

Instructor: Dr. M. Brauer, mbrauer@uoguelph.ca x 53795 Science Complex 3520.

Lectures: Monday Wednesday Friday 12:30 - 1:20, MacK 115.

Office Hours: Monday Wednesday Friday 1:30 - 2:20, OR e-mail me!

Suggested Textbooks (**not required**):

Very Highly recommended:

Nelson and Cox, *Lehninger's Biochemistry* - 6th Edition, 2013, Voet and Voet, *Biochemistry* - 4th Edition, 2011 or Mathews, Van Holde, Appling, Cahill, *Biochemistry* 4th Edition, 2013. Detailed and comprehensive texts, esp. for metabolism and chemical mechanisms.

Other Highly recommended:

Voet and Voet, *Biochemistry* - 3^d Edition, 2004, Berg, Tymoczko and Stryer, *Biochemistry* - 6th Edition, 2006; Voet and Voet 2nd Edition, 1995; Matthews, Van Holde, Ahern, *Biochemistry* - 4th Edition, 2012; McKee and McKee, *Mol. Basis of Life*, 5th Edition 2012; or *Lehninger's Biochemistry*, Nelson & Cox, 2005.

You need **not** buy a new book, if you already have any of these. These books are on reserve at the library.

Objectives:

This course presents an in-depth study of metabolic pathways. The governing role of **free energy** in determining the extent and direction of reactions will be used as a guiding principle to demonstrate the patterns and associations that contribute to the ordered functioning of a complete biochemical system. Principles of **organic reaction mechanisms** will be introduced and used to demonstrate the chemical logic governing synthesis and breakdown of the major groups of biochemical substances. A basic organic chemistry background (nucleophiles, electrophiles, electron pushing) is *assumed*. **Regulatory mechanisms** and their roles in integrating complete biochemical systems will be studied.

Presentation:

There will be three lectures a week. There are no labs or assigned readings, but you are responsible for **everything** that occurs in lecture. Problem sets will be given out to reinforce the lecture material. Solutions to these problems will be given out.

Policy on Missed Examinations:

If you miss an exam or assignment, you **must** have documentation. Only valid excuses (medical or compassionate reason) will prevent a grade of zero for any missed test. It is the student's responsibility to arrange for the necessary verification from the Medical or Psychological Services or the Director of Student Affairs. *Make-up tests will not be given.*

Course Evaluation:

The course grade will be based on performance on two midterms (in class, 16% each), assignments (10%), a term paper on a current research paper (24%) and a cumulative final examination (34%).

Learning Outcomes:

By the end of this course, successful students will be able to:

1. Critically evaluate a scientific claim with human health implications for a primary research article published in the last year.
2. Explain the role of entropy and enthalpy, Gibbs free energy change, equilibrium constants, coupled reactions and redox reactions in biochemical processes.
3. Understand the four basic types of metabolic reactions, and the general mechanisms that most enzymes use to catalyze these reactions. Be able to predict how an enzyme should work, and what cofactors (vitamins) it needs to work.
4. Describe the key metabolic pathways, i.e. the overall purpose, reactants and products, tissue distribution and metabolic regulation and coordination between glycolysis, the TCA cycle (catabolic and anabolic), electron transport, oxidative phosphorylation, fat breakdown and biosynthesis, ketone bodies, cholesterol biosynthesis, amino acid breakdown and biosynthesis and nucleic acid metabolism.
5. Explain how disorder of metabolic regulation results in important medical consequences, such as increased glycolysis in tumours, insulin resistance and diabetes in obesity, reactive oxygen species and free radical damage in electron transport disruption, atherosclerosis in high cholesterol states and neurotransmitter imbalance in amino acid metabolic dysfunction.

Examination Schedule:

Midterm Examinations: There will be 2 in-class midterm exams. Persons with a scheduled academic conflict should inform the instructor immediately. Alternative midterm exams will be arranged where appropriate and possible.

Final Examination: The Registrar sets the time (Friday, Dec. 16, 11:30 - 1:30 pm) and location (to be determined.) The final exam is cumulative, but will stress material since the last midterm. A metabolic map will be provided on the final exam.

Exam aids: No materials may be brought to the exam except for pencils, pens and an eraser. No electronic devices (other than calculators), pencil cases, purses, bags, tissue boxes or other containers may be present. All materials are subject to inspection.

Academic Misconduct: The University of Guelph is committed to upholding the highest standards of academic integrity and it is the responsibility of all members of the University community - faculty, staff, and students - to be aware of what constitutes academic misconduct and to do as much as possible to prevent academic offences from occurring. University of Guelph students have the responsibility of abiding by the University's policy on academic misconduct regardless of their location of study; faculty, staff and students have the responsibility of supporting an environment that discourages misconduct. Students need to remain aware that instructors have access to and the right to use electronic and other means of detection.

Students who are in any doubt as to whether an action on their part could be construed as an academic offence should consult with a faculty member or faculty advisor.

The Academic Misconduct Policy is detailed in the Undergraduate Calendar:

<http://www.uoguelph.ca/registrar/calendars/undergraduate/current/c08/c08-amisconduct.shtml>.

Detailed Course Outline - Approximate Time Line

1. Introduction to Thermodynamics - forms of energy, life and the second law.
- 2 & 3. Free Energy - free energy of formation, coupled reactions.
4. Free Energy Calculations - free energy of hydrolysis, bioenergetic status.
5. Redox Reactions and Free Energy - standard potentials, Nernst equation.
6. Metabolic Flux and Metabolomics.
7. Introduction to Reaction Mechanisms.
- 8 & 9. Glycolysis - Reaction Mechanisms.
- 10 & 11. Glycolysis - Bioenergetics and Regulation.
12. Start and End of Glycolysis - glycogen, glucose, lactate, ethanol, tumours.
13. Pyruvate Dehydrogenase - Mechanism of Action.
- 14 & 15. TCA Cycle - Mechanisms, Bioenergetics and Control.
16. TCA Cycle - Anaplerotic Reactions, Fat vs. CHO.
17. Electron Transport-components, leakage of electrons, free radical scavengers.
- 18 & 19.

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- 20. Compartmentation and Transport in the Mitochondria.
- 21. Triglycerides and Fatty Acids - lipoproteins, transport and β oxidation.
- 22 & 23. Ketone Bodies, Terpenoids.
- 24 & 25. Cholesterol Metabolism, Steroid Biosynthesis and Function.
- 26 & 27. Amino-acid catabolism, Mechanism of Action of Pyridoxal Phosphate.
- 28. The Urea Cycle.
- 29 & 30. Amino Acid and Neurotransmitter Biosynthesis.
- 31. Beyond Amino Acid Biosynthesis - nitric oxide synthase, folate.
- 32. Amino Acids and Porphyrin Biosynthesis.
- 33 & 34. Pyrimidine Biosynthesis, Purine Catabolism - xanthine oxidase and hypoxia.
- 35 & 36. Review of Coenzymes, Metabolic Regulation and Integration of Pathways.