

Welcome to Biochemistry! You are embarking on a semester's study of what is, in my humble opinion, the most fascinating material in the intellectual world -- the molecular analysis of life as we know it on earth. This course will touch on many topics that you've visited before, but we are likely to be looking at these familiar issues in new ways, and I hope that you will be delighted to see how many nuggets of knowledge from earlier coursework fit together in the new analyses you'll be undertaking this term.

I have designed this course, but I strive to create an environment where you will be sufficiently comfortable and sufficiently excited that you will really make this YOUR course, rather than mine. What you are holding in your hands is what I call my "syllabook" -- it is a (lengthy) description of the philosophy motivating my design of this course as well as the usual course logistics and scheduling details. It is my sincere hope that it should help you

- get a sense for how I have structured the class
- begin to formulate questions about the course and about Biochemistry
- prepare yourself for what I hope will be an exciting and challenging exploration of the Chemistry of Life.

What I want to achieve in this course this semester:

- What we term "biochemistry" includes a huge -- HUGE -- realm of knowledge. I expressly do NOT hope to teach you all of it. Rather, I hope to introduce you to a selection of topics in biochemistry, and through these topics, to a set of analytical approaches for probing the molecular underpinnings of life. It is my intent that by mastering these analytical tools that you will be prepared to master the many domains of biochemical topics that we won't have time to explore this term.
- My main "content" goal for this course is to guide you to a deep-seated understanding of the relationships between molecular structure and biological function for the major classes of biological macromolecules. By the end of this course, you should have begun to develop the ability to *predict* the change in function that might accompany a particular change in structure of a molecule that you have never seen before. To approach this goal, I intend to introduce you to lots of examples of biologically-important macromolecules, with many of these 'molecular case studies' drawn from the primary research literature.
- My main "process" goal for this course is to motivate your desire for more sophisticated ways of thinking about biochemical data and biochemical systems. This objective will also lead us into the research literature, and involve the use of 'professional-grade' tools for laboratory analysis, molecular modeling, and data analysis. The goal of stimulating your curiosity and your hunger for more sophisticated knowledge underlies much of the format of this course, and is the greatest goal (in my opinion) that any educator can strive for. I hope that we can achieve it together.

Who I am and how to get in touch with me:

Instructor: Peter Kuhlman

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Office hours: To optimize our opportunities to meet outside of class hours to discuss any questions or difficulties you are having, I don't have regular "office hours", but instead set up individual or group appointments. I will make every effort to ensure that you and I can find a time to meet outside of class hours to discuss any topics that are of concern to you. *I will be available for at least 3 hours of appointments each week*, as long as they are scheduled by the end of the preceding week.

Course resources:

- Texts: *Biochemistry, Sixth Edition*, Berg/Tymoczko/Stryer (2006).
A laboratory manual will be handed out on the first day of lab (free of cost to you).
- Problem sets: A variety of sample problems will be available to you in order to help you review, deepen your understanding, and prepare for tests. The first installment is online at http://personal.denison.edu/~kuhlman/courses/biochem/samples/sample_probs.html
- Study session: I will hold an extra one-hour session each week to provide interested students an opportunity to spend more time in explanation, review, and application of material that we've covered in class and lab. The time of this session will be decided during week 2.

How we'll achieve the course goals:

Research into how humans learn suggests that education is most effective if we encounter a new concept or skill in several different ways, followed by the opportunity to practise it and then to apply it to new situations. I have tried to embrace this theory in my design of this course. For most topics, you'll have the opportunity to read about them, to hear me talk about them, to think about them on your own and in class, to answer questions on them, to apply them both in your mind and with your hands, and then to try them out in novel situations. In order to give you multiple ways to explore new concepts, I will structure some of our class meetings differently than a conventional lecture. And because it is my fundamental assumption that I am here as your *partner* in learning, I invite you to join me in taking responsibility for your education. For instance, I expect that you, as an experienced student at Denison, have learned to read textbooks in a sophisticated fashion, and I will therefore typically NOT simply re-cover the material in your text. Rather, I expect you to come to class each day prepared to actively engage the material, and I will intentionally spend much of our class time in ways that I feel *complement* the text rather than reiterate it. I will be disappointed if you have not spent enough time outside of class with your text and notes in order to understand and be able to contribute to the class conversation. To help focus your reading and thinking, I will often provide comments and questions to follow up on the day's class and prepare for the next session.

I will structure our class time in ways intended to help you review, reinforce, and synthesize the material in the text. I will do some lecturing, we will do some (both large and small) group discussions, and I will at times ask probing questions. There will be opportunities over the course of the term for you to practice making observations and reaching conclusions on the basis of those observations. In keeping with my goals for this course, there will be many times when I will ask you to make predictions of the behavior of biochemical systems on the basis of what you have already learned. Throughout, I will be looking more for evidence that you are trying to learn and to think than for evidence that you have the "right" answers. I will ask questions *not* to be cruel or "tough", but rather because I believe it is my job to help you *learn to learn* and *learn to think critically*. That said, please note that although I will endeavor to structure this class to maximize your benefit from it, I recognize that I am fallible (!) and that we don't all learn in the same ways, so I strongly encourage you to share your feelings about the class with me as we go along!

This class format is most effective when every member of the class is engaged. If class members either dominate, distract from, or withdraw from the class, we are all likely to learn less. I will therefore base part of your grade on my evaluation of your contribution to the class discourse. That doesn't mean that you have to say a lot in class, or that every comment or answer you give has to be "right". On the contrary, we often learn much more from our mistaken answers than from our correct ones. Accordingly, I will note only whether your comments and answers indicate (a) that you are coming to class prepared and (b) that you are thinking. Of course, this also means that you must generally be present in class (and you must arrive on time), for if you aren't there, it will be difficult for you to contribute to the class and to show me that you're exploring and thinking.

More specifically, if you *must* be absent from any laboratory or exam day, please see me beforehand if at all possible, and in any case be prepared to rigorously justify your absence (with supporting documentation from, for example, Student Health or the Academic Support office). Absence on a test date will result in a score of zero for that test if you have not *previously* made an arrangement

with me to take the test at another time. You're responsible for all class material whether you're present at all class meetings or not, so be sure to make arrangements with me and with your classmates to obtain the information that we covered in class on any days that you are not present.

In order to extend your classroom learning experiences, to give you exposure to useful tools and techniques, and to give you a sense for what sorts of questions I am apt to put on the tests before you sit down to take them, I will occasionally recommend problems from the textbook or give you challenge questions. In addition, I have compiled a long list of questions to stimulate your studying and reflecting. These are available online at the URL listed above under "Course Resources".

I will strive to keep the format and content of this class flexible so that I can respond to your needs and interests as we go through the semester. Consequently, you should view the course calendar and even the grading scheme as approximations of the final outcomes at the end of the course. I agree with past students that this flexibility enhances my ability to make this Biochemistry course *your* Biochemistry course. I also realize, however, that this very flexibility can be unsettling, and I will therefore also strive to make it very clear what my view of the class structure and priorities are. Furthermore, in order to make changes to the course on the fly, we need to be in ready communication, and so I ask that you make it a habit to *check your e-mail daily* in case we need to be in touch about class-related matters.

Several of the assignments for this course involve writing. In science, as in nearly all aspects of professional and personal life, clear and effective communication skills are a tremendous asset. I encourage each of you to take advantage of the campus Writing Center to improve your written communication skills. Although there is a widespread perception that writing in the sciences is somehow "different" from writing in other disciplines, I regard that as a myth. Styles certainly differ between fields, but the fundamentals of good communication are nearly universal. The Center is a free resource available to all Denison students. Student writing consultants from many majors help writers one-on-one in all phases of the writing process, from deciphering the assignment, to discussing ideas, to developing an argument, to finalizing a draft. Because proofreading is a last step in that process, writers should leave plenty of time for getting their ideas right before expecting proofreading help. Consultants also can help writers with personal documents, like job and internship applications. The Center is located on the fourth floor of Barney-Davis Hall; satellite locations are on the third floor of the Library (the Main level) and the first floor of Fellows near the Computer Lab. Appointments between 4 p.m. and 9 p.m., Sunday through Thursday, can be made in the Barney location by phoning 587-JOT1. The satellite locations are drop-in; check the website at <http://www.denison.edu/writingctr/> for those hours.

Finally, I think that it is important for you to learn how to decide which of the many, many bits of information that you encounter in this class are more important and which are less important. Similarly, I want to encourage you to reflect on which aspects of the material *I* think are important and am apt to stress on exams. To stimulate these kinds of higher-order learning, I'll give you one extra point for every exam question that you predict I will ask. Of course, I don't expect you to come up with the exact questions, but with some work I think that you'll be able to predict the *types* of questions I'll ask. I will accept up to four of these sample questions for each exam. In order to receive credit for your submissions, you must send me *sample questions and correct answers in plain (unformatted) text by email before the test is administered*. I'll tell you more about this in class.

Building on your previous knowledge

This course has an uncommonly long list of prerequisite courses: 2 semesters of General Chemistry, 2 semesters of Organic Chemistry, and one semester of Cellular and Molecular Biology. And we really will build explicitly and implicitly on material from all of those courses. To underscore the importance of those prerequisites and to ensure that you learned material from those courses that is fundamental to this one, *you will be required to pass a Fundamentals Test in order to pass this course*. Your score on the Fundamentals Test will not be reflected in your final course grade, and the test will be offered

weekly for eight weeks so that you have ample opportunity to solidify your knowledge and demonstrate to me that you have mastered the fundamental concepts you will need to build on in this course. The second-to-last page of this Syllabook provides a list of the concept areas you will be responsible for.

Laboratory participation:

The laboratory component of this course is an integral part of it. This is reflected in its large numerical weight in the overall grade scheme of the course. To pass this course, you **MUST** complete all assigned laboratory work. Period. As noted above, you'll receive the laboratory manual on the first day of lab.

Learning from your mistakes

I believe very firmly that learning is an iterative process; very few of us get things exactly right the first time through, and there is often a great opportunity for learning in repeating an assignment after receiving feedback on it. This philosophy underlies much of my approach to grading and point values for assignments in this class. I want you to feel that you can learn and benefit from your mistakes, that you will be rewarded for getting it right the second time around. Accordingly, if you ever want to revise an assignment and submit it for reconsideration, you are welcome to come and discuss that with me. And for *any* assignment on which you receive a grade of 50% or less, you are strongly encouraged to revise and submit the assignment for regrading.

In the same vein, if you receive any assignment back on which any part of one of your answers has been marked in orange highlighter, you should interpret this as an invitation to revise your answer and submit it for regrading. Typically this will indicate that I had trouble understanding the logic behind your answer, or felt that you answered a different question from the one I asked. In any event, this indicates that I think you have a better grasp on the material than your answer shows, and I'd like to give you another chance to demonstrate your mastery.

In any resubmission situation, please

- ensure that you include the original graded version of the assignment so that I can compare my original comments with your revised version. Resubmissions that are not accompanied by the original version will not be regraded. I strongly encourage you to make a copy of your original assignment before giving it back to me, so that you can study from it. Resubmissions get the lowest priority on my grading to-do list, and I won't guarantee getting them back to you before the end of finals week.
- ensure that you carefully address the deficiencies of the original. I try to put care and time into the comments on your assignments when I hand them back, with the intent that my comments will help you think more carefully about your work. Revised versions that come back to me with the original problems un-addressed are likely to receive a less-than-generous review. If you have any questions about my comments, by all means come to talk with me about them *before* making your revisions.
- be aware that I grade at least as stringently on revisions as on the originals -- on the revision, I assume that you understand my expectations, so I am less likely to give you the benefit of the doubt when your intent or procedure is not clear from your work.
- understand that your final grade for the assignment will be the average of your original and revised grades. With a substantial improvement over the original assignment, this can make a very meaningful difference in your overall grade.

Special Needs

Different students come to this class with different training, different backgrounds, and different abilities. If you feel that because of personal factors you would benefit from some modification of course procedures, such as special test-taking arrangements, I ask that you contact me privately *at your earliest convenience*. I will work with you and with the Academic Support and Enrichment Center (Doane Hall, room 104) to optimize your learning experience. Certain accommodations will require verification of disability based on documentation on file in the Academic Support office.

Academic honesty

My fundamental assumption about this class is that you are here to learn. All feedback that I provide you, all learning opportunities that I set up, are predicated on that assumption. For you to effectively learn, and for me to effectively advise you on your learning, you must be honest with me and with yourself about what you do and do not know. If the atmosphere of trust and learning that I try to create in this class is compromised by individuals behaving in an academically dishonest manner -- for instance, passing off someone else's work as their own -- I will be deeply disappointed and quite upset. Academic dishonesty is tantamount to intellectual theft. This standard applies to all work ranging from simple lab assignments to the final exam. I recommend that you carefully read the Denison University Academic Dishonesty Policy as printed in the student handbook, and the Denison handbook entitled "Writing With Sources". Neither ignorance nor carelessness is an acceptable defense in cases of plagiarism.

The grade penalty associated with a confirmed case of dishonesty will ordinarily be a score of zero for that assignment. Furthermore, all instructors must refer every act of academic dishonesty to the Associate Provost, and violations may result in failure in the course, suspension, or expulsion.

How will your learning be assessed?

As I currently envision the course (and subject to feedback from you), there will be four types of opportunities (in addition to class discussions) for you to demonstrate to me your mastery of biochemical concepts -- tests, the laboratory exercises, a written Protein Profile report, and a final exam:

Laboratory		225 points (details in lab manual)
Subjective evaluation of intellectual engagement and contribution to the class		50 points
Hour-long tests	4 x 50 pts =	200 points (5 tests; best 4 count toward final grade)
Protein Profile		50
Final exam (including a take-home portion)		<u>250 points</u>
	TOTAL	825 points

Please note:

- The five hour exams only account for 24% of your grade in this course, and the final exam for 30%. I've done this for three reasons. **First**, it makes each in-class exam significantly shorter; I want to test how well you understand the material, not how quickly you can write. **Second**, it allows you to learn from your mistakes -- you can do poorly on a test, but if you learn what you did wrong and you address your deficiencies, then you will have the chance to score well on the final and come out of the class with a grade that reflects *what you learned in the end*. **Third**, this scoring system reflects my belief that what you know at the end of the semester is really important -- I don't want to reward you for cramming for one test and then immediately forgetting the material. Rather, I want to reward you for truly learning the material and for integrating each new topic into your mental picture of how the world works.
- Grades will be assigned *roughly* according to the scale below. Note that I may change the scale so that it more accurately reflects what I feel to be the performance of members of the class. For instance, if everyone does poorly on the tests and if I conclude that it is because I did something wrong, then I will likely adjust all grades upward from the following distribution. On the other hand, if I think that the tests are sufficiently challenging but everyone does very well and is earning "A" marks, then I will be pleased as punch and am *unlikely* to change the scale. For the most part, you may consider these to be the most demanding standards that I am apt to apply.

90% and up	flavors of A
80 to 89%	flavors of B
70 to 79%	flavors of C
60 to 66%	flavors of D
below 60%	F

- Finally, I wish to make clear my interpretation of letter grades.
I view an "F" as a strong indication that the level of preparation and/or commitment brought to the class by a student are incompatible with the goals of this course. I hope not to give your class any "F"s.
I view a "D" as an indication that a student is passing the class, but performing well below my standards and failing to achieve a substantial portion of the course goals. Usually, this means that the student is performing well below her or his true abilities. I hope not to give your class any "D"s.
I view a "C" as notice that the student is doing only a fair job. Frequently, this means that the student is present but not fully motivated or engaged. A "C" student is doing adequately but probably came to the class with insufficient preparation and/or has not committed the personal resources to the class to learn most effectively.
I view a "B" as a very respectable grade. The student to whom I give a "B" may be trying very hard but still struggling with mastery of the material, or may be working less hard and stopping short of achieving excellence.
I view a "B+" as an indication that a student is doing a truly good job. This grade indicates to me that the student is expending significant care and effort to ensure that s/he is learning the material.
I view an "A-" as a very good grade. I do not give this grade lightly or without evidence that a student is nearly approaching mastery of the material; this grade indicates that a student has met my expectations for the course.
I view an "A" as an indication of true excellence. In order to achieve an "A" in my course, a student must demonstrate to me that s/he has not only committed the necessary resources to master the material, but also that s/he is *aggressively engaging the questions that we explore*. This is a grade to be proud of, a grade to be earned by serious work and mental sharpness.

"Base Topics" for Biochemistry 302: concepts and techniques that we are *assuming* you are conversant with as you enter this class

General and organic chemical principles

- **fluency** with metric units of measurement and prefixes (pico-, nano-, micro-, milli-, centi-, kilo-)
- **fluency** with scientific notation
- stoichiometry (gram \leftrightarrow mole relationships)
- solution properties and solution stoichiometry (concentration, dilution, ionic strength)
- periodic trends in bonding and reactivity of non-metals
- types and magnitudes of intermolecular interactions/forces
- the structure of small molecules and the impact of structure on reactivity, intermolecular forces, etc.
- dynamic chemical equilibrium (Le Chatelier's principle, K_{eq})
- basic pH effects and calculations (K_a , K_b , K_w , the Henderson-Hasselbalch equation, buffers)
- the interaction of light with matter (i.e., spectroscopy; especially Beer's Law and standard curves)
- kinetics (reaction order, Arrhenius equation, catalysis, collision geometry)
- thermodynamics (reaction coordinate diagrams; S, H, G; relationship of kinetic properties to thermodynamic properties; relationship of thermodynamic properties to equilibrium constant and behavior)
- structure and reactivity of common organic functional groups
- organic reaction mechanisms and "electron pushing"
- identification of nucleophiles/electrophiles and rationalization of their chemical behavior
- stereochemistry

Molecular and cellular biology

- cellular organization of prokaryotes and eukaryotes
- intracellular transport
- cellular information organization (the "central dogma": DNA \rightarrow RNA \rightarrow protein; basic molecular players in these processes)
- basic elements of gene structure and mRNA structure
- basic aspects of molecular cloning
- general understanding of proteins (what are enzymes?, the link between structure and function)

Lab Techniques/Skills

- pH meter use
- stir/heat plate use
- balance use (top-load and analytical and *when to use each*)
- column chromatography -- basic principles
- electrophoresis (protein and DNA)
- micropipet use (if you have any questions about proper use of micropipetters, *please* ask in lab!)
- **basic solution preparation** (e.g., how would you make 1.00 L of a 0.3 M solution of NaCl?)
- spectrophotometer principles and use
- **statistical treatment of data (averages, standard deviations, confidence intervals for collections of numbers and for lines)**

Computer/Technology Skills

- basic use of Microsoft Word, Excel (including linear regression), and PowerPoint
- Web searching of data bases
- Web/online searching of literature sources
- E-mail use
- Network file sharing and information exchange

In addition, you will be expected to gain full familiarity (immediate recall) with the structures, names, one-letter-codes, and physicochemical properties of the 20 amino acids most commonly found in proteins. This information can be found in detail in chapter 2 of your text; it is summarized on the next page. This is an ideal focus for your first few days of the semester.

Name	one-letter ID	notable physicochemical properties
All of them	X	pK_A of the amino group is about 8 (an oversimplification, but...) pK_A of the carboxyl group is about 3
Alanine	A, as in A lanine	small; in many ways this is the generic amino acid is often interchangeable, biochemically and evolutionarily, with G, S, or T
Glycine	G, as in G lycine	very small; can fit in tight spots is often interchangeable, biochemically and evolutionarily, with A (and less often w/ S, T)
Proline	P, as in P roline	unusual and constrained cyclic backbone geometry
Serine	S, as in S erine	small and modestly hydrophilic -OH group is a target for some covalent modifications as we'll discuss later is often interchangeable, biochemically and evolutionarily, with A and T
Threonine	T, as in T hreonine	-OH group is a target for some covalent modifications is often interchangeable, biochemically and evolutionarily, with A and S
Cysteine	C, as in C ysteine	contains sulfur can form a (covalent) disulfide bond with another C is sometimes interchangeable, biochemically and evolutionarily, with S; less often with A, T
Valine	V, as in V aline	bulky and hydrophobic is often interchangeable, biochemically and evolutionarily, w/ I, L, M; less often w/ F, Y (&W)
Isoleucine	I, as in I soleucine	bulky and hydrophobic is often interchangeable, biochemically and evolutionarily, w/ V, L, M; less often w/ F, Y (&W)
Leucine	L, as in L eucine	bulky and hydrophobic is often interchangeable, biochemically and evolutionarily, w/ V, I, M; less often w/ F, Y (&W)
Methionine	M, as in M ethionine	contains sulfur bulky and hydrophobic is often interchangeable, biochemically and evolutionarily, w/ V, I, L; less often w/ F, Y (&W)
Phenylalanine	F, as in F enylalanine	bulky and hydrophobic weakly absorbs UV light around 280 nm (see Berg/Tymoczko/Stryer, page 46) is often interchangeable, biochemically and evolutionarily, with Y; less often with I, V, L, M, W
Tyrosine	Y, as in tY rosine	bulky and hydrophobic absorbs UV light around 280 nm (see Berg/Tymoczko/Stryer, figure 3.11) -OH group is a target for some covalent modifications is often interchangeable, biochemically and evolutionarily, with Y; less often with I, V, L, M, W
Tryptophan	W, as in tW ryptophan (just say it with a lisp!)	bulky and hydrophobic absorbs UV light around 280 nm (see Berg/Tymoczko/Stryer, figure 3.11) occurs only rarely, but is generally interchangeable, biochemically and evolutionarily, with F and Y
Asparagine	N, as in a sparagi N e	hydrophilic releases ammonia by amide hydrolysis when treated with strong acid is often interchangeable, biochemically and evolutionarily, w/ Q; sometimes with D, E
Glutamine	Q, as in Q tamine	hydrophilic releases ammonia by amide hydrolysis when treated with strong acid is often interchangeable, biochemically and evolutionarily, w/ N; sometimes with D, E
Aspartic acid	D, as in a spar D ic acid	acidic pK_A , about 4 negative charge at pH above pK_A is often interchangeable, biochemically and evolutionarily, w/ E; sometimes with N, Q
Glutamic acid	E, as in gluE -tamic acid	acidic pK_A , about 4 negative charge at pH above pK_A is often interchangeable, biochemically and evolutionarily, w/ D; sometimes with N, Q
Histidine	H, as in H istidine	acidic pK_A , about 6 neutral charge at pH above pK_A , positive charge at pH < pK_A
Lysine	K, as in the letter before L for lysine	basic pK_A , about 11 positive charge at pH < pK_A is often interchangeable, biochemically and evolutionarily, w/ R
Arginine	R, as in R ginine	basic pK_A , about 12.5 positive charge at pH < pK_A is often interchangeable, biochemically and evolutionarily, w/ K

Overall Course Calendar

Topical Outline	When we'll be there	Recommended chapters in B/T/S	Important dates and Assignments
I. The Basics			
A. Introduction to the context of biochemistry	week 1	1	
B. Introduction to the molecules	week 2	(4,11,12) 2.1, 2.2	
C. Introduction to protein analysis			<i>test #1, Fri 15 Sep</i>
i. proteins in their native habitat			
ii. protein architecture	week 3	2.3-2.5	
iii. how proteins interact with themselves and other molecules	week 4	2.6	
iv. protein purification and characterization	week 5	3	
v. testing hypotheses in protein biochemistry via the central dogma of molecular biology		5,6; this may largely be review for you	<i>test #2, Mon 2 Oct</i>
II. Towards a predictive understanding of protein architecture, function, and regulation			
A. Case studies in protein S/F			
i. hemoglobin	week 6/7	7	
ii. receptor proteins	week 7		
B. Thermodynamic and kinetic tools in protein analysis	week 8/9	8	<i>lab practical, Weds 18 Oct</i> <i>test #3, Weds 25 Oct</i>
C. Control of protein function by modification of protein structure			
i. allosteric inhibition/activation	week 9/10	9, 10.1, 10.2	
ii. selective proteolysis	week 10	10.4	
iii. covalent modification	week 11	10.3, 21.2-3	
iv. further case studies in enzyme action and control	week 12		<i>test #4, Fri 17 Nov</i> <i>Draft of Protein Profile due, 13-17 Nov</i>
III. Proteins in the wild			
Topics of your choosing (possibilities include Sensory systems, Metabolic systems, and Protein or Drug Design)	weeks 13/14/15	To Be Decided	<i>test #5, Weds 6 Dec</i> <i>lab poster presentations, Thu 7 Dec?</i> <i>final exam, Mon 11 Dec, 9:00 a.m.</i>