Dr. HM Lacker Fall 2006

BME 381
Engineering Physiology I

The Department of Biomedical Engineering

CLASS HOURS
Monday 1-2:30 pm (Cullimore: Lecture Hall III)
Wednesday 1-2:30 pm (Cullimore: Lecture Hall III)

Recitation Sessions: (go over homework and review class material)

OFFICE HOURS (Fenster 615)
Email: hmlacker@aol.com

TEXT
Modeling and Simulation in Medicine and the Life Sciences, 2nd Edition, Hoppensteadt & Peskin
ISBN:0-387-95072-9 (required)

Human Physiology, From Cells to Systems, 4th Edition, Sherwood,
ISBN: 0-534-56826-2 (reference)

COURSE DESCRIPTION
Prerequisites: Math 111, Math 112, CIS 101, Phys 111, Phys 121, Chem 125, Chem 126, BME 106

This is the first of a pair of 1 semester courses (BME 381,382) that introduce students to the modeling of organ function and organ systems of the human body. The subjects covered are similar to those taught in introductory systemic physiology courses in medical school, biology or biomedical engineering departments (BME 106). The approach, however, is that of an engineer integrating and applying quantitative concepts acquired in basic undergraduate physics, chemistry, mathematics, and computer science courses to the modeling of dynamical systems of the human body with feedback control. Emphasis will be placed on feedback control, mathematical modeling, and numerical simulation.

BME 381 and BME 382 are similar courses and differ primarily in the physiological systems for which the students learn to develop models.

COURSE OBJECTIVES
The course objectives are to enable biomedical engineering students to apply some of the basic tools that they have learned in electrical and mechanical engineering analysis, mathematics, computer science, general physics and chemistry courses so that they can develop models that quantitatively predict the functioning of physiological systems in the human body. Such models provide quantitative insight into the normal feedback mechanisms that control physiological variables of the human body. This quantitative approach applies engineering systems analysis to systemic physiology and employs the ideas of feedback control, signal processing, mathematical modeling and numerical simulation. This engineering approach to physiological function is designed to give the student the potential to better understand human disease and to use this understanding for the construction of new technologies for diagnosis and treatment.

TOPICS COVERED

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Topics covered in this course include: Electrical properties of cells and cell membranes; design of the nervous system, regulation of cell volume, the Hodgkin-Huxley voltage clamp, the spaced-clamp action potential, introduction to cable properties of neurons, propagating action potential, and synaptic transmission, Gas exchange in the lungs; single alveolus model, multiple alveolar models with non-uniform ventilation and perfusion, transport of gases that dissolve in blood as simple solutions and gases like oxygen that are bound to carriers (oxyhemoglobin), ventilation perfusion ratios that achieve optimal transport, deviation from optimal transport as measured by the difference between arterial partial pressure of a gas and its partial pressure at end expiration (mixed alveolar air) ,computer projects concerning oxygen transport by the lung.

LEARNING OUTCOMES

By the end of the course you should be able to do the following:

- **Modeling:** Apply knowledge of math, engineering and science to understand the principles of modeling physiological and biophysical systems.

- **Computer Simulation:** Learn to utilize Matlab software to program numerical solutions to physiological and biophysical processes.

- **Physiological Applications:** Apply knowledge of math, engineering and science to identify formulate, and solve problems in physiology and biophysics and learn theoretical tools and methodology that are needed to design effective, efficient and safe equipment that interact with and assist physiological systems.

COURSE OUTLINE*

Date	**Topic**	**Material**	**Recitation Class Work (Weekly Meeting)**	**Assignment**
9/6	Osmotic problem posed by impermeable intracellular proteins. Simple models of Cell Volume Regulation in Plant and Animal Cells (formulation of flux equations for uncharged solutes, water flow, and Na-K pump)	Chapters 3.1, 3.2		Start Reading Chapter 3, Sections 1 and 2.Exercise problem: 3.1

9/11	Steady-State Solution of Simple (Uncharged) Volume Regulation Model and interpretation of the effect of physiological parameters: on steady-state intracellular concentrations and cell volume	Chapter 3.1,3.2	Formulate, Solve and Analyze system equations when sign convention for positive flux is changed and when the Na-K pump directions and ratios change. Consider the case of theoretical artificial membranes that have both pumps and significant material elasticity	Finish Reading Chapter 3, Sections 1 and 2 Exercise problem: 3.2
:9/13	Derivation of the Osmotic Pressure Equation from energetic arguments and the work of concentrating an ideal gas	Chapter 3.1,3.2		Exercise Problem 3.3
9/18	Dynamics of the Uncharged Cell Volume Regulation Model	Class Notes	Review HW problems 3.1 -3.3	Study Class Notes
:9/20	Numerical Solution of the Initial Value Problem (Euler's Method) for the Uncharged Dynamic Model of Cell Volume Regulation	Class Notes		Create Computer Program to Solve for Transients to Hand out Initial Value Problems for Uncharged Cell Volume Regulation Model (1 wk. assignment)
9/25	Generalization of the Numerical Method for other First Order Dynamical Systems, application to the single pendulum with small and large amplitude oscillation, with and without friction, multiple (stable and unstable) steady states	Class Notes	Review Numerical Solutions to Assigned Initial Value Problems and Check for consistency of sufficiently large time values with Analytic Solutions of the Steady State	(same as above)
9/27	Movement of Charged Ions across Cell Membranes, Derivation of the linear Hodgkin Huxley Current-Voltage Equations and the Equilibrium Nearnst Potential from Energetic arguments	Chapter 3.3		Exercise Problem 3.4
10/2	Reformulation of the Cell Volume Regulation	Chapter 3.4	Review Solution to Problem 3.4	Read Section 3.4

	Model with charged ions and the interaction of electrical and osmotic effects			
10/4	Solution of the Steady State (charged) Cell Volume Regulation Model in the limit of small membrane Capacitance: interpretation of the physiological parameters including pump rate on steady-state intracellular ion concentrations and cell volume and resting membrane potential	Chapter 3.4		Exercise Problem 3.5
10/9	Dynamics of (charged) Cell Volume Regulation Model with voltage independent ion conductances (non – excitable cells)	Class Notes	Review Solution to Exercise 3.5	Study Class Notes
10/11	Introduction to Transient Changes in Membrane Potential in Nerve and Muscle: Model 1: Small Capacitance limit, K and Na time dependent conductances given, derivation of membrane potential as a weighted average of ion equilibrium potentials (Goldman Equation)	Chapter 3.5		Read Chapter 3.5(pp.124-125) Exercise Problem 3.6
10/16	Hodgkin-Huxley Membrane Voltage Clamp.Experiment and the Measurement of Voltage Dependent Transients in K and Na Conductance	Chapter 3.5 and Class Notes	Review Solution to Exercise Problem 3.6	Read Chapter 3.5 and Class Notes
10/18	Model first order equation for K (n gated) channel	Chapter 3.5 and Class Notes		Read Chapter 3.5 and Class Notes
10/23	Steady state and transient solutions for K conductance in the voltage clamped membrane	Chapter 3.5 and Class Notes	Applications of Goldman Equation in predicting membrane voltage and ion currents in artificial	Read Chapter 3.5 and Class Notes on Graphical and Exponential Solutions to First Order Linear Differential Equations

			membranes with given conductances separating infinite baths with given ionic concentration	with Constant Coefficients
10/25	Model first order equations for Na (m and h gated) channel)	Chapter 3.5 and Class Notes		Read Chapter 3.5 and Class Notes on Graphical and Exponential Solution to First Order Linear Differential Equations with Constant Coeffiecinets
10/30	Steady state and transient solutions for Na conductance in the voltage clamped membrane		Review time dependent K and Na conductance curves of Hodgkin Huxley Voltage Clamp Experiments and relate curves to theoretical solutions to model equations for n, m and h dynamics with given step changes in membrane voltage	
11/1	Formulation of the time dependent Hodgkin Huxley Model Equations for Nerve Axon Membrane Potential	Chapter 3.5 and 3.6		Finish Chapter 3.5 and begin reading Chapter 3.6
11/6	Numerical Solution of the time dependent Hodgkin Huxley Equations for small initial voltage deviations from the steady state resting potential. Local stability of the Resting potential.	Chapter 3.6 and 3.7	Review Euler Method for Numerical Solution of First Order Systems of Differential Equations (discussed and applied in week 3)	Read Chapter 3.6 Write Computer Code to Solve Nerve Impulse Simulation Problems (1 wk. assignment)
11/8	Action Potential Solution of the Hodgkin Huxley Equations for initial voltage deviations above the threshold voltage. Numerical solution of the threshold membrane voltage using the method of bisection	Chapter 3.7		Solve Nerve Impulse Simulation Project (1 wk. assignment)

	Introduction to the space and time dependent Hodgkin Huxley Equations in a 1-dimensional model of the Nerve axon. The wave propagated action potential and saltatory conduction in myelinated nerve	Class Notes and Animation Materials	Review numerical solution to Nerve Impulse Simulation Project. Exam Review	Study for Exam
11/15	Exam on Nerve			
11/20	Introduction to Gas Exchange in the Lungs: Review of Anatomy, Ideal Gas Law and Gas Solubility in Blood	Chapter. 2.1		Read Chapter 2.1
11/22	No class – classes follow a Friday schedule			
11/27	Equations of Gas Transport in One Alveolus and the significance of the Ventilation-Perfusion Ratio	Chapter 2.2	Review Exam Solutions	Read Chapter 2.2 Exercise Problem 2.1
11/29	Gas Transport in the Lung as a whole (Multiple Alveolar System with non-uniform distribution of ventilation and perfusion)	Chapter 2.3		Read Chapter 2.3 Exercise Problem 2.2
12/4	Optimal Gas Transport in the Lung: Review of Langrange's Method for Obtaining Critical Points of Functions with Constraints	Chapter 2.4 & 2.5	Review Solution to Exercise Problems 2.1 and 2.2	Read Chapter 2.4 & start Chpater 2.5 Exercise Problem 2.3 and 2.4
12/6	Transport of Oxygen: Non linear solubility due to the presence of Hemoglobin (Oxygen Dissociation Curve)	Chapter 2.6		Finish Chapter 2.5, Start Chapt 2.6 Exercise Problem 2.5
12/11	Qualitative Analysis of Oxygen Transport and the Dual Optimization Transport Problem	Chapter 2.6 & 2.7	Review solutions to Exercises 2.3,2.4,2.5	Finish Chapter 2.6 begin Chapter 2.7 Exercise Problem 2.6
12/13	Computer Solution of the Equations for Oxygen Transport	Finish Chapter 2.7		Review for Final Exam
TBA	Final Exam		Review solution to Exercise 2.6	

			Review for Final Exam	

***The Course Outline may be modified at the discretion of the instructor or in the event of extenuating circumstances. Students will be notified in class of any changes to the Course outline and schedule of studio sessions.**

GRADING
4 Quizzes (Unannounced): 40%
Midterm Exam: 30%
Final Exam: 30%

Attendance is mandatory. Failure to attend class regularly will result in a failing grade.
No makeup examinations will be administered. If a valid, documented excuse for a missed exam is provided, the weight of the Final Exam will increase to compensate for the missed grade.

Honor Code Violations/Disruptive Behavior: NJIT has a zero-tolerance policy regarding cheating of any kind and student behavior that is disruptive to a learning environment. Any incidents will be immediately reported to the Dean of Students. In the cases the Honor Code violations are detected, the punishments range from a minimum of failure in the course plus disciplinary probation up to expulsion from NJIT with notations on students' permanent record. Avoid situations where honorable behavior could be misinterpreted. No eating or drinking is allowed in class. Cellular phones must be turned off during the class hours.

CONTRIBUTION OF COURSE TO MEETING THE PROFESSIONAL COMPONENT
This course meets the professional component by introducing students to the general study and function of each of the major organs and systems of the human body. Students are taught to approach hypothetical situations by employing engineering concepts and ideas of feedback control, signal processing, mathematical modeling, and numerical simulation. In this way a hierarchy of models will be constructed. This course prepares students for careers which can include heath-related professions as well as various professional within biomedical engineering.

RELATIONSHIP OF COURSE TO PROGRAM OUTCOMES
Successful understanding and application of quantitative physiology requires an integration of multiple disciplines including chemistry, physics, electrical engineering, mechanical engineering, mathematics and computer science. Students will engage in studio lab projects that will involve programming skills to build models and simulate solutions to physiological and pathological conditions such as exercise or hemorrhage. The ability to identify, formulate, and solve problems related to physiological processes is practiced throughout the course through the use of in-class examples, homework problems, and exams. The ability to communicate effectively and to write well is exercised on exams through the use of short-answer and essay type questions in which students must clearly explain and justify their answers not only through calculations.

BME 381: Learning Outcome Summary

Outcome # 1. Apply knowledge of math, engineering and science to understand the principles of modeling physiological and biophysical systems		
Strategies & Actions	**Program Outcomes**	**Assessment Methods**
Hierarchical Models of Physiological and Biophysical Systems are formalized into self-consistent and complete mathematical systems; available data is used to identify normal and/or pathological model parameters; steady-state and dynamical closed form and/or numerical solutions are constructed; solution analysis related to model limiting behavior, model self-consistency, physical and physiological plausibility are explored.	A,E,K,L,M	Homework, Recitation Sessions, Quizzes, Examinations
Outcome # 2. Learn to utilize Matlab software to program numerical solutions to physiological and biophysical processes		
Strategies & Actions	**Program Outcomes**	**Assessment Methods**
Numerical Solutions to non-linear systems of differential equations are obtained using simple (Euler) explicit finite difference equations. Root finding algorithms (Bisection, Newton or Newton like methods) are employed to solve algebraic implicit systems when explicit solutions to variables can not be obtained in closed form. Numerical solutions are compared to limiting analytic solutions to test for logical coding errors and self-consistency.	A,E,K,L,M	Homework, Recitation Sessions, Quizzes, Examinations
Outcome # 3. Physiological Applications: Apply knowledge of math, engineering and science to identify formulate, and solve problems in physiology and biophysics and learn theoretical tools and methodology that are needed to design effective, efficient and safe equipment that interact with and assist physiological systems.		
Strategies & Actions	**Program Outcomes**	**Assessment Methods**
(see also Strategies & Actions for Outcome #1) Model Solutions are analyzed to strengthen intuition and insight into physiological system behavior and possible implications for effective, efficient and safe equipment design.	A, E,K,L,M,O	Homework, Recitation Sessions, Quizzes, Examinations

Person(s) who prepared this description and date of preparation: Dr. H. Michael Lacker, January 2006

ABET Outcomes expected of graduates of BME BS program by the time that they graduate:

(A) an ability to apply knowledge of mathematics, science, and engineering
(B) an ability to design and conduct experiments, as well as to analyze and interpret data
(C) an ability to design a system, component, or process to meet desired needs within realistic constraints such as economic, environmental, social, political, ethical, health and safety, manufacturability, and sustainability
(D) an ability to function on multi-disciplinary teams
(E) an ability to identify, formulate, and solve engineering problems
(F) an understanding of professional and ethical responsibility
(G) an ability to communicate effectively
(H) the broad education necessary to understand the impact of engineering solutions in a global, economic, environmental, and societal context
(I) a recognition of the need for, and an ability to engage in life-long learning
(J) a knowledge of contemporary issues
(K) an ability to use the techniques, skills, and modern engineering tools necessary for engineering practice.
(L) an understanding of biology and physiology
(M) the capability to apply advanced mathematics (including differential equations and statistics), science, and engineering to solve problems at the interface of engineering and biology
(N) an ability to make measurements on and interpret data from living systems
(O) an ability to address problems associated with the interaction between living and non-living materials and systems