Advanced Topics in Modern Biology BISP194
Protein Folding and Human Diseases

Winter Quarter 2021
Monday 1:00-2:20 pm
Zoom: https://ucsd.zoom.us/j/98750190668; Meeting ID: 987 5019 0668

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Office Hours: Thursday 4:00-4:50 pm

Goals: In this class, we will read and discuss research papers together that have brought breakthrough discoveries in our understanding of human diseases, with the goal of learning how to read research papers effectively. For each paper, we will discuss how most research papers are structured, how to identify common pit holes, how to read/analyze the data in a paper independent of the authors' arguments, and how to identify new conclusions and contributions in light of our current understanding of the specific diseases caused by misfolding proteins.

Logistics: Students will be asked to read a different research paper each week before coming to class so that everybody can participate in the discussion. Papers will be posted one week ahead of time. Note that some papers may be relatively old, but are considered very important papers as they changed the course of our thinking.

In addition, each student will be assigned to a specific paper as a part of a small group (3 or 4 people) to present to the class.

During the first class on January 4, 2021, we will discuss some details, but briefly, a paper to discuss will be posted on Canvas a week ahead of the presentation. I will post a list of the presenting groups after the first lecture on Jan 4, 2021. Please make sure that you appear in one of the groups, and take note of the date of your presentation.

IMPORTANT: When you are not presenting, you are still required to read the paper and participate in questions and discussion during the class presentation by your fellow students.

Grading Policy:

No midterm and no final exams.

Attendance of each lecture will count as 5% (5% x 8 lectures= 40% total).

Grades will be determined by (1) attendance (40%), (2) participation in discussion including asking questions each week (30%), and (3) presentation (30%).

A: 90% or higher
B: 70-89%
C: 50-69%

Course Objectives: Revealing the sequence of the entire human genome brought excitement in the fields of molecular and cellular biology, medicine, pharmacology, and biotechnology. Rapid advances in technologies and methods also opened possibilities for researchers to undertake previously regarded difficult or impossible questions. Furthermore, there has been an increase in public interest and funding directed towards finding the causes and cures of human diseases and developing more effective diagnoses. Among the areas that have experienced rapid growth are human diseases that are caused by mis-regulation and accumulation of misfolded proteins or by the failure of protein handling in the cell. In this class, we will read and discuss papers that have brought breakthrough discoveries or paradigm shifts in our understanding of human diseases.

Proteins are by far the most abundant class of macromolecules in cells (approximately 50% of dry mass) and are involved in nearly all aspects of cell structure and physiology. Proteins are assembled from a set of 20 different amino acids, each linked to its neighbor through a chemical “peptide” bond. Initially, proteins are translated as linear polypeptide chains. To perform their intended functions, these chains must first fold into precise three-dimensional configurations. The process of protein folding requires assistance from proteins collectively referred to as the “protein folding machinery” and molecular chaperonin. The critical nature of protein folding capacity is underscored by the many different types of human diseases caused by mis-regulation of protein folding events, including cystic fibrosis, type 2 diabetes, and Alzheimer’s disease.

How to prepare for a presentation:

1. **Important technical information:**

Using PowerPoint is a good way to put together materials for making a presentation, although you do not necessarily have to use PowerPoint. The classroom (YORK 3010) is equipped to handle an overhead projector.

If your group decides to give a PowerPoint presentation, please bring a laptop. Mac users will need to bring an adaptor for the projector. Note that different Macs use different adaptors.

2. **Preparation for presentation:**

   A. PLEASE read the entire paper and discuss how to divide up the presentation.

   Normally, it makes sense to divide the result section by figures. For instance, if the paper has six figures, each student can present the results described in two figures. In addition, divide the introduction, discussion, and future directions among the members. Please see #4 (below) for more specific instructions.

   B. I hold office hours every Thursday at 4:00 pm. I would like to meet with **all the members** of the presenting group via zoom (I will send out a zoom link) to go over any questions you might have on the paper.

   Even if you do not have any questions, I would still like to meet with you to discuss the content of the paper in a smaller group setting. I can also talk to you about what makes a good presentation in general and give specific advice for the assigned paper. After graduating from UCSD, almost all of you will have some opportunities to make presentations to wide ranges of audiences. The ability to communicate science effectively is extremely important.

3. **Evaluation**: The ability to give constructive criticism is also a very important skill for everybody. Therefore, after each presentation, non-presenting students in the class will be asked to write a short paragraph or two on the presentation, specifically focusing on (1) what was good and (2) what would have improved the presentation. I will also discuss this in detail during the first lecture.

4. **What to present**

   a. Brief overview-------What is the point of the paper? Why is the question/topic important? What are the overall conclusions?

b. Introduction----------(1) What was known prior to the study described in the paper? (This is generally considered the background of the study)

(2) What is the specific question (or questions) addressed in the paper? Discuss the background information on the specific biological process (or mechanism).

For example, let's say that the paper discusses the discovery that a loss-of-function mutation of a new translation elongation factor causes a specific human disease phenotype. I would expect you to discuss:

(i) the specific disease,
(ii) the overall mechanism (or steps) of translation (with a focus on elongation steps).
(iii) what motivated the authors to set up the experiments that resulted in the discovery of the link between a new elongation factor and human disease?
(iv) What was the authors' question(s)? Why is this question(s) important?
(v) What were the approaches used?

c. Results section------- Discuss the results of the experiments described in each figure. If there are multiple panels, discuss each individually. I will discuss this in detail during the 1st (01/04/2021) lecture.

Important points to consider for each figure panel:

*What did the authors want to demonstrate?
*What was the experimental method?
*What were the results (which band(s) on the gel or which signals in the microscope picture demonstrate their conclusion?)
*What was the conclusion(s) drawn from each panel?
*Do you agree with their conclusion? –(Is the data convincingly clear? Can you see the same changes (or no change) that the authors claim?)
*Is there other experimental method to demonstrate the same issue? If so, why may one be better than the other?

d. Discussion and future directions----------
*What were the overall conclusion(s) drawn from the paper?

*Do you agree with the authors conclusions overall? Why?

*What future questions need to be addressed?
*Is there anything missing from the paper?