

SAAM II Version 2.2

Basic Tutorials

Working with Experimental Inputs

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Working with Experimental Inputs

Prerequisites

The prerequisite for this tutorial is having worked through the SAAM II introductory tutorial, “Getting Started with **SAAM II Compartmental**.”

What you will learn in this tutorial

The purpose of this tutorial is to show you how to specify different input formats for your experiment in SAAM II. You will learn

- How to specify single and multiple boluses (Part 1)
- How to specify single and multiple constant infusions (Part 2)
- How to specify a primed infusion (Part 3)
- How to specify an input as an equation (Part 4)

Files Required

Study Files: The study file for this tutorial is

study_0_ExpInp.stu

This file is included as part of this tutorial. The file **study_0_ExpInp.stu** is the same as **study_0.stu** that is installed in the SAAM II program folder and referred to in the **SAAM II** examples and tutorials with the exception there are no data in the **Data** window and the parameters have been set to “fixed.”

Remember **study_0** is a study file for an experiment lasting 9 days. In this tutorial, the time of the experiment may be adjusted so specific points can be illustrated.

Data Files: There are no data files for this tutorial.

Introduction

This tutorial focuses on how to use the options in the **Exogenous Input** dialog box to specify different input formats for your experiment in SAAM II. Several input types are permitted. The default input is the bolus. Because of their frequency of use, the bolus, the constant infusion and the primed constant infusion are predefined. The equation input allows the user to specify any input as long as the terms of the equation are recognized by SAAM II.

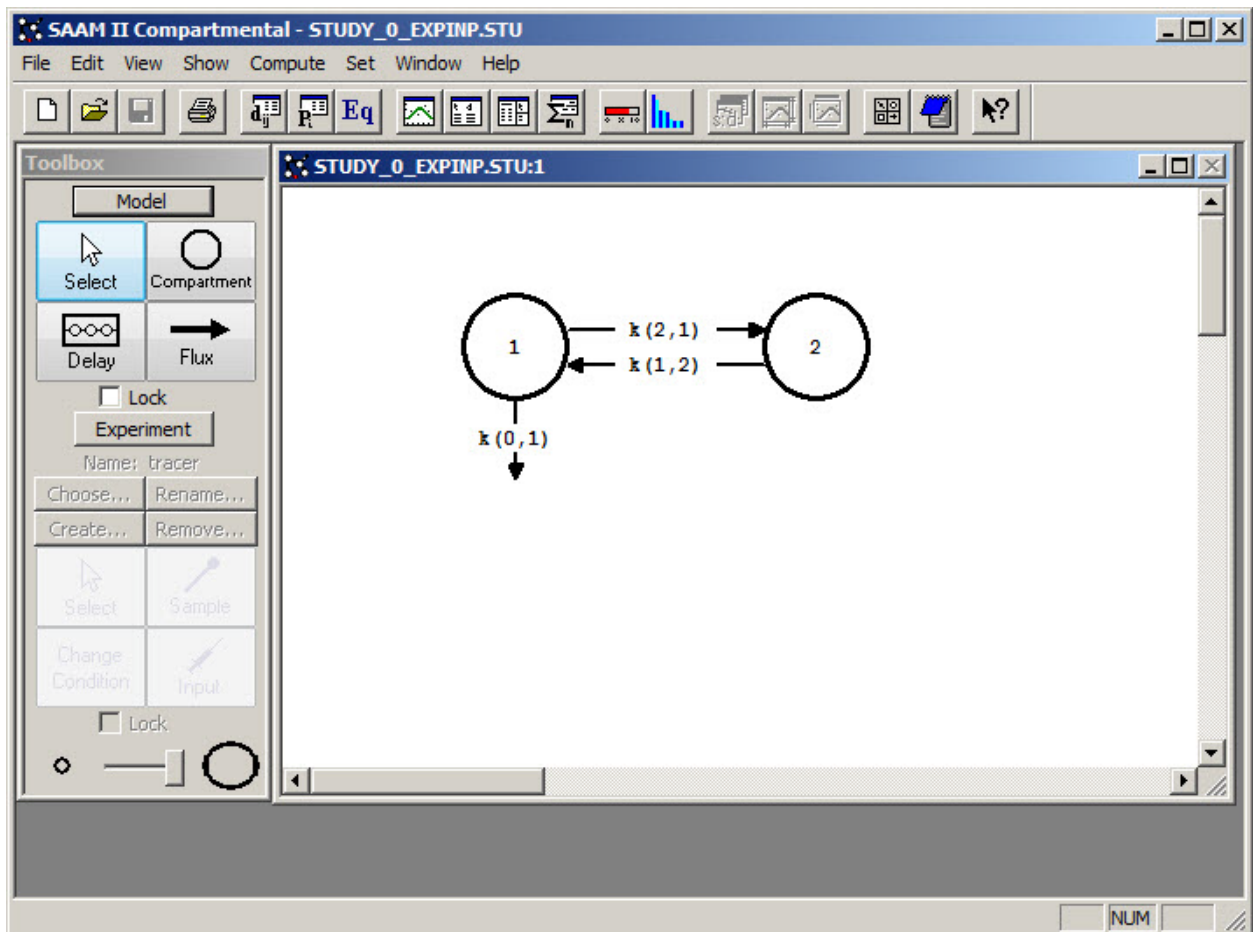
Other ways of specifying the input dosage and other applications of the **Exogenous Input** dialog box are included in the tutorial **Experimental Inputs, Advanced**. These include:

- Specifying the amount of a dose as a constant in the data file.
- Specifying the dose as an adjustable parameter.
- Split inputs (an input into more than one compartment)
- Parametric deconvolution

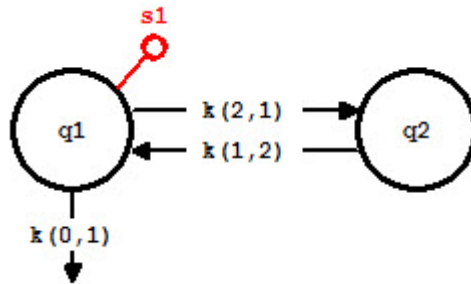
Part 1. The bolus input (single and multiple)

The bolus input is the most common method by which test material or drugs are introduced into the system. The part of the tutorial will show you how to specify both the single bolus dose, and multiple boluses.

1. **Start** the **SAAM II Compartmental** application. The **SAAM II Compartmental** main window will open.
2. Open the **SAAM II Compartmental** study file **study_0_ExpInpUS**.
 - a. The file **study_0_ExpInpUS.stu** should appear in the file list; if it does not, find the folder where you put this file.
 - b. In the **File** menu, click **Open**. The **SAAM II Compartmental** main window will appear as shown below:



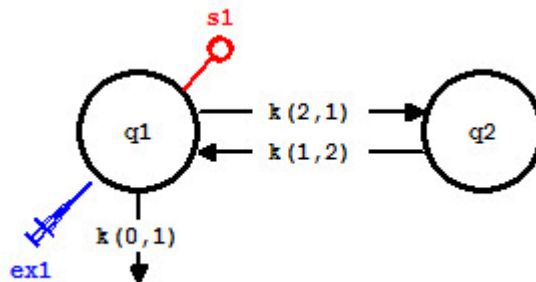
3. View the model and the experiment on the model. In the **SAAM II Toolbox**, click **Experiment**. The model of the experiment will appear on the **Drawing Canvas** as follows:



Notice the difference between this model and the experimental model developed and used in the **Getting Started with Compartmental** tutorial. Here there is no experimental input, **ex1**, and the sample circle, **s1**, is not filled because there are no data in the study file.

You may wish to review the **Parameters** dialog box and the **Samples Attributes** dialog box. The parameters are the initial values from **study_0** except they have been fixed since this tutorial involves only simulations and no data fitting. The sample equation is “ $s1 = q1/vol$ ”. The transfer coefficients are all set at 0.1 and the volume, $vol=2000$.

4. Create a bolus injection of 100 mg into Compartment **q1**.
 - a. In the **SAAM II Toolbox**, click **Input**.
 - b. Click Compartment **q1** and then click on the **Drawing Canvas**. The experimental input **ex1** will appear associated with the model as shown below:



- c. Double-click **ex1** to open the **Exogenous Input** dialog box. The **Exogenous Input** dialog box will appear as follows:

The screenshot shows the 'Exogenous Input' dialog box with the following details:

- Name:** ex1
- Reference:** (empty)
- Units:** (empty)
- Input Type:** Bolus (selected), Infusion, Primed Infusion, Equation
- Initial Amount:** (empty)
- Constant Rate:** (empty)
- Event Start:** (empty)
- Event Stop:** (empty)
- Repeat Every:** (empty)
- Nr. of Repeats:** (empty)
- Equation:** ex1 =
- Buttons:** Save, Edit, Add, Delete, Split Input..., Done, Cancel, Help

Notice in the **Input Type** pane, **bolus** is selected.

- d. Enter a bolus injection of 100 mg.
 - (1) In the **Initial Amount** box, type “100”.
 - (2) Click **Add**. The **Exogenous Input** dialog box will appear as follows:

Exogenous Input [X]

Name: Reference: Units:

Type	Initial	Constant	Start	Stop	Repeat Every	Nr. Repeats
Bolus	100.000	-	0.000	-	-	-

Input Type:

Bolus
 Infusion
 Primed Infusion
 Equation

Initial Amount:

Constant Rate:

Event Start:

Event Stop:



Repeat Every:

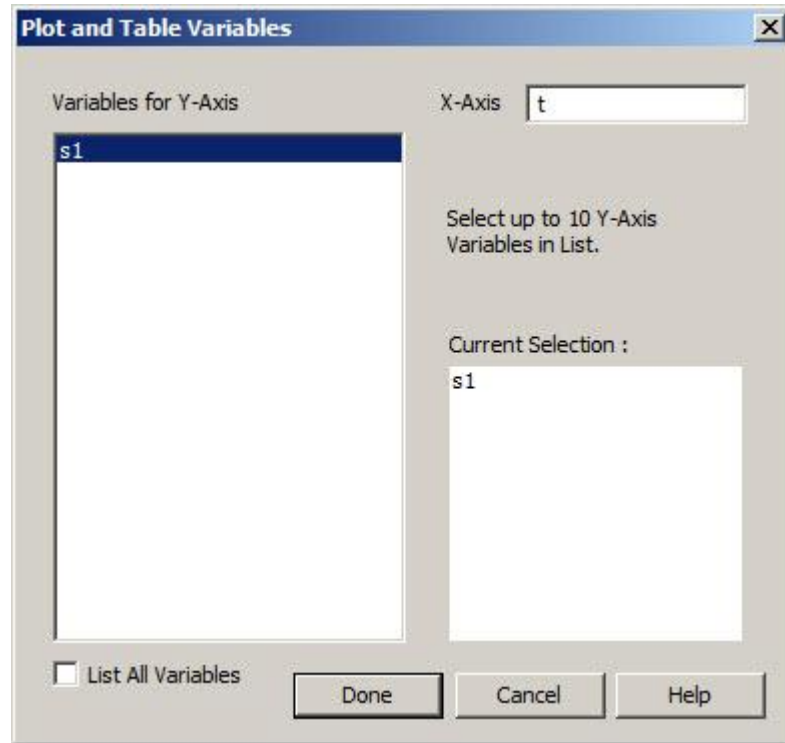
Nr. of Repeats:

Equation:

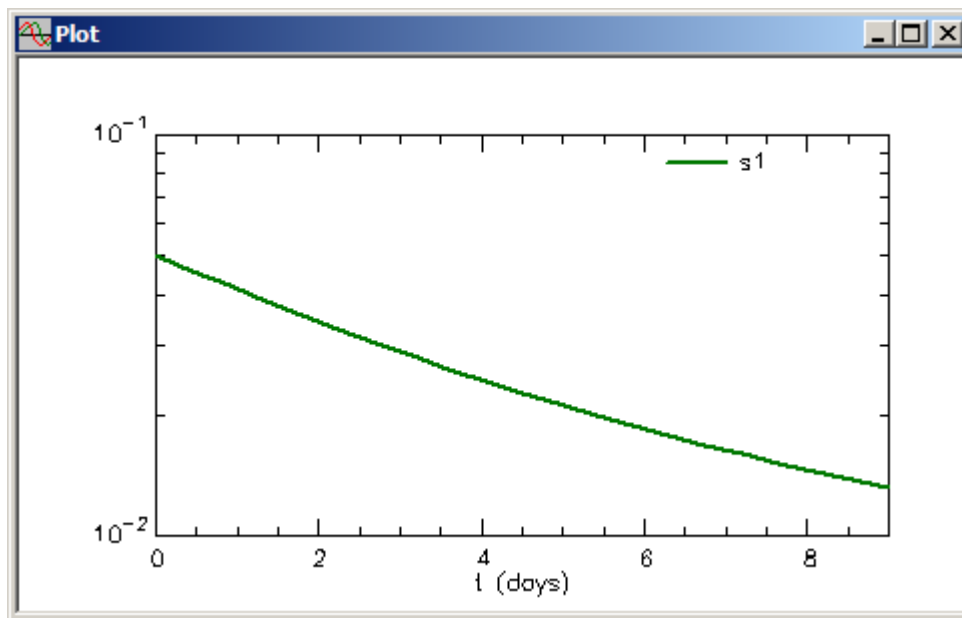
(3) Click **Done**.

5. Solve the model and view the solution.

- a. In the **Compute** menu, click **Solve**, or alternatively, on the **SAAM II Toolbar**, click **Solve** .
- b. In the **Show** menu, click **Plot**, or alternatively, on the **SAAM II Toolbar**, click **Plot** . The **Plot and Table Variables** dialog box will open. Be sure the **List All Variables** check box is not selected so **s1** is the only option in the **Variables for Y-Axis** pane.
- c. Click **s1** to add this to the **Current Selection** pane. The **Plot and Table Variables** dialog box will appear as shown below:



- d. Click **Done**. A plot of **s1** will appear in semilog mode in the **Plot** window as shown below (if it is not in semilog mode, in the **View** menu, click **Semilog**):



- e. Close the **Plot** window.
6. Create multiple bolus injections of 100 mg every 12 hours (every half-day).
- a. Double-click **ex1** to open the **Exogenous Input** dialog box.

- b. Click **Delete** to remove the original bolus injection.
- c. Create the multiple bolus injections.
 - (1) In the **Initial Amount** box, type “100”.
 - (2) In the **Event Start** box, type “0”.
 - (3) In the **Repeat Every** box, type “0.5”.
 - (4) In the **Nr. of Repeats** box, type “17”.
 - (5) Click **Add**. The **Exogenous Input** dialog box will appear as shown below:

Type	Initial	Constant	Start	Stop	Repeat Every	Nr. Repeats
Bolus	100.000	-	0.000	-	0.500	17



- (6) Click **Done**.

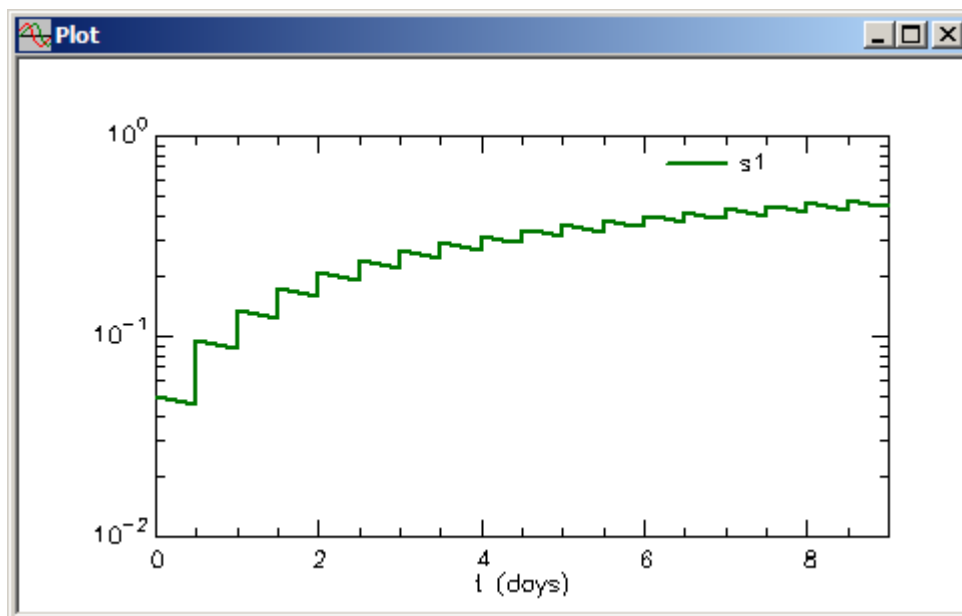


The multiple bolus input. In the situation above, the units of the experiment are in days. Thus the bolus injection every 12 hours in days will be 0.5. This is why 0.5 was entered in the **Repeat Every** box. Starting at time zero, there will be a bolus every 0.5 days for 8.5 days. Thus the number of repeats is 17.



- d. Solve the model and view the solution.

- (1) In this part of the tutorial, it will be useful to increase the resolution of your plot. In the **Compute Menu**, click **Computational Settings**. Type “200” in the **Min. Nr. of Calculation Intervals** box. Click **Done**.
- (2) In the **Compute** menu, click **Solve**, or alternatively, on the **SAAM II Toolbar**, click **Solve** .
- (3) In the **Show** menu, click **Plot**, or alternatively, on the **SAAM II Toolbar**, click **Plot** . Your plot of **s1** should appear as follows. (If it does not, open the **Plot and Table Variables** dialog box, and click **s1** to move it to the **Current Selection** pane.)



You can see the expected saw-toothed nature of the model predicted values following the multiple boluses.

- (4) Close the **Plot** window.
7. Create multiple bolus injections three times a day every six hours.

In what follows, you will simulate an experiment in which three 100 mg doses were given daily at 6 hour intervals. The first dose can be assumed to be at 8:00am, the second at 2:00pm and the third at 8:00pm. There is no dosing between 8:00pm and 8:00am. It will be more convenient to work in units of hours rather than days, so the first step will be to change the units of the independent variable “t” from days to hours.



Changing the time units of the experiment. In what follows, you will change the time units of the experiment from day to hours. You will change “9” days to “216” hours. However, the units of the $k(i,j)$ are /day, not /hr. The values of all $k(i,j)$ in study_0 are 0.1/day. To convert these to /hr, you need to multiply each of the $k(i,j)$ by 1/24. Thus each value for $k(i,j)$ should be 0.042. Since the purpose of this tutorial is to illustrate different methods of input, these changes to the rate constants will not be made. If you were actually using the model on a particular system and changed the units, you would have to make these changes.



- a. On the **Set** menu, click **Experiment Attributes**. The **Experiment Attributes** dialog box will open.
- b. In the **Units** box, type “hours”. In the **End At** box, type “216”. Remember 9 days equals 216 hours. The **Experiment Attributes** dialog box will appear as follows:

The screenshot shows a dialog box titled "Experiment Attributes". It contains four input fields: "Independent Variable:" with the value "t", "Units:" with the value "hours", "Start at:" with the value "0.0", and "End at:" with the value "216". At the bottom of the dialog box, there are three buttons: "Done", "Cancel", and "Help".

- c. Click **Done**.
- d. Double-click **ex1** to open the **Exogenous Input** dialog box.
- e. Click **Delete** to clear the information in the **Exogenous Input** dialog box.
- f. Specify the input of 100 mg every six hours daily.
 - (1) In the **Name** box, change “ex1” to “dose”.
 - (2) In the **Reference Name** box, type “ThreeDoses”.
 - (3) In the **Units** box, type “mg”.
 - (4) In the **Initial Amount** box, type “100”.

- (5) In the **Event Start** box, type “0”.
- (6) In the **Repeat Every** box, type “24”.
- (7) In the **Nr. of Repeats** box, type “8”.
- (8) Click **Add**. The **Exogenous Input** dialog box should appear as follows:

Type	Initial	Constant	Start	Stop	Repeat Every	Nr. Repeats
Bolus	100.000	-	0.000	-	24.000	8

At this point, you have specified the 100 mg dose daily. You must also specify the second dose 6 hours after the first, and then 6 hours after that.

- (9) The dose does not change. To start the next dosing at 6 hours, in the **Event Start** box, type “6”. To have this repeat every 24 hours, you do not have to change the entry in the **Repeat Every** box or the **Nr. of Repeats** box.
- (10) Click **Add**.
- (11) To start the dosing at 12 hours, in the **Event Start** box, type “12”.
- (12) Click **Add**. The **Experiment Attributes** dialog box will appear as follows

Exogenous Input

Name: Reference: Units:

Type	Initial	Constant	Start	Stop	Repeat Every	Nr. Repeats
Bolus	100.000	-	0.000	-	24.000	8
Bolus	100.000	-	6.000	-	24.000	8
Bolus	100.000	-	12.000	-	24.000	8

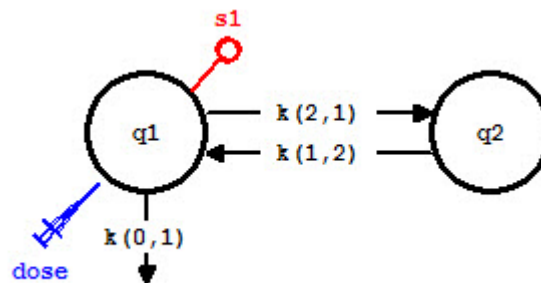
Input Type:

Bolus
 Infusion
 Primed Infusion
 Equation

Initial Amount:
Constant Rate:
Event Start:
Event Stop:
Repeat Every:
Nr. of Repeats:



Equation:

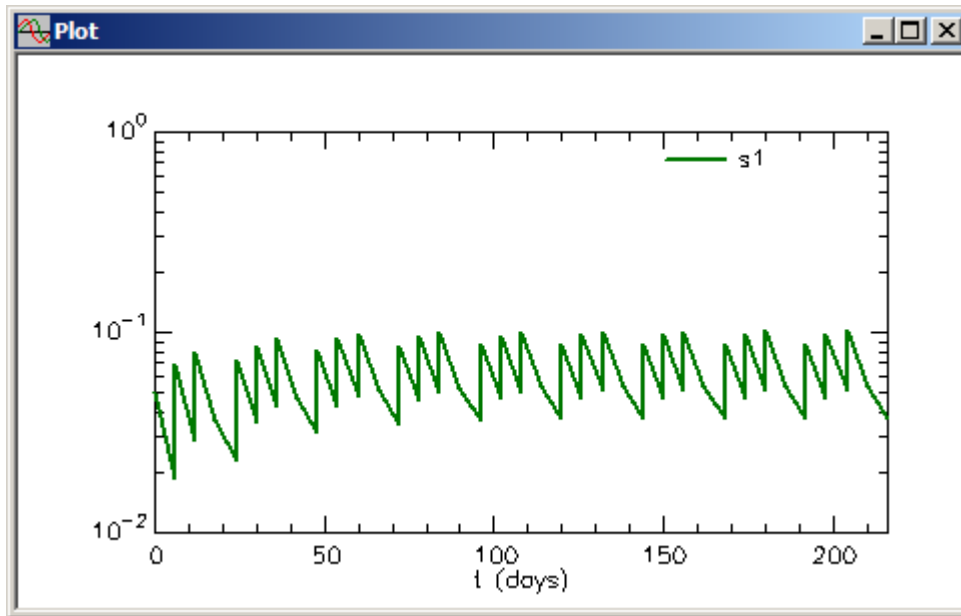
(13) Click **Done**. Your experiment will appear as follows:



Exogenous input name. The default **Name** for exogenous inputs is **ex_i** for the i^{th} input. This is the name that will appear associated with input tool unless you change it. In this case, you changed the name from “ex1” to “dose”; “dose” will now appear as the name of the input on the drawing canvas (as shown in the figure above), and in the list of variables associated with the model. The **Reference Name**, in this case “Three Doses”, is for convenience; it is not used by SAAM II. Similarly **Units** is for convenience.



- g. In the **Compute** menu, click **Solve**, or alternatively, on the **SAAM II Toolbar**, click **Solve** .
- h. In the **Show** menu, click **Plot**, or alternatively, on the **SAAM II Toolbar**, click **Plot** . Your plot of **s1** should appear as follows. If it does not, open the **Plot and Table Variables** and select **s1**.



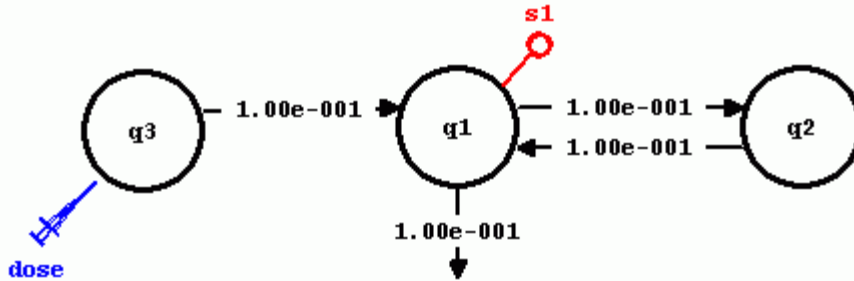
Now you see the saw-tooth nature of the model solution changing to reflect three inputs (doses) every 12 hours followed by 12 hours with no inputs (dosing). You may view the solution in linear mode as well if you wish.

- i. Close the **Plot** window.

Quit the SAAM II Compartmental application. Do not save the changes to study_0_ExpInp.

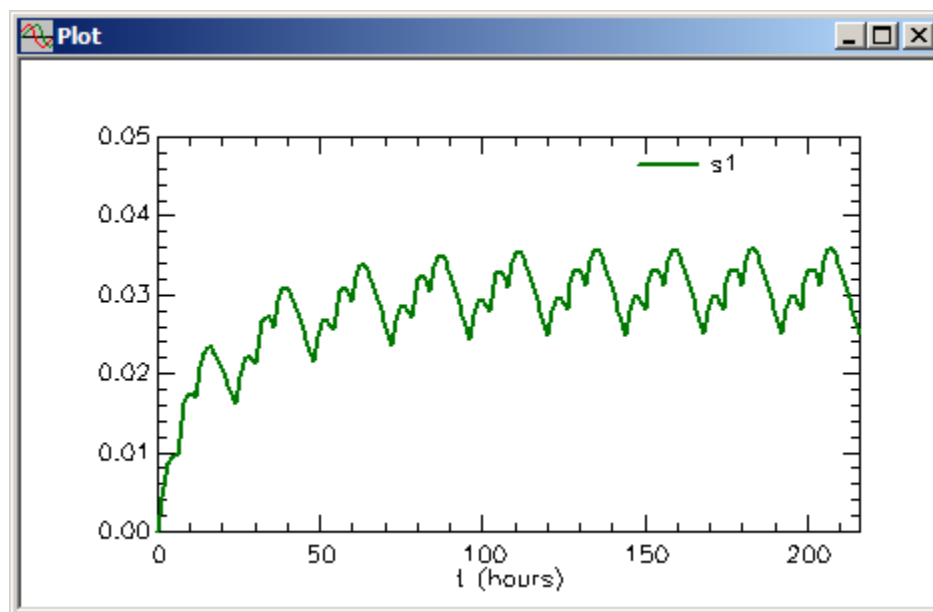


The bolus input. The bolus input has been illustrated using the **study_0** model. This involves input into the compartment from which samples are taken, usually plasma. Exactly the same strategy could be applied if you were administering the dose, for example, orally. Consider the following modification of the **study_0** model:



As shown in the figure above, Compartments **q1** and **q2** together with the rate constants are those from **study_0**. A third compartment, **q3**, has been added. This model is now a three-compartment model with input into one compartment and samples from another compartment. In pharmacokinetics, this model is sometimes called the two-compartment model with absorption. (Model parameters are as shown and for $s1=q1/vol$ where $vol=2000$)

It would be worthwhile for you to create this model, and repeat the different input exercise you did above. If, for example, you recreate the 100 mg dose every 6 hours daily, you solution, plotted in linear mode (with the **Y Axis Maximum** set at “0.05”), will appear as follows:



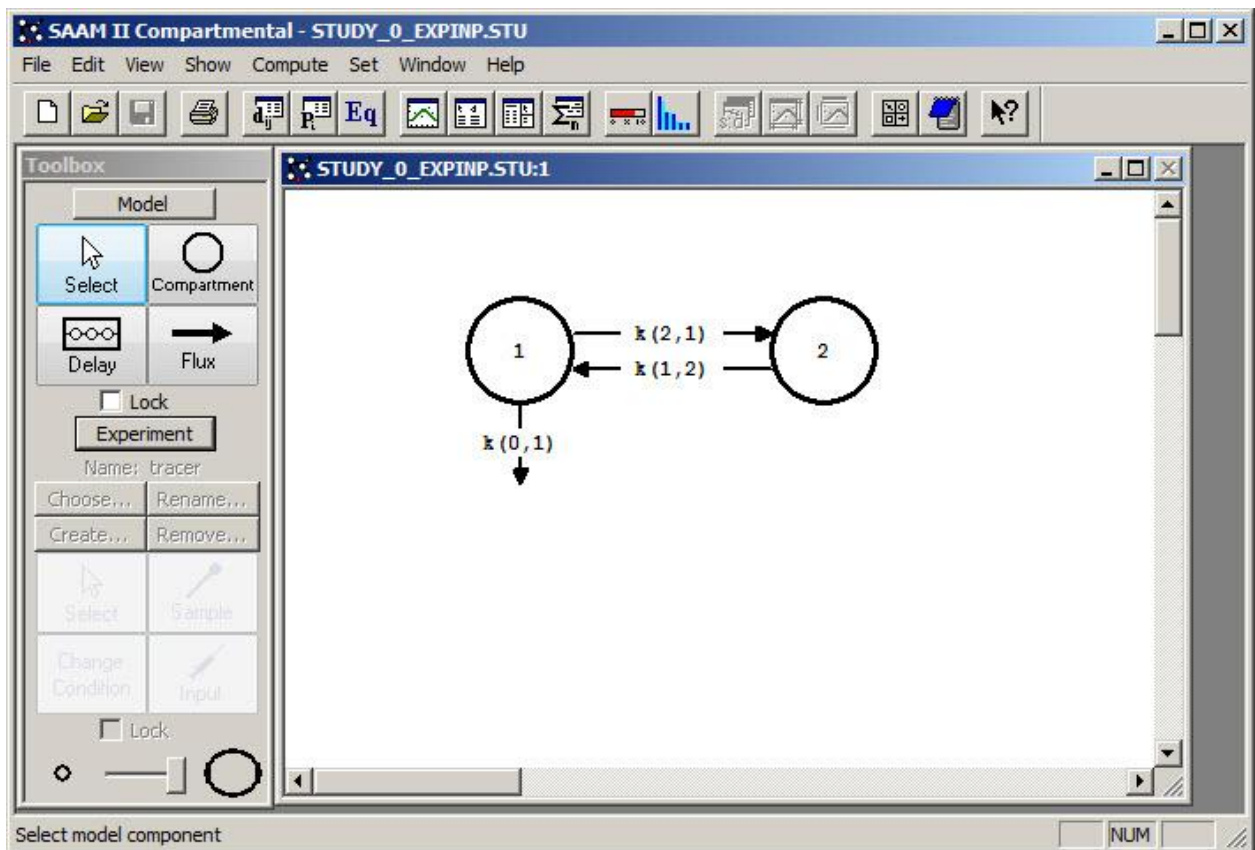
This shows it is very easy to simulate many different kinds of inputs in the bolus format. The example here is very useful in simulating different oral dosing regimens.



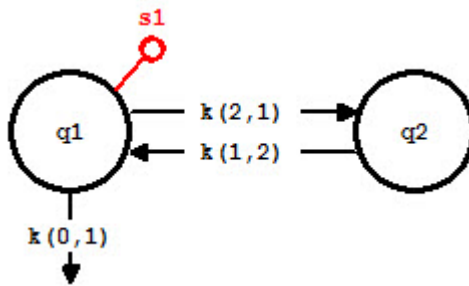
Part 2. The constant infusion input (single and multiple)

The constant infusion input is probably the second most common method by which test material or drugs are introduced into the system. The part of the tutorial will show you how to specify both a single constant infusion, and multiple infusions.

1. **Start** the **SAAM II Compartmental** application. The **SAAM II Compartmental** main window will open.
2. Open the **SAAM II Compartmental** study file **study_0_ExpInp**.
 - a. The file **study_0_ExpInp.stu** should appear in the file list; if it does not, find the folder where you put this file.
 - b. In the **File** menu, click **Open**. The **SAAM II Compartmental** main window will appear as shown below:



3. View the model and the experiment on the model.
 - a. In the **SAAM II Toolbox**, click **Experiment**. The model of the experiment will appear on the **Drawing Canvas** as follows:



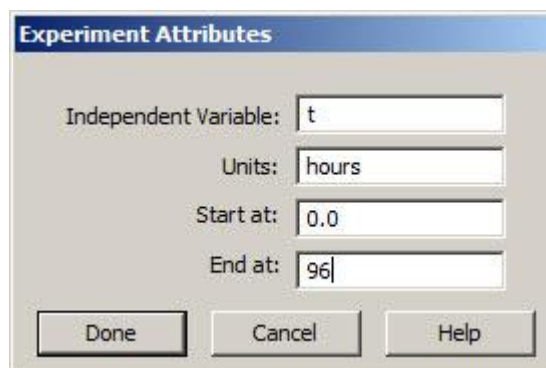
Notice the difference between this model and the experimental model developed and used in the **Getting Started with Compartmental** tutorial. Here there is no experimental input, **ex1**, and the sample circle, **s1**, is not filled because there are no data in the study file.

You may wish to review the **Parameters** dialog box and the **Samples Attributes** dialog box. The parameters are those from **study_0** except they have been fixed since this tutorial involves only simulations and no data fitting. The sample equation is “ $s1 = q1/vol$ ”.

- b. Change the time of the experiment from 9 days to 96 hours.

It will be more convenient to work in units of hours rather than days which are the original units of **study_0**. The experiment in **Study_0** lasted 9 days. In the simulations that follow, it is assumed that the experiment lasted 96 hours (4 days).

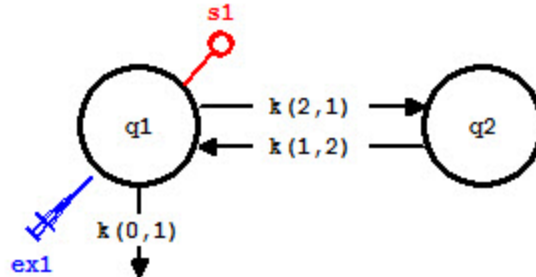
- (1) On the **Set** menu, click **Experiment Attributes**. The **Experiment Attributes** dialog box will open.
- (2) In the **Units** box, type “hours”. In the **End At** box, type “96”. The **Experiment Attributes** dialog box will appear as follows:



- (3) Click **Done**.

4. Create a constant infusion equal to 500 mg over four hours into Compartment **q1**.

- a. In the **SAAM II Toolbox**, click **Input**.
- b. Click Compartment **q1** and then click on the **Drawing Canvas**. The experimental input **ex1** will appear associated with the model as shown below:



- c. Double-click **ex1** to open the **Exogenous Input** dialog box. The **Exogenous Input** dialog box will appear as follows:

Notice in the **Input Type** pane, **Bolus** is selected.

- d. Create the infusion.
 - (1) In the **Input Type** pane, select **Infusion**.
 - (2) The total amount of substance infused is 500 mg over 4 hours. Thus the infusion rate is 125 mg/hr. In the **Constant Rate** box, type “125”.

(3) In the **Event Start** box, type “0”.



(4) In the **Event Stop** box, type “4”.

(5) Click **Add**. The **Exogenous Input** dialog box will appear as follows:

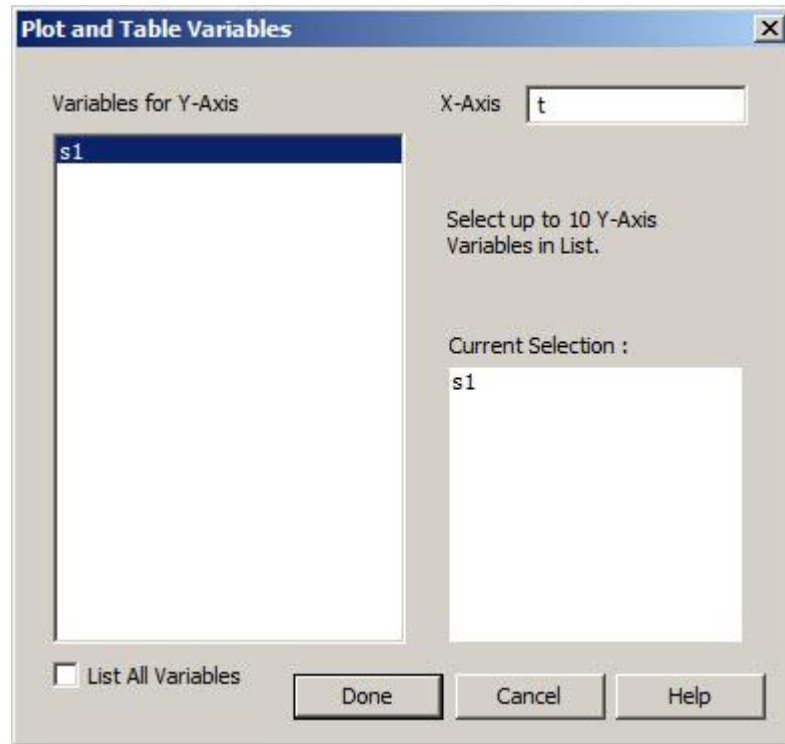
Type	Initial	Constant	Start	Stop	Repeat Every	Nr. Repeats
Infusion	-	125.000	0.000	4.000	-	-

(6) Click **Done**.

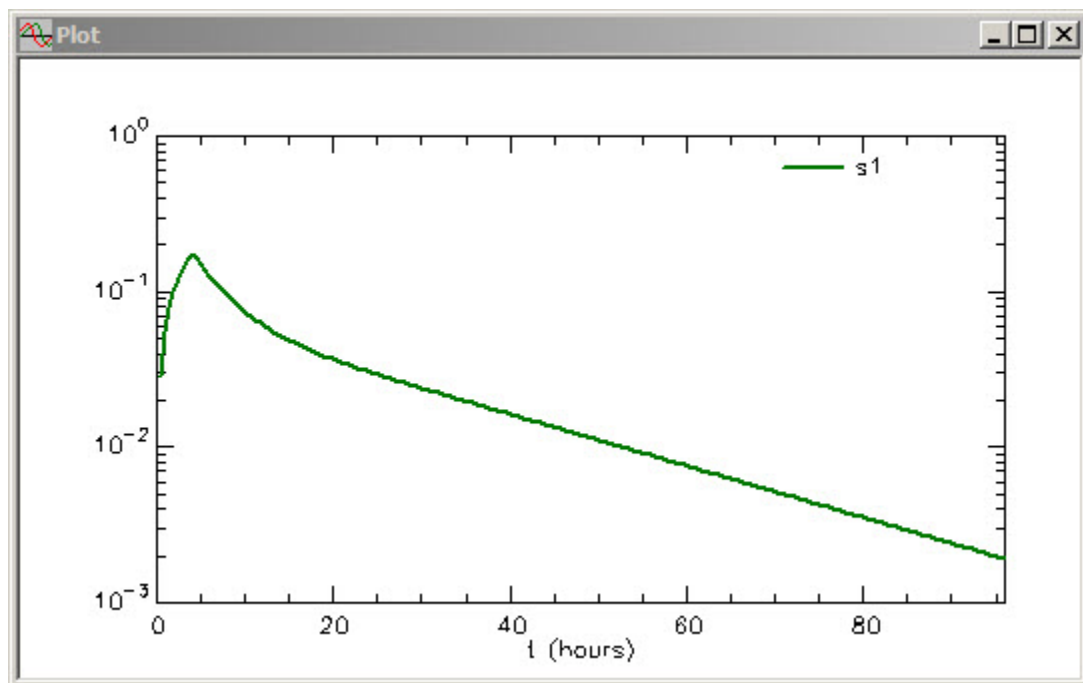
5. Solve the model and view the solution.

- It will be useful to increase the resolution of your plot. In the **Compute Menu**, click **Computational Settings**. Type “200” in the **Min. Nr. of Calculation Intervals** box. Click **Done**.
- In the **Compute** menu, click **Solve**, or alternatively, on the **SAAM II Toolbar**, click **Solve** .
- In the **Show** menu, click **Plot**, or alternatively, on the **SAAM II Toolbar**, click **Plot** . The **Plot and Table Variables** dialog box will open. Be sure the **List All Variables** check box is not selected so **s1** is the only option in the **Variables for Y-Axis** pane.

- d. Click **s1** to add this to the **Current Selection** pane. The **Plot and Table Variables** dialog box will appear as shown below:

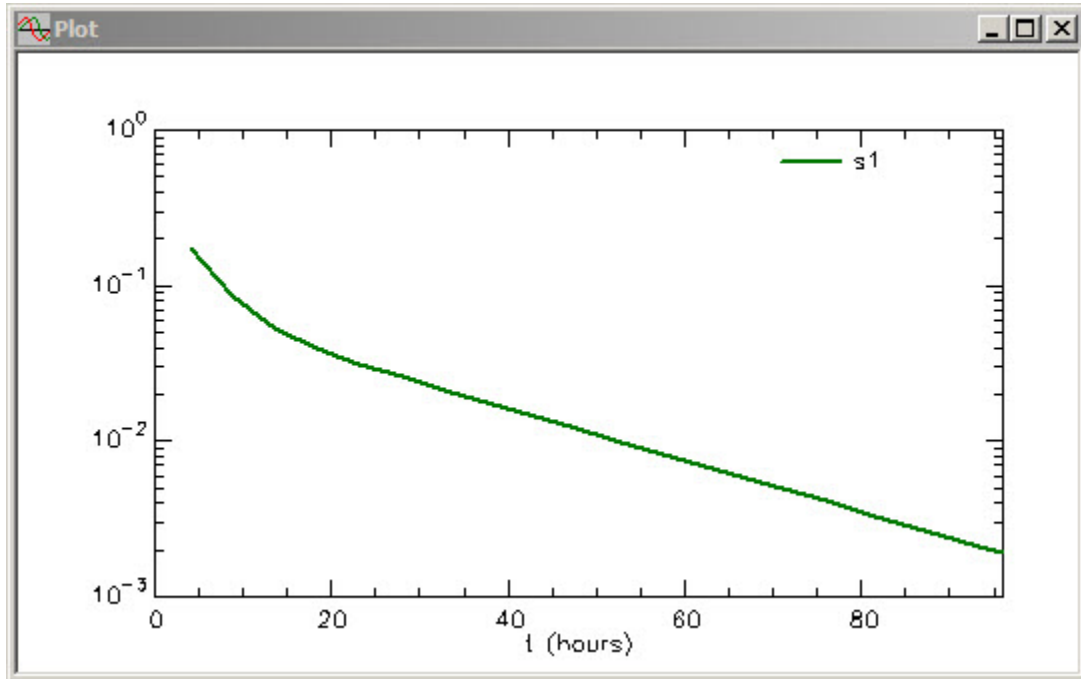


- e. Click **Done**. A plot of **s1** will appear in semilog mode in the **Plot** window as shown below (if it is not in semilog mode, in the **View** menu, click **Semilog**):





Plot resolution. In this simulation, if you had not set the minimum number of calculation intervals equal to 200, you would not see the initial rise during the infusion. To see this, you can set the minimum number of calculation intervals equal to 20 and Resolve. The updated plot will appear as follows:



This is why it is important to be aware of the role that plot resolution can play, especially in simulation studies, or studies where some data collection times are close together and others far apart.



- f. Close the **Plot** window.
6. Create a 500 mg infusion for 4 hours daily for an experiment lasting 96 hours.

In this case, you will want to create four infusions lasting 4 hours at a rate of 125 mg/hr.

- a. Double-click **ex1** to open the **Exogenous Input** dialog box.
- b. Click **Delete** to clear the information in the **Exogenous Input** dialog box.
- c. Specify the 125 mg/hr infusion for 4 hours daily for three days.
 - (1) In the **Input Type** pane, be sure **Infusion** is selected.

- (2) In the **Name** box, change “ex1” to “dose”.
- (3) In the **Reference Name** box, type “Three Infusions”
- (4) In the **Units** box, type “mg/hr”.
- (5) In the **Constant Rate** box, type “125”.
- (6) In the **Event Start** box, type “0”.
- (7) In the **Event Stop** box, type “4”.
- (8) In the **Repeat Every** box, type “24”.
- (9) In the **Nr. of Repeats** box, type “3”.
- (10) Click **Add**. The **Exogenous Input** dialog box will appear as follows:

Exogenous Input

Name: Reference: Units:

Type	Initial	Constant	Start	Stop	Repeat Every	Nr. Repeats
Infusion	-	125.000	0.000	4.000	24.000	3

Input Type:

Bolus
 Infusion
 Primed Infusion
 Equation

Equation:

Initial Amount:

Constant Rate:

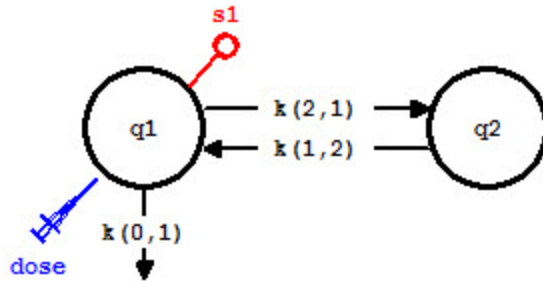
Event Start:

Event Stop:

Repeat Every:



Nr. of Repeats:

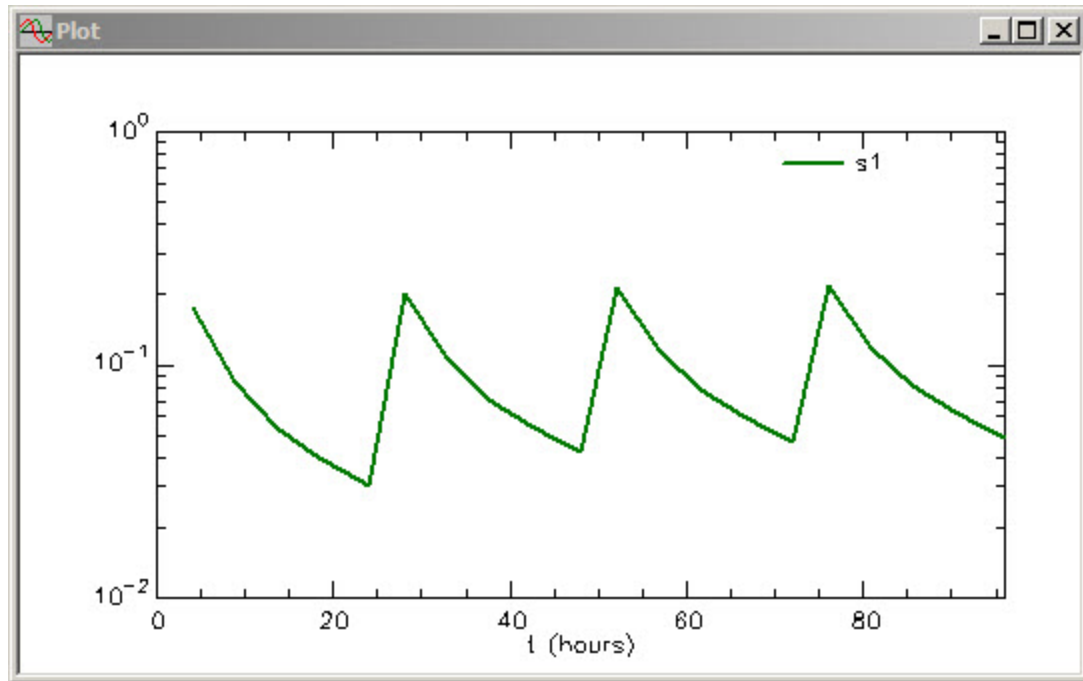
- (11) Click **Done**. Your model will appear as follows:



Exogenous input name. The default **Name** for exogenous inputs is **exi** for the i^{th} input. This is the name that will appear associated with input tool unless you change it. In this case, you changed the name from “ex1” to “dose”; “dose” will now appear as the name of the input on the drawing canvas (as shown in the figure above), and in the list of variables associated with the model. The **Reference Name**, in this case “Three Infusions”, is for convenience; it is not used by SAAM II. Similarly **Units** is for convenience.



- d. In the **Compute** menu, click **Solve**, or alternatively, on the **SAAM II Toolbar**, click **Solve** .
- e. In the **Show** menu, click **Plot**, or alternatively, on the **SAAM II Toolbar**, click **Plot** . Your plot of **s1** should appear as follows. If it does not, open the **Plot and Table Variables** and select **s1**.

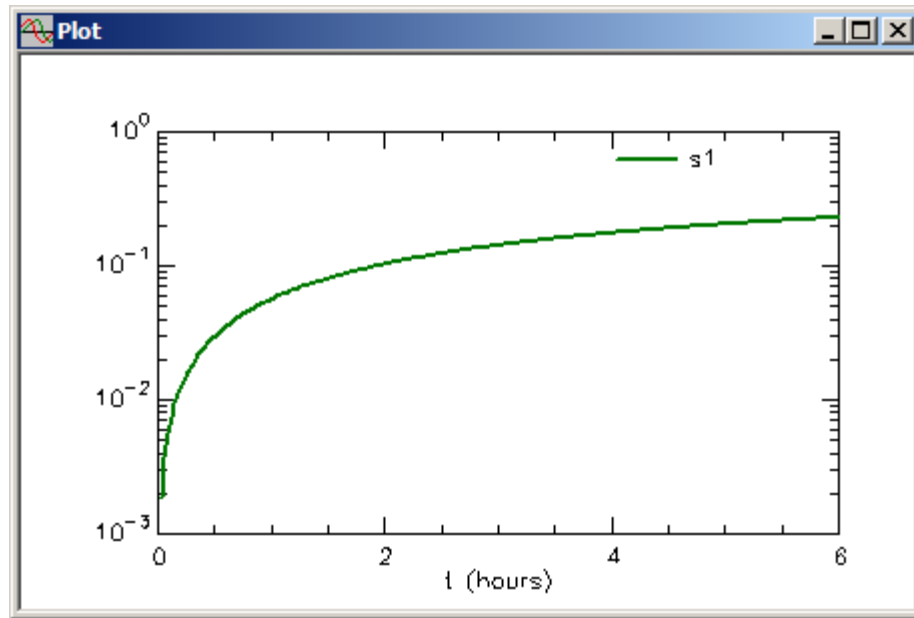


f. Close the **Plot** window.

Quit the **SAAM II Compartmental** application. Do not save the changes to **study_0_ExpInp**.



The constant infusion input. Constant infusion inputs are used in a variety of ways in experimental design. In short duration experiments, the infusion can last the duration of the experiment. The idea in this design is to design the experiment and infusion so that a plateau value is reached. For example in the current study file **study_0_ExpInp**, if you set the duration of the experiment equal to 6 hours instead of 96 hours, and set the infusion of 125 mg/hr to last the entire six hours, the model would predict the following:

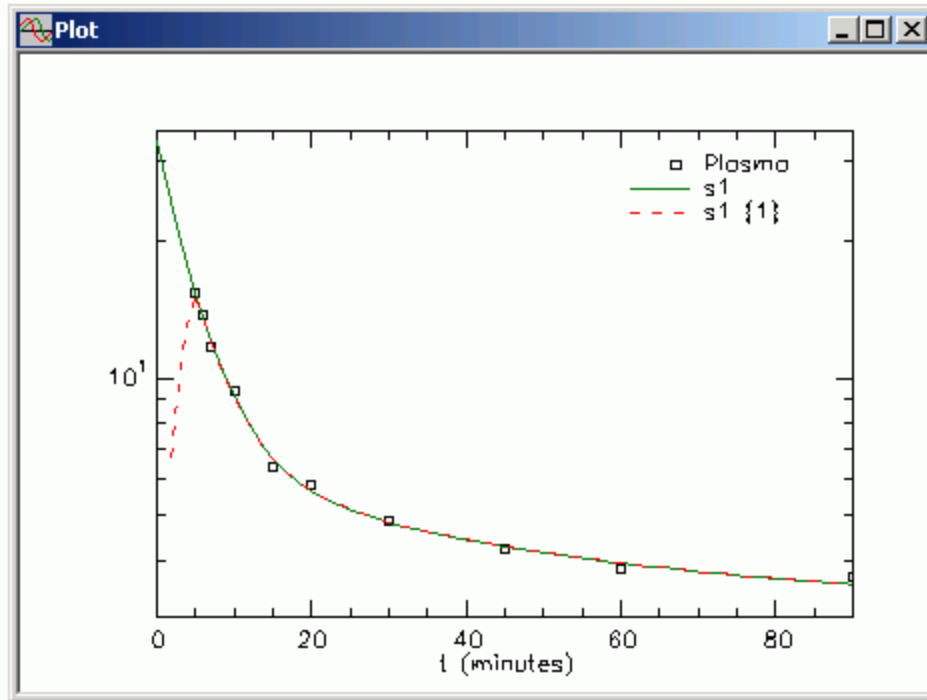


Obviously at this infusion rate, the experiment had not been carried out long enough to achieve a plateau.

Many investigators feel the constant infusion method is superior to the bolus injection, but this is not the case. The differential equations represented by the model “don’t care” about the input; this is just a term added to one of the differential equations. The model “does care” about the nature of the data – how many and how precise. Some investigators feel that only the plateau is of value, and hence delay in taking the first sample hoping the samples taken are only on the plateau. If you do this, the transient nature of *how* the plateau was reached won’t be available, and you will not be able to estimate the rate constants in your model.

Short constant infusions are often used in place of a bolus in introducing material into the system. Such short infusions may last 2 – 5 minutes. These constant infusions cannot be modeled as boluses! Your input in your model must describe what you did in the laboratory. It can be shown that, if you treat a short constant infusion as a bolus, some parameters such as volumes will be estimated in error!

Consider the following situation shown in the figure below:



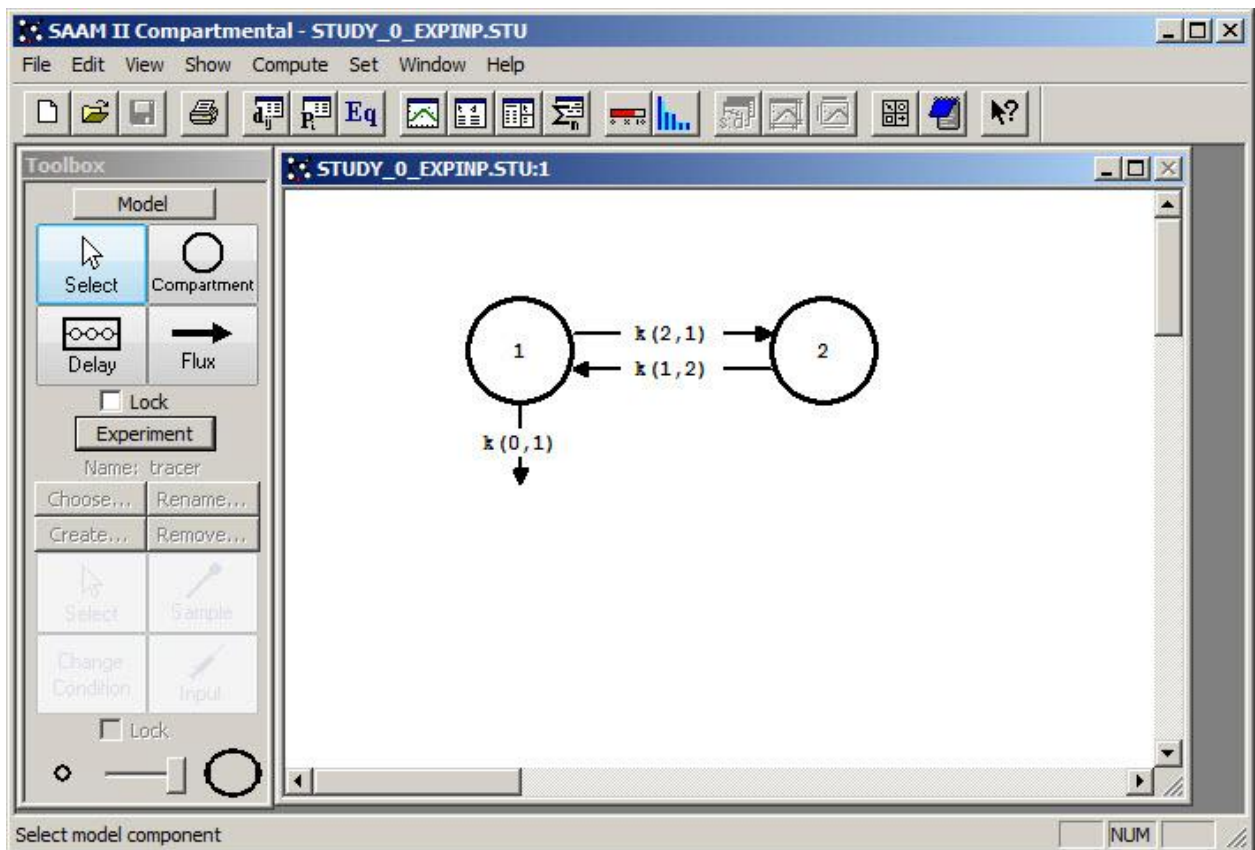
This is an experiment in which 200 mg of a drug was infused into plasma for 5 minutes. The dotted line shows the model solution when the infusion input is specified. The solid line shows the model solution when the data are fitted assuming a bolus injection of 200 mg. What is different? Using the infusion model, the estimated plasma volume is 9.4L while using the bolus injection model, the estimated plasma volume is 6.0L, a difference of more than 30%. Thus any pharmacokinetic parameter in which volume plays a role will be off by this amount!



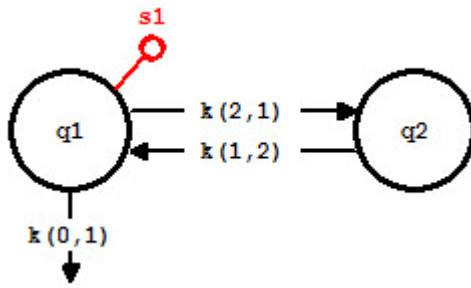
Part 3. The primed constant infusion

The primed constant infusion is sometimes used as a method to introduce test material or a drug into the system. This part of the tutorial will illustrate how to specify a primed, constant infusion.

1. **Start** the **SAAM II Compartmental** application. The **SAAM II Compartmental** main window will open.
2. Open the **SAAM II Compartmental** study file **study_0_ExpInp**.
 - a. The file **study_0_ExpInp.stu** should appear in the file list; if it does not, find the folder where you put this file.
 - b. In the **File** menu, click **Open**. The **SAAM II Compartmental** main window will appear as shown below:



3. View the model and the experiment on the model.
 - a. In the **SAAM II Toolbox**, click **Experiment**. The model of the experiment will appear on the **Drawing Canvas** as follows:



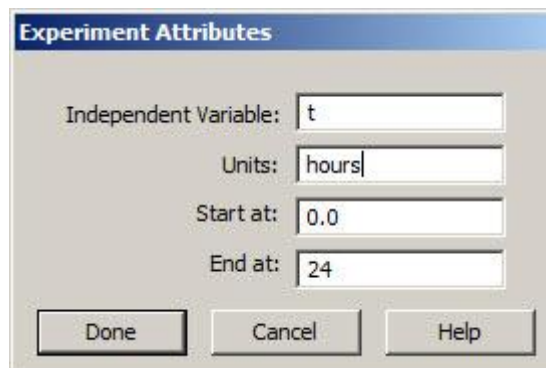
Notice the difference between this model and the experimental model developed and used in the **Getting Started with Compartmental** tutorial. Here there is no experimental input, **ex1**, and the sample circle, **s1**, is not filled because there are no data in the study file.

You may wish to review the **Parameters** dialog box and the **Samples Attributes** dialog box. The parameters are those from **study_0** except they have been fixed since this tutorial involves only simulations and no data fitting. The sample equation is “ $s1 = q1/vol$ ”.

- b. Change the time of the experiment from 9 days to 24 hours.

It will be more convenient to work in units of hours rather than days which are the original units of **study_0**. The experiment in **Study_0** lasted 9 days. In the simulations that follow, it is assumed that the experiment lasted 24 hours.

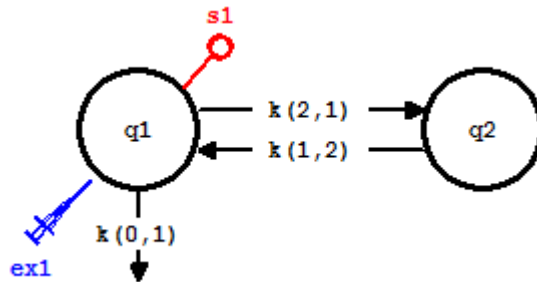
- (1) On the **Set** menu, click **Experiment Attributes**. The **Experiment Attributes** dialog box will open.
- (2) In the **Units** box, type “hours”. In the **End At** box, type “24”. The **Experiment Attributes** dialog box will appear as follows:



- (3) Click **Done**.

4. Create a primed infusion into Compartment **q1** with a priming dose of 100 mg and a constant infusion of 25 mg/hr for 12 hours.

- a. In the **SAAM II Toolbox**, click **Input**.
- b. Click Compartment **q1** and then click on the **Drawing Canvas**. The experimental input **ex1** will appear associated with the model as shown below:



- c. Double-click **ex1** to open the **Exogenous Input** dialog box. The **Exogenous Input** dialog box will appear as follows:

Exogenous Input

Name: Reference: Units:

Type	Initial	Constant	Start	Stop	Repeat Every	Nr. Repeats

Input Type:

Bolus

Infusion

Primed Infusion

Equation

Initial Amount:

Constant Rate:

Event Start:

Event Stop:

Repeat Every:

Nr. of Repeats:

Equation:

Notice in the **Input Type** pane, **Bolus** is selected.

- d. Create the infusion.

(1) In the **Input Type** pane, select **Primed Infusion**.

- (2) In the **Name** box, change “ex1” to “dose”.
- (3) In the **Reference Name** box, type “Primed Infusion”
- (4) In the **Units** box, type “mg/hr”.
- (5) In the **Initial Amount** box, type “100”.
- (6) In the **Constant Rate** box, type “25”.
- (7) In the **Event Start** box, type “0”.
- (8) In the **Event Stop** box, type “12”.
- (9) Click **Add**. The **Exogenous Input** dialog box will appear as follows:

Type	Initial	Constant	Start	Stop	Repeat Every	Nr. Repeats
P.Infus.	100.000	25.000	0.000	12.000	-	-

Input Type:

Bolus

Infusion

Primed Infusion

Equation

Initial Amount: 100

Constant Rate: 25

Event Start: 0

Event Stop: 12

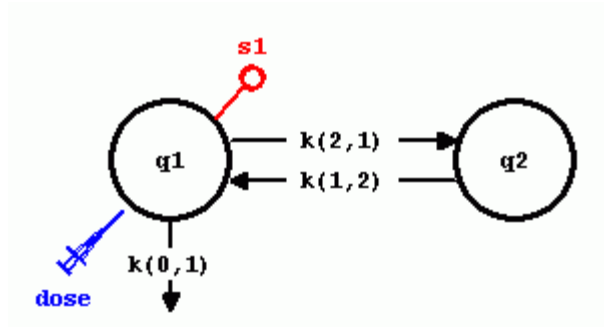
Repeat Every:

Nr. of Repeats:

Equation: ex1 =



Buttons: Save, Edit, Add, Delete, Split Input..., Done, Cancel, Help

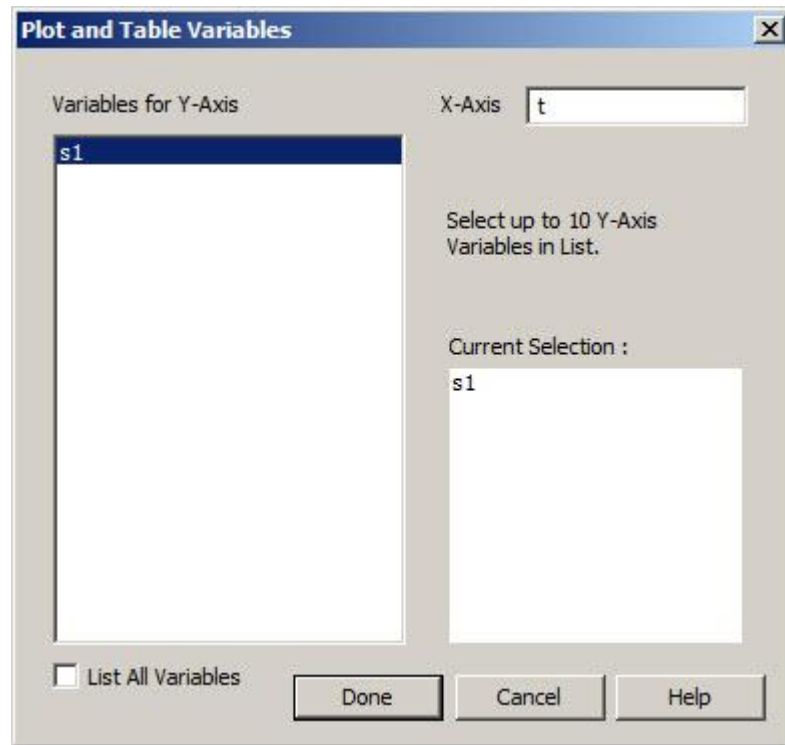
- (10) Click **Done**. Your model will appear as follows:



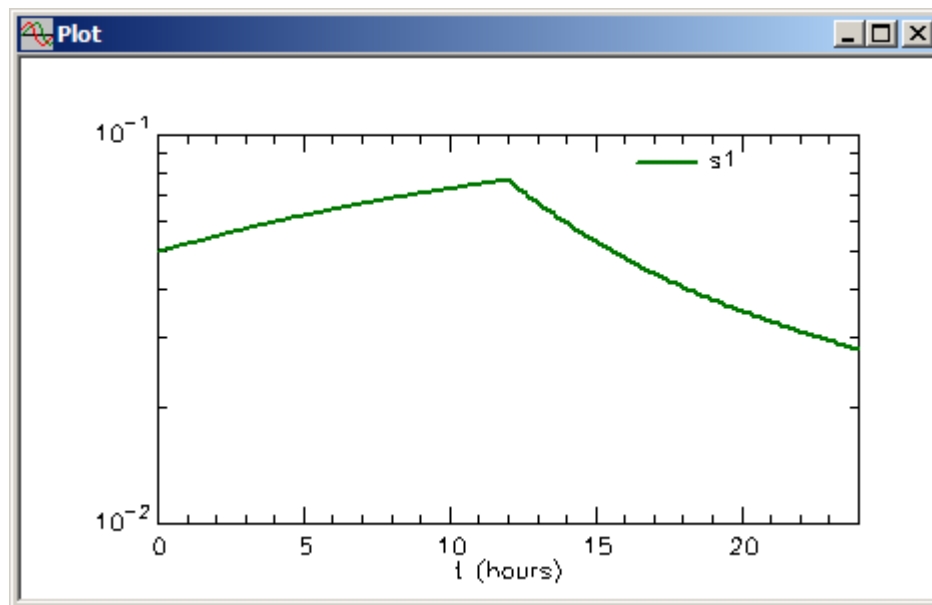
Exogenous input name. The default **Name** for exogenous inputs is **ex_i** for the i^{th} input. This is the name that will appear associated with input tool unless you change it. In this case, you changed the name from “ex1” to “dose”; “dose” will now appear as the name of the input on the drawing canvas (as shown in the figure above), and in the list of variables associated with the model. The **Reference Name**, in this case “Primed Infusion”, is for convenience; it is not used by SAAM II. Similarly **Units** is for convenience.



5. Solve the model and view the solution.
 - a. It will be useful to increase the resolution of your plot. In the **Compute Menu**, click **Computational Settings**. Type “200” in the **Min. Nr. of Calculation Intervals** box. Click **Done**.
 - b. In the **Compute** menu, click **Solve**, or alternatively, on the **SAAM II Toolbar**, click **Solve** .
 - c. In the **Show** menu, click **Plot**, or alternatively, on the **SAAM II Toolbar**, click **Plot** . The **Plot and Table Variables** dialog box will open. Be sure the **List All Variables** check box is not selected so **s1** is the only option in the **Variables for Y-Axis** pane.
 - d. Click **s1** to add this to the **Current Selection** pane. The **Plot and Table Variables** dialog box will appear as shown below:



- e. Click **Done**. A plot of **s1** will appear in semilog mode in the **Plot** window as shown below (if it is not in semilog mode, in the **View** menu, click **Semilog**):



- f. Close the **Plot** window.

Quit the SAAM II Compartmental application. Do not save the changes to study_0_ExpInp.



The primed infusion input. The primed infusion works similarly in many ways to the constant infusion (see Part 2 of this tutorial). The difference is the priming dose. In the example above, a single priming dose and a single constant infusion was used. It is clear that, using the capabilities in the **Exogenous Input** dialog box, multiple kinds of inputs can be specified. You can specify a single priming dose followed by several constant infusions. You can specify multiple priming doses and several constant infusions. In using the **Exogenous Input** dialog box with multiple inputs, it is simply a matter of bookkeeping to be sure you specify on your model what you did in the laboratory.



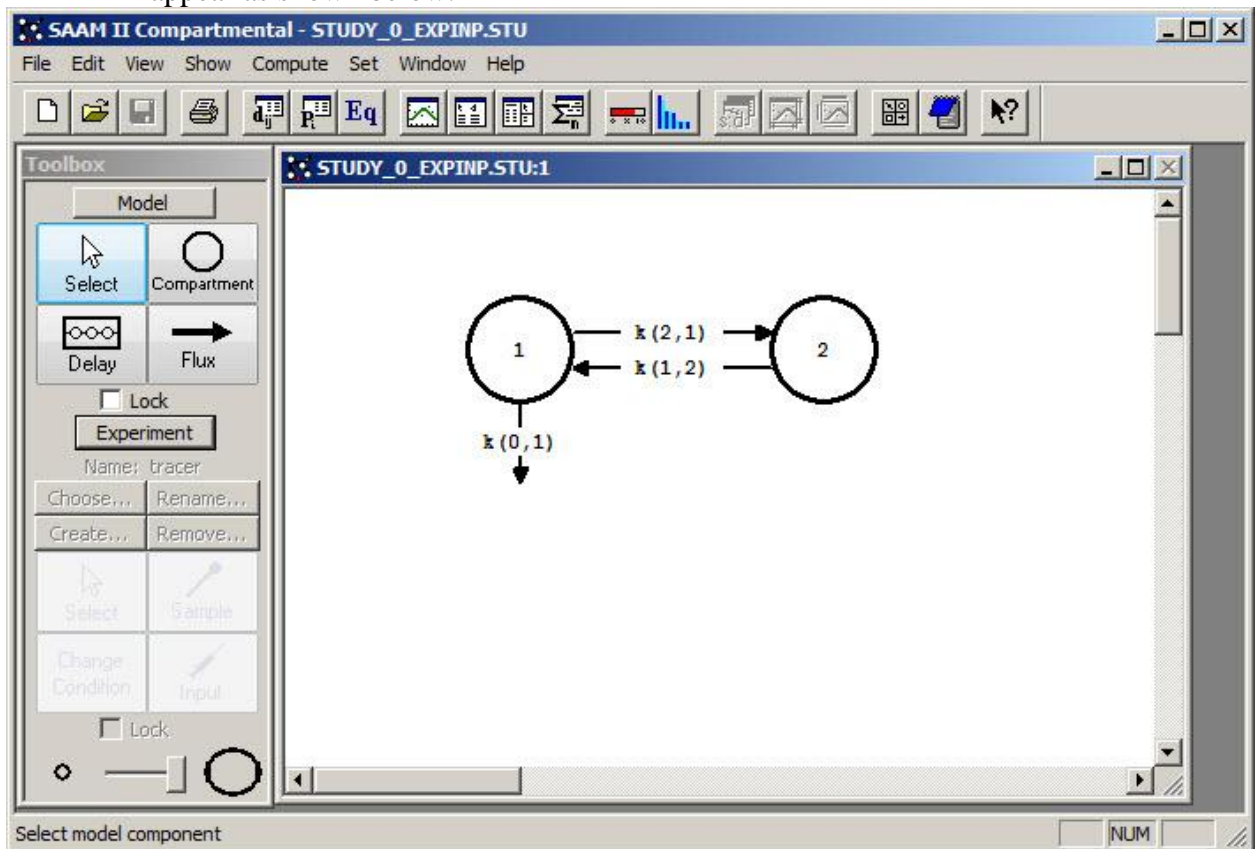
Part 4. Equation input

While the most common specification of inputs into a model are the bolus, the constant infusion or the primed constant infusion, there are times when you may want to specify an input using an equation.

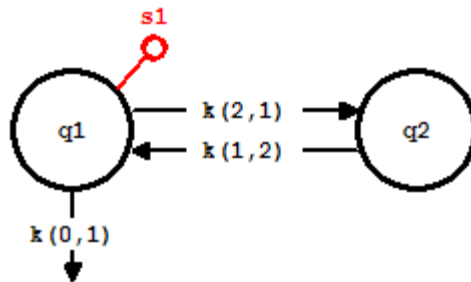
Equation inputs are used in two common ways. One is to specify the equation as a constant, the value of which can either be specified in the **Parameters** dialog box, or read in from a data file. The other is to specify a particular equation input.

This tutorial will illustrate how to specify an input that is a sum of exponentials. Any equation that is recognized by SAAM II can, however, be used.

1. **Start** the **SAAM II Compartmental** application. The **SAAM II Compartmental** main window will open.
2. Open the **SAAM II Compartmental** study file **study_0_ExpInp**.
 - a. The file **study_0_ExpInp.stu** should appear in the file list; if it does not, find the folder where you put this file.
 - b. In the **File** menu, click **Open**. The **SAAM II Compartmental** main window will appear as shown below:



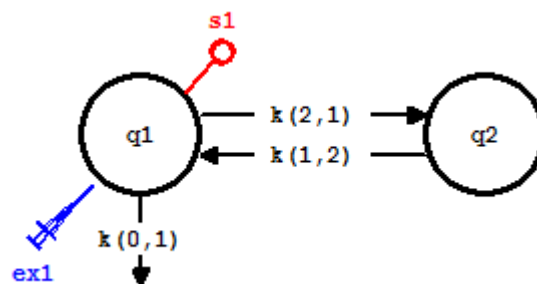
3. View the model and the experiment on the model. In the **SAAM II Toolbox**, click **Experiment**. The model of the experiment will appear on the **Drawing Canvas** as follows:



Notice the difference between this model and the experimental model developed and used in the **Getting Started with Compartmental** tutorial. Here there is no experimental input, **ex1**, and the sample circle, **s1**, is not filled because there are no data in the study file.

You may wish to review the **Parameters** dialog box and the **Samples Attributes** dialog box. The parameters are those from **study_0** except they have been fixed since this tutorial involves only simulations and no data fitting. The sample equation is “ $s1 = q1/vol$ ”.

4. Create an equation input into Compartment **q1** where the input equation is $A*(exp(-a*t)-exp(-b*t))$.
 - a. In the **SAAM II Toolbox**, click **Input**.
 - b. Click Compartment **q1** and then click on the **Drawing Canvas**. The experimental input **ex1** will appear associated with the model as shown below:



- c. Double-click **ex1** to open the **Exogenous Input** dialog box. The **Exogenous Input** dialog box will appear as follows:

The screenshot shows the 'Exogenous Input' dialog box with the following fields and controls:

- Name:** ex1
- Reference:** (empty)
- Units:** (empty)
- Input Type:**
 - Bolus
 - Infusion
 - Primed Infusion
 - Equation
- Initial Amount:** (empty)
- Constant Rate:** (empty)
- Event Start:** (empty)
- Event Stop:** (empty)
- Repeat Every:** (empty)
- Nr. of Repeats:** (empty)
- Equation:** ex1 =
- Buttons:** Save, Edit, Add, Delete, Done, Cancel, Help, Split Input...

Notice in the **Input Type** pane, **Bolus** is selected.

d. Create the equation input.

(1) In the **Input Type** pane, select **Equation**.

(2) In the **Name** box, change “ex1” to “input”.

(3) In the **Reference Name** box, type “Sum of Exponential”

(4) In the **Equation** box, type “input = A*(exp(-a*t)-exp(-b*t))”.

(5) In the **Event Start** box, type “0”.

(6) In the **Event Stop** box, type “9”.

(7) Click **Add**. The **Exogenous Input** dialog box will appear as follows:

Exogenous Input [X]

Name: Reference: Units:

Type	Initial	Constant	Start	Stop	Repeat Every	Nr. Repeats
Equation	input = A*(exp(-a*		0.000	9.000	-	-

Input Type:

Bolus
 Infusion
 Primed Infusion
 Equation

Initial Amount:

Constant Rate:

Event Start:

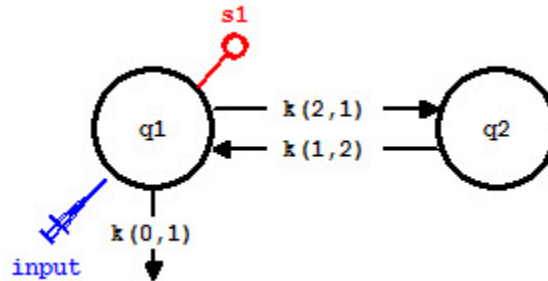
Event Stop:

Repeat Every:

Nr. of Repeats:

Equation:

(8) Click **Done**. Your model will appear as follows:



Exogenous input name. The default name for exogenous inputs is **ex_i** for the *i*th input. This is the name that will appear associated with input tool unless you change it. In this case, you changed the name from “ex1” to “input”; “input” will now appear as the name of the input on the drawing canvas, and in the list of variables associated with the model. You can also add a reference name (in this case “Sum of Exponentials”) and specify the units of the input if you wish.

When you specify an equation input type, the **Equation** box will open with “ex1” as the default to match the default Exogenous Input name seen in the upper left hand corner of the Exogenous Input dialog box.

When you enter the equation, if you had typed

$$\text{"ex1 = A*(exp(-a*t)-exp(-b*t))"}$$

you would have received an error when you closed the **Exogenous Input** dialog box. SAAM II will check that the names in the **Name** box and on the left hand side of the equation are the same. For this reason, you entered


$$\text{"input = A*(exp(-a*t)-exp(-b*t))"}$$

in the **Equation** box.



5. Solve the model and view the solution.

Because of the way in which you specified the equation input, you have introduced three new parameters in your model, A , a and b . Before you can solve your model, you must provide values for these parameters.

- a. In the **Show** menu, click **Parameters**, or alternatively, on the **SAAM II Toolbar**, click **Parameters** . The **Parameters** dialog box will open, as shown below:

Name	Type	Current	Low Limit	High Limit
A	Adj			
a	Adj			
b	Adj			
k(0,1)	Fix	0.1000		
k(1,2)	Fix	0.1000		
k(2,1)	Fix	0.1000		
vol	Fix	2000.0000		

Name: A Value:

Type: Fixed Adjustable Low Limit: High Limit:

Adjust value:

Auto solve

Done Cancel Help

- b. Enter A , a , and b as fixed parameters. For A , enter “100”; for a , enter “0.05” and for b , enter “0.5”. The **Parameters** dialog box will appear as follows:



The screenshot shows the 'Parameters' dialog box with a table of parameters and a detailed view for parameter 'b'.

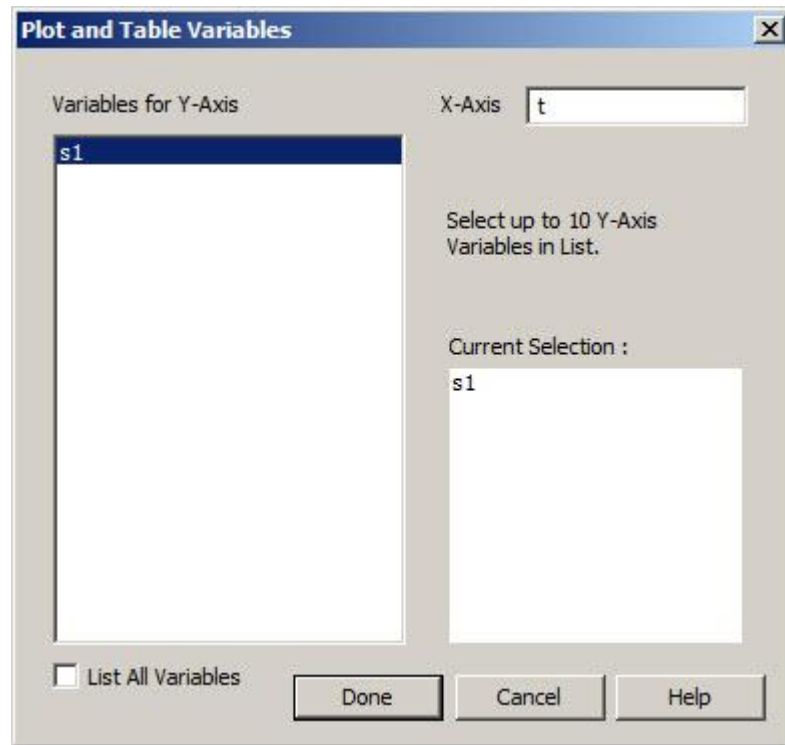
Name	Type	Current	Low Limit	High Limit
A	Fix	100.0000		
a	Fix	0.0500		
b	Fix	0.5000		
k(0,1)	Fix	0.1000		
k(1,2)	Fix	0.1000		
k(2,1)	Fix	0.1000		
vol	Fix	2000.0000		

The detailed view for parameter 'b' shows:

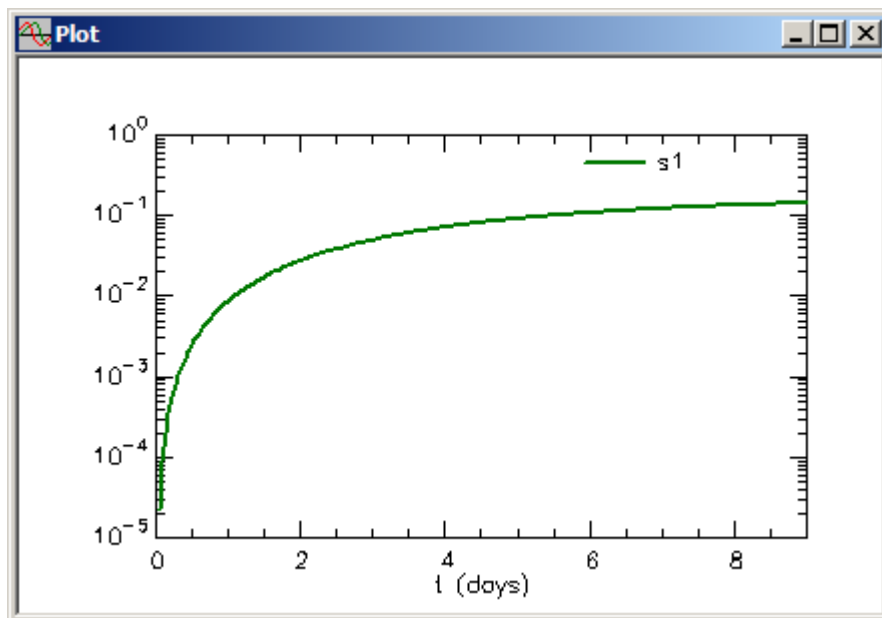
- Name: b
- Value: 0.5
- Type: Fixed, Adjustable
- Low Limit: 0.05000000
- High Limit: 5.00000000
- Buttons: Edit, Save
- Auto solve:
- Buttons: Done, Cancel, Help

Click **Done**.

- c. It will be useful to increase the resolution of your plot. In the **Compute Menu**, click **Computational Settings**. Type “200” in the **Min. Nr. of Calculation Intervals** box. Click **Done**.
- d. In the **Compute** menu, click **Solve**, or alternatively, on the **SAAM II Toolbar**, click **Solve** .
- e. In the **Show** menu, click **Plot**, or alternatively, on the **SAAM II Toolbar**, click **Plot** . The **Plot and Table Variables** dialog box will open. Be sure the **List All Variables** check box is not selected so **s1** is the only option in the **Variables for Y-Axis** pane.
- f. Click **s1** to add this to the **Current Selection** pane. The **Plot and Table Variables** dialog box will appear as shown below:

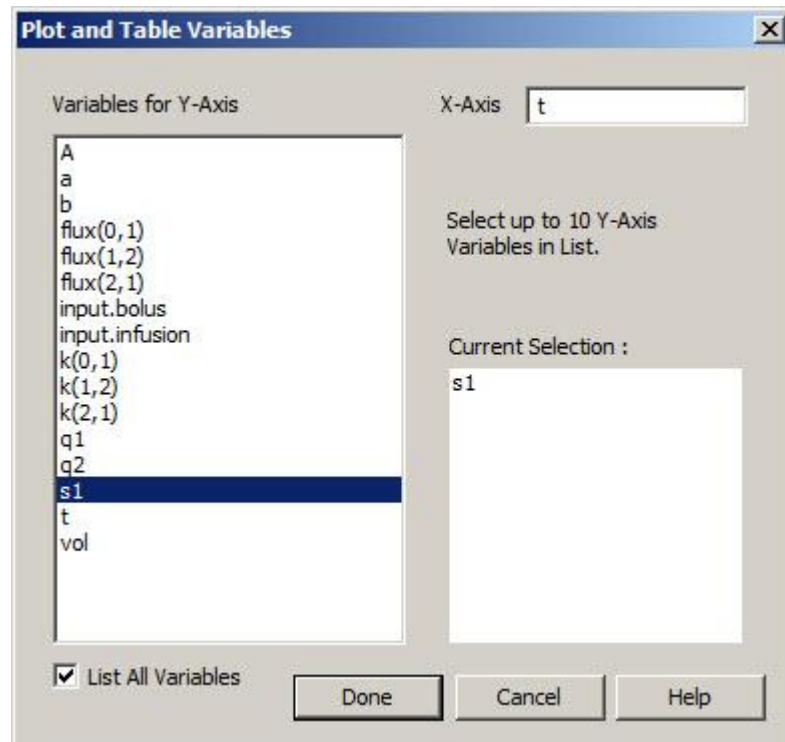


- g. Click **Done**. A plot of **s1** will appear in semilog mode in the **Plot** window as shown below (if it is not in semilog mode, in the **View** menu, click **Semilog**):



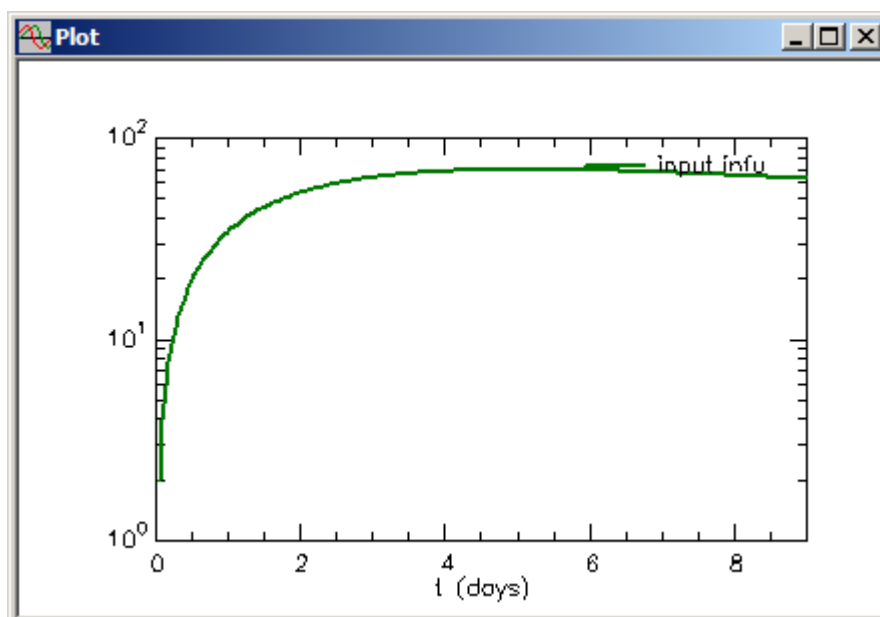
- h. View the input equation.

- (1) In the Set menu, click **Plot/Table Variables**. The **Plot and Table Variables** dialog box will open. Be sure the **List All Variables** check box is selected. . The **Plot and Table Variables** dialog box will appear as shown below:



The variable **s1** is in the **Current Selection** pane because this was your last plot. Notice that “input.infusion” appears in the **Variables for Y-Axis** pane. The name “input” is because you changed the name of the input from “ex1” to “input” in the **Exogenous Input** dialog box.

- (2) Click **input.infusion** to move this to the **Current Selection** pane.
- (3) Click **Done**. The plot of the input equation will appear as follows:



(4) Close the **Plot** window.

Quit the **SAAM II Compartmental** application. Do not save the changes to **study_0_ExpInp**.