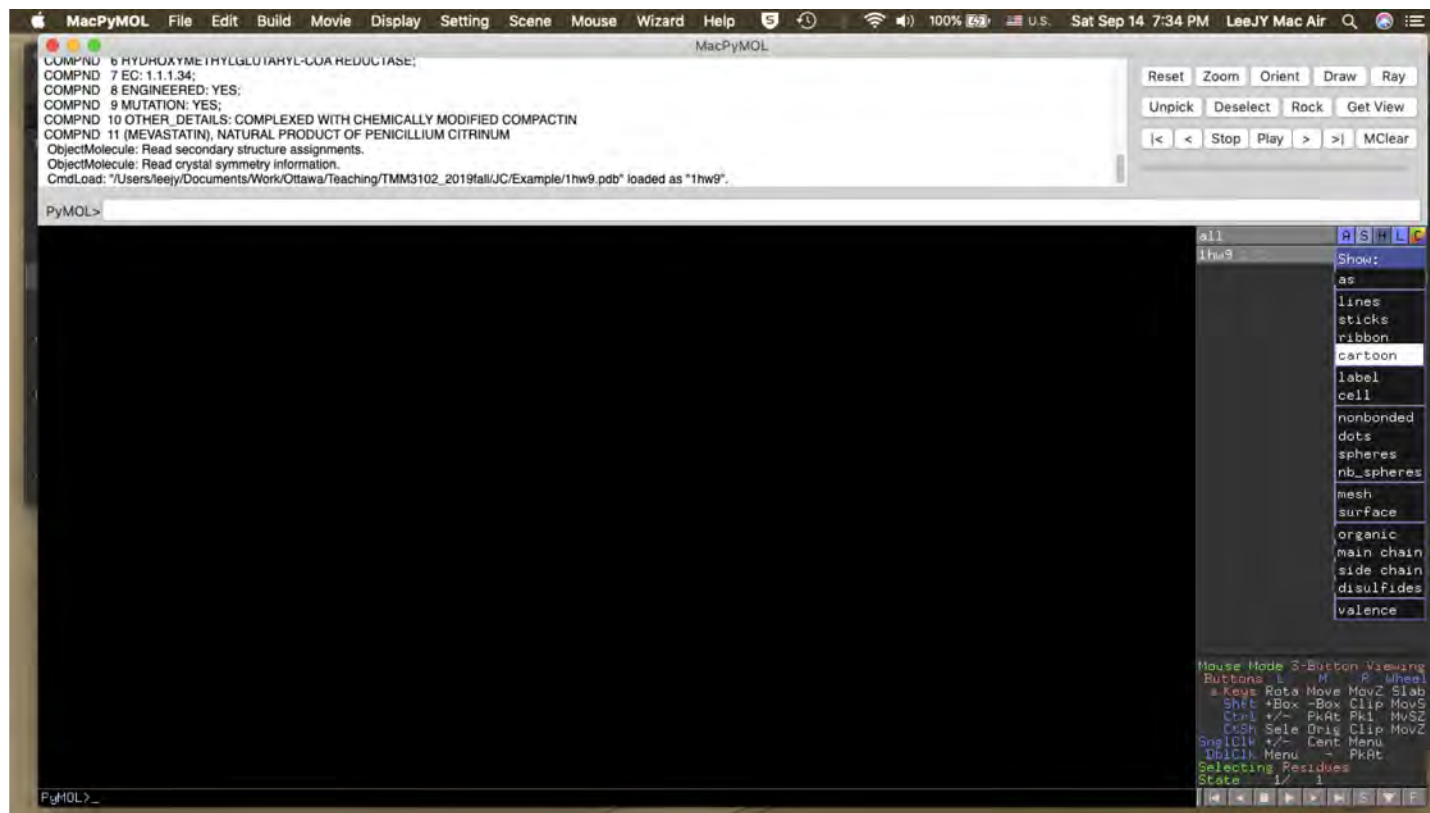
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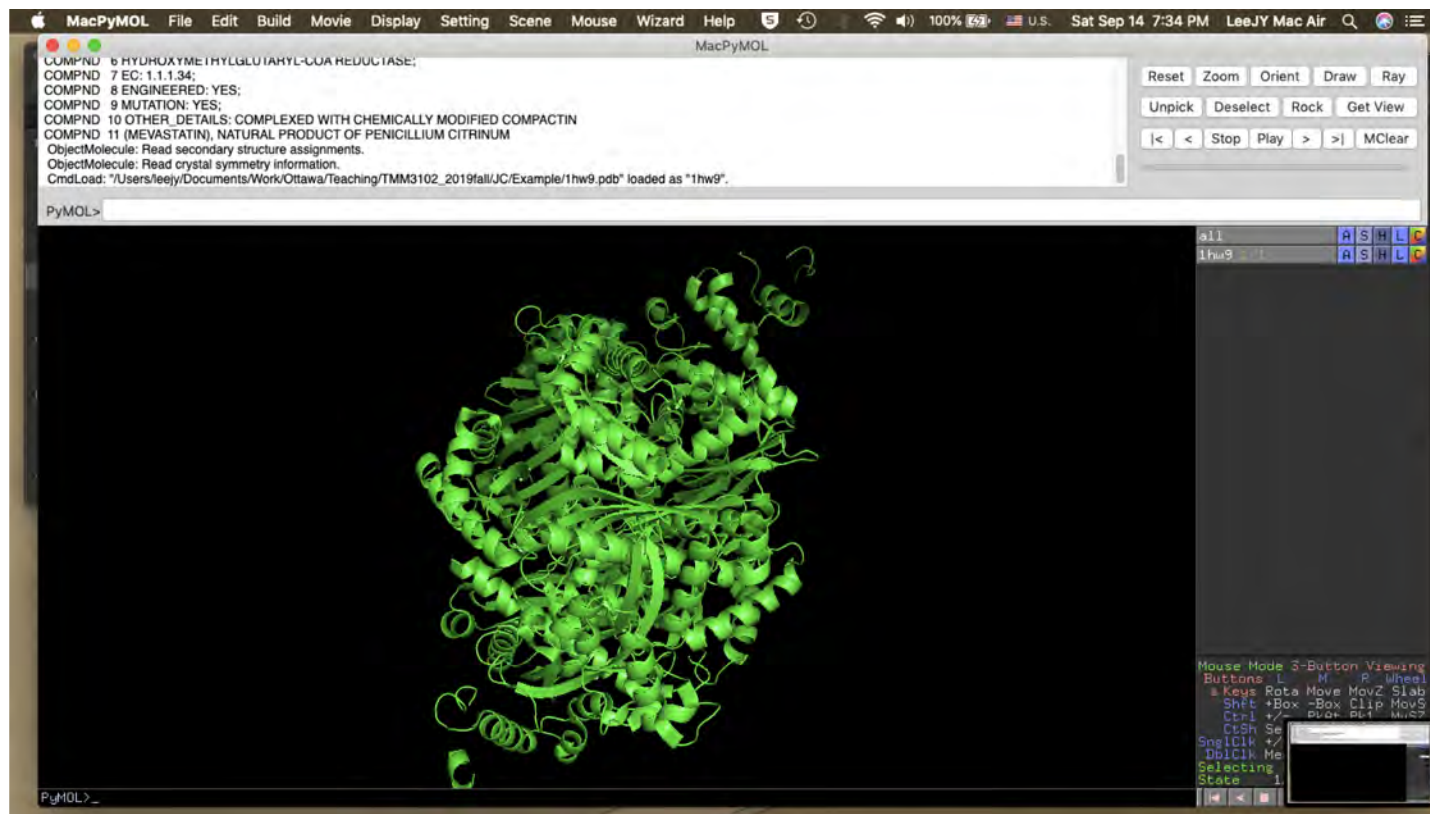
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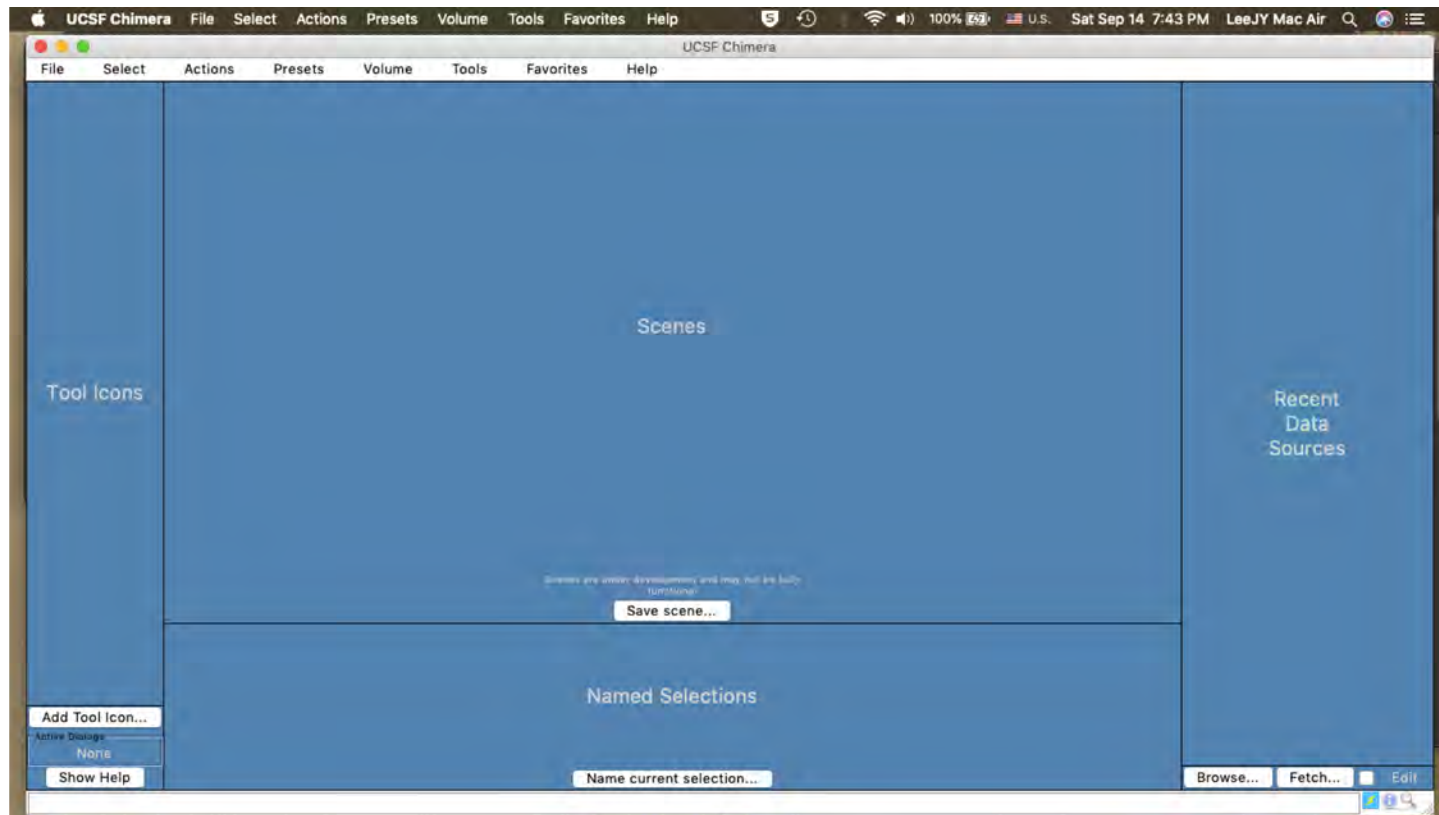
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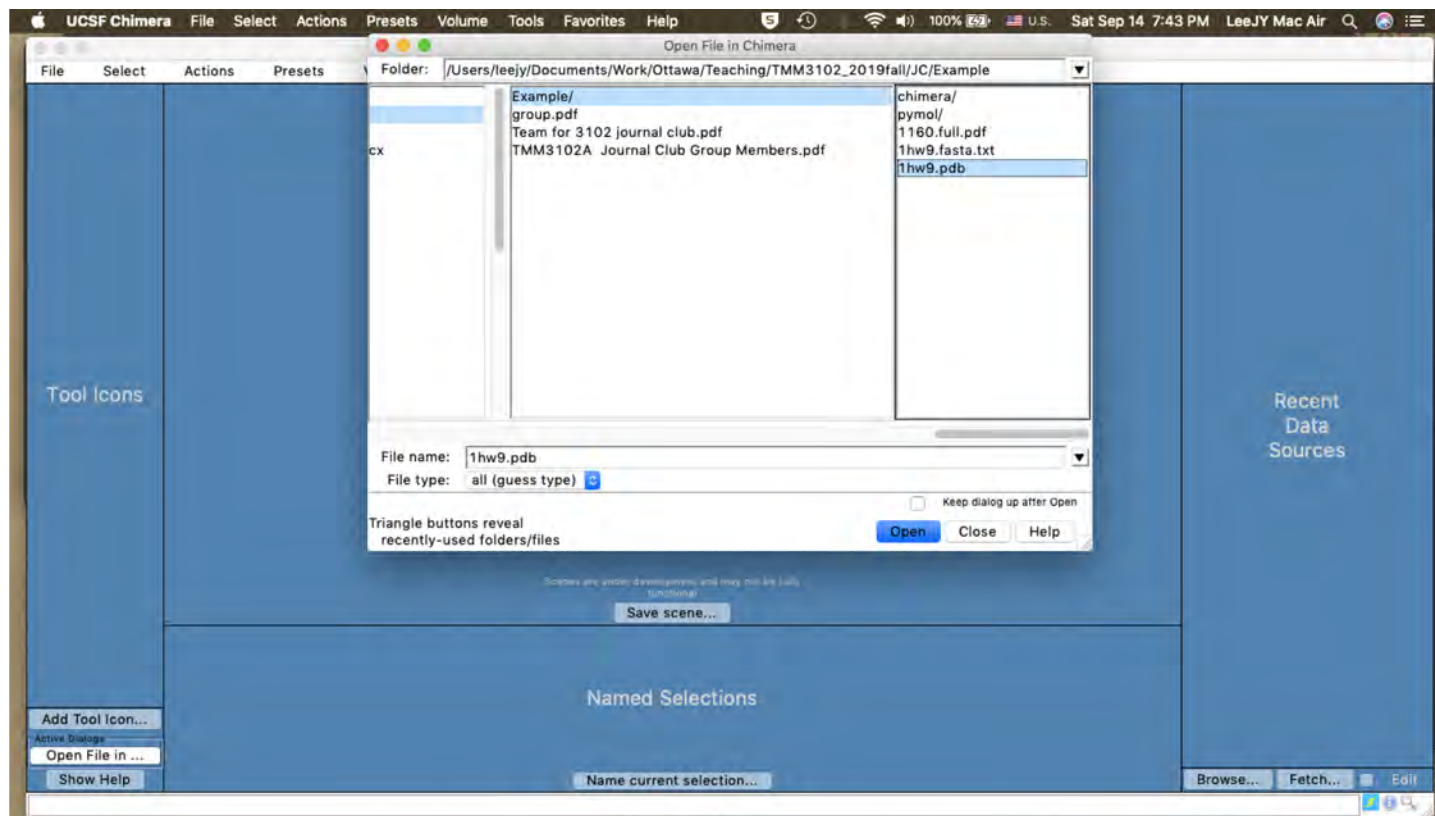
Protein in action at atomic resolution

Demo example: statin and HMG-CoA reductase; Chimera



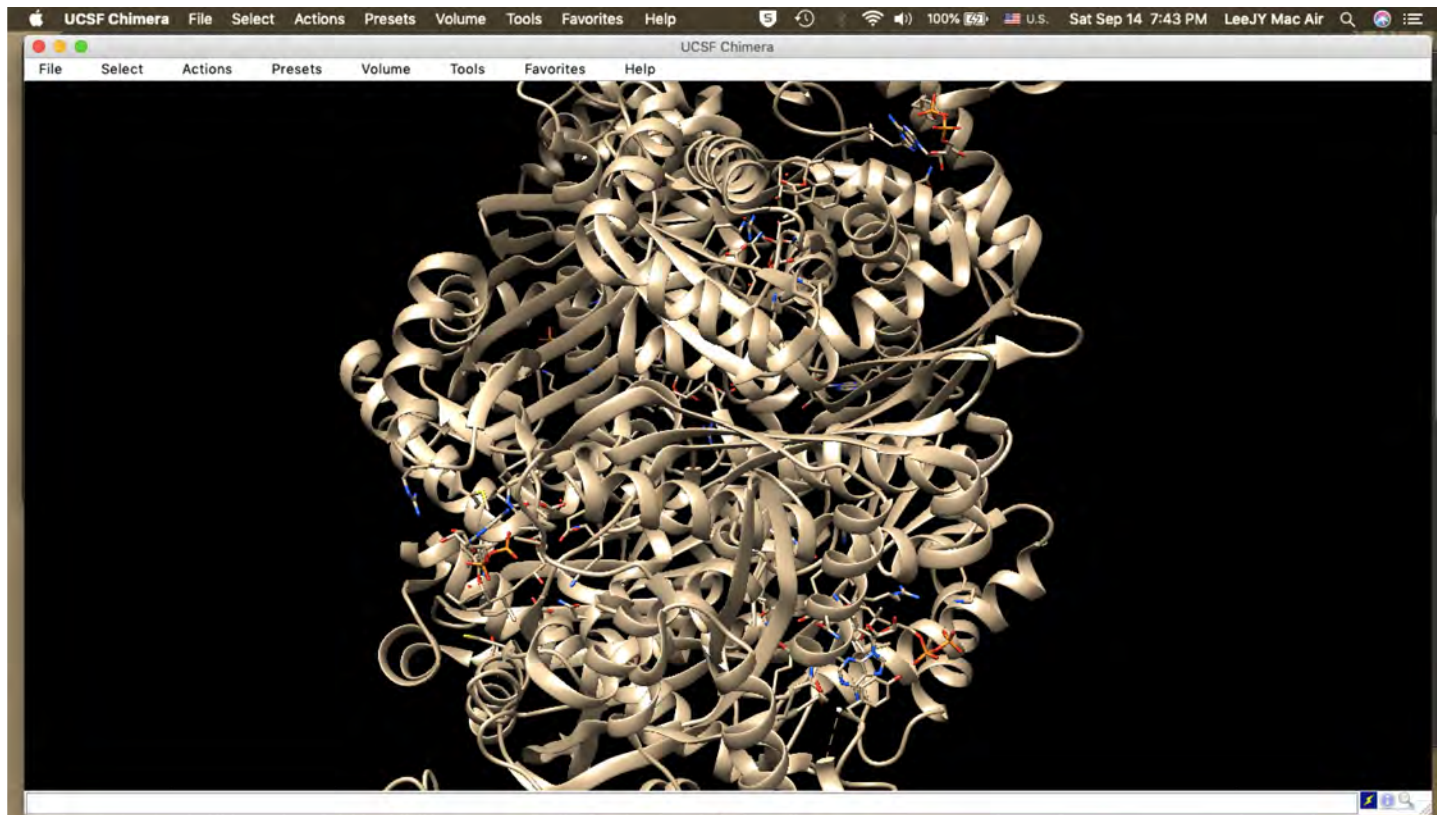
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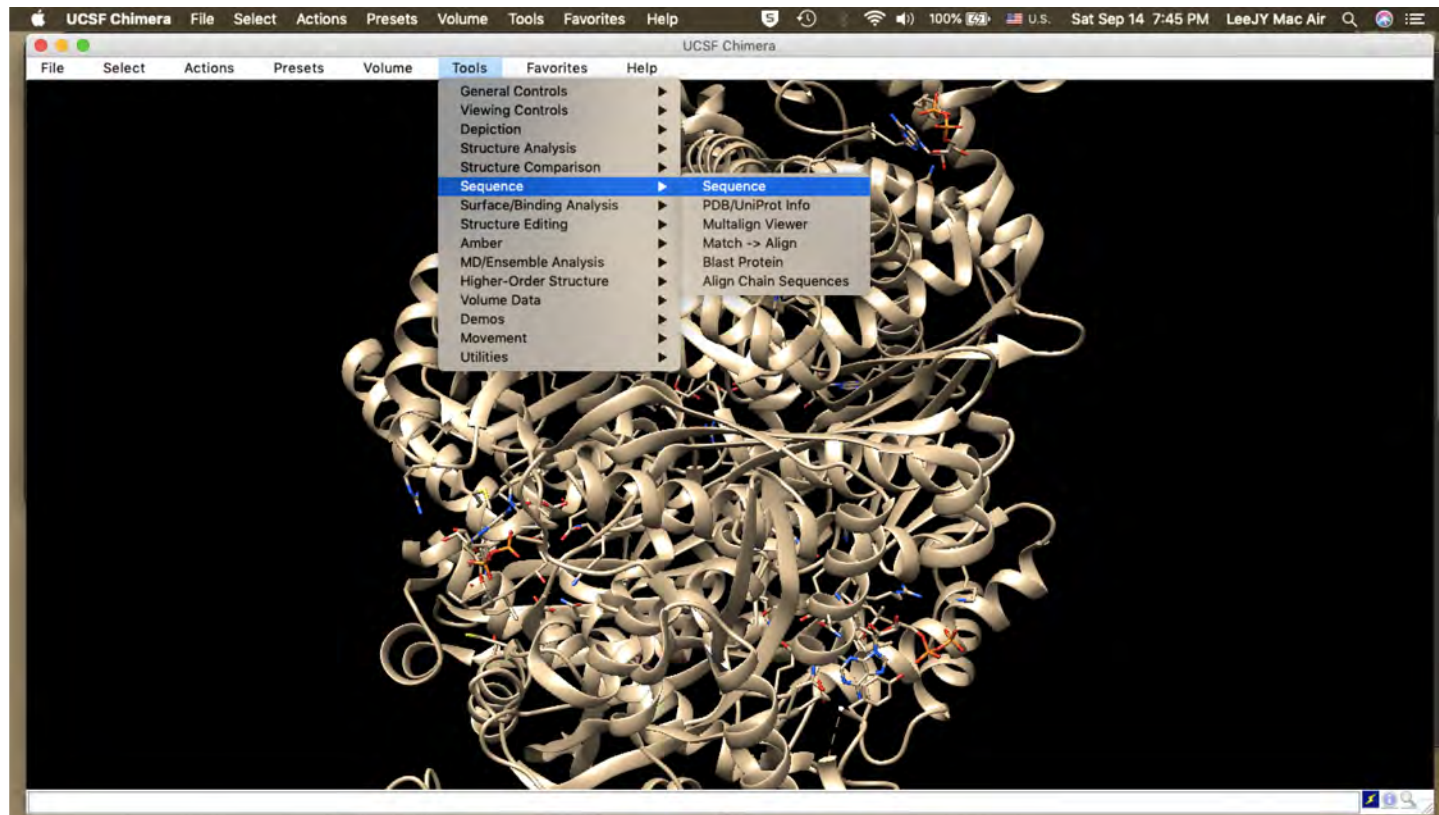
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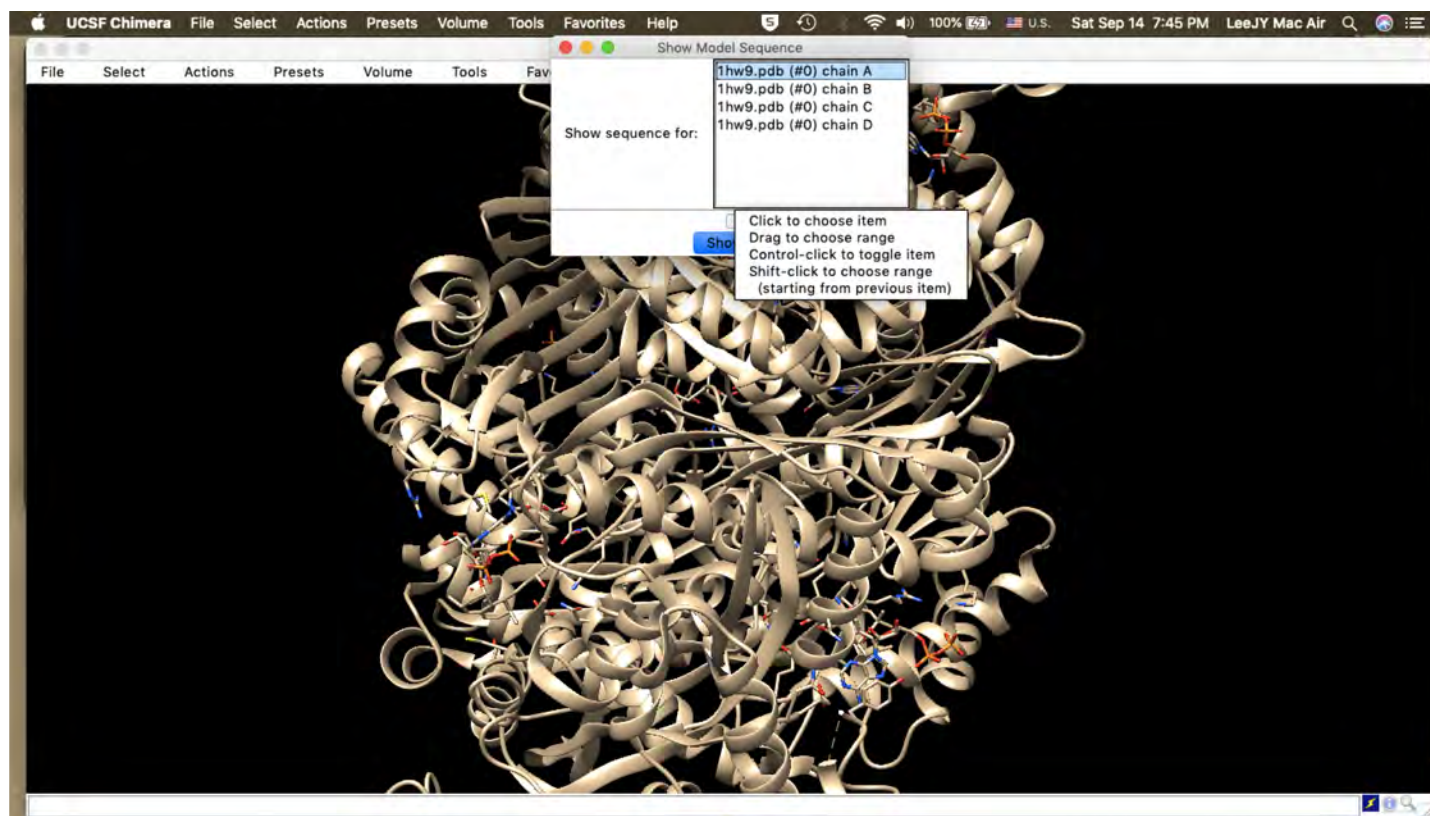
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Demo example: statin and HMG-CoA reductase; Chimera



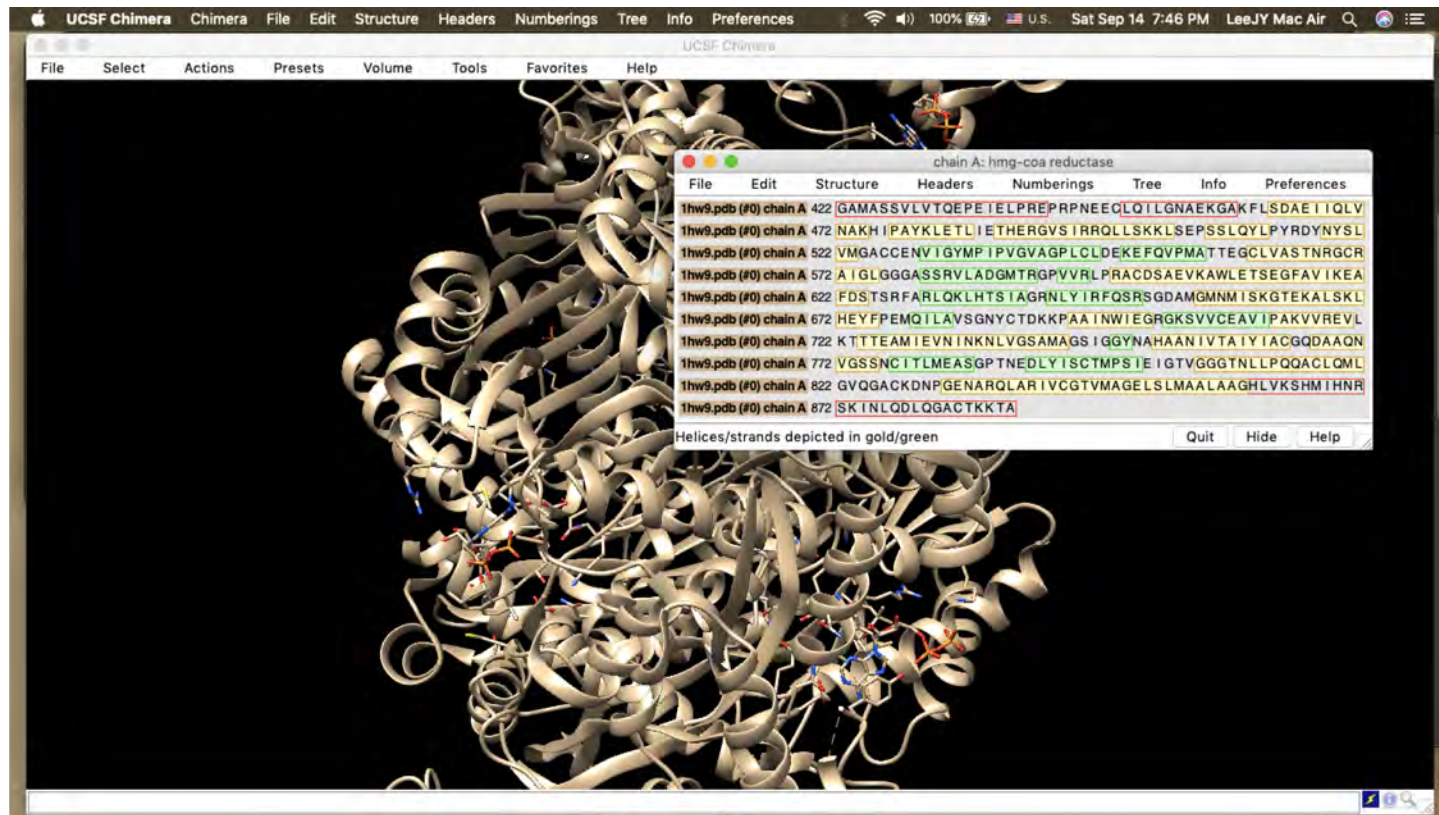
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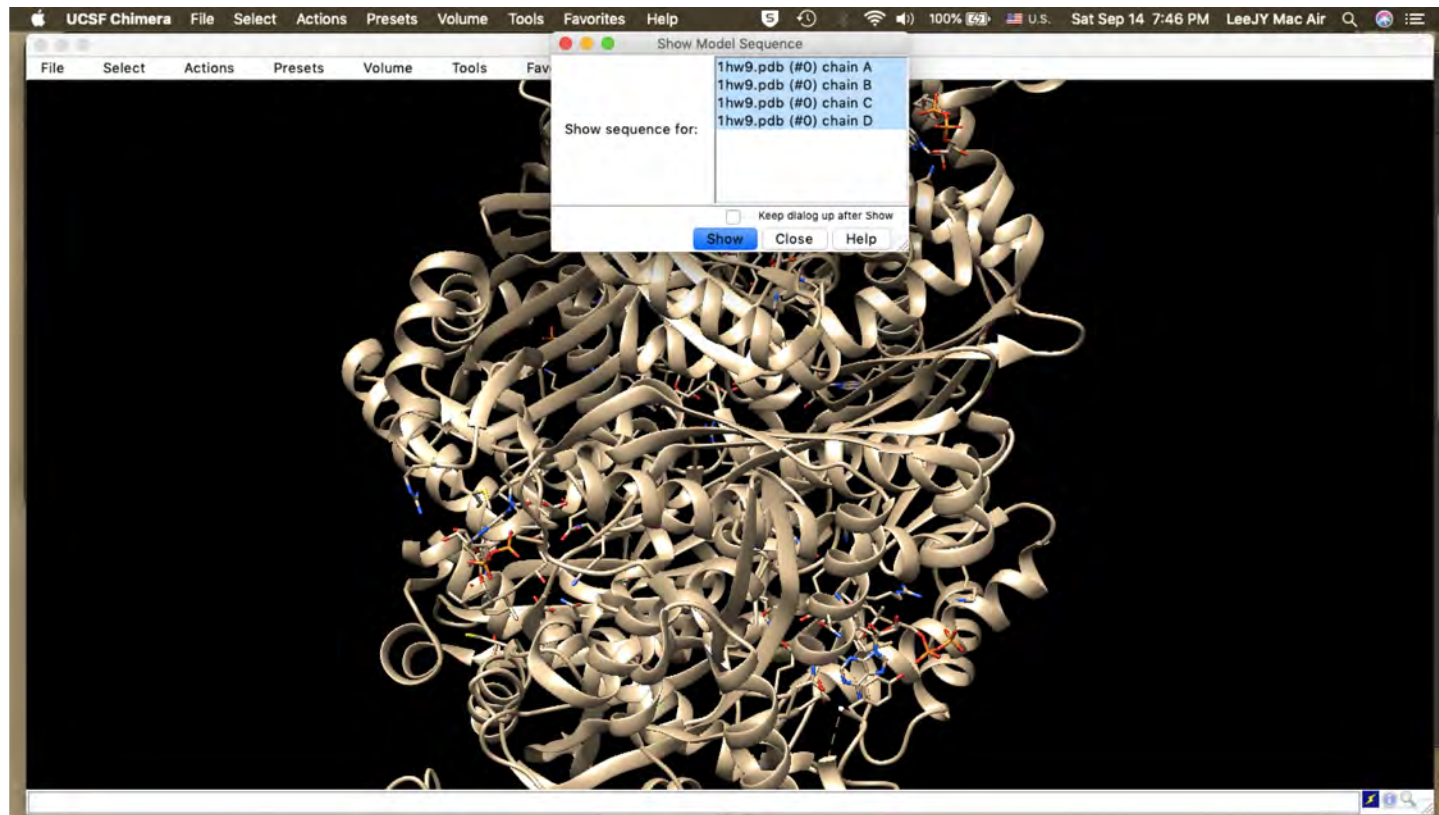
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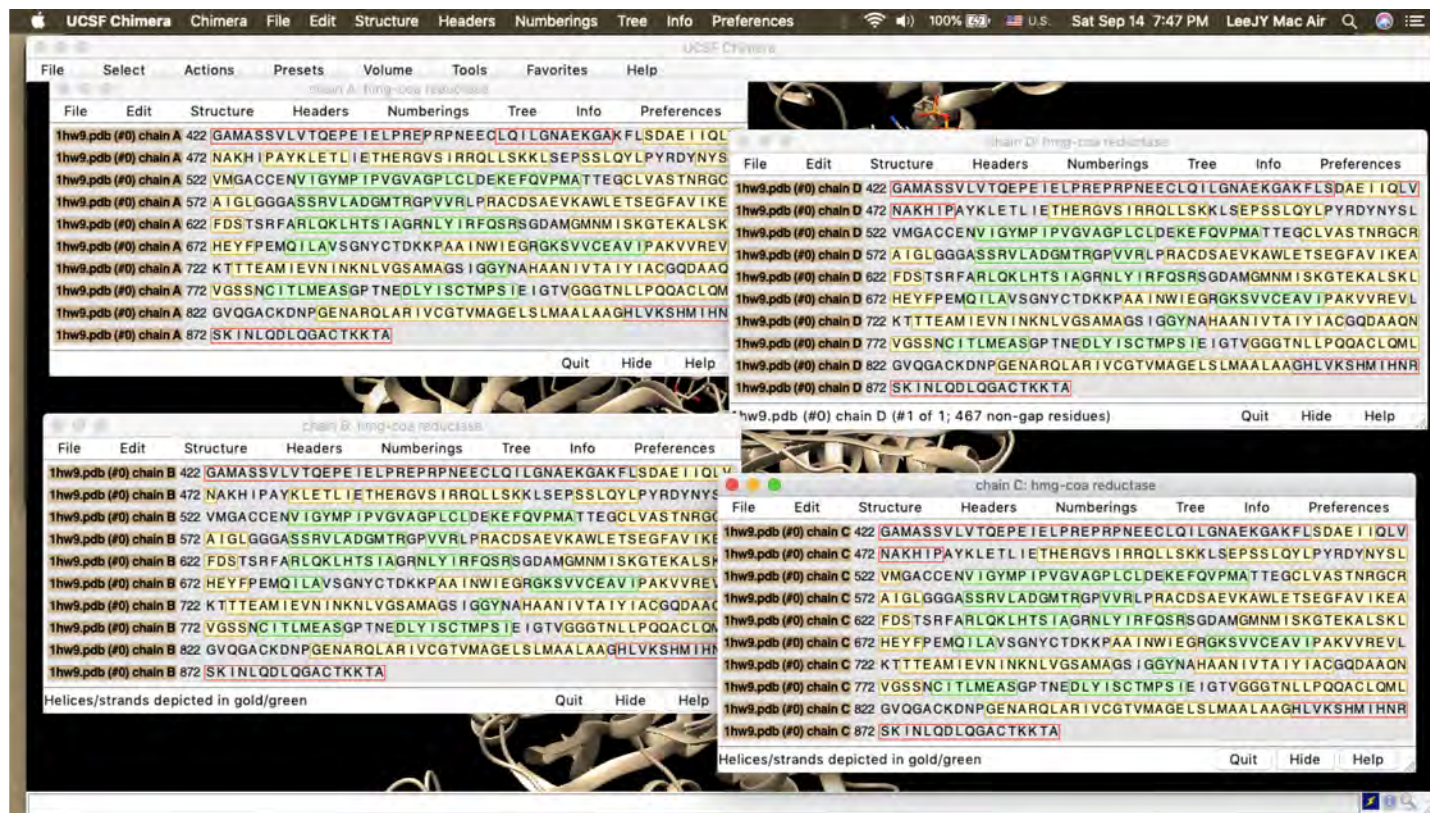
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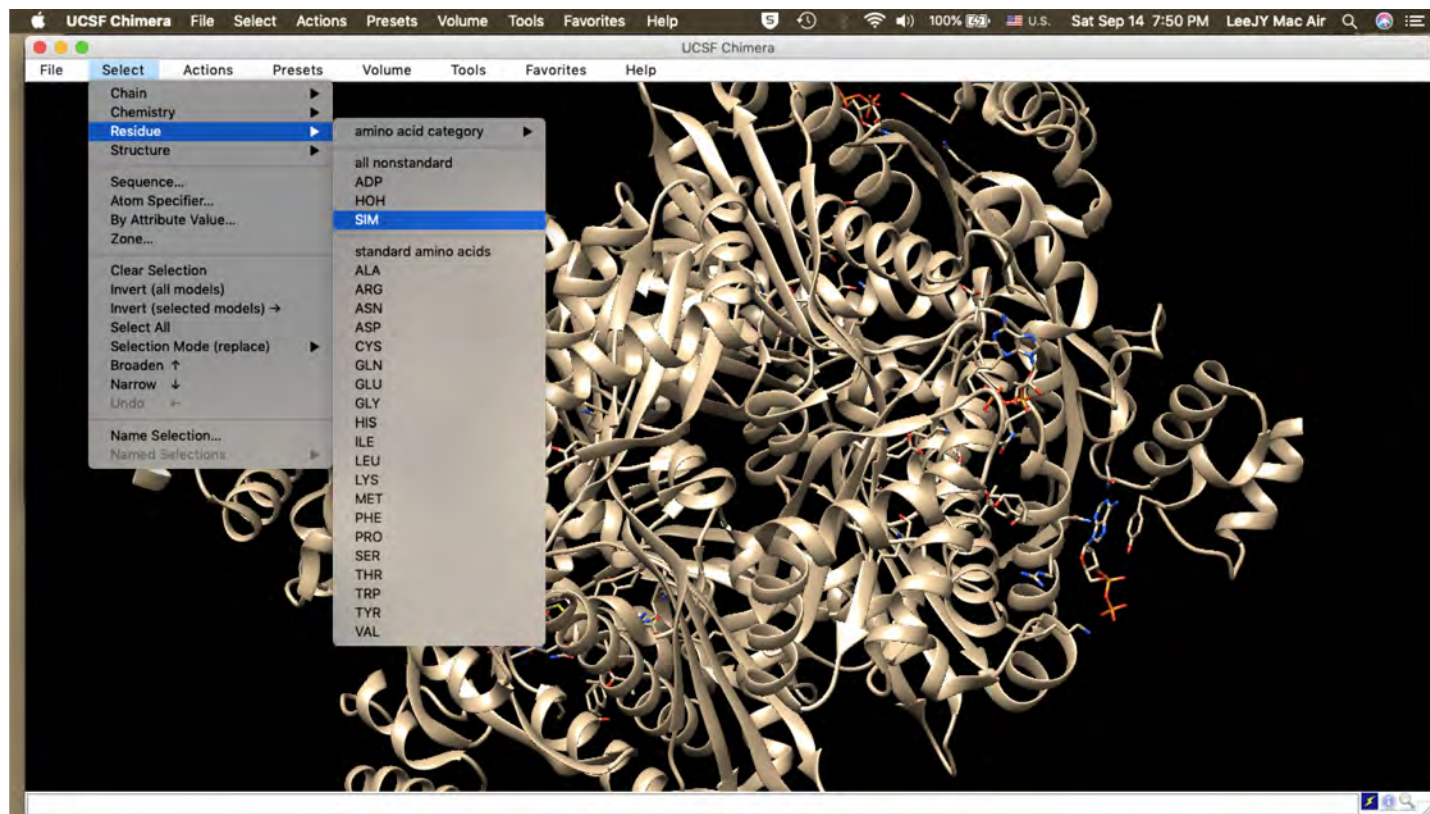
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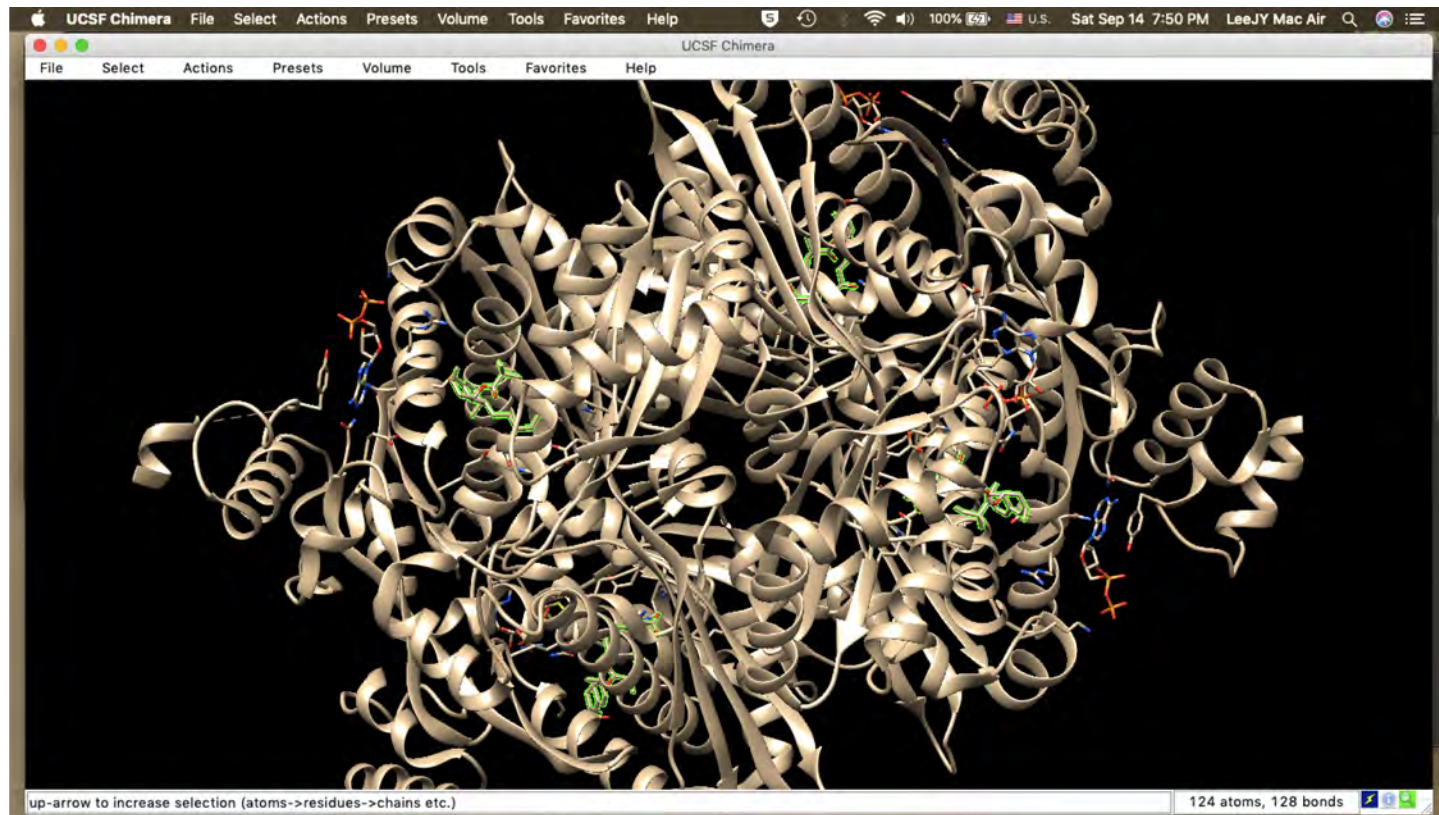
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