



iGEM 2009

Tutorial Modelling

What?

- **Model**

A model in science is a symplified 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.

- **Modelling**

Modelling refers to the process of generating a model as a conceptual representation of some phenomenon.

Why?

- Costs of experiments reduce
- 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, ...)

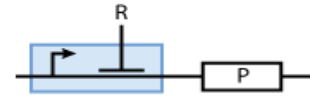
We will work with white box models

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



inhibition

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

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

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

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

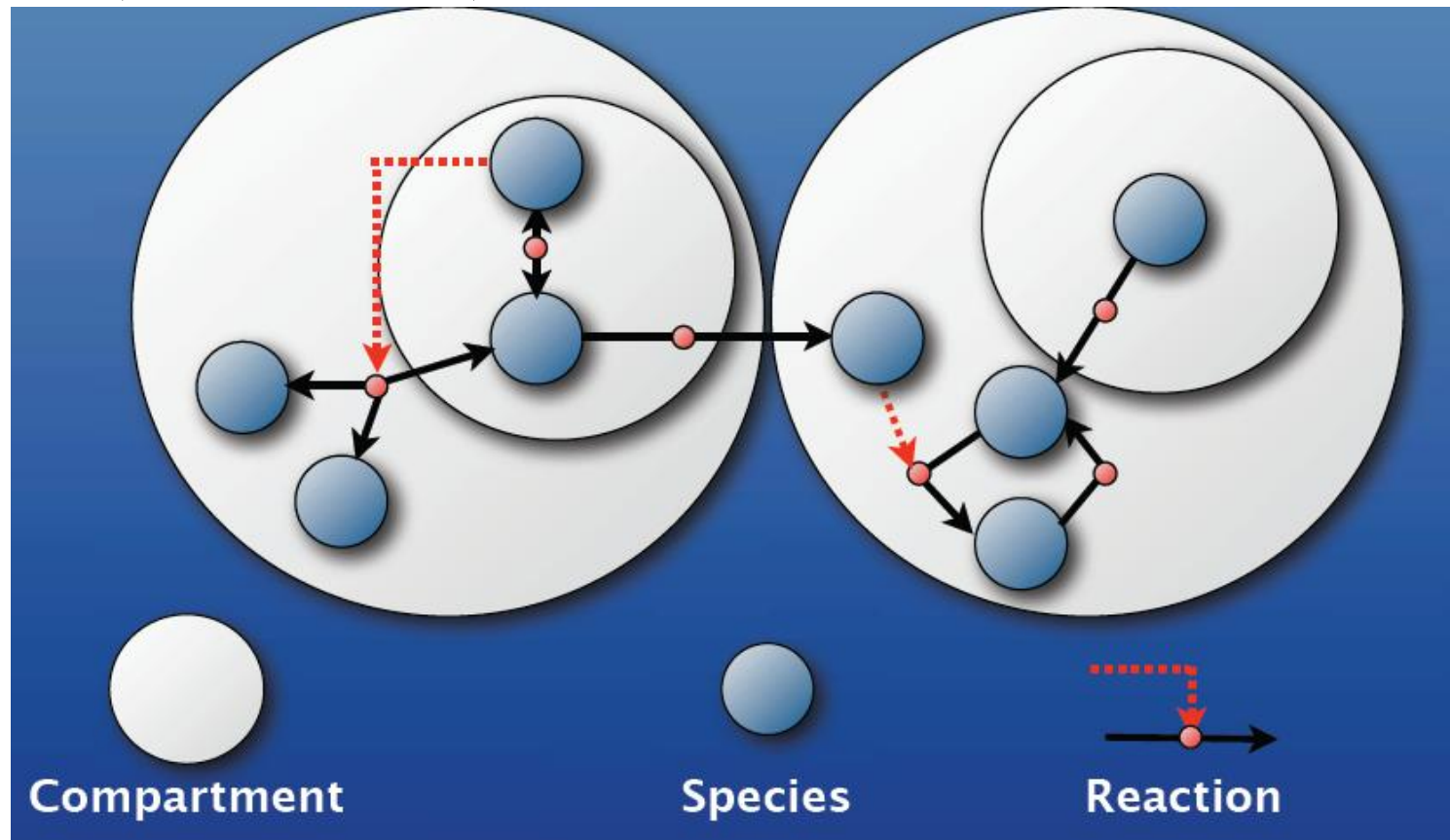
The screenshot displays the SimBiology software interface. The top window shows the 'Model Session - apoptosis' settings. The main window displays a detailed biological model diagram with nodes for casp-3, casp-8, casp-9, casp-3* casp-3, casp-3* XIAP, casp-3* ub, casp-8, and XIAP. A plot window shows the time course of these variables. The bottom window displays a table of simulation results and the underlying reaction network.

Species	Initial Amount
Species1	0.000
Species2	0.1
Species3	0.05
Species4	0.000
Species5	0

```
%% Model reaction code
function reactionCode
%
% Species:
% 1: casp-3
% 2: casp-8
% 3: casp-9
% 4: casp-3* casp-3
% 5: casp-3* XIAP
% 6: casp-3* ub
% 7: casp-8
% 8: XIAP
%
% Reactions:
% 1: casp-3 + casp-8 -> casp-3* casp-3
% 2: casp-3 + casp-9 -> casp-3* casp-3
% 3: casp-3* casp-3 + XIAP -> casp-3* XIAP
% 4: casp-3* XIAP -> casp-3* ub
% 5: casp-3* XIAP -> casp-3 + XIAP
```


Systems Biology Markup Language (SBML)

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



iGEM-modelling

- **Role of modelling**

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

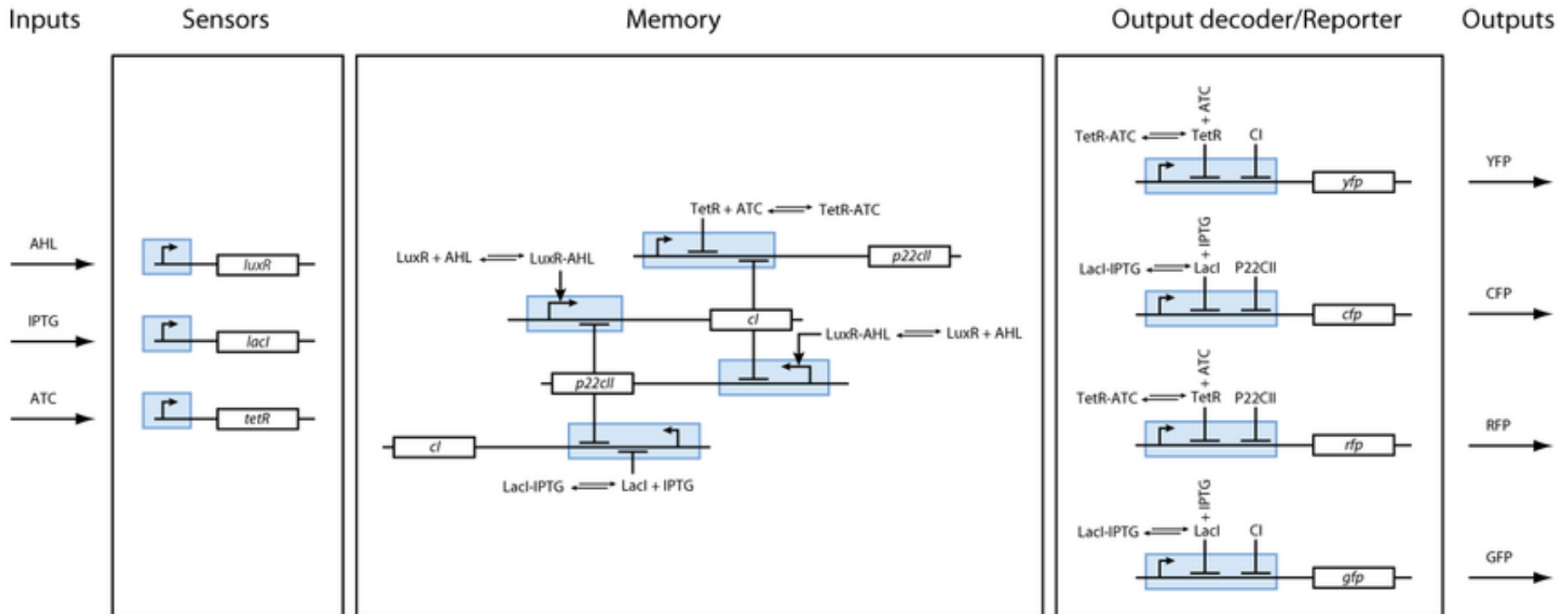
- **Detailed Model**

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 modelling
- Most parameters not known
- 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