41. Protein structure

1 unit Stephen Long, October 28, 2025

Topics covered:

Non-covalent interactions that determine the properties of macromolecules.
Electrostatic interactions, van der Waals interactions, hydrogen bonds, hydrophobic effect
Introduction to protein structure.
Peptide bonds, phi/psi angles, α helix, β sheet, topology, structural motifs, active sites
Techniques of x-ray crystallography and cryo-EM
Viewing structures and protein density with PyMOL and ChimeraX

Discussion Paper:

Koehl, A., Hu, H., Feng, D., Sun, B., Zhang, Y., Robertson, M. J., et al. (2019). Structural insights into the activation of metabotropic glutamate receptors. Nature, 1–22. http://doi.org/10.1038/s41586-019-0881-4

Information regarding the maps and coordinates from the paper: "The atomic coordinates of apo mGlu5 and active mGlu5 in complex with Nb43 and L-quisqualate have been deposited in the Protein Data Bank under accession codes 6N52 and 6N51, respectively." The corresponding maps are emd_0346.map and emd_0345.map.

***Before class, download and inspect both sets of coordinates (with pymol) and the associated maps (with ChimeraX). Please have these loaded on your laptop before class.* More information is below. A three-button mouse for use with PyMOL and ChimeraX is HIGHLY recommended.**

Instructions to install the program **PyMOL** on your laptop, if you don't have it already:
https://pymol.org/edu/?q=educational/ You can call the helpdesk (x3337) if you have trouble.
PyMOL is a molecular graphics program that allows you to visualize 3D structures. Download the coordinates for each of the structures that we will be looking at from www.pdb.org by searching for the accession numbers 6N51 and 6N52. Then, click "download files" -> "pdb format". This will save the coordinates file (6n51.pdb or 6n52.pdb) to your computer (usually in the downloads folder). Open the file in PyMOL by selecting open from the file menu within PyMOL (or drag the file onto the PyMOL applicaton).
Please learn the basis before class – here is a tutorial:
www.pymolwiki.org/index.php/Practical_Pymol_for_Beginners
And an informational sheet: https://pymolwiki.org/index.php/CheatSheet

Install the program **ChimeraX** on your laptop: https://www.cgl.ucsf.edu/chimerax/
This program is useful for viewing cryo-EM maps and atomic models.
Open the mGlu5 maps in ChimeraX. This can be achieved by typing "open 0345 from emdb" and "open 0346 from emdb" in the command window of ChimeraX, or by downloading the maps from the pdb (Download files -> EM Map) and then opening them in ChimeraX. (These are big files ~50 MB so they may take a while to load)

Background paper:

Niswender, C. M., & Conn, P. J. (2010). Metabotropic glutamate receptors: physiology, pharmacology, and disease. Annual Review of Pharmacology and Toxicology, 50, 295–322. http://doi.org/10.1146/annurev.pharmtox.011008.145533