BIOCHEMISTRY 465 (BIOCHEMISTRY III: MOLECULAR GENETICS) — SPRING, 2001
TuTh, 9:30-10:45 a.m., Chemistry 0127

Prof. Jason D. Kahn, Dept. of Chemistry and Biochemistry, UMCP

Office: Chemistry 2505 (Biochemistry, Wing 5 of the Chemistry complex)

Office hours: Weds. 2-3 p.m., Thurs. 1-2 p.m., Chemistry 2505; there is no TA for the course

Contacting me: kahn@adnadn.umd.edu much preferred to 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.

Class web site: http://www.chem.umd.edu/biochem/kahn/bchm465; there will also be an e-mail reflector.

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, emphasize common logic and mechanisms. Topics are as follows:

- Chemistry and structure of DNA and RNA, from nucleotides to chromosomes.
- Interactions between nucleic acids and proteins.
- Selected aspects of the biochemistry and regulation of DNA replication, transcription, recombination, and repair, and how these processes interact with each other.
- Translation, RNA splicing, and RNA catalysis.

Texts: (Note that the course is primarily lecture-based).

Required: Weaver, R. F. (1999). *Molecular Biology*. 1st ed., WCB/McGraw-Hill, Boston. Excellent source for historical and modern experiments.

Occasional required reading from the primary or review literature may be provided.

Recommended: Any of the standard Biochemistry texts you have used for 461 and/or 462.

Other recommended sources, available on reserve in the White Memorial Chemistry Library:

Bates, A. D. and Maxwell, A. (1993). *DNA Topology*. Oxford: IRL Press at Oxford University Press. Excellent short monograph on this difficult topic.

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

Kornberg, A. and Baker, T. A. (1992). *DNA Replication*. 2nd ed. New York: W.H. Freeman and Co. Great source for historical background, good breadth.

Ptashne, M. (1992). *A Genetic Switch: Phage λ and Higher Organisms*. 2nd ed. Cambridge, MA: Cell Press and Blackwell Scientific. Heuristics of gene regulation.

Schleif, R. (1993). *Genetics and Molecular Biology*. 2nd ed. Baltimore: The Johns Hopkins University Press. Eclectic, emphasizing experiments leading to conclusions.

Travers, A. (1993). *DNA-Protein Interactions*. London: Chapman & Hall. Focuses on DNA structure.

Wolffe, A. (1999). *Chromatin: Structure and Function*. 3rd ed. San Diego: Academic Press, Inc. Covers from structure to biology.

Grading Policy:

There will be two 75-minute midterm exams (100 pts each), group class projects in lieu of a third exam (75 pts), and a two hour final (150 pts). Exams will be about 50% short-answer questions, testing your comprehension of lecture material, and about 50% essay or computational questions, testing your ability to apply and extend this basic knowledge. The final will explicitly cover only the latter part of the course but will inevitably draw on older material. There will be a review session before each exam, and past years' exams will be on reserve.

Your final letter grade will be based on your performance relative to the class as a whole and to my expectations (*i.e.* it's curved, but I draw the lines between grade levels depending on how I felt the class as a whole performed). Final grades will be given out only through the MARS system. 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.

If you absolutely must miss a midterm exam, you must call me in advance or within 24 hours after the exam, and you must also present a valid University excuse, in order to be eligible for the assignment of a grade based on the remaining course work. If you miss the final, do not turn in a project, or miss both hour exams, you will receive a failing grade. You are expected to adhere to the University code of conduct.

The class projects, to be conducted by small groups, are intended to give you an understanding of the sources of our knowledge of molecular machines. Each group of 4-5 students will study a type of DNA/RNA transaction (e.g. replication, transcription, repair, RNA splicing, recombination, translation). The panoply of components involved in the process will be schematized in web page form, with links to pages on the experiments in which they were first identified, their essential functions identified, and their structures if available. This is an experiment—suggestions are welcome. Project presentations will comprise the last class.

Lecture Schedule (approximate)

READING ASSIGNMENTS ARE FOR REFERENCE, NOT REQUIRED UNLESS EXPLICITLY STATED.

I. Nucleic Acid Structure and Chemistry, Protein-Nucleic Acid Interaction (12 lectures)

1.	Introduction; nucleic acid building blocks Central dogma, nucleotide structure, primary structure, chemical stability, nomenclature	Weaver, Chapters 1, 2	1/30/01
2.	Structures of double helices A, B, and Z form helices, base pairing and hydrogen bonding	Chapter 2	2/1/01
3.	DNA and RNA hybridization and thermodynamics Base-pair stability rules, melting, hypochromism, hybridization, gene chips	Chapter 2, 5	2/6/01
4.	RNA structure and triple helices Tertiary structure and tRNA, prediction of RNA folding, antisense	Chapter 2, 19	2/8/01
5.	DNA bending, twisting, and supercoiling; topoisomerases Persistence length, linking number, superhelix structure, topo reaction mechanisms	Chapter 6, 7, 20	2/13/01
6.	Enzymatic manipulation of nucleic acids Restriction enzymes, nucleases, radiolabeling, basic genetic engineering, polymerases, PCR	Chapter 4, 5	2/15/01
7.	Sequencing and synthesis of DNA and RNA Maxam-Gilbert and Sanger sequencing, genomics, bioinformatics **LECTURE ON 2/20 IS CANCELLED, TO BE RESCHEDULED AT A MUTUALLY AGREED TIME**	Chapter 5	TBA
8.	Methods for studying protein-nucleic acid complexes Binding curves, footprinting, in vitro and in vivo crosslinking, structural methods	Chapter 5, 9	2/22/01
9.	Catch-up day		2/27/01
10.	Protein structural motifs for nucleic acid binding Helix-turn-helix, zinc fingers, bZIP proteins, TBP, hnRNP, etc.	Chapter 9, 12	3/1/01

—> EXAM I <— Covers through lecture 9 **3/6/01**

11.	Recognition of nucleic acids Major groove vs. minor groove, hydrogen bonding, direct vs. indirect readout, deformability	Chapter 9, 12	3/8/01
12.	Chromosome structure Nucleosomes, chromatin, higher-order structure, telomeres, effects on transcription	Chapter 13	3/13/01

II. DNA Transactions (10 lectures)

13.	DNA replication: fundamental mechanisms Polymerization reaction mechanisms, fidelity, structure	Chapter 20, 21	3/15/01

Spring Break March 17-24

14.	Genome replication Origin recognition and polymerase holoenzyme in *E. coli*; the cell cycle	Chapter 20, 21	3/27/01
15.	Transcription: fundamental mechanisms RNA polymerases, transcription cycle, transcription bubble, supercoiling	Chapter 6	3/29/01
16.	Regulation of transcription in prokaryotes Repression and activation paradigms: lac operon, araC, ntrC; searching mechanisms	Chapter 7, 8	4/3/01
17.	Transcription in eukaryotes Holoenzyme vs. initiation complex assembly, activators, chromatin, recruitment	Chapter 10, 11, 12	4/5/01
18.	Catch-up day **PROJECT OUTLINES DUE**		4/10/01
19.	Homologous recombination Holliday junctions, recABCD	Chapter 22	4/12/01

—> EXAM II <— Covers through Lecture 18 **4/17/01**

20.	Site-specific recombination λ phage integration/excision, HIV integrase	Chapter 22	4/19/01
21.	DNA repair BER, NER, mismatch repair, cancer	to be provided	4/24/01
22.	"Interprocess communication" Review of regulatory and biochemical connections among replication, transcription, repair	to be provided	4/26/01

III. RNA Transactions (5 lectures)

23.	Translation: fundamental chemistry, fidelity tRNA synthetases, peptidyl transferase chemistry, proofreading	Chapter 18, 19	5/1/01
24.	Translation: mechanism and regulation ribosome structure, elongation cycle, mRNA lifetime	Chapter 18, 19	5/3/01
25.	Catalytic RNA Self-splicing RNA, ribozymes, origin of life	Chapter 14	5/8/01
26.	RNA splicing mRNA splicing mechanisms **PROJECTS ARE DUE**	Chapter 16	5/10/01
27.	Review: **PRESENTATION OF STUDENT PROJECTS**		5/15/01

FINAL EXAM: Covers Lectures 19-27 Friday, 5/22/01, 1:30-3:30 p.m., Chem. 0127