I use the book and slides of Chris J. Myers

Lecture 0: Preface
Engineering is the art or science of making practical.
Robert Heinlein

One man’s “magic” is another man’s engineering.
Biology is now both a lab-based science and an information science.
Biologists have had to draw assistance from those in mathematics, computer science, and engineering.
Result was development of *bioinformatics* and *computational biology*.
Major goal is to extract new biological insights from large and noisy sets of data generated by high throughput technologies.
Must create and maintain databases with massive amounts of data.
Must be able to efficiently access, submit, and revise this data.
Latest software must even analyze and interpret this data.
In this course, we use the term bioinformatics to refer to the analysis of *static* data such as sequence analysis of DNA and protein sequences, techniques for finding genes or evolutionary patterns, and *cluster analysis* of microarray data.
Bioinformatics algorithms are not covered in this course.
The focus of this course is the modeling, analysis, and design methods for *systems biology*.

Systems biology is the study of the mechanisms underlying complex molecular processes as integrated into systems or pathways made up of many interacting genes and proteins.

Concerned with the analysis of *dynamic* models.

Made possible by new experimental methods such as:

- cDNA microarrays and oligonucleotide chips.
- Mass spectrometric identification of gel-separated proteins.
- 2-hybrid systems.
- Genome-wide location analysis (ChIP-to-chip)
Systems Biology (cont)

- Systems biology involves:
  - Collection of large experimental data sets,
  - Constructing mathematical models from this data,
  - Designing software to accurately and efficiently analyze these models \textit{in silico} (i.e., on a computer),
  - Comparing numerical simulations with the experimental data, and
  - Designing new synthetic biological systems.

- Ultimate goal is to develop methods which can give reasonable predictions of experimental results.

- While it will never replace experimental methods, may help experimentalists make better use of their time.

- Also may gain insight into mechanisms used by these biological processes which may not be obtained by experiments.

- Eventually, may be possible that they could have substantial impact on our society such as aiding in drug discovery.
Biological Networks

- **Metabolic networks** are enzymatic processes that transform food into energy, and perform both biosynthesis and biodegradation.

- **Protein networks** are communication and signaling networks which are composed of basic reactions between two or more proteins.

- **Genetic regulatory networks**, or *genetic circuits*, regulate gene expression at many molecular levels.

- **The focus of this course are methods for modeling, analysis, and design of genetic circuits.**
Standards for sequence data were absolutely essential.

For systems biology, standard data formats are being developed.

One is the *systems biology markup language* (SBML).

XML-based language to represent chemical reaction networks.

All networks described in this lecture can be reduced to a set of bio-chemical reactions.

SBML model consists of a list of the species and their reactions.

A reaction includes a list of reactants, products, and modifiers.

Also includes a mathematical description of the kinetic rate law governing the dynamics of this reaction.

SBML is ugly, but GUIs have been developed.
Another essential item in the genomic-age was the development of *biological databases*.

These provide repositories for storing large bodies of data that can be easily updated, queried, and retrieved.

Databases store many things ranging from nucleotide sequences within GenBank to biomedical literature at PubMed.

Recently, a database for SBML models has been started.
The last essential piece is tools.

Excellent list of bioinformatics tools at the NCBI website.

List of systems biology tools that support SBML can be found at the SBML website.

The remainder of this course concentrates on describing the methods used by tools being developed for systems and synthetic biology.
Engineers have experience in modeling and analyzing systems.
- Can take a circuit view of a genetic circuit (Science1995).
- Collaborations needed between engineers and biologists.
- **Goal of this course is to facilitate these collaborations.**
The Engineering Approach

- Genetic Circuit
- Insert into Host
- Plasmid
  - Construct Plasmid
  - DNA Sequence
    - TechMap
      - Library
  - Logic Equations
    - Synthesis
      - HDL
  - Abstraction/Simulation
    - Simulation Data
      - Construct Experiments
  - Learn Model
    - Models
      - Construct Experiments
  - Experimental Data
    - Perform Experiments
      - Set of Experiments

Modeling
Analysis
Design
Chapter 1: An Engineer’s Guide to Genetic Circuits

Set of Experiments → Perform Experiments → Experimental Data → Learn Model → Models → Construct Experiments

Genetic Circuit

Insert into Host ➔ Plasmid ➔ Construct Plasmid

Biological Knowledge ➔ DNA Sequence ➔ TechMap ➔ Library

Abstraction/Simulation ➔ SBML Model ➔ Logic Equations ➔ Synthesis ➔ HDL

Models ➔ Construction

Simulation Data ➔ Synthesis ➔ HDL

Modeling  Analysis  Design
Chapter 2: Learning Models

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Set of Experiments

**Modeling**

**Analysis**

**Design**

Chris J. Myers (Lecture 0: Preface) Engineering Genetic Circuits
Chapter 3: Differential Equation Analysis

Set of Experiments → Perform Experiments

Genetic Circuit ← Insert into Host

Plasmid

Construct Plasmid

DNA Sequence

TechMap

Library

Learn Model

Experimental Data

Models

SBML Model

Abstraction/Simulation

Simulation Data

Synthesis

HDL

Logic Equations

Construct Experiments

Analysis

Design

Modeling
Chapter 4: Stochastic Analysis

Set of Experiments → Perform Experiments → Experimental Data → Learn Model → Models → Construct Experiments

Genetic Circuit ← Insert into Host ← Plasmid

Biological Knowledge

Construct Plasmid ← DNA Sequence ← TechMap ← Library

SBML Model

Abstraction/Simulation

Simulation Data

Synthesis ← HDL

Logic Equations

Construct Experiments

Models

Learn Model

Perform Experiments

Set of Experiments

Engineering Genetic Circuits

Modeling Analysis Design
Chapter 6: Logical Abstraction

Set of Experiments → Perform Experiments → Experimental Data → Learn Model → Models → Construct Experiments.

Genetic Circuit → Insert into Host → Plasmid → Construct Plasmid → DNA Sequence → TechMap → Library.

Biological Knowledge → Learn Model → SBML Model → Abstraction/Simulation → Logic Equations → Synthesis → HDL.

Construct Experiments → Simulation Data → Analysis → Design.