Topics in Biophysics (3 or 4 credits)

Department of Physics, Universidad de los Andes

Course code: FISI4882 (graduate) y FISI3882 (undergraduate)

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Office hours: Wednesday 3-4 pm.

Guide Texts: Physical Biology of the Cell, First or Second Edition, Phillips, Kondev, Theriot, Orme (Main Text). Biological Physics, Energy, Information, Life. Philip Nelson, Updated First Edition

Thermal Biophysics of Membranes, Thomas Heimburg.

Course Instructors: Chad Leidy (Department of Physics).

1. **Description of the Course**

**What is Biophysics?**

Biophysics is the field that applies the theories and methods of physics to understand how biological systems work. Biophysics has been critical to understanding the mechanics of how the molecules of life are made, how different parts of a cell move and function, and how complex systems in our bodies—the brain, circulation, immune system, and others— work. Biophysics is a vibrant scientific field where scientists from many fields including math, chemistry, physics, engineering, pharmacology, and materials sciences, use their skills to explore and develop new tools for understanding how biology—all life—works.

In this course, we will begin by introducing the basic theoretical theories that biophysicists apply to do their work. In the second half, we focus our attention on cell membranes, which are fascinating biological assemblies with interesting properties and important physiological functions. These complex structures protect cells from outside conditions, and help the cell communicate with outside world, and respond to external factors. Their complexity and importance in cell processes makes them an interesting topic of study for the second part of this course.

**Objective of this course**

In this course, we will introduce students (coming from different fields, including physics, chemistry, biology, math, engineering) to the following main ideas:

**a)** Biological structures and the relation between structure and function for the main biomolecules.

**b)** The basic biophysical theory used to quantify and understand the behavior of biological systems, including the harmonic oscillator, free-energy and equilibration, tow-state systems. reaction kinematics, diffusion, hydrodynamics, and electrostatics in electrolyte solutions.

**c)** The basic experimental and computational techniques used to observe, measure, and quantify the biophysical processes.

**Learning objective:**

At the end of the course, students will be able to:

1. Describe molecular and structural aspects of biological molecules and their function in cells.
2. Be capable of analyzing the behavior of biological systems by modeling these systems using basic concepts in thermodynamics, statistical physics, electrostatics, and diffusion theory.
3. Identify the basic experimental and computational techniques needed to study biological systems.
4. Narrow down a scientific question in biophysics and write a research proposal regarding the proposed question.
5. **Prerequisites**

**1)** Thermodynamics or equivalent. Students that have taken Physical Chemistry may take the course.

1. **Evaluation system**

**Activities and points (3 credits)**

1. **(35%) Homework.**  Five homework assignments will be turned in throughout the semester. The homework assignments will include problems from Phillips and Nelson.
2. **(5%) First draft of essay analyzing two research publications in biophysics.** The student will choose two research publication that apply biophysical models to analyze a biological system. The student needs to introduce the topic, describe and discuss the theoretical models and findings. This first draft only identifies the papers and presents a small introduction of the general topic.
3. **(40%) Five quizzes.** Students will be required to write explanations about certain concepts covered in class and analyze mathematical models.
4. **Final presentations.**
5. **(10%)** Students will give brief 15 minute presentations of two selected papers during the time slot allocated for the final exam.
6. **(10%)** Final version of the essay describing and comparing in detail the findings of the two selected publications (maximum 6 pages).
7. Introduction to the topic
8. Description of results including a description of experimental, computational or theoretical techniques used.
9. Description and discussion and comparison of the results presented in the two selected publications.

**Activities and points (4 credits)**

1. **(20%) Homework.**  Five homework assignments will be turned in throughout the semester. The homework assignments will include problems from Phillips and Nelson.
2. **(10%) First Draft of Research Proposal.** These research proposals are written in teams of two students, and in English. Write the proposal using the rules of an R03 grant from the National Insitute of Health (6 pages maximum). This first draft is only a dirty outline of the grant, including the topic of research, an initial draft of its significance and innovation, an outline of the aims with brief descriptions, and some bibliography.
3. **(40%) Five quizzes every three weeks.** Students will be required to write explanations about certain concepts covered in class and analize mathematical models.

**Final presentations and final research projects.**

1. **(10%)** Students will give brief 15 minute presentations of their research proposals during the time slot allocated for the final exam.
2. **(20%)** Final version of the research proposal. The final version of the research proposal will include the following sections:
3. Specific Aims with extended descriptions.
4. Significance. General description of why the topic is important
5. Innovation. Why will this proposed research provide a significant advancement in this problem or field of research.
6. Approach. A more careful description of the experimental, computational, or theoretical methods used to address the specific aims.

(Entrega del 30%) more than 40% of the total grade will be turned in at the end of week 8, which includes grades for HW 1 and 2, preproposal or essay, and 20% from Quizes.

1. **Week to Week activities.**

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| **Class** | **Readings** | **Topic** |
| **Class #1**  What is Biophysics? What differentiates life from inert matter? Building models. | Phillips. Read read chapter 1 | 1.1 to 1.6   1. Description of program. 2. What does biophysics do? 3. What distinguishes Life from inert matter. 4. Biomolecules, structure and function. 5. Building models. |
| **Class #2**  Cell structures and size scales. | Phillips. Please read chapter 2. | 2.1 to 2.3   1. *E.coli* as our standard ruler. 2. Cells and structures within them. 3. Multicelular structures. |
| **Class #3**  Time scales, clocks and timelines in cells. | Phillips. Please read chapter 3. | 3.1 to 3.4   1. Temporal scales in biophysics 2. Procedural time in cell processes 3. Clocks and oscillators 4. Relative Time and the order of events. 5. Formation of bacterial flagellum 6. Killing the cell. Life cycle of viruses. 7. Manipulated time (chemical kinetics, breaking the diffusion limit in transport). |
| **Class #4**  Bless the little beasties. Model biological systems. | Phillips. Please read chapter 4. | 4.1 to 4.6   1. Choosing an adequate biological system to model behavior. 2. Hemoglobin as a model protein. 3. Bacteriophages and molecular biology 4. *E.coli* as a model system 5. Yeast as a eukaryote model. |
| **Class #5**  Mechanical and chemical equilibrium in living cells. | Phillips. Please read chapter 5. Sections 5.1 and 5.2 | 5.1 to 5.2   1. Energy and the life of cells. 2. Biological systems as minimizers |
| **Class #6**  Mechanical and Chemical equilibrium in cells. | Phillips. Please read chapter 5. Sections 5.3 to 5.6  **QUIZ#1**  **HW#1 due** | 5.3 to 5.6   1. Maximizing and minimizing to find equilibrium. 2. Configurational energy 3. Structures as free energy minimizers. |
| **Class #7**  Entropy rules! | Phillips. Please read chapter 6. Sections 6.1 and 6.2 | 6.1 to 6.2   1. The analytical engine of Statistical Mechanics. 2. Ideal gases and solutions. |
| **Class #8.**  Entropy rules! | Phillips. Please read chapter 6. Sections 6.3 and 6.4 | 6.3 to 6.4   1. Law of mass action. 2. Applications of the calculus of equilibrium. |
| **Class #9**  Two-state systems: From ion channels to cooperative binding. | Phillips. Please read  7.1 and 7.2 | 7.1 to 7.2   1. Macromolecules with multiple states. 2. State variable description of binding. |
| **Class #10**  Two-state systems: From ion channels to cooperative binding. | Phillips. Please read  7.1 and 7.2 | 1. Bacteriorhodopsin. |
| **Class #11**  Random walks and the structure of macromolecules | Phillips. Please read 8.1 and 8.2 | 8.1 and 8.2   1. Macromolecules and random walks |
| **Class #12**  Random walks and the structure of macromolecules | Phillips. Please read 8.3 and 8.4  **QUIZ#2**  **HW#2 due** | 8.3 and 8.4   1. Single molecule mechanics 2. Proteins as random walks |
| **Class #13**  Electrostatics in salty solutions | Phillips. Please read 9.1 and 9.2 | * 1. and 9.2  1. Chemistry and behavior of water 2. Electrostatics in salty solutions. |
| **Class #14**  Electrostatics in salty solutions | Phillips. Please read 9.1 and 9.2 | 9.2   1. Electrostatics in salty solutions. |
| **Class #15**  Beam theory | Phillips. Please read 10.1 and 10.2 | 10.1 and 10.2   1. Beams are everywhere: From flagella to the cytoskeleton. 2. Geometry and energetics of beam deformation. |
| **Class #16**  Beam theory | Phillips. Please read 10.3 and 10.4  **(3 credits) Draft of article analysis is due.**  **(4 credits) Draft of research proposal is due.** | 10.3 and 10.4   1. The mechanics of transcriptional regulation. 2. DNA packing: from viruses to eukaryotes |
| **Class #17**  Beam theory | Phillips. Please read 10.5 and 10.6 | 1. The cytoskeleton and beam theory 2. Beams and biotechnology |
| **Class #18**  Biological membranes | Phillips. Please read 11.1 and 11.2  **QUIZ#3**  **HW#3 due** | * 1. and 11.2   1) Nature of biological membranes  2) Springiness of biological membrane |
| **Class #19**  Biological membranes | Phillips. Please read 11.3 and 11.4 | 11.3 and 11.4   1. Structure and energetics of vesicles 2. Membrane and shapes |
| **Class #20**  Biological membranes | Phillips. Please read 11.5 | 11.5   1. The active membrane 2. Membrane domains |
| **Class #21**  Biological membranes | Heimburg Please read Chapter 6 and 7 | 1. Lipid phases transitions. 2. Lipid domains. |
| **Class #22**  Statistical view of biological dynamics | Phillips. Please read 13.1 to 13.2 | 13.1 and 13.2   1. Diffusion in the cell 2. Concentration fields and diffusive dynamics. |
| **Class #23**  Statistical view of biological dynamics | Phillips. Please read 13.3 | 13.3   1. Concentration fields and diffusive dynamics. |
| **Class #24**  Rate equations and dynamics of the cell. | Phillips. Please read 15.1 and 15.2  **QUIZ#4**  **HW#4 due** | 15.1 and 15.2   1. Biological statistical dynamics. 2. A chemical picture of biological dynamics. |
| **Class #25**  Rate equations and dynamics of the cell. | Phillips. Please read 15.3 | 15.3   1. The cytoskeleton is always under construction. |
| **Class #26**  Rate equations and dynamics of the cell. | Phillips. Please read 15.4 | 15.4   1. Simple models of cytoskeletal polymerization. |
| **Class #27**  Biological Electricity and the Hodgkin-Huxley Model | Phillips. Please read 17.1 to 17.3 | * 1. to 17.3   1) The role of electricity in cells.   1. The charge state of the cell. 2. Membrane permeability: pumps and channels. |
| **Class #28**  Biological Electricity and the Hodgkin-Huxley Model | Phillips. Please read 17.4 | 17.4   1. The action potential. |
| **Class #29**  Molecular motors. | Phillips. Please read 16.1 | 16.1   1. The life of molecular motors. Life in the noisy lane. |
| **Class #30**  Molecular motors. | Phillips. Please read 16.2  **QUIZ#5**  **HW#5 due** | 1. Rectified Brownian motion and molecular motors. |