

Using SAAM II

Experimental Inputs, Advanced

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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 the amount of your input in a data file (Part 1)
- How to specify the amount of the input as an adjustable parameter (Part 2)
- How to specify split inputs (an input into more than one compartment (Part 3)
- How to perform parametric deconvolution (Part 4)

Files Required

Study Files: The study files for this tutorial are

study_0_ExpInp.stu
study_0.stu

These files are 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** User Guide 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: The data files for this tutorial are

paradecon_ExpInp
study_0.dat

Introduction

This tutorial focuses on how to use the options in the **Exogenous Input** dialog box to specify less common or more advanced types of input dosage and to conduct parametric deconvolution.

The tutorial covers

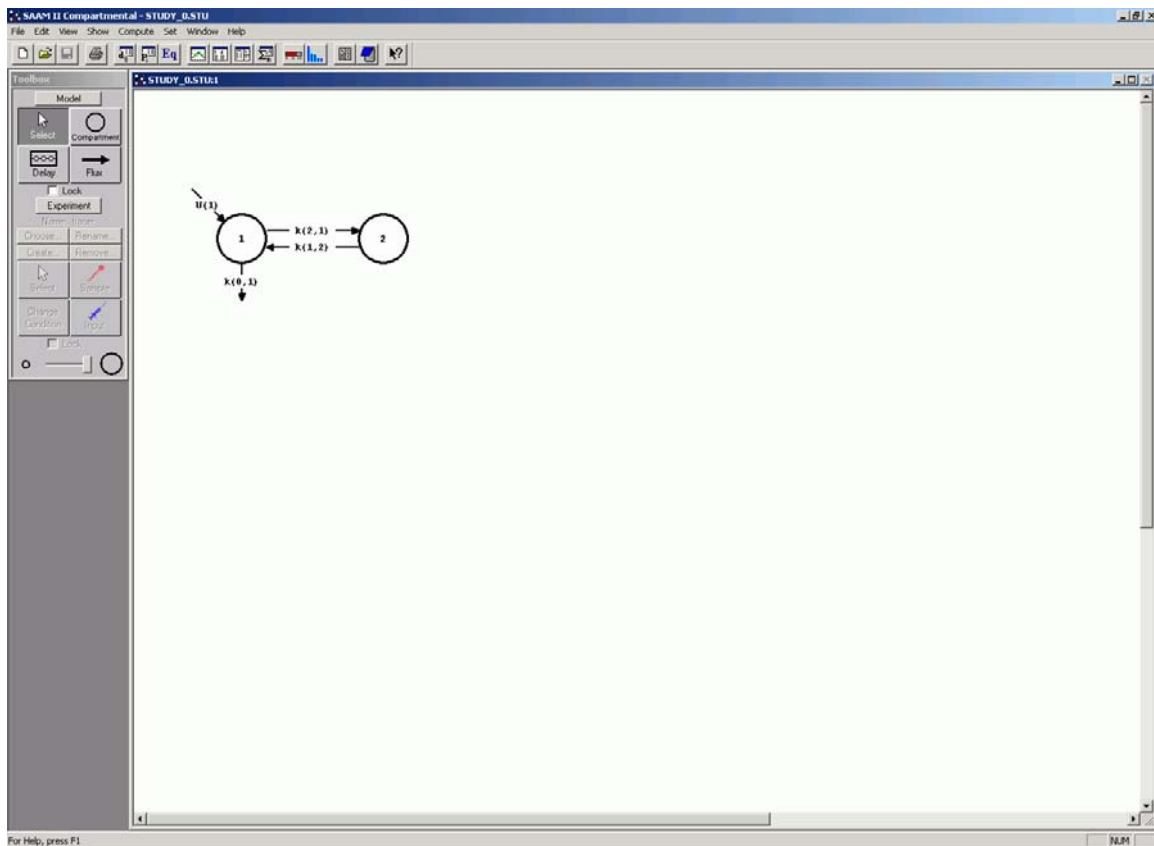
- Specifying the amount of a dose as a constant in the data file.
- Specifying the dose as an adjustable parameter.
- Split inputs (an input into more than one compartment)
- Parametric deconvolution

The most frequently used types of dosage inputs are covered in the tutorial Experimental Inputs, Basic. These input types are the bolus, the constant infusion and the primed constant infusion and 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.

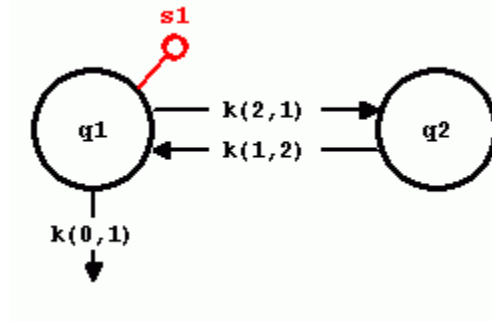
Part 1. Specifying the amount of an input from the Data window

You can specify information about dosing from the data window. To do so, you use the equation input option in the **Exogenous Input** dialog box. This part of the tutorial will illustrate how to specify the amount of a bolus injection in the **Data** window.

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:



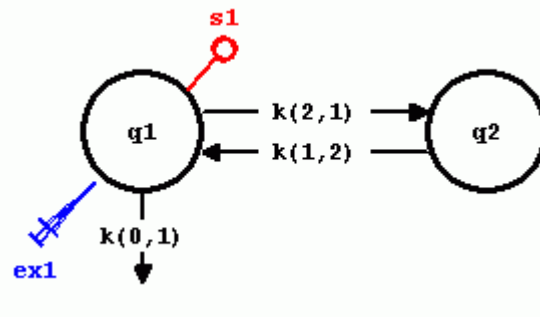
3. View the model and the experiment on the model. In the **SAAM II Toolbox**, click **Experiment**. The model of the experiment will appear on the **Drawing Canvas** as follows:



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 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 a bolus injection into Compartment **q1** where the amount of the bolus is specified in the **Data** window.
 - 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 Name: Units:

Type Initial Constant Start Stop Repeat Every Nr. Repeats

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:

Save Edit Add Delete

Split Input... Done Cancel Help

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

- d. Enter a bolus injection of “dose” specified by an equation.
 - (1) In the **Input Type** pane, select **Equation**.
 - (2) In the **Equation** box, type “ex1 = dose”.
 - (3) In the **Event Start** box, type “0”.
 - (4) In the **Event Stop** box, type “0”.
 - (5) Click **Add**. The **Exogenous Input** dialog box will appear as follows:

Type	Initial	Constant	Start	Stop	Repeat Every	Nr. Repeats
Equation	ex1 = dose		0.000	0.000	-	-




Specifying an equation as a bolus input. The effect of the above is the following. The equation is specified “ex1 = dose”. However, the start and stop times being equal to zero, specifies the bolus. The result will be a bolus dose at time zero equal to an amount “dose”. “dose” can either be entered as a parameter or in the **Data** window.

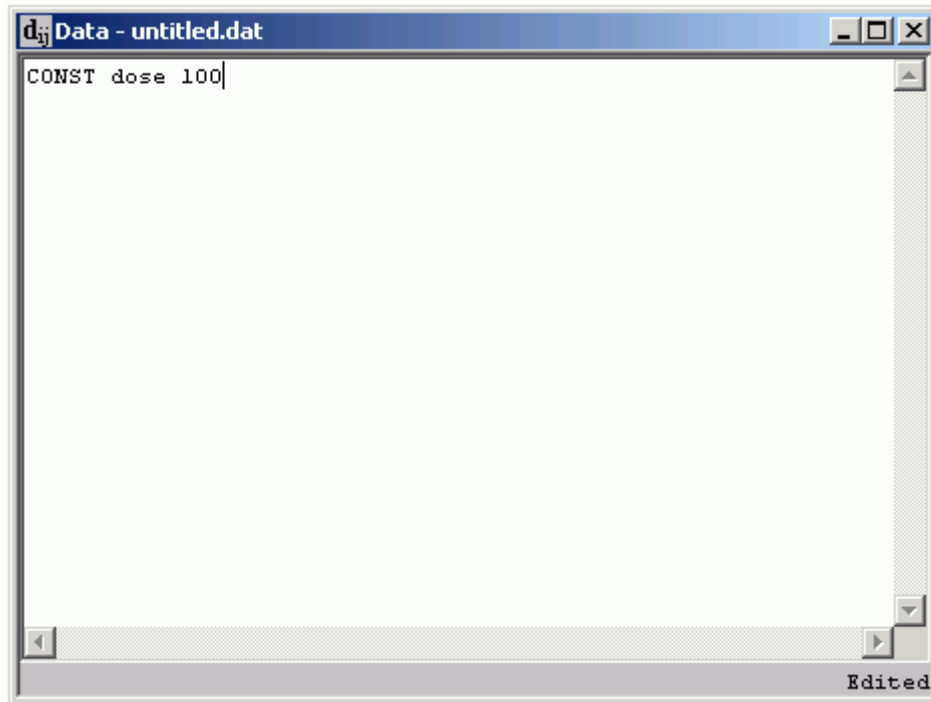


(6) Click **Done**.

e. Enter the amount of the dose in the **Data** window.

(1) In the **Show** menu, click **Data**, or alternatively, on the **SAAM II Toolbar** click **Data** . The **Data** window will open as blank since there are no data associated with this study file.

(2) In the **Data** window, type “CONST dose 100”. The **Data** window will appear as follows:





*Specifying constants in the **Data** window.* You can specify constants in the data window using the **CONST** designator. In this case **CONST** is used to define the constant “dose” equal to “100.”

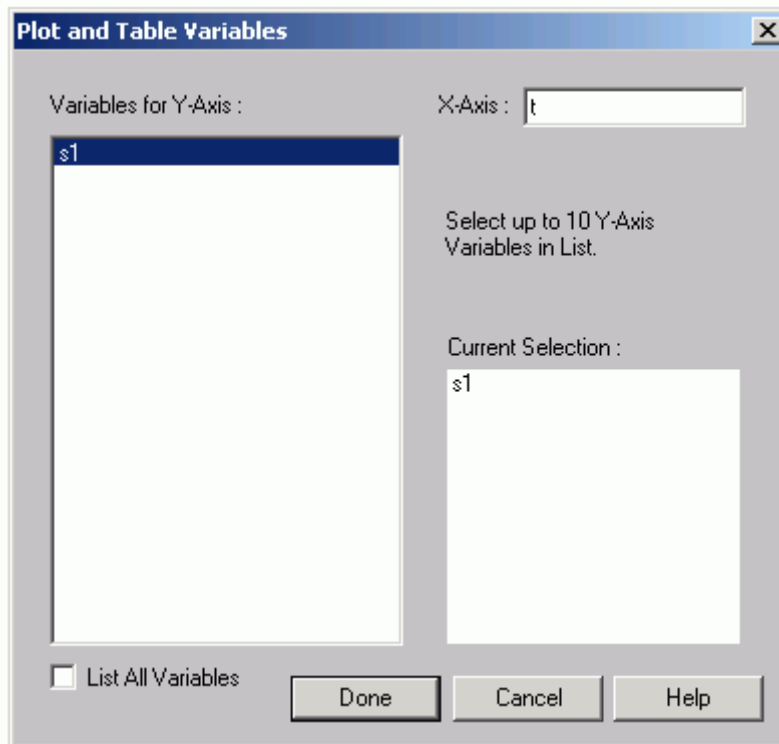


(3) Close the **Data** window.

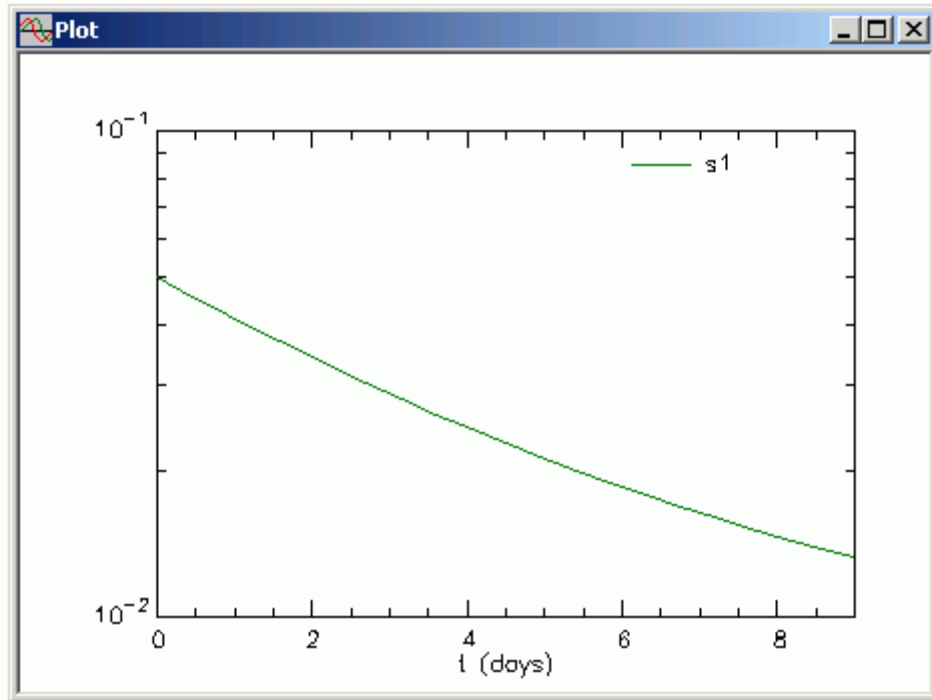
5. Solve the model and view the solution.

- 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**.



Specifying the amount of an input in the **Data** window using the **Equation** type of **Exogenous Input**. The above is an example of how to specify the amount of a bolus injection where the amount of the bolus is specified in the Data window. It is clear that multiple boluses, constant infusions, multiple constant infusions and primed infusions can be specified similarly. It is simply a matter of how the equation input is specified. Suppose, for example, you wanted to specify a primed constant infusion where the priming dose was 100 and the infusion rate was 25 for a specified time interval. If in the Data window, there were two constants entered, for example

CONST dose 100

and

CONST dose1 25

were entered, the **Exogenous Input** dialog box could look as follows:

Exogenous Input [X]

Name: Reference Name: Units:

Type	Initial	Constant	Start	Stop	Repeat Every	Nr. Repeats
Equation	ex1 = dose1		0.000	4.000	-	-
Equation	ex1 = dose		0.000	0.000	-	-

Input Type:

Bolus
 Infusion
 Primed Infusion
 Equation

Initial Amount:

Constant Rate:

Event Start:

Event Stop:

Repeat Every:

Nr. of Repeats:

Equation:

Here the bolus is specified equal to “dose” since it starts and stops at time zero. It is followed by a constant infusion equal to “dose1” starting at time 0 and ending at time 4.

Thus the **Equation** input type gives you great flexibility in specifying inputs where information about the input can be contained in the data file.

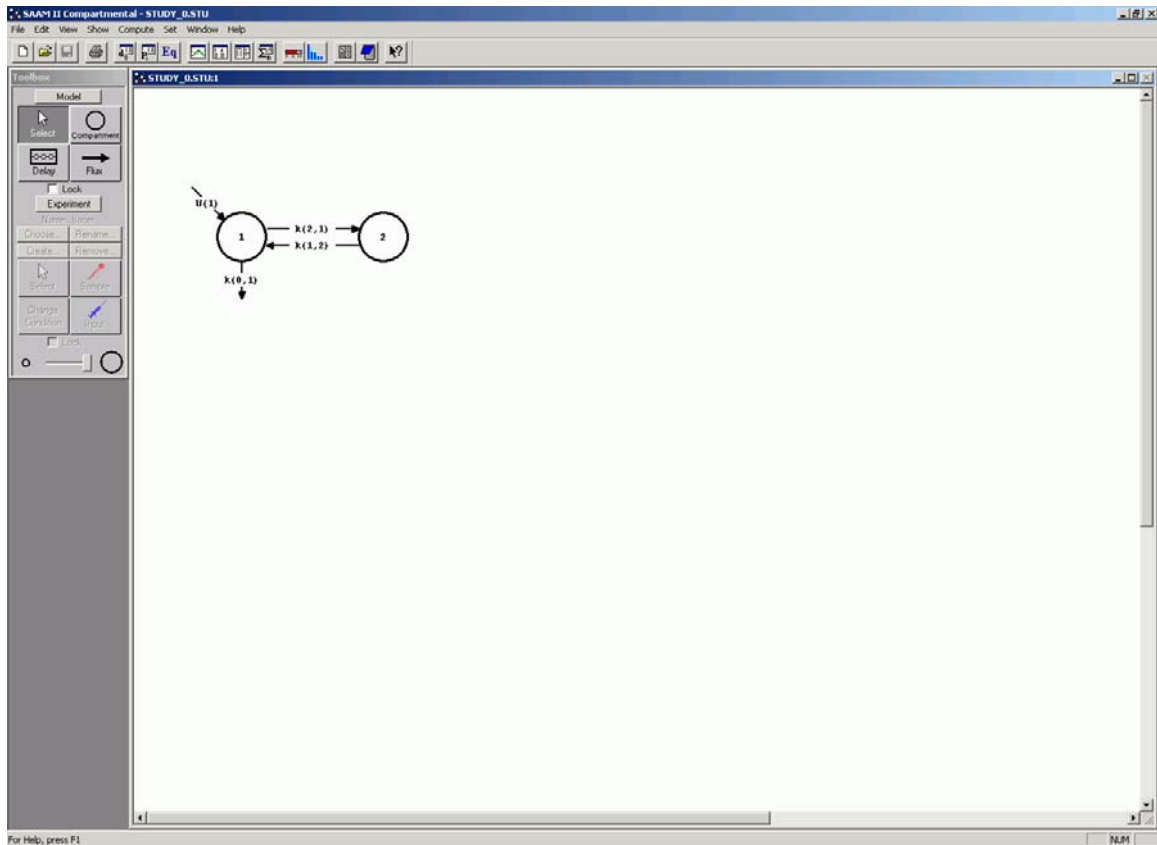


Part 2. Dose as an adjustable parameter

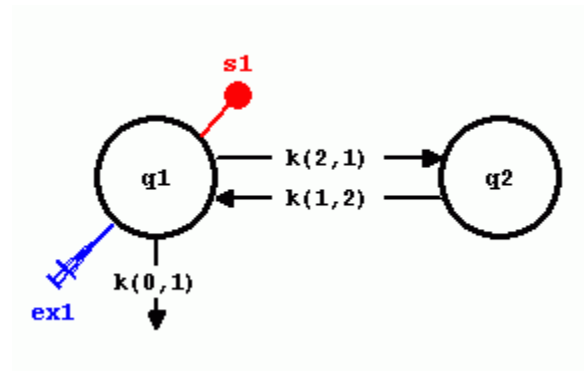
It is not often that the amount of material in the dose can be an adjustable parameter. This is because, under normal circumstances, the volume of the pool into which the test substance is administered needs to be estimated. To obtain an estimate of this volume, it is necessary to know the dose precisely.

There are instances, however, when the amount of the dose can be an adjustable parameter. Normally this occurs when one has a single input-multiple output experimental design. An example would be a bolus injection into plasma with plasma and urine samples. Another example would be if volume were precisely known. This is the example that will be illustrated in this part of the tutorial.

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**.
 - a. The file **study_0.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:



You may wish to review the **Parameters** dialog box and the **Samples Attributes** dialog box. The sample equation is “ $s1 = q1/vol$ ”.

4. Create a bolus injection into Compartment **q1** where the amount of the dose is an unknown parameter.
 - a. Double-click **ex1** to open the **Exogenous Input** dialog box. The **Exogenous Input** dialog box will appear as follows:

Exogenous Input

Name: Reference Name: Units:

Type	Initial	Constant	Start	Stop	Repeat Every	Nr. Repeats
Bolus	1.04e+8	-	0.000	-	-	-

Input Type:

Bolus
 Infusion
 Primed Infusion
 Equation

Initial Amount:

Constant Rate:

Event Start:

Event Stop:

Repeat Every:

Nr. of Repeats:

Equation:

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

This is the bolus input specified in **study_0**. It assumes the dose is known and the volume *vol* is unknown. In what follows, the situation will be reversed. The dose will be assumed unknown and the volume known.

- b. Click **Delete** to remove the bolus injection.
- c. Create the input.
 - (1) In the **Input Type** pane, select **Equation**.
 - (2) In the **Equation** box, type “ex1 = dose”.
 - (3) Be sure the **Event Start** and **Event Stop** times are set equal to zero.
 - (4) Click **Add**. The **Exogenous Input** dialog box will appear as follows:

Exogenous Input

Name: Reference Name: Units:

Type	Initial	Constant	Start	Stop	Repeat Every	Nr. Repeats
Equation	ex1=dose		0.000	0.000	-	-

Input Type:

Bolus
 Infusion
 Primed Infusion
 Equation

Initial Amount:

Constant Rate:

Event Start:

Event Stop:


Repeat Every:

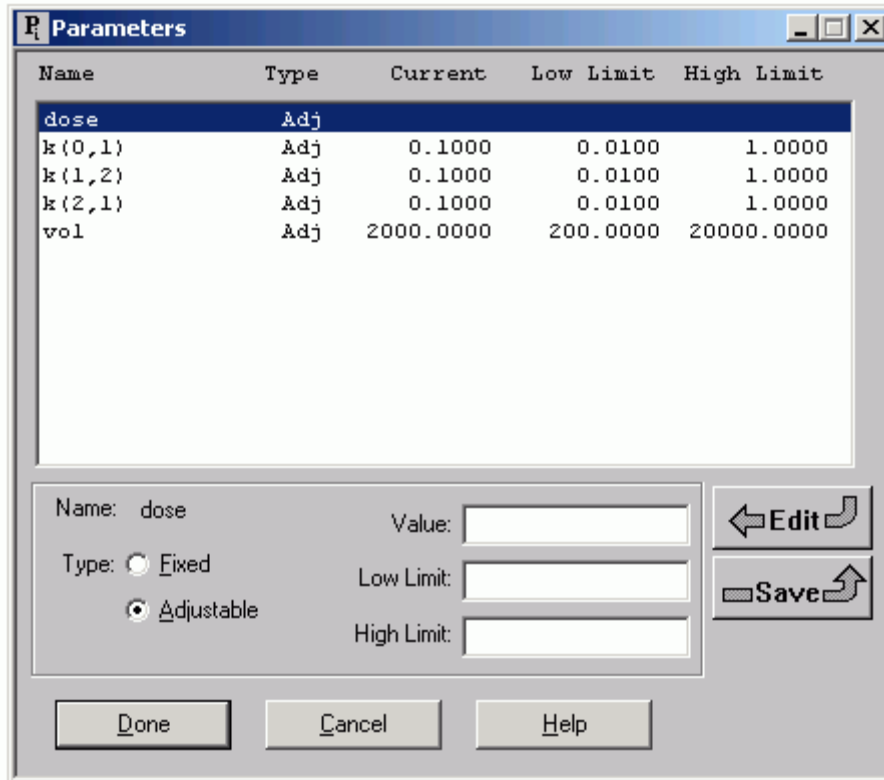
Nr. of Repeats:

Equation:

(5) Click **Done**.

The input now has been defined as an equation where the equation is a constant “dose”. “dose” will appear as a parameter when you open the **Parameters** dialog box. The event start and stop times being zero specifies the equation as a bolus. Since a new parameter has been introduced, a value for it must be specified in the **Parameters** dialog box.

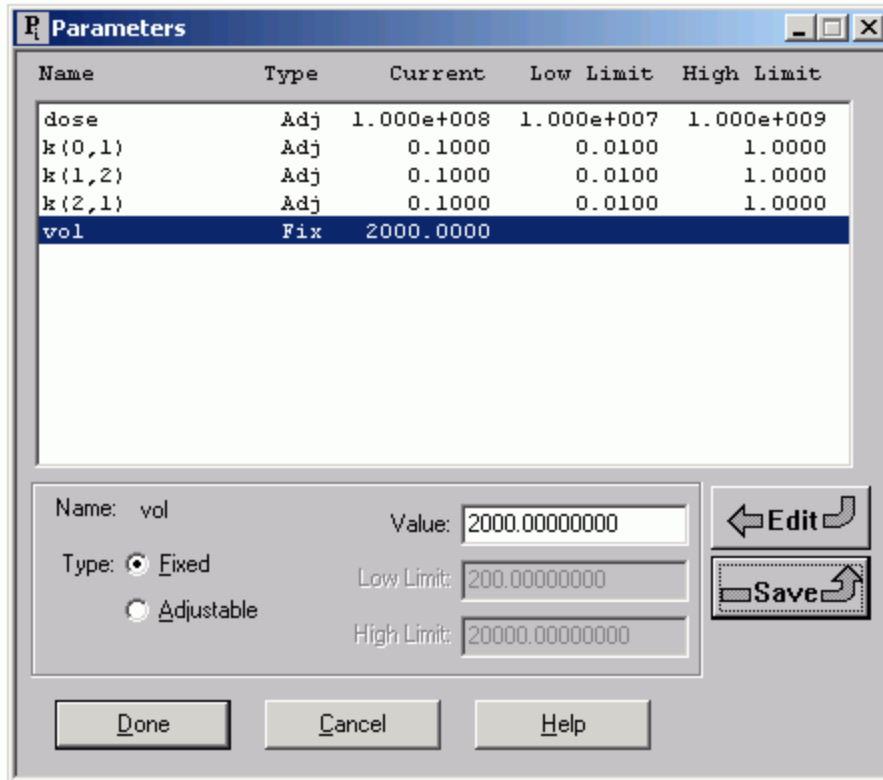
5. Specify the model parameters.
 - a. In the **Show** menu, click **Parameters**, or alternatively, on the **SAAM II Toolbar**, click **Parameters** . The **Parameters** dialog box will open, as shown below:



You can see *dose* now appears as a parameter. If you specify a value for the dose and leave all the other parameters adjustable, you will not be able to fit the model to the data because there are too many parameter values. In this example, it will be assumed that the volume *vol* is known, and equal to 2000 ml.



b. Set the parameters are follows:

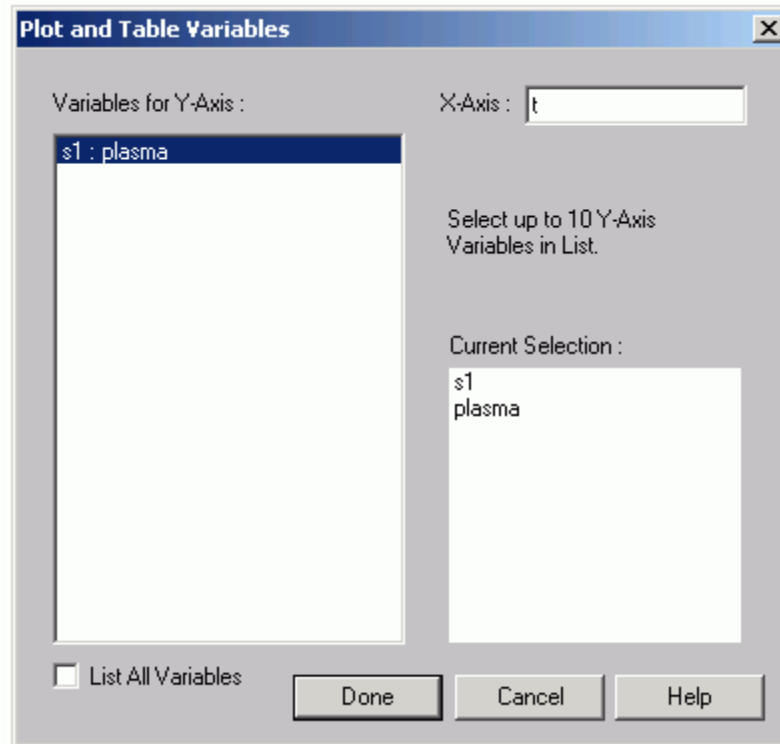
- (1) Double-click *dose* to select it.
- (2) In the **Value** box, type “1.0e+08”.
- (3) Click **Save**.
- (4) Double-click *vol* to select it.
- (5) Select **Fixed** as the **Type**.
- (6) Click **Save**. The **Parameters** dialog box will appear as follows:



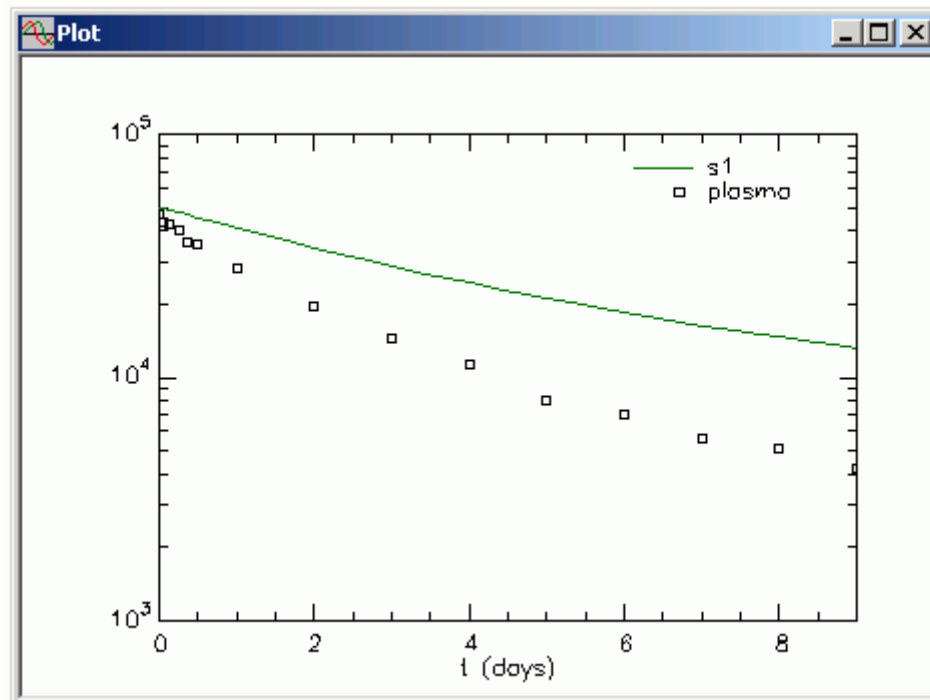
(7) Click **Done**.

6. 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:plasma** is the only option in the **Variables for Y-Axis** pane.
- c. Click **s1:plasma** to add this to the **Current Selection** pane. The **Plot and Table Variables** dialog box will appear as follows:

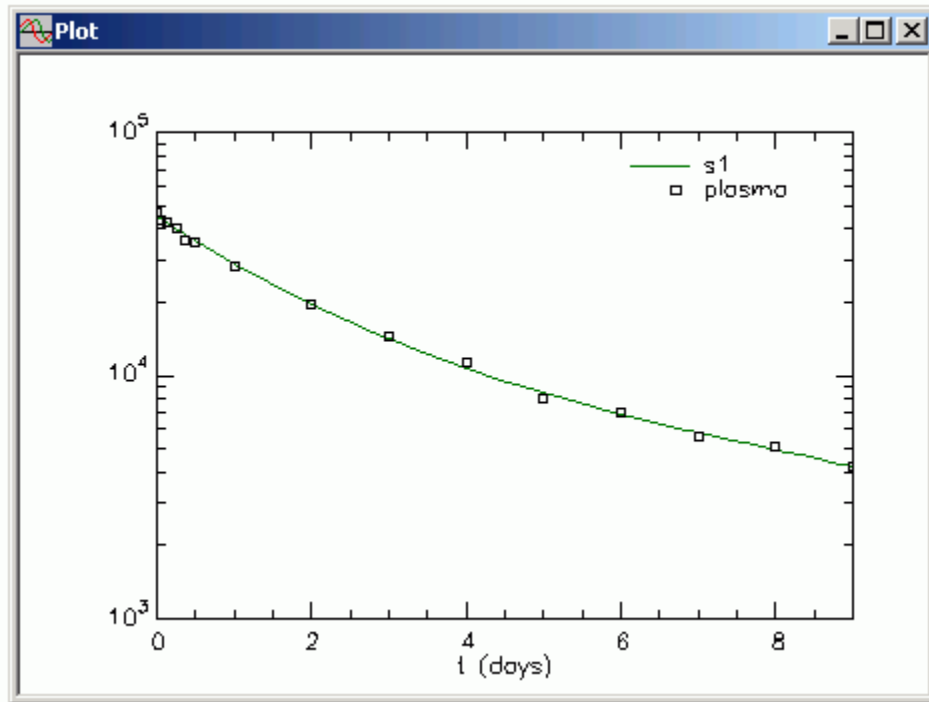



- d. Click **Done**. A plot of **s1** and plasma will appear in semilog mode in the **Plot** window as shown below (if it is not in semilog mode, in the **View** menu, click **Semilog**):

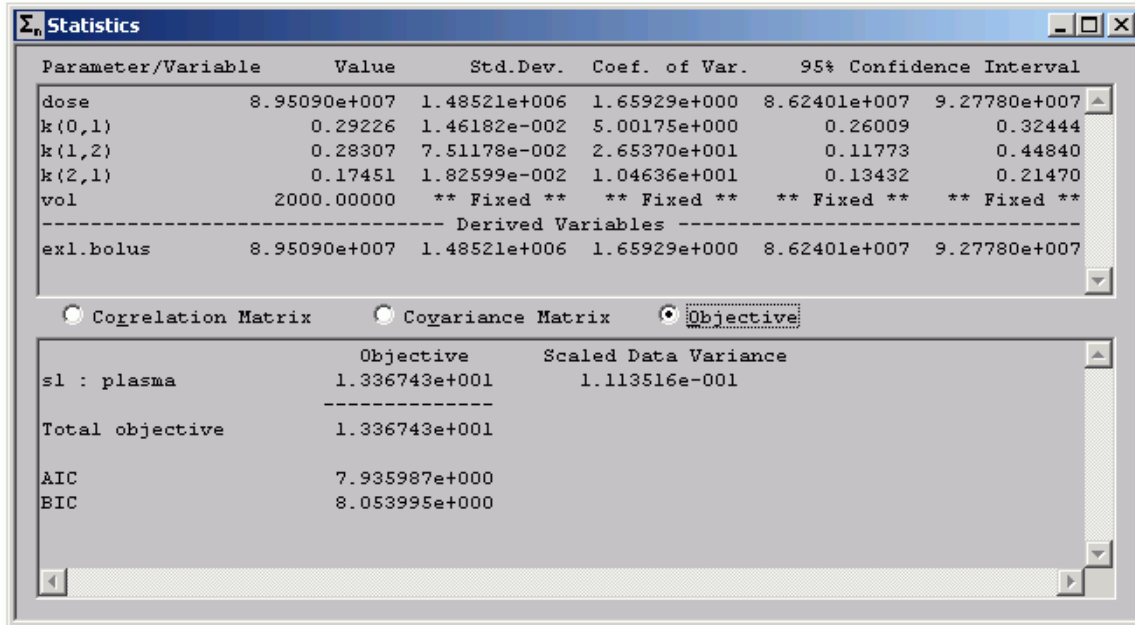


Leave the **Plot** window open.

7. Fit the model to the data and view the solution.
 - a. In the **Compute** menu, click **Fit**, or alternatively, on the **SAAM II Toolbar**, click **Fit** . Your plot will be updated as follows:



- b. In the **Show** menu, click **Statistics**, or alternatively, on the **SAAM II Toolbar**, click **Statistics** . The **Statistics** window will open as follows:



Parameter/Variable	Value	Std.Dev.	Coef. of Var.	95% Confidence Interval	
dose	8.95090e+007	1.48521e+006	1.65929e+000	8.62401e+007	9.27780e+007
k(0,1)	0.29226	1.46182e-002	5.00175e+000	0.26009	0.32444
k(1,2)	0.28307	7.51178e-002	2.65370e+001	0.11773	0.44840
k(2,1)	0.17451	1.82599e-002	1.04636e+001	0.13432	0.21470
vol	2000.00000	** Fixed **	** Fixed **	** Fixed **	** Fixed **
----- Derived Variables -----					
ex1.bolus	8.95090e+007	1.48521e+006	1.65929e+000	8.62401e+007	9.27780e+007

	Objective	Scaled Data Variance
sl : plasma	1.336743e+001	1.113516e-001
Total objective	1.336743e+001	
AIC	7.935987e+000	
BIC	8.053995e+000	

The model parameters are estimated with good precision. Notice, of course, *vol* is a fixed parameter. *ex1.bolus* appears as a derived parameter because of the specification of the input as an equation.

- c. Close the **Statistics** and **Plot** windows.

Quit the **SAAM II Compartmental** application. Do not save the changes to **study_0**.

Part 3. Split inputs (an input into more than one compartment)

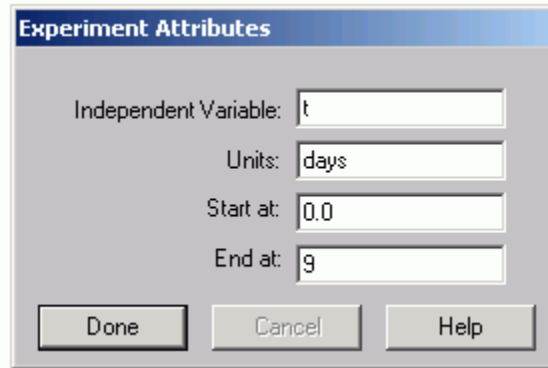
There may be occasion when you have an experimental input into more than one compartment, and you may not know how the input distributes among the compartments. One example is injecting radioiodinated low density lipoproteins (LDL) where the radioactive iodide distributes between two subpopulations of LDL particles. Another example would be an injected material with an unknown amount of contaminants where the material and contaminant have different kinetics. Thus what is known is the total amount of material administered; what may not be known is how it is distributed. This situation is accommodated in SAAM II using the split input capability in the **Exogenous Input** dialog box.

1. **Start the SAAM II Compartmental** application. The **SAAM II Compartmental** main window will open.
2. Create the following system model.

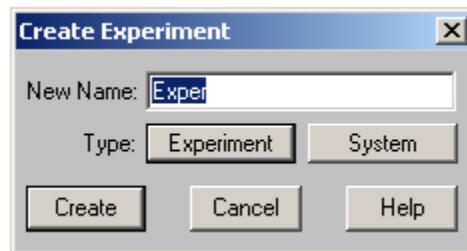


Notice this is a two-compartment model where there is no interconnection between the two compartments; there is only a loss from each.

3. Create the experiment on the model.
 - a. In the **SAAM II Toolbox**, click **Experiment**. Notice that the **Model** tools are unavailable and the **Experiment** tools are available. The **Experiment Attributes** dialog box will open.
 - b. Change the entry in the **Units** box from “minutes” to “days.”
 - c. Type “9” in the **End at** box. The **Experiment Attributes** dialog box will appear as shown below:




- d. Click **Done**. The **Create Experiment** dialog box will appear on the **Drawing Canvas**. The choice is to create an **Experiment (Exper)** or **System** experiment. The **Exper** experiment is selected as follows:

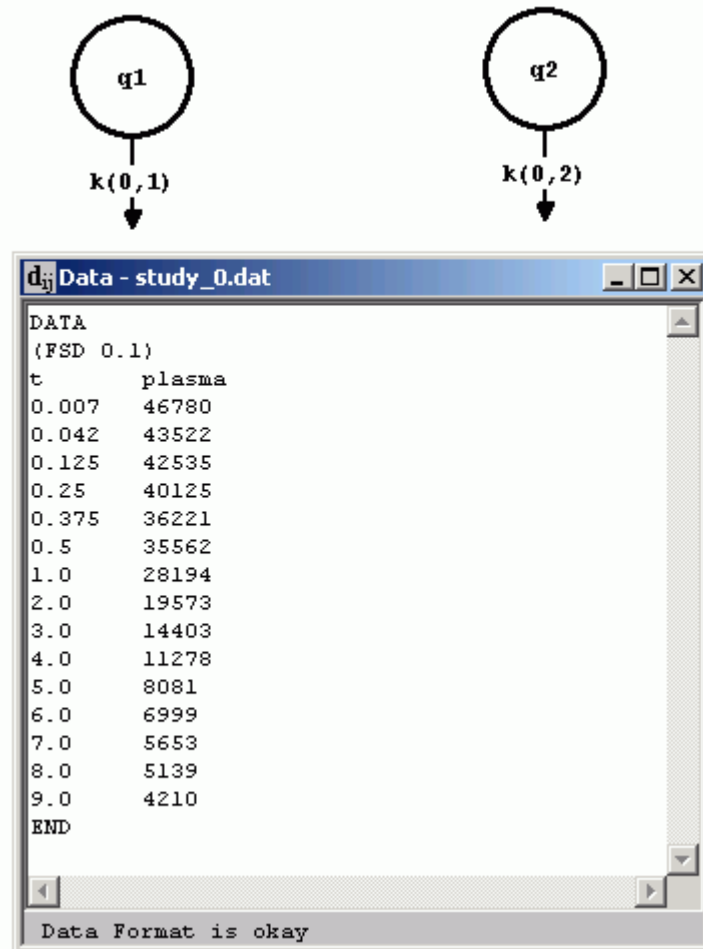


- e. Click **Create** (since **Exper** is selected, and this is the type of experiment you want to create). Your model will appear as follows:



4. Add the data
- On the **Show** menu, click **Data**, or alternatively, on the **SAAM II Toolbar**, click **Data** . The **Data** window will open.
 - On the **File** menu, click **Open**. The file **study_0.dat** should appear in the list (if it does not, find the folder where you put this data file).

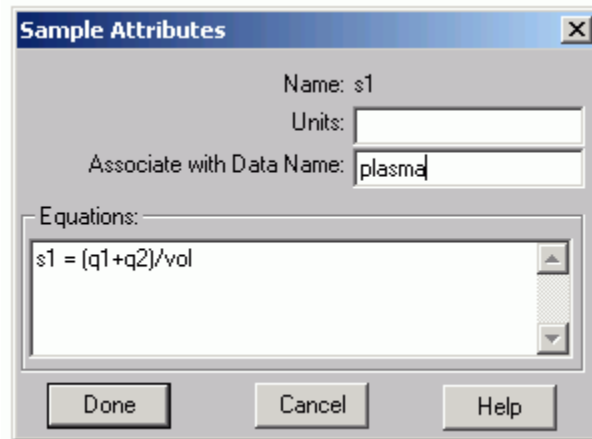
- c. Double-click **study_0**. The data in this file will appear in the **Data** window. The model and the **Data** window should appear with the model on the **Drawing Canvas** as follows:



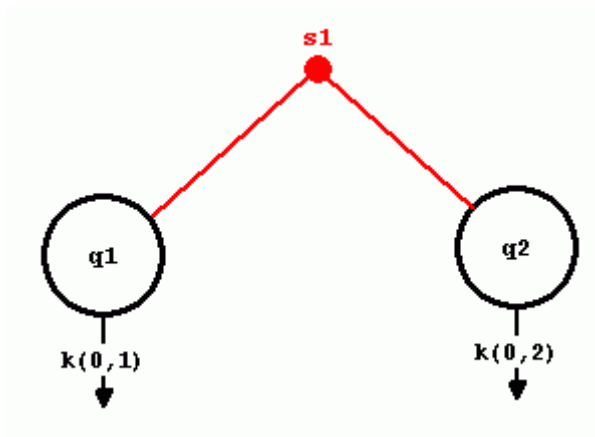
- d. Close the **Data** window.
5. Create the sample on the model.
- In the **SAAM II Toolbox**, click **Sample**.
 - Click Compartment **q1**, then Compartment **q2**, and then click on the **Drawing Canvas**.

A sample object, **s1**, will appear on the **Drawing Canvas** attached to Compartments **q1** and **q2**. This means your sample was from plasma. Notice that the circle at the top of the sample object is an open circle; data have not yet been associated with the sample. The sample object can be moved on the **Drawing Canvas** to a location you desire.

- c. Double-click **s1** to open the **Sample Attributes** dialog box.
- d. Type “plasma” in the **Associate with Data Name** box.
- e. Edit the sample equation “ $s1 = q1+q2$ ” to read “ $s1 = (q1+q2)/vol$ ” in the **Equations** pane. The **Sample Attributes** dialog box will appear as follows:

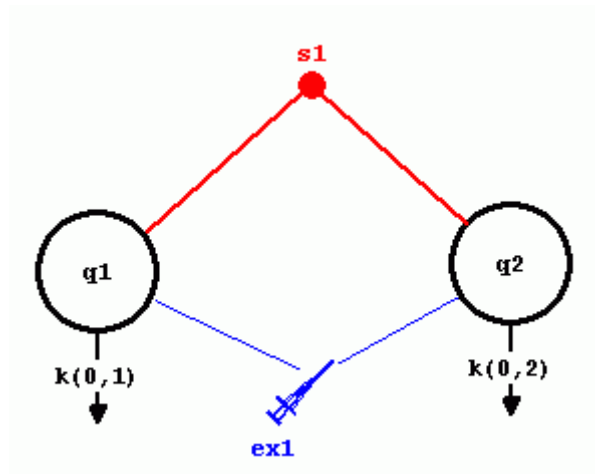


- f. Click **Done**. The model will appear as follows:



7. Create the experimental input
 - a. In the **SAAM II Toolbox**, click **Input**.
 - b. Click Compartment **q1**, then Compartment **q2**, and then click on the **Drawing Canvas**.

An input arrow named **ex1** will appear on the **Drawing Canvas** attached to Compartments **q1** and **q2**. The input syringe can be moved to a desired location. The model will appear as follows:



- c. Double-click **ex1** to open the **Exogenous Input** dialog box.
- b. Type “1.04e+08” in the **Initial Amount** box.
- e. Click **Add**. The **Exogenous Input** dialog box should appear as follows:

Exogenous Input

Name: Reference Name: Units:

Type	Initial	Constant	Start	Stop	Repeat Every	Nr. Repeats
Bolus	1.04e+8	-	0.000	-	-	-

Input Type:

Bolus
 Infusion
 Primed Infusion
 Equation

Initial Amount:

Constant Rate:

Event Start:

Event Stop:

Repeat Every:

Nr. of Repeats:

Equation:

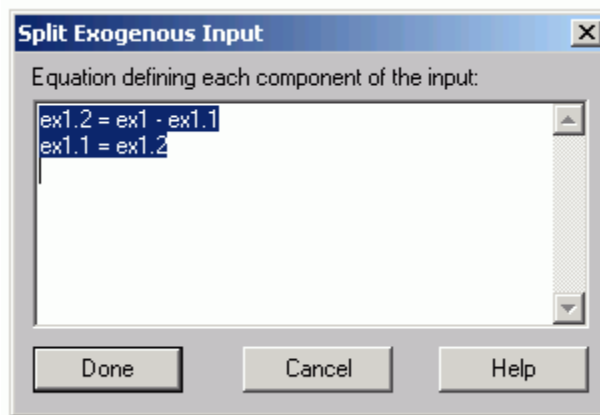
Notice the **Split Input** button is active.



Split inputs. Split inputs occur when your injected test substance is not kinetically homogeneous, but kinetically heterogeneous. This means the input consists of two or more substances with different kinetics. This can be due to a variety of factors including contamination. It is important to be aware when this can happen, and incorporate it into your model.



- f. In the **Exogenous Input** dialog box, click **Split Input**. The **Split Exogenous Input** dialog box will open as follows:



Split Exogenous Input. When you have a split input, you know the total amount of substance given, but you may not know how the substance distributes among different compartments. You must write equations which relate the amounts in the different compartments to the total. In this example where the input is a bolus, **ex1** is the total dose. The doses in Compartments **q1** and **q2** are respectively **ex1.1** and **ex1.2**.



- g. In the **Equation** box in the **Split Exogenous Input** dialog box, edit the equations to read:

$$\begin{aligned} \text{ex1.1} &= \text{frac} * \text{ex1} \\ \text{ex1.2} &= (1 - \text{frac}) * \text{ex1} \end{aligned}$$

The **Split Exogenous Input** dialog box together with the **Exogenous Input** dialog box will appear as follows:

Exogenous Input

Name: Reference Name: Units:

Type	Initial	Constant	Start	Stop	Repeat Every	Nr. Repeats
Bolus	1.04e+8	-	0.000	-	-	-

Input Type:

Bolus
 Infusion
 Primed Infusion
 Equation

Initial Amount:

Constant Rate:

Event Start:

Event Stop:

Repeat Every:

Nr. of Repeats:

Equation:

Split Exogenous Input

Equation defining each component of the input:


```
ex1.1=frac*ex1
ex1.2=(1-frac)*ex1
```

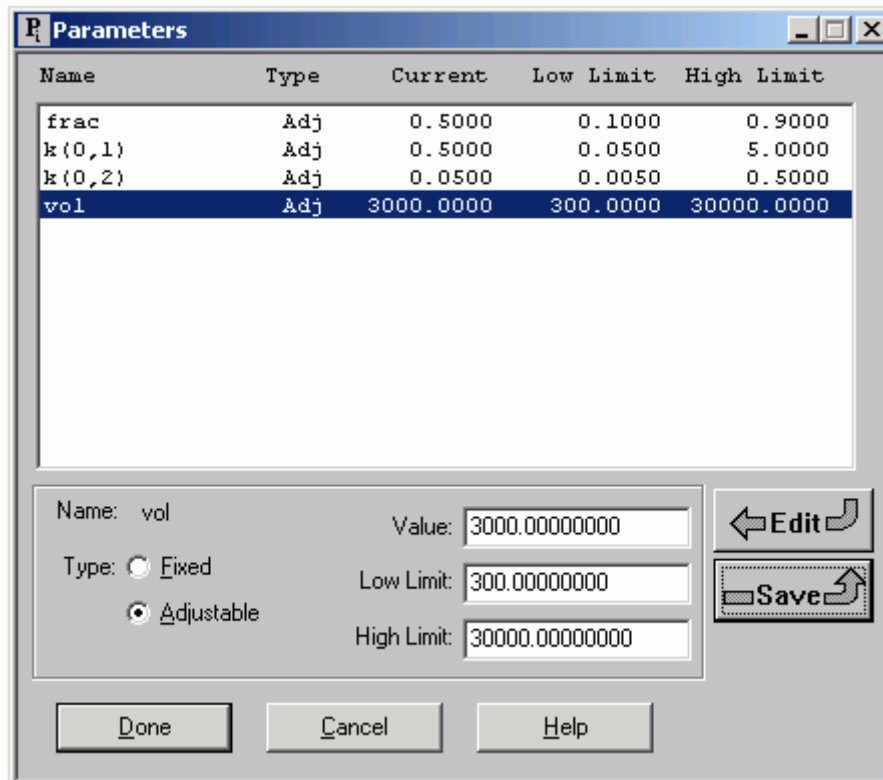


Split exogenous input. The above equations partition the total dose, **ex1**, into two fractions. *frac* will become a parameter whose value lies between 0 and 1. It will be the fraction of the total dose in Compartment **q1**. The value $1 - \textit{frac}$ will be the total dose in Compartment **q2**.



- h. In the **Split Exogenous Input** dialog box, click **Done**. The **Exogenous Input** dialog box will remain as shown above. The only indication of the split input is the **Split Input** option is active.

- i. In the **Exogenous Input** dialog box, click **Done**.
8. Add parameter values to the model.
 - a. In the **Show** menu, click **Parameters**, or alternatively, on the **SAAM II Toolbar**, click **Parameters** . The **Parameters** dialog box will open.
 - b. Add the parameters as shown in the **Parameters** dialog box below:



Name	Type	Current	Low Limit	High Limit
frac	Adj	0.5000	0.1000	0.9000
k(0,1)	Adj	0.5000	0.0500	5.0000
k(0,2)	Adj	0.0500	0.0050	0.5000
vol	Adj	3000.0000	300.0000	30000.0000

Name: vol Value: 3000.00000000

Type: Fixed Low Limit: 300.00000000

Adjustable High Limit: 30000.00000000



Buttons: Done, Cancel, Help, Edit, Save

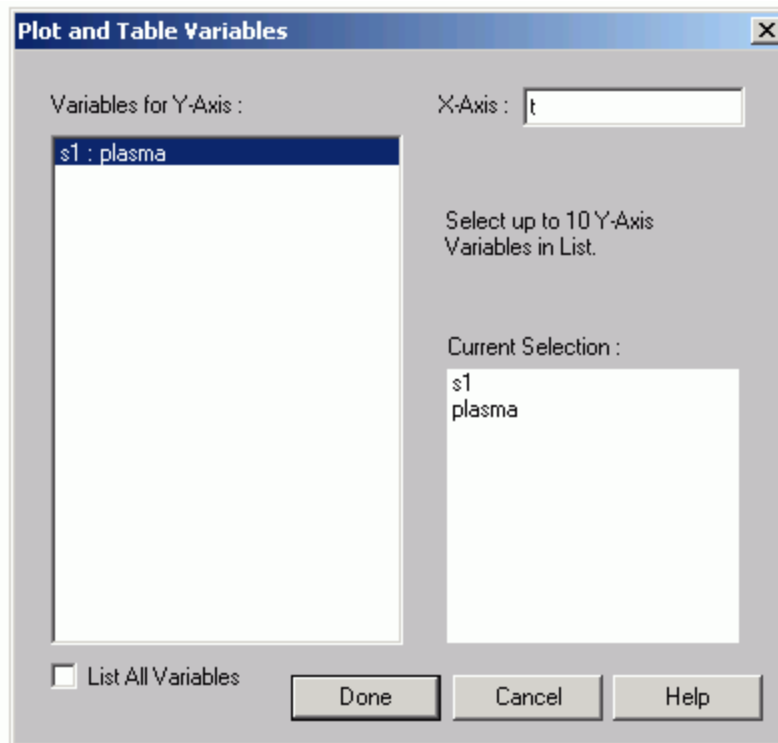


Split exogenous input. In the above, *frac* is a parameter whose value lies between 0.1 and 0.9. Notice also there are four parameters to estimate, the two losses, the volume, and *frac*.

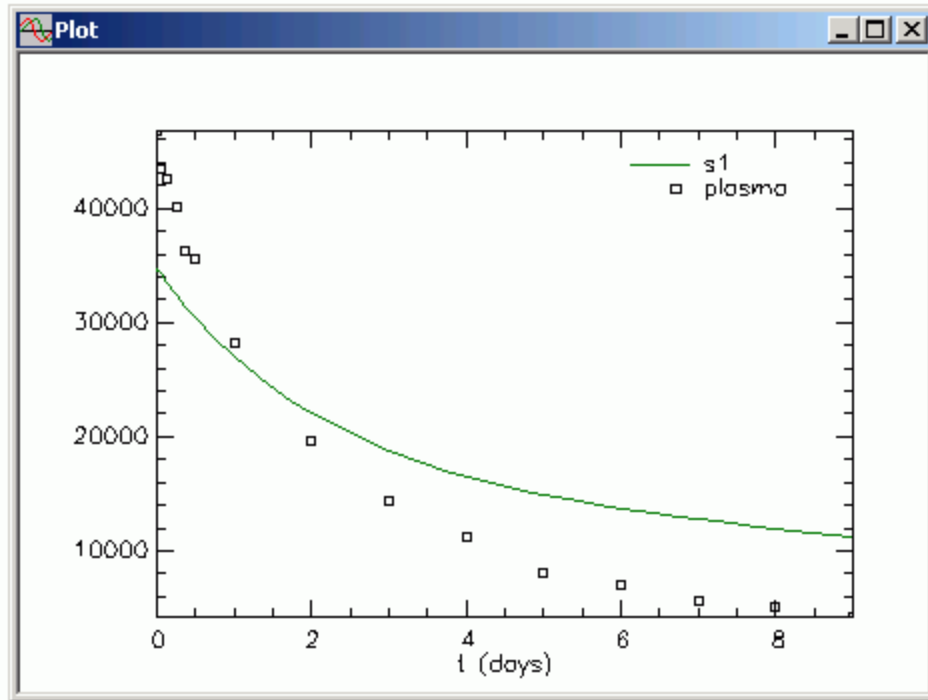


- c. Click **Done**.
9. Solve the model, and view the solution.


- 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:plasma** is the only option in the **Variables for Y-Axis** pane.
- c. Click **s1:plasma** to add this to the **Current Selection** pane. The **Plot and Table Variables** dialog box will appear as follows:

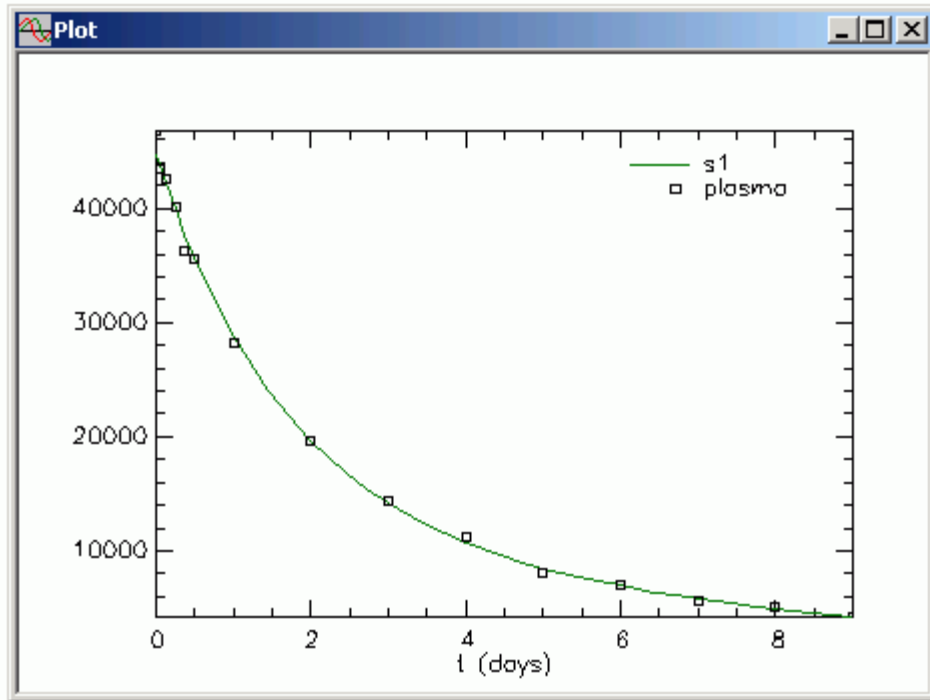



- d. Click **Done**. A plot of **s1** and **plasma** will appear in semilog mode in the **Plot** window as shown below (if it is not in linear mode, in the **View** menu, click **Semilog**):



Leave the **Plot** window open.

7. Fit the model to the data and view the solution.
 - a. In the **Compute** menu, click **Fit**, or alternatively, on the **SAAM II Toolbar**, click **Fit** . Your plot will be updated as follows:



- b. In the **Show** menu, click **Statistics**, or alternatively, on the **SAAM II** **Toolbar**, click **Statistics** . The **Statistics** window will open as follows:

Parameter/Variable	Value	Std.Dev.	Coef. of Var.	95% Confidence Interval	
frac	0.69063	7.13487e-002	1.03310e+001	0.53359	0.84767
k(0,1)	0.61580	7.74012e-002	1.25693e+001	0.44544	0.78616
k(0,2)	0.13455	2.59813e-002	1.93097e+001	0.07737	0.19173
vol	2323.68590	3.85664e+001	1.65971e+000	2238.80155	2408.57024
----- Derived Variables -----					
ex1.1.bolus	7.18255e+007	7.42026e+006	1.03310e+001	5.54936e+007	8.81574e+007
ex1.2.bolus	3.21745e+007	7.42026e+006	2.30625e+001	1.58426e+007	4.85064e+007

		Objective		Scaled Data Variance	
s1 : plasma	1.336743e+001			1.113512e-001	

Total objective	1.336743e+001				
AIC	7.935986e+000				
BIC	8.053994e+000				

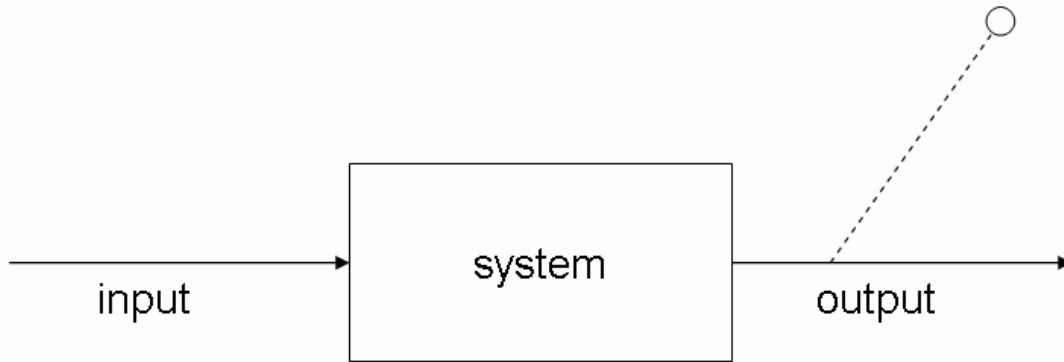
The model parameters are estimated with good precision. The value for *frac* is 0.69 which means 69% of the original injected dose is into Compartment **q1**. Under **Derived Variables**, you can see the exact amount of dose in each compartment predicted by the model.

- c. Close the **Statistics** and **Plot** windows.

Quit the **SAAM II Compartmental** application. You may save the study file if you wish.

Part 4. Parametric deconvolution

Deconvolution is the technique used to address the following problem. There is a known system and a known output from an unknown input. The problem is to calculate the unknown input. The problem is shown diagrammatically as follows:



There are basically two ways to deal with this problem. One is called nonparametric deconvolution. This is an extremely difficult problem. The other is called parametric deconvolution.

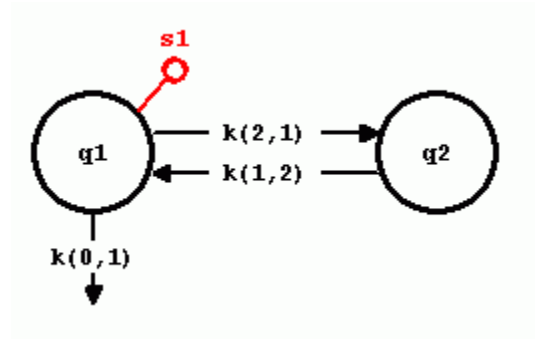
In parametric deconvolution, the following are assumed:


- The exact specification of the system model (in terms of a compartmental model, this means the structure and all parameter values).
- There are output data.
- The specification of the input is known (in terms of the situation here, this means the equation for the input is known but the parameters of the equation are unknown and will be estimated from the data).

This part of the tutorial will illustrate how to perform parametric deconvolution using SAAM II.

1. **Start** the **SAAM II Compartmental** application. The **SAAM II Compartmental** main window will open as shown below:
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. In the **SAAM II Toolbox**, click **Experiment**. The model of the experiment for **study_0_ExpInp.stu** will appear on the **Drawing Canvas** as follows:




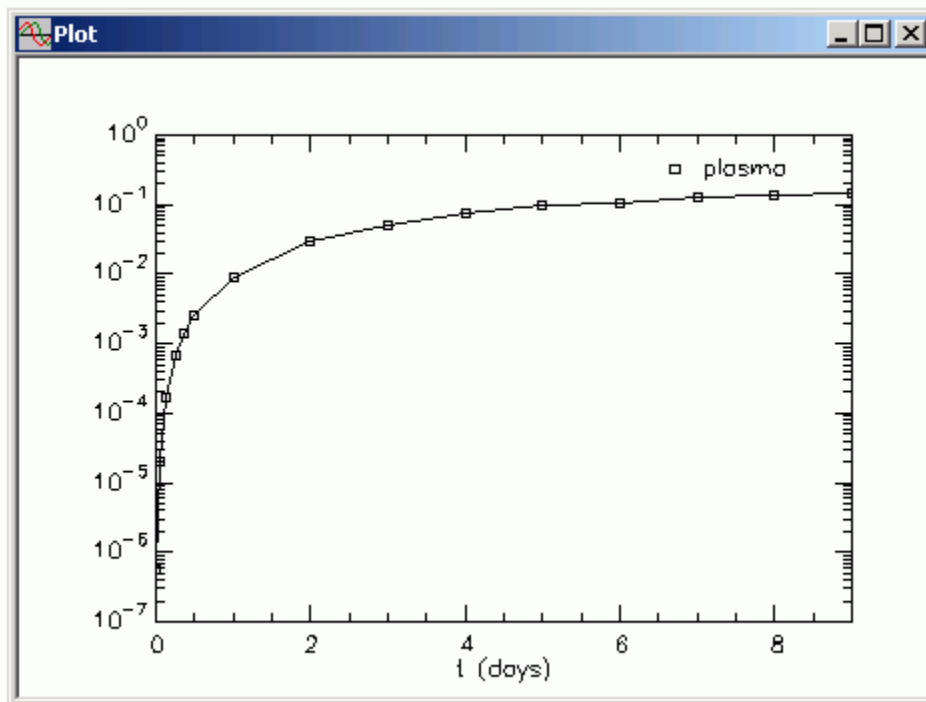
3. Enter and view the data.
- In the **Show** menu, click **Data**, or alternatively, on the **SAAM II Toolbar**, click **Data** . The **Data** window will open.
 - In the **File** menu, click **Open**. The file **paradecon_ExpInpUS.dat** should appear in the list (if it does not, find the folder where you put this data file).
 - Double-click **paradecon_ExpInpUS.dat**. The data in this file will appear in the **Data** window as follows:

```

DATA
(FSD 0.1)
plasma
0.007 5.44E-07
0.042 1.98E-05
0.125 1.74E-04
0.250 6.74E-04
0.375 1.39E-03
0.50 2.60E-03
1.0 8.92E-03
2.0 2.90E-02
3.0 4.92E-02
4.0 7.51E-02
5.0 9.60E-02
6.0 0.104
7.0 0.125
8.0 0.137
9.0 0.142
END
Data Format is okay
  
```

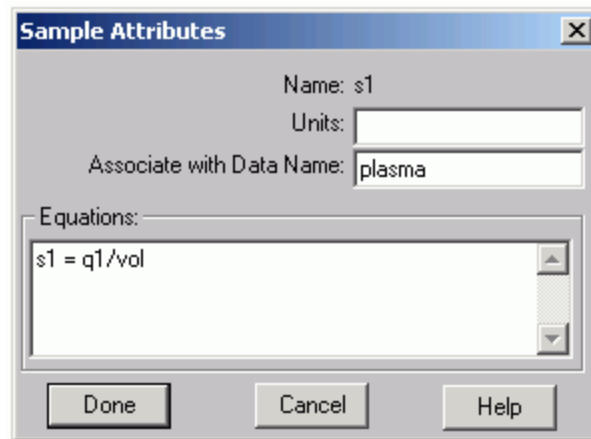
These are simulated data obtained when an exponential input was specified and samples were created at the same time samples were taken in the data file **study_0.dat**.

- d. Close the **Data** window.
- 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.
- f. Be sure the **List All Variables** check box is selected. (Click this box if it is not selected).
- g. Click **plasma** to move it to the **Current Selection** pane.
- h. Click **Done**. A plot of the data will appear in the **Plot** window.
- i. In the **View** menu, click **Line Plot**.
- j. In the **View** menu, be sure **Semilog** is selected. Your plot will appear as follows:



These are the output data. The problem is to specify an input function format, and to estimate the parameters of this input from the data.

- k. Close the **Plot** window.
4. Associate the sample **s1** with the **plasma** data.
 - a. Double-click **s1** to open the **Sample Attributes** dialog box.
 - b. In the **Associate with Data Name** box, type “plasma”. The **Sample Attributes** dialog box will appear as follows:



- c. Click **Done**.
5. Specify and define the input function.

In this example, the input function is assumed to be known, and be equal to $A * (\exp(-a*t) - \exp(-b*t))$. This will be entered as equation input, and the parameters A , a and b estimated from the data.

- a. In the **SAAM II Toolbox**, click **Input**.
- b. Click on Compartment **q1** and then the **Drawing Canvas**. The input **ex1** will appear.
- c. Double-click **ex1** to open the **Exogenous Input** dialog box.
- d. Specify the equation input.
 - (1) In the **Input Type** pane, select **Equation**
 - (2) In the **Equation** box, type “ $ex1=A*(\exp(-a*t)-\exp(-b*t))$ ”.
 - (3) In the **Event Start** box, type “0”.

- (4) In the **Event Stop** box, type “9”. (Remember the time of the experiment in **study_0** is 9 days). Click **Add**. The **Exogenous Input** dialog box will appear as follows:

Exogenous Input

Name: Reference Name: Units:

Type	Initial	Constant	Start	Stop	Repeat Every	Nr. Repeats
Equation	ex1 = A*(exp(-a*t))	0.000	9.000	-	-	-

Input Type:

Bolus
 Infusion
 Primed Infusion
 Equation

Initial Amount:

Constant Rate:

Event Start:


Event Stop:

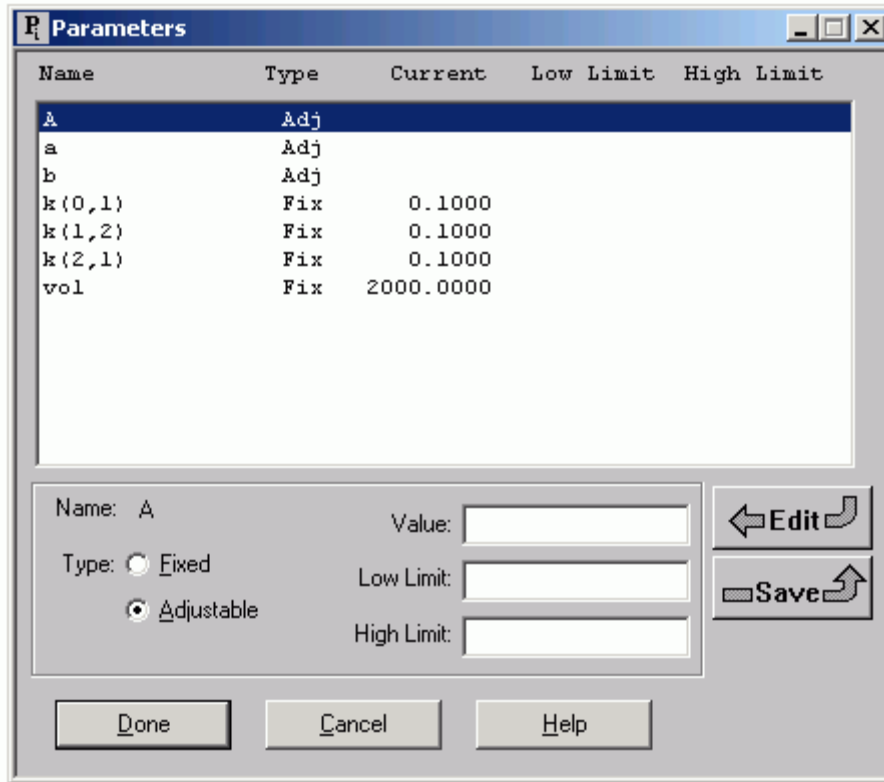
Repeat Every:

Nr. of Repeats:

Equation:

- (5) Click **Done**.

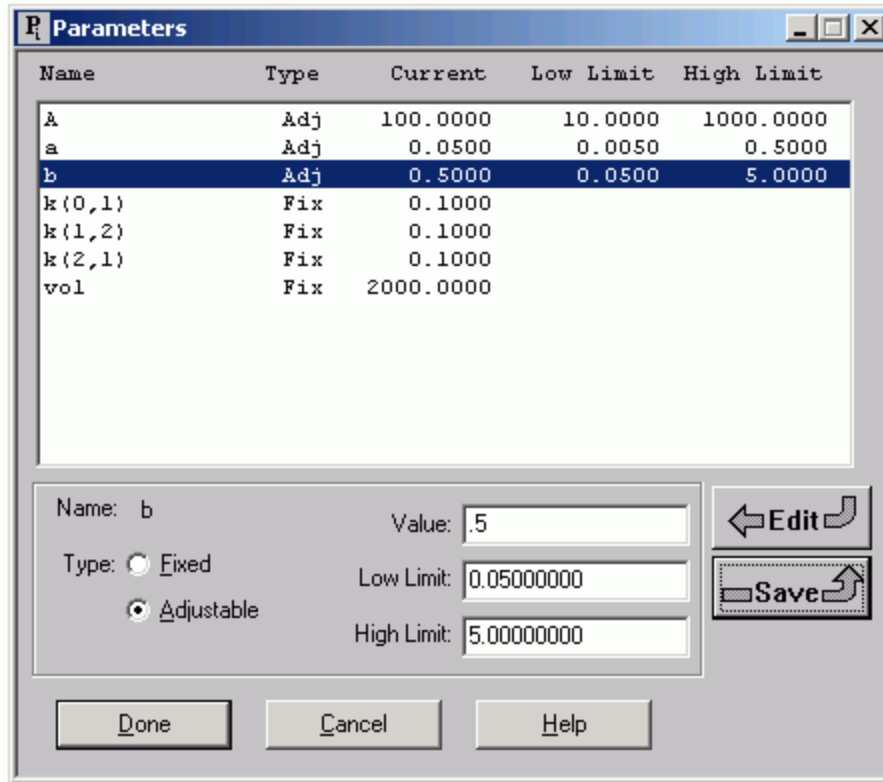
6. Specify the parameter values.
- a. In the **Show** menu, click **Parameters**, or alternatively, on the **SAAM II Toolbar**, click **Parameters** . The **Parameters** dialog box will open, as shown below:



The model parameters are all present and fixed. These are the $k(i,j)$ and vol . In parametric deconvolution, the model parameters are assumed to be known precisely, and hence must be fixed.



The unknown model parameters are those characterizing the input function. In parametric deconvolution, the “type” of input function is assumed to be known but the parameters of the function are unknown. In this case, these parameters are A , a and b .

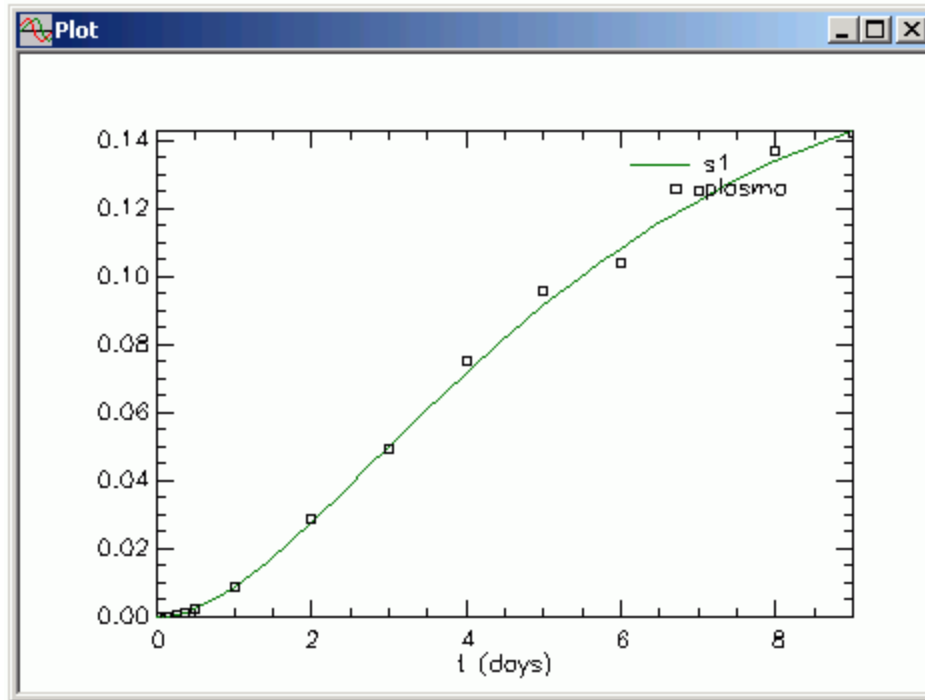
- b. Enter the parameter values.
 - (1) If A is not selected, double-click A to select it. Type “100” in the **Value** box, and click **Save**.
 - (2) Double-click a to select it. Type “0.05” in the **Value** box, and click **Save**.
 - (3) Double-click b to select it. Type “0.5” in the **Value** box, and click **Save**.
The **Parameters** dialog box will appear as follows:




(4) Click **Done**.

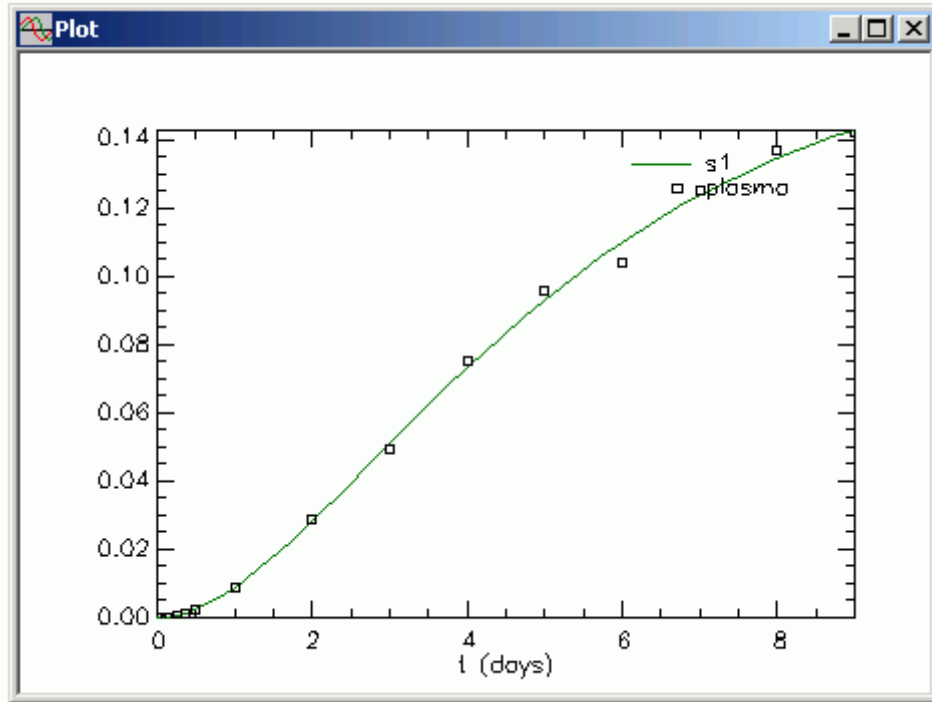
7. Solve the model and view the solution.

- 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.
- c. Click **s1:plasma** to move this to the **Current Selection** pane. Your plot will appear as shown below (in linear mode).




Leave the **Plot** window open.

8. Fit the model to the data and view the results.
 - a. In the **Compute** menu, click **Fit**, or alternatively, on the **SAAM II Toolbar** click **Fit** . The plot will be updated as follows:



Close the **Plot** window.


- b. In the **Show** menu, click **Statistics**, or alternatively, on the **SAAM II** **Toolbar**, click **Statistics** . The **Statistics** window will open as follows:

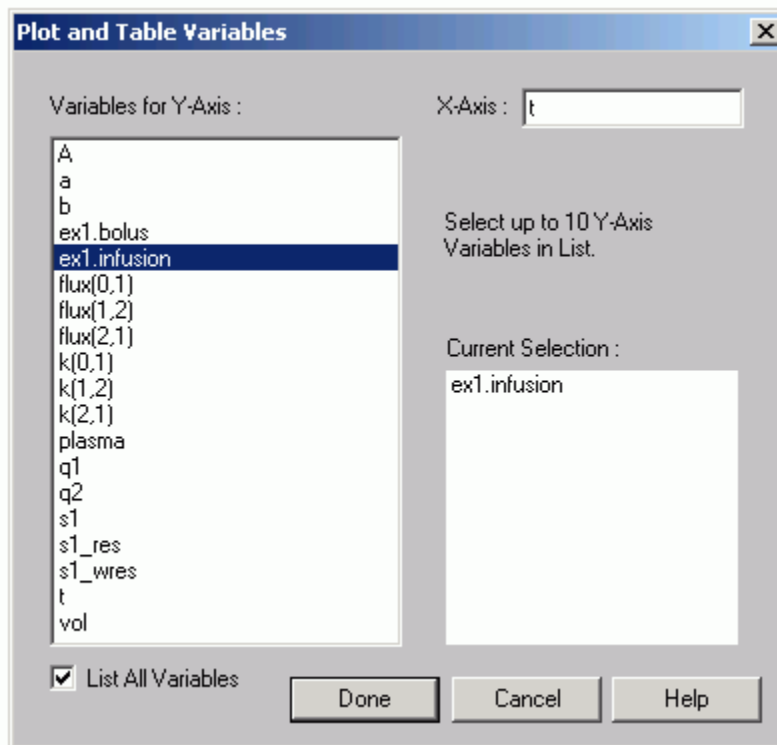
Parameter/Variable	Value	Std.Dev.	Coef. of Var.	95% Confidence Interval	
A	114.82347	2.50059e+001	2.17777e+001	60.34040	169.30655
a	0.06763	2.88858e-002	4.27142e+001	0.00469	0.13056
b	0.46192	5.99843e-002	1.29858e+001	0.33123	0.59262
k(0,1)	0.10000	** Fixed **	** Fixed **	** Fixed **	** Fixed **
k(1,2)	0.10000	** Fixed **	** Fixed **	** Fixed **	** Fixed **
k(2,1)	0.10000	** Fixed **	** Fixed **	** Fixed **	** Fixed **
vol	2000.00000	** Fixed **	** Fixed **	** Fixed **	** Fixed **

Correlation Matrix
 Covariance Matrix
 Objective

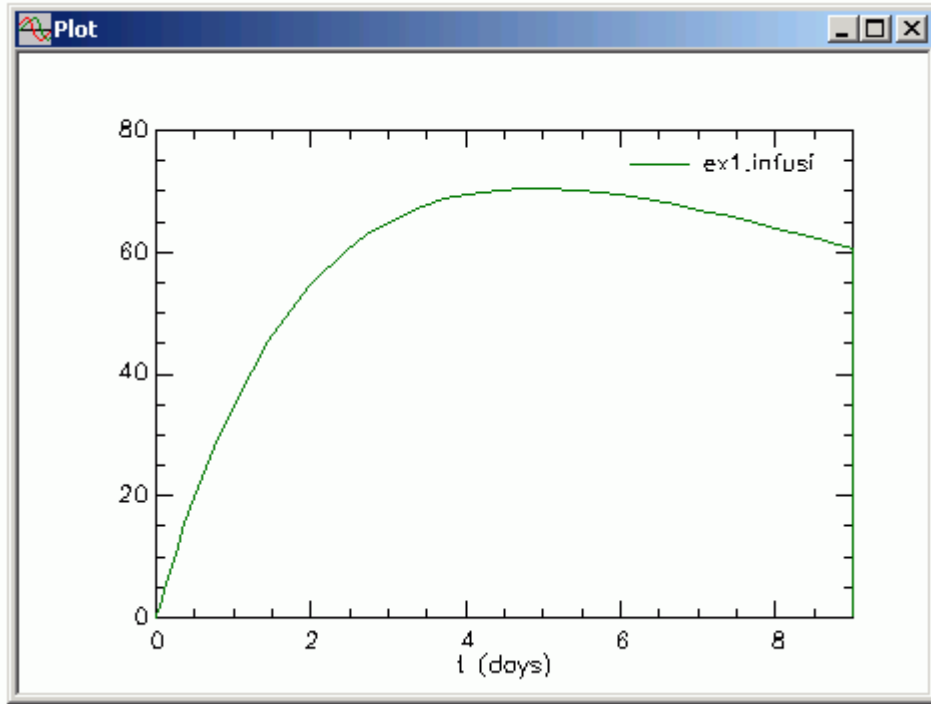
	Objective	Scaled Data Variance
s1 : plasma	-1.662886e+001	9.349419e-002
Total objective	-1.662886e+001	
AIC	-7.128827e+000	
BIC	-7.034420e+000	

Close the **Statistics** window.

9. View the unknown input function.
 - a. In the **Show** menu, click **Plot**, or alternatively, on the **SAAM II Toolbar**, click **Plot** . Your previous plot should open.
 - b. 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.
 - c. Click **ex1.infusion** to move this to the **Current Selection** pane. The **Plot and Table Variables** dialog box will appear as follows:



- d. Click **Done**. The plot of the unknown input function will appear as follows (the plot is in linear mode, and the **Y Axis maximum** has been set equal to 80):



e. Close the **Plot** window.

Quit the SAAM II Compartmental application. Do not save the changes to **study_0**.