CHEM 761

Advanced Topics in Biochemistry

Goals:

Up until this point, you have learned many of the basic pathways and concepts that are relevant to the cellular metabolism of all species. These include the utilization of carbohydrates and fatty acids for energy, the storage of energy in carbohydrates and fatty acids, the metabolism of amino acids, the structure and role of proteins, the biosynthesis of lipids and biological membranes, and some very basic aspects of the coordination of these activities. Depending on the other courses you have taken, you may have learned some aspects of genetics and the storage of protein sequence information in the DNA sequence of every organism.

The goals of this course are two-fold. The first goal is to cover several topics not covered in BIOL 402: Principles of Biochemistry, including:

1. **DNA and RNA.** The structure, chemistry, and function of nucleic acids.
2. **DNA Replication and DNA Repair.** Maintaining the fidelity of the DNA sequence and passing this sequence on to future generations is central to sustained life.
3. **DNA Transcription and the many uses of RNA.** DNA sequence is converted to RNA, which codes for various proteins, but can also have many other purposes within the cell.
4. **RNA Translation and Protein Synthesis.** Ribosomes are huge RNA-based enzymes that are capable of reading the RNA sequence and generating proteins with very specific amino acid sequences.
5. **Regulation of Gene Expression.** Gene expression can be regulated at many different levels and by many different methods, including direct control through protein binding to DNA or RNA, and indirect control (epigenetics) through chemical modification of nucleic acids or proteins bound to DNA. There are also examples of gene regulation at the RNA level.
6. **Regulation of Enzyme Function.** Enzyme activity can be regulated directly, either through binding of various biomolecules or proteins, or through chemical modification, especially phosphorylation of specific amino acid side-chains.
7. **Hormones and Control of Mammalian Pathways.** In organisms that have multiple organs and tissues, the function of these tissues must be coordinated to benefit the organism. The primary method of control is through the release, binding, and exerted action of various types of hormones and neurotransmitters.

The goal of this course is to introduce you to how scientists advance the field of biochemistry through incremental improvements in our knowledge of very specific topics. We don't just wake up one day with a fully formed understanding of how an enzyme or pathway works. Based on prior studies and theories, we formulate various hypotheses, decide which ones are worth testing, and devise various types of experiments that can hopefully unambiguously prove or disprove a hypothesis. In this section, you will pick an area of science you find most interesting, study the literature to arrive at some understanding of the current state of knowledge, and prepare a written proposal that will organize your hypotheses and hypothetical experimental plans. This will be written in the style of an NSF grant proposal.

Throughout this course, I want you to start moving beyond the information in textbooks. Most textbooks are at least 10 years out-of-date and many contain factual errors. You are quickly reaching the point where most of what you learn will not come from textbooks. Where does the information in textbooks come from? I want you to start asking the questions: "How do they know that the system works like that?" "What types of experiments could they have used to demonstrate it works like that?" "Is it possible that there is another way to explain all of the observations?"

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Lectures
Tues & Thurs
10:30 – 11:45 am
Bilger 341c

Office Hours
Mon
9:30 am – 11:00 am
(or email for an appt)

Text: **Lehninger: Principles of Biochemistry, 6th Edition**
Authors: Daniel L. Nelson and Michael M. Cox
Publisher: W.H. Freeman & Co., New York, NY
We are using this textbook because it was already used for BIOL 402. Much of the information content is excellent, but the images are not particularly interesting. We will jump around and cover roughly 9 chapters in this book.

Additional material for slides may be taken from **Biochemistry**, 4th edition, by Voet and Voet, and **Fundamentals of Biochemistry**, 3rd edition, by Voet, Voet, and Pratt, both from Wiley. These books are available used on Amazon.com for about $40 and are much better textbooks in terms of the chemical explanations.

Lectures:
- The class will be divided into 8 sections with ~4 lectures per section.
- Most lectures will be based on the textbook.
- Where possible, I will also hand out journal articles and we will begin to spend some class time examining these articles so we can begin to understand how scientists arrive at the information that eventually ends up in textbooks.

Homework, Quizzes & Exams:
- Reading assignments will be given prior to each lecture.
- Online multiple choice quizzes are available at http://bcs.whfreeman.com/lehninger6e/. These are optional and will not be graded, but might help you check how much you remember from the reading.
- For each chapter, there will be a short quiz. Typically the quiz will be short answer questions that will take ~15-20 min.
- There will be 2 midterm exams and the ACS Biochemistry exam.

Writing Assignments:
- This course is a designated upper-division writing intensive (WI) course. **Students must adequately complete all writing assignments to pass the course with a D grade or better. Students who do not complete all writing assignments will get a D- or an F and will not earn W Focus credit.**
- Students will prepare an NSF style research proposal based upon an independent research idea. This idea can be based on a journal article or the work of a specific scientist, but should be a new idea or concept that extends the current published work. The final proposal must be at least 12 pages, including figures and references (12 pt font, 1.5 line spacing)
- Draft versions of each component of the proposal will be turned in or uploaded to Laulima with specific due dates.
- Feedback on content and writing style will be provided:
  - project summary (abstract) and specific aims – email feedback from the instructor
  - intro and background – peer review from another student
  - experimental design – in-class writing workshops studying successful proposals from UH faculty
- The final version of the proposal will be due in class on the last day of the semester.

Student-Led Journal Presentations: You will need to pick a topic from weeks 3 – 14 and lead a 30 min discussion of a journal article of my choosing. If you have a particular topic you would like to claim, let me know and I will put you down for that topic and date.

Grading:

- Quizzes worth 20% total.
- Two midterm exams each worth 20% of the final grade.
- Presentation worth 10% of the final grade.
- Research proposal worth 30% of the final grade.
  - -Hypothesis & Abstract (draft), 5%
  - -Specific Aims (draft), 5%
  - -Intro and background (draft) for peer review (at least 5 pages), 5%
  - -Final version, 15%
- The finished version of the proposal will serve as your final project and will be due on the last day of class. There will be NO final exam.

Student Learning Outcomes:

- Students will understand the chemical principles that underlie DNA replication and transcription, and RNA translation and protein synthesis.
- Students will understand the interplay between methods for regulating networks of biochemical reactions, including genetic regulation, hormones and signal transduction, and protein activation and inhibition.
- Students will understand how biochemical reactions can be described at an atomic level, including how enzyme catalysts and cofactors can accelerate difficult reactions.
- Students will use literature search processes to gain knowledge of recent advances in biochemistry, develop a hypothesis-driven research proposal, and will write an NSF-style grant proposal.

Week #	Date	Topic	Reading
1	1/12	Nucleic acid structure and chemistry.	L: Ch 8 VVP: Ch 3, 24
2	1/17	Chromosome structure in prokaryotes and eukaryotes.	L: Ch 24 VVP: Ch 24
	1/19	Prokaryotic DNA replication. Journal Article	L: Ch 25 VVP: Ch 3, 25
3	1/24	Eukaryotic DNA replication. DNA repair mechanisms.	L: Ch 25 VVP: Ch 25
	1/26	More on repair & recombination. Journal Article	L: Ch 25 VVP: Ch 25
4	1/31	Selected methods for manipulating DNA in the laboratory	L: Ch 9 VVP: Ch 3, 24, 25, handouts
	2/2	*In vivo* DNA editing methods Journal Article	Handouts
5	2/7	Proposal development: Where do you get a new idea? Generating a hypothesis.	Hypothesis due 2/9
	2/9	Proposal development: Abstract and Specific Aims.	Draft abstract due 2/14
6	2/14	DNA transcription/RNA Polymerase Retroviral RNA synthesis	L: Ch 26 VVP: Ch 26
	2/16	Eukaryotic DNA transcription Journal Article	L: Ch 26 VVP: Ch 26
7	2/21	RNA translation/protein synthesis	L: Ch 27 VVP: Ch 27
	2/23	Protein degradation Journal Article	L: Ch 27 Handouts
8	2/28	**EXAM 1** – All material covered in weeks 1-4,6,7	L: Ch. 8, 24-27 (selected sections)
	3/2	Proposal development: Specific aims or objectives	Draft specific aims due 3/7
9	3/7	Proposal development: Developing a detailed outline.	
	3/9	Regulation of gene expression Journal Article	L: Ch 28 VVP: Ch 28
10	3/14	More regulation of gene expression, epigenetics	L: Ch 28 and Handouts
	3/16	Eukaryotic epigenetic mechanisms Journal Article	L: Ch 28 and Handouts
10	3/21	T.B.D.	
	3/23	**American Chemical Society Biochemistry Assessment Exam**	No need to study. Do your best with what you've already learned at UH.
	3/27-3/31	Spring Break	

Week #	Date	Topic	Reading
12	4/4	Proposal development: introduction, background, and preliminary results.	
	4/6	Regulation of enzyme function: cooperativity and allostery	L: Ch 5 & 6 VVP: Ch 12
13	4/11	Regulation of enzyme function: kinases, phosphatases. Journal Article	L: Ch 6 & 15 VVP: Ch 12
	4/13	Signal transduction pathways	L: Ch 12 VVP: Ch 13
14	4/18	Hormones and neurotransmitters Journal Article	L: Ch 15 VVP: Ch 13, 22
	4/20	**EXAM 2** – All material covered in weeks 9-14	L: Ch. 5, 6, 12, 15, 28 (selected sections)
15	4/25	Proposal development: describing experimental proposals.	Turn in a draft for peer comments
	4/27	Proposal development: the importance of backup plans and alternative methods	Return your comments
16	5/2	**Final proposals due** End of semester celebration: free lunch on me.	Turn in your final proposal