BIOCHEMISTRY 465 (BCHM 465, BIOCHEMISTRY III): BIOLOGICAL INFORMATION PROCESSING SPRING, 2006: TU TH, 9:30-10:45 A.M., CHEMISTRY 0128

Assoc. Prof. Jason D. Kahn, Dept. of Chemistry and Biochemistry, Univ. Maryland, College Park

Office: Chemistry 2500A (Biochemistry, Wing 5 of the Chemistry complex)

Office hours: Tues. 1-2 p.m., Thurs. 1-2 p.m., Chemistry 2500A; there is no TA for the course

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

Web and email: The course web site is http://www.biochem.umd.edu/biochem/kahn/bchm465-06. You should already be subscribed to the e-mail reflector for the course. To email everyone on the list, send to bchm465-0101-spr06@coursemail.umd.edu. No spam!

WileyPlus: Some on-line assignments will be provided through the textbook publisher's web site: http://edugen.wiley.com/edugen/class/cls17790/. You also have access to the full text of the textbook through the site. You may be surveyed on your on-line experience.

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), a poster presentation (see below, 100 pts), a two hour final examination (170 pts), and 30 points for completion of WileyPlus or other assignments. Exams will emphasize lecture 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. Your course grade will be based on exam

and poster 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 an exam viewing and you can get final grades there or through Testudo.

The poster will concern societal impacts of nucleic acid oriented science. Topics could include the evolutionary history of humans or pathogens, the impact of DNA forensics, personalized medicine, the hype and reality of nucleic-acid based drugs, the stock market performance of biotechnology companies, the bioethics of genetic testing, what makes us human, the origin of life, DNA in literature. You will work on the posters in seven groups of 5 or 6 students. Funds will be provided to print out professional posters. We will have a poster session outside of class on or about May 5. Your grade will be based on the quality of the poster, on a brief oral presentation by one or more group members, and on the perceptiveness of your evaluation of others' posters: you will turn in a paragraph on each four of the other posters, total one page, for 20 points of the 100 points on the poster.

If you absolutely must miss an hour exam or the poster presentation, 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 will then be assigned a grade based on the remaining exams and the poster. 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.

Textbooks

Required: Voet, D., Voet, J.G., and Pratt, C.W. (2006). Fundamentals of Biochemistry: Life at the Molecular Level. 2nd edition. Chapters 3 and 23-27(photocopies provided) and ancillary material.

Additional Sources:

Bates, A. D. and Maxwell, A. (1993). *DNA Topology*. Oxford: IRL Press at Oxford University Press. 114 pp. Excellent short 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.

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

Weaver, R. F. (2002). *Molecular Biology*. 3rd 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.

Lecture Outline

Chapters 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 3 — 1/26/06
   Introduction, central dogma, nucleotide structure, primary structure, chemical stability, nomenclature
2. Structures of double helices; Chapter 23 — 1/31/06
   A, B, and Z form helices, base pairing and hydrogen bonding
3. DNA and RNA hybridization and thermodynamics; Chapter 23 — 2/2/06
   Base-pair stability rules, melting, hybridization, hypochromism, microarrays
4. RNA structure and triple helices; Chapter 23 — 2/7/06
   Tertiary structure and tRNA, prediction of RNA secondary structure, RNA tertiary folding
5. DNA bending, flexibility, and cyclization; Chapter 23 — 2/9/06
   Bending and twisting flexibility, sequence-directed bending, methods for detection and quantitation
6. Topology, supercoiling, topoisomerases; Chapter 23 — 2/14/06
   Linking number, superhelix structure, topoisomerase reaction mechanisms
7. Enzymatic manipulation of nucleic acids; Chapter 3 — 2/16/06
   Basic genetic engineering, restriction enzymes, radiolabeling, polymerases, PCR
8. DNA sequencing and bioinformatics; Chapter 3, Chapter 27 — 2/21/06
   DNA sequencing methods, genomics, homology, BLAST
9. Review/catch-up day — 2/23/06

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

10. Biochemical methods for studying protein-nucleic acid complexes; Chapter 23 — 2/28/06
    Binding curves, gel mobility shift, footprinting/interference, crosslinking, filter binding, FRET, ChIP

→ EXAM I ← Covers through Section I. — 3/2/06

11. Sequence- and structure-specific recognition of nucleic acids; Chapter 23 — 3/7/06
    Major groove vs. minor groove, hydrogen bonding, direct vs. indirect readout, deformability, RNA recognition
12. Protein structural motifs for nucleic acid binding; Chapter 23 — 3/9/06
    Helix-turn-helix, zinc fingers, bZIP proteins, TBP, hnRNP, etc. Molecular visualization.
13. Chromosome structure; Chapter 23 — 3/14/06
    Nucleosomes, chromatin, higher-order structure, telomeres
14. Review/catch-up day — 3/16/06

→ Spring Break← No lectures — 3/21/06, 3/23/06

III. DNA Transactions (9 lectures)

15. DNA replication: fundamental mechanisms; Chapter 24 — 3/28/06
    Polymerization reaction mechanisms, fidelity, structure
16. Genome replication; Chapter 24 — 3/30/06
    Origin recognition and polymerase holoenzymes in *E. coli*; the cell cycle.
17. Transcription: fundamental mechanisms; Chapter 25 — 4/4/06
    RNA polymerases, transcription cycle, transcription bubble, supercoiling

18. Regulation in prokaryotes; repression, activation, looping; Chapter 27 4/6/06
    Paradigms: lac operon, araC, ntrC. Searching mechanisms.
19. Transcription in eukaryotes: chromatin and complexity; Chapter 27 4/11/06
    Assembly, activators, enhancers, chromatin remodeling, histone code, recruitment

→ Poster Preview Due ← **4/13/06**

20. Regulation of transcription by RNA; Chapter 27 4/13/06
    RNAi, siRNA, microRNA, riboswitches
21. Recombination; Chapter 24 4/18/06
    Holliday junctions, homologous recombination by RecABCD

→ EXAM II ← Covers through Lecture 20 **4/20/06**

22. DNA repair; Chapter 24 4/25/06
    BER, NER, mismatch repair, cancer
23. "Interprocess Communication" 4/27/06
    Review of regulatory and biochemical connections among replication, transcription, repair

IV. RNA Transactions (4 lectures)

24. Catalytic RNA; Chapter 25 5/2/06
    Self-splicing RNA, ribozymes, origin of life
25. RNA splicing, processing, and degradation; Chapter 25 5/4/06
    Splicing mechanisms, control of mRNA lifetime, nonsense-mediated decay

→ Poster Session (Time/date will be finalized according to everyone's schedules) ← **Friday, 5/5/06**

26. Translation; Chapter 26 5/9/06
    Chemistry of protein biosynthesis, ribosome structure, the translation cycle

→ Evaluation of Posters Due ← **5/9/06**

27. Review/catch up day. 5/11/06

→ FINAL EXAM← Emphasizes 21-27 **Monday, 5/15/06, 8:00-10:00 a.m., Chemistry 0128**

The final will explicitly cover only 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.