

SIMBIOLOGY 3.0

A graphical modeling environment for pharmacokinetic and pharmacodynamic modeling

OVERVIEW

The MathWorks provides software tools for your entire pharmacokinetic/pharmacodynamic (PK/PD) workflow, from modeling to analysis, within a single graphical environment. The SimBiology® environment provides point-and-click tools to make PK/PD modeling and analysis accessible, even if you have little to no programming experience. Built on MATLAB®, SimBiology provides direct access to an industry-tested simulation solver suite and enables you to integrate PK/PD modeling with other functionality such as parallel computing, statistics, and optimization. SimBiology also lets you experiment with new approaches, such as integrating PK models with mechanistic or physiologically based PK models.

Visualizing and Preprocessing the Data

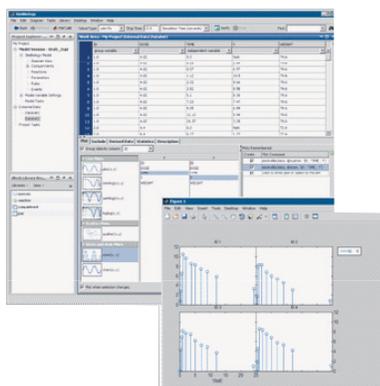
You can import into SimBiology PK and PD data of various sorts, including text files, Microsoft® Excel® files, and MAT-files. You can also import data from other sources, such as databases or SAS files, using the MATLAB workspace as an intermediate. If a data file has common headers, such as ID or Time, SimBiology automatically recognizes and stores the headers as the group and independent variables.

The external data panel in SimBiology gives you easy access to plotting tools that enable you to quickly visualize your data in various ways. The external data panel also includes features that let you exclude outliers or bad data points either by selecting rows in the data table or by specifying rules. Excluding a data point does not remove it from the data set permanently, but rather flags the data point to be ignored during analysis. You can also perform statistical analyses on the data, such as calculating the mean, area under the curve (AUC), area under the first moment curve (AUFMC), and mean residence time (MRT).

Creating a PK Model

In SimBiology, you can create a PK model by specifying your desired model options in the PK model wizard. Model options include number of compartments, dosing type, and elimination route. Alternatively, you can create a PK or PD model using the graphical, tabular, or programmatic interfaces.

The external data panel in SimBiology. Data from external sources can be imported, visualized, and used for fitting parameters.



KEY FEATURES

- > Graphical and programmatic interfaces
- > Functionality for fitting data and estimating parameters using nonlinear mixed effects
- > Industry-tested simulation solver suite
- > Pharmacokinetics wizard for automatically selecting PK models
- > Diagnostic plots of individual and population fits
- > Seamless MATLAB integration for pre- and postprocessing of data

ABOUT THE MATHWORKS

Employing more than 2,000 people, The MathWorks was founded in 1984 and is headquartered in Natick, Massachusetts, with offices and representatives throughout the world. The company has been profitable every year since its inception and is privately held. Over 1,000,000 scientists and engineers in more than 100 countries, on all seven continents, use MathWorks products.

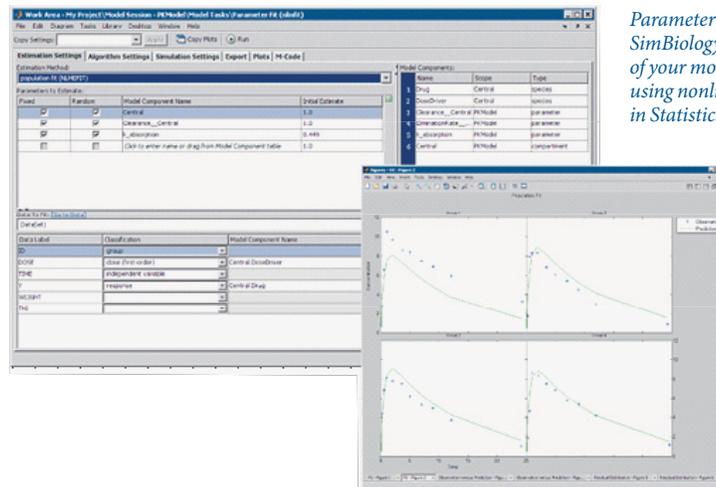
Fitting the Model to Data

With the Fit Parameters task in SimBiology, you can interactively configure your parameter estimation task. You can specify parameters to estimate as well as parameters for which you want to calculate random effects. You can also identify key model variables such as the dosed and response variables.

SimBiology generates two types of outputs to determine how well a parameter fit performed: a data panel summarizing the results, and diagnostic plots specified in the Fit Parameters task. The data panel includes fixed estimates for the parameters, a table of the random effects for each parameter for each subject, a summary of statistics on the fit, and the estimated covariance matrix. You can iterate on the PK/PD modeling workflow by using the goodness-of-fit statistics, such as Akaike and Bayesian information criteria (AIC and BIC, respectively), to decide the best model for your data.

The SimBiology desktop offers several prepackaged diagnostic plot types, including the trellis plot, which plots both the observed and predicted time courses of drug concentration for each patient. Other plot types include observed versus predicted concentration values, box plots of the random effects calculated for each parameter, residual errors over time, and the distribution plots of residuals.

A SimBiology project stores all components used in the workflow—such as multiple models, data sets, reports, and analysis tasks—in one file, making it easy to manage and organize associated components. You can capture your work by automatically creating an HTML or XML report with the SimBiology report generator.



Parameter fitting in SimBiology. SimBiology lets you fit the response of your model to population data sets using nonlinear mixed-effects models in Statistics Toolbox™.

Extending This Approach

Because SimBiology is based on MATLAB, SimBiology users can use MATLAB functionality to extend the PK/PD modeling workflow. MATLAB capabilities such as parallel computing, optimization, statistics, and curve fitting can help you further analyze the results of your PK/PD modeling.

More information is available at www.mathworks.com/simbiology.