BIOCHEMISTRY 465 (BCHM 465, BIOCHEMISTRY III): BIOLOGICAL INFORMATION PROCESSING FALL, 2008: TU TH, 8:00-9:15 A.M., CHEMISTRY 1402

Assoc. Prof. Jason D. Kahn, Dept. of Chemistry and Biochemistry, Univ. Maryland, College Park
Teaching Assistant: Sarah Sucayan, graduate student in Chemistry and Biochemistry

Office hours: JDK: Mon. 2-3 p.m., Weds. 1-2 p.m., Chemistry 2500A (Biochemistry, Wing 5)
SS: Tues. 3-4 p.m., Thurs. 9:30-10:30 a.m., Chemistry 2510 (Biochemistry, Wing 5)

Contacting us: **jdkahn@umd.edu** much preferred to 301-405-0058. **ssucayan@umd.edu** much preferred to 301-405-1815. Please do not drop in to our offices or lab outside of office hours, but we will be happy to set up appointments if necessary.

Web and email: The course web site will be handled through ELMS (elms.umd.edu). There is also a wealth of material at http://www.biochem.umd.edu/biochem/kahn/teach_res.
You should already be subscribed to the e-mail reflector for the course. To email everyone on the list, send to bchm465-0101-fall08@coursemail.umd.edu. No spam!

Course Description

This course concerns the structure and function of nucleic acids and the mechanisms of nucleic acid transactions: a biochemical approach to molecular genetics. We will generally cover both prokaryotic and eukaryotic systems, emphasizing common logic and mechanisms. We will emphasize bioenergetics and fidelity. Topics are as follows:

- **Chemistry and structure of DNA and RNA, from nucleotides to chromosomes and genomes, and some methods for studying, synthesizing, sequencing and manipulating nucleic acids. Rudimentary bioinformatics and systems biology.**
- **Interactions between nucleic acids and ligands such as cations, drugs, and especially proteins. Principles, structures, experiments, and molecular visualization.**
- **DNA Biology: Selected aspects of the biochemistry and regulation of DNA replication, transcription, recombination, and repair, and how these processes interact with each other.**
- **RNA Biology: Regulation of gene expression by RNA, RNA processing, RNA catalysis, translation.**

Assignments, Procedures, and Grading

This course is primarily lecture-based. Required reading from the textbook or other sources will also be assigned for some lectures, as indicated on the Course Outline below. The reading can be done after the lecture, and study questions or problem set assignments will be provided. The textbook and other materials will be on reserve at the White Memorial Chemistry Library or otherwise provided to you.

There will be **two 80-minute exams (100 pts each), two problem sets (50 pts each), and a two hour final examination (200 pts)**. The problem sets will cover some of the bioinformatics methods used by practicing molecular biologists and also an exploration of the research literature. Details will be provided later. Exams will emphasize lecture and problem set material. You are responsible for material covered solely in the reading only when it is specifically assigned; in general, the reading is for improving your understanding of lecture material. On exams, you may be asked to design and interpret experiments as well as to recapitulate facts. Review sessions will be held and past exams are available. The exams are

quite difficult, but in the past I have had few complaints about final grades. I encourage questions and discussion in class, but class participation does not affect grading. I encourage you to form study groups, but **any written work that you turn in must be done independently of anyone else**. Your course grade will be based on exam and problem set performance relative to a curve and to my expectations (*i.e*. I move borders depending on how the class as a whole did). I anticipate roughly 30:30:30 A:B:C. The curve does not require D's or F's but I will give them without hesitation if necessary. Plus/minus final grades will be given. There will be a final exam viewing and you can get final grades there or through Testudo.

If you absolutely must miss an hour exam, you must call me in advance or within 24 hours after the exam, and you must also present a valid University excuse (please secure a note from the Health Services if possible). You can then take a comprehensive makeup exam or be assigned a grade based on the remaining exams and the problem sets. If you miss the final or both hour exams, you will receive a failing grade. I expect and enforce adherence to the University's Code of Academic Integrity, found at http://www.studenthonorcouncil.umd.edu/code.html. I expect you to write out and sign the University honor pledge on each exam: "**I pledge on my honor that I have not given or received any unauthorized assistance on this assignment/examination."** Also, you are hereby notified that "plagiarism" will be interpreted in its broadest sense: ideas from others must be referenced; words from others must be in quotation marks and referenced. Paraphrasing without referencing will be considered plagiarism. Extensive paraphrasing from a single source is unacceptable, referenced or not. As a condition of remaining in the class, you are specifically directed to read my own web page on this: http://www.biochem.umd.edu/biochem/kahn/plagiarism.html.

Please try to be on time for class. Please make sure that your cell phone does not ring during class. Cell phones must be stored out of reach and sight during exams. If you bring a laptop to class, I expect you to make sure that it will not be a source of distraction to other students.

Textbooks and other Sources

Required: Nelson, D.L. and Cox, M.M. (2008). ***Lehninger: Principles of Biochemistry.*** 5th edition. W. H. Freeman and Co., New York. ISBN 978-0-7167-7108-1.

Recommended (NOT in addition to the required text!): If it saves you money, you can get by with the 4th edition of Lehninger, or else Berg, Tymoczko, and Stryer (2007), *Biochemistry*. 6th edition.

Additional Sources:

Bates, A. D. and Maxwell, A. (2005). *DNA Topology*. 2nd ed. Oxford University Press. 198 pp. Excellent monograph on this difficult topic.

Blake, R.D. (2004). *Informational Biopolymers of Genes and Gene Expression*. University Science Books, Sausalito, CA. The chemistry of molecular biology.

Bloomfield, V.A., Crothers, D.M., and Tinoco, I., Jr. (2000). *Nucleic Acids: Structure, Properties and Functions*. University Science Books, Sausalito CA. Biophysical chemistry.

Calladine, C.R., Drew, H.R., Luisi, B.F., and Travers, A.A. (2004). *Understanding DNA: The Molecule and How It Works*. 3rd edition. Elsevier Academic Press, Amsterdam. Focuses on explaining protein-DNA complexes.

Ptashne, M. and Gann, A. (2002). *Genes & Signals*. Cold Spring Harbor Laboratory Press. 192 pp. Heuristics of gene regulation.

Weaver, R. F. (2007). *Molecular Biology*. 4th ed., McGraw-Hill, Boston. Excellent source for historical and modern experiments.

Wolffe, A. (1999). Chromatin: Structure and Function. 3rd ed. San Diego: Academic Press, Inc. 400 pp. Covers from structure to biology. Becoming of historical interest.

Lecture Outline

Chapters in Lehninger 5/e containing relevant sections to be read for background or amplification are specified for each lecture. You are not responsible on exams for material covered only in the book unless this is specifically announced. You are, however, responsible for the answers to any study questions assigned or handed out in class.

I. Nucleic Acid Sequence, Structure, and Chemistry (9 lectures)

1. Introduction and nucleic acid building blocks; Chapter 1.4-1.5, 8.1 — 9/2/08
   Introduction, central dogma, nucleotide structure, primary structure, chemical stability, nomenclature
2. Structures of double helices; Chapter 8 — 9/4/08
   A, B, and Z form helices, base pairing and hydrogen bonding
3. DNA and RNA hybridization and thermodynamics; Chapter 8, 9.1, 9.3 — 9/7/08
   Base-pair stability rules, melting, hybridization, hypochromism, microarrays
4. RNA structure and triple helices; Chapter 8.2, 27.2 — 9/9/08
   Tertiary structure and tRNA, prediction of RNA secondary structure, RNA tertiary folding
5. DNA bending, flexibility, and cyclization; Chapter 8.2 — 9/16/08
   Bending and twisting flexibility, sequence-directed bending, methods for detection and quantitation
6. Topology, supercoiling, topoisomerases; Chapter 24.2, 24.3 — 9/18/08
   Linking number, superhelix structure, topoisomerase reaction mechanisms
7. Enzymatic manipulation of nucleic acids; Chapter 9 — 9/23/08
   Basic genetic engineering, restriction enzymes, radiolabeling, polymerases, PCR
8. DNA sequencing and bioinformatics; Chapter 9, Chapter 24 — 9/25/08
   DNA sequencing methods, genomics, BLAST
9. Review/catch-up day — 9/30/08

II. General Features of Protein-Nucleic Acid Interaction (4 lectures)

10. Biochemical methods for studying protein-nucleic acid complexes; Chapter 5.1, 26.1 — 10/2/08
    Binding curves, gel mobility shift, footprinting/interference, crosslinking, filter binding, FRET, ChIP

→ EXAM I ← Covers through Section I. — **10/7/08**

11. Sequence- and structure-specific recognition of nucleic acids; Chapter 28.1 — 10/9/08
    Major groove vs. minor groove, hydrogen bonding, direct vs. indirect readout, deformability, RNA recognition
12. Protein structural motifs for nucleic acid binding; Chapter 28.1, 28.3 — 10/14/08
    Helix-turn-helix, zinc fingers, bZIP proteins, TBP, hnRNP, etc. Molecular visualization.
13. Chromosome structure; Chapter 24.3 — 10/16/08
    Nucleosomes, chromatin, higher-order structure, telomeres
14. Review/catch-up day — 10/21/08

III. DNA Transactions (9 lectures)

15. DNA replication: fundamental mechanisms; Chapter 25 — 10/23/08
    Polymerization reaction mechanisms, fidelity, structure
16. Genome replication; Chapter 25 — 10/28/08
    Origin recognition and polymerase holoenzymes in *E. coli*; the cell cycle.
17. DNA repair; Chapter 25.2 — 10/30/08
    BER, NER, mismatch repair, cancer
18. Transcription: fundamental mechanisms; Chapter 26.1 — 11/4/08

RNA polymerases, transcription cycle, transcription bubble, supercoiling

19. Regulation in prokaryotes; repression, activation, looping; Chapter 28.1-28.2 11/6/08
    Paradigms: lac operon, araC, ntrC. Searching mechanisms.
20. Transcription in eukaryotes: chromatin and complexity; Chapter 28.3 11/11/08
    Assembly, activators, enhancers, chromatin remodeling, histone code, recruitment
21. Regulation of transcription by RNA; Chapter 28.3 11/13/08
    RNAi, siRNA, microRNA, riboswitches
22. Recombination; Chapter 25.3 11/18/08
    Holliday junctions, homologous recombination by RecABCD

→ EXAM II ← Covers through Lecture 21 **11/20/08**

23. "Interprocess Communication" 11/25/08
    Review of regulatory and biochemical connections among replication, transcription, repair

→ Thanksgiving Break← **11/27/08**

IV. RNA Transactions (4 lectures)

24. Catalytic RNA; Chapter 26.2 12/2/08
    Self-splicing RNA, ribozymes, origin of life
25. RNA splicing, processing, and degradation; Chapter 26.2-26.3 12/4/08
    Splicing mechanisms, control of mRNA lifetime, nonsense-mediated decay
26. Translation; Chapter 27 12/9/08
    Chemistry of protein biosynthesis, ribosome structure, the translation cycle
27. Review/catch up day. 12/11/08

→ FINAL EXAM← Emphasizes 22-27 **Friday, 12/19/08, 10:30-12:30 a.m., Chemistry 1402**

The final will explicitly cover mainly the latter part of the course but will inevitably draw on older material. You get a few more points per minute for the final than on the midterms as a reward for improvement.