Modeling and Control of Biomolecular Machines
EML 6934
Fall 2021, M W F, 7th Period, 1:55 PM – 2:45 PM
Zoom/MAE-B 238

Modifications to this syllabus may be required during the semester. Any changes that are made will be reflected in a posted version of the syllabus and announced in class.

Instructor
Assistant Professor Jing Pan, Ph.D.
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Observer: Assistant Professor Amor Menezes, Ph.D.
Department of Mechanical and Aerospace Engineering

Office Hours
• M F, 2:45 PM – 3:45 PM, Wertheim 485
• Or via confirmed email appointment

Course Description
This course overviews biomolecular systems engineering. The course introduces models of biological macromolecules, biochemical kinetics and thermodynamics, biomolecular interaction dynamics, models of cellular processes, energy transduction and mass transport, common gene regulatory network motifs, and the design of synthetic biology circuits. The course format consists of lectures, literature discussions, and problem sets. Literature case studies will show how the introduced concepts are implemented in experimental design to study/engineer biomolecular systems. (Credits: 3)

Course Objectives
This course introduces theoretical and experimental techniques to model molecular and cellular machinery in biological systems. By the end of the course, students will know how to:
• Use kinetic and thermodynamic concepts to understand biomolecular and cellular mechanisms;
• Construct rigorous mathematical models of these mechanisms; and
• Design experiments with these models to study and engineer the dynamics of biomolecular machines and networks.

Course Pre-Requisites
Differential equations (e.g., MAP 2302), and senior undergraduate or graduate standing

Materials and Supply Fees
None.

Required Textbooks, Software, and Hardware
• Python;
• Scientific calculator (not your phone).
• No required textbook. All reading materials will be provided.

Recommended Textbooks
• Uri Alon, *An Introduction to Systems Biology: Design Principles of Biological Circuits*, 2nd Ed.
• Domitilla Del Vecchio and Richard M. Murray, *Biomolecular Feedback Systems*
• Leah Edelstein-Keshet, *Mathematical Models in Biology*
• Terrell Hill, *Free Energy Transduction and Biochemical Cycle Kinetics*
• Brian Ingalls, *Mathematical Modelling in Systems Biology: An Introduction*
• John Kuriyan et al., *The Molecules of Life: Physical and Chemical Principles*
• Rob Phillips et al., *Physical Biology of the Cell*, 2nd Ed.

**Important Dates**
- Classes Begin: Aug 23rd (Monday)
- Holidays/Reading Days: Sep 6 (Monday), Oct 8 (Friday), Nov 24-26 (Wednesday – Friday)
- Classes End: Dec 8 (Wednesday)
- Homework dates stated in this syllabus will be confirmed in class

**Attendance Policy**
- The class has no attendance policy. Students are expected to attend.
- Absences are excused consistent with university policies in the graduate catalog ([https://catalog.ufl.edu/graduate/regulations/](https://catalog.ufl.edu/graduate/regulations/)) and require appropriate documentation.
- **Make-up Policy:** Instructor notifications are required in all circumstances. See [https://care.dso.ufl.edu/instructor-notifications](https://care.dso.ufl.edu/instructor-notifications). Note that, “Professors have the right to accept or reject the notification.”

**Class Expectations**
- The student is solely responsible for their education. The professor is the guide to their understanding of the field.
- Respect and disruption: the professor and students will be respectful at all times. Classroom disruption of any kind will not be tolerated.
- **COVID-related requirements:**
  - You are expected to wear approved face coverings at all times during class and within buildings even if you are vaccinated. Please continue to follow healthy habits, including best practices like frequent hand washing. Following these practices is our responsibility as Gators.
  - If you are sick, stay home and self-quarantine. Please visit the UF Health Screen, Test & Protect website about next steps, retake the questionnaire and schedule your test for no sooner than 24 hours after your symptoms began. Please call your primary care provider if you are ill and need immediate care or the UF Student Health Care Center at 352-392-1161 (or email covid@shcc.ufl.edu) to be evaluated for testing and to receive further instructions about returning to campus. UF Health Screen, Test & Protect offers guidance when you are sick, have been exposed to someone who has tested positive or have tested positive yourself. Visit the UF Health Screen, Test & Protect website for more information.
  - You must be cleared to be on campus if attending in-person class. If you are withheld from campus by the Department of Health through Screen, Test & Protect, you are not permitted to use any on campus facilities. Students attempting to attend campus activities when withheld from campus will be referred to the Dean of Students Office.
  - **The principles of the honor code must be adhered to at all times.** Individual effort is required on homework assignments and exams. The honor pledge that you explicitly or implicitly sign is:

  *On my honor, I have neither given nor received unauthorized aid in doing this homework/quiz/report/exam.*

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The Honor Code ([https://sccr.dso.ufl.edu/process/honor-code/](https://sccr.dso.ufl.edu/process/honor-code/)) specifies a number of behaviors that are in violation of this code and the possible sanctions. You are obligated to report any condition that facilitates academic misconduct to appropriate personnel. If you have any questions or concerns, please consult with the professor or TA.

**Homework:** The purpose of homework is to learn and understand the material. **Students are responsible for performing and understanding the homework problems and solutions on their own.**

**Software:** All faculty, staff, and students of the University are required and expected to obey the laws and legal agreements governing software use. Failure to do so can lead to monetary damages and/or criminal penalties for the individual violator. Because such violations are also against University policies and rules, disciplinary action will be taken as appropriate. We, the members of the University of Florida community, pledge to uphold ourselves and our peers to the highest standards of honesty and integrity.

**Commitment to a Safe and Inclusive Learning Environment**
The Herbert Wertheim College of Engineering values broad diversity within our community and is committed to individual and group empowerment, inclusion, and the elimination of discrimination. It is expected that every person in this class will treat one another with dignity and respect regardless of gender, sexuality, disability, age, socioeconomic status, ethnicity, race, and culture.

If you feel like your performance in class is being impacted by discrimination or harassment of any kind, please contact your instructor or any of the following:
- Your academic advisor or Graduate Program Coordinator
- Jennifer Nappo, Director of Human Resources, 352-392-0904, jpennacc@ufl.edu
- Curtis Taylor, Associate Dean of Student Affairs, 352-392-2177, taylor@eng.ufl.edu
- Toshikazu Nishida, Associate Dean of Academic Affairs, 352-392-0943, nishida@eng.ufl.edu

**Student Privacy**
There are federal laws protecting your privacy with regards to grades earned in courses and on individual assignments. For more information, please see: [https://registrar.ufl.edu/ferpa.html](https://registrar.ufl.edu/ferpa.html)

**Students Requiring Accommodations**
Students with disabilities who experience learning barriers and would like to request academic accommodations should connect with the disability Resource Center by visiting [https://disability.ufl.edu/students/get-started/](https://disability.ufl.edu/students/get-started/). It is important for students to share their accommodation letter with their instructor and discuss their access needs, as early as possible in the semester.

**In-Class Recording**
Students are allowed to record video or audio of class lectures. However, the purposes for which these recordings may be used are strictly controlled. The only allowable purposes are (1) for personal educational use, (2) in connection with a complaint to the university, or (3) as evidence in, or in preparation for, a criminal or civil proceeding. All other purposes are prohibited. Specifically, students may not publish recorded lectures without the written consent of the instructor.

A “class lecture” is an educational presentation intended to inform or teach enrolled students about a particular subject, including any instructor-led discussions that form part of the presentation, and delivered by any instructor hired or appointed by the University, or by a guest instructor, as part of a University of Florida course. A class lecture does not include lab sessions, student presentations,
clinical presentations such as patient history, academic exercises involving solely student participation, assessments (quizzes, tests, exams), field trips, private conversations between students in the class or between a student and the faculty or lecturer during a class session.

Publication without permission of the instructor is prohibited. To “publish” means to share, transmit, circulate, distribute, or provide access to a recording, regardless of format or medium, to another person (or persons), including but not limited to another student within the same class section. Additionally, a recording, or transcript of a recording, is considered published if it is posted on or uploaded to, in whole or in part, any media platform, including but not limited to social media, book, magazine, newspaper, leaflet, or third party note/tutoring services. A student who publishes a recording without written consent may be subject to a civil cause of action instituted by a person injured by the publication and/or discipline under UF Regulation 4.040 Student Honor Code and Student Conduct Code.

Campus Resources
Health and Wellness
U Matter, We Care:
Your well-being is important to the University of Florida. The U Matter, We Care initiative is committed to creating a culture of care on our campus by encouraging members of our community to look out for one another and to reach out for help if a member of our community is in need. If you or a friend is in distress, please contact umatter@ufl.edu so that the U Matter, We Care Team can reach out to the student in distress. A nighttime and weekend crisis counselor is available by phone at 352-392-1575. The U Matter, We Care Team can help connect students to the many other helping resources available including, but not limited to, Victim Advocates, Housing staff, and the Counseling and Wellness Center. Please remember that asking for help is a sign of strength. In case of emergency, call 9-1-1.

Counseling and Wellness Center: https://counseling.ufl.edu, and 392-1575; and the University Police Department: 392-1111 or 9-1-1 for emergencies.

Sexual Discrimination, Harassment, Assault, or Violence
If you or a friend has been subjected to sexual discrimination, sexual harassment, sexual assault, or violence contact the Office of Title IX Compliance, located at Yon Hall Room 427, 1908 Stadium Road, (352) 273-1094, title-ix@ufl.edu

Sexual Assault Recovery Services (SARS)
Student Health Care Center, 392-1161.

University Police Department at 392-1111 (or 9-1-1 for emergencies), or http://www.police.ufl.edu/.

Academic Resources
E-learning technical support, 352-392-4357 (select option 2) or e-mail to Learning-support@ufl.edu. https://lss.at.ufl.edu/help.shtml.


Library Support, http://cms.uflib.ufl.edu/ask. Various ways to receive assistance with respect to using the libraries or finding resources.
Course Evaluation

Students are expected to provide professional and respectful feedback on the quality of instruction in this course by completing course evaluations online via GatorEvals. Guidance on how to give feedback in a professional and respectful manner is available at https://gatorevals.aa.ufl.edu/students/. Students will be notified when the evaluation period opens, and can complete evaluations through the email they receive from GatorEvals, in their Canvas course menu under GatorEvals, or via https://ufl.bluera.com/ufl/. Summaries of course evaluation results are available to students at https://gatorevals.aa.ufl.edu/public-results/.

Evaluation of Grades and Grading Policy

Evaluation Mechanism on a Percent Basis

<table>
<thead>
<tr>
<th>Homeworks</th>
<th>70%</th>
</tr>
</thead>
<tbody>
<tr>
<td>1- or 2-page summaries of assigned journal paper sets (graded on completion)</td>
<td></td>
</tr>
</tbody>
</table>

| Problem sets |
| Final project |
| 30% |

Homework

Students will submit solutions of the homework problems only via the course website. Students who turn in homework before the due date and time will have their homework graded. Not all homework problems will be graded; instead, a selection of problems will be randomly chosen for grading after the homework due date and time. Submitted homework that is partially- or fully-missing solutions to these chosen problems will not be eligible for partial or any credit for those problems, respectively, even if other non-chosen homework problems were completed. Homework solutions will be posted on the class website after the due date.

Final Grade

Final grades may be calculated by the following table. For example, if a student earns 86.60% (Percent Grade Earned %GE = 86.60) then their grade point will be 3.33 (B+). %GE are rounded to the hundredths decimal place. For example, if a student earns 77.995% (Percent Grade Earned %GE = 77.995) it will be rounded up to 78.00%, and their grade point will be 2.67 (B-). Shifts in the grading table are at the discretion of the professor.

Table 1. Grading Table. %GE = Percent Grade Earned.

<table>
<thead>
<tr>
<th>Percentage Range</th>
<th>Grade Point</th>
</tr>
</thead>
<tbody>
<tr>
<td>92.00 ≤ %GE &lt; 100.00</td>
<td>4.00</td>
</tr>
<tr>
<td>88.00 ≤ %GE &lt; 92.00</td>
<td>A- 3.67</td>
</tr>
<tr>
<td>85.00 ≤ %GE &lt; 88.00</td>
<td>B+ 3.33</td>
</tr>
<tr>
<td>81.00 ≤ %GE &lt; 85.00</td>
<td>B 3.00</td>
</tr>
<tr>
<td>78.00 ≤ %GE &lt; 81.00</td>
<td>B- 2.67</td>
</tr>
</tbody>
</table>

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Grade Corrections
Corrections of grades should be submitted promptly in writing within three business days of the grade posting. Include a concise statement of why you believe there has been an error. Note that the professor has the final determination in the grade assigned. If a grade change is determined it may result in a lower or higher grade.

Tentative Topic List
1. Preliminaries
   a. Biological macromolecules (nucleic acids, protein)
   b. Core cellular processes
   c. Designing synthetic biomolecular machinery: Synthetic Biology and DNA Nanotechnology
2. Basic concepts and theories
   a. Weak and strong forces at the molecular scale
   b. Multistate system and statistical mechanics
   c. Energy landscape and kinetic theory
   d. Analyses of dynamic behavior: stability analyses, time-scale separation, chemical master equation, robustness and sensitivity analyses, limit cycles, bifurcations
   e. Analyses of stochastic behavior: Monte Carlo methods, the Gillespie algorithm
   f. Energy, entropy, and work
   g. Molecular recognition and binding equilibria
   h. Allostery and cooperativity
   i. Diffusion and pattern formation
3. Modeling biological macromolecules and biomolecular networks
   a. The gene regulatory machinery: activation, repression, autoregulation and common gene regulatory network motifs
   b. The electron transport machinery: photosynthesis and respiration
   c. The cell signaling machinery: quorum sensing, phase separation, ultrasensitivity, and trigger wave
   d. The mechanotransduction machinery: mechanoenzymes, mechanotransduction, force generation
4. Design and control of synthetic biomolecular systems
   a. Synthetic biology foundations: bistability (toggle switch) and oscillation (repressilator)
   b. Integral control, adaptation, applications in synthetic biology
   c. Logic gates, digital vs. analog genetic circuits
   d. Noise in gene regulatory networks: benefits and mitigation
   e. DNA Nanotechnology foundations: molecular junctions and strand displacement
   f. DNA chemical reaction networks and DNA computing
   g. DNA self-assembly and DNA origami