

Biochemistry 766: Nucleic Acids

<http://www.biosci.ohio-state.edu/~mfoster/biochem766/>

<http://carmen.osu.edu>

Winter Quarter 2009, 3 cr., MWF 10:30-11:20, BI 668

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Primary Text:

Nucleic Acids in Chemistry and Biology. Blackburn, Gait, Loakes and Williams, eds. Royal Society of Chemistry, 2006, 3rd edition. ISBN: 978-0-85404-654-6.

Grading:

Problem Sets: 20%, Paper reviews: 10%, Oral Presentations: 10%, Midterm: 30%, Final: 30%

Lecture Topics

Introduction

Nucleic acids biochemistry; history and context

Nucleic acid nomenclature; tautomerism; ionization

Structure

Base pairing, helical structure, ion binding, hydration

Computer-aided structure analysis (RASMOL/PYMOL; BPL computing lab)

Chemical and Biochemical Methods

Synthesis

Reactivity

Sequencing, identification of modified nucleosides

DNA/RNA structure analysis by chemical/enzymatic probing and phylogenetic data

Nucleoside analogs, phosphorothioates, NAIM

SELEX

RNA Interference

Physical Methods

Nucleic acid crystallography

NMR of Nucleic Acids

Spectroscopy of nucleic acids

Conformational changes

Single molecule methods

Interactions

Ligand binding in the major and minor grooves, intercalation, drug design

Protein-DNA interactions; motifs, major and minor groove recognition, bending

RNA-protein interactions

Protein enzymes

RNA catalysis

Ribozymes

The ribosome

Oral Presentations/Literature Discussions

Final Exam: Thursday, March 19, 9:30-11:18 am; location TBA

Class Materials

Materials for the course will include assigned text readings, handouts provided in class, and materials available on-line via Carmen (<http://carmen.osu.edu>). Other sources of information include the current research literature as well as literature and structural databases.

Computer-Aided Structure Analysis

We will be making use of molecular visualization software to learn about nucleic acids structure and interactions. You will be encouraged to learn to use the Pymol visualization program, although similar alternative programs may be also used. Pymol is available in the computing lab on the second floor of the BPL, versions are freely available and can be installed on your own (or laboratory) computer. A tutorial on the use of the software will be provided in one class session.

Oral Presentations & Written Paper Reviews

Students will be required to read, discuss and present essential aspects of selected research papers orally and in writing. During the last week, students will make oral presentations on a selected paper topic; one evening session may be scheduled to complement the in-class sessions.

Other texts (on reserve in BPL)

Nucleic Acids: Structure, Properties and Functions. Bloomfield, Crothers & Tinoco. University Science Books, 2000, ISBN 0-935702-49-0

Principles of Nucleic Acid Structure. Saenger, Springer Verlag, New York, 1984

Bioorganic Chemistry: Nucleic Acids. Hecht, Oxford University Press, 1996

Molecular Biology. Weaver, McGraw-Hill, 3rd ed., 2005

Computer and web resources

Data

Protein Data Bank (PDB) <http://www.rcsb.org/pdb>
Nucleic Acid Database <http://ndbserver.rutgers.edu:80>
BMRB <http://www.bmrw.wisc.edu>

Software

PyMOL <http://pymol.sourceforge.net>
RASMOL <http://www.umass.edu/microbio/rasmol>
MOLMOL <http://www.mol.biol.ethz.ch/wuthrich/software/molmol>
Chimera (UCSF) <http://www.cgl.ucsf.edu/chimera/>
VMD (UIUC) <http://www.ks.uiuc.edu/Research/vmd/>
Mfold <http://www.bioinfo.rpi.edu/applications/mfold/old/rna/form3.cgi>
(PDB repository) <http://www.rcsb.org/pdb/software-list.html>

Literature

Entrez/PubMed <http://www3.ncbi.nlm.nih.gov/Entrez>
Ohio-Link Journal Center <http://journals.ohiolink.edu/cgi-bin/sciserv.pl?collection=journals>
OSCAR databases <http://www.lib.ohio-state.edu/find/subject.php>

Journals (by no means a comprehensive list)

Biochemistry <http://pubs.acs.org/journals/bichaw/index.html>
Cell <http://www.cell.com>
Curr Opin Struct Biol <http://www.current-opinion.com/jstb/about.htm?jcode=jstb> (OhioLink)
EMBO J <http://www.emboj.org>
J Mol Biol <http://www.academicpress.com/jmb> (OhioLink)
Nature <http://www.nature.com>
Nature Struct Biol <http://www.nature.com/nsmb/>
Nucleic Acids Res <http://www.oup.co.uk/nar/contents>
Proc Natl Acad Sci USA <http://www.pnas.org>
RNA <http://www.rnajournal.org/>
Science <http://www.sciencemag.org/>

Biochemistry 766 Preliminary lecture schedule:

Week	Day	Date	Topic	Instructor	Reading	Assignment
1	Mon	1/5	Intro/Nomenclature	Mark	Ch. 1, 2.1; Watson & Crick Nature 1953	
	Wed	1/7	Structure, part 1	Karin	2.1.2, 2.2	Read Moran & Kool PNAS 1997
	Fri	1/9	Structure, part 2	Karin	2.3, 2.4	PS #1 available (Karin)
2	Mon	1/12	Physical Properties: Thermodynamics Computer-aided structure analysis	Karin	2.1.3, 2.4.4.1, 2.5	
	Wed	1/14	(PyMOL; BPL computing lab)	Mark		
	Fri	1/16	Higher order structure; RNA/DNA folding	Karin	2.6, 7.1	PS #1 due; PS #2 available (Mark)
3	Mon	1/19	MLK Day, no class			
	Tue	1/20	OSBP Seminar, 4 PM, 170 H&L, Lynne Maquat			
	Wed	1/21	DNA, RNA sequencing, modified nucleosides	Mark	5.1-5.3, 7.2, 11.6	PS #2 due; PS #3 available (Mark)
	Fri	1/23	Phylogenetic co-variation; SELEX	Mark	Massire 1998 JMB; Hermann & Patel 2000	
4	Mon	1/26	Chemical and enzymatic probes	Mark	Zarrinkar & Williamson 2004 Correll et al. 1997	
	Wed	1/28	Nucleoside analogs, phosphorothioates	Mark	4.3-4.4, NAIM Review	PS #3 due
	Fri	1/30	NAIM	Mark		
5	Mon	2/2	X-ray crystallography	Mark	11.3	
	Wed	2/4	X-ray cont. NMR Spectroscopy	Mark	11.2	
	Thu	2/5	Exam I (evening)			
	Fri	2/6	NMR Spectroscopy	Mark	11.2	Paper selections for oral presentations approved by today
6	Mon	2/9	Optical Spectroscopy, FRET	Karin	11.1	Assign papers to review
	Wed	2/11	RNA interference/ micro RNAs	Karin	5.7.2	
	Fri	2/13	Catalytic RNAs	Karin	7.6.2	
7	Mon	2/16	Catalytic RNAs	Karin		Paper review discussion
	Wed	2/18	Catalytic RNAs	Karin		Written reviews due. Assign PS#4 (Karin)
	Fri	2/20	Protein-DNA interactions	Karin	10.1-10.4	
8	Mon	2/23	Protein-DNA interactions	Karin	10.5-10.8	
	Tue	2/24	OSBP Seminar, 4 PM, 170 H&L Jamie Williamson			
	Wed	2/25	Protein-RNA interactions	Karin	10.9	
	Fri	2/27	Protein-RNA interactions	Karin		PS #4 due
9	Mon	3/2	Single Molecule Methods	Mark	11.5, Bustamante 2003; Ha 1999	
	Wed	3/4	Ligand binding in major/minor groove, intercalation, drug design	Mark	9	
	Fri	3/6	Ribosome	Mark		
10	Mon	3/9	Paper presentations (+ one evening)			
	Wed	3/11	Paper presentations			
	Fri	3/13	Paper presentations			
Final	Thu	3/19	Final Exam (9:30-11:18)			