

# Mathematical modeling with CellDesigner

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# Overview

- Introduction of CellDesigner
  - What kind of model you can build
- How to build a model with CellDesigner
  - From scratch
  - Import a model, kinetic law and parameters from existing databases

# Installation



CellDesigner-  
4.3beta2-wind  
ows-installer.  
exe

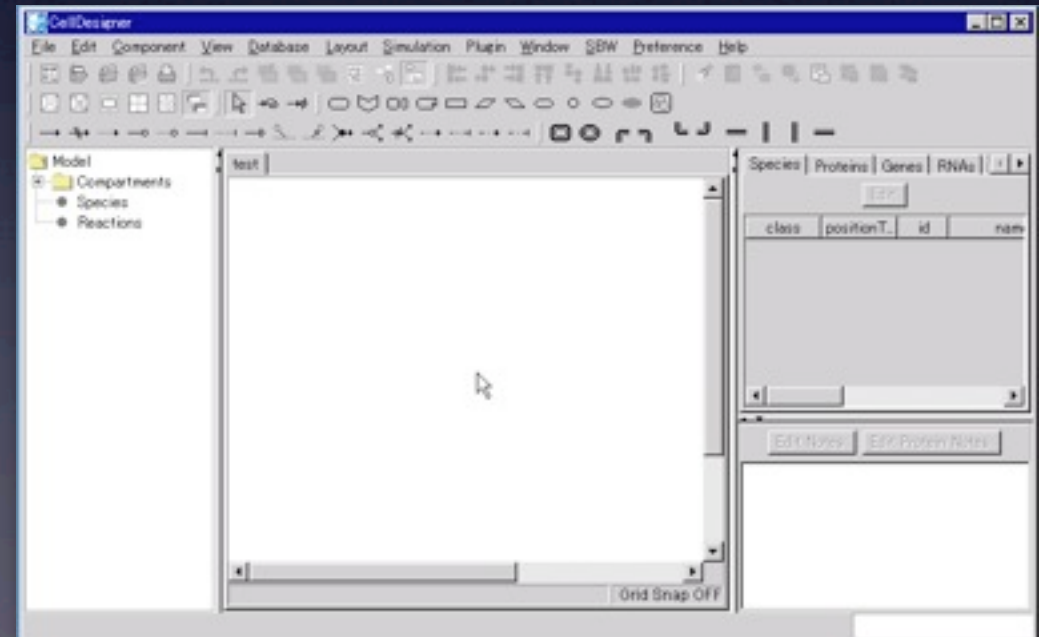
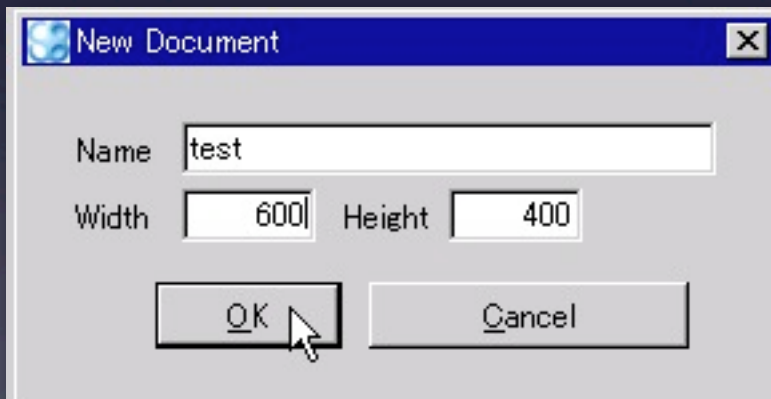
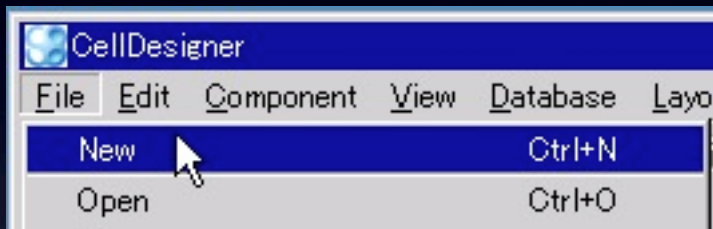


CellDesigner4.  
3beta

# Create model

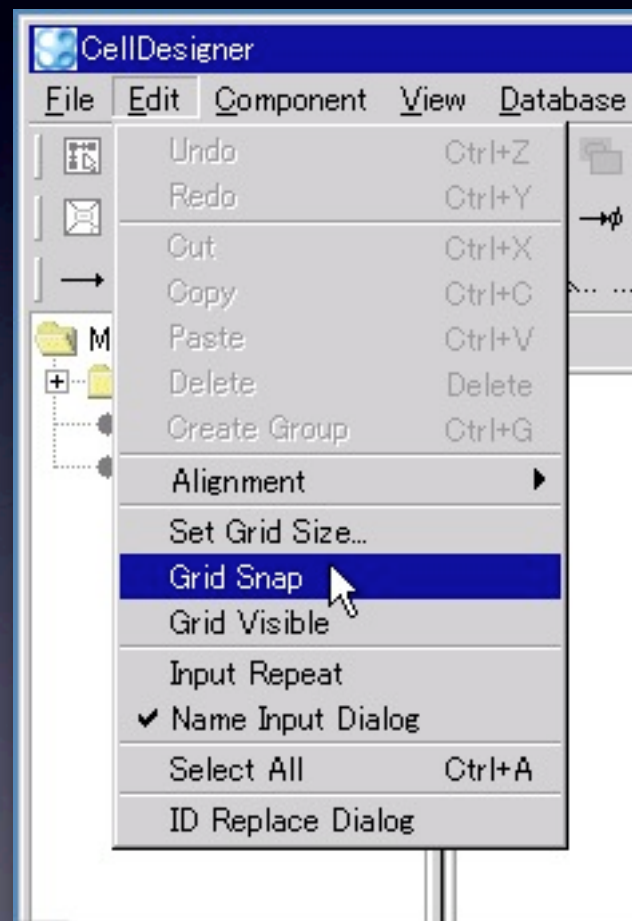
- Create new model:

- [File] → [New] → input title → [OK]

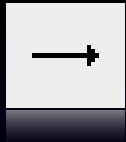


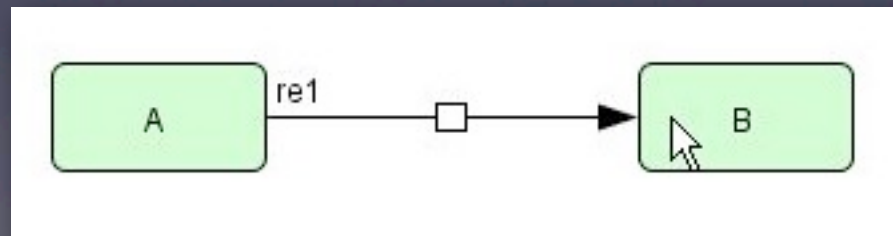
# Tips

- **Enable [Grid Snap] will help you draw your model much easier**



# Create Reaction

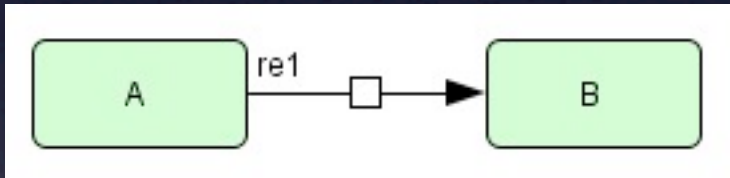
- Create Protein “A” and “B”
- Draw “State transition”  arrow from “A” to “B”





# Simulation (ex1)

- Create following biochemical reaction
- Click [Simulation] → [ControlPanel] and call SBML ODE Solver

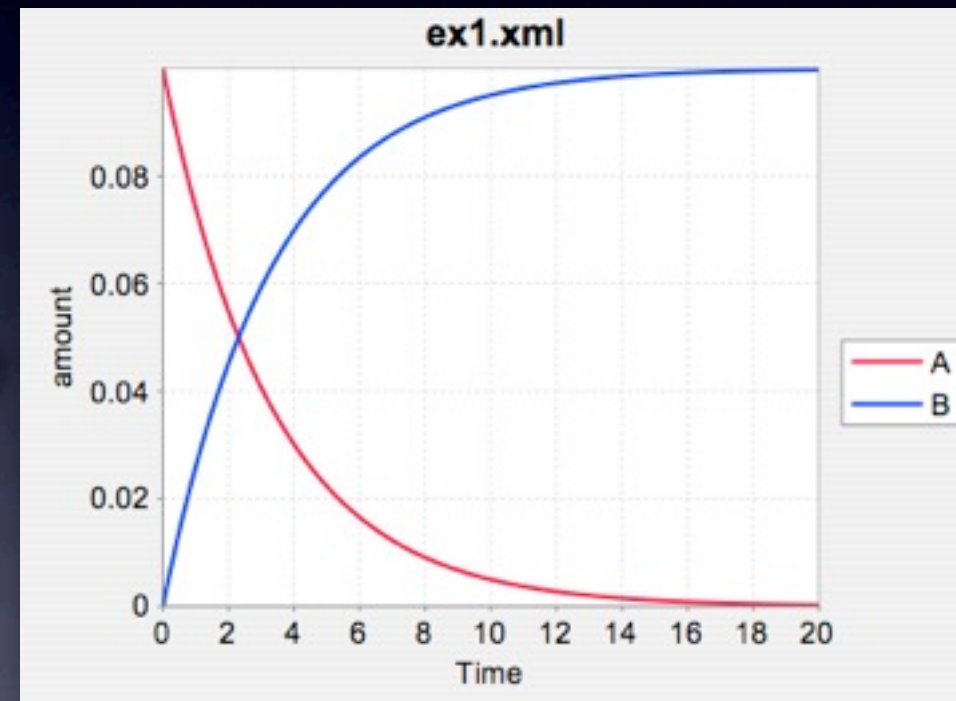


$$v = k[A]$$

$$k = 0.3$$

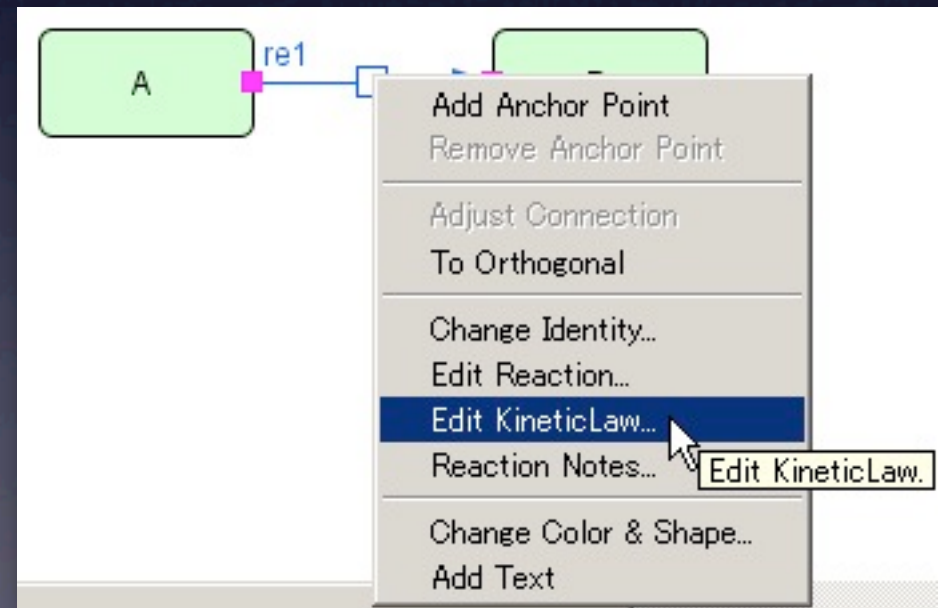
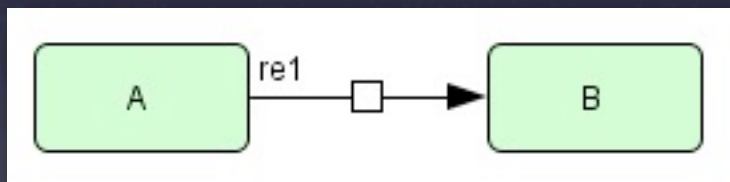
$$A = 0.1$$

$$B = 0$$



# Simulation (ex1)

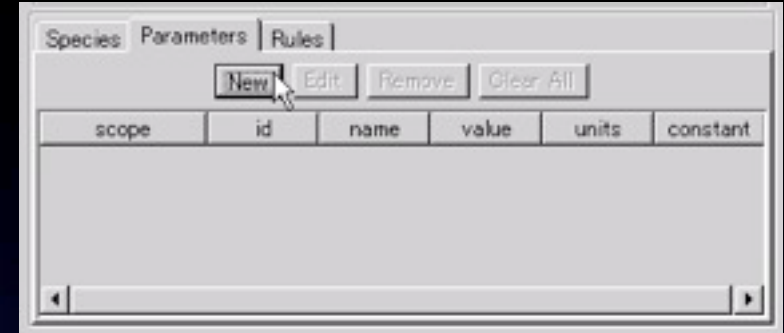
- Right click on the reaction and select [Edit KineticLaw...]





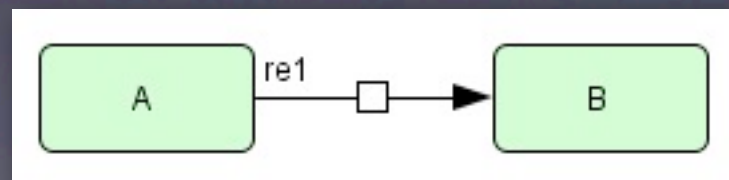
# Simulation (ex1)

- Click [New] button on [Parameters] tab



- Input values as follows:

- id: **k**
- name: **k**
- value: **0.3**



$$v = k[A]$$

$$k = 0.3$$

$$A = 0.1$$

$$B = 0$$

# Simulation (ex1)

- Click top most text field
- Type  $k *$  (k times)
- Select Protein “A”
- Click [Name] checkbox  
(  $k*s1 \rightarrow k*A$  )

$$v = k[A]$$

$$k = 0.3$$

$$A = 0.1$$

$$B = 0$$

The screenshot shows the KineticLaw software interface. The 'math' field contains the expression  $k*s1$ . The 'Name' checkbox is checked, and the 'SelectedReaction' panel shows a reaction from species A to species B. The 'Predefined Functions' panel lists 'NonPredefinedFunction', 'Mass\_Action\_Kinetics', and 'Irreversible\_Simple\_Michaelis-Menten'. The 'Parameters' tab is active, showing a table with the following data:

| scope            | id | name | value | units | constant |
|------------------|----|------|-------|-------|----------|
| localReaction/r_ | k  | k    | 0.3   |       | true     |

Buttons for 'Update' and 'Cancel' are at the bottom.

math

☐ Math
 ☐ Name

+

-

\*

/

(

)

SelectedReaction

s1

A

→

s2

B

Predefined Functions

NonPredefinedFunction

Mass\_Action\_Kinetics

Irreversible\_Simple\_Michaelis-Menten

Species Parameters Rules

New

Edit

Remove

Clear All

| scope            | id | name | value | units      | constant |
|------------------|----|------|-------|------------|----------|
| local:Reactio... | k  | k    | 0.3   | substan... | true     |

Update

Cancel

Species

Edit

Export

| class  | id | name |
|--------|----|------|
| ROTEIN | s1 | A    |
| ROTEIN | s2 | B    |

NOTE

MIRIAM

Edit Notes

reaction (id=re1, name=;  
 est)

# Simulation (ex1)

- Double click [initialQuantity] column for Protein “A”

The screenshot shows the MAPK software interface. On the left, a reaction diagram shows a green box labeled 'A' with a pink border, connected by a blue arrow labeled 're1' to another green box labeled 'B'. On the right, a table with columns 'Species', 'Proteins', 'Genes', 'RNAs', 'asRNAs', and 'Reactions' is visible. The 'Proteins' tab is selected, and the 'initialQuantity' column is highlighted. A mouse cursor is clicking on the '0.0' value in the 'initialQuantity' column for Protein 'A'. Below the table, there are buttons for 'Edit Notes' and 'Edit Protein Notes'. At the bottom, text indicates 'Species (id=s1, name=A; ex1)' and 'Protein (id=pr1, name=A)'.

| Species | Proteins | Genes  | RNAs | asRNAs | Reactions |
|---------|----------|--------|------|--------|-----------|
| default | inside   | Amount | 0.0  |        |           |
| default | inside   | Amount | 0.0  |        |           |

Species (id=s1, name=A; ex1)  
Protein (id=pr1, name=A)

- Set value as 0.1

$$v = k[A]$$

$$k = 0.3$$

$$A = 0.1$$

$$B = 0$$

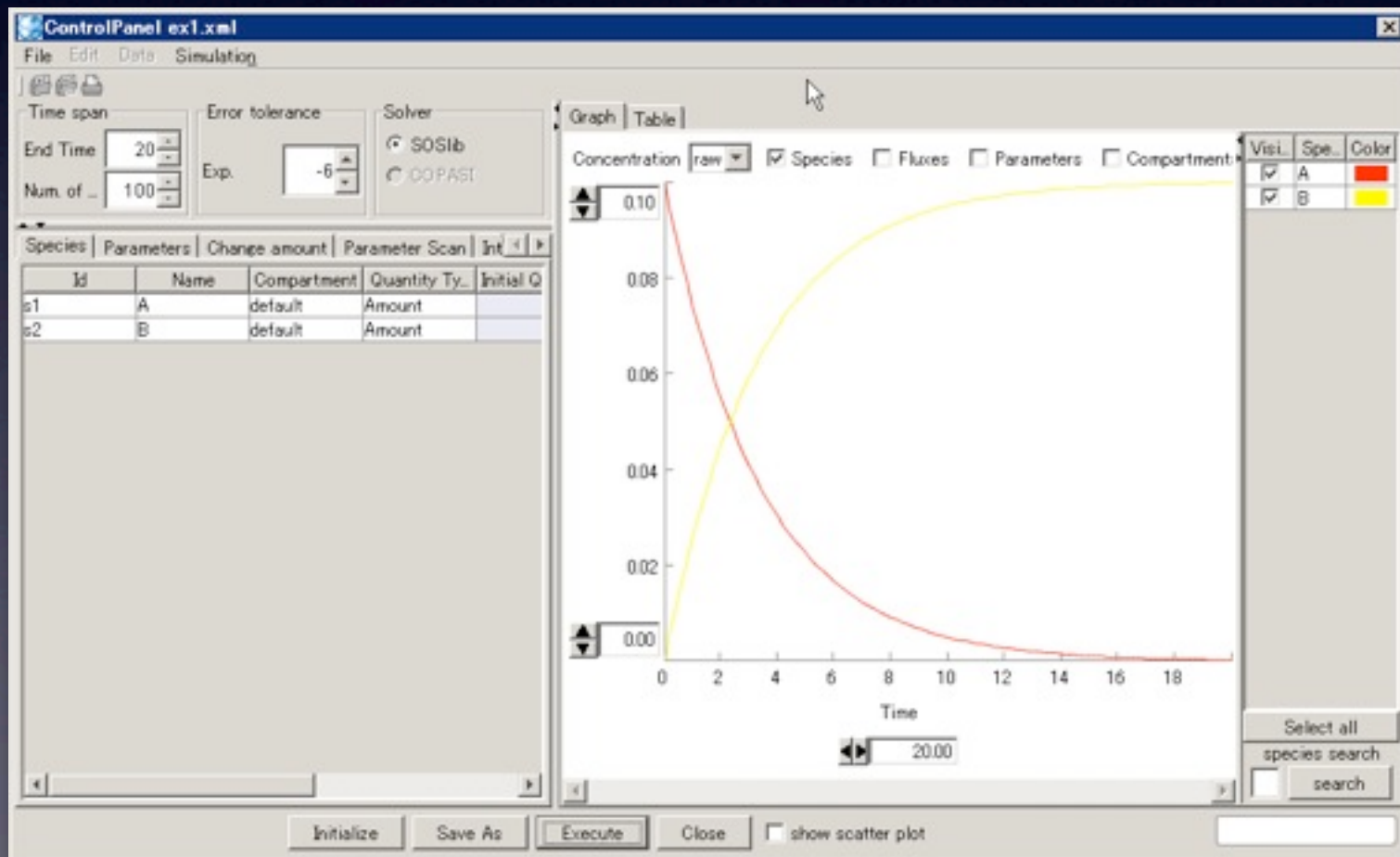
# Simulation (ex1)

- Click [Simulation] → [ControlPanel]
- Set [End Time] to 20
- Click [Execute] button

Time span

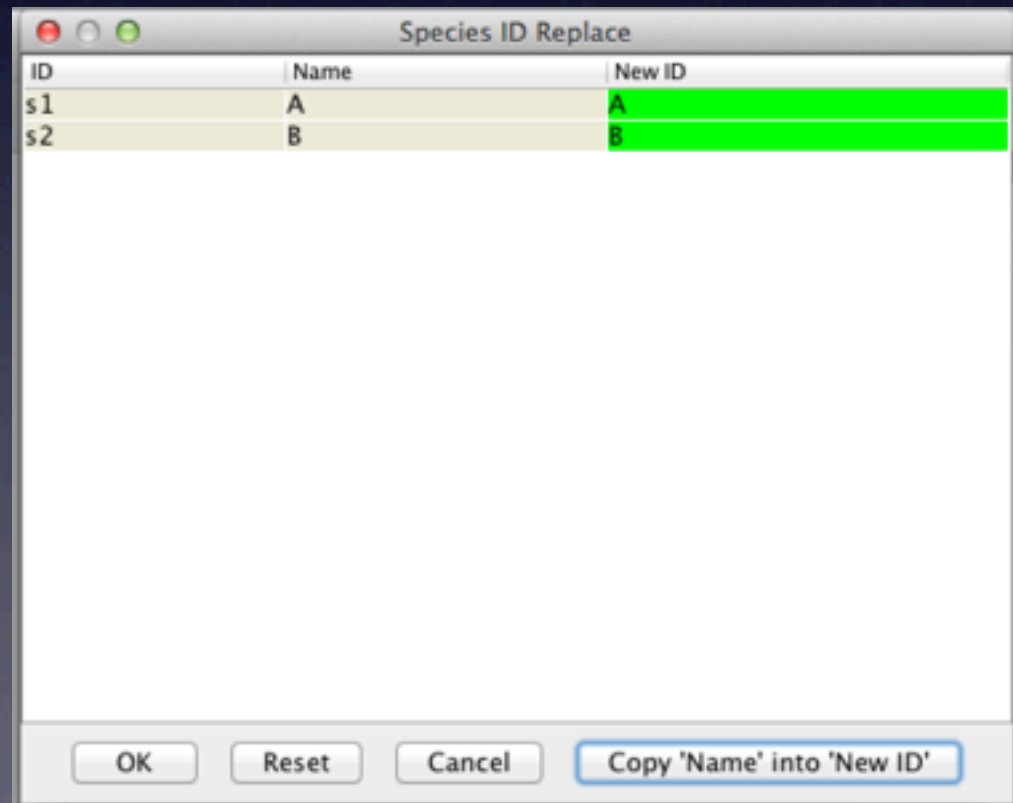
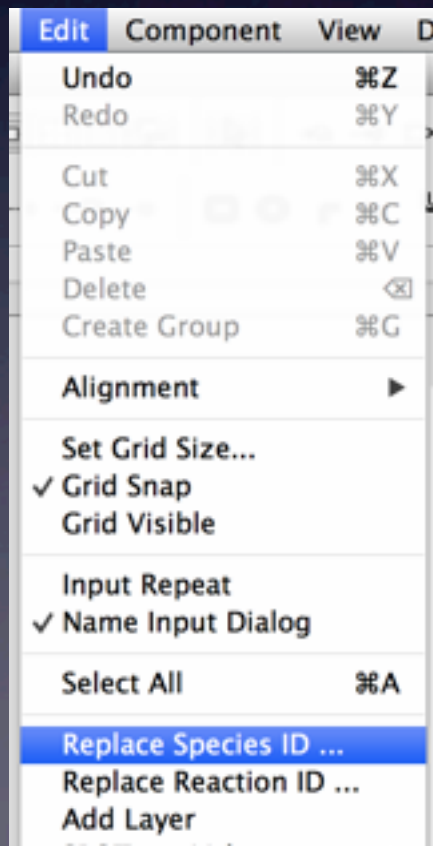
End Time

Num. of Points



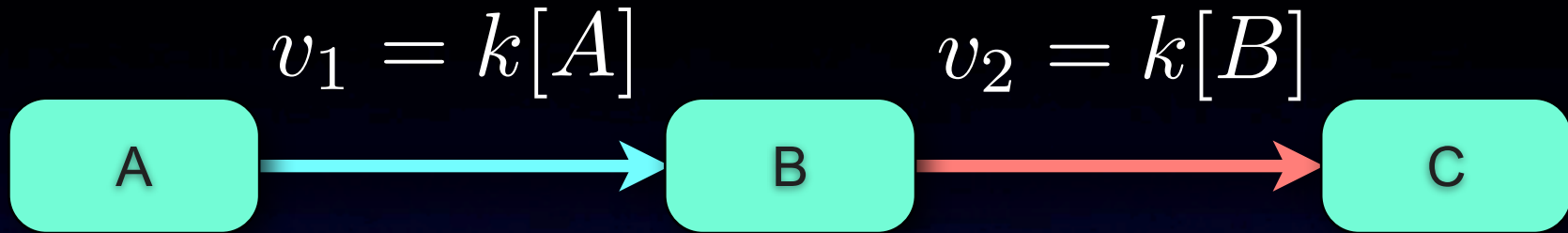
# Rename Species ID (s1 → A)

- Click [Edit] → [Replace Species ID]
- Click [Copy 'Name' into ...] button
- Use “Species Name” in KineticLaw Editor





# Network $\rightarrow$ Equation



$$\frac{d[A]}{dt} = -k[A]$$

$$\frac{d[B]}{dt} = k[A] - k[B]$$

$$\frac{d[C]}{dt} = k[B]$$

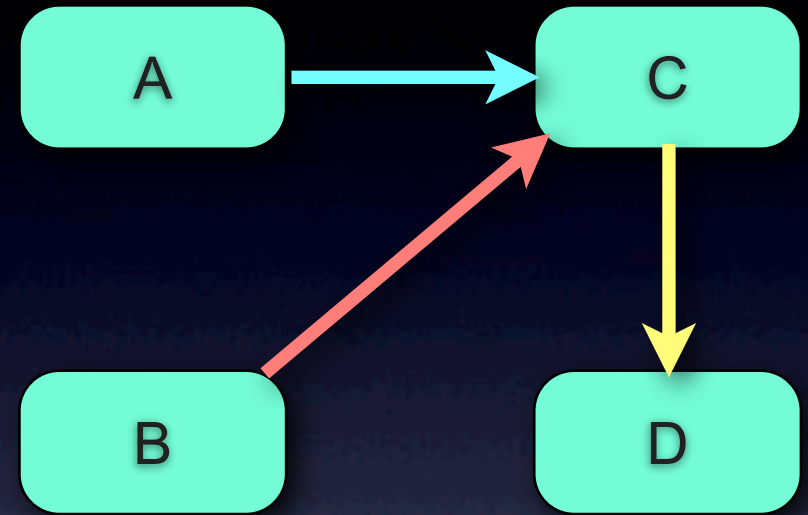
# Equation $\rightarrow$ Network

$$\frac{dA}{dt} = -k_1 A$$

$$\frac{dB}{dt} = -k_2 B$$

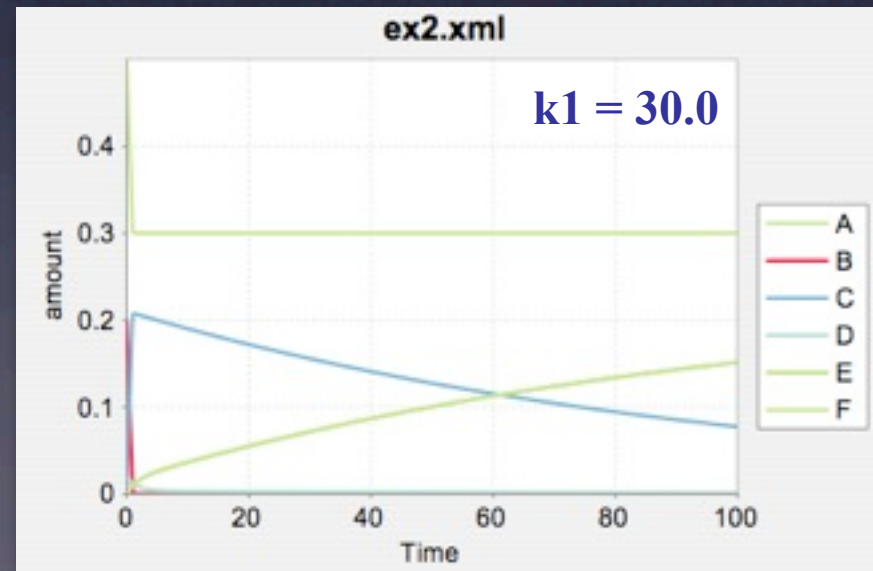
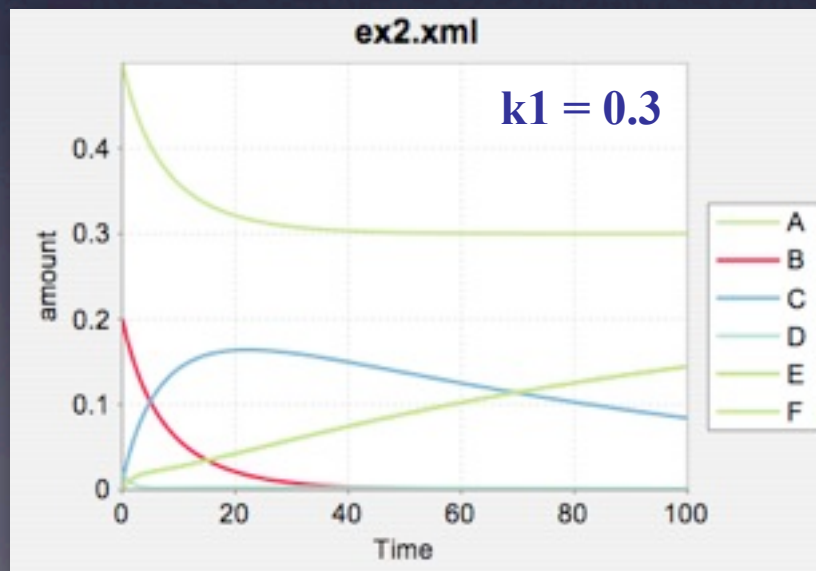
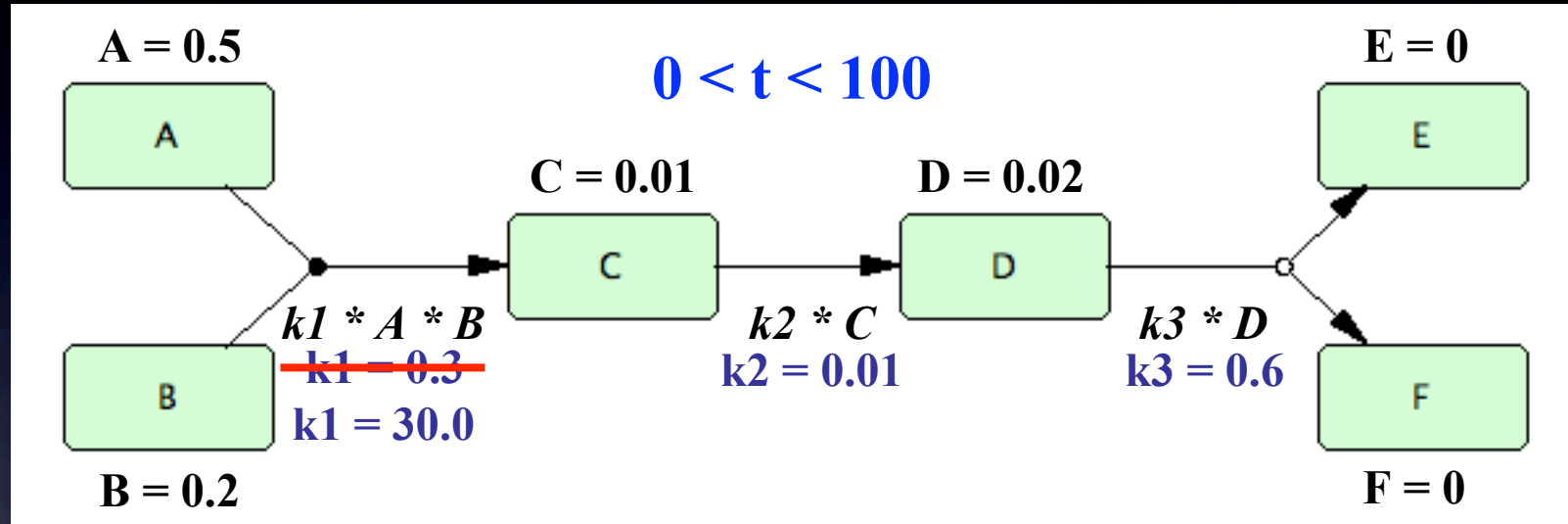
$$\frac{dC}{dt} = k_1 A + k_2 B - k_3 C$$

$$\frac{dD}{dt} = k_3 C$$



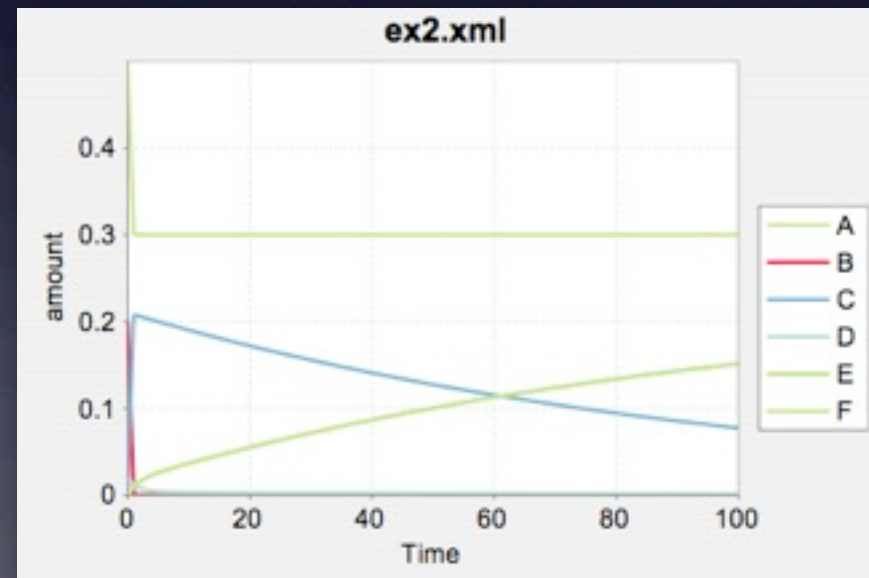
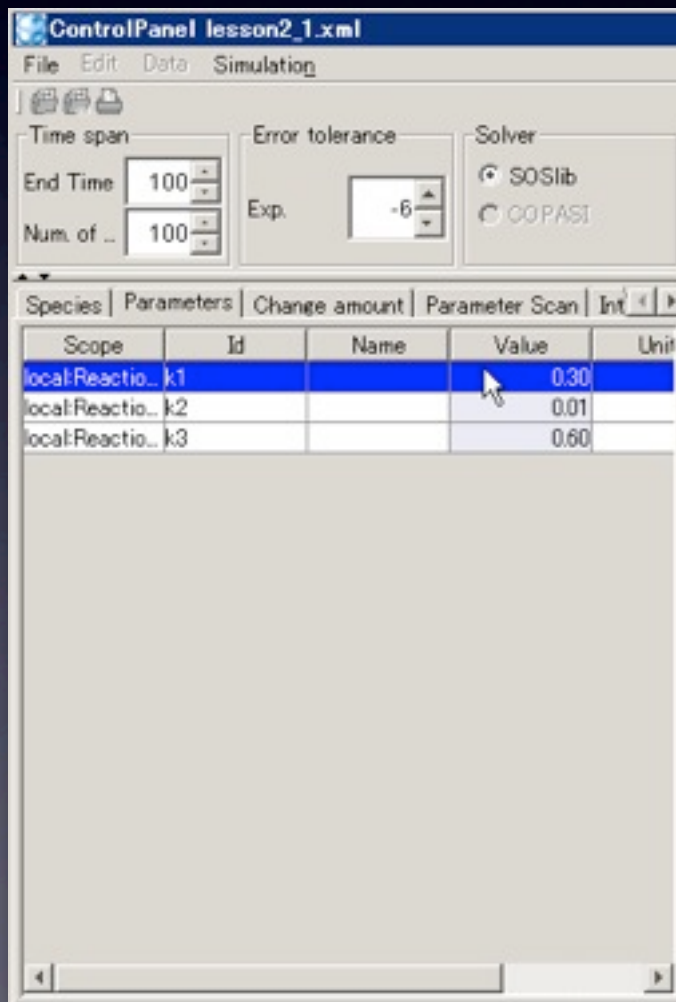
# Simulation (ex2)

- Change parameter  $k_1$  to 30.0



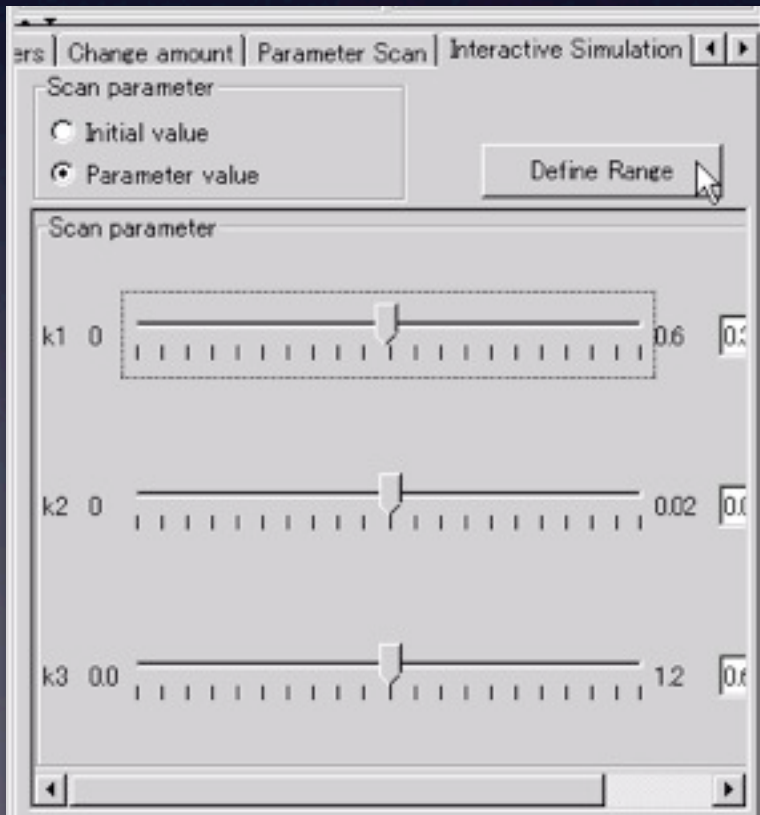
# Simulation (ex2)

- Click [Parameters] tab
- Double click [Value] column for k1
- Change parameter k1 to **30.0**



# Simulation (ex2)

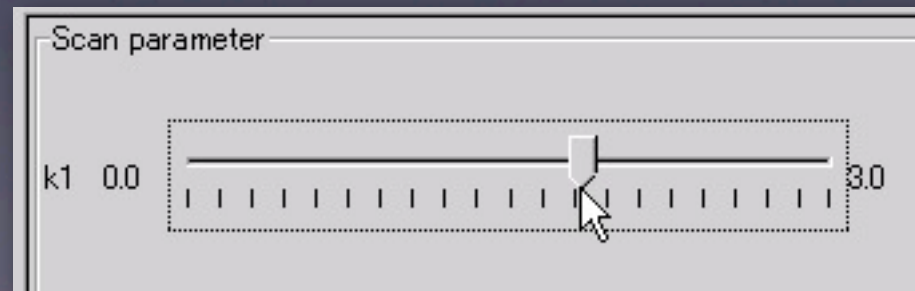
- Click [Interactive Simulation] tab
- Click [Parameter value] radio button
- Click [Define Range] button
- Click [Max] column for k1 and set value as 3.0



The 'Define Slider Range' dialog box displays a table with four columns: Id, Min, Max, and Current. The table contains three rows of data for parameters k1, k2, and k3. A mouse cursor is pointing at the 'Max' value for k1, which is 3.00.

| Id | Min | Max  | Current |
|----|-----|------|---------|
| k1 | 0.0 | 3.00 | 0.30    |
| k2 | 0.0 | 0.02 | 0.01    |
| k3 | 0.0 | 1.20 | 0.60    |

Drag sliderbar for k1



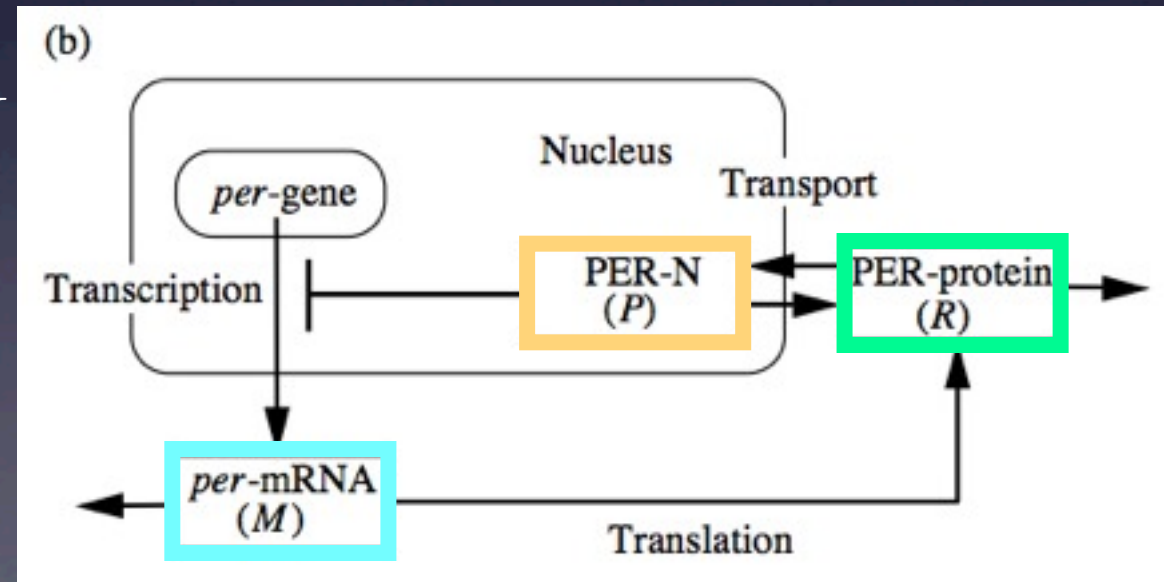
# Circadian clock model

- Protein (**P**) **inhibits** transcription of mRNA (**M**)
- **M** is translated to Protein (**R**)
- **P** / **R** will be transported to cytosol / nucleus

$$\frac{dM}{dt} = \frac{1}{1 + (P/h)^n} - aM - sM$$

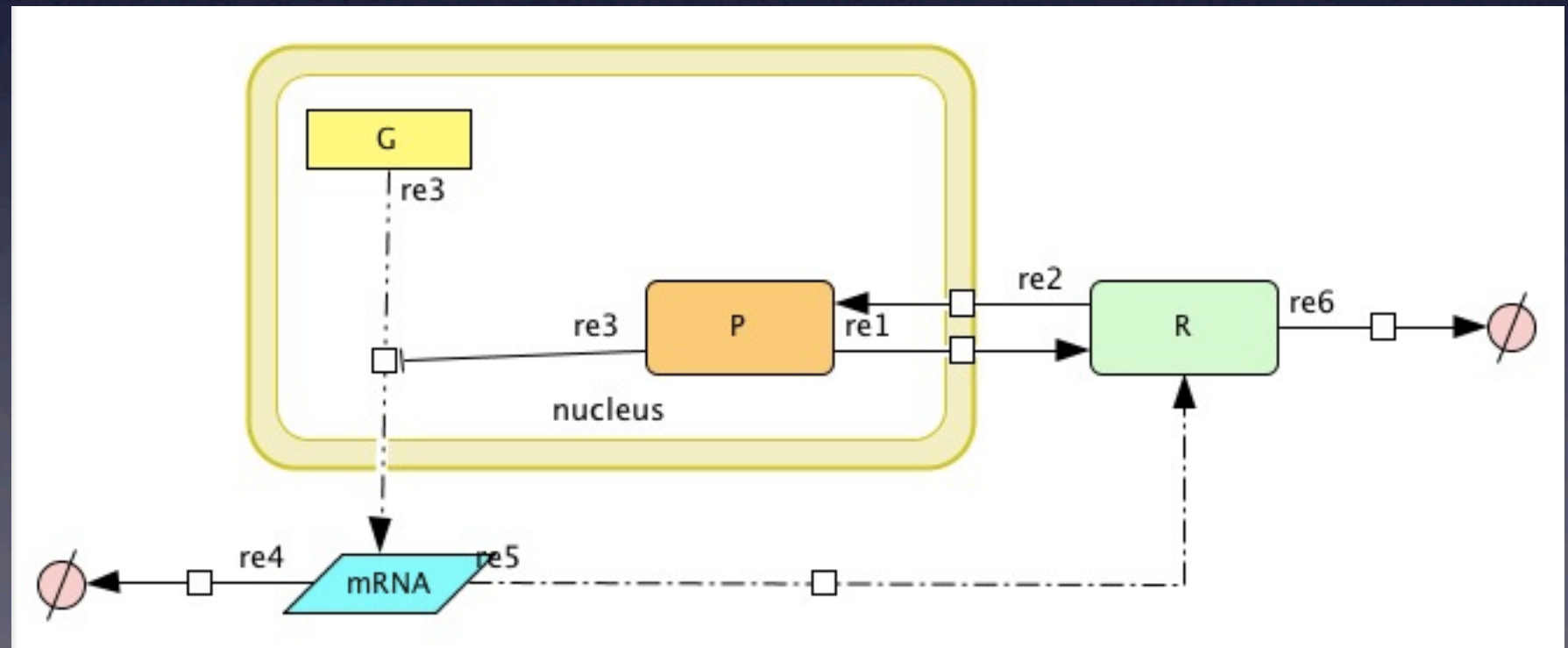
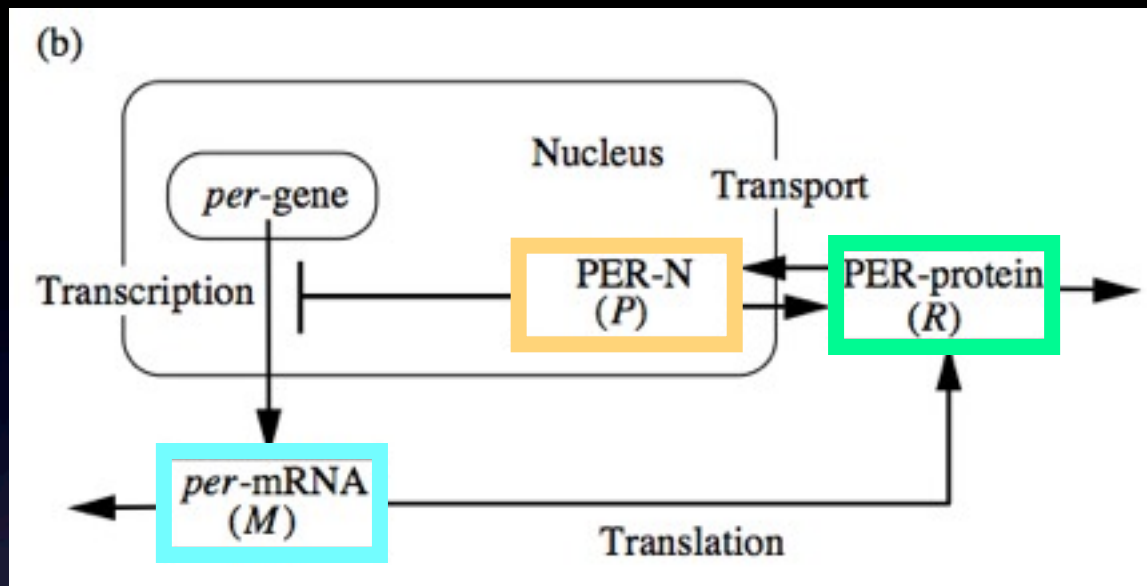
$$\frac{dR}{dt} = sM - (d + u)R + vP$$

$$\frac{dP}{dt} = uR - vP$$





# Circadian clock model



# Circadian clock model

$$\frac{dM}{dt} = \frac{1}{1 + (P/h)^n} - aM - sM$$

$$a = s = d = v = 1.0$$

$$\frac{dR}{dt} = sM - (d + u)R + vP$$

$$x^n = \text{pow}(x, n)$$

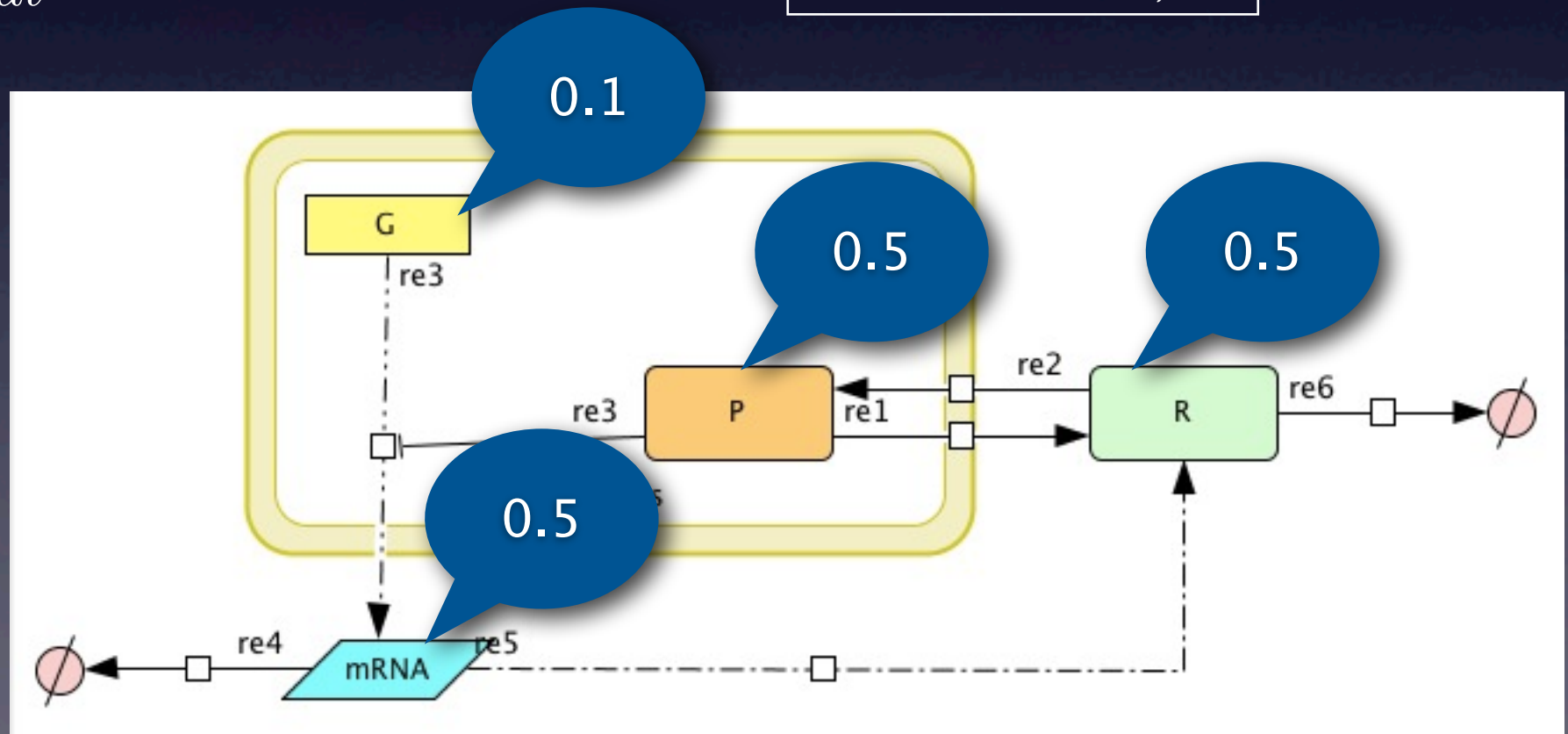
$$u = 0.1$$

$$h = 0.01$$

$$\frac{dP}{dt} = uR - vP$$

End Time: 50  
Num. of Points: 1,000

$$n = 40$$



# Circadian clock model

$$\frac{dM}{dt} = \frac{1}{1 + (P/h)^n} - aM - sM$$

$$a = s = d = v = 1.0$$

$$\frac{dR}{dt} = sM - (d + u)R + vP$$

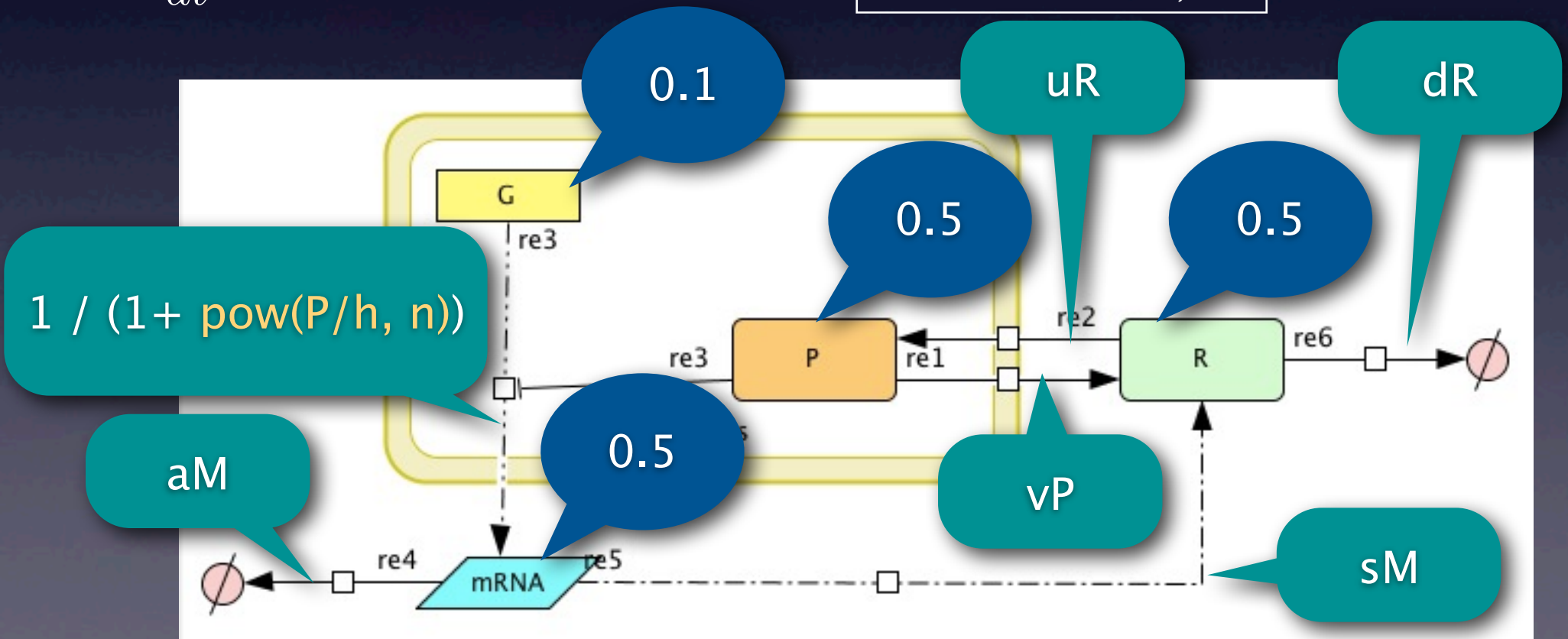
$$u = 0.1$$

$$h = 0.01$$

$$\frac{dP}{dt} = uR - vP$$

$$n = 40$$

End Time: 50  
Num. of Points: 1,000



# Boundary condition



| name   | speciesType | compar... | positio... | included | quantit... | initialQuantity | sub... | hasO... | b.c.  |
|--------|-------------|-----------|------------|----------|------------|-----------------|--------|---------|-------|
| G      |             | c1        | inside     |          | Amount     | 0.1             |        | true    | true  |
| mRNA   |             | default   | inside     |          | Amount     | 0.5             |        | true    | false |
| P      |             | c1        | inside     |          | Amount     | 0.5             |        | true    | false |
| R      |             | default   | inside     |          | Amount     | 0.5             |        | true    | false |
| waste  |             | default   | inside     |          | Amount     | 0.0             |        | true    | true  |
| waste2 |             | default   | inside     |          | Amount     | 0.0             |        | true    | true  |

Species

id: s1

name: G

speciesType: [dropdown]

compartment: c1

initial...: ☒ Amount ☐ Concentration  
0.1

substanceUnits: [dropdown]

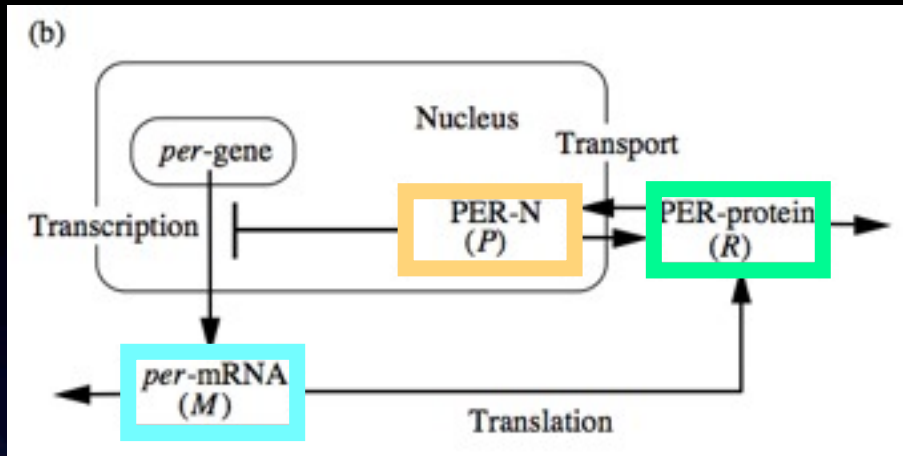
hasOnlySubstanceUnits: ☒ true ☐ false

**boundaryCondition: ☒ true ☐ false**

constant: ☐ true ☒ false

Update Cancel

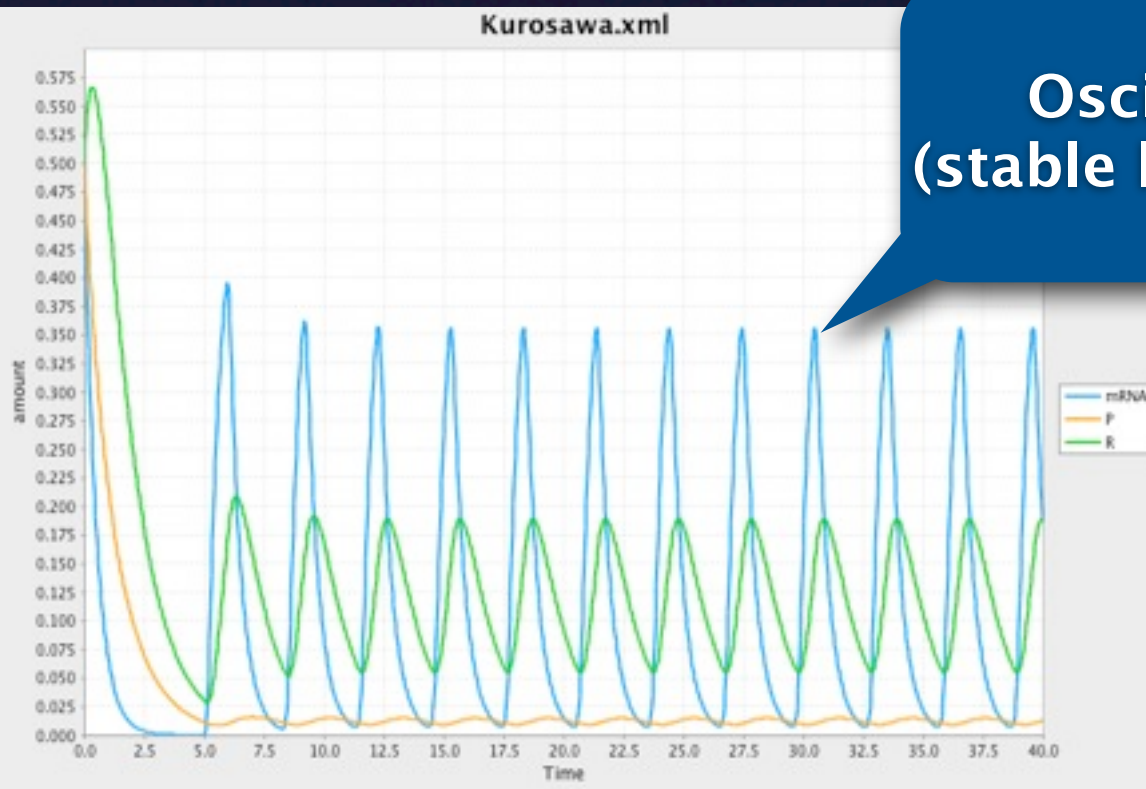
# Qualitative change by 'n'



$$\frac{dM}{dt} = \frac{1}{1 + (P/h)^n} - aM - sM$$

$$\frac{dR}{dt} = sM - (d + u)R + vP$$

$$\frac{dP}{dt} = uR - vP$$

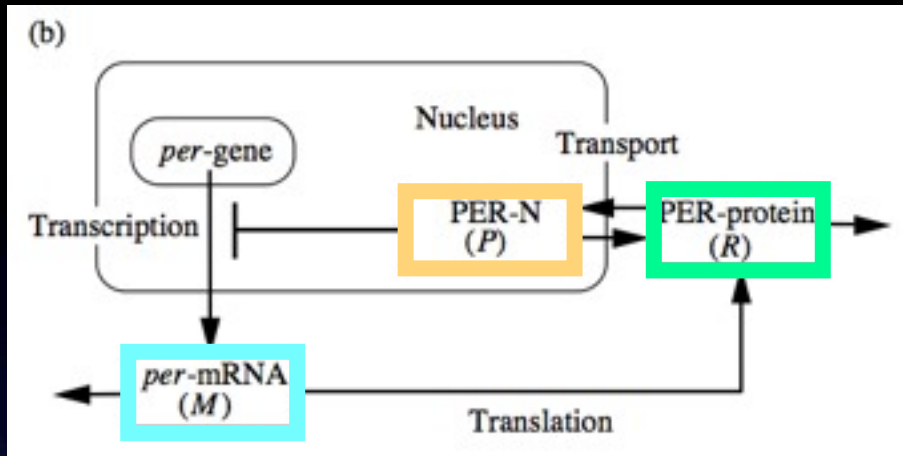


Oscillation  
(stable limit cycle)

$$n = 40$$

End Time: 50  
Num. of Points: 1,000

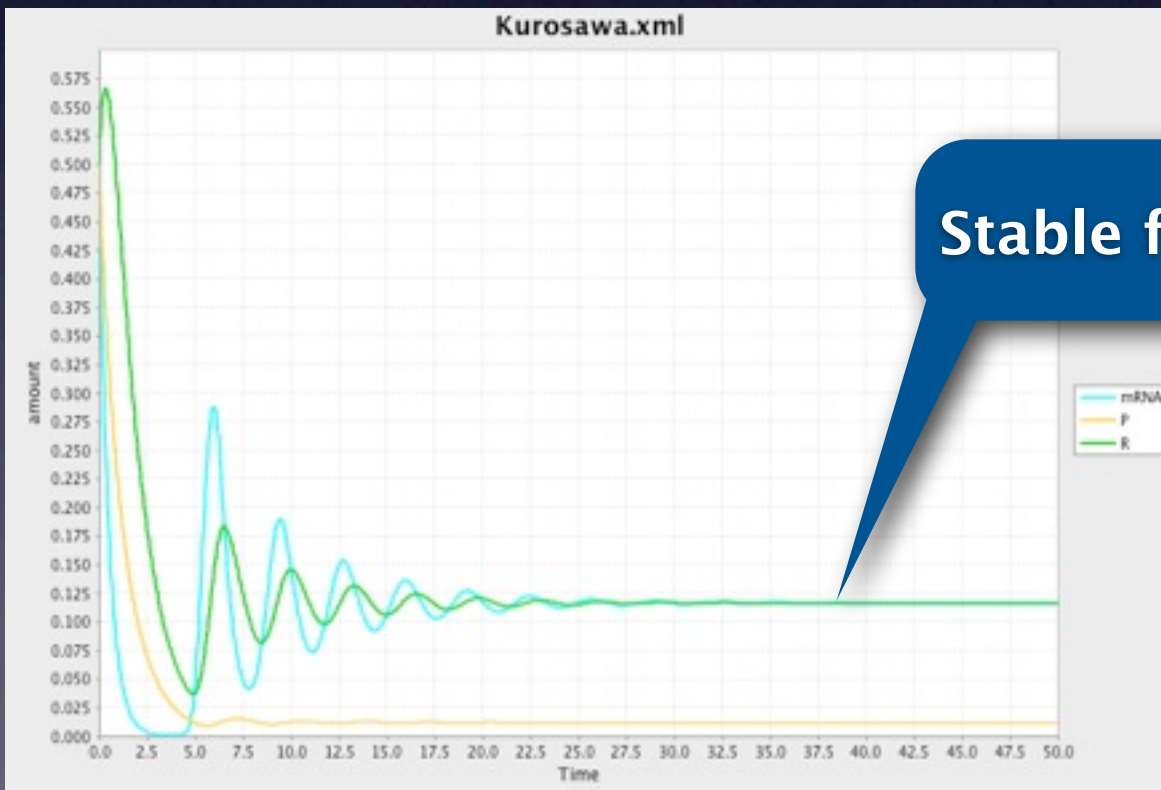
# Qualitative change by 'n'



$$\frac{dM}{dt} = \frac{1}{1 + (P/h)^n} - aM - sM$$

$$\frac{dR}{dt} = sM - (d + u)R + vP$$

$$\frac{dP}{dt} = uR - vP$$



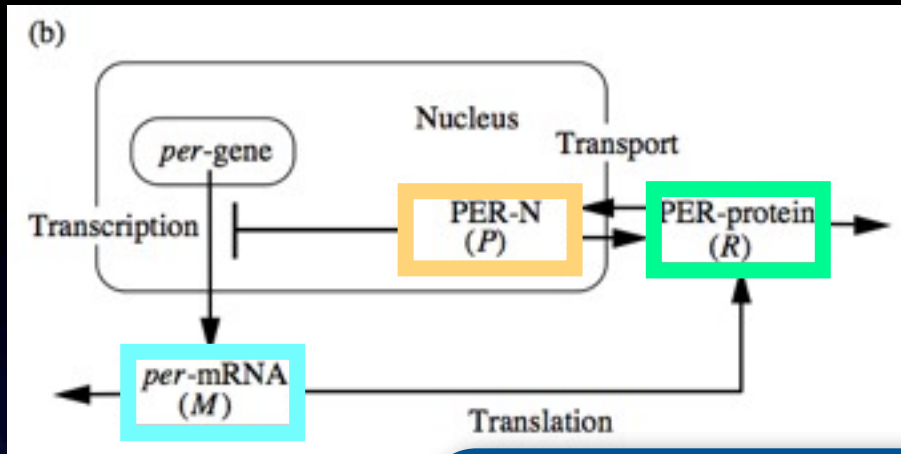
Stable fixed point

$$n = 8$$

End Time: 50  
Num. of Points: 1,000



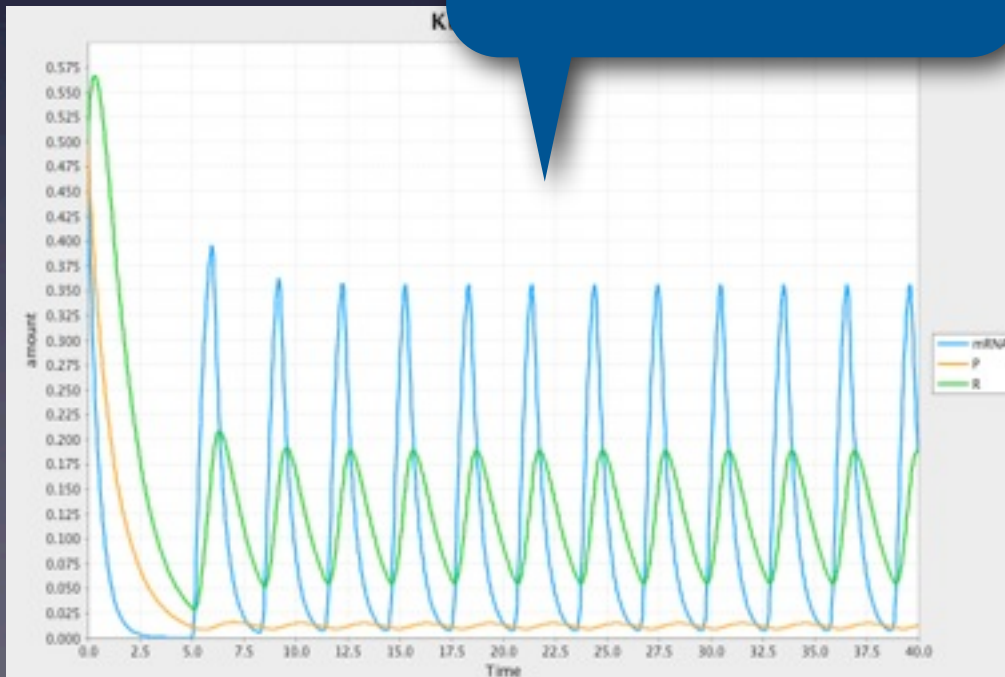
# Why we simulate a model?



Mathematical model and **Quantitative** evaluation (Simulation) will reach a **Qualitative** conclusion

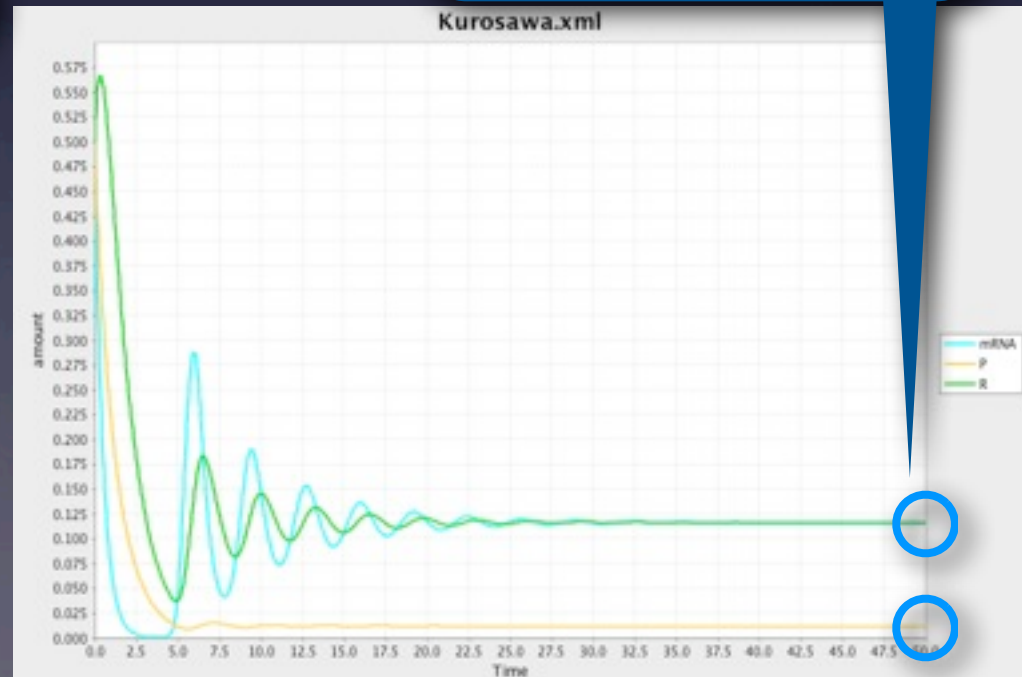
$n = 40$

Oscillation  
(stable limit cycle)



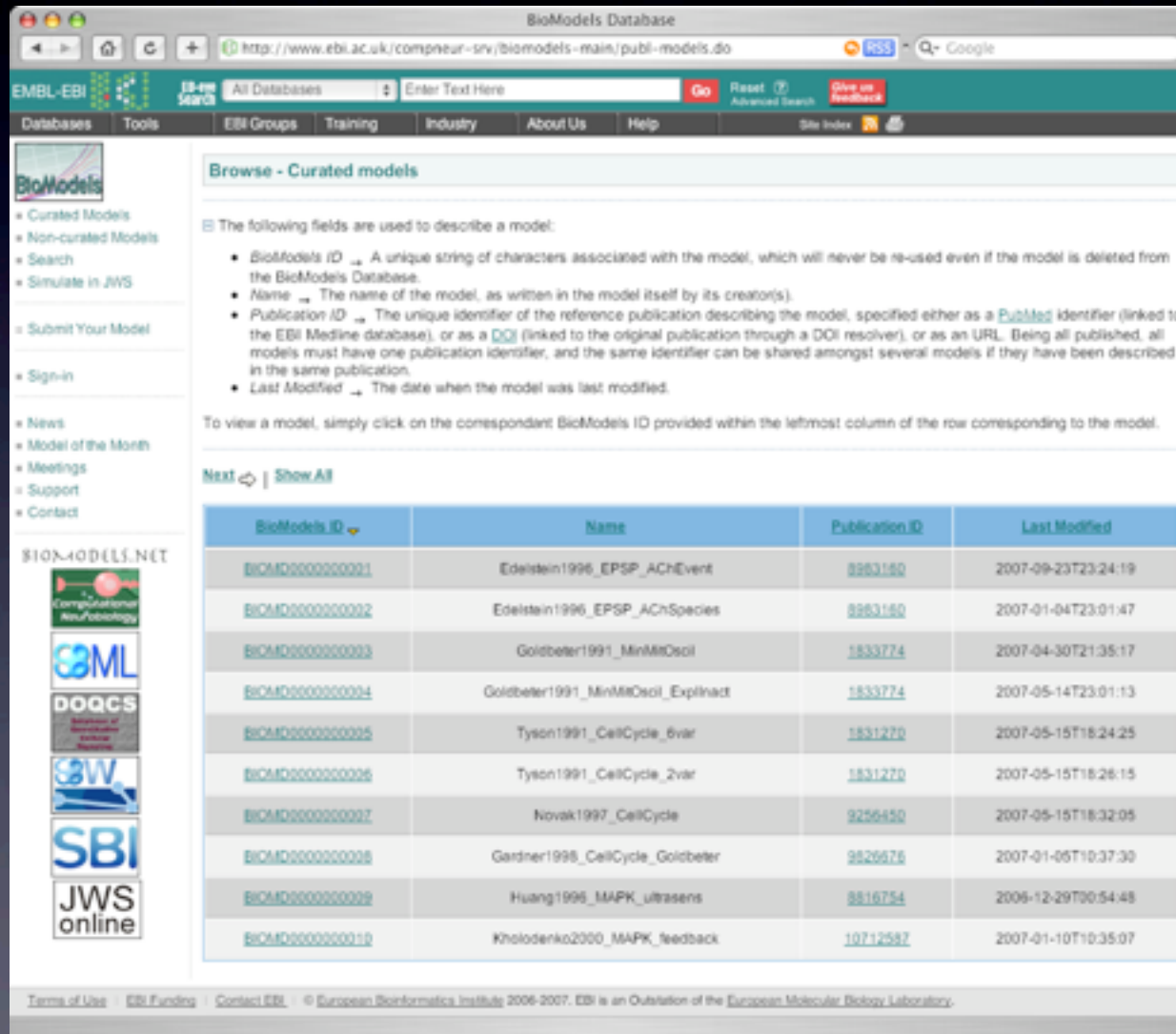
$n = 8$

Stable fixed point



# Database connection

## ● Import model from BioModels.net



The screenshot shows the BioModels Database website. The browser address bar displays the URL: <http://www.ebi.ac.uk/computeur-srv/biomodels-main/publi-models.do>. The page features a search bar with the text "All Databases" and a "Go" button. A sidebar on the left contains navigation links: "Curated Models", "Non-curated Models", "Search", "Simulate in JWS", "Submit Your Model", "Sign-in", "News", "Model of the Month", "Meetings", "Support", and "Contact". Below these links are logos for "COMBML", "DOACS", "SBI", and "JWS online". The main content area is titled "Browse - Curated models" and includes a section explaining the fields used to describe a model: "BioModels ID", "Name", "Publication ID", and "Last Modified". Below this explanation is a table listing 10 models.

| BioModels ID                    | Name                                | Publication ID           | Last Modified       |
|---------------------------------|-------------------------------------|--------------------------|---------------------|
| <a href="#">BICMD0000000001</a> | Edelstein1996_EPSP_AChEvent         | <a href="#">9863160</a>  | 2007-09-23T23:24:19 |
| <a href="#">BICMD0000000002</a> | Edelstein1996_EPSP_AChSpecies       | <a href="#">9863160</a>  | 2007-01-04T23:01:47 |
| <a href="#">BICMD0000000003</a> | Goldbeter1991_MinMitOscil           | <a href="#">1833774</a>  | 2007-04-30T21:35:17 |
| <a href="#">BICMD0000000004</a> | Goldbeter1991_MinMitOscil_ExplInact | <a href="#">1833774</a>  | 2007-05-14T23:01:13 |
| <a href="#">BICMD0000000005</a> | Tyson1991_CellCycle_6var            | <a href="#">1831270</a>  | 2007-05-15T18:24:25 |
| <a href="#">BICMD0000000006</a> | Tyson1991_CellCycle_2var            | <a href="#">1831270</a>  | 2007-05-15T18:26:15 |
| <a href="#">BICMD0000000007</a> | Novak1997_CellCycle                 | <a href="#">9256450</a>  | 2007-05-15T18:32:05 |
| <a href="#">BICMD0000000008</a> | Gardner1998_CellCycle_Goldbeter     | <a href="#">9826676</a>  | 2007-01-06T10:37:30 |
| <a href="#">BICMD0000000009</a> | Huang1996_MAPK_ultrasens            | <a href="#">8816754</a>  | 2006-12-29T00:54:48 |
| <a href="#">BICMD0000000010</a> | Kholodenko2000_MAPK_feedback        | <a href="#">10712587</a> | 2007-01-10T10:35:07 |

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# Database connection

## ● Import model from BioModels.net

The screenshot shows the CellDesigner software interface. The 'Database' menu is open, and 'Import model from BioModels.net...' is selected. The 'BioModels.net' dialog box is open, showing a list of models. The model 'Kholodenko2000\_MAPK\_feedback' is selected. Below the dialog, a diagram of the MAPK feedback model is shown.

**BioModels.net**

| ID               | Name                                 |
|------------------|--------------------------------------|
| BIO MD0000000001 | Edelstein1996_EPSP_AChEvent          |
| BIO MD0000000002 | Edelstein1996_EPSP_AChSpecies        |
| BIO MD0000000003 | Goldbeter1991_MinMitOscil            |
| BIO MD0000000004 | Goldbeter1991_MinMitOscil_ExplInact  |
| BIO MD0000000005 | Tyson1991_CellCycle_6var             |
| BIO MD0000000006 | Tyson1991_CellCycle_2var             |
| BIO MD0000000007 | Novak1997_CellCycle                  |
| BIO MD0000000008 | Gardner1998_CellCycle_Goldbeter      |
| BIO MD0000000009 | Huang1996_MAPK_ultrasens             |
| BIO MD0000000010 | Kholodenko2000_MAPK_feedback         |
| BIO MD0000000011 | Levchenko2000_MAPK_noScaffold        |
| BIO MD0000000012 | Elowitz2000_Repressilator            |
| BIO MD0000000013 | Poolman2004_CalvinCycle              |
| BIO MD0000000014 | Levchenko2000_MAPK_Scaffold          |
| BIO MD0000000015 | Curto1998_purineMetabol              |
| BIO MD0000000016 | Goldbeter1995_CircClock              |
| BIO MD0000000017 | Hoefnagel2002_PyruvateBranches       |
| BIO MD0000000018 | Morrison1989_FolateCycle             |
| BIO MD0000000019 | hodgekin-huxley squid-axon 1952      |
| BIO MD0000000020 | Leloup1999_CircClock                 |
| BIO MD0000000021 | Ueda2001_CircClock                   |
| BIO MD0000000022 | Rohwer2001_Sucrose                   |
| BIO MD0000000023 | Scheper1999_CircClock                |
| BIO MD0000000024 | Smolen2002_CircClock                 |
| BIO MD0000000025 | Markevich2004_MAPK_orderedElementary |

**Diagram:**

The diagram illustrates the MAPK feedback model. It shows the following components and interactions:

- Species:** MAPK, MAPK-P, MAPKK, MAPKK-P, MAPKK-PP.
- Reactions:** J0, J1, J2, J3, J4, J5, J6, J7, J8, J9.
- Input:** uVol.

The diagram shows a feedback loop where MAPK is activated by MAPKK, which is activated by MAPKK-P. MAPKK-P is activated by MAPKK, which is activated by MAPKK-PP. MAPKK-PP is activated by MAPK, which is activated by MAPK-P. MAPK-P is activated by MAPK, which is activated by MAPK-PP. The input uVol is connected to the MAPK-PP reaction.

# SABIO-RK

- Web-accessible database
- <http://sabio.h-its.org/>
- Contains information about biochemical reactions, related kinetic equations and parameters



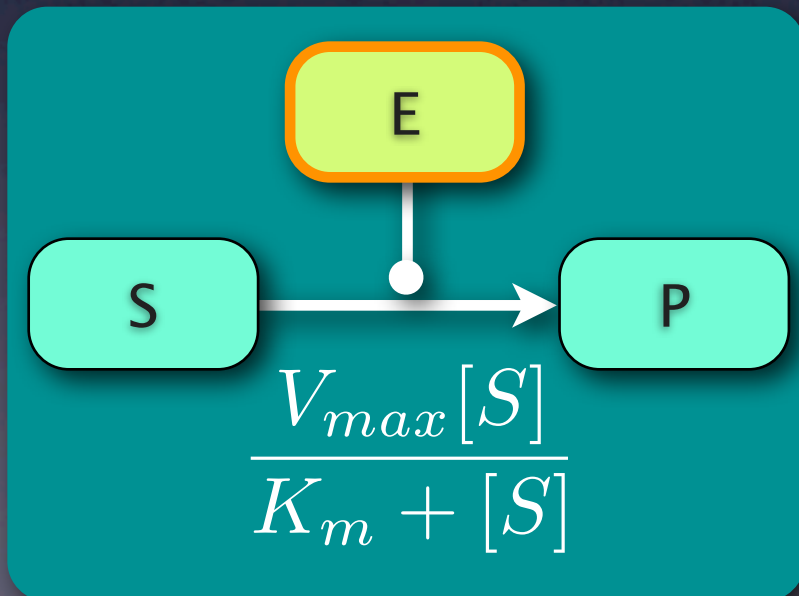
A screenshot of the SABIO-RK website interface. The page title is "Welcome to the SABIO Reaction Kinetics Database". The URL in the browser is "http://sabio.h-its.org/index2.jsp". The page features a search bar, a "Search Results" section, and a table of reactions. The table has columns for "Reactions", "Select Reaction(s)", "Kinetic Data for this reaction", "Enzyme EC#", and "Kinetic data for enzymes". The table lists several reactions, including "D-Glucose + ATP &lt;-&gt; D-Glucose-6-phosphate + ADP" and "ATP + Glucose &lt;-&gt; ADP + Glucose-6-phosphate". The "Kinetic Data for this reaction" column shows "none" for the first reaction and "yes" for the second. The "Enzyme EC#" column shows "2.7.1.1" for both reactions. The "Kinetic data for enzymes" column shows "yes" for both reactions. The page also includes a "Send Selected Reactions to SBML File" button and a "Display" button.



# CellDesigner $\Leftrightarrow$ SABIO RK

- Users can import additional information to each object (reaction) on-the-fly
- SBML (Systems Biology Markup Language) is used to exchange information

CellDesigner



Name, EC number

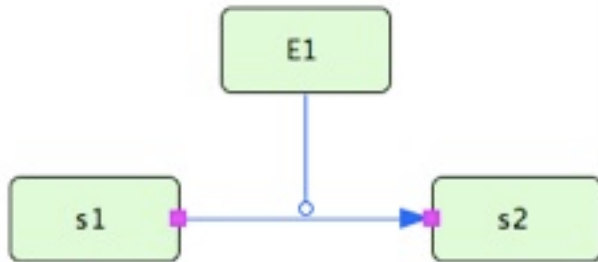


kinetic law, parameters,  
function / unit definitions



# Integration

- Import kinetic law, parameters to the model from SABIO-RK



KineticLaw

math k \* s1

timeUn...

substanceUnits

listOfParameters

| scope               | id | name | value | units | constant |
|---------------------|----|------|-------|-------|----------|
| local:Reaction(re1) | k  | k    | 0.5   |       | true     |



# Annotating a model

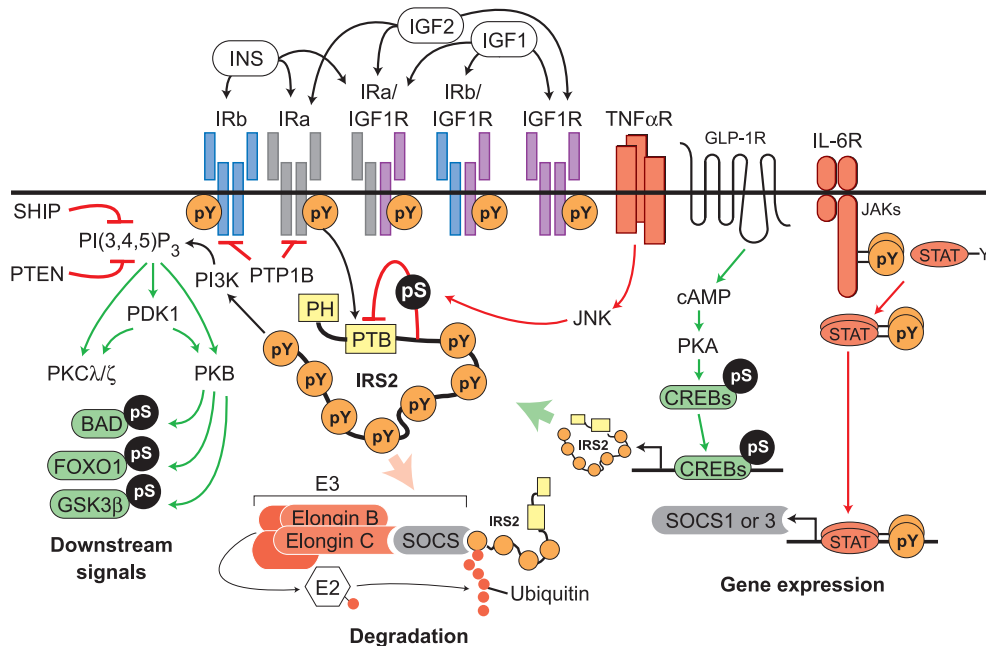
Akira Funahashi & Noriko Hiroi & Yuta Tokuoka  
Keio University, Japan  
6th Aug. 2017



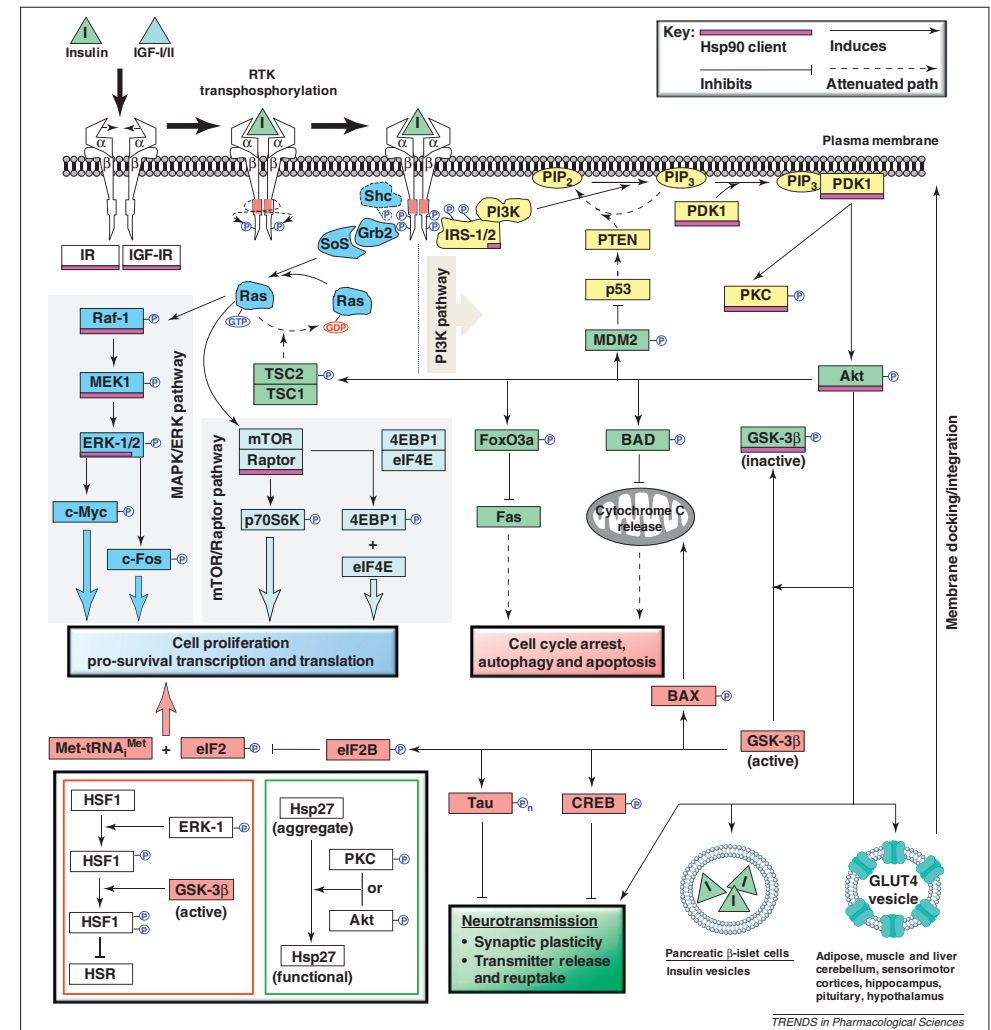
Keio University  
1858  
CALAMVS  
GLADIO  
FORTIOR



# IGF signaling pathway



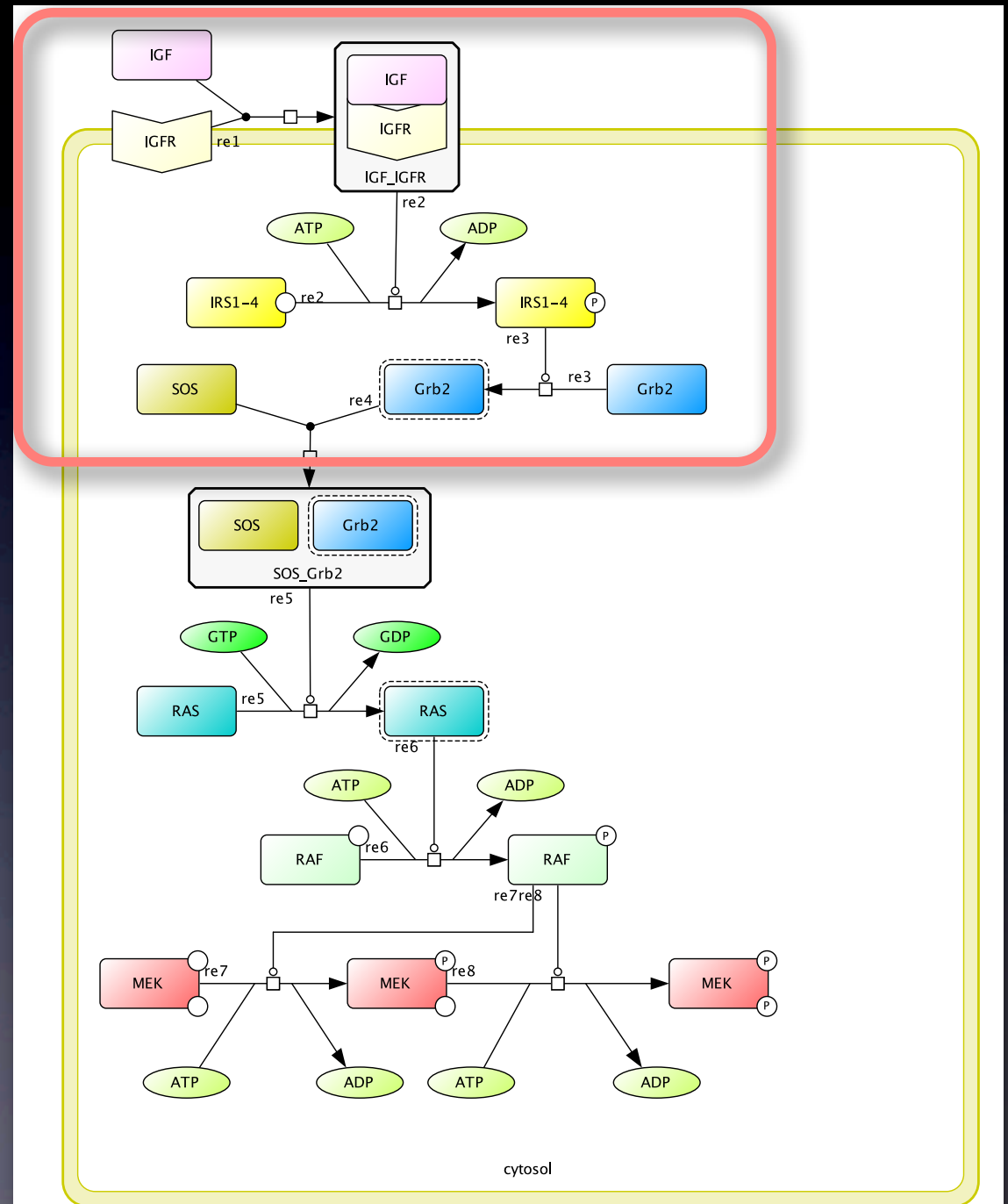
**Fig. 1.** Regulation of insulin and IGF signaling. Insulin and IGF1 receptors form hybrids that modulate the selectivity and affinity for insulin and insulin-like growth factors (IGF1 and IGF2). Insulin or IGF binding stimulates tyrosine autophosphorylation in the receptor β subunits, which activates the kinase and recruits cellular substrates—IRS1 and IRS2—for tyrosine phosphorylation. Recruitment is regulated by serine phosphorylation of the IRS proteins, which inhibits the interaction between its PTB domain and the phosphorylated receptor. Proinflammatory cytokines increase the synthesis of SOCS1 or SOCS3, which promote ubiquitination and degradation of IRS1 and IRS2. Production of cAMP enhances expression of IRS2 through the activity of phosphorylated CREB. Tyrosine phosphorylation of IRS1 or IRS2 recruits and activates various SH2 domain-containing proteins, including the PI 3-kinase, which activates the PKB cascade. Abbreviations: pY, phosphotyrosine; pS, phosphoserine; PKCλ/ζ, protein kinase C λ or ζ; E2, ubiquitin conjugating enzymes; TNFαR, tumor necrosis factor-α receptor; GLP-1R, glucagon-like peptide-1 receptor; IL6R, interleukin-6 receptor; for other abbreviations, see the text.



**Insulin Signaling in Health and Disease**  
Science 302 (5651), 2003, 1710.

**Heat shock response and insulin-associated neurodegeneration**  
Trends in Pharmacological Sciences, 33(3), 2012, 129-137

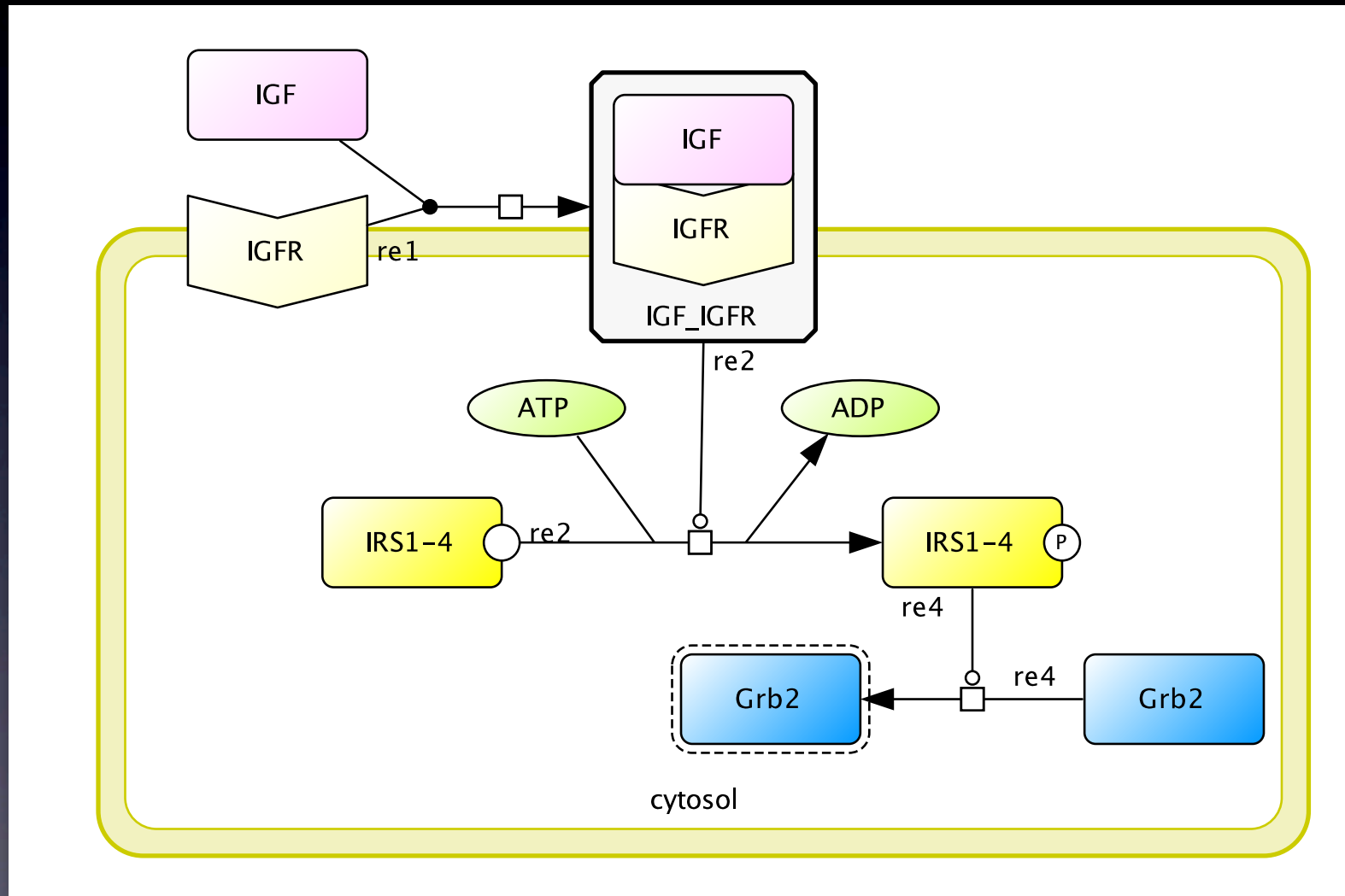
# IGF signaling pathway



[http://www.sbgng.org/  
Documents/PD\\_L1\\_Examples](http://www.sbgng.org/Documents/PD_L1_Examples)

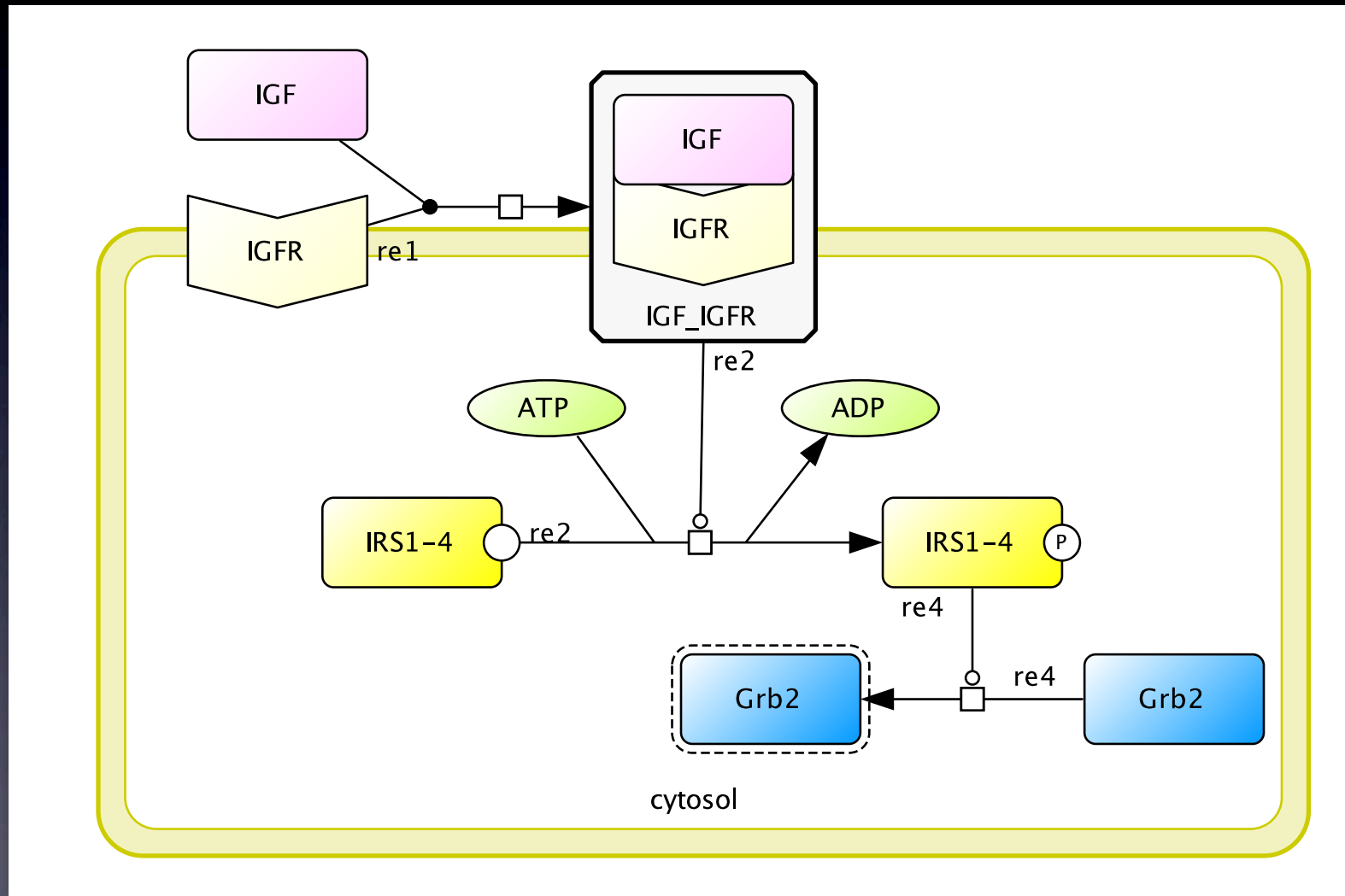
# Exercise

- Create a following model on CellDesigner



# Exercise

- Search Database from CellDesigner



# Database Connection

## ● Search Database by Notes:

- PubMed: **PMID: 123456**

- Entrez Gene: **GeneID: 4015**

The screenshot displays a database interface with two main panels. The left panel shows a diagram with two green boxes labeled 'A' and 'B' connected by a horizontal arrow labeled 're1'. A small white square is positioned on the arrow. Below this diagram is a blue box labeled 'LOX'. The right panel features a table with columns 'id', 'type', and 'name'. The table contains three rows: 'pr1' (GENERIC, A), 'pr2' (GENERIC, B), and 'pr3' (GENERIC, LOX). The 'pr3' row is highlighted. Below the table are buttons for 'Edit' and 'Export'. At the bottom of the right panel, there are buttons for 'Edit Notes' and 'Edit Protein Notes'. Below these buttons, the text 'Species (id=s3, name=LOX; test5)' and 'Protein (id=pr3, name=LOX) GeneID: 4015' is displayed. The bottom status bar indicates 'Grid Snap ON'.

| id  | type    | name |
|-----|---------|------|
| pr1 | GENERIC | A    |
| pr2 | GENERIC | B    |
| pr3 | GENERIC | LOX  |

Species (id=s3, name=LOX; test5)

Protein (id=pr3, name=LOX)  
GeneID: 4015



# Database Connection

## ● Search Database by Notes:

- PubMed: **PMID: 123456**

- Entrez Gene: **GeneID: 4015**

The screenshot displays a database interface with two main panels. The left panel shows a diagram with two green boxes labeled 'A' and 'B'. A horizontal arrow points from 'A' to 'B', with a small square box on the arrow labeled 're1'. Below this, there is a blue box labeled 'LOX'. The right panel features a table with columns 'id', 'type', and 'name'. The table contains three rows: 'pr1' (GENERIC, A), 'pr2' (GENERIC, B), and 'pr3' (GENERIC, LOX). The 'pr3' row is highlighted. Below the table, there are buttons for 'Edit Notes' and 'Edit Protein Notes'. A red box highlights the text 'Protein (id=pr3, name=LOX) GeneID: 4015'.

database.xml test5 \*

Species Proteins Genes RNAs asRNAs Rea

Edit Export

| id  | type    | name |
|-----|---------|------|
| pr1 | GENERIC | A    |
| pr2 | GENERIC | B    |
| pr3 | GENERIC | LOX  |

Edit Notes Edit Protein Notes

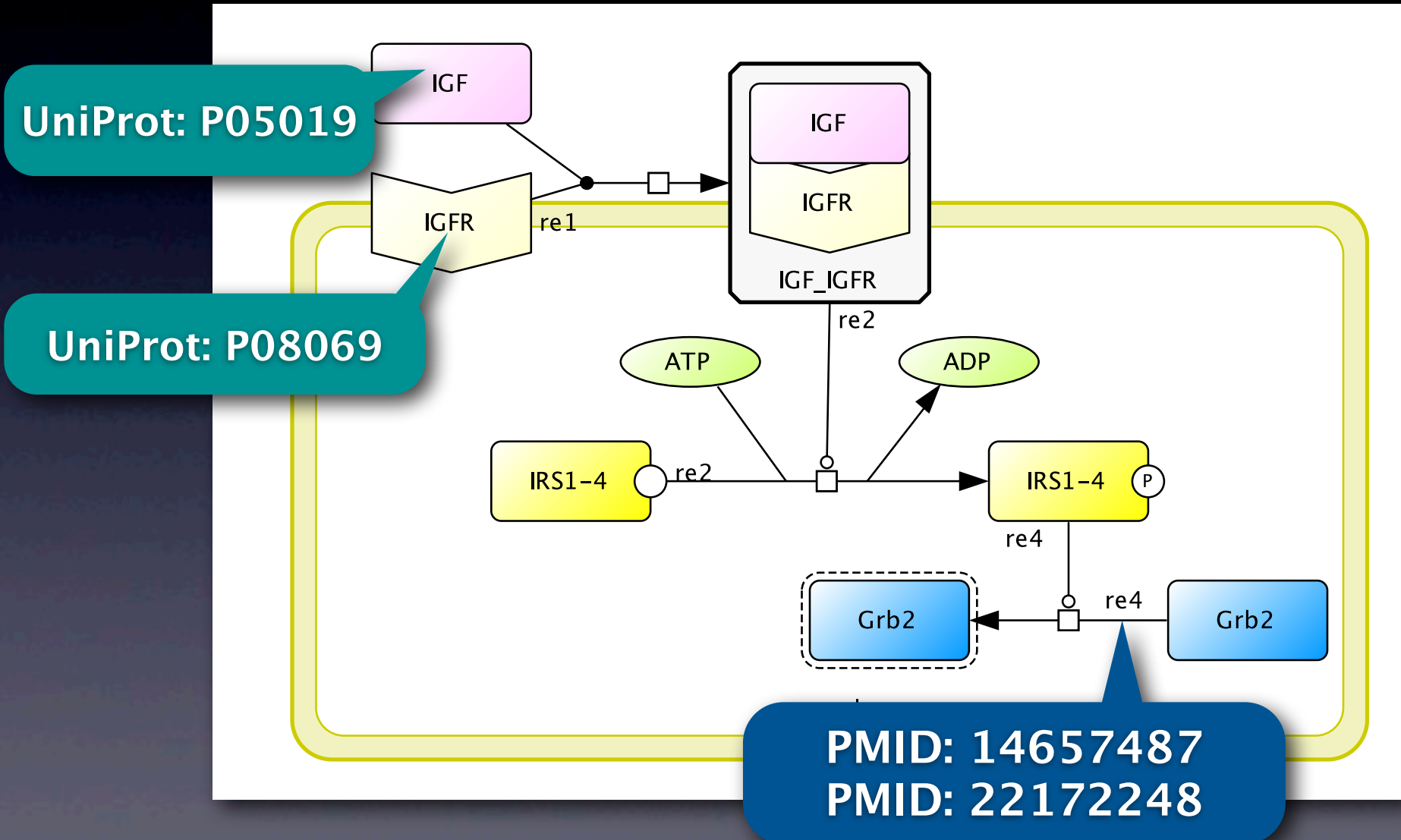
Species (id=s3, name=LOX; test5)

Protein (id=pr3, name=LOX)  
GeneID: 4015

Grid Snap ON

# Exercise

- **Add UniProt ID for Proteins, PubMed ID for reactions and call “Connect to UniProt”**



# MIRIAM annotation



computational  
BIOLOGY

## PERSPECTIVE

### Minimum information requested in the annotation of biochemical models (MIRIAM)

Nicolas Le Novère<sup>1,15</sup>, Andrew Finney<sup>2,15</sup>, Michael Hucka<sup>3</sup>, Upinder S Bhalla<sup>4</sup>, Fabien Campagne<sup>5</sup>, Julio Collado-Vides<sup>6</sup>, Edmund J Crampin<sup>7</sup>, Matt Halstead<sup>7</sup>, Edda Klipp<sup>8</sup>, Pedro Mendes<sup>9</sup>, Poul Nielsen<sup>7</sup>, Herbert Sauro<sup>10</sup>, Bruce Shapiro<sup>11</sup>, Jacky L Snoep<sup>12</sup>, Hugh D Spence<sup>13</sup> & Barry L Wanner<sup>14</sup>

Most of the published quantitative models in biology are lost for the community because they are either not made available or they are insufficiently characterized to allow them to be reused. The lack of a standard description format, lack of stringent reviewing and authors' carelessness are the main causes for incomplete model descriptions. With today's increased interest in detailed biochemical models, it is necessary to define a minimum quality standard for the encoding of those models. We propose a set of rules for curating quantitative models of biological systems. These rules define procedures for encoding and annotating models represented in machine-readable form. We believe their application will enable users to (i) have confidence that curated models are an accurate reflection of their associated reference descriptions, (ii) search collections of curated models with precision, (iii) quickly identify the biological phenomena that a given curated model or model constituent represents and (iv) facilitate model reuse and composition into large subcellular models.

During the genomic era we have witnessed a vast increase in availability of large amounts of quantitative data. This is motivating a shift in the focus of molecular and cellular research from qualitative descriptions of biochemical interactions towards the quantification of such interactions and their dynamics. One of the tenets of systems biology is the use of quantitative models (see Box 1 for definitions) as a mechanism for capturing precise hypotheses and making predictions<sup>1,2</sup>. Many specialized models exist that attempt to explain aspects of the cellular machinery. However, as has happened with other types of biological information, such as sequences, macromolecular structures or

#### Box 1 Glossary

Some terms are used in a very specific way throughout the article. We provide here a precise definition of each one.

**Quantitative biochemical model.** A formal model of a biological system, based on the mathematical description of its molecular and cellular components, and the interactions between those components.

**Encoded model.** A mathematical model written in a formal machine-readable language, such that it can be systematically parsed and employed by simulation and analysis software without further human translation.

**MIRIAM-compliant model.** A model that passes all the tests and fulfills all the conditions listed in MIRIAM.

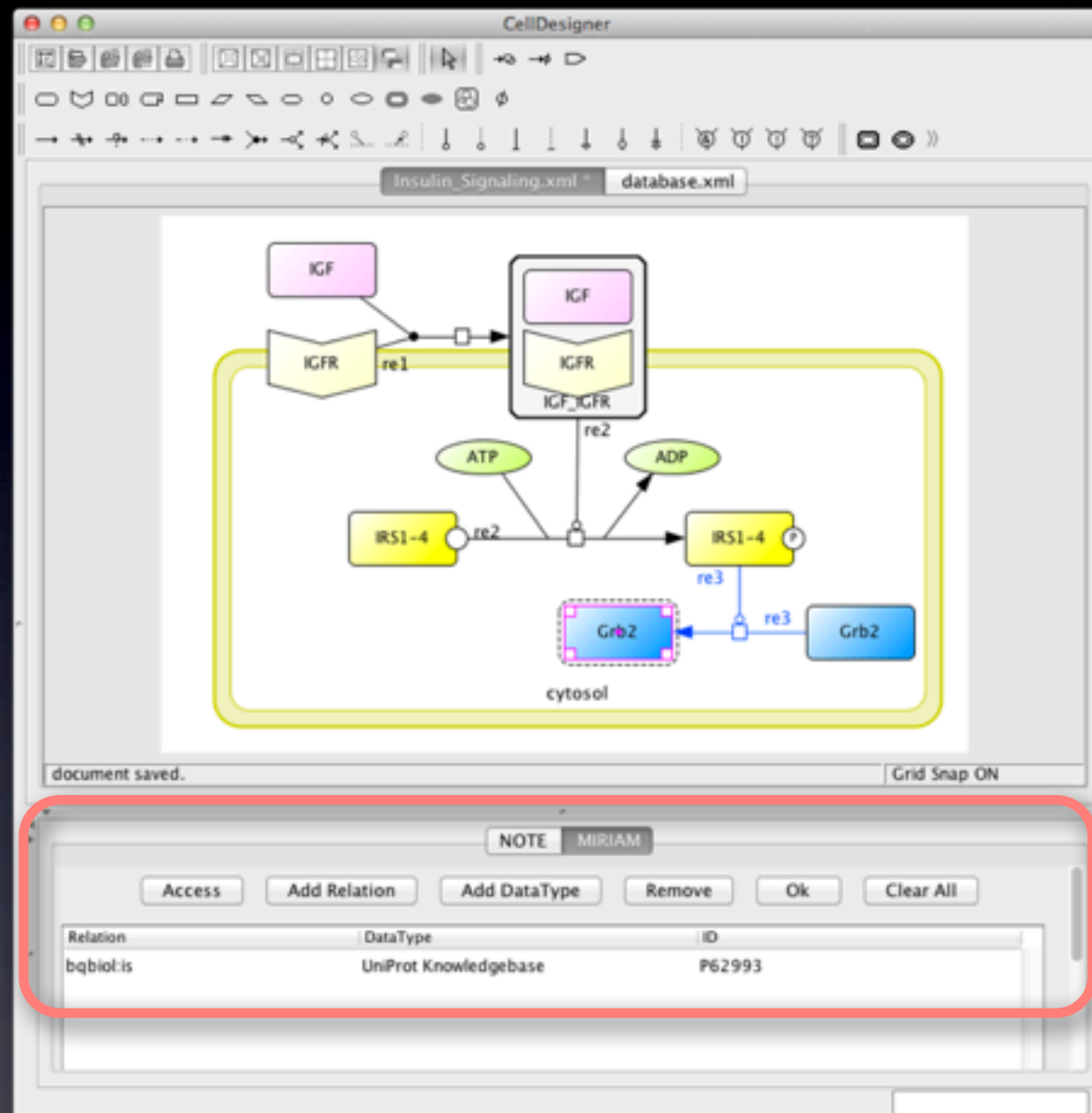
**Reference description.** A unique document that describes, or references the description of the model, the structure of the model, the numerical values necessary to instantiate a simulation from the model, or to perform a mathematical analysis of the model, and the results one expects from such a simulation or analysis.

**Curation process.** The process by which the compliance of an encoded model with MIRIAM is achieved and/or verified. The curation process may encompass some or all of the following tasks: encoding of the model, verification of the reference correspondence and annotation of the model.

**Reference correspondence.** The fact that the structure of a model and the results of a simulation or an analysis match the information present in the reference description.

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<sup>5</sup>Institute for Computational Biomedicine, Weill Medical College of Cornell University, New York, New York 10021, USA.  
<sup>6</sup>Center for Genomic Sciences, Universidad Nacional Autónoma de México, Av. Universidad s/n, Cuernavaca, Morelos, 62100, Mexico.  
<sup>7</sup>Bioengineering Institute and Department of Engineering Science, The University of Auckland, Private Bag 92019, Auckland, New Zealand.  
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<sup>9</sup>Virginia Bioinformatics Institute, Virginia Tech, Washington St., Blacksburg, Virginia 24061-0477, USA.  
<sup>10</sup>Keck Graduate Institute, 535 Watson Drive, Claremont, California 91711, USA.  
<sup>11</sup>Jet Propulsion Laboratory, California Institute of Technology, Pasadena, California 91109, USA.  
<sup>12</sup>Triple-J Group for Molecular Cell Physiology, Department of Biochemistry, Stellenbosch University, Private Bag X1, Matieland 7602, South Africa.  
<sup>13</sup>Department of Scientific Computing & Mathematical Modeling, GlaxoSmithKline Research & Development Limited, Medicines Research Centre, Gurneys Wood Road, Stevenage, Herts, SG1 2NY, UK.  
<sup>14</sup>Purdue University, Department of Biological Sciences, Lilly Hall of Life Sciences, 915 W. State Street, West Lafayette, Indiana 47907-2054, USA.  
<sup>15</sup>These authors have contributed equally to the work. Correspondence should be addressed to N.L.N. (e-mail: lenov@ebi.ac.uk).

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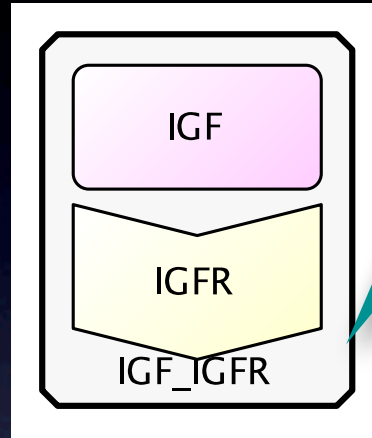


Minimum information requested in the annotation of biochemical models (MIRIAM)  
Nature Biotechnology 23, 1509 – 1515 (2005)

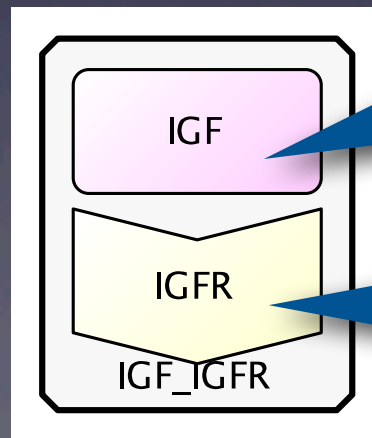
# MIRIAM annotation

● <http://www.ebi.ac.uk/miriam/main/qualifiers/>

- is
- hasPart
- isPartOf
- hasVersion (isoform)
- isVersionOf (superclass, parent)



IGF\_IGFR hasPart: **IGF**  
IGF\_IGFR hasPart: **IGFR**

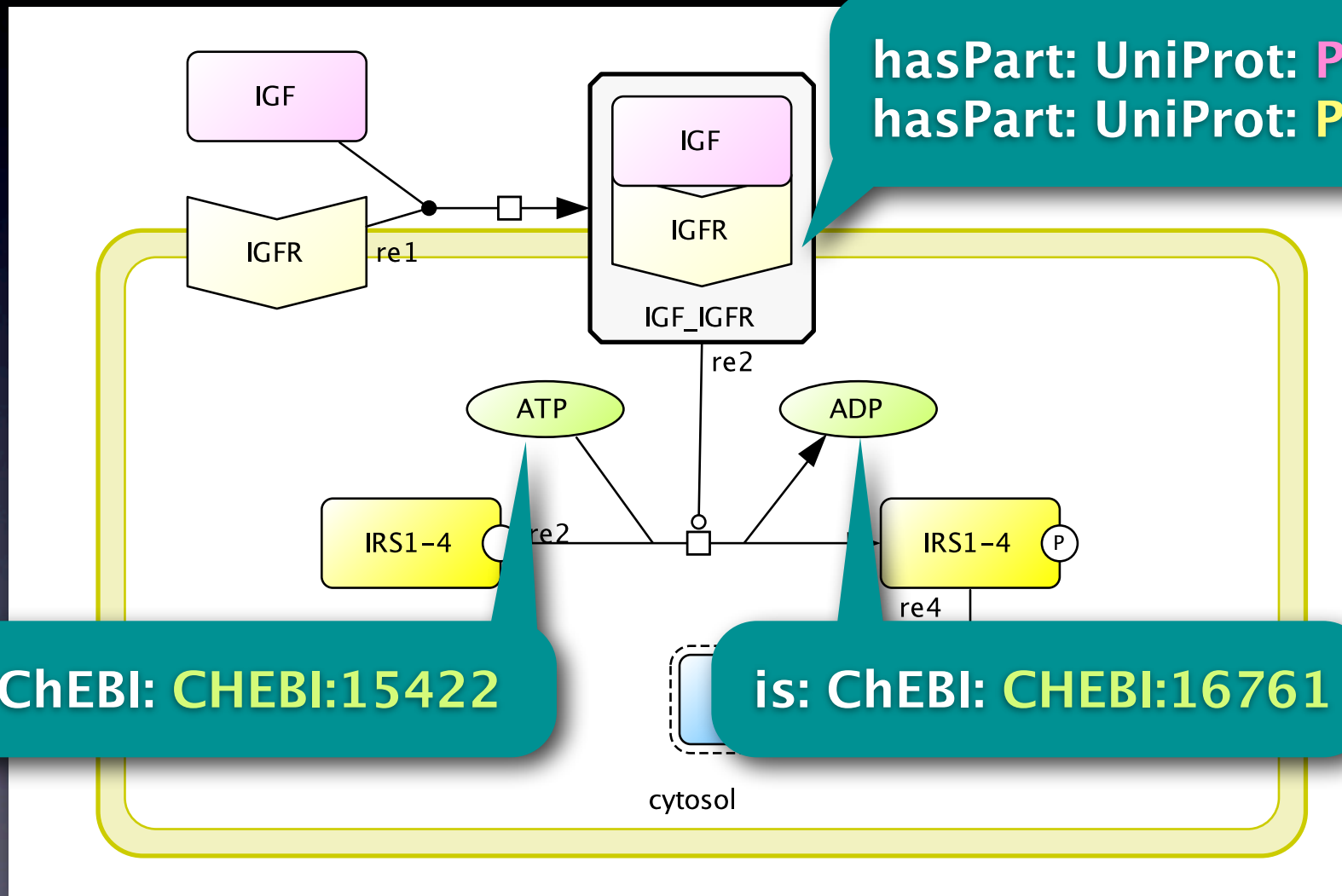


**IGF** isPartOf: IGF\_IGFR

**IGFR** isPartOf: IGF\_IGFR

# Exercise

- Add MIRIAM annotation



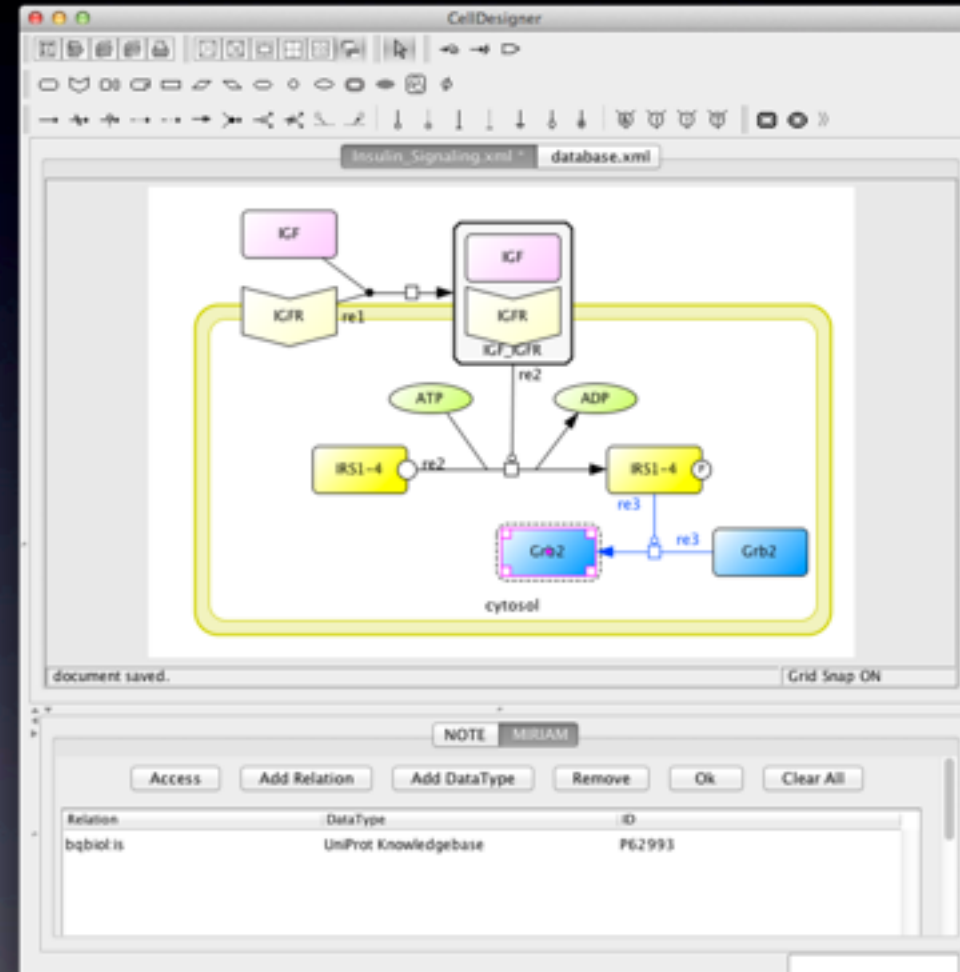
# Notes or MIRIAM?

- CellDesigner Notes

- Easy to add (text)

- MIRIAM

- Tool neutral (SBML)
- Precise annotation





# Summary

- **Introduction of CellDesigner**
  - **What kind of model you can build**
    - **Mathematical model**
    - **Pathway map**
- **How to build a model with CellDesigner**
  - **From scratch**
  - **Import a model from BioModels.net**
  - **Import kinetic law and parameters from SABIO-RK**