

RuleBuilder 1.0

Getting Started Guide

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Introduction

RuleBuilder enables you to define, generate, and simulate graphical rule-based models of biochemical systems. Objects and rules created in RuleBuilder are passed to the BioNetGen program in the form of a BioNetGen Language (BNGL) file in order to generate and simulate the reaction network. RuleBuilder enables you to control both the network generation and simulation steps and to view the generated network and plot the simulation results. This guide takes you through all of the basic steps involved in using RuleBuilder.

RuleBuilder Layout

The screenshot displays the RuleBuilder 1.40 Beta software interface. At the top is a menu bar with 'File', 'Edit', 'View', and 'Help'. Below it is a toolbar with various icons for drawing and editing. The main workspace is divided into several panels:

- Drawing Board:** The central area where a reaction rule is being constructed. It shows two reactants, labeled 'A' and 'B', each represented by a circle containing a smaller circle with the letter 'b'. These are followed by a plus sign and an arrow pointing to the products, which are two circles labeled 'A' and 'B' connected by a horizontal line. A yellow callout box explains: "The Drawing Board is where containers, components, edges and operators can be placed in order to create the molecules, species, reaction rules, observables, and patterns that form a BioNetGen model."
- Molecule Templates Palette:** A panel on the right side containing two molecule templates, labeled 'A' and 'B', each consisting of a circle with a smaller circle inside labeled 'b'. A yellow callout box states: "Defined objects, such as Molecule Templates, Species, and Reaction Rules are displayed in separate windows."
- Reaction Rules:** A panel at the bottom of the interface, currently empty.

At the bottom left, the text 'Object Manipulation Mode' is visible. The bottom of the window features a blue bar with a small window icon.

Adding Containers and Components

The screenshot displays the Rule Builder 1.40 Beta software interface. The main window is titled "Rule Builder 1.40 Beta - gsg_example" and contains a menu bar (File, Edit, View, Help) and a toolbar with various icons. The central area is the "Drawing Board", which currently shows a small molecule structure consisting of a carbon atom (C) and a circle. A yellow callout box points to the "Add Container Mode" icon in the toolbar, which is a circle with a plus sign. Another yellow callout box explains that a component is added by entering "Add Components" mode and left-clicking in the Drawing Board. To the right of the Drawing Board are two panels: "Molecule Templates Palette" and "Seed Species". At the bottom of the interface is a "Reaction Rules" panel and a status bar.

Rule Builder 1.40 Beta - gsg_example

File Edit View Help

Drawing Board

Add Container Mode.

A component is added by entering "Add Components" mode on the toolbar and left-clicking in the Drawing Board.

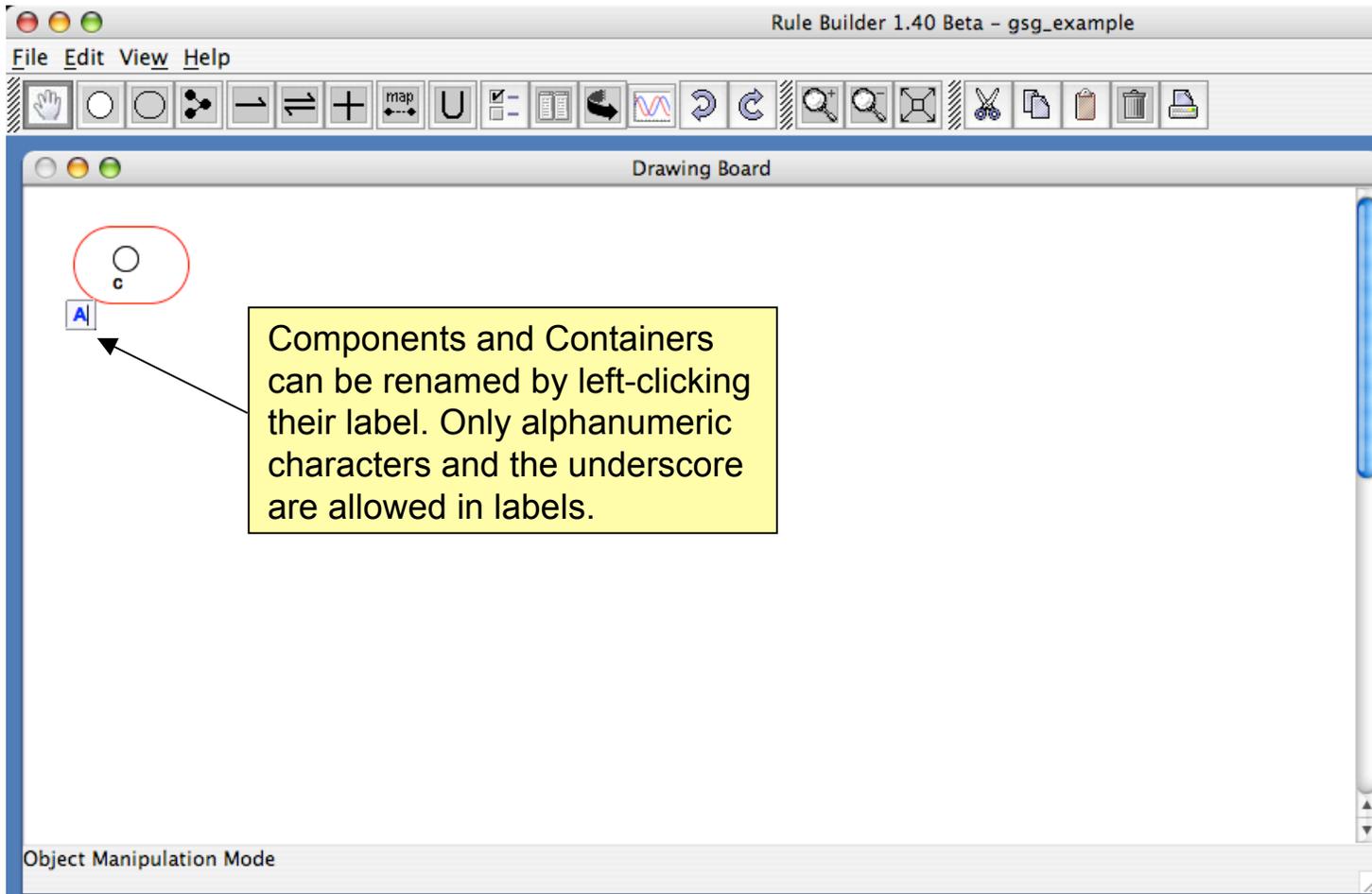
Object Manipulation Mode

Molecule Templates Palette

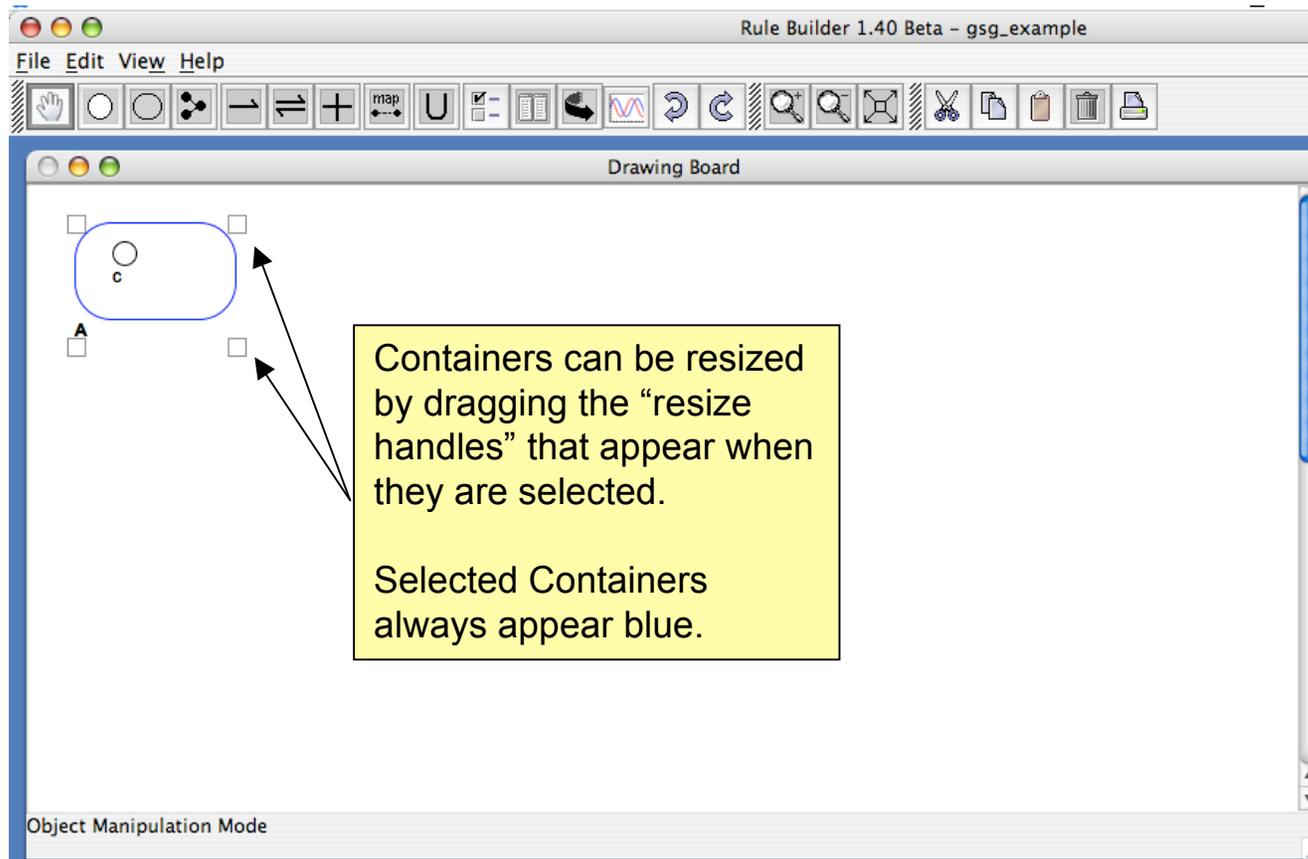
Seed Species

Reaction Rules

Renaming Components and Containers

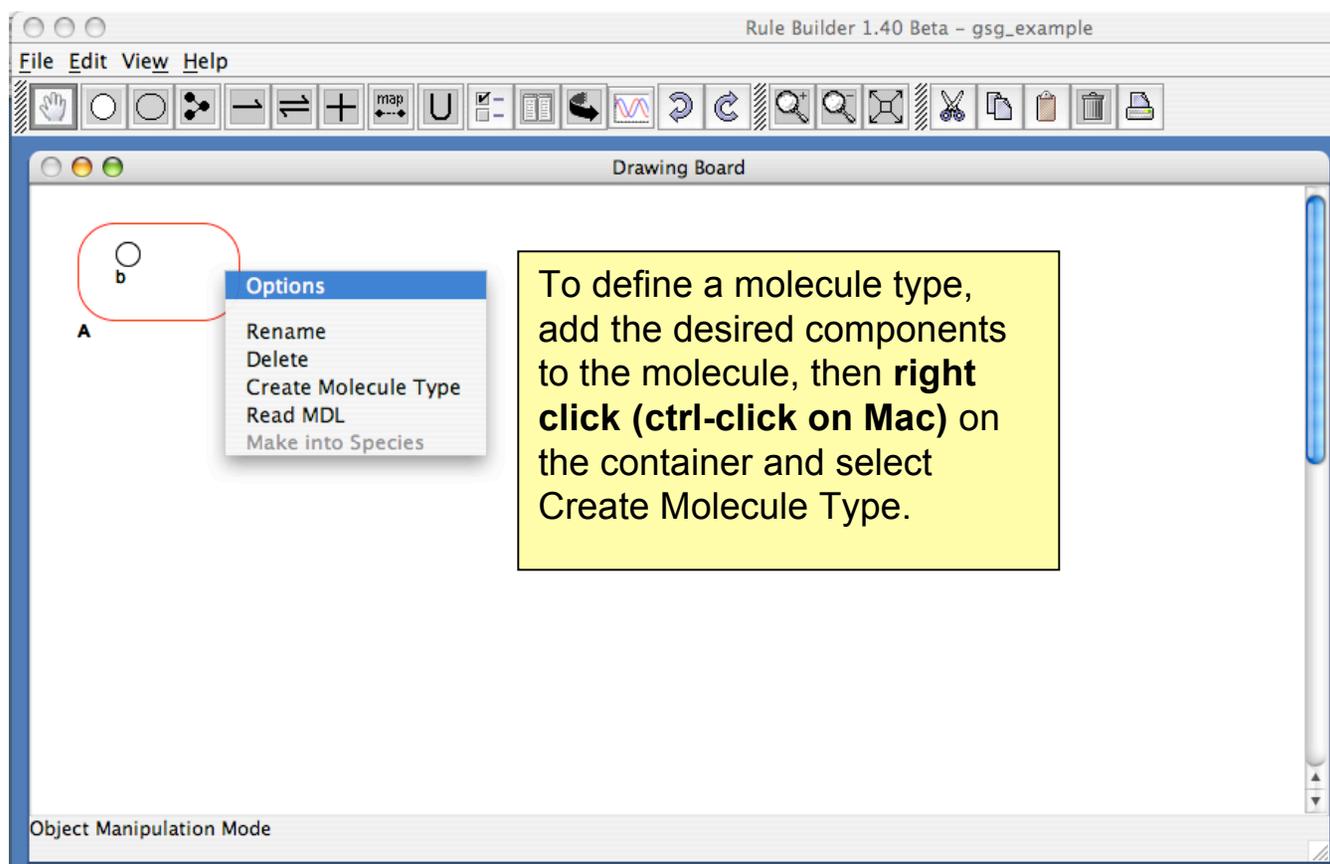


Resizing Containers



Creating Molecule Types

Molecules used in a model have to be defined and registered as a “Molecule Type” before they can be used in reaction rules and species.



The screenshot shows the Rule Builder 1.40 Beta software interface. The main window is titled "Drawing Board" and contains a drawing area with a small circle labeled "b" inside a container labeled "A". A context menu is open over the circle, listing options: "Rename", "Delete", "Create Molecule Type", "Read MDL", and "Make into Species". A yellow text box on the right provides instructions: "To define a molecule type, add the desired components to the molecule, then **right click (ctrl-click on Mac)** on the container and select Create Molecule Type." The status bar at the bottom indicates "Object Manipulation Mode".

Rule Builder 1.40 Beta - gsg_example

File Edit View Help

Drawing Board

Options

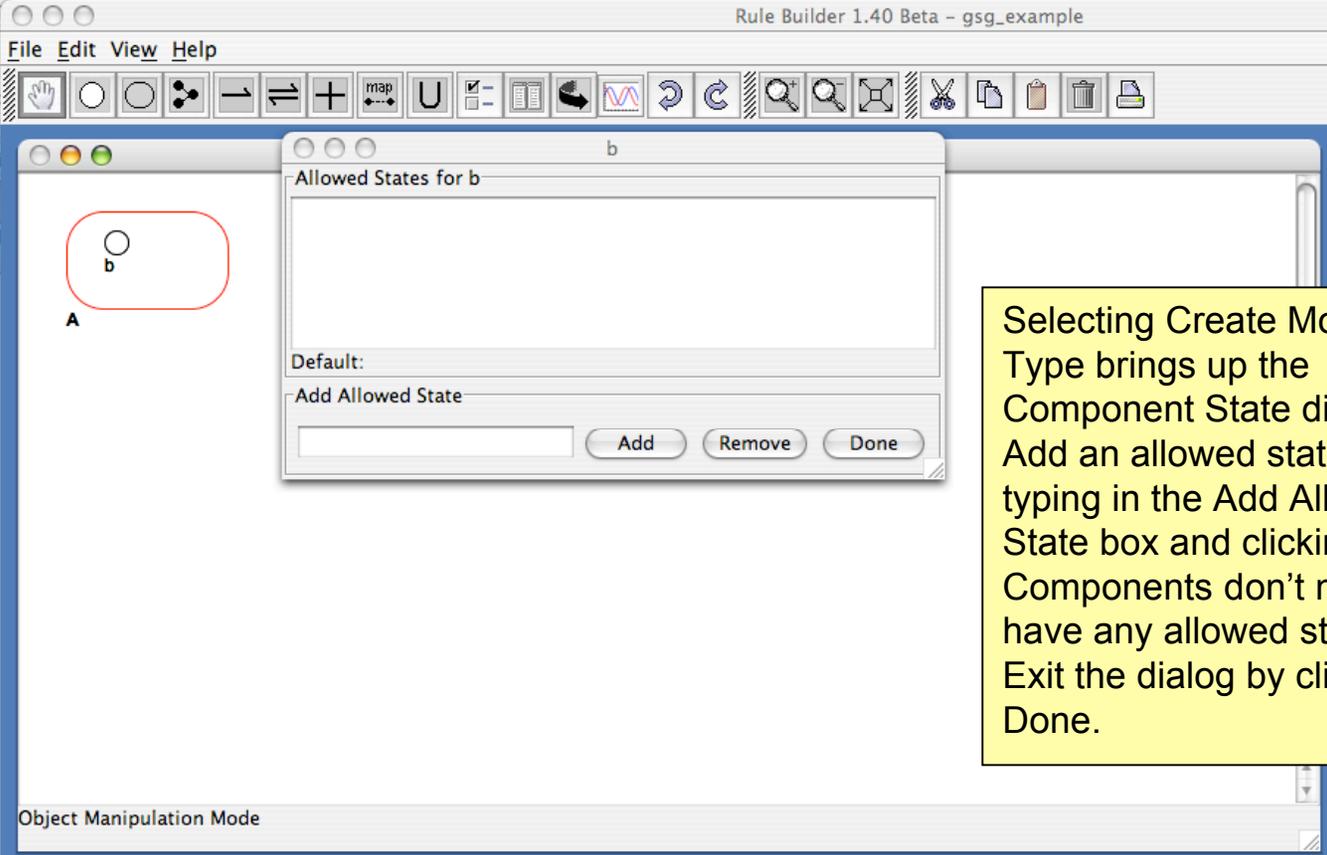
- Rename
- Delete
- Create Molecule Type
- Read MDL
- Make into Species

To define a molecule type, add the desired components to the molecule, then **right click (ctrl-click on Mac)** on the container and select Create Molecule Type.

Object Manipulation Mode

Setting Allowed Component States

Components may take on different states to indicate conformation or covalent modification, such as phosphorylation.



The screenshot shows the 'Rule Builder 1.40 Beta - gsg_example' application window. The main workspace contains a diagram with a component labeled 'b' inside a rounded rectangle labeled 'A'. A dialog box titled 'Allowed States for b' is open, showing a list of allowed states (currently empty), a 'Default:' field, and an 'Add Allowed State' section with a text input box and 'Add', 'Remove', and 'Done' buttons. The status bar at the bottom indicates 'Object Manipulation Mode'.

Selecting Create Molecule Type brings up the Component State dialog. Add an allowed state by typing in the Add Allowed State box and clicking Add. Components don't need to have any allowed states. Exit the dialog by clicking Done.

Identifying Valid and Invalid Molecules

The screenshot displays the Rule Builder 1.40 Beta software interface. The main window is titled "Rule Builder 1.40 Beta - gsg_example" and contains a "Drawing Board" and a "Molecule Templates Palette".

The Drawing Board shows three molecules labeled A:

- A molecule with a green outline and a small circle labeled 'b' inside, labeled 'A'. A yellow callout box next to it states: "Containers matching valid types are **green**."
- A molecule with a red outline and a small circle labeled 'b' inside, labeled 'B'. A yellow callout box next to it states: "Containers not matching a valid type are **red**."
- A molecule with a dashed green outline and a small circle labeled 'b' inside, labeled 'A'. A yellow callout box next to it states: "Dashed line indicates an incomplete match."

The Molecule Templates Palette on the right shows a single molecule template labeled 'A' with a small circle labeled 'b' inside. A yellow callout box at the top right of the palette area states: "Molecule Types appear here".

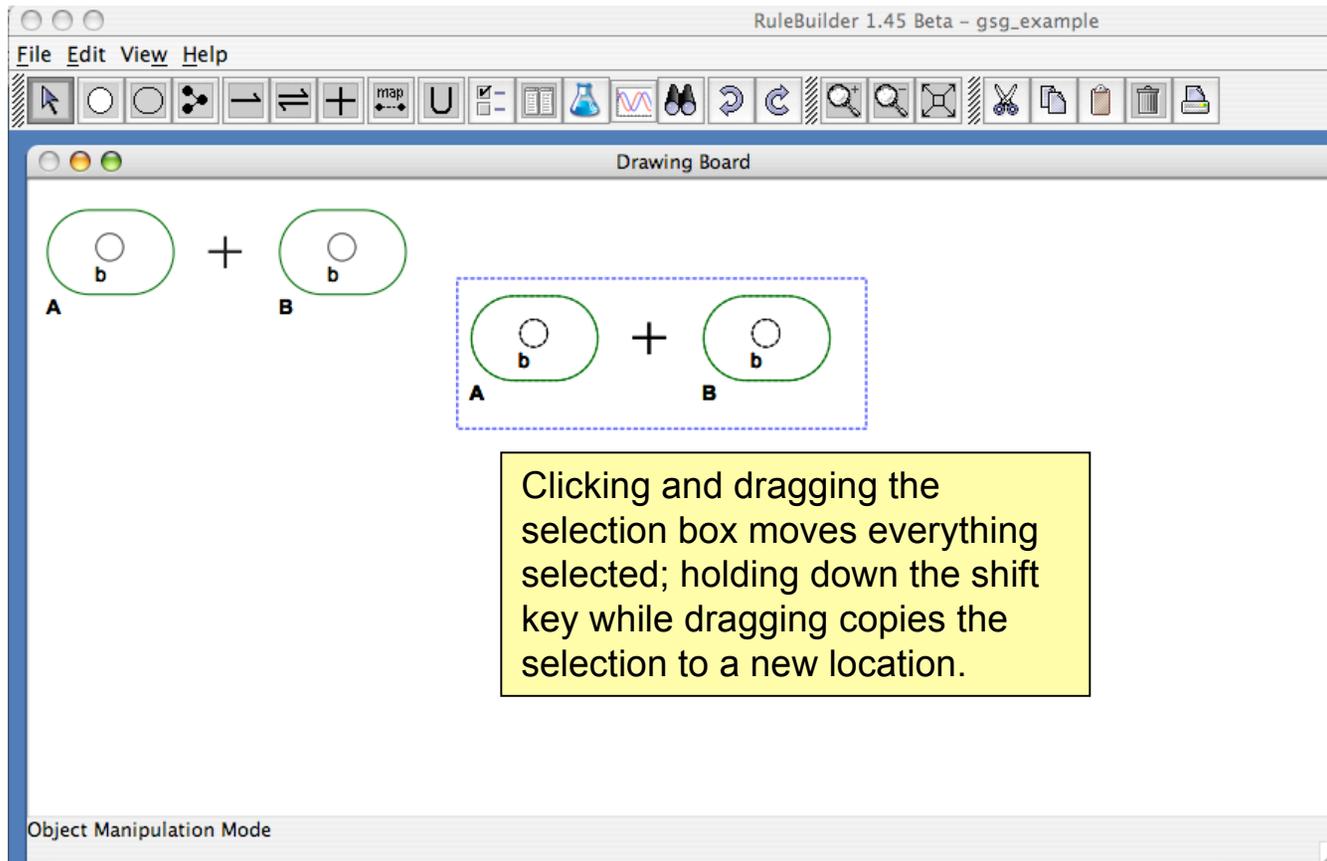
The bottom status bar of the software indicates "Object Manipulation Mode".

Copying Objects with the Selection Box

Draw a box around objects on the Drawing Board to select them. Partially enclosed objects are not selected.

Object Manipulation Mode

Copying Objects with the Selection Box



Creating a Reaction Rule

Reaction rules are created by arranging containers and operators to construct a formula for the reaction.

The screenshot displays the 'Rule Builder 1.40 Beta - gsg_example' application window. The main 'Drawing Board' contains two rounded rectangular containers, 'A' and 'B'. Container 'A' contains a small circle with the letter 'b' inside, and container 'B' contains a small circle with the letter 'a' inside. A red '+' operator is positioned between containers 'A' and 'B', and a red '-' operator is positioned to the right of container 'B'. Two yellow callout boxes provide explanations: one points to the '+' operator with the text 'The '+' operator separates reactants or products in a list.', and another points to the '-' operator with the text 'The arrow operator separates reactants and products.'. The software interface includes a menu bar (File, Edit, View, Help), a toolbar with various icons, and two side panels: 'Molecule Templates Palette' and 'Seed Species'. The status bar at the bottom indicates 'Object Manipulation Mode'.

Creating a Reaction Rule

The type of arrow determines whether a reaction is reversible or irreversible.

The screenshot displays the Rule Builder 1.40 Beta software interface. The main window is titled "Rule Builder 1.40 Beta - gsg_example" and contains a menu bar (File, Edit, View, Help) and a toolbar. The toolbar includes various icons for drawing and editing, with a red box highlighting the reversible reaction arrow icon (two horizontal arrows pointing in opposite directions). Below the toolbar is the "Drawing Board" window, which shows a chemical reaction rule. On the left, a rounded rectangle labeled "A" contains a small circle with the letter "b" inside. To its right is a plus sign (+). Further right is another rounded rectangle labeled "B" containing a small circle with the letter "a" inside. To the right of "B" is a single-headed arrow (→). On the right side of the interface is a "Molecule Templates Palette" window, which contains two rounded rectangles: the top one labeled "A" with a circle containing "b", and the bottom one labeled "B" with a circle containing "a". Below the palette is a "Seed Species" window, which is currently empty. At the bottom left of the main window, the text "Object Manipulation Mode" is visible.

Defining Products

RuleBuilder 1.45 Beta - gsg_example

File Edit View Help

Drawing Board

A + B → A B

Use Add Edges to create a bond between the components

Object Manipulation Mode

Defining Products

RuleBuilder 1.45 Beta - gsg_example

File Edit View Help

Drawing Board

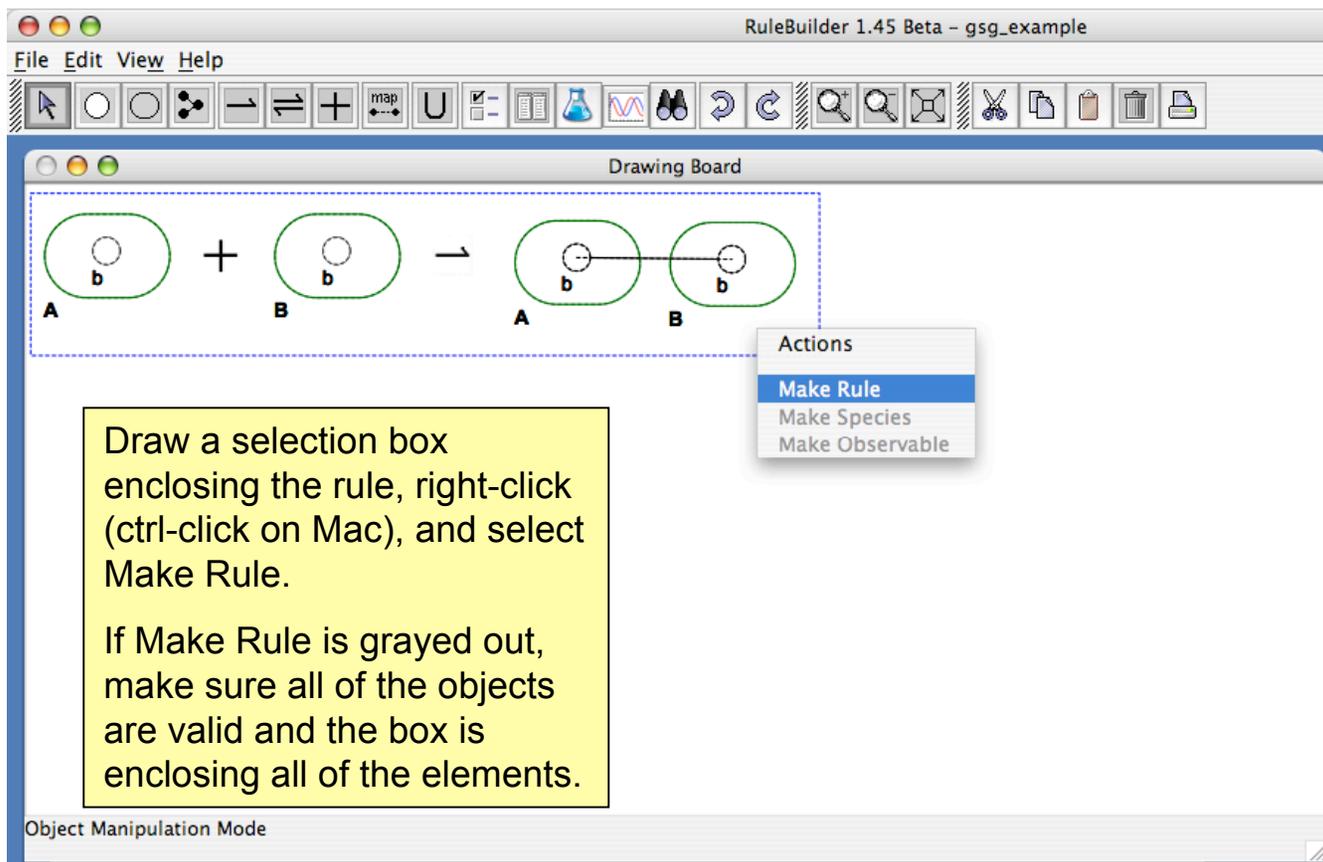
A + B → A B

b b b b

Create the bond by clicking on the two components to be linked.

Add Edge Mode

Creating the Rule



The screenshot shows the RuleBuilder 1.45 Beta software interface. The main window is titled "RuleBuilder 1.45 Beta - gsg_example" and contains a "Drawing Board" window. The drawing board displays a chemical rule: two green ovals labeled "A" and "B" (each containing a smaller white circle with a "b" inside) are separated by a plus sign and an arrow. To the right of the arrow, the two ovals "A" and "B" are connected by a horizontal line, representing a reaction product. A blue dashed selection box encloses the entire rule. A context menu is open over the drawing board, listing "Actions": "Make Rule" (highlighted in blue), "Make Species", and "Make Observable".

File Edit View Help

RuleBuilder 1.45 Beta - gsg_example

Drawing Board

A + B → A B

Actions

- Make Rule
- Make Species
- Make Observable

Draw a selection box enclosing the rule, right-click (ctrl-click on Mac), and select Make Rule.

If Make Rule is grayed out, make sure all of the objects are valid and the box is enclosing all of the elements.

Object Manipulation Mode

Make Rule Dialog

RuleBuilder 1.45 Beta - gsg_example

File Edit View Help

Reaction Properties

Rule Name

Label: Rule1

Forward Rate

Name: kp1

Rate:

BNGL Annotation

Done Cancel

Drawing Board

Object Manipulation Mode

Set Rule Name, rate constants, and optional annotation in the dialog box.

For a parameter being used for the first time, set a numerical value in the Rate box.

Reaction Rules Window

The screenshot displays the RuleBuilder 1.45 Beta software interface. The main window is titled "RuleBuilder 1.45 Beta - gsg_example" and contains a "Drawing Board" and a "Reaction Rules" window. The "Drawing Board" shows a chemical reaction rule: two separate molecules, each consisting of a circle labeled 'b' inside an oval labeled 'A' or 'B', react to form a single molecule where two 'b' circles are connected by a line, each still within its respective 'A' or 'B' oval. The "Reaction Rules" window at the bottom shows the same reaction rule, but with a rate constant $kp1$ above the reaction arrow. A yellow callout box points to this window with the text: "Rule now appears in the Reaction Rules Window." To the right of the main workspace, there are two palettes: "Molecule Templates Palette" containing two templates labeled 'A' and 'B', and "Seed Species" which is currently empty. The interface includes a menu bar (File, Edit, View, Help) and a toolbar with various icons for drawing and editing.

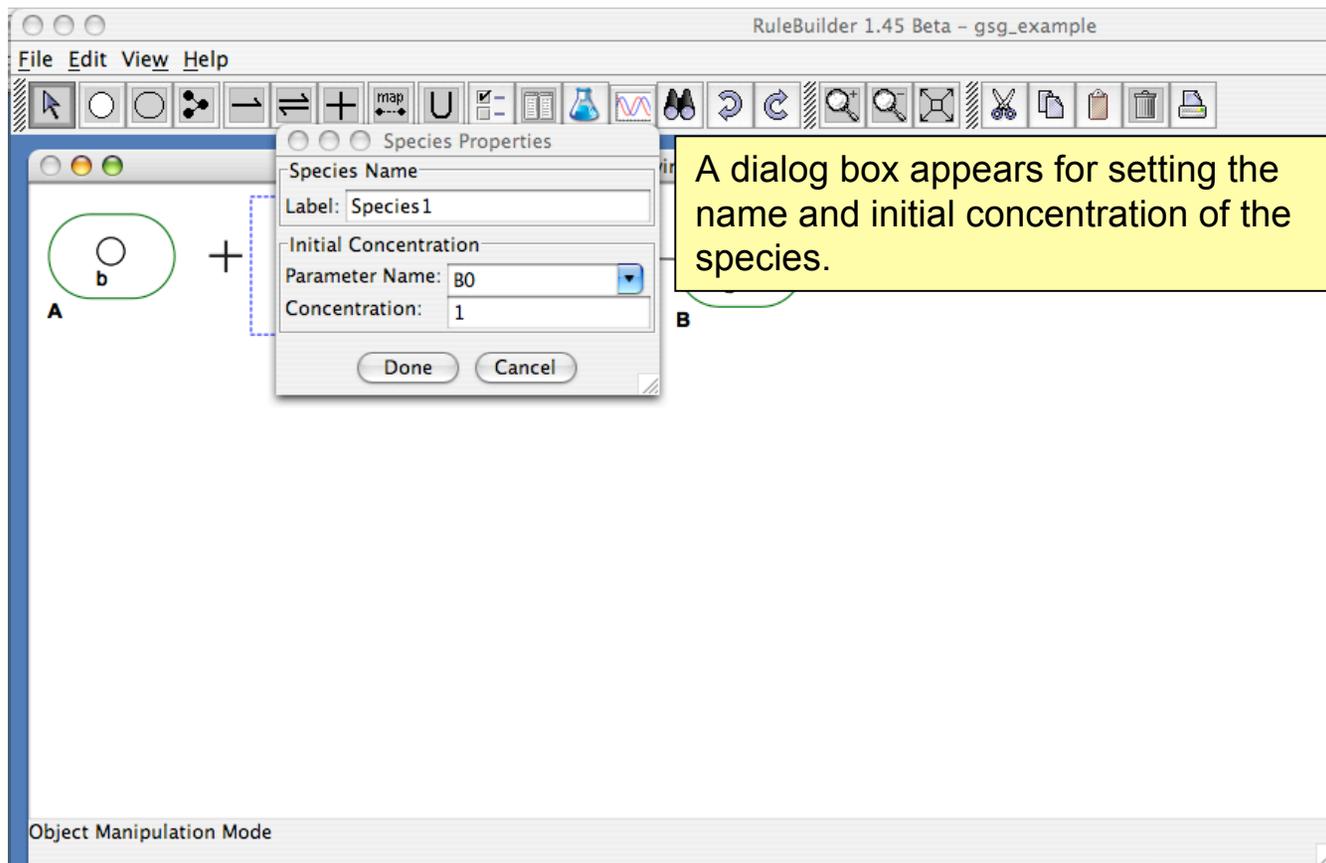
Defining Seed Species

The network is defined by applying the reaction rules to a set of seed species.

Draw a selection box around a connected set of molecules and right-click (ctrl-click on Mac) to define a species.

All items in selection box should have solid green lines, indicating the the molecules are fully defined.

Species Dialog Box



Seed Species Window

The screenshot displays the RuleBuilder 1.45 Beta interface. The main window, titled "RuleBuilder 1.45 Beta - gsg_example", contains a "Drawing Board" and a "Molecule Templates Palette".

The Drawing Board shows a chemical reaction: two separate molecules, labeled A and B, each consisting of a small circle 'b' inside a larger oval, are added together (+). An arrow points to the product, which consists of two such molecules, A and B, connected by a horizontal line.

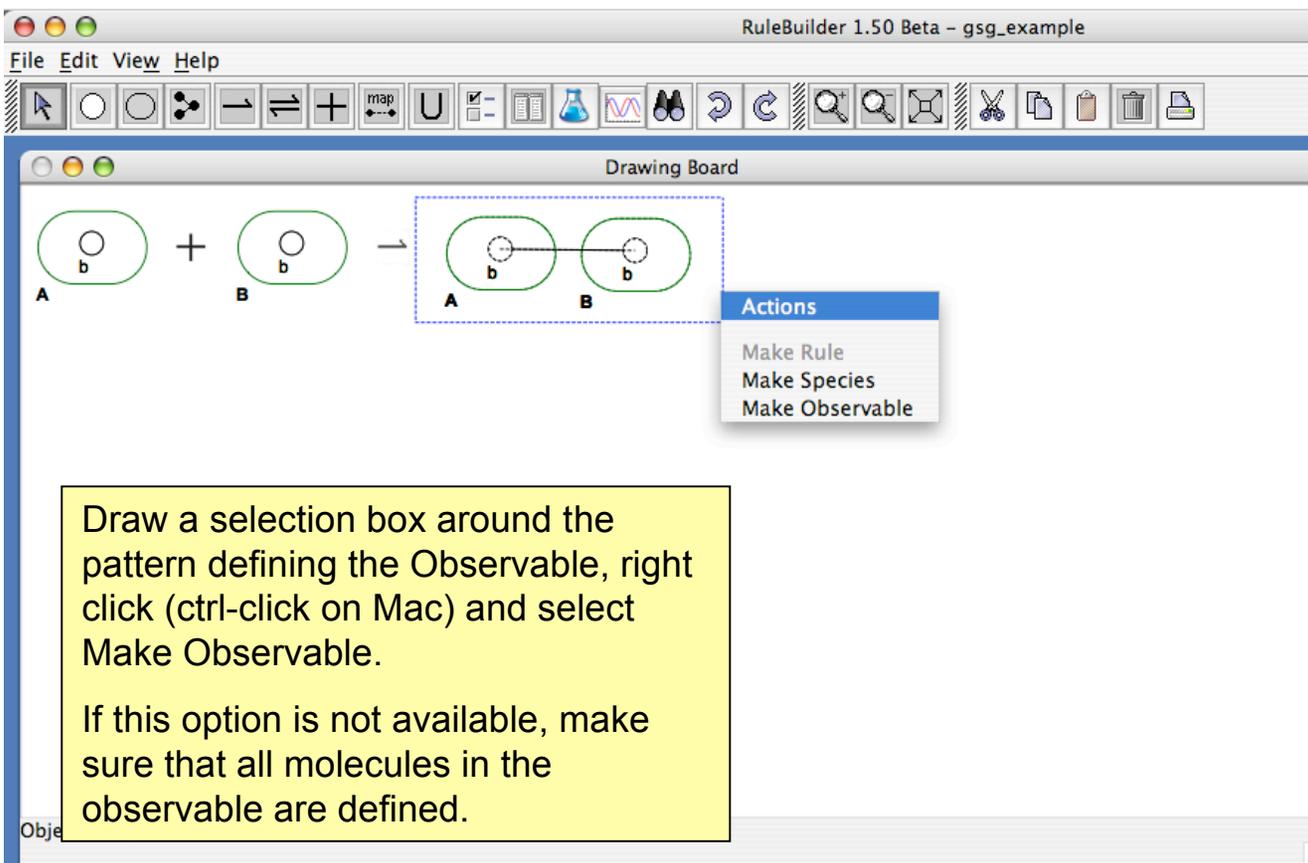
The Molecule Templates Palette on the right shows two templates: A (a small circle 'b' inside a larger oval) and B (a small circle 'b' inside a larger oval).

The Seed Species window, located below the Molecule Templates Palette, shows two species: A Species0 and B Species1. Each species is represented by a small circle 'b' inside a larger oval. A yellow callout box with the text "New species appears in the Seed Species Window." has an arrow pointing to the B Species1 entry.

At the bottom left of the interface, the text "Object Manipulation Mode" is visible.

Defining Observables

Observables are concentration sums over species with particular properties and correspond to model outputs, such as total phosphorylation of a protein.



The screenshot shows the RuleBuilder 1.50 Beta software interface. The main window is titled "RuleBuilder 1.50 Beta - gsg_example" and contains a "Drawing Board" window. On the drawing board, a chemical reaction is shown: two molecules, labeled A and B, each containing a smaller circle labeled 'b', are combined to form a single molecule consisting of two such circles connected by a horizontal line, also labeled A and B. A dashed blue selection box is drawn around the product molecule. A context menu is open over the selection box, with the following options: "Make Rule", "Make Species", and "Make Observable".

Draw a selection box around the pattern defining the Observable, right click (ctrl-click on Mac) and select Make Observable.

If this option is not available, make sure that all molecules in the observable are defined.

Make Observables Dialog

RuleBuilder 1.50 Beta - gsg_example

File Edit View Help

Properties

Name:

Type: Molecules

Done

Set Rule Name and Type.

Type **Molecules** weights the concentration of each matching species by the number of times the defined pattern matches the species.

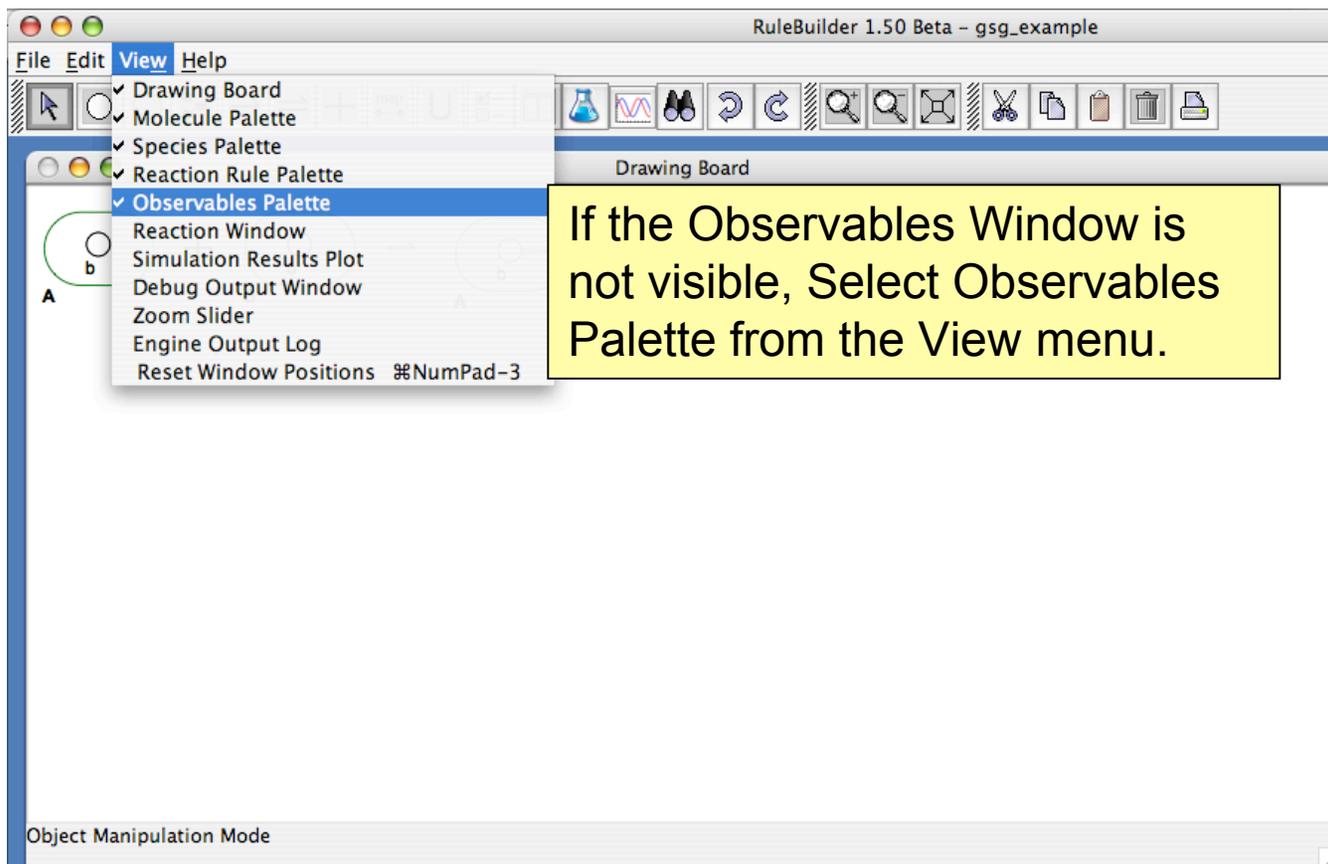
Use this for quantities like total phosphorylation of a site on a protein or total number of receptors in aggregates.

Type **Species** gives unit weight to the concentration of each matching species.

Use this type to get the concentration of complexes of a particular type.

Object Manipulation Mode

Observables Window



Observables Window

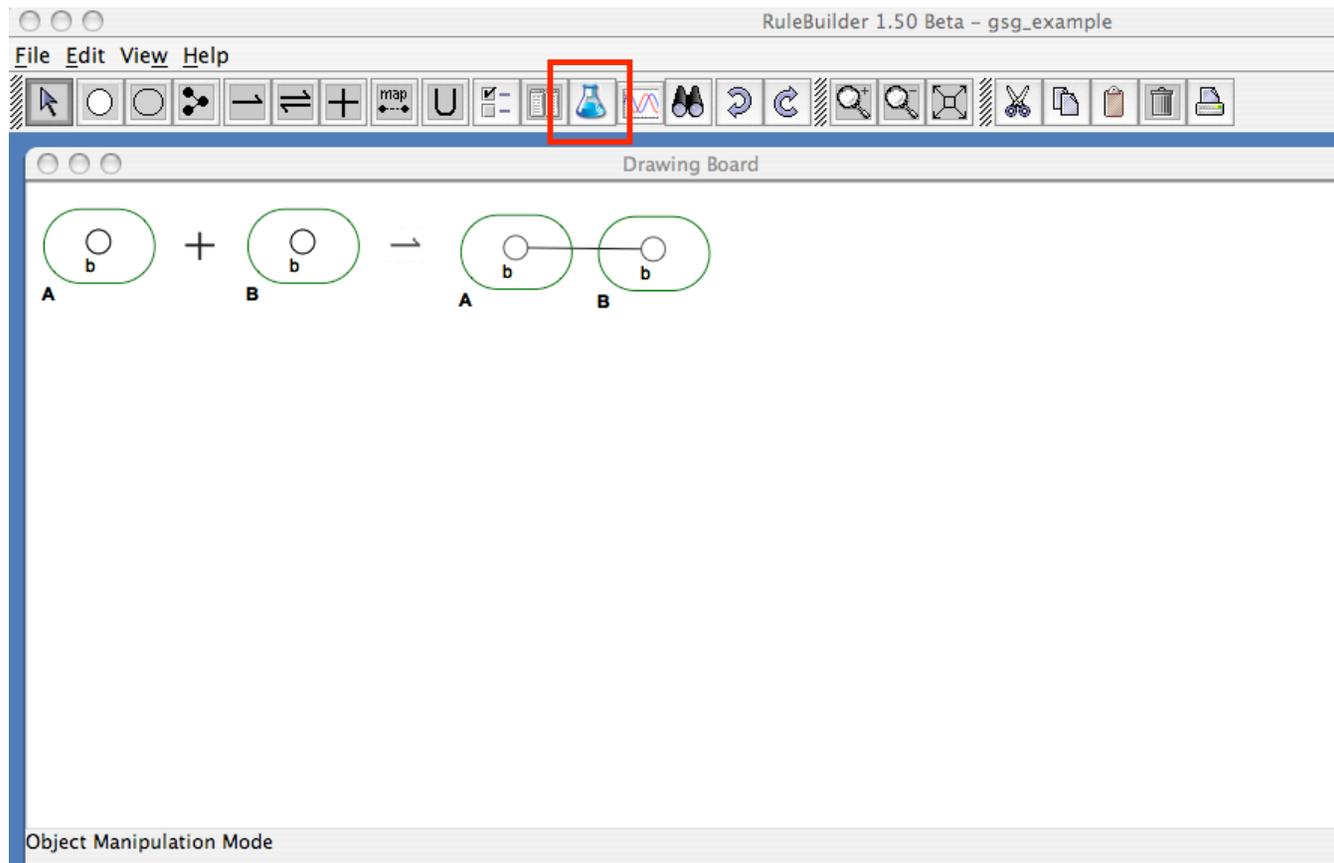
The screenshot displays the RuleBuilder 1.50 Beta software interface. The main window is titled "RuleBuilder 1.50 Beta - gsg_example" and contains several panels:

- Drawing Board:** Shows a chemical reaction where two separate molecules, labeled A and B, react to form a single molecule labeled AB. Each molecule consists of a small circle labeled 'b' inside a larger circle labeled 'A' or 'B'.
- Molecule Templates Palette:** Contains two templates, A and B, each consisting of a small circle 'b' inside a larger circle.
- Seed Species:** Contains two species, Species0 (template A) and Species1 (template B).
- Reaction Rules:** Shows the reaction rule for the reaction, labeled "Rule1", with a rate constant k_{01} .
- Observables:** A window titled "Observables" that displays the resulting molecule AB, which is a larger circle containing two smaller circles 'b'.

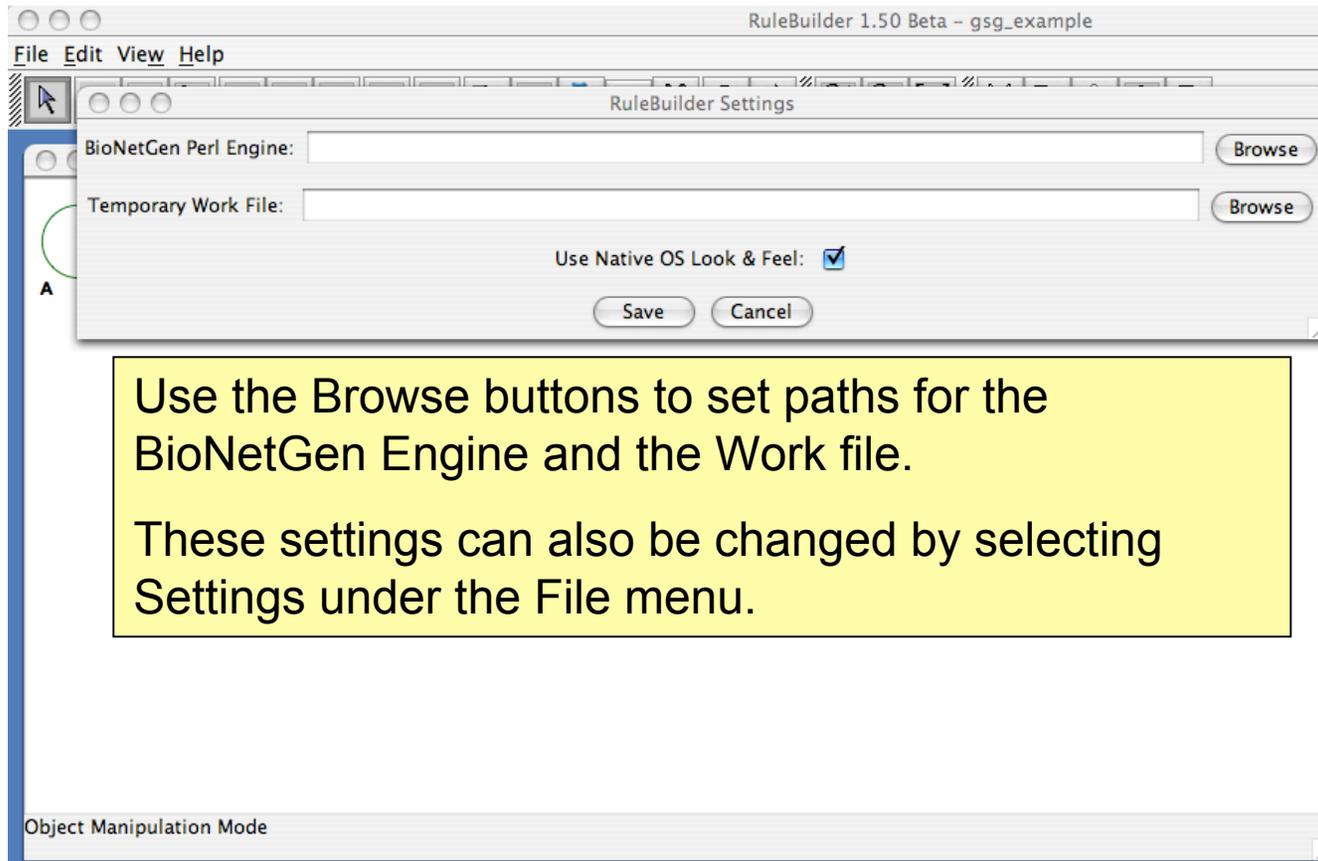
A yellow box highlights the text "The Observables Window" in the Reaction Rules panel.

Running the Model

Once Reaction Rules, Seed Species, and Observables (optional) have been defined, the model can be simulated by pressing Run BioNetGen button.

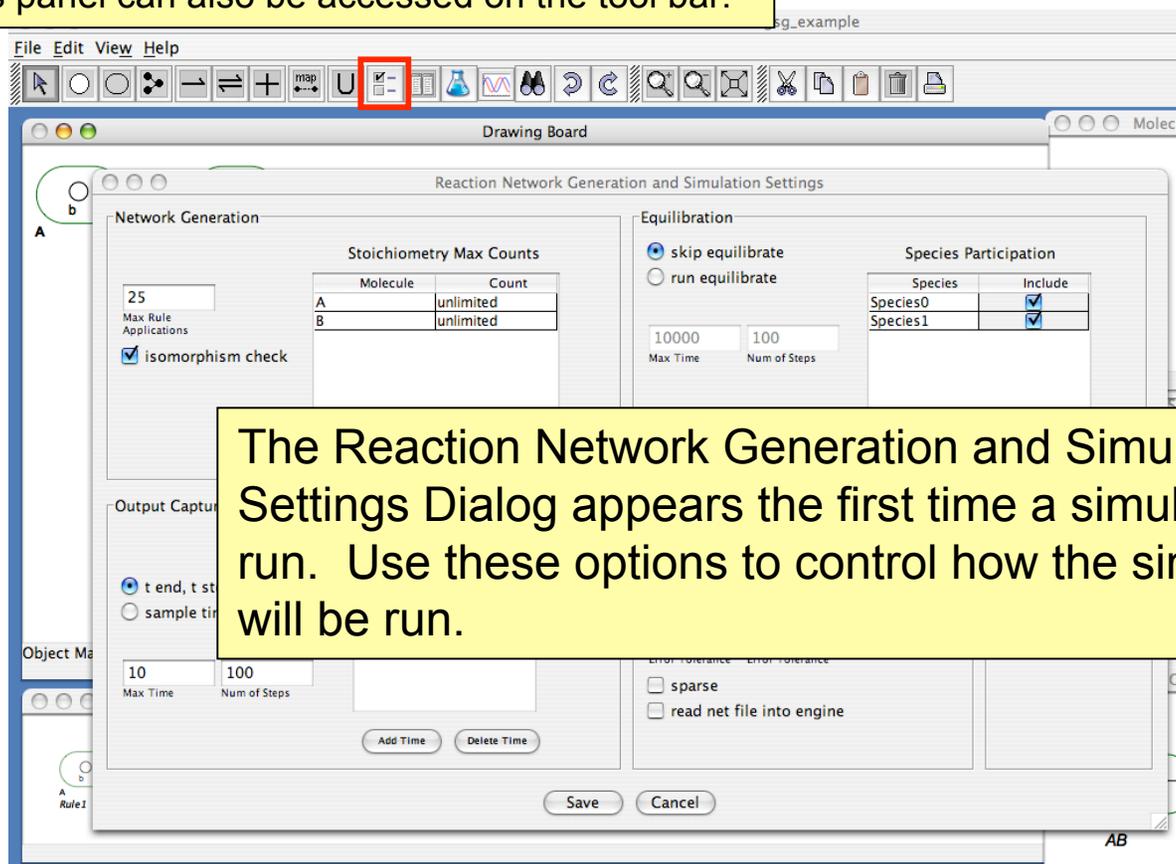


BioNetGen Engine Settings



The SimConfig Panel

This panel can also be accessed on the tool bar.



The Reaction Network Generation and Simulation Settings Dialog appears the first time a simulation is run. Use these options to control how the simulation will be run.

The SimConfig Panel

RuleBuilder 1.50 Beta - gsg_example

File Edit View Help

Drawing Board

Reaction Network Generation and Simulation Settings

Network Generation

25
Max Rule Applications

isomorphism check

Molecule	Count
A	unlimited
B	unlimited

Equilibration

skip equilibrate
 run equilibrate

10000 100
Max Time Num of Steps

Species Participation

Species	Include
Species0	<input checked="" type="checkbox"/>
Species1	<input checked="" type="checkbox"/>

Integration Method

Options

SBML output

1e-12 1e-12
Abs Integration Error Tolerance Rel Integration Error Tolerance

sparse
 read net file into engine

10 100
Max Time Num of Steps

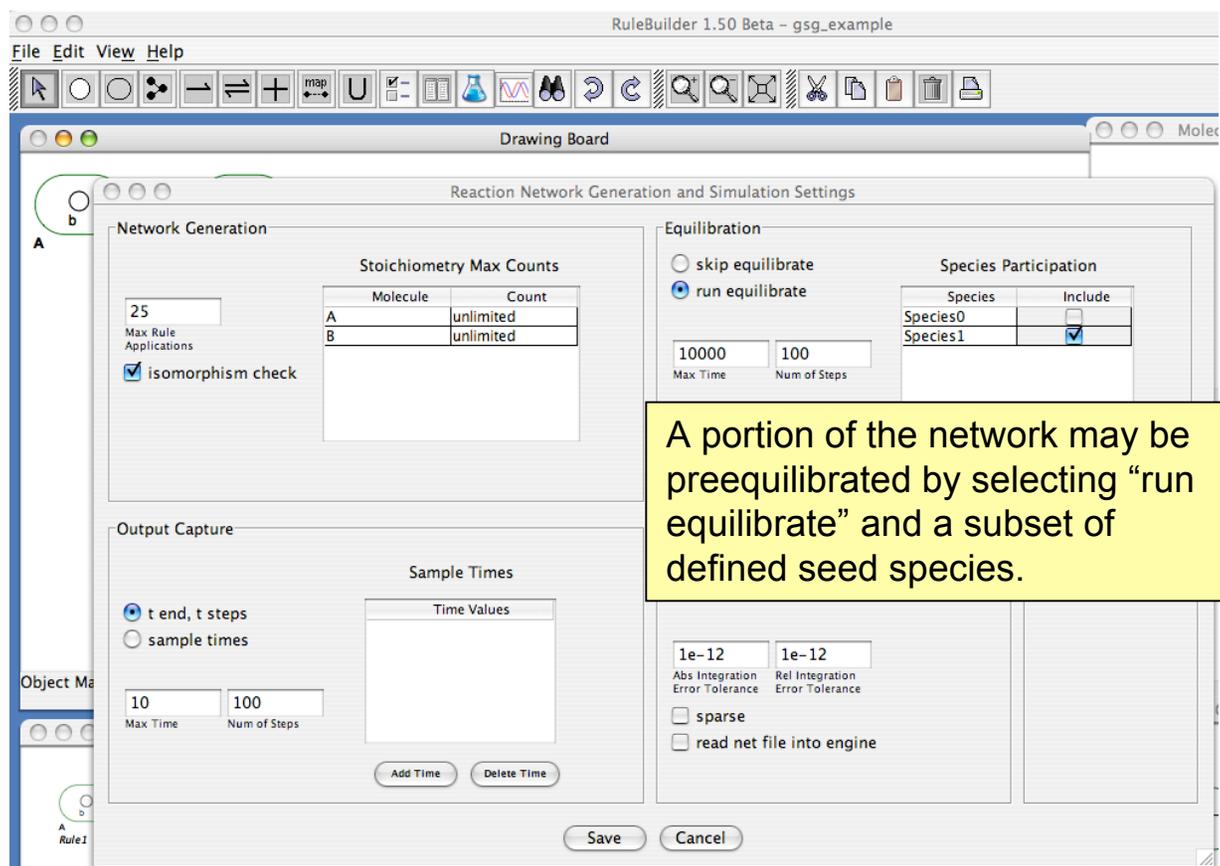
Add Time Delete Time

Save Cancel

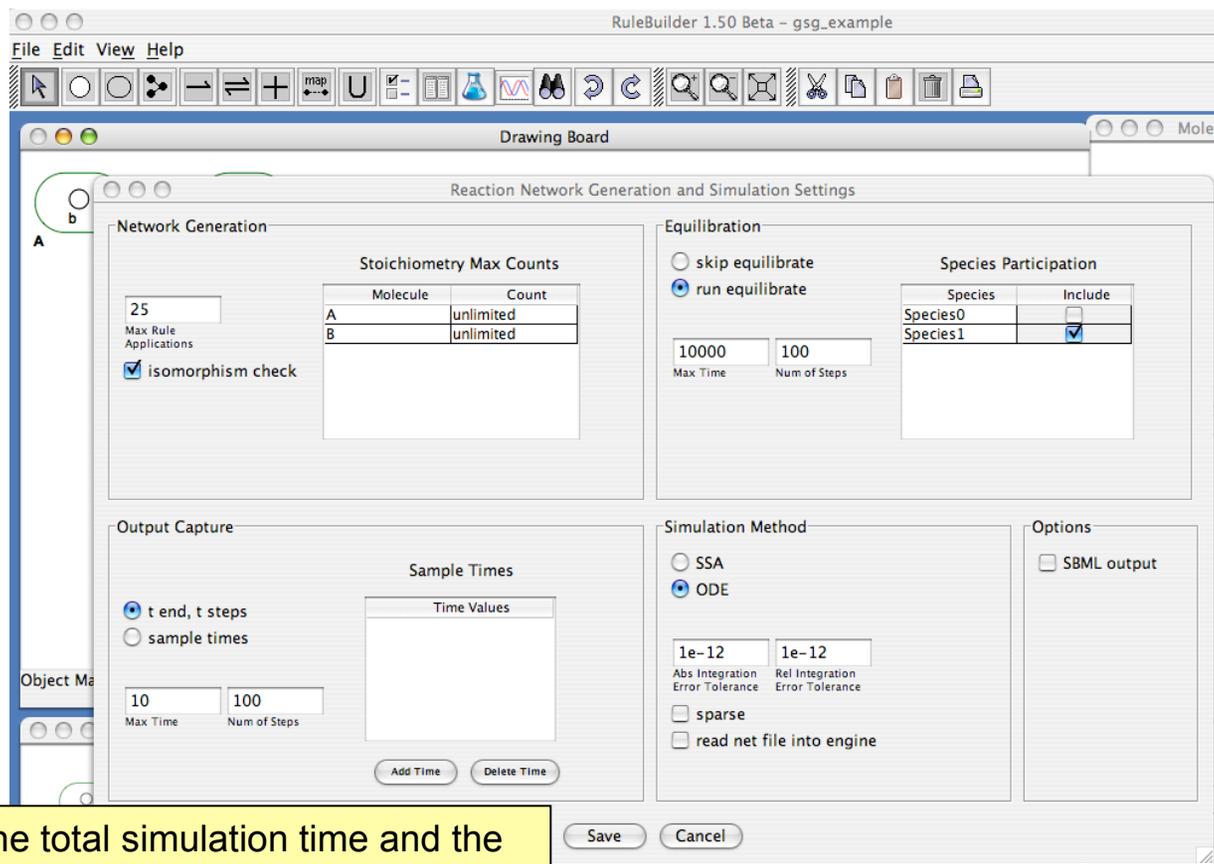
AB

The size of complexes and the reaction network can be limited by setting maximum values for the stoichiometry of molecules.

The SimConfig Panel

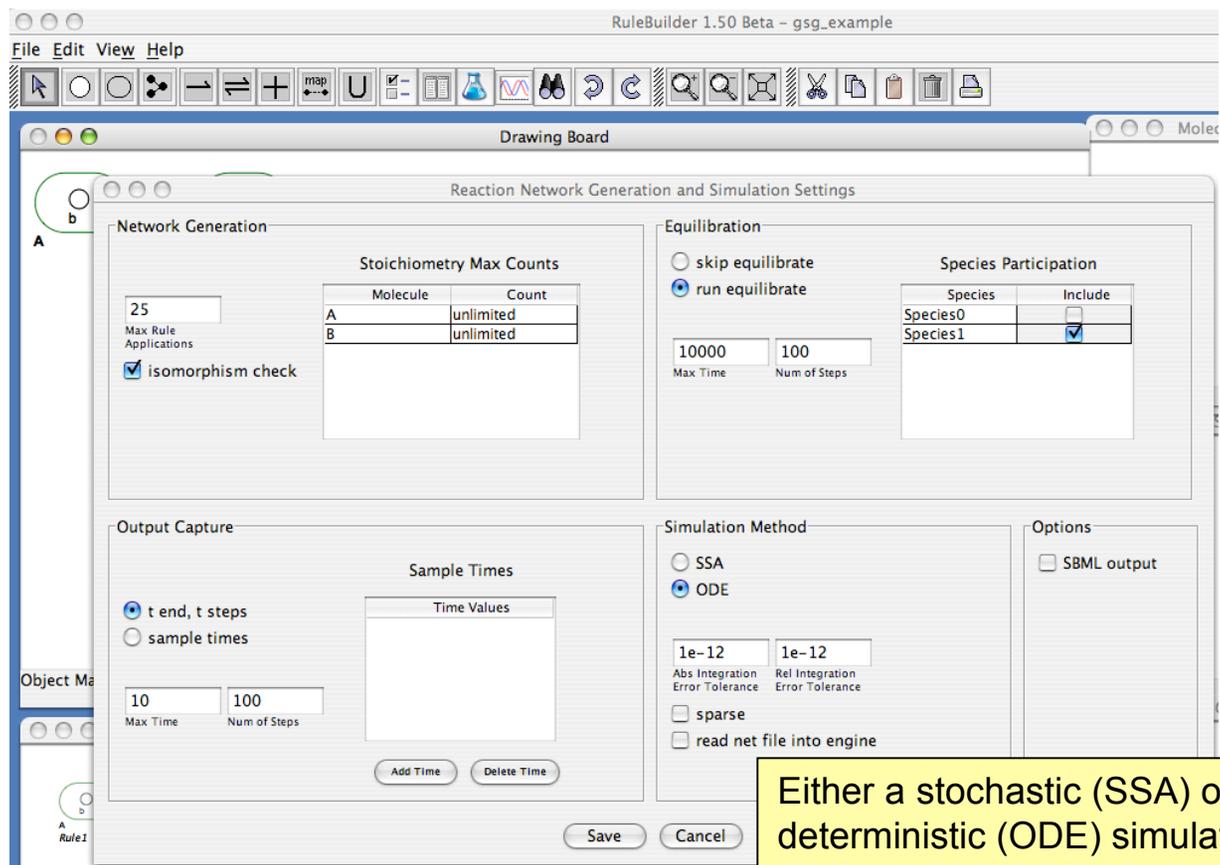


The SimConfig Panel



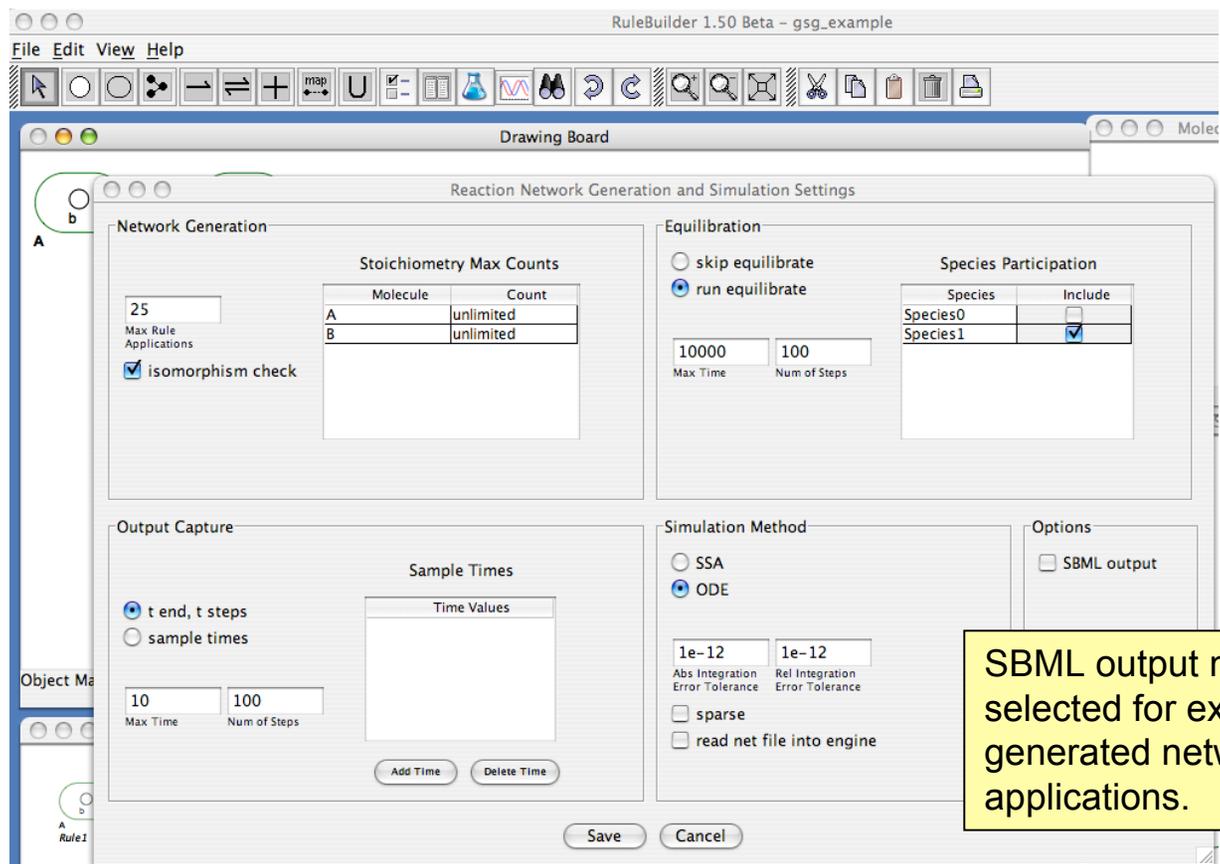
The total simulation time and the times at which concentrations are sampled are set here.

The SimConfig Panel



Either a stochastic (SSA) or a deterministic (ODE) simulation method may be chosen.

The SimConfig Panel



The Log Window

Running the simulation brings up the BioNetGen Output Log or Log Window

RuleBuilder 1.40 Beta - gsg_example

Drawing Board
BioNetGen Output Log

7.70	594	646
7.80	596	648
7.90	598	650
8.00	600	652
8.10	602	654
8.20	604	656
8.30	606	658
8.40	608	663
8.50	611	666
8.60	613	668
8.70	615	670
8.80	617	672
8.90	619	674
9.00	621	676
9.10	623	678
9.20	625	680
9.30	627	682
9.40	630	685
9.50	632	687
9.60	634	689
9.70	636	691
9.80	638	693
9.90	640	695
10.00	642	697

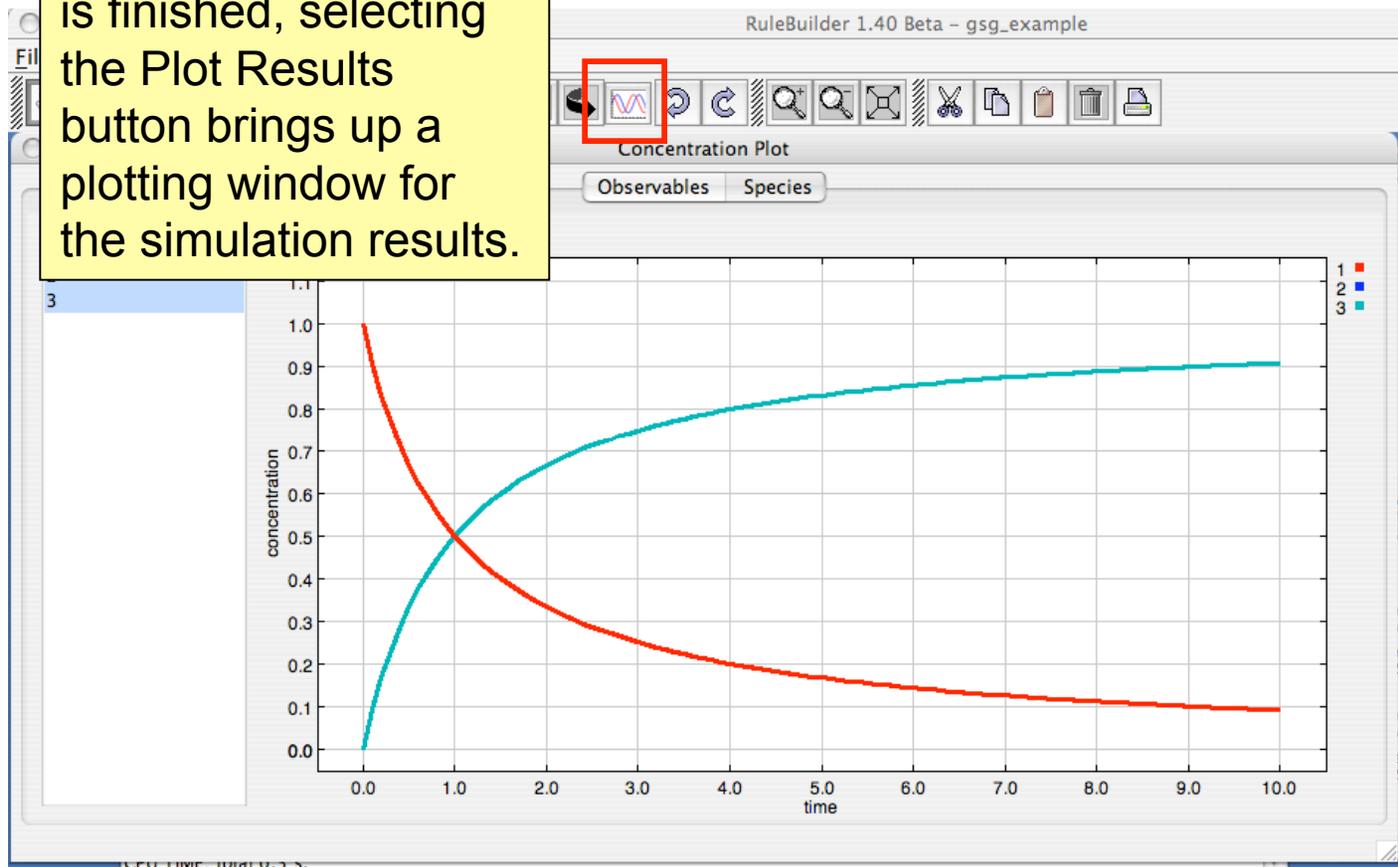
Time course of concentrations written to file /Users/faeder/shared/Projects/BioNetGen_develop/temp.cdat.
Propagation took 0.00 CPU seconds
Program times: 0.01 CPU s 0.00 clock s
Updating species concentrations from /Users/faeder/shared/Projects/BioNetGen_develop/temp.cdat
CPU TIME: simulate_ode 0.0 s.
Finished processing file /Users/faeder/shared/Projects/BioNetGen_develop/temp.bngl
CPU TIME: total 0.3 s.

Object Ma

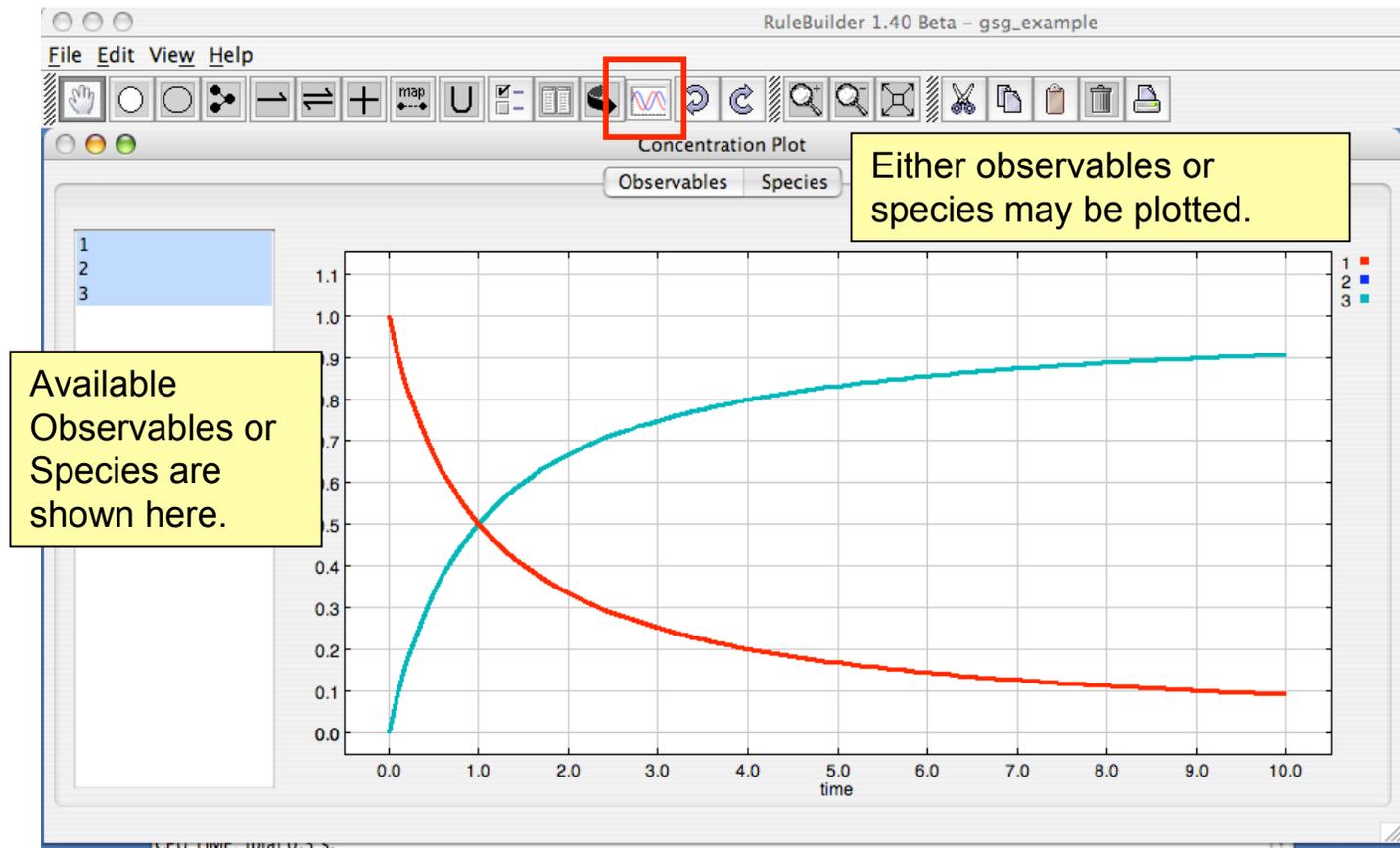
The Log Window displays the output of BioNetGen.

Plotting the Results

Once the simulation is finished, selecting the Plot Results button brings up a plotting window for the simulation results.



Plotting the Results



Plotting the Results

