

**Instructor:** Jim Russo

**How to reach me:**

**via Email:** [russo@whitman.edu](mailto:russo@whitman.edu)

**via Voicemail:** 527-5228

**via Office:** S-352. Office hours: M 1-2 pm; T 3-4 pm; W 9-10; F. You are welcome to drop in anytime my door is open or make an appointment for other times as well. I'm in the biochem lab on W,Th afternoons (S-317) and that also provides good time for questions.

**In case of emergency:** You may call me at home.

**How to reach others in class:** The email address for our class list is [bbmb325@whitman.edu](mailto:bbmb325@whitman.edu)

**Class meets:** In Rm S-142 325 A M,T,Th 9:00-9:50 a.m. AND 325 B M,T,Th 11:00-11:50 a.m.

**Text:** *Biochemistry*, by Jeremy Berg, John Tymoczko, and Lubert Stryer. 6E, 2007.

**Course Goal:** To enhance your understanding of and appreciation for the relationship of molecular structure to biological function.

**Course Content:** In this semester of the BBMB trilogy (biochemistry, biophysics, and molecular biology), we will focus on the role of proteins in conferring specificity in molecular recognition and catalysis. We will also study protein interactions with lipids and carbohydrates, since these molecular complexes participate in signal transduction and cell recognition. The analysis of nucleic acids and gene expression is the prime focus for the BBMB 326 (Molecular Biology) course. The physical methods for studying and predicting biomolecular structure and function will be the focus for the BBMB 324 (Biophysics) course.

<b>Assessment:</b>	Examlets 1 - 4 (70 pts. ea. x 4)	280	(56 %)
	Biochemistry Update (BU)	60	(12 %)
	In-class problems & contributions	20	( 4 %)
	Comprehensive Final	140	(28 %)

**Examlet schedule:** Note **February 5, February 26, March 31, April 23, May 15/19**, the **near-immutable** exam dates. You must make arrangements with me at least three days before the exam to arrange an alternate time to take the exam if you have a legitimate schedule conflict. Make-up exams will only be given when an absence is excused in writing by the Student Health Center or the Dean of Students. If you have any known exam or other needs due to disability, please see me during the first week of class.

**Classroom etiquette:**

- 1) Class starts @ 9:00 & 11:00. Late entry to the classroom can be very disruptive. If you are having difficulty getting out of a previous class on time, please come talk with me.
  - 2) Cell phones & earbuds: OFF. Hats: NO. Shoes: YES. Eating and drinking in class: OK if discreet. (fyi, my coffee preference is medium roast, all the caffeine nature provided, no adulterants)
- Lack of adherence to classroom etiquette may result in a lowering of your course grade.

**Class materials:** via **CLEo**. This site will contain folders with files for: Course syllabus, Class outlines & images, Biochem Update papers and presentations, Exams and reviews. PDF files are best opened by Acrobat Reader.

**In-class time:** Our class periods will include a wide mix of learning opportunities, including: lecture time; viewing, interpretation, and discussion of visual images, data, and animations; in class problem solving; general question and discussion time; and the biochem update presentations and discussions. I strongly recommend bringing your textbooks to class if you like to make notes in the margins or on the figures used in class and copies of the class outlines. In addition, the BU papers are essential for those presentation days.

• **In-class problems (ICP)/ graphics interpretations/summaries:** You will be asked to contribute by proposing strategies and solutions to the ICPs or by providing interpretations of data, figures and images used in class. The ICPs, frequently exams problems from the past year(s), are embedded in the class outlines. Quality time spent

thinking about, struggling with, and working through problems and figures is one of the best indicators of your comprehension of course material and your preparedness for exams.

• **Biochemistry Updates (BU):** There are many fascinating new developments in biochemistry, which can't be incorporated into the text. Part of the excitement of these events comes from learning about them first hand, and sharing that knowledge and excitement with one's peers. Therefore, you will have an opportunity to present a **15-minute** summary of a recent, primary research paper which complements or extends our text readings and class discussion.

**BU Guidelines:** The presenters will be expected to give a cogent summary of the salient points of the assigned article(s). The use of pertinent graphics will be essential. A short outline (1-2 pages max) handed out in class before your presentation is essential and a well-crafted outline will serve as a useful guide for your colleagues. Your presentation to the class will require advanced planning. I expect that you will come by to see me to discuss strategies for presenting your topic (what to include, questions on pronunciations, use of graphics). All articles will be available as PDF files on CLEo. They can also be obtained as full-text articles online (Free full-text access to *Science* is available from terminals in Penrose or our classroom; *J Biol Chem*, *PNAS* and *Nature* are available from any Whitman networked terminal). You will want to obtain high-resolution images or video from the original, full-text articles. Original articles in *Science*, *PNAS*, and *Nature* also have supplementary information (additional figures or methods) that can only be obtained online.

#### *Oral Presentation of BU*

Some essentials for quality oral presentations:

- A well-crafted, 1-2 page outline for your audience.
- Practice your talk to make sure it fits into the designated time frame. You will not be rewarded for going beyond 15 minutes!
- Be familiar with the operation of your high-tech presentation devices (overhead projector or computer). Check your presentation at least 1 day in advance to confirm formatting and compatibility with our class computer or your laptop.
- Part of the success of oral communication resides in how you present yourself to your audience. Eye contact, good posture, voice projection, confidence, style of dress (hats and shorts, no; shoes, yes)... all contribute to how well your message is received.
- Some of you may not be comfortable speaking in front of your colleagues. If you find standing in front of an audience of your peers challenging, please come talk with me before your talk. I would be happy to discuss strategies for effective oral presentations.

**Out of class time:** I, and students who have taken this class before you, strongly recommend that you make your **first** read of the text AND class outline **prior** to coming to class. The class outlines will contain topics for each chapter in our text. They will highlight the text material that I want you to focus on, as well as add topics/vocabulary that are not in the text. Write down questions or comments so that you can ask them in class (or in lab, in office hours, or post your questions to the class e-mail list). Don't procrastinate with questions or confusions which arise from vocabulary or concepts presented in class, from your readings, or your class outlines. Sources of problems may include the suggested end-of-chapter problems in our text (see below), previous course exams, questions addressed in class, biochemistry updates, and your own intellectual curiosity.

• **Suggested end-of-chapter problems from your text:**

Ch 1 – 10	Ch 9 – 2,4,10,13	Ch 15 – 1,3,7,8,9	Ch 27 – 1,2,8,9,10,11,12
Ch 2 – 3,4,6,9	Ch 10 – 7,19	Ch 16 – 3,8,9,10,14,16	
Ch 3 – 1,7,9,10,14,17	Ch 11 – 2,5,14	Ch 17 – 1,7,9,12	
Ch 7 – 3,5,6	Ch 12 – 7,8,9,11,12,13	Ch 18 – 1,3,4,5,6,10,14,15	
Ch 8 – 2,4ab,6,11,12	Ch 14 – 1,2,3,6,13,14	Ch 21 – 3,5,11,12	

**1/29 # 1 Novel molecular function: H<sub>2</sub>S as a Physiologic Signaling Molecule**

Yang G et al. H<sub>2</sub>S as a Physiologic Vasorelaxant: Hypertension in Mice with Deletion of Cystathionine  $\gamma$ -Lyase. *Science* 322:587-590, 2008. Also, see Newsfocus *Science* 320:1155-1157, 2008.

Methods: knock-out mice; cell culture; Western blot; immunohistochemistry; cardiac physiology

**2/3 #2 Experimental techniques: Genomic and Proteomic Analysis**

Tarun AS et al. A combined transcriptome and proteome survey of malaria parasite liver stages. *PNAS* 105:305-310, 2008.

Methods: *Plasmodium* ; GFP-tags; cell culture; drug targeting; SDS-PAGE; microarrays; mass spec

**2/12 # 3 Protein regulation: NO binding to hemoglobin**

Reynolds J et al. S-nitrosohemoglobin deficiency: A mechanism for loss of physiological activity in banked blood. *PNAS* 104:17058-17062, 2007.

Methods: RBCs; chemiluminescence; dogs; hemodynamics; quantitation of SNO

**2/19 # 4 Enzyme Structure & Mechanism: Active Site of an Hydrogenase**

Shima S et al. The Crystal Structure of [Fe]-Hydrogenase Reveals the Geometry of the Active Site. *Science* 321:572-5705, 2008. (Also see Perspective 321:498-99, 2008)

Methods: *Archaea*; purification; site-directed mutagenesis; x-ray crystallography; metal complexes

**3/2 Vis Ed Barry Stoddard Protein Engineering: Computational Design of Enzymes**

Jiang L et al. De-Novo Computational Design of Retro-Aldol Enzymes. *Science* 319:1387-1391, 2008.

Methods: computational design; enzyme kinetics; x-ray crystallography; molecular dynamics/modeling

**3/5 #5 Membrane topology: Inhibition of a membrane protease**

Rajendran L et al. Efficient Inhibition of the Alzheimer's Disease  $\beta$ -Secretase by Membrane Targeting. *Science* 320:520-523, 2008.

Methods: cell culture; protease assays; in vitro/in vivo inhibition assays; fluorescence microscopy.

**3/12 #6 Glycobiology: Engineering human glycoproteins in yeast**

Hamilton SR et al. Humanization of Yeast to Produce Complex Terminally Sialylated Glycoproteins. *Science* 313:1441-1443, 2006.

Methods: yeast glycoengineering; HPLC; SDS-PAGE & glycosidase assays

**4/9 #7 Insulin Resistance: O-glycosylation**

Yang X et al. Phosphoinositide signaling links O-GlcNAc transferase to insulin resistance. *Nature* 451:964-970, 2008.

Methods: cell culture; mice; transfection; immunoblotting; fluorescence; phosphorylation assays

**4/16 #8 Glucose Metabolism: Gestational diabetes**

Karnik, S et al. Menin controls Growth of Pancreatic  $\beta$ -Cells in Pregnant Mice and Promotes Gestational Diabetes Mellitus. *Science* 318:806-809, 2007. (Also see Perspective 318:729, 2007.)

Methods: transgenic mice; western blot; northern blot; immunofluorescence

**4/30 #9 Mitochondrial Disease: Mutations in Complex 1 of Electron Transport Chain**

Malfatti E et al. Novel mutations of *ND* genes in complex I deficiency associated with mitochondrial encephalopathy. *Brain* 130:1894-1904, 2007.

Methods: muscle biopsy; cybrid culture; in-gel activity assay; mtDNA analysis

**5/7 #11 Integration of metabolism: Lifespan, Type 2 Diabetes, and Diet**

Milne J et al. Small molecule activators of SIRT1 as therapeutics for the treatment of type 2 diabetes. *Nature* 450: 712-716, 2007.

Methods: enzyme kinetics; glucose/insulin profiles; molecular screening

## I. Protein Structure

- a. Amino acids
- b. 1° - 4° structure: covalent and non-covalent interactions of amino acids
- c. Protein folding and degradation
- d. Experimental techniques for
  - 1) purifying proteins
  - 2) characterizing/quantitating proteins
  - 3) characterizing/quantitating proteomes
- e. Regulatory strategies: allosterism

## II. Enzymes: Catalytic Specificity

- a. Biochemical reactions
- b. Role of catalyst: lower  $E_{act}$  by stabilizing transition state
- c. Kinetics of enzyme catalyzed reactions: Michaelis-Menten Model
- d. Substrates, products, and inhibitors at the active site
- e. Vitamins and cofactors (nutritional requirements)
- f. Mechanisms: flow of electrons from S  $\rightarrow$  P; role of active site groups

## III. Signal Transduction Across Membranes

- a. Molecular composition of membranes
  - Lipids, Carbohydrates, & Proteins
- b. Kinetics: Receptor - Ligand binding
- c. Regulatory strategies: kinases and phosphatases
- d. Case studies of receptor types
  - 1)  $\beta$ -adrenergic receptor coupled to trimeric  $G_s$ -protein (GPCRs)
  - 2) Insulin receptor as tyrosine kinase receptor (RTKs)
- e. Integration of signal transduction pathways

## IV. Energy metabolism

- a. Bioenergetics: Coupled reactions and ATP
- b. Nutritional requirements and food
- c. Origins and fates of Glucose
  - 1) glycolysis
  - 2) gluconeogenesis
  - 3) glycogen metabolism
- d. Catabolism of glucose to carbon dioxide coupled to ATP synthesis
  1. glucose to pyruvate to acetyl CoA
  - 2) citric acid cycle
  - 3) electron transport chain and oxidative phosphorylation
- e. Fatty acid oxidation
- f. Integration of metabolism: from starvation to obesity

## BBMB 325 Syllabus 2009

Date	Topic	Chap	In-class activity
20 Jan T	Introduction	1	
22 Jan Th	Amino acids	2	ICP Ch 2 Amino acid structure/charge
26 Jan M	Protein structure: 1° to 4°	2	
27 Jan T	Protein folding	2,23.2	
29 Jan Th	Experimental Techniques I	3	BU#1 H <sub>2</sub> S as physiologic vasorelaxant
2 Feb M	Experimental Techniques II	3	ICP Ch3 PAGE
3 Feb T	Experimental Techniques III	5.3,6	BU#2 Malaria Proteomics
<b>5 Feb Th</b>	<b>EXAMLET I</b>		
9 Feb M	Case study: Globins	7	ICP Ch 7 Hb-O <sub>2</sub> saturation curves
10 Feb T	Enzyme catalyzed reactions	8	
12 Feb Th	Enzyme kinetics	8	BU#3 S-NO Hemoglobin & Blood Donation
16 Feb M	NO CLASS- PRES DAY		
17 Feb T	Enzyme inhibition	8,35	ICP Ch 8 Kinetic plots
19 Feb Th	Enzyme mechanisms I	9	BU#4 Crystal Structure of an Hydrogenase
23 Feb M	Enzyme mechanisms II	9	
24 Feb T	Enzyme mechanisms III	9	ICP Ch 9 Drug binding at active site
<b>26 Feb Th</b>	<b>EXAMLET II</b>		
2 Mar M	Vis Ed: Enzyme design		Barry Stoddard, FHCRC
3 Mar T	Membrane molecules I	12	ICP Ch 12 Lipid structure
5 Mar Th	Membrane molecules II	11	BU#5 Membrane targeted inhibitor of β-secretase
9 Mar M	Signal Transduction/Kinases	35,10.3	ICP Ch 11 Oligosaccharide structure
10 Mar T	Receptors: GPCRs	14	
12 Mar Th	Receptors: RTKs	14	BU#6 Human Glycosylation in yeast
16-27 Mar	SPRING BREAK		
30 Mar M	Receptors: Integration	14	ICP Ch14 signal transduction
<b>31 Mar T</b>	<b>EXAMLET III</b>		
2 Apr Th	Intro Bioenergetics	15	
6 Apr M	Glycolysis I	16	ICP Ch 16 Glycolytic rxns
7 Apr T	NO CLASS- WUC		
9 Apr Th	Glycolysis II	16	BU# 7 O-GlcNAc & Insulin Resistance
13 Apr M	Gluconeogenesis	16	
14 Apr T	Glycogen metabolism	21	ICP Ch16/21 Fates of glucose
16 Apr Th	Pyruvate to Acetyl CoA	17	BU# 8 Menin & Gestational Diabetes
20 Apr M	Citric acid cycle	17	ICP Ch 17 Vitamin co-factors in AcCoA
<b>21 Apr T</b>	<b>Metabolism I: Integration</b>		
<b>23 Apr Th</b>	<b>EXAMLET IV</b>		
27 Apr M	Ox phos I	18	
28 Apr T	Ox phos II	18	ICP Ch18 Electron transfer and ATP syn
30 Apr Th	Ox phos III	18,19	BU #9 Mito complex I Deficiencies
4 May M	Fatty Acid oxidation	21	
5 May T	Fatty Acid oxidation	21	ICP Ch21 Fates of C in FA metabl
7 May Th	Malnutrition: obesity	27	BU#10 Sirt1 Activators: Diabetes & Lifespan
11 May M	Malnutrition: starvation	27	
12 May T	Metabolism II: Integration	27	
<b>FINAL EX</b>	Sect A (9:00) F 5/15 9-11 am Sect B (11:00) T 5/19 9-11		