

MB&B 300A/600A: BIOCHEMISTRY - Fall 2015
11:35 - 12:50 TUESDAYS & THURSDAYS, WLH 201

INSTRUCTORS:

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TEXT: Lehninger Principles of Biochemistry, 6th edition, W. H. Freeman (New York, 2013).

This text is available at the Yale Bookstore. It is also possible to buy a cheaper e-book.

WEB SITE: Important course materials will be posted on the classes*v2 site for the course. We will post old exams, problem sets, answer keys for exams and problem sets, announcements, etc. There is also a piazza.com web site for the course on which students can post questions that are answered by the instructors and/or other students.

EXAMS will be based exclusively on the material either discussed in the main lectures or as specifically assigned as part of one of the main lectures. Information in the supplemental readings that is not discussed in lectures will not be on the exams. The textbook covers the same concepts we discuss in lecture using different examples and perspectives. Reading the book carefully will strongly enhance your understanding of the lectures and your performance on exams. We will often present information in lectures that is not covered in the textbook: you are responsible for this information. The content of the "special topic" lectures given at the end of class will not be on the exams.

Two midterms: 25% each. October 8 and November 19 during class hours.

Two quizzes: 2.5% each. 15 minutes in class on September 17 and November 5.

Final Exam: 35%. December 19, 2 pm, location TBA.

Problem sets: make up the remaining 10% of the grade. You can drop your lowest problem set score.

Make-ups to the mid-term exams (by Dean's excuse only) will be given orally; a written make-up for the final exam will be given in January.

Exams from last year are available on the web site.

GRADING:

The score cutoffs for various grades are chosen each year by the professors based on student performance. As a guide to what we are likely to do this year, in past years the cutoffs typically had these results: A=top 20%, A-=20th-40th percentiles, B+=40th-60th percentiles, B=60th-80th percentiles, B- and lower for 80th-100th percentiles.

PROBLEM SETS:

Problem sets will be posted on classes*v2 on Thursdays and due via classes*v2 by 11:15 the next Tuesday. Answers will be posted on classes*v2. The TAs will choose one problem at random from each problem set to correct and score. These scores make up 10% of your grade. Problem sets will cover lectures up to and including the date they are posted. Problems will be derived from exams given in this course in past years. Problem sets and their answers will be discussed at discussion sections. You may discuss the problems with classmates but must compose and write the answers independently.

DISCUSSION SECTIONS:

There will be discussions each week, Tuesday 7-8 PM (2 sections), Tuesday 8-9 PM (1 section), Wednesday 7-8 PM (2 sections), Wednesday 8-9 PM (1 section), locations TBA. Sign up for one section and attend it unless special circumstances arise. In that case, you may go to another section. Attendance is strongly recommended. Sections will begin the week of September 14. You must sign up using Yale's [preference selection system](#), with selection starting August 31 and closing September 8 at 9 AM.

MB&B 300 - Biochemistry - Syllabus in Brief
11:35 - 12:50, Tuesdays & Thursdays, Fall, '15, WLH 201
Michael R. Koelle (in charge), Matthew Simon

September 3– (MRK/MS) What is Biochemistry? / Thermodynamics Review

September 8 – (MS) Chemical Principles of Biochemistry

September 10 - (MS) Amino Acids, Peptides and Secondary Structure

September 15 - (MS) Fibrous and Globular Proteins

September 17 - (MS) **15 min. quiz on amino acids.** Lecture: Protein Folding and Dynamics

September 22 - (MS) Protein Purification and Analysis

September 24 - (MS) Allostery (Hemoglobin)

September 29 - (MS) Enzymes: Basic Concepts and Kinetics

October 1 – (MS) Enzymes: Catalysis

October 6 - (MS) Regulation at the Protein Level

October 8 - **Midterm Exam** - covers lectures up to and including October 1

October 13 - (MS) Membranes: Bilayers and Compartments

October 15 - (MS) Membranes: Protein structures, Ion channels and Pores

October 20 - (MS) Membranes: Active transport

October 27 - (MRK) Carbohydrates

October 29 - (MRK) Principles of Metabolism

November 3 - (MRK) Glycolysis

November 5- (MRK) **15 min. quiz on glycolysis.** Lecture: Glycolysis and Gluconeogenesis

November 10- (MRK) Citric Acid Cycle

November 12- (MRK) Electron transport and oxidative phosphorylation

November 17 - (MRK) Lipid metabolism

November 19 –**Midterm Exam** - covers lectures up to and including November 12

December 1 - (MRK) Glycogen metabolism and other metabolic pathways

December 3 - (MRK) Integration of metabolism

December 8 – (MRK) Hormone signaling

December 10 – (MRK) Protein engineering for optogenetics

FINAL EXAM – December 19, 2 pm, location TBA

MB&B 300 - Biochemistry - Detailed Syllabus

11:35 - 12:50, Tuesdays & Thursdays, Fall, '15, **Location TBA**

Michael R. Koelle (in charge), Matthew Simon

September 3 - (MRK/MS) What is Biochemistry? / Physical

Chemistry and Thermodynamics Review

What is biochemistry?

Why study biochemistry?

Course logistics

Principles of Biochemistry

Review: Physical Chemistry and Thermodynamics

Special topic: Energy from disorder.

September 8 - (MS) Chemical principles of Biochemistry

Drawing biochemical mechanisms

Energies of formation

Common reactive groups in biology

Concentrations of the biomolecules

Rates of biochemical reactions

Thermodynamic selectivity

Kinetic selectivity

September 10- (MS) Amino Acids, Peptides and Secondary Structure

Review of amino acid structures and sidechain chemistry

Dissociable groups and titration

The peptide bond: formation and chemical properties

Secondary structure: helices, sheets, turns

Ramachandran plots

Non-random coils

Secondary structure propensities of amino acids

September 15 - (MS) Fibrous and Globular Proteins

Tertiary and quaternary structure

Protein structure determination by X-ray crystallography

Fibrous proteins: Keratin, Collagen, Fibrin

Folds, motifs and domains of soluble, globular proteins

Properties of protein interiors and surfaces

Multimeric proteins

September 17 - (MS) **15 min. quiz** on amino acids.

Lecture: Protein Folding and Dynamics

Folding overview: the Levinthal paradox

Protein folding landscapes

Catalysis and assistance of protein folding

Marginal stability

Amino acid sequence variation

Membrane protein folding

September 22 - (MS) Protein Purification and Analysis

Ultracentrifugation and fractionation

Column chromatography and dialysis

Electrophoresis

Antibodies as tools

Mass spectrometry

Peptide chemistry - sequencing and synthesis

Protein structure determination by NMR

Special topic: The first chromatography.

September 24 - (MS) Allostery and Hemoglobin

Myoglobin structure and oxygen binding

Hemoglobin subunits

Cooperativity, the Hill coefficient

Quaternary structure changes

Sickle cell and other molecular diseases

September 29 - (MS) Enzymes: Basic Concepts and Kinetics

General concepts in catalysis

Thermodynamic principles

Enzyme-substrate complex formation

Michaelis-Menten kinetics and analysis

Competitive inhibition

Non-competitive inhibition

October 1 - (MS) Enzymes: Catalysis

Lysozyme: structure

Lysozyme: enzyme mechanism

Ribonuclease

Carboxypeptidase

Chymotrypsin

Proteases

Catalysis by folded RNA

October 6 - (MS) Regulation at the Protein Level

Amount of enzyme

Compartmentalization

Feedback regulation of ATCase

Phosphorylation - mechanism

Activation by proteolytic cleavage

Endogenous Inhibitors

Clotting

October 8 - **Midterm Exam** - covers material through October 1

October 13 - (MS) Membranes: Bilayers and Compartments

Lipid structure

Micelles and bilayers

Bilayer dynamics

Permeability

Partitioning into bilayers: protein sidechains

Protein secondary structures in bilayers

Prediction of transmembrane helices

October 15 - (MS) Membranes: Protein structures, Ion channels and

Pores

Gap junctions: structure and properties

Porins: a structural alternative

Patch clamps and conductance measurements

The acetylcholine receptor

How a channel works: potassium channel structure

Sodium channels

Potassium channels

Permeases

October 20 - (MS) Membranes: Active transport

Active transport requires net energy input

The sodium-potassium ATPase

Calcium pumps

Symport and antiport

Bacteriorhodopsin: a light-driven proton pump

October 27 - (MRK) Carbohydrates

What are carbohydrates?

Monsaccharides

Oligosaccharides

Polysaccharides

Glycoproteins

Special topic: discovery of lysozyme and penicillin: is there luck in science?

October 29 - (MRK) Principles of Metabolism

What is metabolism?

Six principles:

1. Metabolism is controlled kinetically by enzymes
2. Metabolic reactions occur in many small steps - "pathways"
3. A few important molecules carry the "currencies" of metabolism
4. Coupled reactions drive energy-requiring processes
5. Metabolic pathways are regulated and integrated
6. Biosynthetic and degradative pathways are distinct

Special topic: How is biomedical research organized and funded? Who sets policy?

November 3 - (MRK) Glycolysis

What is glycolysis?

The 10 steps of glycolysis

The chemical logic of glycolysis

Mechanisms of important glycolytic enzymes

Regulation: theoretical considerations

Special topic: History of glycolysis research

November 5 - (MRK) **15 min. quiz** on glycolysis. Lecture:

Glycolysis and Gluconeogenesis

15 minute quiz: write down the glycolytic pathway

Regulation of glycolysis: how it works in practice

Chemical steps of gluconeogenesis

Coordination of glycolysis and gluconeogenesis

November 10 - (MRK) Citric Acid Cycle

What is the citric acid cycle?

The chemical steps of the cycle.

The unprecedented stereospecificity of aconitase

Pyruvate dehydrogenase - a multienzyme complex

Regulation of the cycle

Plants are more clever than humans

Special topic: vitamins and nutrition

November 12 - (MRK) Electron transport and oxidative phosphorylation

What is electron transport & ox. phos?

Energetics of the process

What are the electron transport carriers

Cytochrome reductase: how it pumps protons

Coupling of electron transport to ATP synthesis

ATP synthase makes ATP by spinning

Efficiency of the complete oxidation of glucose

Special topic: imaging a single molecule of ATP synthase spinning

November 17 - (MRK) Lipid metabolism

Fat (triacylglycerols) for energy storage

Transport of fats in the bloodstream

Oxidation of fat for energy

Synthesis of fat for storage

Regulation of fat utilization

Cholesterol biosynthesis and regulation

Cholesterol transport

Cholesterol and heart disease

Special topic: miracle cures for obesity

December 1 - (MRK) Glycogen metabolism and other metabolic pathways.

Reactions and logic of glycogen metabolism

What other metabolic pathways are there?

Review of the principles of metabolism

Extra special topic: Photosynthesis

December 3 - (MRK) Integration of metabolism

Crossroads in metabolism

Organ specialization

Starvation

Hormones that control metabolism

Special topic: Research in the Koelle lab

December 8 - (MRK) Hormone signaling

What are hormones?

Mechanism of signaling by the hormone epinephrine

Diseases caused by signaling defects

Special topic: Signaling for survival.

December 10 - (MRK) Protein engineering for optogenetics

Green fluorescent protein (GFP)

Engineering GFP to make different colors

Engineering brains for optical clarity

Engineering split GFP

Engineering GFP as a Ca²⁺ sensor

Engineering optical control of neurons

Summary: the power and value of biochemistry

FINAL EXAM:

December 19, 2 pm, location TBA

November 19 - **Mid-term Exam** covers lectures through November 12