BIOCHEMISTRY 674 (NUCLEIC ACIDS) — FALL, 2001
TuTh, 8:00-9:15 a.m., Chemistry 0127

Assoc. 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@adnahn.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.biochem.umd.edu/biochem/kahn/bchm674; there is also 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, emphasizing common logic and mechanisms. Topics are as follows:

- Chemistry and structure of DNA and RNA, from nucleotides to chromosomes, and some methods
  for studying, synthesizing, sequencing and manipulating nucleic acids. Bioinformatics.
- Interactions between nucleic acids and ligands such as cations, drugs, and especially proteins.
- Selected aspects of the biochemistry and regulation of DNA replication, transcription, recombination,
  and repair, and how these processes interact with each other.
- RNA splicing, RNA catalysis, translation, and selection-amplification methods.

Required papers from the literature will be assigned for some lectures (may be read after the lecture), as
indicated on the Course Outline below. All papers will be on reserve at the White Memorial Chemistry
Library. In addition, two textbooks are strongly recommended for the course, for background and for
reference in your research careers. I may also provide occasional handouts with some figures, hints on what
you should take away from the assigned reading, and additional entries into the literature. Some of these
additional sources, especially books, are on reserve.

There will be two 75-minute exams (100 pts each), a short (7-10 pp.) paper (100 pts), and a two hour
final examination (150 pts). Exams will emphasize lecture material, with some coverage of key concepts
from the reading. You will be asked to design and interpret experiments as well as to recapitulate assigned
material. Review sessions will be held and past exams will be on reserve. The paper will be an examination
of the historical development of our understanding of a particular topic, with emphasis on critical
experiments and how they caused reinterpretation of earlier work. I encourage questions and discussion in
class, but class participation does not affect grading. Plus/minus final grades will be given.

If you absolutely must miss an 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 two exams and the paper. If you miss the final or both hour exams, you will receive
a failing grade. The exams are quite difficult, but in the past I have had few complaints about final grades.
Your course grade will be based on exam and paper performance relative to a curve and to my expectations.

I expect and enforce adherence to the University’s Code of Academic Integrity, found at
http://www.inform.umd.edu/CampusInfo/Departments/JPO/code_acinteg.html. Specifically, "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.
Course Outline

Recommended texts, available at the University Book Center. Chapters to be read for background or amplification are specified for each lecture (W3 = Weaver, Chapter 3, etc.). You are not responsible for material covered only in the book unless this is specifically announced.


I. Nucleic Acid Sequence, Structure, and Chemistry (10 lectures)
   1. Nucleic acid building blocks; BCT2, W1, 2, 3
      Central dogma, nucleotide structure, primary structure, chemical stability, nomenclature
      8/30/01
   2. Structures of double helices; BCT4, W2
      A, B, and Z form helices, base pairing and hydrogen bonding
      Watson and Crick, 1953; Dickerson, 1983
      9/4/01
   3. DNA and RNA hybridization and thermodynamics; BCT8, W5
      Base-pair stability rules, melting, hybridization, hypochromism, gene chips
      Holstege et al., 1999
      9/6/01
   4. RNA structure and triple helices; BCT8, W19
      Tertiary structure and tRNA, prediction of RNA folding, antisense
      Moser and Dervan, 1987
      9/11/01
   5. Sequencing and synthesis of DNA and RNA; BCT3, W5, 24
      Maxam-Gilbert and Sanger sequencing, chemical and enzymatic synthesis, genomics and bioinformatics
      Fleischmann et al., 1995
      9/13/01
   6. Drug and cation binding, chemical probing methods; BCT11, 12
      Intercalation, groove-binding, ion atmosphere, reactivity of nucleotides, altered backbone chemistries
      9/18/01
   7. DNA bending, flexibility, and cyclization; BCT9
      Bending and twisting flexibility, sequence-directed bending, methods for detection and quantitation
      Zinkel and Crothers, 1987
      9/20/01
   8. Topology, supercoiling, topoisomerases; BCT10, W20
      Linking number, superhelix structure, topoisomerase reaction mechanisms, knots and catenanes
      Bauer et al., 1980
      9/25/01
   9. Enzymatic manipulation of nucleic acids; BCT3, W4, 5
      Restriction enzymes, nucleases, radiolabeling, basic genetic engineering, polymerases, PCR
      Arnheim and Levenson, 1990
      9/27/01
   10. Catch-up day
      10/2/01

II. General Features of Protein-Nucleic Acid Interaction (4 lectures)
      Binding curves, gel mobility shift, footprinting/interference, crosslinking, filter binding, ChIP
      10/4/01
   12. Protein structural motifs for nucleic acid binding; BCT13, W9, 12
      Helix-turn-helix, zinc fingers, bZIP proteins, TBP, hnRNP, etc.
      Harrison, 1991; Nikolov et al., 1995
      10/9/01

→ EXAM I ← Covers through Section I. 10/11/01

13. Sequence- and structure-specific recognition of nucleic acids; BCT13, W9
    Major groove vs. minor groove, hydrogen bonding, direct vs. indirect readout, deformability, RNA recognition
    Seeman et al., 1976
    10/16/01
14. Chromosome structure; BCT14, W13  
   Nucleosomes, chromatin, higher-order structure, telomeres  
   Luger et al., 1997

III. DNA Translations (8 lectures)

15. DNA replication: fundamental mechanisms; W20, 21  
   Polymerization reaction mechanisms, fidelity, structure  
   Brutlag and Kornberg, 1972

16. Genome replication; W20,21  
   Origin recognition and polymerase holoenzymes in E. coli; the cell cycle.  
   Naktinis et al., 1996

17. Transcription: fundamental mechanisms; W6  
   RNA polymerases, transcription cycle, transcription bubble, supercoiling  
   Nudler et al., 1997; Liu and Wang, 1987

18. Regulation in prokaryotes; repression, activation, looping; W7, 8  
   Paradigms: lac operon, araC, ntrC. Searching mechanisms.

19. Transcription in eukaryotes: chromatin and complexity; W10, 11, 12, 13  
   Holoenzyme vs. initiation complex assembly, activators, enhancers, chromatin, recruitment  
   Struhl, 1999; Cosma et al., 1999

20. Recombination; W22, 23  
   Holliday junctions, recABCD, λ phage integration and excision

→ Paper Topics Due ←  

21. DNA repair; W20  
   BER, NER, mismatch repair, cancer

→ EXAM II ← Covers through Lecture 20.  

22. “Interprocess Communication”  
   Review of regulatory and biochemical connections among replication, transcription, repair

→ Thanksgiving ← No lecture

IV. RNA Transactions (5 lectures)

23. Catalytic RNA; W14  
   Self-splicing RNA, ribozymes, origin of life

24. RNA splicing and degradation; W14, 16  
   Splicing mechanisms, control of mRNA lifetime  
   Nilsen, 1994

25. Translation; W18, 19  
   Chemistry of protein biosynthesis, ribosome structure, the translation cycle  
   Nissen et al., 2000

→ Paper Due ←  

26. Selection-amplification methods for nucleic acids  
   Selection of optimal DNA and RNA ligands or catalysts, in vitro evolution  
   Ellington and Szostak, 1990

27. Review and/or catch up day.

→ FINAL EXAM ← Emphasizes 21-27  
   Sat., 12/15/01, 8:00-10:00 a.m., Chem. 0127
Reading List

This list may change as the semester progresses. In the required papers, I have tried to strike a balance among review articles, classic papers, and current research. Please let me know if there are difficulties with the amount or depth of the reading.

General texts for further reading and background:

Monographs for more in-depth discussion of particular topics:

Required Papers:


