

## Supplement 1: Authoring a Molecular Case Study: A Partial CURE Project

**Overall project goal:** Make a clear link between the structure and function of a protein that plays a critical role for a specific biological function.

There is a set of parallel goals from the ASBMB Foundational Concepts that may be provided by the instructor or chosen by the students.

(see

[https://docs.google.com/document/d/1CgooZ9ttEidXpEX55H\\_ib2WW3TOnTsLTkEAWLUIUcPM/edit#heading=h.kkqdf8gto1](https://docs.google.com/document/d/1CgooZ9ttEidXpEX55H_ib2WW3TOnTsLTkEAWLUIUcPM/edit#heading=h.kkqdf8gto1))

### How does this project fit in with biochemistry curricular goals?

Through this project you will have the opportunity to:

1. Apply foundational knowledge about protein identity, structure, and function to a protein of special interest to you.
2. Find and interpret biochemical literature and/or data related to your protein or system of interest.
3. Study examples of how similar biochemical principles are applied to solve a diverse set of biological and biomedical problems.

### Steps for authoring molecular case study as a partial CURE: (Figure 1b)

#### A. Molecular Case Study Examples

Complete and/or critically review a published or late-stage draft of an example molecular case study (MCS). Share your experience with your peers on the available discussion board where you can ask questions, critique what was done well, what should be improved, and what you learned from the way these cases are written.

#### B. Project Proposal

1. **Review scientific literature:** Select a biological system of interest or learn about the biological system you are assigned for your case
2. **Identify case context:** Outline the specific scientific question(s) you would like to answer within this biological system and identify the protein players that are involved in the chosen biological context.
3. **Identify relevant PDB structures:** Perform preliminary search in the Protein Data Bank (PDB, [www.rcsb.org](http://www.rcsb.org)) to determine if adequate structural information is available for the proteins identified in the previous step and determine the main protein structure you want to build your case around.
  - **Explore the PDB.** Look at all the relevant structures for the protein of interest. Which one(s) would be most valuable in answering the functional question at hand? What are additional structures that can be compared/contrasted to the original structure to make a point?

#### Consider:

- What do you want your audience to learn from the 3D structure that cannot be learned by looking at its primary sequence alone?
- Should the audience be able to describe the structural method(s) used to elucidate its structure and report the strengths and limitations of the method?

- Referencing the paper where the structure was originally published, why did the authors seek the 3D structure?
- What are some of the interesting/unique features and spatial organization of the protein molecule (such as domains, motifs, secondary structures, etc) that are relevant to the function investigated?
- What is the quality of the structure? (Examine validation reports where possible)
- What unique information could be obtained or hypothesized about the protein based on the deposited structural information?
- Are there other forms of your protein for which there are additional PDB structures available (e.g. from other species, as co-structures with a drug, as a mutant)?
- Is a comparison of multiple structures helpful?
- What compromised functional state(s) is/are affiliated with the protein, and what leads to this state?
- Are there any 3D structures available with binding partners (e.g. co-structures with drugs) or mutations?
- How can examination of the 3D structure of the protein clarify its role in altered functional states?
- Are there specific published examples describing these altered states?
- How can you lead others through the structure to look and understand it at an amino acid molecular level and draw structural and functional conclusions?

**4. Explore other bioinformatics resources:** Expand your structural search into online databases and tools beyond PDB to supplement your story line. Consider resources that look both at DNA/RNA sequences and protein sequences/structures:

NCBI Genbank: <https://www.ncbi.nlm.nih.gov/genbank/>,

UniProt: <https://www.uniprot.org/>,

JPred: <https://www.compbio.dundee.ac.uk/jpred/>,

Pfam: <http://pfam.xfam.org/>,

KEGG PATHWAY Database: <https://www.genome.jp/kegg/pathway.html>,

BLAST: <https://blast.ncbi.nlm.nih.gov/Blast.cgi>,

CLUSTAL Omega: <https://www.ebi.ac.uk/Tools/msa/clustalo/>, etc.

Consider:

- What can be learned quickly/easily from the primary and/or secondary structure of proteins, and what cannot?
- How can you use the DNA or RNA sequences to learn more about the wild-type or a mutant protein?
- Are there proteins with related/redundant functions? Is your protein part of a metabolic pathway? Signaling pathway? Multi-protein complex?
- How conserved is the protein across species? Does it make sense to do a multi-species alignment in CLUSTAL OMEGA?

**5. Justify choices made:** The justification should be supported by primary literature and/or data supporting experimental data for the claimed link between the structure and function of the central protein. The structure(s) and bioinformatics data selected should help answer the problem or question in the case.

**6. Receive mentor approval**

## C. Case Writing

1. **Identify learning objectives:** All major projects should begin and end with the objective of the study. Your learning objectives should be appropriate for the specific audience you are targeting. Each of the sections of your case should have 2-3 learning objectives that all tie to one main overall learning goal for the case. Learning objectives should be matched to existing standards whenever possible. You can find a simple introduction to writing clear learning objectives here:

[https://www.bu.edu/cme/forms/RSS\\_forms/tips\\_for\\_writing\\_objectives.pdf](https://www.bu.edu/cme/forms/RSS_forms/tips_for_writing_objectives.pdf)

2. **Define research problem:**

- **Function and altered function:** A well defined specific function and a change in that function that is being investigated. Within the introduction section of the case, there should be a well articulated question that clearly ties the hook to the investigated functional question. There should be a dedicated section in the case that delivers adequate biological and chemical background to explain the biological system at hand and help appreciate the importance of the investigated question. Furthermore this section should clearly describe all the important cellular players within the biological system, how they are related functionally with respect to each other, and how they individually or collectively impact the investigated function. The case should include several specific questions (and answers) about this section that assess the audience's understanding of the functional information related to the case.
- **Structure and altered structure** (Sequence is a part of this line as it is the primary structure of a protein). A central protein around which the case will be built. There should already be a minimal amount of available structural information in the protein data bank about this protein and its altered form relevant to the functional change investigated. There should be a dedicated section in the case that delivers adequate background information as well as specific structural information at a molecular level about the central protein investigated. Furthermore this section should clearly describe the structural relationship between the central protein and its interacting partners within the investigated biological system. The case should include several specific questions (and answers) about this section that assess the audience's understanding of the structural information related to the case.

Consider using literature or online bioinformatics tool to investigate:

- What biological phenomenon is affiliated with your protein under normal and disease contexts?
- How/why was your protein named as it is?
- What are its substrates, ligands, reaction mechanisms, or binding partners?
- What organism does it come from? How conserved is the protein across species?
- What are the physical stats of the protein (e.g. MW, pI, amino acid length)?
- How is your protein regulated in the cell? What are the post-translational modifications on the protein (if any), and what role do they play in its function?

3. **Develop a creative/ engaging storyline:** A context for the molecule that is delivered in a non-scientific language aimed to capture the interest of the audience. This "hook," which can be in the form of an image, a short audio/video or written piece (such as a newspaper article or story), will constitute the introduction to the case and convey the

biochemical question to be addressed in the study.

Consider:

- Who is your audience and what is the take home message you would like them to have after completing this case study? Are there YouTube videos (or home-made videos) or articles to get a reader hooked into your story?
- Are you going to create a fictional story line or can you use a real life example from a newspaper story or clinical publication?
- Is your storyline entirely scientifically plausible?
- Make sure that any images, videos, stories used for the case are appropriately attributed. All necessary permissions should be obtained if using any copyrighted materials.

**4. Write case and assessment questions:**

- **Decide the number of subsections/modules your case study will have under each of the five mandatory MCS sections.** Each MCS needs to include the following five sections: Preparation (case context), getting to the structure(s), exploring the structure(s), modeling, and skill assessment. You can have multiple subdivisions or modules under each of these sections
- **List the literature data, bioinformatic tools, and PDB structures** you will use in each section to meet your stated objectives. You must explore molecular interactions within the protein as well as between the protein and a binding partner for the structure/function relation sections of the case.
- **Write the instructions** for how to obtain information.

Consider:

- Where and how will readers find information? How can you provide or help them obtain information?
  - Some of your information should be described in embedded text, figures, or tables—keep the text short and sweet and custom tailor your figures/tables.
  - Can you use some already-written instructions or a YouTube tutorial for finding specific details like a hydrogen bond or coloring an individual residue, etc?
  - Are you asking students to do things in a logical order?
- **Write your case questions.** Each learning objective should be measured with 1-2 questions (assessments) to determine if students have met the objective.

Consider:

- After the student obtains the structure, what will they do to gain skills in understanding how to interpret the 3D image?
- How do your questions require the reader to demonstrate the link between molecular structure and function?
- Do you have variety in the kinds of questions you are asking and the ways in which the student can respond (e.g. by pasting an image, a M.C. question, a brief essay, etc.)?
- Do your questions require the students to engage with the figures or structure, or can they just answer the questions without them?

- Are the questions written with the developmental level of the audience in mind?
- **Create a key.** Each team member should read through the case study on their own, make track changes as errors are noticed, and answer every question. Then come together to create a single comprehensive key.
- **Write one additional assessment question (and the associated answer key)** that relates to the case study but requires a student to apply knowledge gained from working through the molecular case study to a slightly different scenario that requires molecular visualization to answer the question. This will be used as a post-test to measure student learning.
- **Format your Literature Cited** section at the end.
  - If referencing specific data or images, use the style of ACS journal *Biochemistry*.
  - A rigorously researched case study will have 5-10 citations.

Example:

Nitric oxide plays a critical role in inflammation<sup>1</sup>.

(And at the bottom of the slide in 12 pt. font:)

<sup>1</sup>Coleman, J. W. (2001) Nitric oxide in immunity and inflammation. *Int. Immunopharmacol.* 1, 1397– 1406.

## 5. Get and give peer and mentor feedback:

- **Work as a team to sort out uncertainties.** One of the big advantages to working together is that someone familiar with your case may know the answer to your question. Create a working document (on Google docs or similar) so your team and mentor can all access the changes. Use a “track changes” feature to ensure that everyone can see what has been changed or contributed. The authorship of this document must be truly collaborative.
- **Touch base with your mentor regularly for small questions.** Insert comments and questions in the margin, and seek assistance when nobody on the team can sort out an answer within a reasonable timeframe. The more specific your questions are, the better (and likely quicker) your feedback will be.
  - Sometimes your mentor will give you additional help but NOT provide a direct answer. It is the team’s responsibility to figure out answers to research questions from the information provided--that’s part of the challenge!
  - You may also seek assistance from another team if you want feedback on whether or not your instructions make sense, for example.
- **A formal peer review assignment** will provide an opportunity for you to receive feedback on your MCS as a whole. The guidelines for this assignment are provided separately at the end of this document. You will be graded on your ability to review another team’s case (not on the quality of your own draft). To participate in the review, you must submit a full-length draft inclusive of all assigned parts (see above).

- When you receive your peer review, **you will submit your final MCS with a one-page cover letter** that responds to the reviews. This letter should describe (briefly) the type of peer feedback you received and highlight how you edited your MCS in response to recommendations. If you disagreed with elements of the peer review, you must respectfully discuss your viewpoint in this letter.

### Peer Review Assignment Questions

Enter brief (<200 word) responses to each question below for the molecular case study (MCS) you have been assigned. Type your general comments for the author here and electronically track shorter comments or brief recommendations on the paper itself. Both items will be turned in as evidence of your review. Save this document in a manner that your name is not included (to keep the peer review confidential).

MCS being reviewed (title, author):

#### The Basics

Check that the length, font, margin, and other basic requirements are met; comment on any issues of structure/formatting. Also note if there are issues with grammar or spelling.

Discuss the title. Does it succinctly convey the main focus of the case study without giving too much away?

Comment on the quality of the stated learning objectives.

-Are they stated clearly and succinctly?

-Do they represent a variety of levels in Bloom's Taxonomy?

How well do the assigned questions align with the stated learning objectives?

Does the storyline serve first and foremost to support the experimental question? Is sufficient introduction provided to help you understand the experimental question?

Look at all of the headings. Are they specific, descriptive, succinct, and logical? Provide examples here for improvement.

Look up a paper in the journal *Cell*, and look specifically at the citation style at the end of it. Now look at the paper. Are there issues of formatting (indentations, spacing), capitalization, or other inconsistencies of style, either in the citation section or in the in-text citations?

### **The Writing**

Does this MCS sustain a single coherent point of view throughout? Why or why not?

How could the readability, clarity, or style of this MCS be improved? Comment briefly here on themes you noticed, but also provide extensive editorial notes on the paper directly as needed.

Provide one example of a section where the author's writing is far too "fluffy". Quote the section here, and on the paper, make extensive marks on how to condense or cut the writing into a more technical form without losing the meaning or content.

Identify all of the following: colloquialisms, informality, clichés, redundancy, and wordiness. Words to avoid include reference to "research," "researchers," "scientist," "studies have shown..." etc. Give a few examples of these problems in the box below.

### **The Scientific Content**

Rate and discuss the strength of this MCS's experimental question and hypotheses explored. Comment on how the authors explore both the function of the wild type protein and altered function (mutation, ligand binding, etc.) Consider language, originality/creativity, scientific legitimacy/logic, justification, and placement within the storyline.

Does each part of the MCS logically progress from the former ones, or are there transitional leaps that are confusing?

Does the logic of this paper's experimental approach [choice of what to look for in the PDB structure and other bioinformatic technique(s)] ever read as incomplete or unsupported? Where? What might be done to correct this?

How smoothly does this MCS integrate specific data from primary literature into its storyline? Does it clearly illustrate connections between the evidence it cites and the ideas they support? Explain.

### **Unique Elements of an MCS**

Discuss the quality, use, creativity, and complexity of the figure(s) and legend(s). Is there any place that would have benefitted from an additional figure or table?

Try to answer the questions provided in the case study. Do you agree with the authors' key and is it complete? Are the questions clearly meeting the objectives stated, or do they feel like random questions? Do the questions being asked lead you forward in the storyline, or are they just latent observations?

Did the author correctly and clearly explain biochemical approaches where appropriate (not gratuitously)? Name at least one spot where the author should better describe the experimental approach taken.

Work through the molecular visualization part of the MCS. Were you able to obtain images of the structure as you believe the authors intended? Were the instructions clear? Explain.

Who do you see as the target audience for this molecular case study? Could it be completed by first-semester biology students? 300-level biochemists? Advanced students? Explain.

Does the additional assessment assignment logically connect to the initial MCS and assess skills a student should be learning in the course of completing the MCS? Explain.