

Student Projects for UMass Chemistry 423 Spring 2016

From Proteopedia

Understanding the chemical basis of disease and life processes

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Instructions

Deadlines

1. Optional Team or Teammate requests in Moodle by 1pm 2/1

You may request one teammate or a complete team of 5 people (including both chemistry and chemical engineering students). Teams of 5 people will be assigned and posted in Moodle, to include both chemistry and chemical engineering majors on most teams.

2. Topic and pdb code due in Moodle Friday 2/5 1pm.

Once you know your team assignment, select an available topic. Must be unique: first-come, first-served, so check the posted list in Moodle to be sure that your topic has not already been chosen. Follow the guidelines for topics (see Moodle). Choose from the list of suggested topics, OR choose another topic of interest and check (1) to be sure it is not on the "Topics to avoid" list, and (2) check with the instructor. You must check your topic (suggested or otherwise) to be sure there is not already a detailed Proteopedia page for the same complex or same pdb code. Team/topic list will be posted in Moodle. Proteopedia 2016 Projects page will have links to each team's sandbox page.

3. Start your team's sandbox page by completing the "See Also" section by Monday 2/8. Are any human-authored Proteopedia pages too similar?

Enter or edit your team's topic name and pdb code, and byline names. Complete the "See Also" section: add links to any related Proteopedia Topic Pages (not pages titled with the pdb code). Search for these, for example at http://proteopedia.org/wiki/index.php/Category:Topic_Page, [Topic_pages](http://proteopedia.org/wiki/index.php/Category:Topic_pages), and [Proteopedia:structure_Index](http://proteopedia.org/wiki/index.php/Proteopedia:structure_Index). If you find another useful search strategy, post it under Help at Sandbox 423. If there is another page describing a complex with the same or a very similar molecule, you will need to choose a new topic.

4. Sandbox page displaying initial structure and one green scene due by end of class workshop 2/12 -- bring your computers to class.

In your assigned sandbox page click "edit this page" (top) and follow the directions to insert your rotating structure on your page. Describe and illustrate with a green scene the secondary structure of your protein.

5. Sandbox page with each section displaying an outline and at least one green scene due by beginning of class 2/24 -- bring your computers to class.

Each team member should read the primary reference for the pdb structure and create an outline for their section and at least one green scene. Teams will meet briefly during class to discuss the overall organization as needed to make it logical and avoid duplication. As individuals proceed to create their sections, they should watch the other sections and stay in contact as

needed to create a coherent overall project.

6. Project completed (all sections) in Proteopedia by Sun 4/10. All team members also submit their text to Turn It In (see class Moodle page).

Project Description

Your proteopedia page should be organized into the following required sections, with each team member responsible for one of sections a-e of the team project. All sections will be within a single scrolling section (single JSmol window) -- I changed to this in March to speed up loading. Provide an interesting description (suitable for non-experts), and illustrate your points about the complex with multiple green scenes. Be concise (<300 words)! Do not include any copyrighted figures! All sections must be written in your own words with citations to your sources, following the reference format in the example below (go into edit this page, to see how these references were done). You may include links to other interesting information or scenes but you must create your own scenes for display on your page.

Make it interesting and accessible to a non-scientist! Show clearly some chemical details to illustrate the chemistry of life processes!

a. Introduction

Introduce the protein function, how it is related to a disease, and what is important about the ligand in the complex. Make 1-2 green scenes suitable for the Molecular Playground: attractive and informative illustrations of (1) the protein complex, and (2) what is especially interesting about it. Include a clever caption for potential display at the Molecular Playground -- caption must be short, ideally < 10 words.

b. Overall structure

Describe the overall structure of your protein in words and make "green scenes" to illustrate your points. What elements of secondary structure are present (ie 5 alpha helices and 2 beta strands) and how are they organized? Additional description and green scenes could illustrate the polar/nonpolar distribution of amino acids (is the inside of the barrel polar or nonpolar?), packing of amphipathic elements, etc.

c. Binding interactions

Describe features of the drug or ligand or protein-protein binding site in words and make "green scenes" to illustrate your points. Show the interactions that stabilize binding of this molecule to the protein (ie H bonds).

d. Additional features

Describe and use green scenes to illustrate additional features of the macromolecule. What you do here depends on what information is available. If a structure of the protein-substrate complex is available, you could compare protein interactions with the substrate vs. with the drug. If the drug is a transition state inhibitor, explain and illustrate that (eg include a reaction scheme with structures of the substrate, transition state and product -- but don't borrow a published scheme).

e. Quiz question

Pose an interesting, quiz-worthy question that involves thinking and investigating the molecule with the green scenes that you provide here. Submit the answer to your question in Moodle and do not share it with other students. Best questions will be chosen for a Moodle quiz, so that students can explore your structure and green scenes to figure out the answer to your quiz question.

f. See also

For the 2/8 deadline, all team members should look for related Proteopedia pages (e.g. same protein but with different ligands) and post links here.

g. Credits -- list who did which portion of the project. If multiple people work on a section, use an asterisk to designate one person with primary responsibility.

Introduction -- name of team member

Overall structure -- name of team member

Binding interactions-- name of team member

Additional features -- name of team member

h. References

This will include the published paper that describes your structure (the reference associated with your pdb code). Everyone should read this primary reference -- you will get much of your information about specific interactions to look for and highlight in the structure from this reference (which is much easier than trying to find these on your own with no guidance!). Additional sources must also be cited in this section.

Help

Tips, Questions, & Answers

Here are some tips/questions/answers from me and previous students. Post new ones at Sandbox423, where you can also find links to past projects.

- For step-by-step instructions on creating example scenes, try Proteopedia:DIY:Scenes.
- A very useful color scheme is "chain" which colors separate proteins or DNA strands in different colors (first select all protein or DNA).
- To show the biological unit, follow directions at Biological Unit: Showing. The pdb file will display the "asymmetric unit" = the smallest unit that can be replicated to generate the full crystal. Example: the protein may function as a dimer (you need biochemical experiments to tell you this -- crystallography and NMR won't tell you), but the pdb file may display a monomer (if the dimer is symmetric) or two dimers (if they have slightly different conformations in the crystals -- perhaps due to crystal contacts or perhaps representing 2 functional states of the protein!).
- Instructions for references are at Help:Editing#Citing_Literature_References. You can follow the format used in the example on the Asp receptor and they will be put in automatically.

You just find out the PMID code (listed in pubmed for example) and insert it into the following, at the place where you want the reference cited (click edit to see what is actually inserted here). ^[1] You also need to add the section:

References

1. ↑ Yeh JI, Biemann HP, Pandit J, Koshland DE, Kim SH. The three-dimensional structure of the ligand-binding domain of a wild-type bacterial chemotaxis receptor. Structural comparison to the cross-linked mutant forms and conformational changes upon ligand binding. J Biol Chem. 1993 May 5;268(13):9787-92. PMID:8486661 (<http://www.ncbi.nlm.nih.gov/pubmed/8486661>)
- Hey guys this is just a useful tip:

If you get an xml error after you try to save your changes it is due to the green scene coding. Our group experienced this issue and it would not let us access our sandbox. In order to fix this go back (or find the page to edit in your history) and delete the green scene code that was just entered. Then save the page and you should be back to your sandbox. This may be trivial to many, but just throwing it out there.

- To highlight some interesting portion of your protein:

Under the selections tab, you can "limit to residue numbers." So for example enter in 60-65, then click "replace selection" below. Then if you go to the colors tab you can pick a color for just the residues you have selected. If it is a loop or if they are hard to see you can go to the representation tab and set selection to ball and stick or spacefill.

It is also useful to click the "selection halos:" box under the picture. That shows you what you have in your selection.

- If you suddenly can't get to your sandbox page (error message XML error: Mismatched tag at line 1), try Help:Errors

Tips from feedback/edits of past year Proteopedia Projects

Each section should start with the line that inserts the Jmol window: then each scene for that section will appear in that window, along side your text (<300 words).

Every jmol window should have a caption so we know what we are looking at (include the name of the molecule and pdb

code) Replace 'insert caption here' with 'your caption'.

Careful with repetition of the same points in multiple sections -- instead organize the topics logically and you can have multiple people contribute to a section if you want.

Feel free to work together on sections and add people to the credits if that helps to make a coherent and organized story.

Follow the correct format for references, including citations in text -- see instructions and link above.

Make green scenes to illustrate your points, and weave your scenes into the text.

Use colored text to help the reader easily see your points in the scene and to keep your text concise. For example "This view shows the **2 alpha helices** packed against the **4-stranded antiparallel beta sheet**." The word "view" would link to a green scene in which the alpha helices are red and the beta sheet is blue. Go into edit mode on this page to copy the colored text section for use on your page. See also Help:Color_Keys.

Avoid a list of miscellaneous facts. Choose the most interesting points to tell us in some detail and illustrate with green scenes.

Tell your story with green scenes and minimal text!

If you are having trouble labeling individual amino acids residues, load your molecule, go to "selections," input the amino acid, residue number, and an atom only contained once in the amino acid (must typically nitrogen), and replace your selection. Then go to "labels" and chose which label you want. This should give you a single label.

Example

This is a complex between a macromolecule and its ligand (but this ligand is not a drug) that illustrates the use of green scenes:

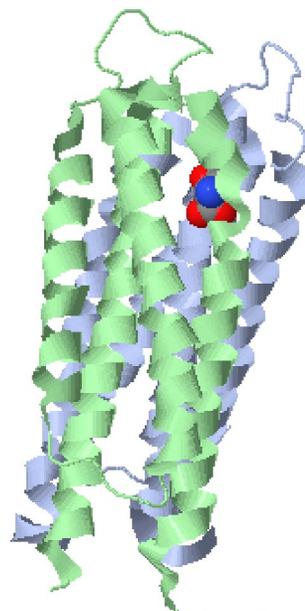
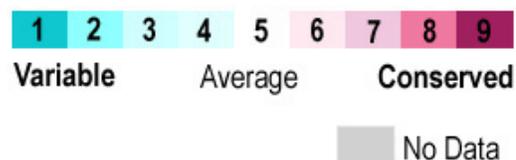
Asp Receptor Ligand-binding domain

Overall structure

The ligand binding domain of the aspartate receptor (**Initial view**) is a dimer of two 4-helix bundles that is shown here with the **aspartate ligand** bound.^[1] In this **rainbow representation** the **N** and **C** termini are at the bottom of the structure; this is where the connections to the transmembrane helices have been truncated.

Ligand binding site

When the protein is colored according to **sequence conservation**, residues at the ligand site are the most conserved.



JSmol

± spin ± quality ± labels popup 🔍+ 🔍-

Bacteria use this protein to "smell" their environment, Iwat

Export Animated Image

Interactions that stabilize ligand binding^[2] include hydrogen bonding from Tyr149 and Gln152 backbone carbonyls and Thr154 sidechain OH to the **ligand amino group** and hydrogen bonding from the sidechain nitrogens of Arg64, Arg69, and Arg73 to the two **ligand carboxyl groups**.

References

1. ↑ Yeh JI, Biemann HP, Pandit J, Koshland DE, Kim SH. The three-dimensional structure of the ligand-binding domain of a wild-type bacterial chemotaxis receptor. Structural comparison to the cross-linked mutant forms and conformational changes upon ligand binding. *J Biol Chem.* 1993 May 5;268(13):9787-92. PMID:8486661 (<http://www.ncbi.nlm.nih.gov/pubmed/8486661>)
2. ↑ Milburn MV, Prive GG, Milligan DL, Scott WG, Yeh J, Jancarik J, Koshland DE Jr, Kim SH. Three-dimensional structures of the ligand-binding domain of the bacterial aspartate receptor with and without a ligand. *Science.* 1991 Nov 29;254(5036):1342-7. PMID:1660187 (<http://www.ncbi.nlm.nih.gov/pubmed/1660187>)

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- Proteopedia is hosted by the ISPC at the Weizmann Institute of Science in Israel

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