Course objectives:
This course will provide a survey of mathematical methods used to model complex biological systems. It is organized into three sections that cover 1) continuous and deterministic state approaches using difference and differential equations, basic feedback models and compartmental models, 2) discrete and stochastic approaches using Markov, Monte Carlo, and discrete event simulation techniques and 3) Agent-based models. Students will be expected to understand these techniques and know when (and how) to apply them to model to understand biological problems. The course will use examples drawn from different levels of analysis (cellular, organism, population) to show how these techniques can be applied to real biological problems. Students will be expected to develop a final project, mentored by the faculty that applies what they have learned to a biological problem of interest to them.

Finally, students will be required to take a topic or domain of interest and provide a lecture and overview to the class. Students with biological backgrounds will be encouraged to pick methodological topics, and students with technical backgrounds will be asked to choose domain problems. These lectures will be selected by the students and presented during regular class.

Course Requirements: Students should be familiar with basic statistics and calculus.

Course Mechanics: The course will consist of lectures, homework assignments, a midterm, and a final course project.

Required text: (none)

Supplemental text:


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Session 1 Aug 29 An Introduction to Simulation I Roberts

Concepts and Topics: In this lecture students will participate in a hands-on simulation that will illustrate first hand the importance of feedback mechanisms to the development of emergent behaviors, and the difficulty in predicting the effect of perturbations of complex systems.

Required Reading:
Supplemental Reading: TBA
Homework Assignment: TBA

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Session 2 Aug 31 An Introduction to Simulation - II Fridsma

Concepts and Topics: This lecture will describe the different types of simulation models useful in medicine, and when each is appropriate. For example, we will discuss discrete vs. continuous models, linear vs. nonlinear, deterministic vs. stochastic, and static vs. dynamic models. This will provide an outline for future lectures and topics, and introduce a “matrix” of clinical problems (of varying granularity) and the modeling methods that have been applied to these problems.
**Concepts and Topics:** Discuss the Rasmussen article in more detail and cover remaining coordination and administrativia.

**Required Reading:**

**Supplemental Reading:**

**Homework Assignment:** TBA

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Session 3  Sept 7  TBA  Fridsma

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**Concepts and Topics:** This model will introduce a model by Carson et al that describes HIV at a cellular level using a 3 variable compound predator/prey model.

**Required Reading:**


**Supplemental Reading:**

**Homework Assignment:** TBA

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Session 4  Sept 12  Modeling Sepsis Using Compound Predator/Prey Models  Gilles

**Concepts and Topics:** In this lecture, we will continue explanations of differential equations, and introduce the use of Matlab and VenSim—examples of two tools that use differential equations for modeling complex systems.

**Required Reading:**


**Supplemental Reading:**

**Homework Assignment:** TBA

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Session 5  Sept 14  Clinical Trials Simulation Talk  Gilles

**Concepts and Topics:** This lecture will describe current and historic models of HIV transmission that have used differential equations and deterministic approaches. Students will read and critique models by Abbas, Krishner and others.

**Required Reading:**


**Supplemental Reading:**

**Homework Assignment:** TBA

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Session 6  Sept 19  Biological HIV Models of Population Dynamics  Gilles

**Concepts and Topics:** This lecture will describe current and historic models of HIV transmission that have used differential equations and deterministic approaches. Students will read and critique models by Abbas, Krishner and others.

**Required Reading:**


**Supplemental Reading:**


**Homework Assignment:** See website
Session 7  Sept 21  Simulation Model Examples: OncoTcap Day

Concepts and Topics: This lecture will review OncoTcap, a simulation that models populations of cells and oncogenesis, and provides a organ/cell level description of how cancers form and can be treated.

Required Reading:

Supplemental Reading:

Homework Assignment: TBA

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Session 8  Sept 26  Introduction to the Final Project /Selecting a Modeling Approach

Concepts and Topics: This lecture will review what is expected for the final project and answer questions as people prepare for their final modeling efforts. This lecture will try to answer the question: “Given the question that I am trying to answer, what are the trade-offs among different modeling approaches?” We will review what has been learned in the course to this point, and describe in more detail some of the strengths and weaknesses of different modeling approaches.

Required Reading:

Supplemental Reading:

Homework Assignment: TBA

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Session 9  Sept 28  Introduction to Discrete State and Stochastic Models

Concepts and Topics: This lecture represents a transition from the deterministic approaches used in the first section of the course to those that have stochastic and discrete states. Students will review Markov models (and some of the problems of state space explosion), Monte Carlo approaches and discrete event simulation (DES) in which time, queues, and resources are important.

Required Reading:

Supplemental Reading:
Homework Assignment: TBA

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Session 10  Oct 3  Review of Markov Models in Medical Decision Making

Required Reading:

Supplemental Reading:

Homework Assignment: TBA
Concepts and Topics: This review will cover the basics of probability and Markov chains, or Markov models as they are known in the medical literature. It will discuss concepts such as independence, conditional independence, states, transitions, distributions, and so on. Of particular interest are those concepts that are needed for Markov decision processes and simulation.

Required Reading:

Supplemental Reading:

Homework Assignment: None

Session 11  Oct 5  Modeling Liver Transplantation Policies  Roberts

Concepts and Topics: This lecture will describe the process of developing a large-scale simulation model of liver transplantation policies. The lecture will describe problems faced early on in the development of the model, and describe how DES techniques circumvented the limitations of earlier approaches.

Required Reading:

Supplemental Reading: None

Homework Assignment: None

Session 12  Oct 10  Discrete Event Simulation  Fridsma/ Schaefer

Concepts and Topics: This lecture will introduce the basics of simulation, including input and output analysis, event queues, verification, and validation. It will discuss the main advantages of simulation, such as its flexibility and ease of use, and the fact that it can model competition for resources. It will also describe the drawbacks of simulation, such as the fact that it can only analyze one policy at a time and that the output is itself a random variable. It will also include a brief demonstration of the simulation software package ARENA.

Required Reading:

Supplemental Reading:

Homework Assignment: TBA

Session 13  Oct 12  Cohort – SIR Model  Smith

Concepts and Topics:
Required Reading:
Supplemental Reading:
Homework Assignment: TBA

Session 14  Oct 17  TBA  Hotskisis

Concepts and Topics:
Required Reading:
Supplemental Reading:
Homework Assignment: TBA
### Session 15  Oct 19  Models of Patient Safety  Fridsma

**Concepts and Topics:** This lecture will describe the application of DES and organizational modeling techniques to the problem of patient safety. In the lecture, we will describe OCCAM, a DES tool that models organizational factors that affect errors, and has been used in other industries to predict error-prone organizations.

**Required Reading:**

**Supplemental Reading:**

**Homework Assignment:** TBA

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### Session 16  Oct 24  No Class – AMIA Conference

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### Session 17  Oct 26  Review  TBA

**Concepts and Topics:** This class will serve to review topics to date in preparation for the midterm.

**Required Reading:**

**Supplemental Reading:**

**Homework Assignment:** TBA

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### Session 18  Oct 31  Midterm Exam  Fridsma

**Concepts and Topics:**

**Required Reading:**

**Supplemental Reading:**

**Homework Assignment:** TBA

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### Session 19  Nov 2  Introduction to the Final Project /Selecting a Modeling Approach  Fridsma

**Concepts and Topics:** This lecture will review what is expected for the final project and answer questions as people prepare for their final modeling efforts. This lecture will try to answer the question: “Given the question that I am trying to answer, what are the trade-offs among different modeling approaches?” We will review what has been learned in the course to this point, and describe in more detail some of the strengths and weaknesses of different modeling approaches.

**Required Reading:**

**Supplemental Reading:**

**Homework Assignment:** TBA

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### Session 20  Nov 7  Arena - I  Fridsma/ Schaeffer

**Concepts and Topics:** In this lecture, we will review modeling in Arena.

**Required Reading:**

**Supplemental Reading:**

**Homework Assignment:** TBA

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### Session 21  Nov 9  Arena - II  Fridsma/ Schaefer

**Concepts and Topics:** This lecture will continue modeling in Arena.

**Required Reading:**

**Supplemental Reading:**

**Homework Assignment:** TBA
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<tr>
<th>Session 22</th>
<th>Nov 14</th>
<th>VenSim – I</th>
<th>Fridsma</th>
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<tr>
<td><strong>Concepts and Topics:</strong></td>
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<th>Session 23</th>
<th>Nov 16</th>
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<th>Fridsma</th>
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<tr>
<td><strong>Concepts and Topics:</strong></td>
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<tr>
<th>Session 24</th>
<th>Nov 21</th>
<th>Data I</th>
<th>Roberts</th>
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<tbody>
<tr>
<td><strong>Concepts and Topics:</strong></td>
<td>First lecture introducing Data as a modeling framework. The basic structure of decision trees, (branch and node definitions) will be presented, and a hands-on tutorial will introduce the use of a specific software system for constructing a decision tree.</td>
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<tr>
<td><strong>Required Reading:</strong></td>
<td>Data Tutorial</td>
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<td><strong>Supplemental Reading:</strong></td>
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<td><strong>Homework Assignment:</strong></td>
<td>If part 1 of the tutorial is not completed in class, the tutorial should be finished prior to the next class meeting</td>
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| Session 25 | Nov 23 | No Class - Thanksgiving Holiday | | |
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<th>Session 26</th>
<th>Nov 28</th>
<th>Data II</th>
<th>Roberts</th>
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<tbody>
<tr>
<td><strong>Concepts and Topics:</strong></td>
<td>Second lecture introducing Data as a modeling framework. In this session, the tutorial will be expanded to include the development of Markov Processes and introduce Monte Carlo simulation as an analysis method and as a sensitivity analysis.</td>
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<td><strong>Required Reading:</strong></td>
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<tr>
<th>Session 27</th>
<th>Nov 30</th>
<th>Simulation Model Examples: BioWar</th>
<th>Fridsma/Carley</th>
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<tr>
<td><strong>Concepts and Topics:</strong></td>
<td>In this lecture, we will describe BioWar, a large-scale simulation tool for modeling biological attacks and developing alternative detection and response strategies. The underlying approach will be reviewed, and some of the insights gained in modeling anthrax, smallpox and other diseases reviewed.</td>
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<tr>
<th>Session 29</th>
<th>Dec 7</th>
<th>Project-Specific Review</th>
<th>Fridsma</th>
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</table>
Concepts and Topics: Students will present their class projects at the end of the course, describing the problem to solve, the methodologies evaluated, and the reason for the chosen approach. They will also present their results and findings and how effectively they answered their question.

Reference List

   Ref Type: In Press
   Ref Type: Abstract