University of Indiana Workshop
SBW and Modeling 8th August to 12th 2011

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Summary of the Week's Course on Pathway Modeling

Text in Blue indicates Hands-on Exercises with Software

The following materials will be provided to participants of the Course:

1. e-book copies of the: "Enzyme Kinetics for Systems Biology" and an option to purchase paper copies at a considerable discount.

> **Visit www.analogmachine.org**
> **Or at Amazon: http://tinyurl.com/3gag92t**

2. A Web site containing additional notes

Schedule:

Morning schedule with start at 9.30 am on day 1 and go on to Noon. Subsequent days will start at 9 am.

There will be breaks through the morning.

The afternoon schedule will start at 1.30 pm and go on to 5 or 6pm with breaks as needed. Evening sessions can also be arranged as required. General discussion and questions are encouraged throughout the workshop.

The purpose of the workshop is to introduce the following:

> **1) Cellular modeling**
> **2) SBW modeling framework**
> **3) Basic operating principles of cellular networks**

Day 1:

1. General Introduction (See http://www.sys-bio.org for downloads and other details.)
2. Cellular Networks
3. **Installation and Introduction to the Software**
4. Basic Concepts (Chapter 1)

    a) Stoichiometric Amounts
    b) Rates of Change, dx/dt
    c) Stoichiometric Coefficients
    d) Reaction Rates. v
    e) Elementary Reaction Rate Laws (Mass-action)
    f) Equilibrium Constant
    g) Mass-Action Ratio
    h) Disequilibrium Constant
    i) Alternative form for mass-action kinetics

5. **Explore simple models**
    a) Introduction to Jarnac, JDesigner and General Simulation Tool
    b) Evolution to equilibrium
    c) Mass-action Ratio Experiments
    d) Closed, Open Systems and boundary species
    e) Equilibrium, Steady State and Transient behavior

6, Network Models, deriving ODEs, **Stoichiometry matrix**

7. Brief discussion on modeling

8. Introduction to the various applications in SBW
    a) Parameter Scans
    b) Perturbations
    c) Collecting Data

Day 2:

1. Survey of Rate Laws
    a) Recap Mass-Action Kinetics
    b) Michaelis-Menten
    c) Hill Equation and Adair
    d) Cooperativity and Allostery **(Parameter scans, 3D plotting)**
    e) Approximations and Generalized Rate Laws
    g) Gene Regulatory Rate Laws **(Parameter scans, 3D plotting**)

2. Elasticities
3. **Investigate Rate laws using the Rate Law Explorer**
4. **Introduction to Stochastic Simulation**
5. **Structural Analysis of Networks**
    a) Moiety Conservation Laws
    b) Flux Conservation and FBA

6. Steady State

7. Stability- **Eigenvalues, Jacobian**

Day 3:

1. Network Design Patterns

2. **Build and Simulate More Complex Networks**
    a) Cascades, b) Feedforward, c) Counters, d) Positive Feedback,
    e) Bistability, f) Negative Feedback, (Response time, Robustness,
    Oscillations) Pos/Neg: Relaxation Oscillators, g) Multi-Output/Sim

Day 4:

1. Properties of Metabolic Pathways

2. Metabolic Control Analysis – **Simulations of Metabolism and Control**
    a) Quantitative Control of metabolic pathways
    b) Front Loading

c) Signal Transfer **- Effect of Irreversible and Reversible Steps**
d)) Effect of Negative Feedback
e) Optimal Protein Allocation
f) Branch Point Effects

Day 5:

Project

a) Find a modeling paper online
b) Extract the model from the paper
c) Reproduce the results given in the paper