iGEM 2009
Tutorial Modeling

What?

- Model

  A model in science is a simplified physical, mathematical, or logical representation of a system of entities, phenomena, or processes.
- Simulation

  A simulation is the implementation of a model over time. A simulation brings a model to life and shows how a particular object or phenomenon will behave. It is useful for testing, analysis or training where real-world systems or concepts can be represented by a model.
- Modeling

  Modeling refers to the process of generating a model as a conceptual representation of some phenomena.

Why?

- Reduction of experiment costs
- Simulations are much faster ➔ number of experiments increase
- No danger!

- BUT simulations represent only part of the real world!
- Models are a simplification of the real world

Models

- Black box:
  Input-output model, no knowledge about how the system works.
  Transferfunction: no relation with physics

- White box:
  Absolute knowledge about how the system works.
  Takes physics into account

Example: Chemical Reactor

White box	Black box
Model based on reaction equations	Model based on input-output data (e.g. ARX, neural network, …)

We will work with white box models

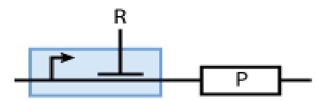
ordinary differential equations (ODE's)

Example:

- **Model described** : $A \xrightarrow{k_1} B$
- **Kinetic Law for 'A'**: $\frac{d[A]}{dt} = -k_1[A]; [A]_{t=0} = A_0 > 0$
- **Kinetic Law for 'B'**: $\frac{d[B]}{dt} = k_1[A]; [B]_{t=0} = 0$

Example: Regulated protein production

$$[\mathrm{DNA}] + n[\mathrm{R}] \underset{k_{-R}}{\overset{k_R}{\rightleftharpoons}} [\mathrm{DNA}{\cdot}n\mathrm{R}]$$



inhibition

$$k_R[\mathrm{DNA}][\mathrm{R}]^n = k_{-R}[\mathrm{DNA}\cdot n\mathrm{R}]$$

$$[\mathrm{DNA}] \sim \frac{1}{1+\left(\frac{[\mathrm{R}]}{K_R}\right)^n}$$

$$\frac{d[P]}{dt} \quad = \quad c^{\max}\frac{1}{1+\left(\frac{[R]}{K_R}\right)^n} - d_P[P]$$

Matlab

- How to model and simulate in Matlab:
  - Basic: m-files
  - Advanced: Simulink
  - Specific: SimBiology toolbox

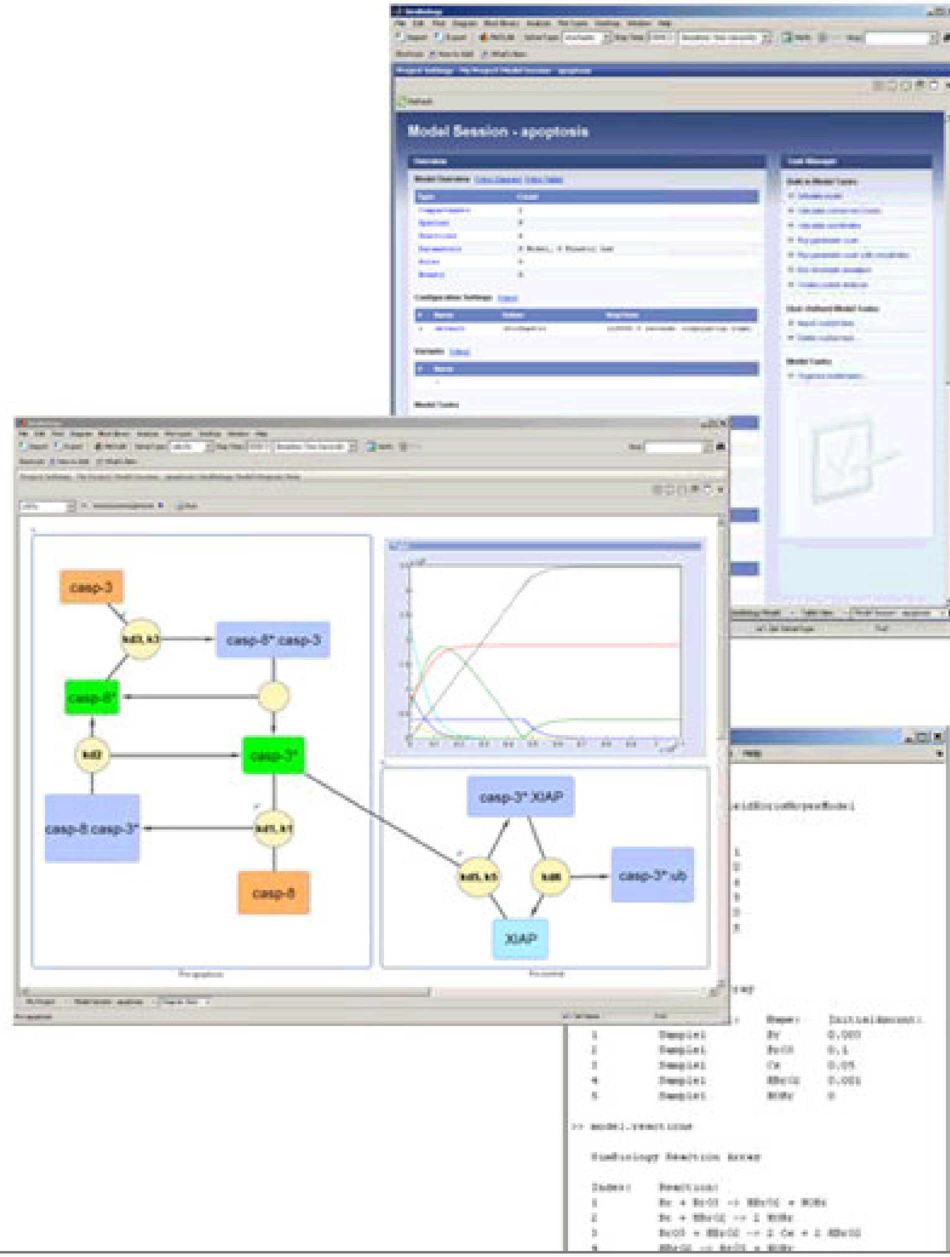
- Alternative: CellDesigner

SimBiology®

- A computational tool for modeling, simulating, and analyzing biological systems

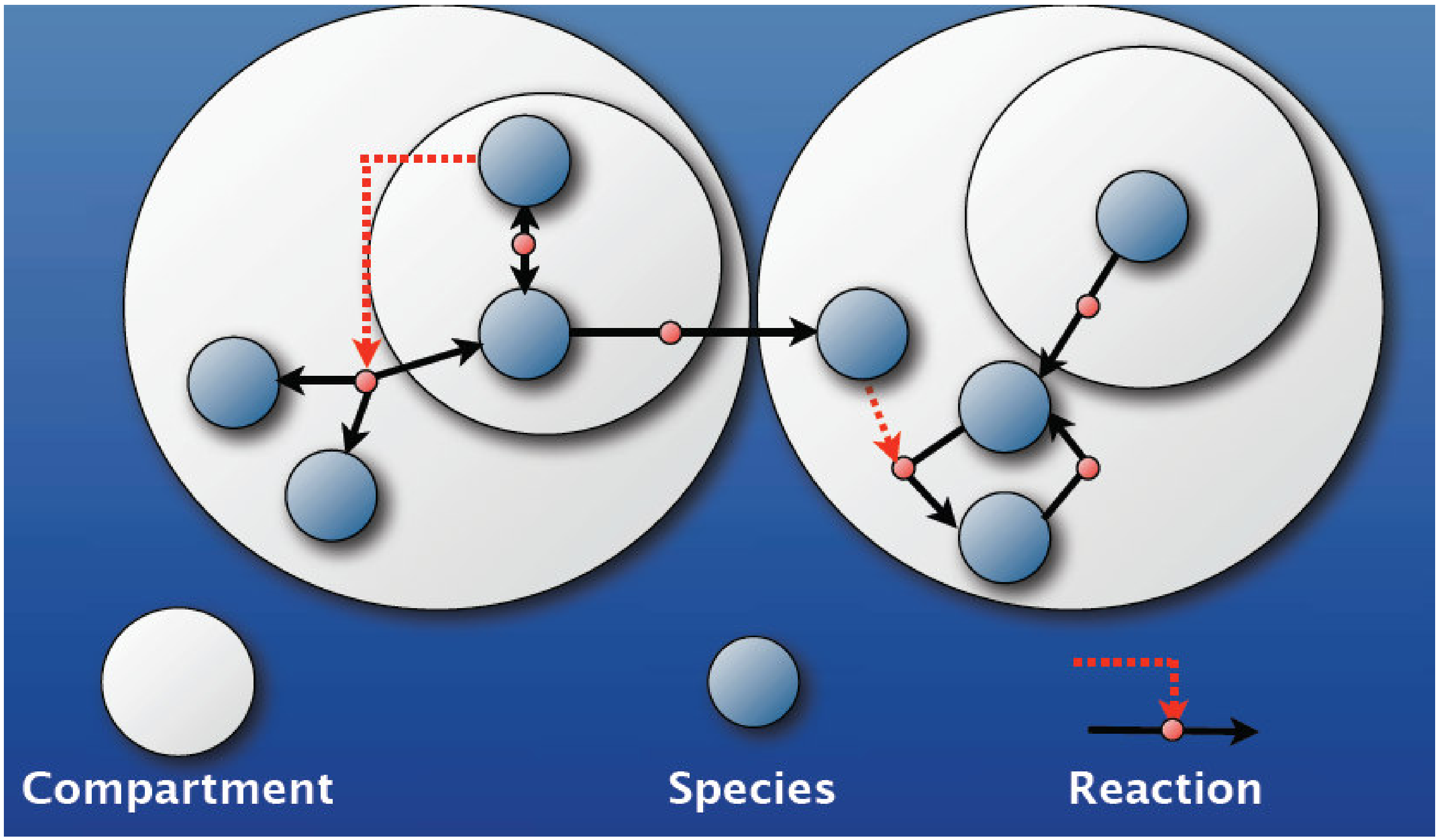
- Provides both a powerful mathematical engine as well as an graphical interface to enable use by all types of researchers

- Built on MATLAB®, which provides extensibility and flexibility



Systems Biology Markup Language (SBML)

- You can create your own block diagram model using predefined blocks. You can manually edit compartments, species, parameters, reactions, events, rules, kinetic laws, and units.



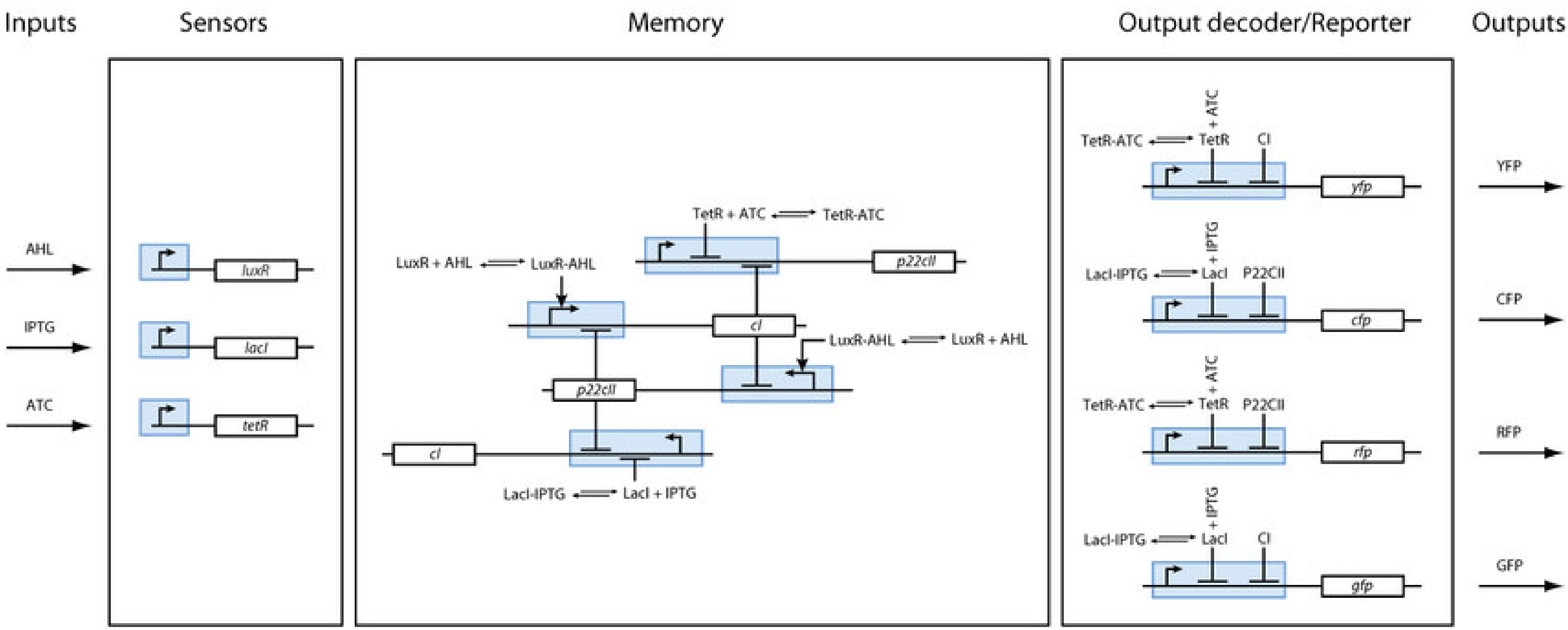
iGEM-modeling

- **Role of modeling**
  Important is the interaction between modeling and experiments: modeling is not a precursor phase of experiment and synthesis, it is part of the design cycle.

- **Detailed Model**
  Detailed model of all interactions in the system:
  define desired behaviour + formalized description of system ➔ identify necessary biological components & interactions

- **Parameter estimation & sensitivity analysis**
  - Most difficult and laborious part of modeling
  - Most parameters unknown
  - Solution: sensitivity analysis
  - Which parameters have effect on which states ?

ETH Zürich 2007 Final Design



- **Mathematical Model**
  The model is given by sets of coupled ordinary differential equations solved with matlab

- **Simulation & Sensitivity Analysis**

Questions