

# SimBiology® 3

## Getting Started Guide

MATLAB®

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*SimBiology*<sup>®</sup> *Getting Started Guide*

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# Introduction

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This chapter introduces SimBiology® functions and features to help you develop a conceptual model for working with the software and your biochemical data.

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## SimBiology Overview

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“Integrated Environment” on page 1-2
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### Integrated Environment

SimBiology software provides an integrated environment for modeling biological processes, simulating the dynamic behavior of these processes, and analyzing the model with simulation and experimental data. Biological processes include metabolic, genetic, and signaling pathways with transform, binding, and transport reactions.

You can also create and analyze pharmacokinetic models. For more information see “Pharmacokinetic Modeling” in the SimBiology documentation.

- **Model** — Design and build models by entering reactions, species, parameters, kinetic laws, rules, and events

Import SBML models created with the SimBiology software or other modeling software that is compliant with the Systems Biology Markup Language (SBML) standard.

Export models you create with the SimBiology desktop to MATLAB® and continue your simulations and analysis with command-line functions.

For more information, see “Modeling”.

- **Analyze Structure** — Verify that the model can be simulated, and use the verification results to fix any incompatibilities in the model. Investigate the structure of your models, including determining conserved moieties, adjacency matrices, and stoichiometry matrices.

For more information, see “Structural Analysis”.

- **Simulate and Analyze** — Observe changes in species amounts and parameter values over time. Convert your model to a system of differential equations and simulate the model numerically with various differential equation solvers. The deterministic solvers include stiff and nonstiff ordinary differential equation (ODE) solvers. The stochastic solvers include a stochastic simulation algorithm with implicit and explicit tau variations. Perform multiple stochastic ensemble runs, save data from a simulation, compare simulation and experimental data, perform sensitivity analysis, species or parameter scans, and parameter estimation.

For more information, see “Simulation and Analysis”.

## Expected Users

The people who use SimBiology software come from a wide range of areas including biology, systems biology, pharmacology, computer science, and engineering. This product is intended for research scientists, computational biologists, and students who need to develop and study biological pathways at the molecular and systems level, develop custom analysis applications, or implement published pathways, and visualize results.

**Industry and Professional** — SimBiology software allows you to model, simulate, and analyze biochemical and system pathways for applications in drug discovery and design, target identification, and pharmacokinetic modeling.

Modeling, simulating, and analyzing a biological system can test hypotheses for a pathway, identify side effects caused by drug interactions with a target compound, and identify biochemical pathways that lead to disease.

**Academia** — Build rigorous, dynamic, quantitative models that allow you to understand and predict system behavior at the molecular level. Build models to explore enzyme kinetics. Leverage the MATLAB foundation to easily manipulate large data sets.

Simulating the dynamic behavior of a model can confirm the validity of the models and identify behaviors and control mechanisms not apparent from studying static models. Validate models experimentally and use the model to predict *in vitro* and *in vivo* behavior.

## Required Software

To use SimBiology software, you must first install the following MathWorks® product:

### MATLAB

Provides a command-line interface and an integrated software environment. For instructions, see the MATLAB installation documentation for your platform.

If you have installed MATLAB and want to check which other MathWorks products are installed, enter `ver` in the MATLAB Command Window.

## Optional Software

### Statistics Toolbox™ (Version 7.0 (R2008b) or later)

Provides fitting tools including functions required to analyze nonlinear mixed effects (NLME).

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**Note** Statistics Toolbox is required to use SimBiology to perform population fitting using `sbionlmeFit` or `sbionlmeFitSA`, or to perform individual fitting using `sbionlinfit`.

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### Global Optimization Toolbox

Solve optimization problems using genetic and direct search algorithms. If this toolbox is installed, you can use various genetic and direct search algorithms for parameter estimation. If this toolbox is not installed, the software uses the optimization algorithms available in MATLAB.

**Optimization Toolbox™**

Optimization Toolbox extends the MATLAB technical computing environment with tools and widely used algorithms for standard and large-scale optimization. These algorithms solve constrained and unconstrained continuous and discrete problems. If the Optimization Toolbox product is installed, you can use some algorithms included this product for parameter estimation in SimBiology software. If the Optimization Toolbox product is not installed, the software uses the optimization algorithms available in MATLAB.

**C Compiler**

Required to prepare the model for accelerating simulations. For a list of supported compilers, see Supported and Compatible Compilers.

**Related Software****Bioinformatics Toolbox™**

Read, analyze, and visualize genomic, proteomic, and microarray data.

# Integrating SimBiology Models into Your Existing Workflow

## In this section...

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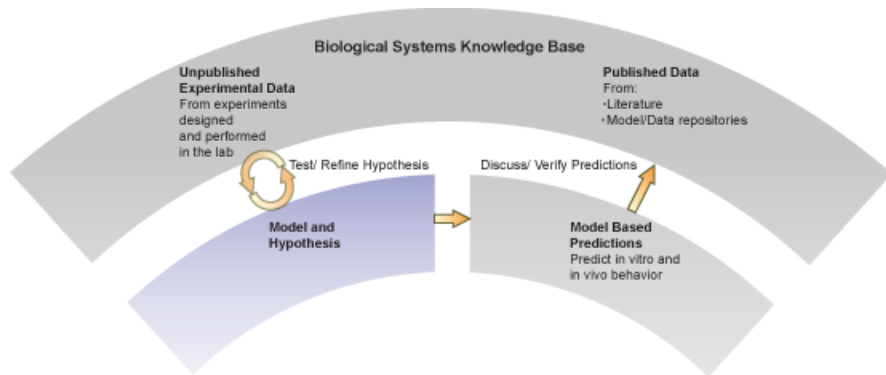
“Workflow Incorporating Mathematical Modeling” on page 1-7

“Workflow Using SimBiology Models for Mathematical Modeling” on page 1-9

## Existing Workflow in Experimental Research

Consider the following typical workflow in experimental research.

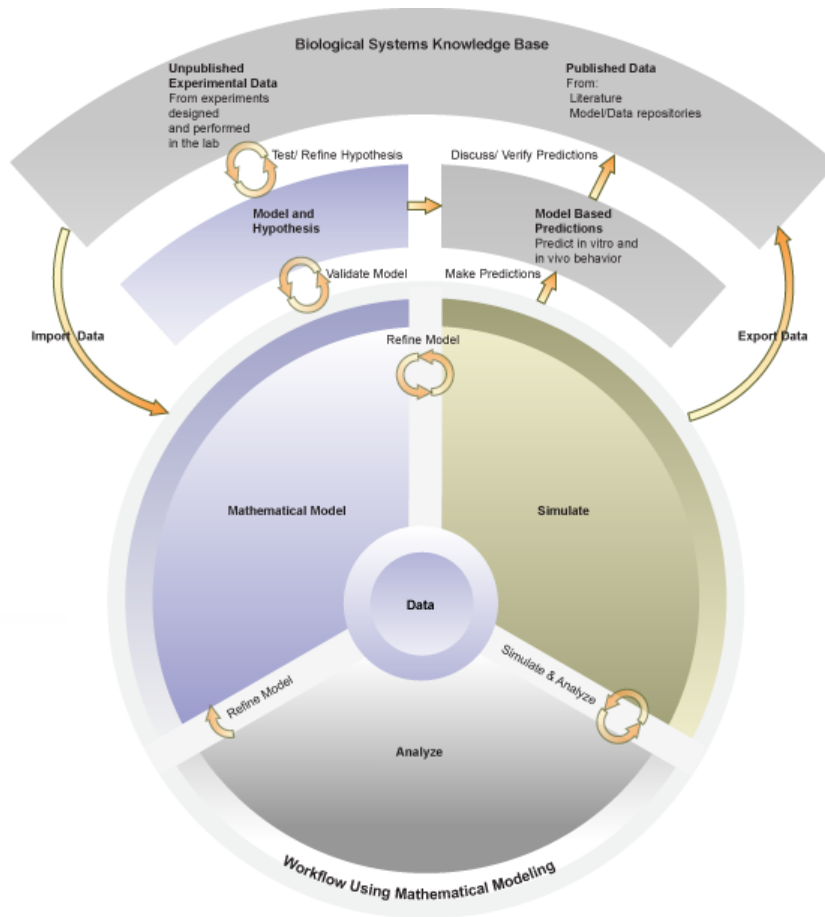
- 1 Use preliminary results and published data to develop a model and hypothesis in your area of interest.
- 2 Validate your model by making predictions and designing experiments to test your model and hypothesis.
- 3 Make further predictions based on your model.
- 4 Publish results and predictions.
- 5 Continue to test predictions experimentally.



## **Workflow Incorporating Mathematical Modeling**

Mathematical modeling integrates into the preceding workflow by providing the means to:

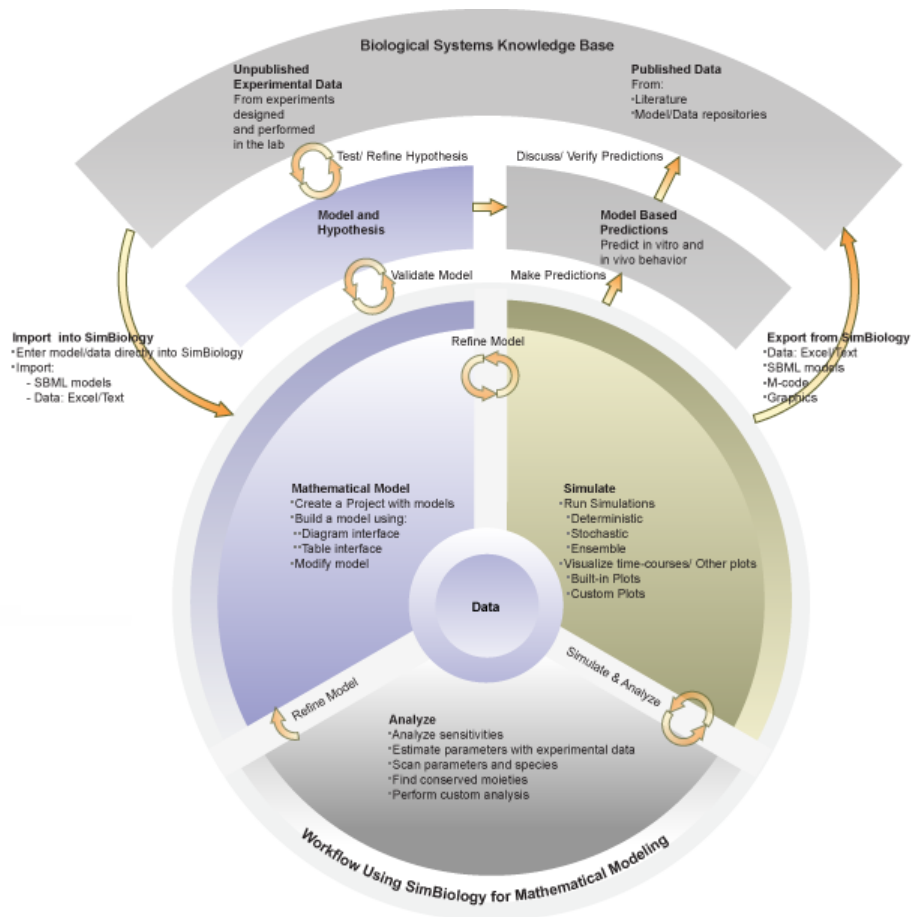
- Consolidate quantitative data into the model.
- Represent large pathways and networks and lay them out in meaningful ways using a software application.
- Study emergent properties of pathways and use these predictions to guide the direction of experimental research in ways that can save time and development costs.





## Workflow Using SimBiology Models for Mathematical Modeling

SimBiology software provides an integrated environment for mathematical modeling and analysis of biological and biochemical pathways. The following figure shows an overlay of features and tasks in the product pictured in the context of the complete workflow in experimental research.



## Using the SimBiology Desktop vs. the Command Line

There are two ways to use SimBiology:

- **SimBiology desktop** — Use the desktop GUI (graphical user interface) to interactively iterate through the model building and analysis workflow. For more information, see Chapter 2, “Getting Started Using the SimBiology Desktop”.
- **Command line** — Use the MATLAB command line to programmatically write and save scripts for batch processing, and to automate the model building and analysis workflow. For more information, see Chapter 3, “Getting Started Using the Command Line”.

There are demos that show you how to use the command line to build a model, simulate, and analyze:

- To access demos included with the software, see SimBiology Demos.
- To access demos on the Web, see SimBiology Demos and Webinars.

# SimBiology and SBML

## In this section...

“What Is SBML?” on page 1-11

“Importing from SBML Files” on page 1-11

“Exporting a SimBiology Model to SBML Format” on page 1-11

## What Is SBML?

Systems Biology Markup Language (SBML) is a standard format for sharing systems biology models among various modeling and simulation software tools. The current specification is available at <http://sbml.org/documents/>.

## Importing from SBML Files

Because SimBiology supports a subset of the SBML Level 2 Version 1 specification, the following SBML features are not imported into the SimBiology model:

- Piecewise kinetics — Models with piecewise kinetics are loaded, but the definitions for piecewise kinetics are ignored.
- Function definitions — Models containing function definitions are loaded, but a warning is displayed, and the function definitions are ignored.
- MATLAB incompatible variable names in `UnitDefinition` — Models that have variable names incompatible with MATLAB in `UnitDefinition` are not loaded and an error message is displayed.
- The `hasOnlySubstanceUnits` field does not have a corresponding property in the SimBiology species object. For more information on dimensions for SimBiology species, see `DefaultSpeciesDimension`.

## Exporting a SimBiology Model to SBML Format

### SimBiology Features Supported by SBML

The following SimBiology model information is included in the SBML format file:

- Compartments, species, parameters, reactions, rules, and events that are defined in the model and have their **Active** property set to true.
- All unit definitions in SBML-compliant format.
- Model component properties with SBML equivalents, such as notes, and unit values for species and parameters.
- The reaction rate equation, but not the kinetic law definition.

### **Example**

In SimBiology, the Henri-Michaelis-Menten equation,  $V_m * S / (K_m + S)$ , is a definition stored in the Kinetic Laws library. Specifically, for a one-substrate enzyme-catalyzed reaction, if you assign  $V_m = V_a$ ,  $K_m = K_a$ , and  $S = A$ , then the reaction rate equation is exported to SBML as  $V_a * S / (K_a + A)$ .

### **SimBiology Features Not Supported by SBML**

The following SimBiology features are not supported by SBML and are not included in the saved SBML format file. You can store this information in a SimBiology project file, which has an `.sbproj` extension.

- **Projects** — Models, analysis tasks, and data.
- **Kinetic law information** — SimBiology models store kinetic law information such as the kinetic law name and a kinetic law definition.
- **Variant information** — Collections of quantities (compartments, species, and/or parameters) that you can use to alter a model's initial or base configuration.
- **Dosing information** — Exogenous increments to the amount (or concentration) of a species in a model.
- Features and properties specific to SimBiology software, such as **Tag** and **Active**.

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**Tip** Because the previous information is not supported by SBML, we recommend saving SimBiology project files to capture this information.

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# Getting Started Using the SimBiology Desktop

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- “SimBiology Desktop Overview” on page 2-2
- “SimBiology Projects” on page 2-3
- “SimBiology Libraries” on page 2-10

# SimBiology Desktop Overview

The SimBiology desktop is a GUI (graphical user interface) that lets you interactively iterate through the model building and analysis workflow. It lets you manage the following:

- **Projects** — Encapsulate models, analysis tasks, results, diagnostic plots, and data into one convenient package. For more information, see “SimBiology Projects” on page 2-3.
- **Libraries** — View and access information, such as units, kinetic laws, and plot types, to use when building models or plotting data. This information is available for use in all projects. For more information, see “SimBiology Libraries” on page 2-10.

## Opening the SimBiology Desktop

Open the desktop by typing the following at the MATLAB command line:

```
simbiology
```

## Using SimBiology Desktop Tools

There are tools in the desktop that you can use for various tasks such as capturing code, viewing errors and warnings, and viewing search results. For a complete list, select the **Desktop** menu.

## Using the Desktop to Learn the Command Line

If you use the SimBiology desktop, you can learn about working at the command line, by using the **MATLAB Code Capture Tool** (accessed from the **Desktop** menu). This tool records and saves your desktop actions as a script of MATLAB and SimBiology commands. You can use the tool to view the script commands. After loading the script into the MATLAB Editor, you can run the script and edit the script.

## SimBiology Projects

### What Is a SimBiology Project?

When using the desktop, *projects* let you manage the model building and analysis workflow.

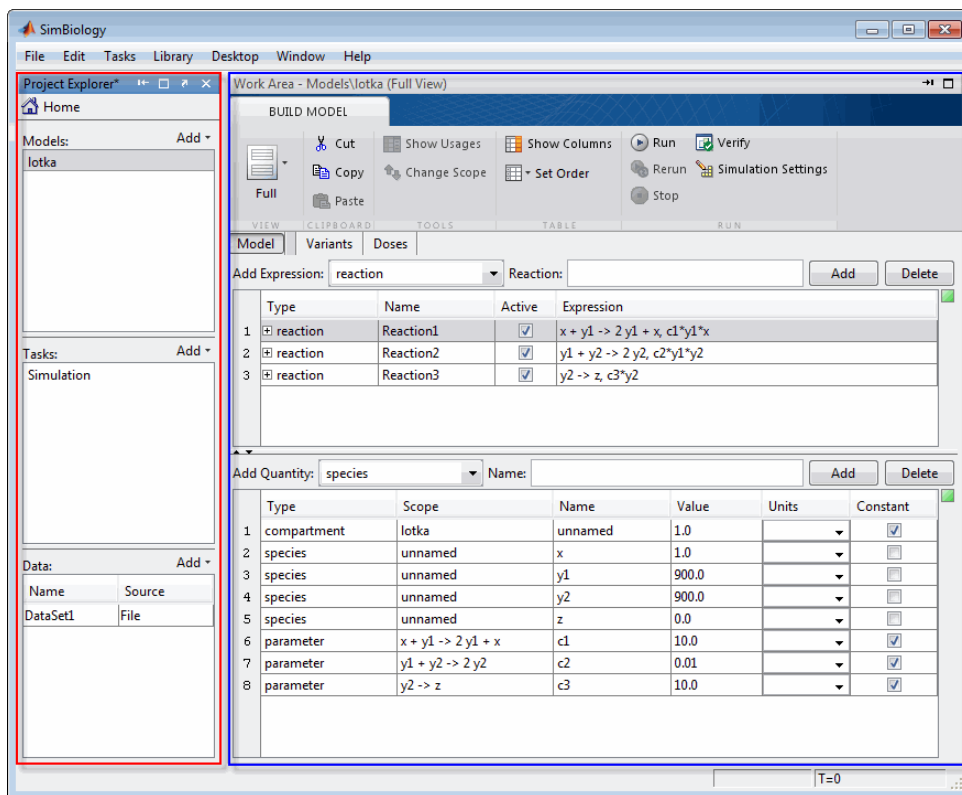
A project encapsulates the following:

- **Models** — Sets of quantities (compartments, species, and parameters) and expressions (reactions, discrete events, and rules, including differential equations, algebraic constants, and assignments) that describe the dynamics of a system.
- **Tasks** — Analyses that operate on a model or project.
- **Data** — Imported data or data generated by analyses.

A project groups and saves related models, tasks, and data into a project file with an `.sbproj` extension.

## Using the Project Explorer to Manage Projects

Use the **Project Explorer** (outlined in red) to manage projects. In the **Models**, **Tasks**, and **Data** sections, use the **Add** button to add these items to a project. Select a model, task, or data in the **Project Explorer**, then view and set related information in the **Work Area** (outlined in blue).







SimBiology® Desktop With Open Project



## Models

Use the **Models** section in the **Project Explorer** to load, create, or select models. After you select a model, you can do the following in the **Work Area**:

- Select a model view (see the following table).
- Create and edit the quantities and expressions that define the model.
- Create and edit modifiers (variants and doses) for the model.

Model View	Description
	<p>Create and edit the following model components in one view:</p> <ul style="list-style-type: none"> <li>• <b>Expressions</b> — Reactions, rules, and events</li> <li>• <b>Quantities</b> — Compartments, species, and parameters</li> <li>• <b>Modifiers</b> — Variants and doses</li> </ul>
	<p>Create and edit a model using visual block representations for compartments, species, and reactions.</p> <ul style="list-style-type: none"> <li>• Add Compartment, Species, and Reaction blocks to the diagram by click-dragging them from the <b>Block Library Browser</b>.</li> <li>• Set block properties by right-clicking the block, then selecting <b>Properties</b>.</li> <li>• Connect Species and Reaction blocks by pressing and holding the <b>Ctrl</b> key (Windows® and Linux®) or the <b>Option</b> key (Macintosh®), then click-dragging a line from one block to another block: <ul style="list-style-type: none"> <li>▪ To mark a species as a reactant, draw the line from the Species block to a Reaction block. This draws a solid line with no arrow.</li> <li>▪ To mark a species as a product, draw the line from a Reaction block to the Species block. This draws a solid line with an arrow pointing to the species.</li> </ul> </li> </ul>
	<p>Create and edit model quantities, expressions, and modifiers using the <b>Compartments, Species, Parameters, Reactions, Rules, Events, Variants, and Doses</b> tabs.</p>
	<p>Create and edit a model using your own custom view, incorporating elements from the Full and Diagram views.</p>

### Analysis Tasks

Use the **Tasks** section in the **Project Explorer** to add or select an analysis task (such as Simulate or Calculate sensitivities). After selecting an analysis task, you can do the following in the **Work Area**:

- Select a model, optionally select a variant or dose, and then define the model's simulation settings.
- Define the settings of the analysis.
- Select the plots to generate when the analysis completes.
- Run the analysis.

For more information on available analysis tasks, see “Simulation and Analysis” in the *SimBiology User's Guide*.

### Creating Plots of Analyses

To visualize data from analyses, you can choose from a list of built-in plot types. You can also create your own plot types that extend or customize the built-in plot types. Create a custom plot type in the **Library Explorer**. For more information, see “SimBiology Libraries” on page 2-10.

### Creating Custom Analysis Tasks

From the **Tasks** section, you can write your own MATLAB code to define an analysis task. You can create a custom analysis task from scratch or use the code of an existing task.

## Data

Use the **Data** section in the **Project Explorer** to manage:

- **Imported data** — Data that you import from external sources for an analysis (such as parameter fitting), or to compare to results from a simulation or analysis.
- **Task data** — Data generated from analysis tasks.

## Working with Imported Data

You can do the following with data that you import:

- **View raw data** — When viewing imported raw data, you can specify the units for the column headers.
- **Plot data** — Select from a list of built-in and user-defined plot types.
- **Exclude data** — Exclude rows of data that meet or don't meet certain criteria, using column headers and relational operators. For example, you can exclude outliers in a data set, such as rows containing a DOSE value > 20.
- **Add derived data** — Create additional columns of data that you derive from the existing columns of data using expressions and relational operators. For example, you can convert a column header to different units, or create a ratio of two columns of data.
- **View data statistics** — View statistics for the data, such as minimum, maximum, mean, and time of maximum.

### Working with Task Data

You can do the following with data generated from an analysis task:

- **Save data** — When you generate data from an analysis task, you can save the data to prevent it from being overwritten by subsequent analysis tasks. Saved data includes the task analysis settings used to create it.
- **View raw data** — Inspect the raw data generated by a simulation or analysis.
- **Plot data** — Select from a list of built-in and user-defined plot types. You can plot data without having to rerun the analysis task.
- **Export data** — Export analysis task data to a file or a variable in the MATLAB Workspace.

### Searching a Project

You can create search criteria to find specific components in the models in a project by creating a **Search model** task from the **Tasks** section in the **Project Explorer**. After editing or loading a project, you must execute a search to have up-to-date results. Like other tasks, a search model task is saved with the project.

### Generating a Report for a Project

You can generate reports with model-specific information, such as analysis task results, imported data, and searches. Select **Generate report** from the **Add** menu in the **Tasks** section in the **Project Explorer**. Like other tasks, a report task is saved with the project.

---

## Importing and Exporting Models, Tasks, and Data

### Models

Use the **Models** section in the **Project Explorer** to import models from any of the following:

- sbproj file
- SBML file
- MATLAB Workspace variable

Use the **Models** section in the **Project Explorer** to export models to any of the following:

- SBML file
- MATLAB Workspace variable

For more information on how SimBiology supports SBML, see “SimBiology and SBML” on page 1-11.

### Tasks

Use the **Tasks** section in the **Project Explorer** to save a task as a MATLAB file.

### Data

Use the **Data** section in the **Project Explorer** to import data from any of the following:

- sbproj file
- Microsoft® Excel® file
- txt or CSV file
- MAT-file
- MATLAB Workspace variable

Use the **Data** section in the **Project Explorer** to export data to a MATLAB Workspace variable.

## SimBiology Libraries

### What Are Libraries?

SimBiology includes the following libraries that contain both built-in and user-defined components to use when building models or plotting data:

- **Units Library**
- **Unit Prefixes Library**
- **Kinetic Laws Library**
- **Plot Types Library** — Contains plot types for plotting results of analysis tasks or plotting data.
- **Blocks Library** — Contains blocks for building models in the **Diagram** view.

The libraries are available for all projects and are not part of any one project.

### Adding User-Defined Components to Libraries

To add user-defined components to a library, select **Desktop > Library Explorer**, then select one of the libraries.

---

**Note** You can add, modify, and delete user-defined components in a library, but you cannot modify or delete built-in components in a library.

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### Exporting and Importing Libraries

You can export user-defined components from a library to an sblib file, which can be imported by another SimBiology user.

# Getting Started Using the Command Line

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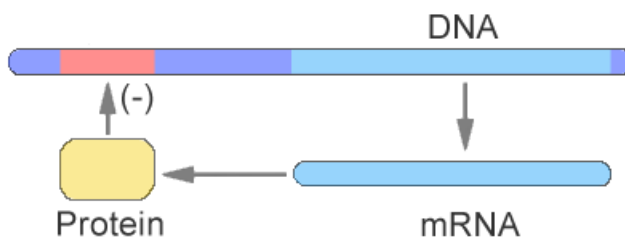
This chapter shows how to model a simple gene-regulation pathway using the command-line interface.

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## About The Gene Regulation Model

### Model Diagram

You can visualize a systems biology model with various levels of detail. One view sketches only the major species and processes. This model is an example of simple gene regulation, where the protein product from translation controls transcription. You could create a more complex model by adding the enzymes, coenzymes, cofactors, nucleotides, and amino acids that are not included in this model. The gene regulation example simplifies the regulatory mechanism by not showing the contributions of RNA polymerase and any cofactors. The protein product from gene expression binds to a regulatory region on the DNA and represses transcription.



Another way of looking at a systems biology model is to list the reactions in a model with the processes they represent.

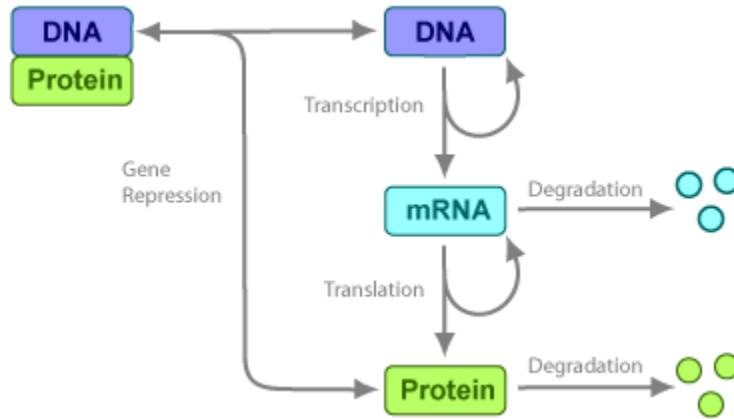
```

DNA -> DNA + mRNA           (transcription)
mRNA -> mRNA + protein       (translation)
DNA + protein -> DNA_protein (binding)
DNA_protein -> DNA + protein (unbinding)
mRNA -> null                 (degradation)
protein -> null               (degradation)

```

Drawing the reaction pathways will help you visualize the relationships between reactions and species. In the gene regulation example, as the amount of a protein increases, the protein forms a complex with the gene responsible for its expression, and slows down protein production.





## Model Reactions

Reaction equations define a systems biology model at the level of detail needed for a software program to simulate the dynamic behavior of the model. The following reactions for transcription, translation, binding, and degradation describe a simple gene-regulating mechanism.

### Transcription

Transcription is where RNAPolymerase and cofactors bind with a DNA molecule. The RNAPolymerase then moves along the DNA and combines nucleotides to create mRNA. A simple model of transcription shows only the DNA and mRNA.



This model simplifies the transcription and the synthesis of mRNA by using a single reaction.

Reaction:  $\text{DNA} \rightarrow \text{DNA} + \text{mRNA}$   
 Reaction rate:  $v = k_1 \cdot \text{DNA}$  molecule/second  
 Species: DNA = 50 molecule  
           mRNA = 0 molecule

Parameters:  $k_1 = 0.2$  1/second

### Translation

After the mRNA moves from the nucleus to the cytoplasm, it can bind with ribosomes. The ribosomes move along the mRNA and create proteins with the help of tRNAs bound to amino acids. A simple model of translation shows only the mRNA and protein product.

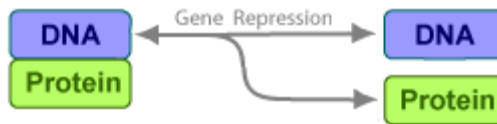


The synthesis of the protein is modeled as a single reaction.

```
Reaction: mRNA -> mRNA + protein
Reaction rate:  $v = k_2 * \text{mRNA}$  molecule/second
Species: mRNA = 0 molecule
         protein = 0 molecule
Parameters:  $k_2 = 20$  1/second
```

### Gene Repression

Transcription of DNA to mRNA is regulated by the binding of the protein product from translation to the DNA. As more protein is produced, the DNA is bound with the protein more often and less time is available for transcription with the unbound DNA.



### Forward Reaction (Binding)

```
Reaction: DNA + protein -> DNA_protein
Reaction rate:  $v = k_3 * \text{DNA} * \text{protein}$  molecule/second
Species: DNA = 50 molecule
         protein = 0 molecule
Parameters:  $k_3 = 0.2$  1/(molecule*second)
```

Notice how the units are described for the parameter  $k_3$ . In the literature, some of the common ways to display second-order rate constants are  $\text{mole}^{-1}\text{second}^{-1}$  or  $1/\text{mole}\cdot\text{second}$ . However, software evaluations of these common ways are sometimes ambiguous.

### Reverse Reaction (Unbinding)

```

Reaction: DNA_protein -> DNA + protein
Reaction rate: v = k3r*DNA_protein molecule/second
Species: DNA_protein = 0 molecule
Parameters: k3r = 1 1/second

```

For this tutorial, model the binding and unbinding reactions as one reversible reaction.

```

Reaction: DNA + protein <-> DNA_protein
Reaction rate: v = k3*DNA*protein - k3r*DNA_protein molecule/second
Species: DNA = 50 molecule
          protein = 0 molecule
Parameters: k3 = 0.2 1/(molecule*second)
           k3r = 1 1/second

```

### Degradation

Protein and mRNA degradation are important reactions for regulating gene expression. The steady-state level of these compounds is maintained by a balance between synthesis and degradation reactions. Proteins are hydrolyzed to amino acids with the help of proteases, and nucleic acids are degraded to nucleotides.



mRNA degradation is modeled as a transformation to the null species.

```

Reaction: mRNA -> null
Reaction rate: v = k4*mRNA molecule/second
Species: mRNA = 0 molecule
Parameters: k4 = 1.5 1/second

```

Likewise, protein degradation is also modeled as a transformation to the null species. The species null is a predefined species name in SimBiology models.



```
Reaction: protein -> null
Reaction rate: v = k5*protein molecule/second
Species: protein = 0.0 molecule
Parameters: k5 = 1.0 1/second
```

## Creating a SimBiology Model

A SimBiology model is a collection of objects that are structured hierarchically. A model object is needed to contain all the other objects.

- 1 Create a model object. For example, to create a model with the name `cell`, in the MATLAB Command Window, type

```
Mobj = sbiomodel('cell')
```

MATLAB creates `Mobj`, a model object in the workspace and displays a summary of the objects in the model.

```
SimBiology Model - cell
```

```
Model Components:
  Compartments:    0
  Events:          0
  Parameters:      0
  Reactions:       0
  Rules:           0
  Species:         0
```

- 2 Display all the model object properties by typing

```
get(Mobj)
```

MATLAB displays a list of properties for the model object and their current values.

```
Annotation: ''
  Events: [0x1 double]
  Name: 'cell'
  Notes: ''
  Parameters: [0x1 double]
  Parent: [1x1 SimBiology.Root]
  Species: [0x1 handle]
Compartments: [0x1 double]
  Reactions: [0x1 double]
  Rules: [0x1 double]
  Tag: ''
```

```
Type: 'sbioModel'  
UserData: []
```

Some of the model properties are themselves objects or arrays of objects.

- 3** Add a compartment named `contents` to the model.

```
compObj = addcompartment(Mobj, 'contents');
```

## Adding the Reaction for Transcription

A simple model of transcription shows only the DNA and mRNA. For more details, see “Transcription” on page 3-3.

- 1 Enter the reaction `DNA -> DNA + mRNA` with reaction rate equation `v=k*DNA`.

```
Robj1 = addreaction(Mobj, 'DNA -> DNA + mRNA');
Kobj1 = addkineticlaw(Robj1, 'MassAction');
```

The `Kobj1` property `KineticLawName` is set to `'MassAction'`. Because the reaction is enough information to determine the rate equation, the property `Expression` is set to `'MassAction'` and the reaction rate expression is assumed to be `'k*DNA'`.

---

**Note** Because this example has only one compartment, you need not specify the compartment to which each species belongs. If there are multiple compartments, here is an example of the reaction syntax:

```
Robj1 = addreaction(Mobj, 'nucleus.DNA -> nucleus.DNA + cytoplasm.mRNA');
```

`nucleus` and `cytoplasm` are the names of the compartments.

---

- 2 Define the reaction rate constant `k1 = 0.2`. For a first-order reaction, the property `ParameterVariableNames` has a single rate constant that needs defining. First create a parameter object named `k1`, and then use the parameter object name to set the rate constant in `ParameterVariableNames` to that object.

```
Pobj1 = addparameter(Kobj1, 'k1', 0.2);
set(Kobj1, 'ParameterVariableNames', 'k1');
```

- 3 Enter the initial amount for the species `DNA = 50` and `mRNA = 0`. Select the species using the function `sbioselect`, which returns an object.

```
Sobj1 = sbioselect(Mobj, 'Type', 'species', 'Name', 'DNA');
set(Sobj1, 'InitialAmount', 50);
```

The value for mRNA defaults to 0.

- 4 Check the initial amounts for the species.

```
Mobj.Species
```

MATLAB displays a summary list.

```
SimBiology Species Array
```

Index:	Compartment:	Name:	InitialAmount:	InitialAmountUnits:
1	contents	DNA	50	
2	contents	mRNA	0	



## Adding the Reaction for Translation

A simple model of translation shows only the mRNA and protein product. For more details, see “Translation” on page 3-4.

- 1 Enter the reaction  $\text{mRNA} \rightarrow \text{mRNA} + \text{protein}$  with reaction rate equation  $v = k \cdot \text{mRNA}$ .

```
Robj2 = addreaction(Mobj, 'mRNA -> mRNA + protein');  
Kobj2 = addkineticlaw(Robj2, 'MassAction');
```

- 2 Define the reaction rate constant  $k_2$ .

```
Pobj2 = addparameter(Kobj2, 'k2', 20.0);  
set(Kobj2, 'ParameterVariableNames', 'k2');
```

## Adding the Reactions for Gene Regulation

Transcription of DNA to mRNA is regulated by the binding of the protein product from translation to the DNA. As more protein is produced, the DNA is bound with the protein more often and less time is available for transcription with the unbound DNA. For more details, see “Gene Repression” on page 3-4.

Enter the reversible reaction for  $\text{DNA} + \text{protein} \leftrightarrow \text{DNA\_protein}$  with a forward reaction rate equation  $v = k3 \cdot \text{DNA} \cdot \text{protein}$  and a reverse rate  $v = k3r \cdot \text{DNA\_protein}$ .

```
Robj3 = addreaction(Mobj, 'DNA + protein <-> DNA_protein');
Kobj3 = addkineticlaw(Robj3, 'MassAction');
Pobj3 = addparameter(Kobj3, 'k3', 0.2);

Pobj3r = addparameter(Kobj3, 'k3r', 1.0);
set(Kobj3, 'ParameterVariableNames', {'k3', 'k3r'});
```

## Adding the Reactions for mRNA and Protein Degradation

Protein and mRNA degradation are important reactions for regulating gene expression. The steady-state level of the compounds is maintained by a balance between synthesis and degradation reactions. Proteins are hydrolyzed to amino acids with the help of proteases, while nucleic acids are degraded to nucleotides.

- 1 Enter the reaction for mRNA degradation to nucleotides.

```
Robj4 = addreaction(Mobj, 'mRNA -> null');  
Kobj4 = addkineticlaw(Robj4, 'MassAction');  
Pobj4 = addparameter(Kobj4, 'k4', 1.5);  
set(Kobj4, 'ParameterVariableNames', 'k4');
```

- 2 Enter the reaction for protein degradation to amino acids.

```
Robj5 = addreaction(Mobj, 'protein -> null');  
Kobj5 = addkineticlaw(Robj5, 'MassAction');  
Pobj5 = addparameter(Kobj5, 'k5', 1.0);  
set(Kobj5, 'ParameterVariableNames', 'k5');
```

## Simulating the Model

After you create a model, you can simulate the dynamic behavior of the model.

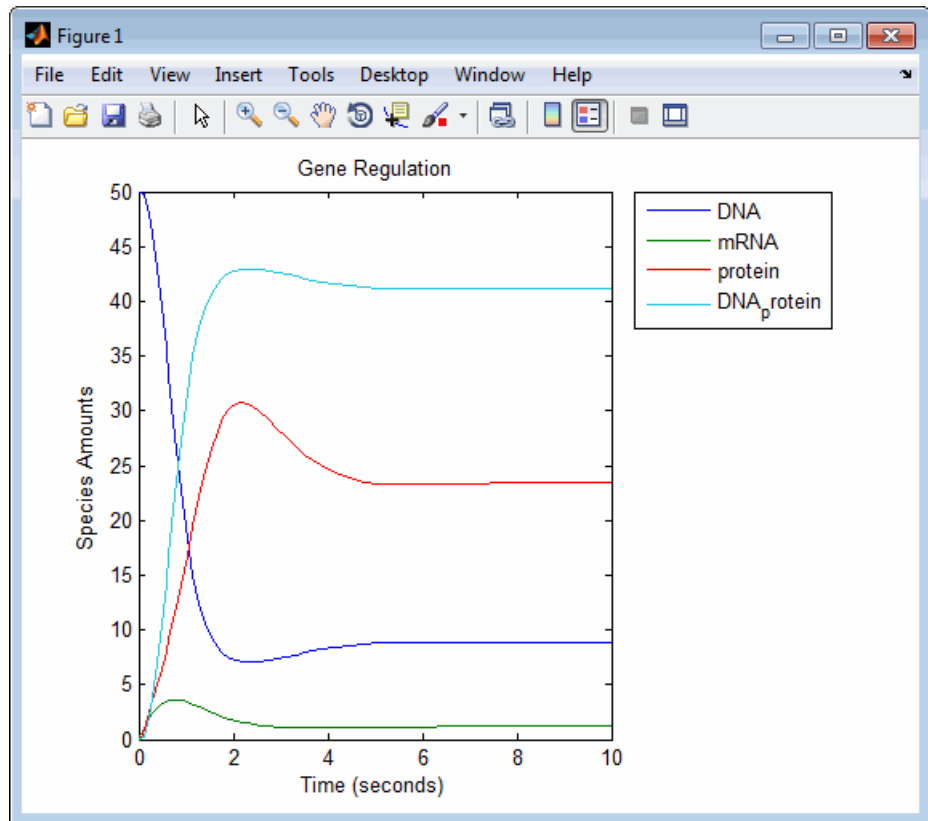
**1** Run the simulation.

```
[t_ode, x_ode, names] = sbiosimulate(Mobj);
```

**2** Plot the results.

```
figure;  
set(gcf, 'color', 'white');  
plot(t_ode, x_ode(:,1:4));  
legend(names, 'Location', 'NorthEastOutside')  
title('Gene Regulation');  
xlabel('Time (seconds)');  
ylabel('Species Amounts');
```

MATLAB plots a figure with the simulation results.



## See Also

- “Simulating Models”
- “ODE Solvers”

## Simulating the Model with a Stochastic Solver

SimBiology software includes three stochastic solvers. The stochastic solvers more accurately calculate the change in species amounts with a small number of molecules.

- 1 Get the active configuration set for the model, `Mobj`.

```
cs = getconfigset(Mobj);

Configuration Settings - default (active)
  SolverType:          sundials
  StopTime:           10

  SolverOptions:
    AbsoluteTolerance: 1.000000e-006
    RelativeTolerance: 1.000000e-003
    SensitivityAnalysis: false

  RuntimeOptions:
    StatesToLog:      all

  CompileOptions:
    UnitConversion:   false
    DimensionalAnalysis: true

  SensitivityAnalysisOptions:
    InputFactors:     0
    Outputs:          0
```

The `configset` object, `cs`, contains all the simulation settings, including the stop time and solver.

- 2 Set the `SolverType` to the `ssa` stochastic solver, and list the configuration set again.

```
set(cs, 'SolverType', 'ssa');
cs
```

Notice that the `SolverOptions` for the stochastic solver are different from the ODE options.

```

Configuration Settings - default (active)
  SolverType:          ssa
  StopTime:           10.000000

  SolverOptions:
    LogDecimation:    1

  RuntimeOptions:
    StatesToLog:      all

  CompileOptions:
    UnitConversion:   false
    DimensionalAnalysis: true

  SensitivityAnalysisOptions:
    InputFactors:     0
    Outputs:          0

```

**3** Change the value for the LogDecimation property.

```
cs.SolverOptions.LogDecimation = 10;
```

Increasing this setting lets you record fewer data points and decrease run time.

**4** Run the simulation.

```
[t_ssa, x_ssa] = sbiosimulate(Mobj, cs);
```

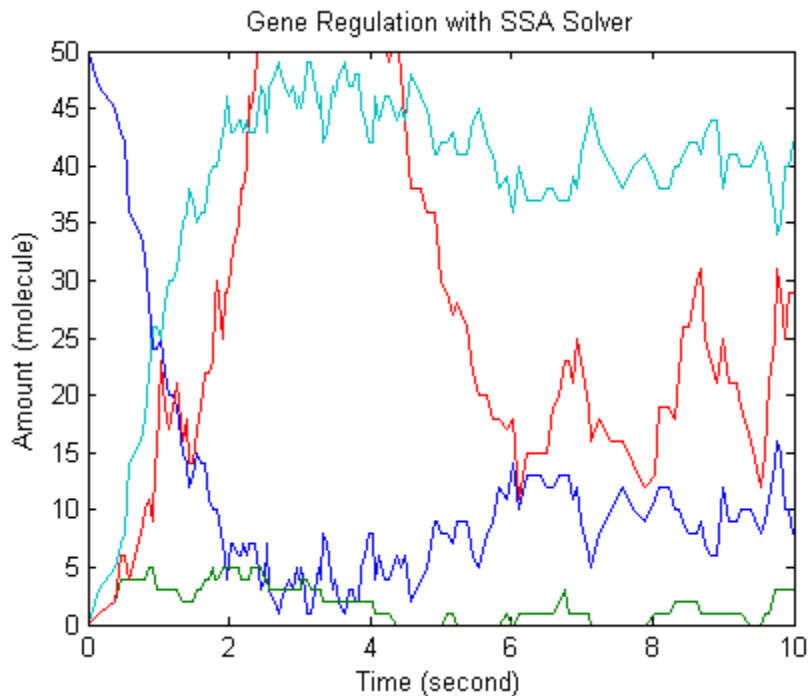
**5** Plot the results.

```

FH1 = figure;
set(gcf, 'color', 'white');
plot(t_ssa,x_ssa(:,1:4));
title('Gene Regulation with SSA Solver');
xlabel('Time (second)');
ylabel('Amount (molecule)');
axis([0, 10, 0, 50]);

```

The resulting plot may resemble the following figure.

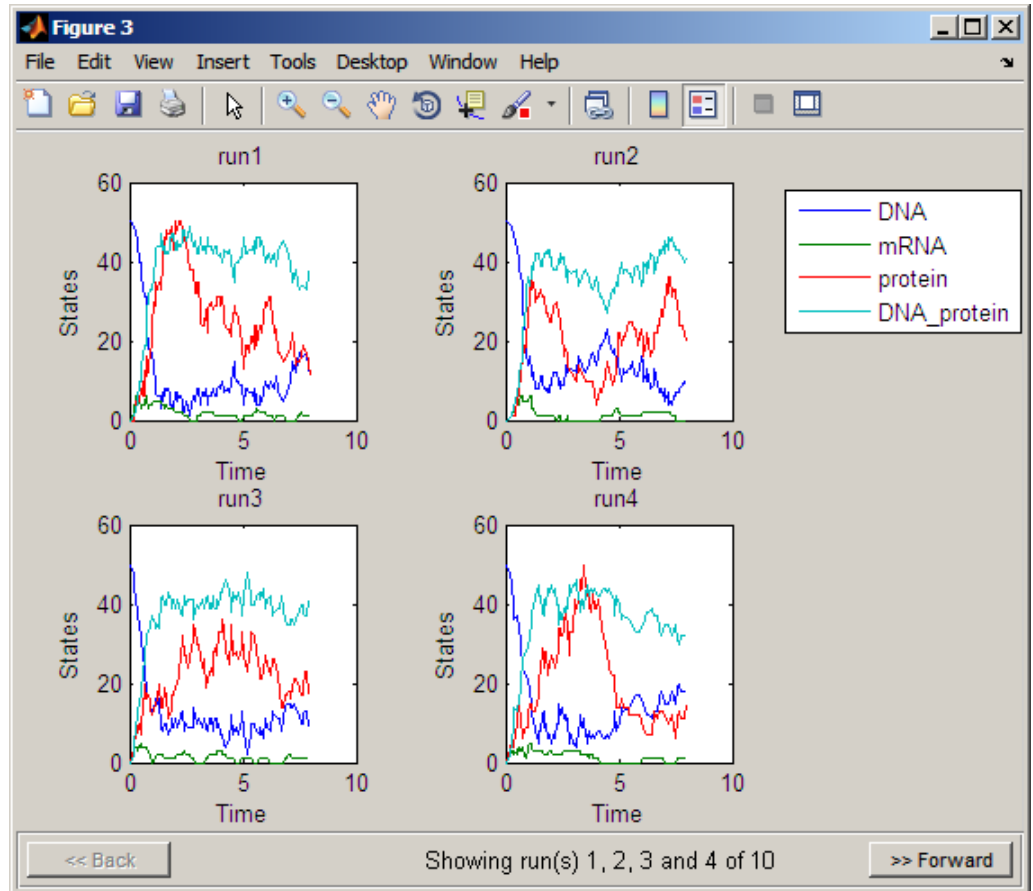


- 6 Another method to visualize stochastic simulations is through ensemble runs.

```
simDataObj = sbioensamplerun(Mobj, 10, cs);  
sbiosubplot(simDataObj);
```

The resulting plot may resemble the following:





- Click **Back** or **Forward** to navigate through the plots.

**Note** To remove the model object from the **Workspace** type

```
delete(Mobj);
```

### See Also

- “Simulating Models”
- “Stochastic Solvers” — Brief description of when to use stochastic solvers and the types available in the software.

## More Examples of Using the Command Line

For more examples of using the command line to build a model, simulate, and analyze, see:

- “Example — Creating A Model That Changes a Species Amount Using an Event”
- “Example — Creating A Model That Changes a Parameter Value Using a Variant”
- “Example — Creating A Model That Uses a User-Defined Function in an Expression”
- “Example — Verifying a Model”
- “Example — Determining Conserved Moieties”
- “Example — Simulating a Model and Viewing Results”
- “Example — Calculating Sensitivities”
- “Example — Estimating Parameters Using sbioparamestim”
- Demos included with the software at [SimBiology Demos](#)
- Demos on the Web at [SimBiology Demos and Webinars](#)



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