Component Based Modeling of Biochemical Networks Using PathwayLab

Mathematical Modeling and Computational Tools
November 19, 2009, Chalmers

Fraunhofer
CHALMERS
Research Centre
Industrial Mathematics

Mats Jirstrand, PhD, Assoc Prof
Head of Department Systems Biology and Bioimaging
Outline

- Introduction

- Component Based Modeling
  - Sample Networks
  - Objects: entities, locations, transformations, controls
  - Example

- The Graphical User Interface
  - Stencils and the Drawing Page
  - The Properties Pane
  - The Preview Plot
  - The Simulation Control
  - Drag and Drop Modeling
  - The Formula Settings Dialog

- Simulation of Models
  - Transient Analysis
  - Steady State Analysis
  - Metabolic Control Analysis

- Import and Export of Data
  - Import of signals (time series)
  - Export of simulation results

- Connectivity to Mathematica and Matlab
  - Interactive Visualization in Mathematica
  - Simulation in Matlab
  - Amount or concentration formulations?

- Overview of Documentation
Fraunhofer-Chalmers Research Centre (FCC)

- Founded in Sept 1, 2001 by Chalmers and Fraunhofer-Gesellschaft (Germany)
- FCC promotes the application of mathematical methods in industry
- FCC undertakes scientific research in projects defined by companies or public institutions

Systems Biology and Bioimaging

- **System Identification** – to build mathematical models of dynamic systems based on measurement data
- **Model Reduction** – to reduce the size and scope of models
- **Image Analysis** – to extract information from images using various tools from mathematics and statistics
- **Software Tools** – to support the model building process and computational analysis of obtained models

Applied/Modeling Projects   Methodology Projects
Computational Tools

Mats Jirstrand
Systems Biology and Bioimaging

- People

Dr Mats Jirstrand
Head of Department

Jonas Hagmar, MSc
Applied Researcher

Joachim Almquist, MSc
Applied Researcher

Kristoffer Andersson, MSc
Applied Researcher

Johan Karlsson, PhD
Applied Researcher

Dr Mats Kvarnström
Group leader Bioimaging

David Wrangborg, MSc
Applied Researcher

Prof Mats Rudemo
Scientific Advisor

Jan Hauth
Andreas Jansson
Atefeh Kazeroonian
Heidar Eyólfsson
Nico Reissmann
Dimitri Koch
Armin Böller

Research students
& Visitors
PathwayLab
A Software for Biochemical Modeling, Documentation, and Computational Analysis

List of Features

- Drag-and-drop GUI (Visio)
- User customizable graphics
- Transient simulation
- Steady-state computations
- Metabolic Control Analysis
- Parametric scanning
- Click-view visualization
- Database connectivity
- Import of data (CSV)
- Model Export
  - SBML
  - Mathematica
  - Matlab

PathwayLab application package
SBtoolbox

Mats Jirstrand
Introduction to Component Based Modeling
- Sample Networks

The mechanism of Anthrax
Introduction to Component Based Modeling
- Sample Networks

The EPO signalling pathway from BioCarta
Introduction to Component Based Modeling
- Sample Networks

Detail from the Roche Applied Science "Biochemical Pathways" wall chart

Mats Jirstrand
Introduction to Component Based Modeling
- Sample Networks

The Glycolysis according to KEGG
Introduction to Component Based Modeling

Three main types of components:

- **Entities**
  - Plain
  - Complexes

- **Interactions**
  - Transformations
  - Controls
  - Complexes

- **Locations**
Introduction to Component Based Modeling

Biochemical *entities* (species):

- Metabolites
- Proteins (enzymes, transporters, building-blocks ...)
- Lipids
- Nucleic Acids (DNA, RNA, ...)
- ...

Mats Jirstrand
Introduction to Component Based Modeling

Quantification:

- **Amount** (1 mol, 1 mmol, 1 nmol, ...)
- **Concentration** (1 mol/m$^3$ = 1 mmol/dm$^3$ = 1 M, ...)
- **Activity** (%,

Also amount per area (e.g., membrane bound proteins) and amount per length (e.g., scaffolding structures)

Different notions are useful in different situations!
Introduction to Component Based Modeling

The biochemical entities are involved in different processes:

- Reactions (catalysis, transfer, binding, assembly/disassembly)
- Translocations (e.g., transport – active/passive)
- Expression
- ...

Note: in all these processes \textit{transformation} of mass from one type of biochemical entity to another (sometimes the same entity but located elsewhere) is essential!
Introduction to Component Based Modeling

The processes themselves might be influenced by other players: (influence ≈ modulate ≈ control)

- Enzymes catalyze reactions (activator)
- Transcription factors facilitates expression (activator)
- Metabolites may inhibit reaction rates (inhibitor)
- ...

Note: these entities only affect the processes by controlling the rates of the processes without being produced or consumed themselves.
Introduction to Component Based Modeling

The processes take place somewhere:

- Reactions of entities within a compartment
- Transport of an entity over a membrane (between compartments)
- Recruitment of proteins to a membrane
- Dimerization of receptors on a membrane
- ...

Note: these processes and the entities that they contain can be associated to different locations (compartments, membranes, scaffolding structures).
Introduction to Component Based Modeling

Example

- Entities
- Locations
- Interactions

Mats Jirstrand
Introduction to Component Based Modeling

Example cont’d

![Diagram](image)

- Cytoplasm
- A
- B
- E
- AB
- I

interaction complex

controls

transformation

Mats Jirstrand
Introduction to Component Based Modeling

Approximations and levels of detail:
- Small or large number of molecules
- Diffusion or “well-stirredness”

Translation to mathematics in different frameworks:
- The Chemical Master Equation
- Stochastic Differential Equations
- Stochastic Simulation Algorithm (SSA)
- Reaction-Diffusion Rate Equations
- Reaction Rate Equations (RRE)
Introduction to Component Based Modeling

Here we use the *reaction rate equations*!

- **Mass Balances**
  
  "The rate of change of an entity equals the differences between the its total production and consumption rates."

- **Rate laws**
  
  "Relations describing the production or consumption rates of processes in terms of the involved entities."

- **Ordinary differential equations (ODEs)**
  
  "The above statements cast in mathematical terms!"

The rest is bookkeeping and number crunching!
Introduction to Component Based Modeling

Here we use the *reaction rate equations*!

- **Mass Balances**
  \[
  \frac{dA}{dt} = r_2 - r_1
  \]

- **Rate laws**
  \[
  r_1 = r_1(A, B, E, I) = \frac{k_0 \, E \, A \, B / K_m}{1 + A / K_m + I / K_i}
  \]
  \[
  r_2 = \text{const}
  \]

Mats Jirstrand
Introduction to Component Based Modeling
- Activators, Inhibitors – Modulators!

- Transformation rates (reaction, transport, ..) are functions of concentration or activity of biochemical entities.
- If an entity only affect the reaction rate without itself being directly affected it is called a modulator or modifier.
- This can be indicated using control arrows (propagation of information without mass transfer)

Note: $r_1$ and $r_2$ are only present in the differential equations for S and P!

Mats Jirstrand
Introduction to Component Based Modeling

Procedure:

- Introduce a variable for each entity
- Formulate its differential equation (mass balance)
  - LHS is the rate of change (notation: \( \frac{dA}{dt} = \ldots, \frac{d[A]}{dt} = \ldots, \dot{x}_1 = \ldots \))
  - RHS is the sum of rate expressions (notation: \( \ldots = r_1 - r_2 + r_3 \), + production, - consumption)
- Formulate expressions for the rates (functions of variables for reactants, products, and modulators)

\[
r_1 = r_1(A, E, I) = \frac{k_0 \frac{E A}{K_m}}{1 + \frac{A}{K_m} + \frac{I}{K_i}} , \quad r_2 = k_1 x_1 x_2 , \ldots
\]

Mats Jirstrand

These steps can be automatized from a consistent graphical notion of the reaction network!
Introduction to Component Based Modeling

Entities

Correspond to
- signals (explicit time dependence)
- dynamic variables (states in ODE)
Introduction to Component Based Modeling

Transformations

Correspond to - rates of mass transfer
Introduction to Component Based Modeling

Controls

Correspond to - propagation of information
Introduction to Component Based Modeling

Locations

Used for
- Volume/area/length dependence
- Naming conventions
Introduction to Component Based Modeling

Links

Used for:
- Hyperlinks
- Reaction complexes

Mats Jirstrand

Fraunhofer CHALMERS Research Centre Industrial Mathematics

Run simulation
Component Based Modeling

– An Example
Example

Entity (dynamic)

\[ A' = \]

Note: A represents the total amount of species A. Initial condition (concentration) is a property of the entity object. Here: \( A(t_{\text{start}}) = [A](t_{\text{start}}) \times V_0 \), where \([A](t_{\text{start}})\) is the concentration at \( t_{\text{start}} \).
Example
Transformation (base)

\[ A' = -r_1 V_0 \]

\[ r_1 = r_1(A, \_\_\_) \]

Note: Transformation rate specified in terms of volumetric flow rate (concentration per time unit), i.e., scaling with volume to obtain absolute rate.
Example
Entity (dynamic)

\[ V_0 = 1.0 \]

\[ A' = -r_1 V_0 \]

\[ B' = r_1 V_0 \]

\[ r_1 = r_1(A, B) \]
Example
Transformation (part)

\[ A' = -r_1 V_0 \]
\[ B' = r_1 V_0 \]

\[ r_1 = r_1(A, B, \_\_\_) \]

\( V_0 = 1.0 \)
Example
Transformation (part)

\[ A' = -r_1 V_0 \]
\[ B' = r_1 V_0 \]

\[ r_1 = r_1(A, B, _, _) \]
Example

Entities (dynamic)

\[
\begin{align*}
A' &= -r_1 V_0 \\
B' &= r_1 V_0 \\
ATP' &= -r_1 V_0 \\
ADP' &= r_1 V_0 \\
r_1 &= r_1 (A, B, ATP, ADP)
\end{align*}
\]

\( V_0 = 1.0 \)
Example
Transformation (base)

\[ V_0 = 1.0 \]

\[ A' = -r_1 V_0 \]
\[ B' = r_1 V_0 - r_2 V_0 \]
\[ ATP' = -r_1 V_0 \]
\[ ADP' = r_1 V_0 \]

\[ r_1 = r_1(A, B, ATP, ADP) \]
\[ r_2 = r_2(B, \_\_) \]
Example

Entity (dynamic)

\[ V_0 = 1.0 \]

\[
A' = -r_1 V_0 \\
B' = r_1 V_0 - r_2 V_0 \\
ATP' = -r_1 V_0 \\
ADP' = r_1 V_0 \\
C' = r_2 V_0
\]

\[
r_1 = r_1(A, B, ATP, ADP) \\
r_2 = r_2(B, C)
\]

Mats Jirstrand
Example

Control

\[ V_0 = 1.0 \]

\[ \begin{align*}
A' &= -r_1 V_0 \\
B' &= r_1 V_0 - r_2 V_0 \\
ATP' &= -r_1 V_0 \\
ADP' &= r_1 V_0 \\
C' &= r_2 V_0
\end{align*} \]

\[ r_1 = r_1(A, B, ATP, ADP; C) \]

\[ r_2 = r_2(B, C) \]
Example

Entity (auxiliary)

\[ A' = -r_1 V_0 \]
\[ B' = r_1 V_0 - r_2 V_0 \]
\[ ATP' = -r_1 V_0 \]
\[ ADP' = r_1 V_0 \]
\[ C' = r_2 V_0 \]

\[ E - E(t) = 1 - e^{-0.2t} \]
\[ r_1 = r_1(A, B, ATP, ADP; C) \]
\[ r_2 = r_2(B, C) \]
Example

Control

\[ V_0 = 1.0 \]

\[ A' = -r_1 V_0 \]

\[ B' = r_1 V_0 - r_2 V_0 \]

\[ ATP' = -r_1 V_0 \]

\[ ADP' = r_1 V_0 \]

\[ C' = r_2 V_0 \]

\[ E - E(t) = 1 - e^{-0.2t} \]

\[ r_1 = r_1(A, B, ATP, ADP; C) \]

\[ r_2 = r_2(B, C; E) \]
Example

Location

\[ A' = - r_1 V_0 \]
\[ B' = r_1 V_0 - r_2 V_0 \]
\[ ATP' = - r_1 V_0 \]
\[ ADP' = r_1 V_0 \]
\[ C' = r_2 V_0 \]
\[ E - E(t) = 1 - e^{-0.2t} \]
\[ r_1 = r_1(A, B, ATP, ADP; C) \]
\[ r_2 = r_2(B, C; E) \]
Example
Entity (dynamic)

\[ V_0 = 1.0 \]
\[ V_{nucleus} = 0.1 \]

\[ A' = -r_1 V_0 \]
\[ B' = r_1 V_0 - r_2 V_0 \]
\[ ATP' = -r_1 V_0 \]
\[ ADP' = r_1 V_0 \]
\[ C' = r_2 V_0 \]

\[ \text{nucleus}_A' = \]
\[ E - E(t) - 1 - e^{-0.2t} \]

\[ r_1 = r_1(A,B,ATP,ADP;C) \]
\[ r_2 = r_2(B,C;E) \]
Example

Transformation (base)

\[ V_0 = 1.0 \]
\[ V_{nucleus} = 0.1 \]

\[ A' = -r_1 V_0 - r_3 \]
\[ B' = r_1 V_0 - r_2 V_0 \]
\[ ATP' = -r_1 V_0 \]
\[ ADP' = r_1 V_0 \]
\[ C' = r_2 V_0 \]
\[ nucleus.A' = r_3 \]

\[ E - E(t) = 1 - e^{-0.2t} \]
\[ r_1 = r_1(A, B, ATP, ADP; C) \]
\[ r_2 = r_2(B, C; E) \]
\[ r_3 = r_3(A, nucleus.A) \]

Note: Transmembrane transport specified in terms of absolute rate (amount per time unit), i.e., no scaling with volume.

Mats Jirstrand
Example
Transformation (base)

\[ V_0 = 1.0 \]
\[ V_{\text{nucleus}} = 0.1 \]

\[ A' = - r_1 V_0 - r_3 \]
\[ B' = r_1 V_0 - r_2 V_0 \]
\[ ATP' = - r_1 V_0 \]
\[ ADP' = r_1 V_0 \]
\[ C' = r_2 V_0 \]
\[ nucleus.A' = r_3 - r_4 V_{\text{nucleus}} \]

\[ E - E(t) - 1 - e^{-0.2t} \]

\[ r_1 = r_1(A, B, ATP, ADP; C) \]
\[ r_2 = r_2(B, C; E) \]
\[ r_3 = r_3(A, nucleus.A) \]
\[ r_4 = r_4(nucleus.A) \]
Example
Rate expressions

\[
\begin{align*}
A' &= -r_1 V_0 - r_3 \\
B' &= r_1 V_0 - r_2 V_0 \\
ATP' &= -r_1 V_0 \\
ADP' &= r_1 V_0 \\
C' &= r_2 V_0 \\
\text{nucleus.A}' &= r_3 - r_4 V_{\text{nucleus}} \\
E - E(t) &= 1 - e^{-0.2t}
\end{align*}
\]

\[
\begin{align*}
 r_1(A, B, ATP, ADP, C) &= \frac{V_m s_1}{K_{m1} + s_1 K_{m2} + s_2 1 + m_1/K_i} \\
 s_1 &= [A] = A/V_0, \quad s_2 = [ATP] = ATP/V_0 \\
 p_1 &= [B] = B/V_0, \quad p_2 = [ADP] = ADP/V_0 \\
 m_1 &= [C] = C/V_0 \\
 V_0 &= 1.0 \\
 V_{\text{nucleus}} &= 0.1
\end{align*}
\]
Example

Rate expressions

\[ A' = -r_1 V_0 - r_3 \]
\[ B' = r_1 V_0 - r_2 V_0 \]
\[ ATP' = -r_1 V_0 \]
\[ ADP' = r_1 V_0 \]
\[ C' = r_2 V_0 \]
\[ nucleus.A' = r_3 - r_4 V_{nucleus} \]
\[ E - E(t) = 1 - e^{-0.2t} \]

\[ r_2(B, C; E) = \frac{V_m s_1}{K_m + s_1} \]
\[ V_m = k m_1 \]
\[ s_1 = [B] = B/V_0 \]
\[ p_1 = [C] = C/V_0 \]
\[ m_1 = [E] = E/V_0 \]

Mats Jirstrand

Fraunhofer CHALMERS Research Centre Industrial Mathematics
Example
Rate expressions

\[ A' = -r_1 V_0 - r_3 \]
\[ B' = r_1 V_0 - r_2 V_0 \]
\[ ATP' = -r_1 V_0 \]
\[ ADP' = r_1 V_0 \]
\[ C' = r_2 V_0 \]
\[ nucleus.A' = r_3 - r_4 V_{nucleus} \]
\[ E - E(t) = 1 - e^{-0.2t} \]

\[ \begin{cases} 
  r_3(A, nucleus.A) = D(s_1 - p_1) \\
  s_1 = [A] = A/V_0 \\
  p_1 = [nucleus.A] = nucleus.A/V_{nucleus} 
\end{cases} \]
Example

Rate expressions

\[ V_0 = 1.0 \]
\[ V_{\text{nucleus}} = 0.1 \]

\[ A' = -r_1 V_0 - r_3 \]
\[ B' = r_1 V_0 - r_2 V_0 \]
\[ ATP' = -r_1 V_0 \]
\[ ADP' = r_1 V_0 \]
\[ C' = r_2 V_0 \]
\[ nucleus.A' = r_3 - r_4 V_{\text{nucleus}} \]
\[ E - E(t) = 1 - e^{-0.2t} \]

\[
\begin{align*}
    r_4(\text{nucleus}.A) &= k s_1 \\
    s_1 &= [\text{nucleus}.A] = \text{nucleus}.A/V_{\text{nucleus}}
\end{align*}
\]
The Graphical User Interface
- Overview

PathwayLab Menu  Pointer Tool  Connector Tool

Stencils

Drawing Page

Properties Pane

Simulation Control

PathwayLab Toolbar

Preview Plot
The Graphical User Interface
- Stencils and the Drawing Page

- Component libraries
- Collections of ready made pathway modeling objects
  - Entities: basic plain shapes
  - Mass Action Reactions: contains mass action kinetics
  - Locations: basic location geometries
The Graphical User Interface
- Stencils and the Drawing Page

- Component libraries
  - Enzymatic Reactions: contain basic enzyme kinetics
  - Interactions (BVT): sample user specified transformations and controls
  - Entities (BVT): sample user specified entities
The Graphical User Interface
- Stencils and the Drawing Page

- Complex interactions can be build by joining basic transformation and control parts together!
- Component libraries
  - Reaction Parts: basic reaction parts
  - Control Parts: basic control parts
The Graphical User Interface
- The Properties Pane

- Information about the currently selected object
- Name: complete, short, and descriptive (show/hide)
- Simulation: properties related to simulations
- Database Info: local display copy of data retrieved from database.
- Notes
The Graphical User Interface
- The Preview Plot

- Preview Plot: Plots graphs of simulation results based on objects selected on the drawing page.

- Time-course plots
  - Select multiple entities by SHIFT-click

- Phase-plane plots
  - First selected entity on x-axis
  - Second on the y-axis
The Graphical User Interface
- The Simulation Control

- Start and final times
- Execute simulation (play)
- Simulation Settings Dialog
  - Start/final simulation times
  - Absolute and relative tolerances
  - # simulation output points
  - Min/Max checking
  - Stationary Analysis etc
The Graphical User Interface
- Drag and Drop Modeling

1. Open a new file using the File menu:
   New->PathwayLab->PathwayLab
2. Drag-and-drop from the "Entities" stencil two copies of the "Entity" object onto the drawing page
3. Rename them by selecting them and type their new name
4. Drag-and-drop from the "Mass Action Kinetics" stencil the symbol for "Reaction" onto the drawing page
5. Click and hold on each end of the reaction arrow to glue the arrow on to the entities (a high lighted red rectangle is shown to indicate that an arrow end is glued to the entity)
The Graphical User Interface
- Drag and Drop Modeling

6. Click on the play button in the Simulation Control to simulate the model

7. Click on the pathway modeling objects (entities and the reaction) to view the simulation result in the Preview Plot.
The Graphical User Interface
- The Formula Settings Dialog

- Open the Formula Setting Dialog by double-clicking on the reaction arrow (or select the reaction and click the Details button in the Properties pane)
- Local variable names to assure portability (a Transformation is not always connected to an entity)
- Parameters: name, value, unit (optional)
- Reaction rate formula (to be specified in terms of variables and parameters)
The Graphical User Interface
- Drag and Drop Modeling

8. Extend the simple reaction arrow by adding other interaction parts (drag-and-drop from the Reaction Parts and Control Parts stencils).

9. Open the Formula Settings dialog and inspect the new local variables that corresponds to the unconnected interaction ends.

10. Use the connector tool to extend an interaction part to connect it to an pathway modeling object.

11. Add and connect entities to the new substrate and product ends.

12. Open the Formula Settings dialog and modify the reaction rate formula to take the new involved entities into account.
The Graphical User Interface
- Drag and Drop Modeling

13. Create or paste some graphics into the drawing area, e.g., the structural formal for pyruvate.

14. Select it and choose Shape Operations ... -> Convert To ... -> Entity from the PathwayLab menu.

15. Use it as any other built-in pathway modeling object: change name, connect it to a reaction, ...
Simulation of Models
- Transient Analysis

- Default analysis performed when the play button in the Simulation Control is pushed.
- Reaction rate equations corresponding to the pathway diagram are simulated.
- Initial conditions are specified per entity in the Properties pane.
- Options for the integration can be set using the ... Button in the Simulation Control.
- The result can be explored by selecting objects and inspecting the graphs in the Preview Plot.

Mats Jirstrand
Simulation of Models
- Transient Analysis

Parameter scanning
- Open the BioCircuit.vsd model.
- Select some pathway modeling objects for preview plot.
- Select Model Properties on the PathwayLab menu.
- Select a parameter, e.g., r10.Vm, to vary and click the Add button.
- Edit the Range for the parameter to 1:0.1:2 to specify that simulations should be done for the values 1 to 2 in steps of 0.1.
Simulation of Models
- Transient Analysis

Parameter scanning

- Click the Play button in the dialog to watch the simulation results to be built up.
- To select other entities the Model Properties dialog needs to be closed.
- It is possible to select multiple parameters for simultaneous scanning.
- Parameter scanning may consume a lot of memory (estimation of runs and memory at the bottom of the dialog).

Mats Jirstrand
Simulation of Models
- Steady State Analysis

- The steady state analysis computes the steady state of the system (explicit functions of time are fixed at time = Start Time)

- The steady state values (entity concentrations and reaction rates) are reported in the Messages pane (available from the PathwayLab menu or PathwayLab tool bar)

- It is possible to initialize a simulation in a steady state (hence, overruling initial conditions given per entity in the preview pane). See check box!
Simulation of Models
- Steady State Analysis

- The steady state analysis computes the steady state of the system (explicit functions of time are fixed at time = Start Time)
- The steady state values (entity concentrations and reaction rates) are reported in the Messages pane (available from the PathwayLab menu or PathwayLab tool bar)
- It is possible to initialize a simulation in a steady state (hence, overruling initial conditions given per entity in the preview pane). See check box!
Simulation of Models
- Steady State Analysis

- The steady state analysis computes the steady state of the system (explicit functions of time are fixed at time = Start Time)
- The steady state values (entity concentrations and reaction rates) are reported in the Messages pane (available from the PathwayLab menu or PathwayLab tool bar)
- It is possible to initialize a simulation in a steady state (hence, overruling initial conditions given per entity in the preview pane). See check box!

Mats Jirstrand

Fraunhofer CHALMERS
Research Centre
Industrial Mathematics
Simulation of Models
- Metabolic Control Analysis

- Pathwaylab performs MCA and compute CCCs and FCCs
  - FCC\(=(\Delta J/J)/(\Delta E/E)\)
  - CCC\(=(\Delta C/C)/(\Delta E/E)\)

- The level of perturbation is set in the Simulation Settings dialog

- The result is given in the Messages pane
  - FCC(name of perturbed transformation, name of response transformation)
  - CCC(name of perturbed transformation, name of response entity)
Import and Export of Data

- Tabulated data can be used as input to a simulation.
- File format: plain ASCII files with comma separated values, CSV.
- Time in one column and corresponding values in another.
- Linear interpolation is used to obtain intermediate values.
- Values beyond the time data is fixed to the last value.
Import and Export of Data

- Tabulated data can be used as input to a simulation
- File format: plain ASCII files with comma separated values, CSV
- Time in one column and corresponding values in another
- Linear interpolation is used to obtain intermediate values
- Values beyond the time data is fixed to the last value
- The time points can optionally be treated as discrete (in plots)
Import and Export of Data

- Simulation data can be exported to file
- The Save Simulation Data dialog can be opened from the PathwayLab menu
- Select type of data to be saved
- Select which data to be saved
Connectivity to Mathematica and Matlab

- Export a model using Export To ... on the PathwayLab menu
  - Mathematica: m-file containing a symbolic expression with all information about the model
  - Matlab: m-file ready to be used with Matlab solvers ode15s, ... 
  - SBML: xml-file

- PathwayLab application package for Mathematica
Connectivity to Mathematica and Matlab
- Interactive Visualization in Mathematica

Example Notebook
Connectivity to Mathematica and Matlab
- Simulation in Matlab

- The exported m-file defines a function which provides
  - state names
  - parameter names
  - parameter values
  - RHS of the ODEs at time t and state x

% Code for parameter scanning
ic = BioCircuit();
clf; hold on
for Vm = 1:0.1:2
    [t, x]=ode15s(@BioCircuit,[0,40],...
        ic,[],['r10_Vm'],[Vm]);
    plot(t,x(:,2),t,x(:,5),t,x(:,6))
end
hold off

Mats Jirstrand
Overview of the Documentation

- The online documentation is available via the PathwayLab menu
- Sections
  - Registering PathwayLab
  - Build Pathway Models
  - Analyze Pathway Models
  - Import and Export
  - Connect to Database
  - Troubleshooting