Dynamical Modeling Methods for Systems Biology

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Outline

Overall course goals

Topics that will be covered

Structure, grading, assessment

Goals

Teach contemporary methods used in systems biology for dynamical modeling

Teach methods for mathematical analysis of biological systems and simulation output

Demonstrate how dynamical mathematical models can provide insight that cannot be gained from experiments only

Different categories of mathematical models

Statistical, top down, models versus dynamical, bottom up, models

Top down

1) Begin with data set (often very large scale)
2) Use statistical methods to find patterns in the data.
3) Generate predictions based on the the structure within the data.

Network analysis
Gene set enrichment
Clustering
Principal components
Partial least-squares regression

See Coursera course taught by Dr. Avi Ma'ayan

Bottom up

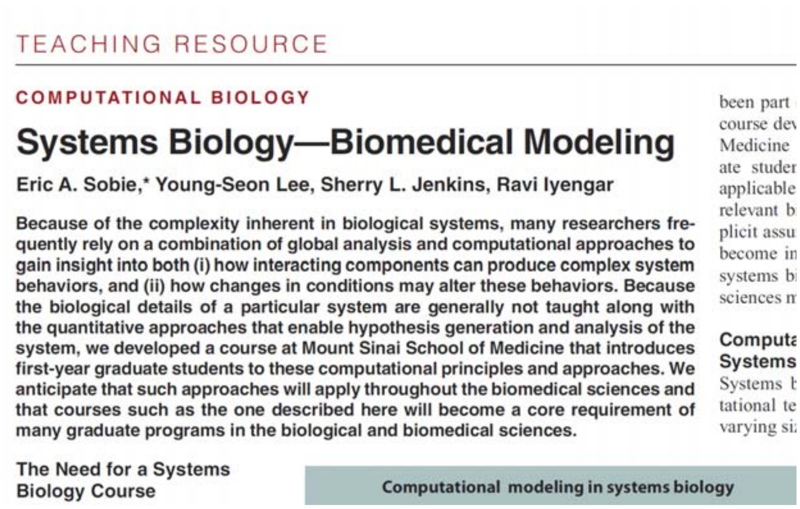
1) Begin with hypothesis of biological mechanism.
2) Write down equations describing how components interact.
3) Run simulations to generate predictions.

Ordinary differential equations
Dynamical systems
Parameter estimation
Partial differential equations
Stochastic models

our focus will be on these

Statistical versus dynamical models

This is discussed in more detail in several review articles



TEACHING RESOURCE

COMPUTATIONAL BIOLOGY

Systems Biology—Biomedical Modeling

Eric A. Sobie,* Young-Seon Lee, Sherry L. Jenkins, Ravi Iyengar

Because of the complexity inherent in biological systems, many researchers frequently rely on a combination of global analysis and computational approaches to gain insight into both (i) how interacting components can produce complex system behaviors, and (ii) how changes in conditions may alter these behaviors. Because the biological details of a particular system are generally not taught along with the quantitative approaches that enable hypothesis generation and analysis of the system, we developed a course at Mount Sinai School of Medicine that introduces first-year graduate students to these computational principles and approaches. We anticipate that such approaches will apply throughout the biomedical sciences and that courses such as the one described here will become a core requirement of many graduate programs in the biological and biomedical sciences.

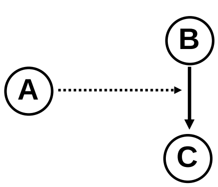
The Need for a Systems Biology Course

Computational modeling in systems biology

Sobie et al. (2011) *Science Signaling* 4:tr2.

Structure of a dynamical modeling study

Mechanism



Equations

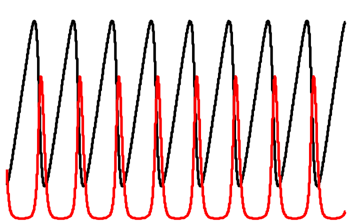
$$\frac{d[G]}{dt} = V_{in} - k_1[G][ATP]$$

$$\frac{d[ATP]}{dt} = 2k_1[G][ATP] - \frac{k_p[ATP]}{[ATP]+K_m}$$

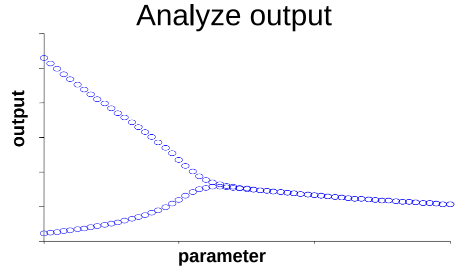
Program to simulate equations

```
a = 20 ;
b = 2 ;
c = 5 ;

dt    = 0.05 ;
tlast = 2 ;

iterations = round(tlast/dt) ;
xall = zeros(iterations,1) ;
```

Simulations



Analyze output



Course Logistics

Format

7 week total course, approximately 25 lectures, 20 minutes each

3-4 lectures posted per week

Self-assessment questions during each lecture

5 homework assignments after lecture blocks

Skills that will be taught

Using MATLAB for data analysis and visualization

Developing models consisting of systems of ordinary differential equations (ODEs)

Implementing ODE models in MATLAB and running simulations with these models

Analyzing ODE models using the tools of dynamical systems analysis

Biological applications

We will see, models are useful for understanding:

Glucose oscillations in yeast

Kinase signaling pathways in mammalian cells

Regulation of the cell cycle

Electrical signaling in neurons

Goal: provide you with the tools necessary to apply these types of models to your own questions of interest

Assessment and Self-Assessment

Self-assessment

1-2 questions posted at the end of each lecture

explanations provided

Assessment

homework assignments to perform simulations with dynamical models

General format: start with MATLAB code written for one purpose, modify it to do something else

Assessment questions designed to verify that code works properly and that biological interpretation is correct

Homework assignments

Designed to reinforce concepts discussed in lectures

Assignments should require you to demonstrate:

- Technical competence (programming)
- Quantitative skills
- Biological insight into the problem