**Writing a Molecular Case Study Project**

**Overall project goal:** Make a clear link between the structure and function of a protein that plays a critical role in your research project.

**How does this project fit in with advanced biochemistry curricular objectives?**

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.

3. Study examples of how similar biochemical principles are applied to solve a diverse set of biochemical challenges.

## *Steps of the Project:*

1. **Select your protein of interest**
* Select a protein or proteins of relevance to your independent research project.
* Perform preliminary searches in the Protein Data Bank (PDB) to determine deposited structures for the identified proteins
	+ Pay close attention to the organism of origin and the coverage of the structure
	+ Choose one of the proteins to build your case study
1. **Introduction to examples of molecular case studies**

We will work through “The Happy Blue Baby” and the “MCS Cycle” papers together as a way of reviewing how we look at 3D protein structures and as an introduction to how MCS are written/structured.

1. **Building and Refining the Case**

## Minimal Components of each case:

1. **Hook:** A storyline delivered in a non-scientific language and aimed to capture the interest of the audience. This hook, which can be in the form of a short audio, video, or written piece, will constitute the introduction to the case and convey the scientific question to be addressed in the study. Reflect upon who your audience is and what message you would like them to have after completing this case study.
2. **Protein function and altered function:** A 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. 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.
3. **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. 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.

***For parts B & C consider:***
* 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?
1. **Literature and/or data supporting structure-function relationship:** A minimal number of additional experimental support for the claimed link between the structure and function of the central protein.

**Recommendations on how to build in the elements of the case study:**

**Write your learning objectives for the whole study.** Your learning objectives should be appropriate for the specific audience you are targeting. Each section of your case should have 2-3 learning objectives that tie to one main overall learning goal for the case. Learning objectives should be matched to existing standards for the course 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>

**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?

C*onsider:*

* 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 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 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?
1. **Explore non-PDB bioinformatic resources** to supplement your story line. Consider resources that look both at DNA/RNA sequences and protein sequences/structures: NCBI, Genbank, UniProt, JPred, Pfam, KEGG, CLUSTALW, etc.

*Consider:*

* What can be learned quickly/easily from the 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?

**List the bioinformatic tools or literature data** 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.

1. **Decide the number of sections your case study will have.** Each case study should include at least four sections: an introduction, a conclusion, a section focused on describing the regular structure/function relationship, and a section focused on describing the altered structure-function relationship.
2. **Write your creative “hook” or story line**.

*Consider:*

* 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?
1. **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?
1. **Write your assessments (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 interpreting 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, answering 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?
1. **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.
2. **Write one additional question** that relates to the case study but requires a student to apply their new knowledge 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 after the case study you wrote.
3. **Format your Literature Cited** section at the end.
* If referencing specific data or images, use the style of Cell.
* A rigorously researched case study will include 5-10 citations, most of which are primary research literature.