Introduction to Systems Biology
Lecture 6 Part A-1

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Simulations with Different Types of Models

Toy Models -- Arbitrary Parameters
Used to make a theoretical points

Plausible Models -- Parameters are experimentally measured or estimated from experiments
Canonical and not cell type specific, hence may not be fully representative of every cell type
Most common type of dynamical models in systems biology

Identifiable Models -- Built to explain experimental data.
System specific and fitted to experimental data
Commonly used in drug action studies
Model parameters are often not connected to molecular details

From Mathematical Representations to Numerical Simulations

Reactions need to be parameterized: initial concentrations and reaction rates are needed
These are often not easy to obtain as biochemical and cell biological experiments were often not geared towards getting rate measurements or absolute levels of components with the cell.

Sometimes parameters need to be guesstimated based on known values for similar components

Often rate parameters need to be estimated from indirect measurements such as time courses

There are curve fitting programs for estimation of parameters such as COPASI

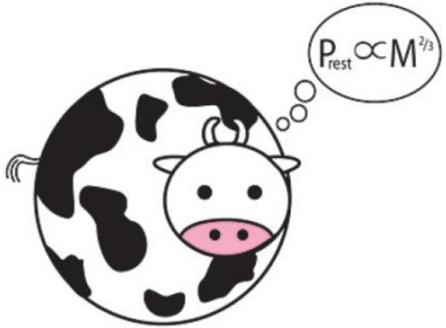
Your simulations are only as real as your model and its kinetic parameters!

1. Do NOT over-simplify the model

2. Build models with enough detail to provide non-intuitive hypotheses from simulations

3. Use available experimental data to obtain realistic (reasonable) parameters

4. Do NOT tweak (change) the parameters so that simulations show a desired behavior



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If you want to know whether your system is capable of displaying a particular behavior or not, start with the parameters that you estimated in an unbiased fashion from experiments, then conduct a systematic parameter variation exercise

Solving ODEs

Forward Euler Integration Method -- From a point on a curve, approximation of another nearby point on the curve can be made by moving a short distance along a line tangent to the curve.

Accuracy of the method depends on how short that distance (time-step) is. Euler methods are historically important but are currently not used often as they are not accurate or versatile

Runge-Kutta Methods (built on the Euler methods) are most commonly used to solve system of ODEs

Several MatLab solvers are available for Runge-Kutta methods

Solving PDEs

Two commonly used approaches

Finite Element Method
Divide the continuous domain into smaller parts called *elements* by enforcing a mesh.
Form a system of equations that governs flow of entities (e.g., proteins) between elements by discretizing PDEs
Numerically solve the system of equations

Finite Volume Method
Use a mesh of defined size
Volume refers to the volume surrounding a point on the mesh
Convert surface integrals into volume integrals and numerically solve
Method most suitable for cell biological models with diffusion

Software for Numerical Computation

Matlab -- Widely used commercial software suite for numerical computation
We teach our courses using Matlab

Mathematica -- Another widely used commercial software suite for numerical computation

GNU Octave -- Free software suite compatible with Matlab

Virtual Cell -- Free modeling and analysis software that has unique capabilities for PDE models in conjunction with imaging experiments