

Using SAAM II

Working with Change Conditions

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Working with Change Conditions

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 use Change Conditions in SAAM II. You will learn

- How to create continuous changes in your model (Part 1)
- How to create instantaneous changes at different times in your model (Part 2)
- How to create instantaneous changes at an equal time interval in your model (Part 3)

Files Required

Study Files: The study files for this tutorial are

cc_cont.stu
cc_instInulin.stu
cc_instLDL

Data Files: The data files for this tutorial are:

cc.cont.dat
cc.instInulin.dat
cc.instLD.dat

These files are included as part of this tutorial.

Introduction

This tutorial will show you how to use Change Conditions, a tool in the SAAM II **Toolbox**. Change conditions allow you to describe experimental perturbations in your model. There are two kinds of perturbations – continuous and instantaneous.

An example of a continuous perturbation would be an experiment in which at some known time, something was done that altered the characteristics of the data. You might want to account for this by changing the value or one or more of your model parameters.

The start would begin at some known time, and continue until the experiment ended, or another experimental perturbation occurred.

An example of an instantaneous perturbation would be urine collections. In the urine collection, the container holding the urine would be emptied at the time specified, and the collection for the next period would begin. You can model this by including a compartment for individual urine samples, and “emptying” it at the end of the collection period.

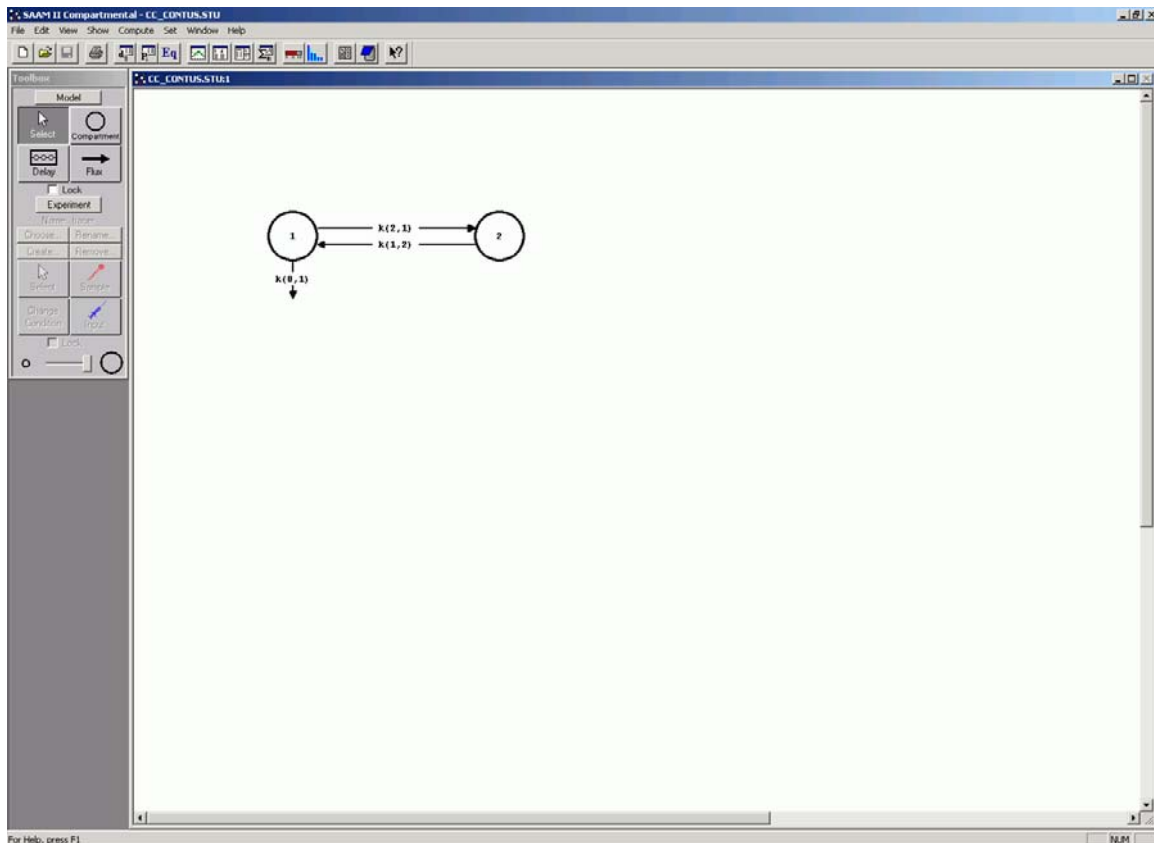
Two examples are presented. Inulin kinetics is a simpler model because inulin is represented by a single plasma compartment. The collection times, however, do not always coincide with a plasma measurement. LDL kinetics is a more complex model because plasma LDL exists in two plasma compartments. The collection times, however, are at 24 (daily) intervals.

Operationally when SAAM II detects a Change Condition, integration (simulation) will stop. The change or changes specified will be made, and integration (simulation) or optimization (fitting) will start again.

Part 1. A continuous Change Condition

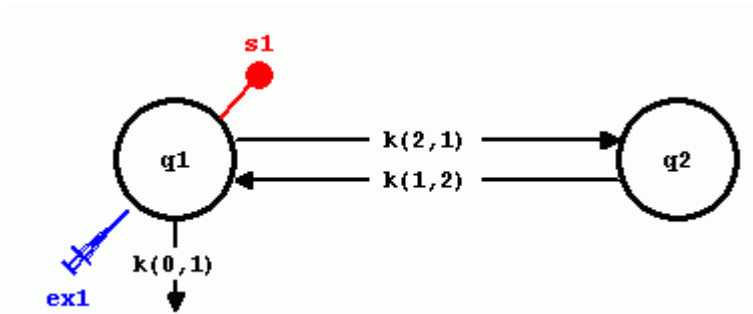
The following study investigated the effect of total parental nutrition (TPN) on the kinetics of low density lipoprotein (LDL) metabolism. Radioiodinated LDL was injected at time zero, and on day 9, TPN was commenced. The experiment lasted 19 days. The question asked was the following: Which of the model parameters change as a result of the TPN?


1. Start the **SAAM II Compartmental** application. The **SAAM II Compartmental** main window will open.
2. Open the **SAAM II Compartmental** study file **cc_cont**.
 - a. The file **cc_cont.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:

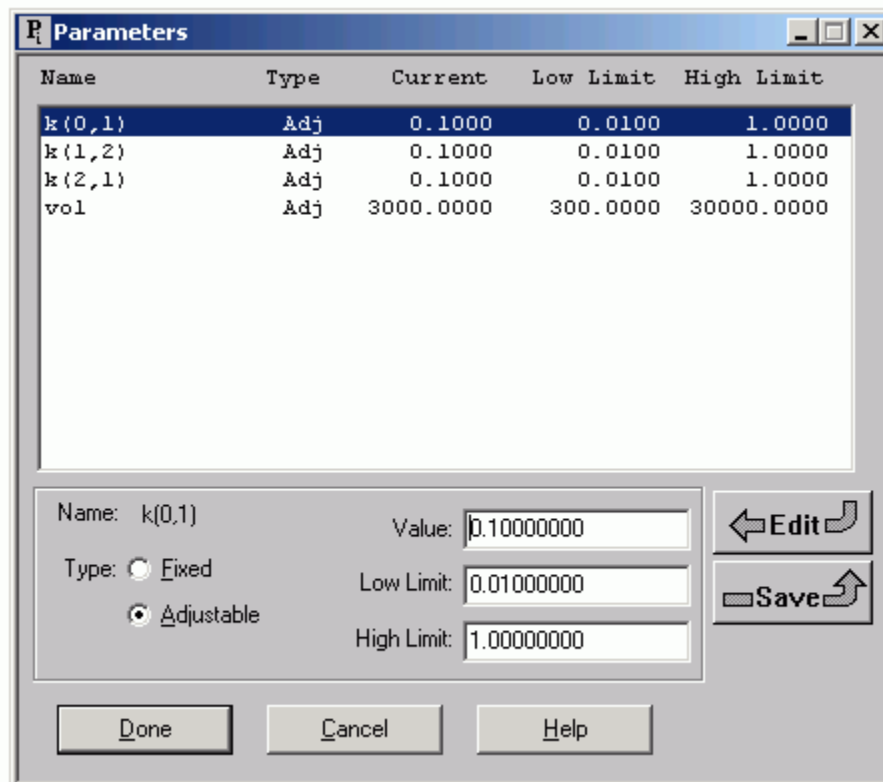


You may recognize this as the model used for **study_0**, the study file supplied with SAAM II. This is in fact the case. The data used for **study_0** are the first 9 days of the data used in this part of the tutorial.

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




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

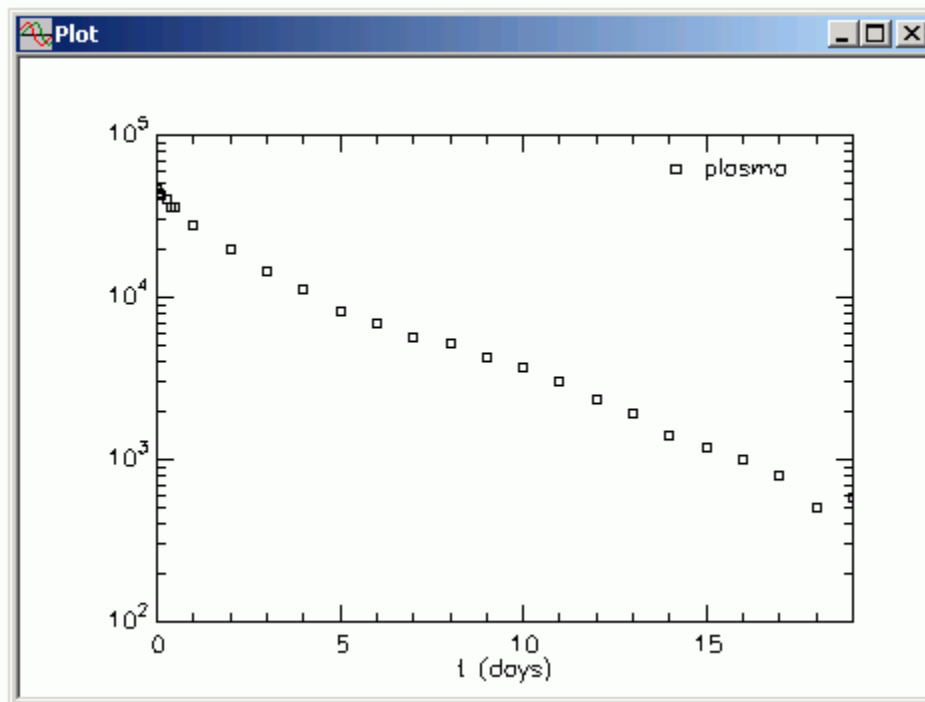


These are the parameters for **study_0**. The question posed in this part of the tutorial is which of these parameters change following TPN starting on day 9.

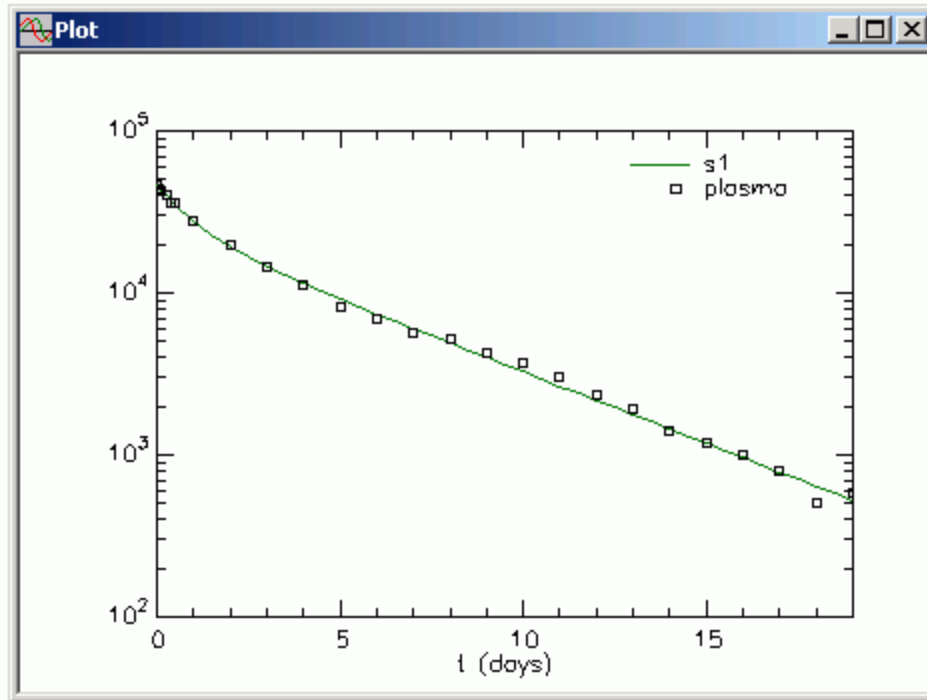
- c. Close the **Parameters** dialog box.
4. View the plasma data.

An important part of deciding how to deal with a continuous change is to look at the raw data to see if a change is obvious.

- a. 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 selected.
- b. Click **plasma** to move this to the **Current Selection** pane.
- c. Click **Done**. The plot of the plasma data will appear in semilog for as follows:



You can see there appears to be a break in the curve at day 9. You can actually solve the model, and see how the model predicts the data. Fit the model to the data, and change the **Plot/Table Variables** to **s1:plasma**. You will obtain the following plot which only further supports a change at day 9:



- d. Close the **Plot** window.
5. Change the value of $k(1,2)$ and $k(0,1)$ from day 9 to 19.

It is hypothesized that these two parameters change following TPN. Such a change will be done using continuous Change Conditions.

You must first provide values for these parameters up to day 9, and then provide values following TPN on day 9. This will be done as described below.

- a. Double-click $k(0,1)$ to open the **Loss Attributes** dialog box.
- b. In the **Equations** box, type the equation “ $k(0,1)=\text{loss_bef}$ ”. The **Loss Attributes** dialog box will appear as follows:

Loss Attributes

Transfer Coefficient: $k(0,1)$

Reference Name:

Flow Rate: $\text{flux}(0,1) = k(0,1) * q1$

Flow Rate Units:

Equations :

Parameter Data

$k(0,1)$

Type:

Fixed

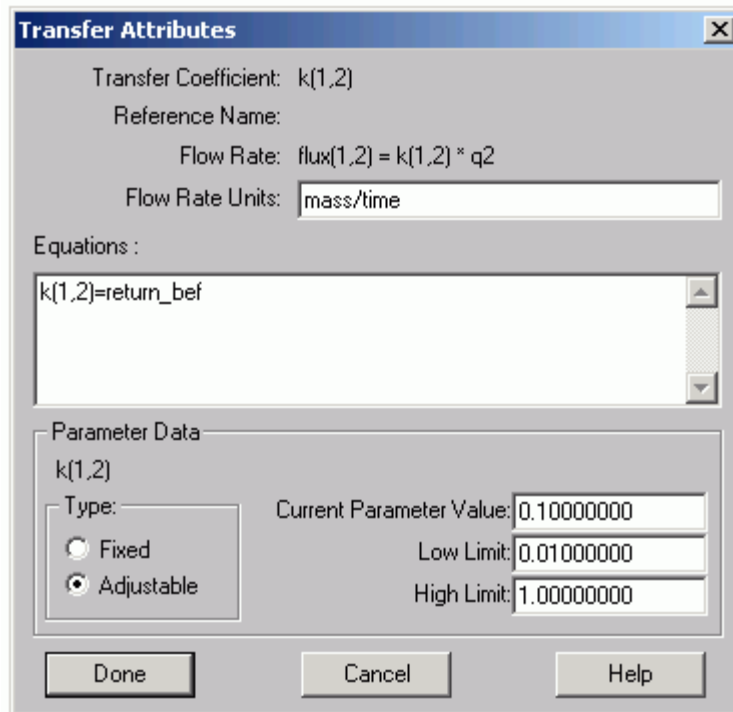
Adjustable

Current Parameter Value:

Low Limit:

High Limit:

- c. Click **Done**. The parameter $k(0,1)$ is now defined by the equation, and *loss_bef* will appear as a parameter in the **Parameters** dialog box.
- d. Double-click $k(1,2)$ to open the **Transfer Attributes** dialog box.
- e. In the **Equations** box, type the equation " $k(1,2)=\text{return_bef}$ ". The **Transfer Attributes** dialog box will appear as follows:



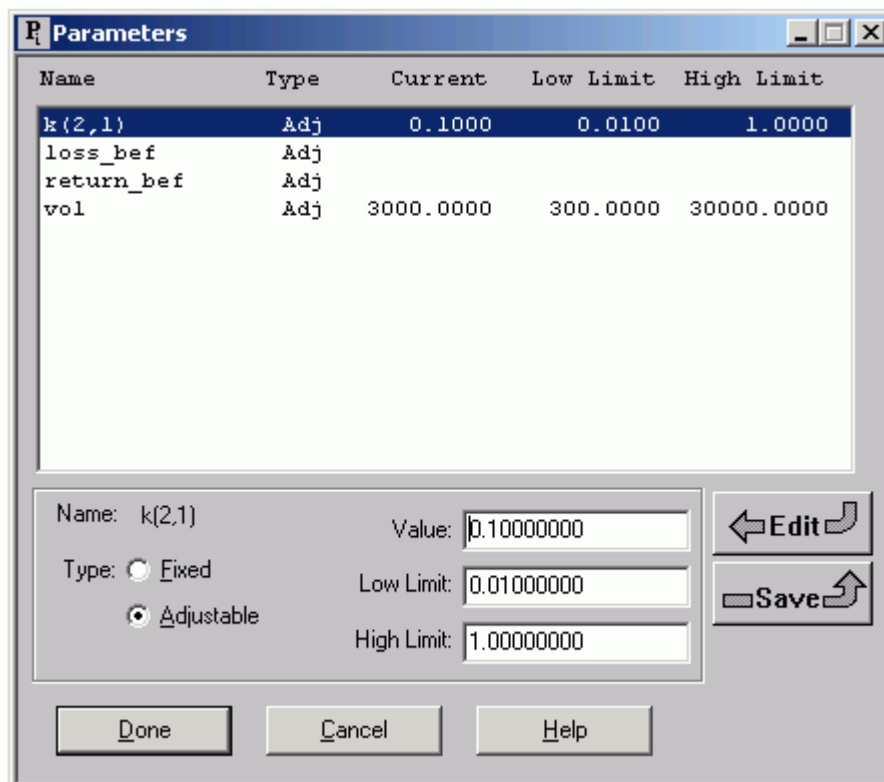
Transfer Attributes

Transfer Coefficient: $k(1,2)$
Reference Name:
Flow Rate: $\text{flux}(1,2) = k(1,2) * q2$
Flow Rate Units:

Equations :

Parameter Data
 $k(1,2)$
Type: Fixed Adjustable
Current Parameter Value:
Low Limit:
High Limit:

- f. Click **Done**. The parameter $k(1,2)$ is now defined by the equation, and *return_bef* will appear as a parameter in the **Parameters** dialog box. If you open the **Parameters** dialog box, it will appear as follows:



Parameters

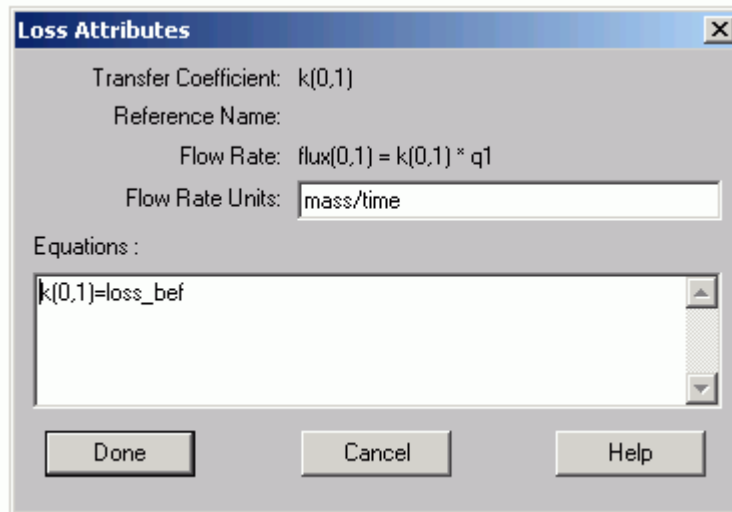
Name	Type	Current	Low Limit	High Limit
$k(2,1)$	Adj	0.1000	0.0100	1.0000
loss_bef	Adj			
return_bef	Adj			
vol	Adj	3000.0000	300.0000	30000.0000

Name: $k(2,1)$ Value:
Type: Fixed Adjustable
Low Limit:
High Limit:

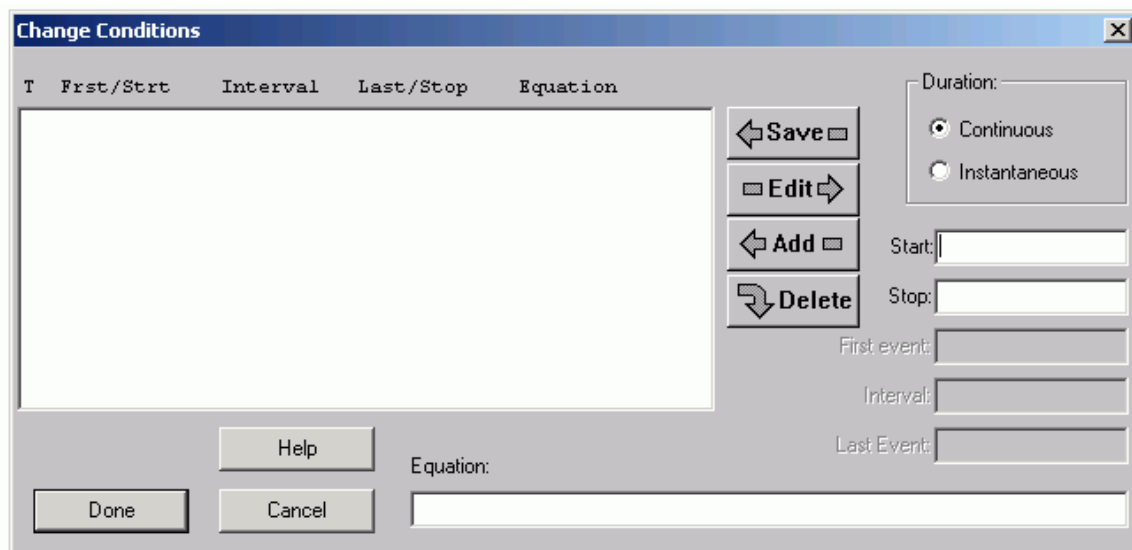
Close the **Parameters** dialog box.



Transfer and Loss Attributes dialog boxes. When you open either of these boxes, they will appear as shown above. However, once you define a parameter by an equation, the lower pane will not appear if you open them again. For example, if you double-click $k(0,1)$ to open the **Loss Attributes** dialog box, it will appear as follows:



- g. In the **SAAM II Toolbox**, click **Change Condition**. The **Change Conditions** dialog box will open as follows:

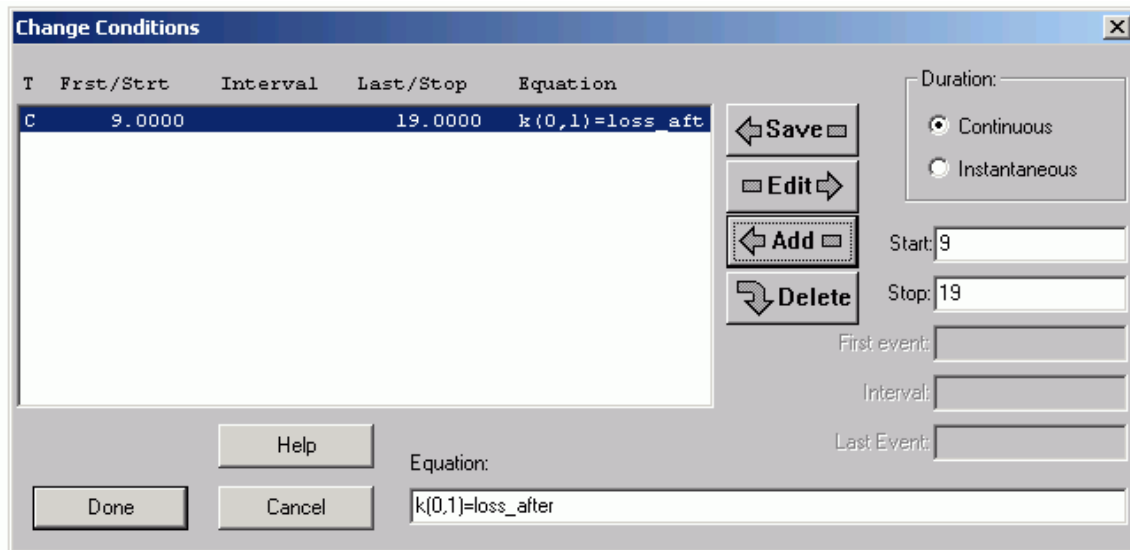




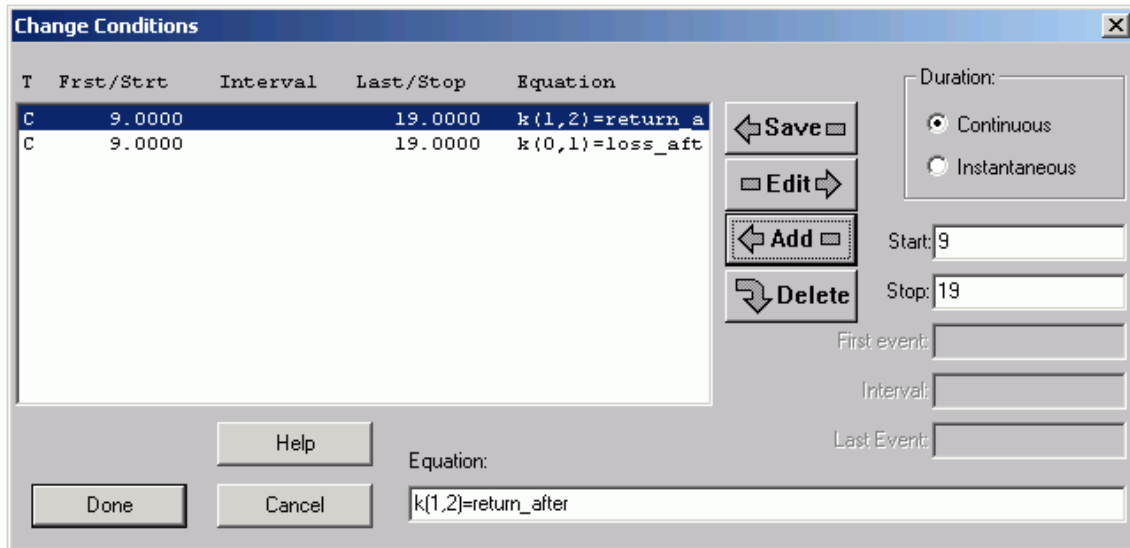
Change Conditions dialog box. The **Change Conditions** dialog box contains the **Duration** pane where you set the Change Condition to be **Continuous** (default) or **Instantaneous**. You set the **Start** and **Stop** times in the boxes below this pane. If the Change Condition is **Instantaneous**, the **First event**, **Interval**, and **Last Event** boxes will be active. You define the change in the **Equation** box.



- h. In the **Start** box, type “9”.
- i. In the **Stop** box, type “19”.
- j. In the **Equation** box, type “k(0,1)=loss_after”
- k. Click **Add**. The **Change Conditions** dialog box will appear as follows:



- l. Edit the equation to read “k(1,2)=return_after”
- m. Click **Add**. The **Change Conditions** dialog box will appear as follows:



n. Click **Done**.



Using Change Conditions. While the above shows you how to change the value of one or more parameters, there are assumptions that must be made about the particular system being studied. In this case, the data are being analyzed using a constant coefficient model. The values of the two parameters $k(0,1)$ and $k(1,2)$ change instantaneously at day 9, and remain at the new value throughout the rest of the experiment. Is this realistic? That is, will the parameter values change that quickly? The assumption here is that, relative to the daily sampling, the change does occur that fast.



6. Add parameter values to the model as shown in the **Parameters** dialog box below:

Name	Type	Current	Low Limit	High Limit
k(2,1)	Adj	0.1000	0.0100	1.0000
loss_aft	Adj	0.3000	0.0300	3.0000
loss_bef	Adj	0.3000	0.0300	3.0000
return_aft	Adj	0.0200	0.0200	2.0000
return_bef	Adj	0.0200	0.0200	2.0000
vol	Adj	3000.0000	300.0000	30000.0000

Name: k(2,1) Value: 0.10000000

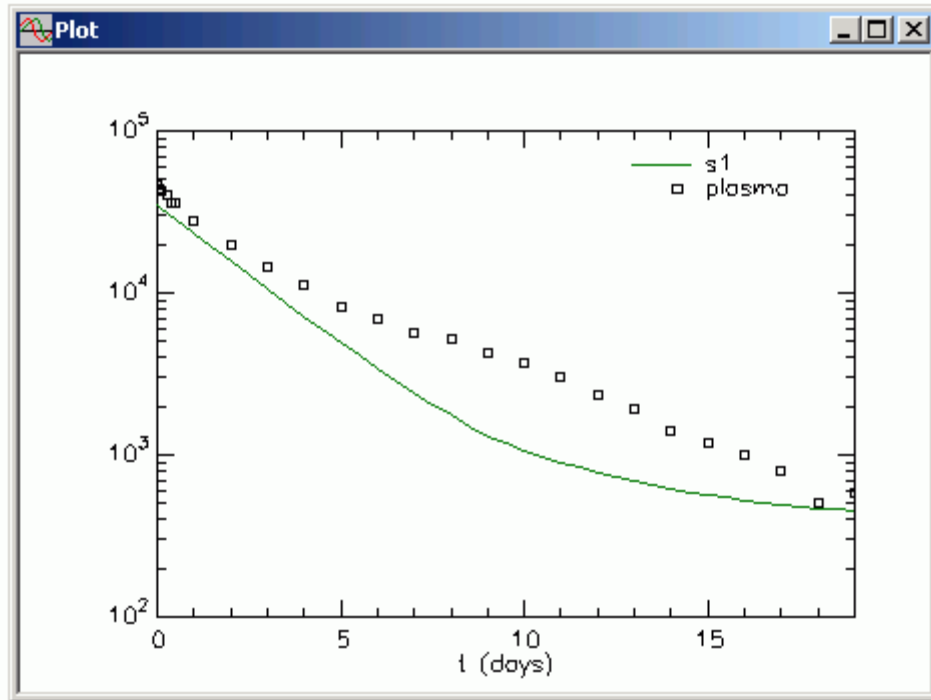
Type: Fixed Adjustable

Low Limit: 0.01000000 High Limit: 1.00000000

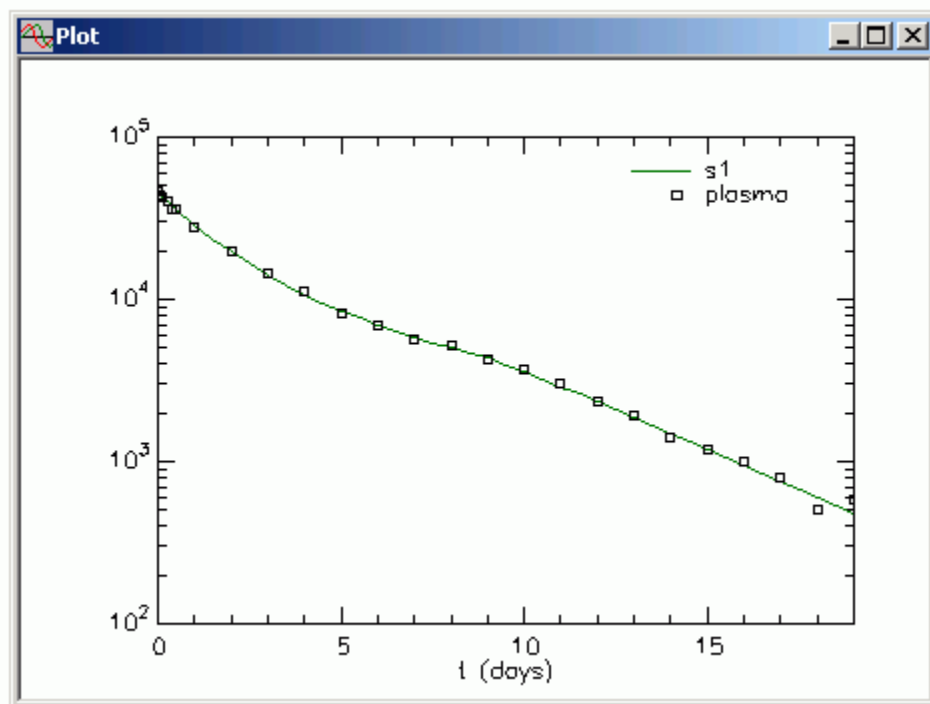
Buttons: Edit, Save, Done, Cancel, Help

Notice the presence now of the values for the loss ($k(0,1)$) and return ($k(1,2)$) before and after the perturbation. All values are the same; they will change when you Fit the model to the data.

7. Solve the model and view the solution. The **Plot** window will appear as follows:



8. Fit the model to the data. The plot will be updated as follows:



You can see that the parameter changes nicely describe the change starting at day 9.

9. View the statistics. The **Statistics** window will appear as follows:

Parameter/Variable	Value	Std.Dev.	Coef. of Var.	95% Confidence Interval	
k(2,1)	0.17849	3.32861e-002	1.86486e+001	0.10882	0.24816
loss_aft	0.48264	1.49857e-001	3.10496e+001	0.16898	0.79629
loss_bef	0.28653	3.20500e-002	1.11855e+001	0.21945	0.35361
return_aft	0.03025	1.38827e-001	4.58984e+002	-0.26032	0.32082
return_bef	0.26165	1.42526e-001	5.44732e+001	-0.03667	0.55996
vol	2323.63441	7.75558e+001	3.33769e+000	2161.30856	2485.96025
----- Derived Variables -----					
k(0,1)	0.28653	3.20500e-002	1.11855e+001	0.21945	0.35361

	Objective	Scaled Data Variance
sl : plasma	1.279055e+001	4.572776e-001

Total objective	1.279055e+001	
AIC	7.594212e+000	
BIC	7.764855e+000	

The statistics are reasonable except that *return_aft* is not well defined, and hence its change is not supported by the data. Open the **Change Conditions** dialog box, and delete the change in $k(1,2)$. Fit the model; the fit will be essentially the same as that shown above. The statistics will change as follows:

Parameter/Variable	Value	Std.Dev.	Coef. of Var.	95% Confidence Interval	
k(2,1)	0.24555	7.93208e-002	3.23027e+001	0.08009	0.41101
loss_aft	0.38529	6.13535e-002	1.59242e+001	0.25730	0.51327
loss_bef	0.31087	2.01238e-002	6.47339e+000	0.26889	0.35285
return_bef	0.48750	1.76706e-001	3.62472e+001	0.11890	0.85610
vol	2279.67858	9.48789e+001	4.16194e+000	2081.76507	2477.59210
----- Derived Variables -----					
k(0,1)	0.31087	2.01238e-002	6.47339e+000	0.26889	0.35285
k(1,2)	0.48750	1.76706e-001	3.62472e+001	0.11890	0.85610

	Objective	Scaled Data Variance
sl : plasma	1.315861e+001	6.276968e-001

Total objective	1.315861e+001	
AIC	7.738242e+000	
BIC	7.884507e+000	

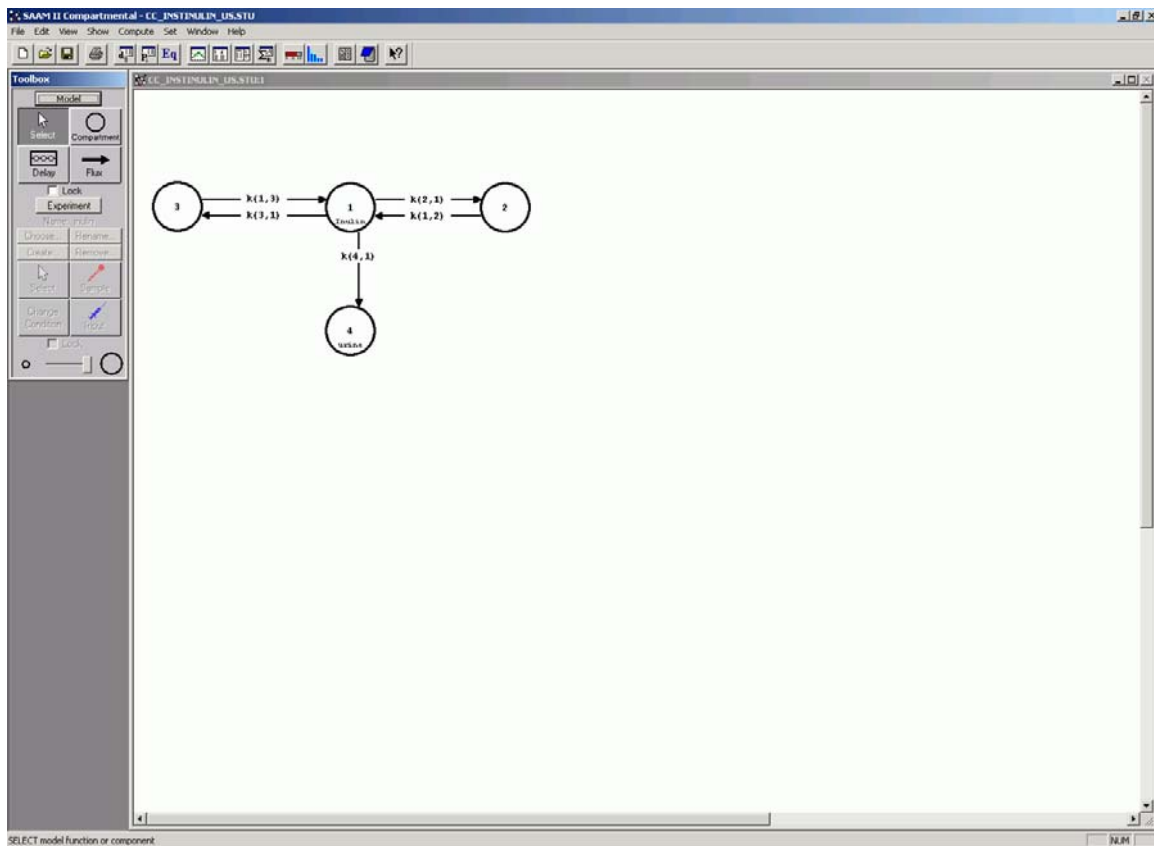
These are better, so a change in the loss is supported by the plasma data. In the actual experiment, urine data were also collected. When these are incorporated into the model, the change in the return is supported by the data.

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

Part 2. An instantaneous Change Condition – inulin kinetics

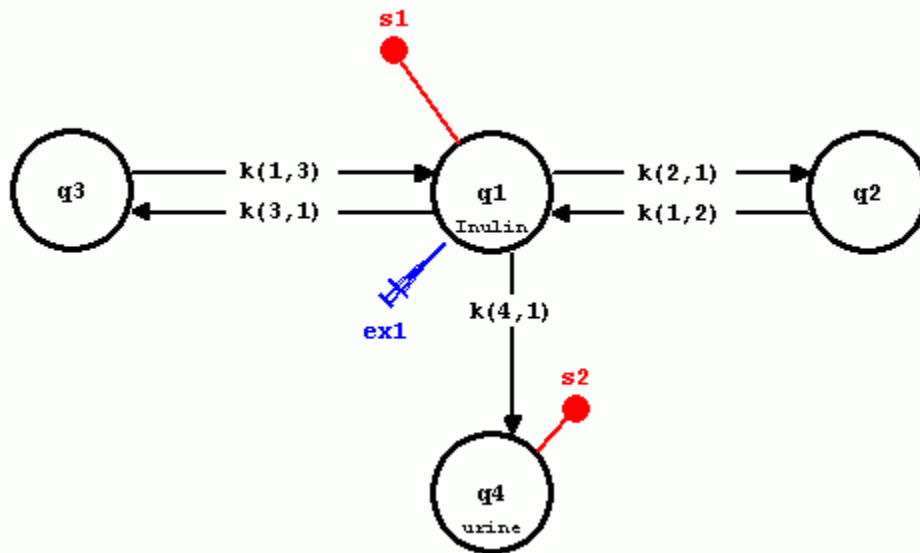
The following study investigated the metabolism of inulin. Inulin is known to be described by a three compartment model, and to be totally excreted in the urine. The experiment lasted 500 minutes. Plasma concentration is mg/L and urine measurements are mg.

1. **Start the SAAM II Compartmental** application. The **SAAM II Compartmental** main window will open.
2. Open the **SAAM II Compartmental** study file **cc_instInulin**.
 - a. The file **cc_instInulin.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:



The model is characterized by a central plasma compartment which exchanges with two peripheral compartments. Excretion in urine, Compartment **4**, is from the plasma compartment, Compartment **1**.

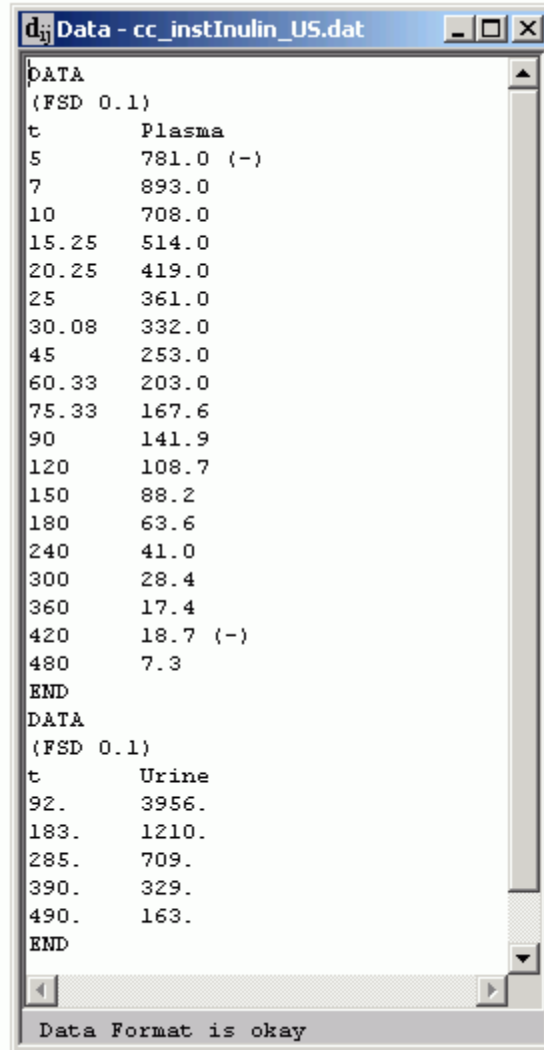
3. View the model and the experiment on the model. In the **SAAM II Toolbox**, click **Experiment**. The model of the experiment will appear on the **Drawing Canvas** as follows:



The plasma samples, **s1**, are the concentration of plasma inulin. Double-click **s1** to view the **Sample Attributes** dialog box. The compartment for the individual urine samples is Compartment **q4**. The sample **s2** links this compartment with the individual urine samples. Double-click **s2** to view the **Sample Attributes** dialog box.

The input is **ex1**. It is a bolus into plasma.

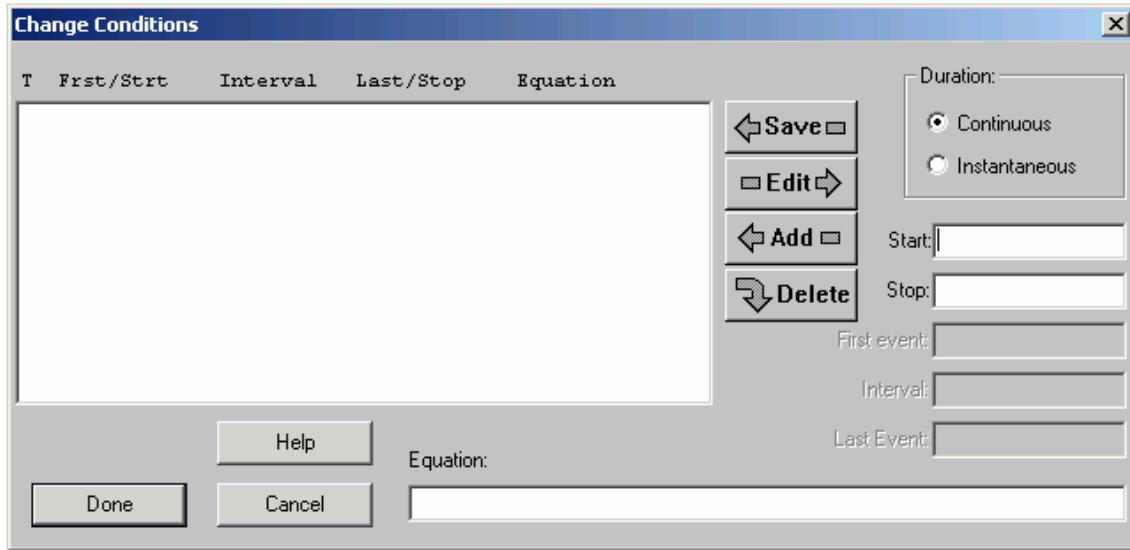
The data to be analyzed are shown in the **Data** window below:



```
DATA
(FSD 0.1)
t      Plasma
5      781.0 (-)
7      893.0
10     708.0
15.25  514.0
20.25  419.0
25     361.0
30.08  332.0
45     253.0
60.33  203.0
75.33  167.6
90     141.9
120    108.7
150    88.2
180    63.6
240    41.0
300    28.4
360    17.4
420    18.7 (-)
480    7.3
END
DATA
(FSD 0.1)
t      Urine
92.    3956.
183.   1210.
285.   709.
390.   329.
490.   163.
END
Data Format is okay
```

The data are entered in two segments, one for plasma and one for the individual urine samples. Notice that the urine collection times do not coincide with the time of plasma samples.

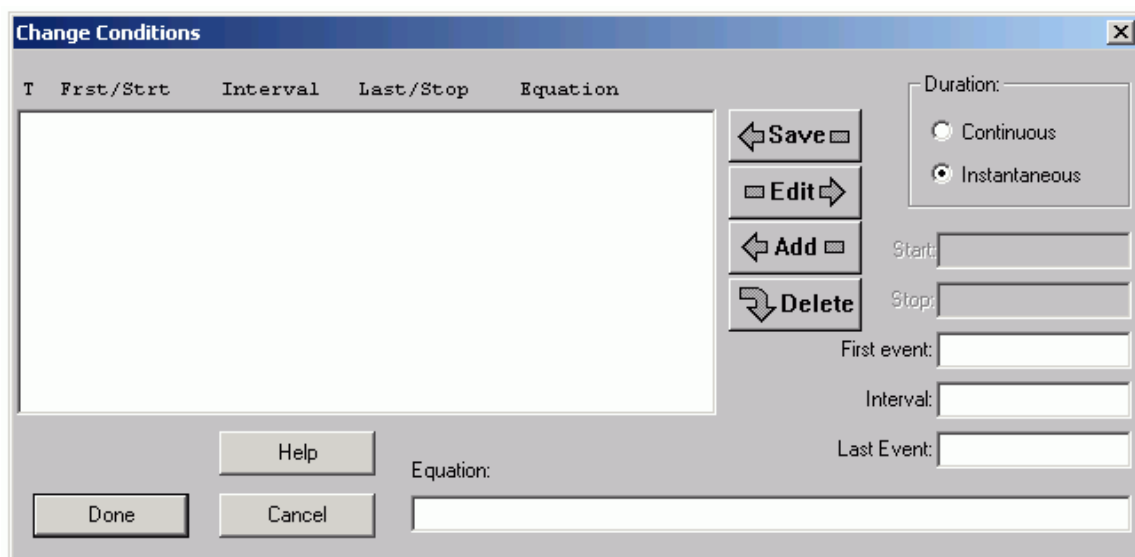
4. Use Change Conditions to model the individual urine collections.
 - a. In the **SAAM II Toolbox**, click **Change Condition**. The **Change Conditions** dialog box will open as shown below:



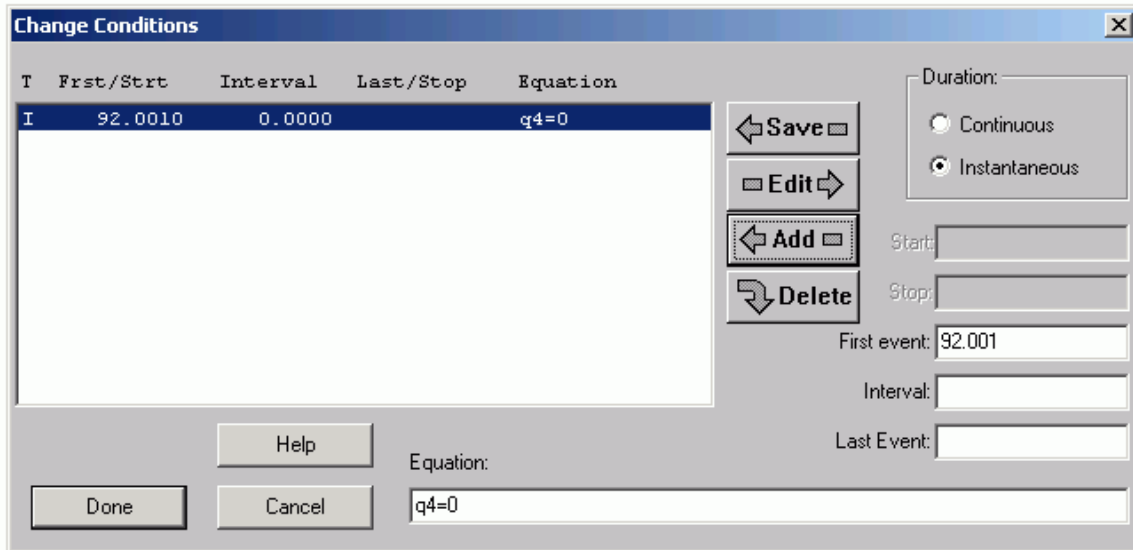
Change Conditions dialog box. The **Change Conditions** dialog box contains the **Duration** pane. The **Duration** pane is where you set the Change Condition to be **Continuous** (default) or **Instantaneous**. You set the **Start** and **Stop** times in the boxes below this pane. If the Change Condition is **Instantaneous**, the **First event**, **Interval**, and **Last Event** boxes will be active. You define the change in the **Equation** box.



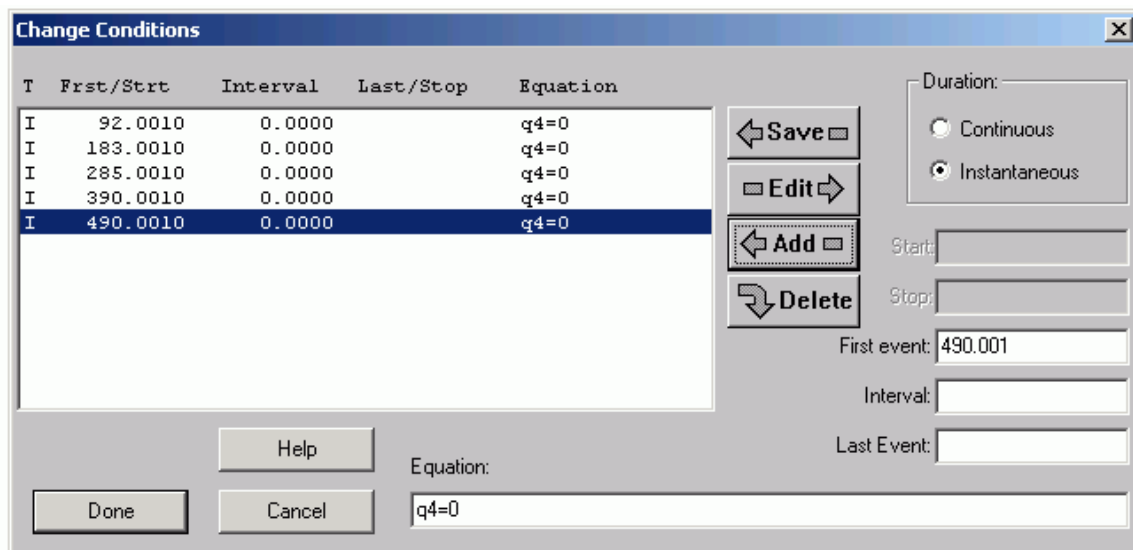
- b. In the **Duration** pane, select **Instantaneous**. The **Change Conditions** dialog box will appear as follows:



- c. In the **First event** box, type “92.001”.
- d. In the **Equation** box, type “q4=0”.
- e. Click **Add**. The **Change Conditions** dialog box will appear as follows:



- f. In the **First Event** box, type “183.001”, and click **Add**.
- g. In the **First Event** box, type “285.001”, and click **Add**.
- h. In the **First Event** box, type “390.001”, and click **Add**.
- i. In the **First Event** box, type “490.001”, and click **Add**. The **Change Conditions** dialog box will appear as follows:



- j. Click **Done**.



Instantaneous Change Conditions. Why do we enter the first event at 92.001? The reason is that the urine collections last for 92 hours. The container is emptied after the volume and concentration of inulin are made. Thus the actual event of emptying the container takes place slightly after the actual sample. Adding 0.001 to the time will accommodate this. The equation “ $q_4 = 0$ ” will reset the value of Compartment **q4** equal to zero at the specified time point. SAAM II will stop integration at, for example, 92.001, reset **q4** equal to zero, and continue integrating.



5. View the model parameters. The parameters have been entered as part of the study file. The **Parameters** dialog box is shown below:

Name	Type	Current	Low Limit	High Limit
V1	Adj	4.5000	0.4500	45.0000
k(1,2)	Adj	0.0250	0.0025	0.2500
k(1,3)	Adj	0.0150	0.0015	0.1500
k(2,1)	Adj	0.0250	0.0025	0.2500
k(3,1)	Adj	0.0150	0.0015	0.1500
k(4,1)	Adj	0.0300	0.0030	0.3000

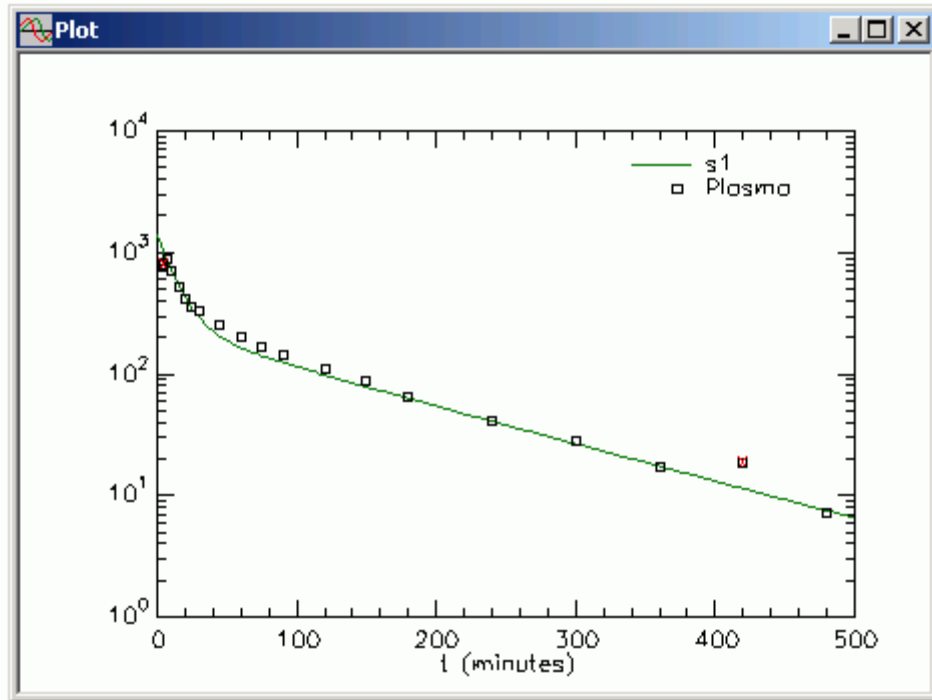
Name: V1 Value: 4.50000000

Type: Fixed Low Limit: 0.45000000

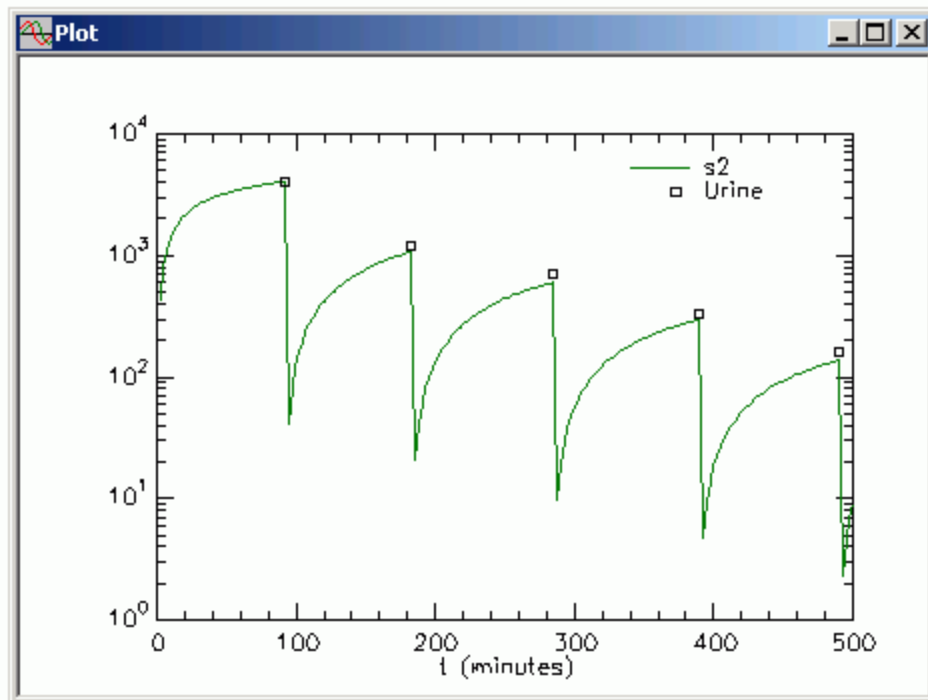
Adjustable High Limit: 45.00000000

Buttons: Edit, Save, Done, Cancel, Help

6. Solve the model, and view the solution. The plot of **s1:Plasma** will appear as follows (in semi-log mode):



Notice the first datum and the datum at 420 are unweighted as indicated by the red x through them. The plot of **s2:Urine** will appear as follows:



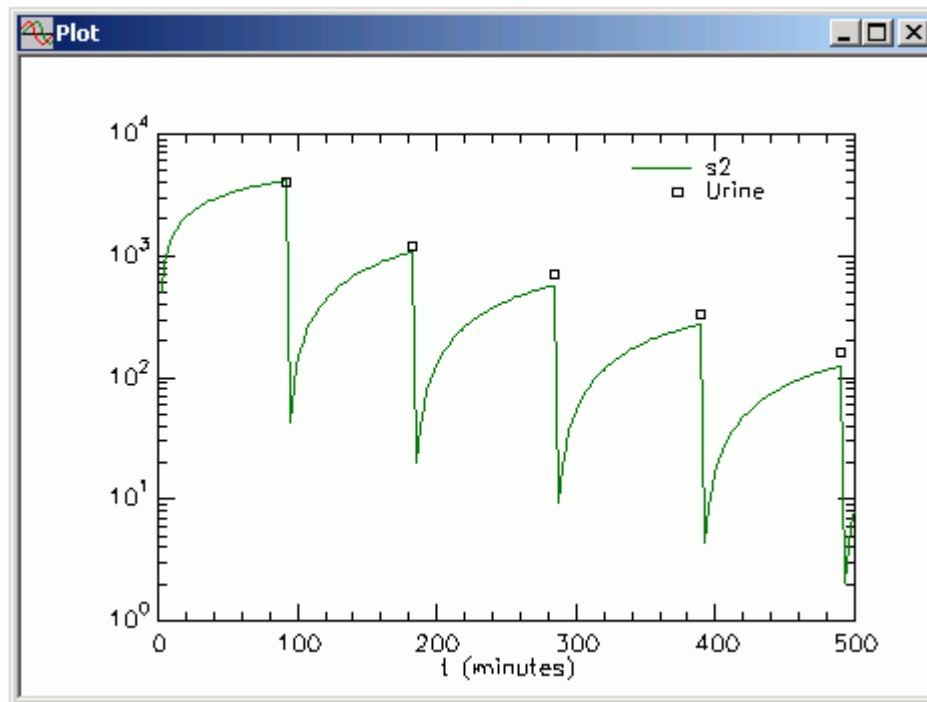


Viewing the individual urine samples. In viewing the individual urine samples, you can clearly see the effect of resetting q_4 equal to zero; this produces the saw-tooth curve. It is also important to note in these situations it is best to reset the **Minimum Number of Computation Intervals** equal to 200 to improve the resolution of the plot. This has been done in the study file. On the **Compute** menu, if you click **Settings**, the **Computational Settings** dialog box will open. You can see that the **Minimum Number of Computation Intervals** is set equal to 200. If you reduce this and resolve the model, you will lose some of the resolution of the plot.

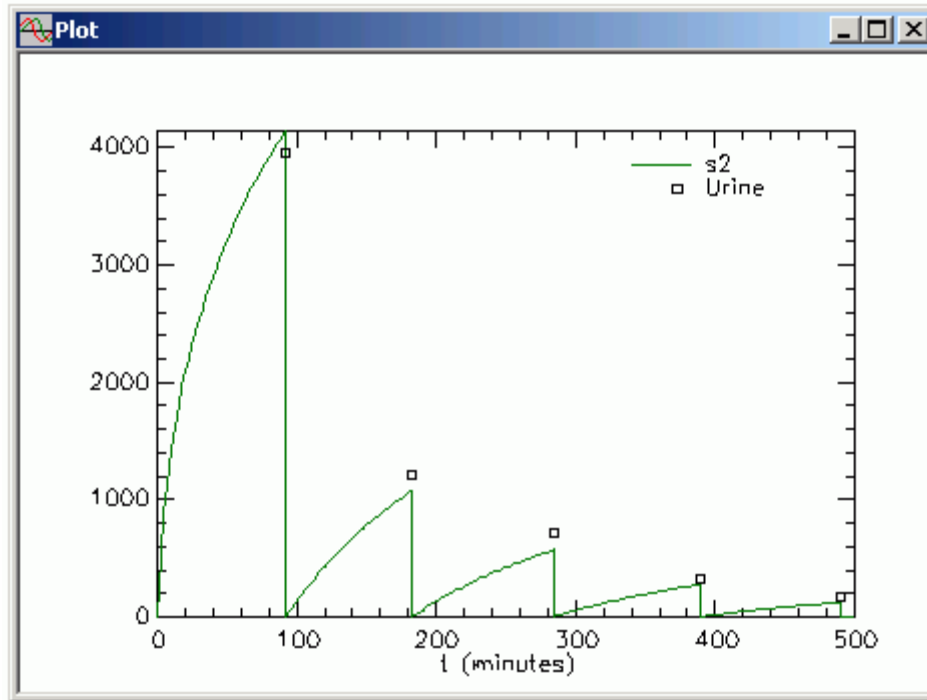


Leave the above plot of **s2:Urine** open.

7. Fit the model to the data, and view the solution.
 - a. The plot of **s2:Urine** will be updated as follows:

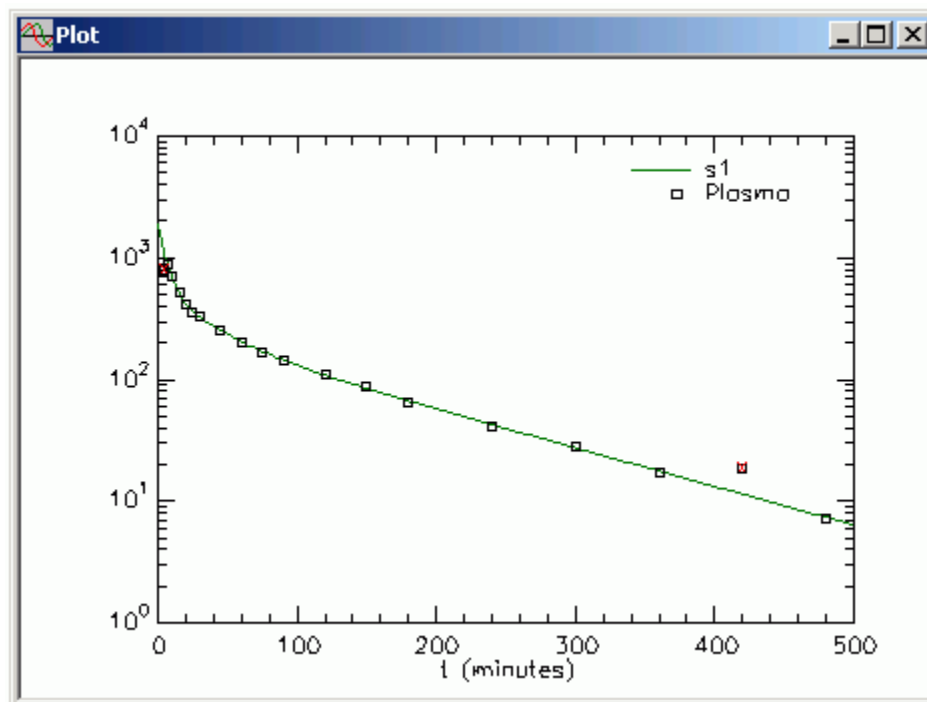


In the linear mode, the plot will appear (the **Y Axis** minimum should be set equal to zero):



Here you can see that **q4** has been reset to zero at the appropriate times.

- b. Plot **s1:Plasma**. The plot will appear as follows (the **Y Axis** scale should be set to autoscale):



You can see that the model describes the data reasonably well.

Close the **Plot** window.

c. View the statistics. The **Statistics** window will appear as follows:

Parameter/Variable	Value	Std.Dev.	Coef. of Var.	95% Confidence Interval
V1	3.32448	4.19753e-001	1.26261e+001	2.43464 4.21432
k(1,2)	0.06864	1.00728e-002	1.46743e+001	0.04729 0.09000
k(1,3)	0.01594	1.02559e-003	6.43439e+000	0.01377 0.01811
k(2,1)	0.06261	1.31064e-002	2.09339e+001	0.03482 0.09039
k(3,1)	0.02644	5.71624e-003	2.16211e+001	0.01432 0.03856
k(4,1)	0.03709	4.22290e-003	1.13866e+001	0.02813 0.04604

Correlation Matrix
 Covariance Matrix
 Objective

	Objective	Scaled Data Variance
s2 : Urine	2.428190e+000	5.860866e+000
s1 : Plasma	2.450978e+000	6.547269e-002

Total objective	4.879168e+000	
AIC	3.722159e+000	
BIC	3.920530e+000	

The statistical information supports the model quite well also.

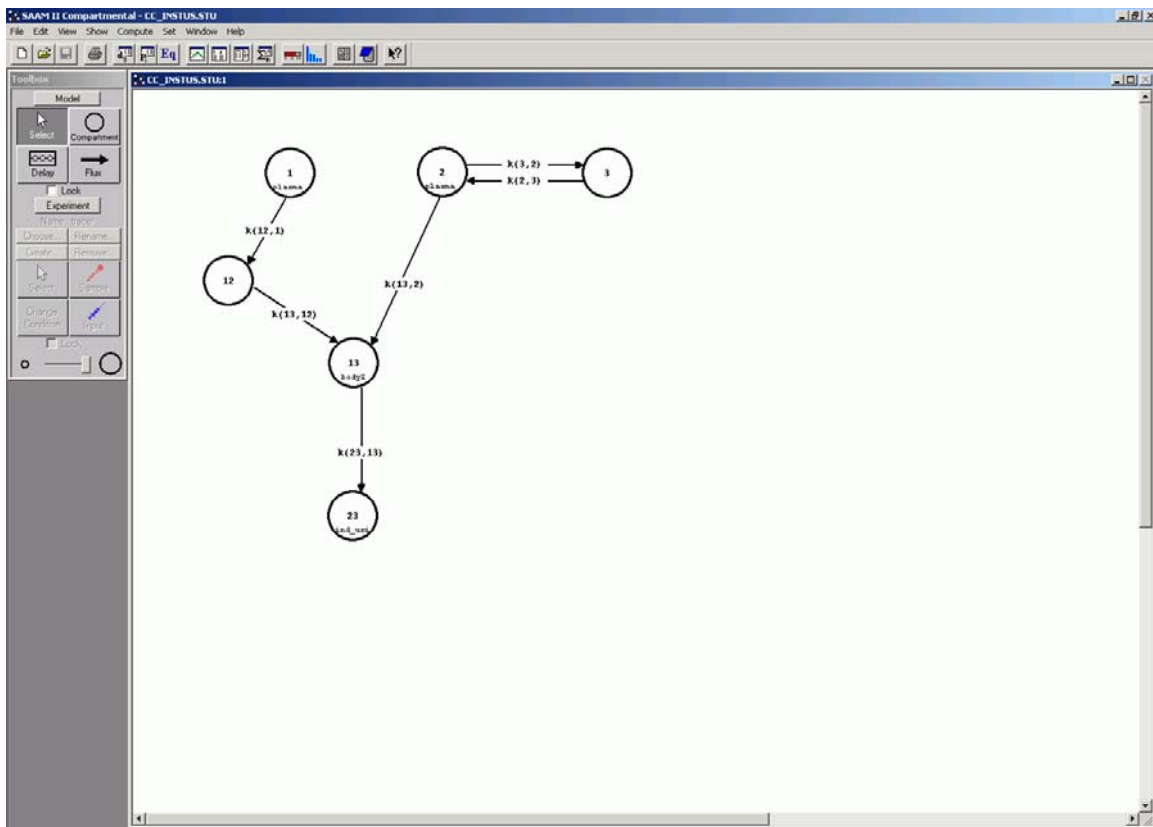
Close the **Statistics** window.

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

Part 3. An instantaneous Change Condition – LDL kinetics

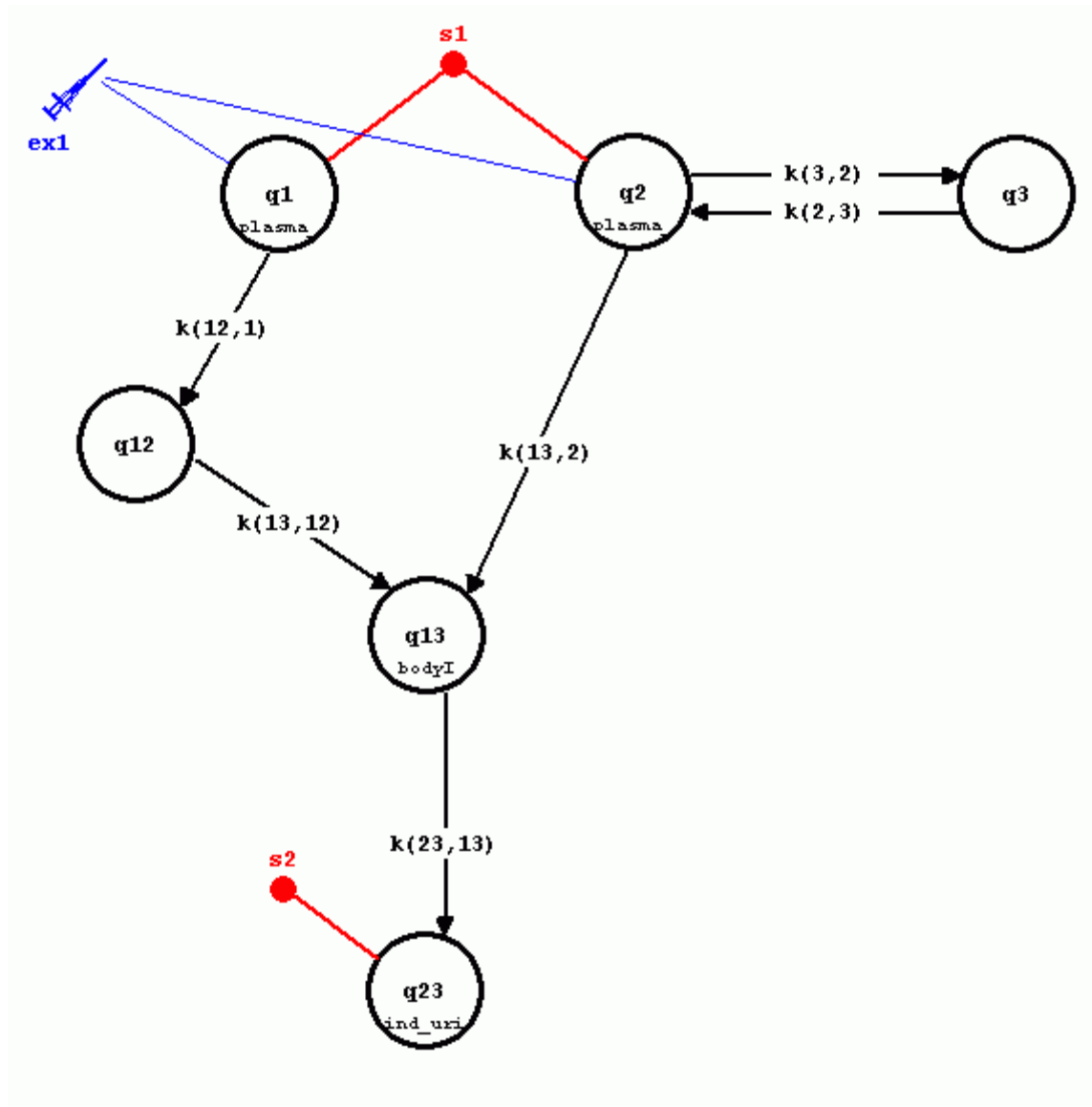
The following study investigated the metabolism of low density lipoproteins (LDL). Radioiodinated LDL was injected, and plasma and urinary radioactivity was determined. 24 hour urine collections were made. This part of the tutorial will show you have to model such collections using instantaneous change conditions.

1. Start the SAAM II Compartmental application. The SAAM II Compartmental main window will open.
2. Open the SAAM II Compartmental study file `cc_instLDL`.
 - a. The file `cc_instLDL.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:



The model is characterized by two plasma pools representing two kinetically distinct subpopulations of LDL particles. Radioiodide leaves the LDL during the metabolic process and enters the total body iodide pool. It is excreted there into the urine.

- 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:



The plasma samples, **s1**, are a sum of the radioactivity in the two plasma compartments, **q1** and **q2**, divided by the plasma volume. Double-click **s1** to view the **Sample Attributes** dialog box. The compartment for the individual urine samples is Compartment **q23**. The sample **s2** links this compartment with the individual urine samples. Double-click **s2** to view the **Sample Attributes** dialog box.

The input **ex1** is a split input. This is because the radiolabeled LDL is split between the two subpopulations of LDL represented by Compartments **q1** and **q2**. Double-click **ex1** to open the **Exogenous Input** dialog box. Then click **Split Input**; the two dialog boxes will appear as follows:

Exogenous Input

Name: Reference Name: Units:

Type	Initial	Constant	Start	Stop	Repeat Every	Nr. Repeats
Bolus	1.00e+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:

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

The parameter *frac* will split the bolus dose between Compartments **q1** and **q2**. For more information on split inputs, see the Using SAAM II (Advanced) tutorial “Working with Experimental Inputs”.

Close the two dialog boxes.

The data to be analyzed are shown in the **Data** window below:

```

d:\Data - cc_instUS.dat
DATA
(FSD 0.1)
t      plasma  ind_urine
(/24)  ()      ()
0      n        n
0.16   29745    n
0.5    31008    n
1      29114    n
2      27907    n
4      27593    n
6      27483    n
9      26610    n
12     25791    n
()     ()      ()
1      20899    6979047
2      13646    1.67E+07
3      9714     1.56E+07
4      6456     1.19E+07
5      4806     8091944
6      3804     5846717
7      3267     3832041
8      2744     2696780
9      2279     1882786
10     2131     1394947
11     1971     985794
12     1720     876272
13     1667     712898
14     1622     643487
END
Data Format is okay

```

The two columns of data are the plasma and the individual urine samples. The initial data were recorded in hours instead of days. The line in the data file

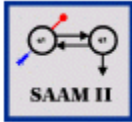
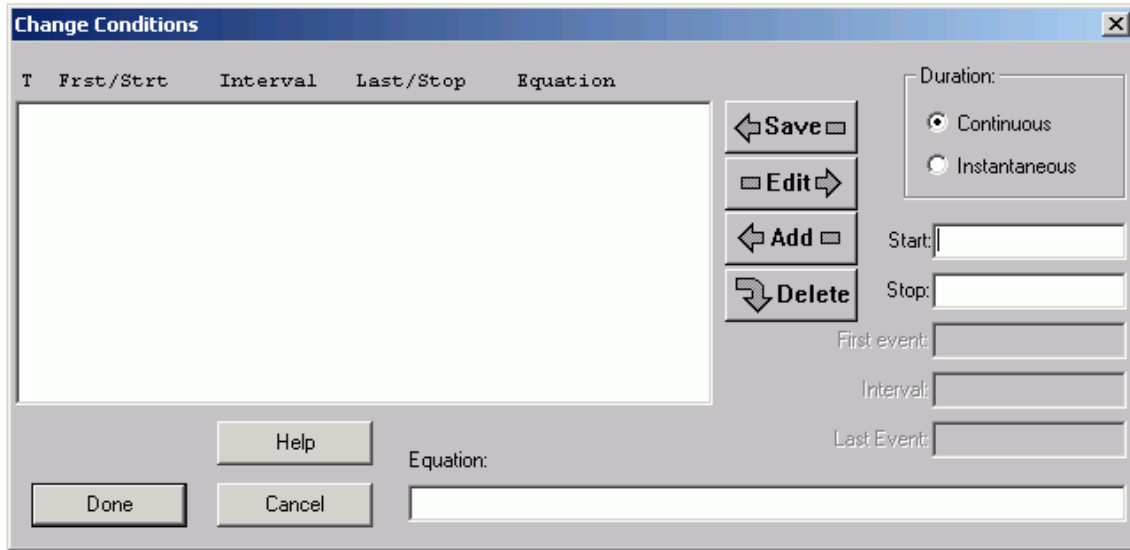
“(/24) () ()”

divides all samples up to 12 hours by 24 converting them to days. The line in the data file

() () ()

will stop the division by 24. The entries “n” in the “ind_urine” column means there are no urine data collected at these times.

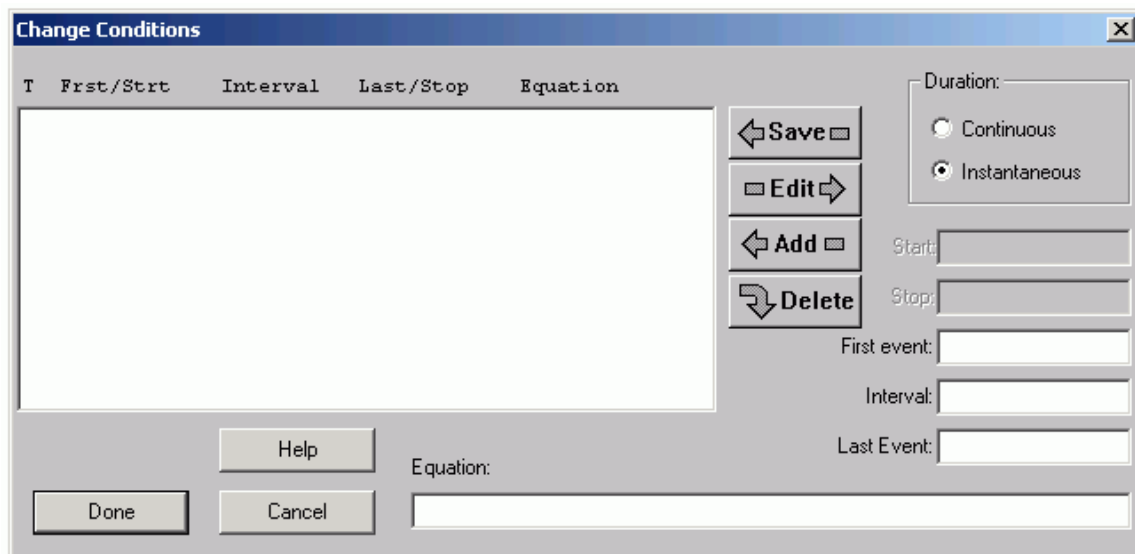
4. Use Change Conditions to model the 24 hour urine collections.
 - a. In the **SAAM II Toolbox**, click **Change Condition**. The **Change Conditions** dialog box will open as shown below:



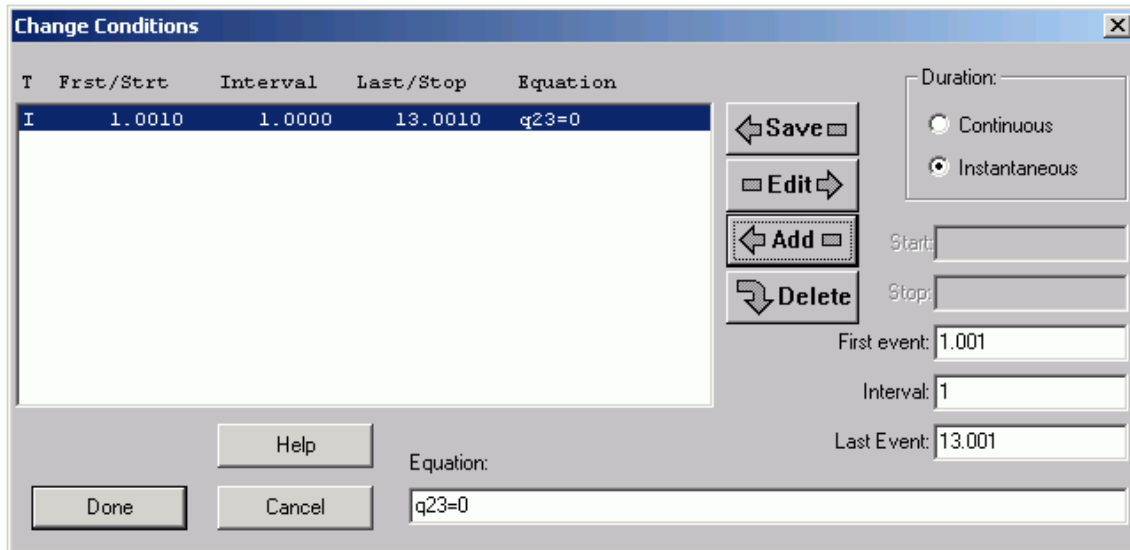
Change Conditions dialog box. The **Change Conditions** dialog box contains the **Duration** pane. The **Duration** pane is where you set the Change Condition to be **Continuous** (default) or **Instantaneous**. You set the **Start** and **Stop** times in the boxes below this pane. If the Change Condition is **Instantaneous**, the **First event**, **Interval**, and **Last Event** boxes will be active. You define the change in the **Equation** box.



- b. In the **Duration** pane, select **Instantaneous**. The **Change Conditions** dialog box will appear as follows:



- c. In the **First event** box, type “1.001”.
- d. In the **Interval** box, type “1”.
- e. In the **Last Event** box, type “13.001”.
- f. In the **Equation** box, type “q23=0”.
- g. Click **Add**. The **Change Conditions** dialog box will appear as follows:



- h. Click **Done**.



Instantaneous Change Conditions. Why do we enter the first event at 1.001? The reason is that the urine collections last for 24 hours, 1 day. The container is emptied after the volume and concentration of radioactivity are measured. Thus the actual event of emptying the container takes place slightly after the actual sample. Adding 0.001 to each day will accommodate this. The equation “q23 = 0” will reset the value of Compartment **q23** equal to zero at the specified time point. SAAM II will stop integration at, for example, 1.001, reset **q23** equal to zero, and continue integrating.



5. View the model parameters. The parameters have been entered as part of the study file. The **Parameters** dialog box is shown below:

Name	Type	Current	Low Limit	High Limit
frac	Adj	0.5000	0.1000	0.9000
k(2,3)	Adj	0.0800	0.0080	0.8000
k(3,2)	Adj	0.2000	0.0200	2.0000
k(12,1)	Adj	0.5000	0.0500	5.0000
k(13,2)	Adj	0.1000	0.0100	1.0000
k(13,12)	Adj	1.0000	0.1000	10.0000
k(23,13)	Fix	2.5000		
vol	Adj	3000.0000	300.0000	30000.0000

Name: frac Value: 0.50000000

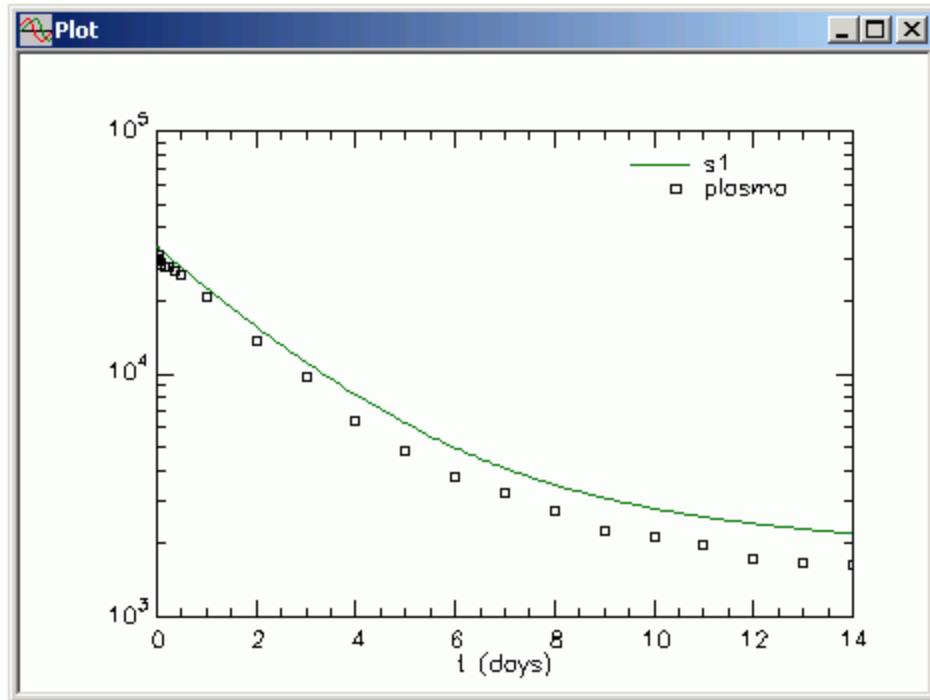
Type: Fixed Low Limit: 0.10000000

Adjustable High Limit: 0.90000000

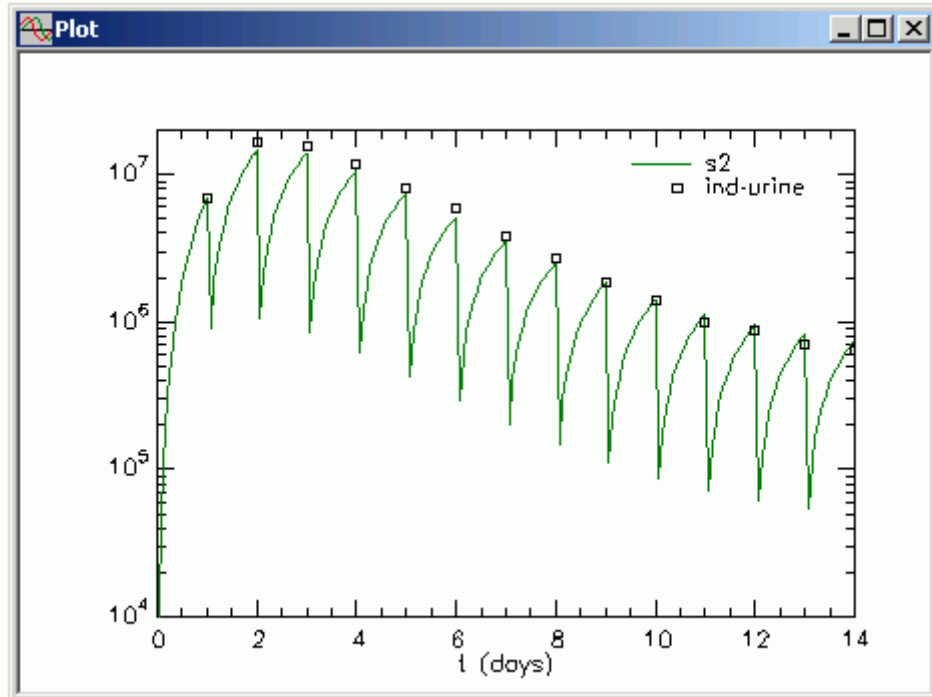
Buttons: Edit, Save, Done, Cancel, Help

Of note in the **Parameters** dialog box is the fact that *frac*, the parameter that distributes the initial dose between the two plasma compartments, lies between 0.1 and 0.9; this parameter cannot be less than zero nor greater than 1. The parameter $k(23,13)$ is fixed equal to 2.5. This is the fractional excretion rate from the body iodide pool, Compartment **q13**; this parameter cannot be determined from the data, and is taken from the literature where it is known that the total body iodide pool turns over at approximately 2.5/day.

- Solve the model, and view the solution. The plot of **s1:plasma** will appear as follows (in semi-log mode):



The plot of **s2:ind_urine** will appear as follows (the **Y Axis** scale has been set with 10000 and 2.0×10^7 as the minimum and maximum respectively):



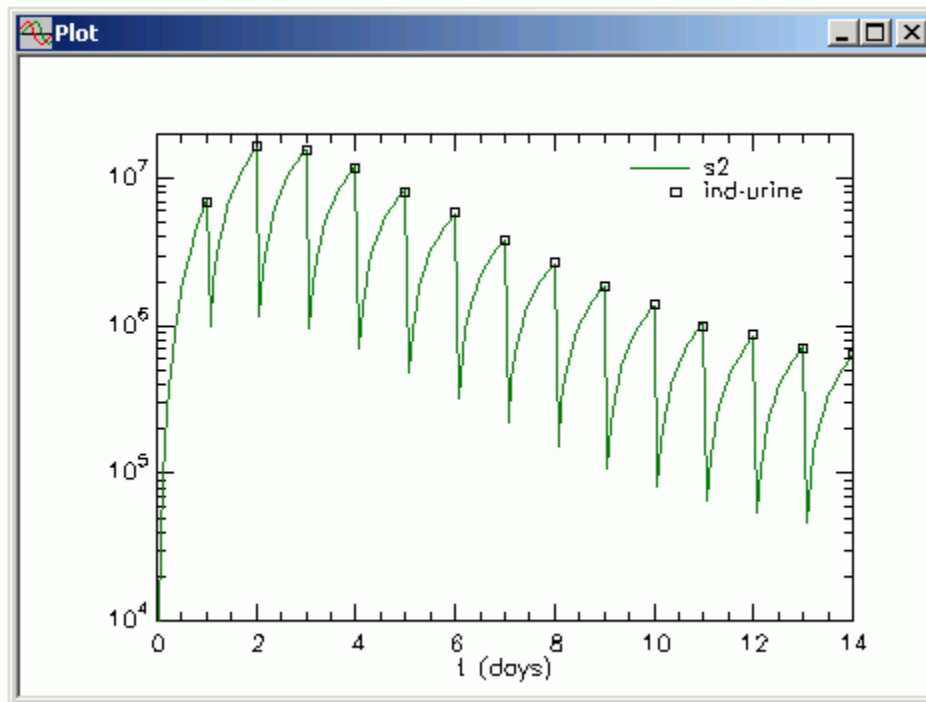


Viewing the individual urine samples. In viewing the individual urine samples, you can clearly see the effect of resetting **q23** equal to zero; this is what produces the saw-tooth curve. It is also important to note in these situations it is best to reset the **Minimum Number of Computation Intervals** equal to 200 to improve the resolution of the plot. This has been done in the study file. On the **Compute** menu, if you click **Settings**, the **Computational Settings** dialog box will open. You can see that the **Minimum Number of Computation Intervals** is set equal to 200. If you reduce this and resolve the model, you will lose the resolution of the plot.

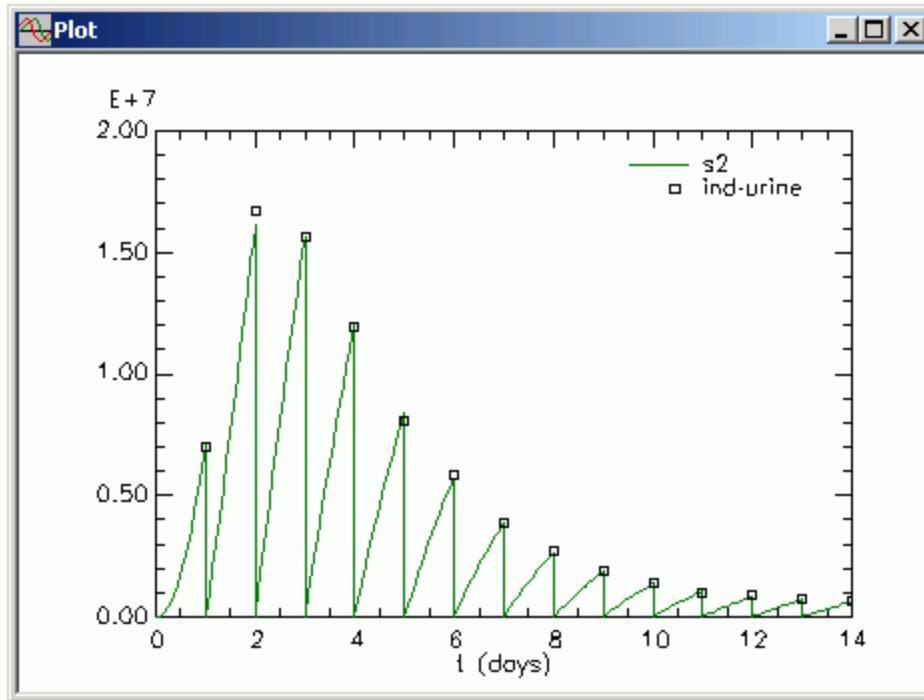


Leave the above plot of **s2:ind_urine** open.

7. Fit the model to the data, and view the solution.
 - a. The plot of **s2:ind_urine** will be updated as follows:

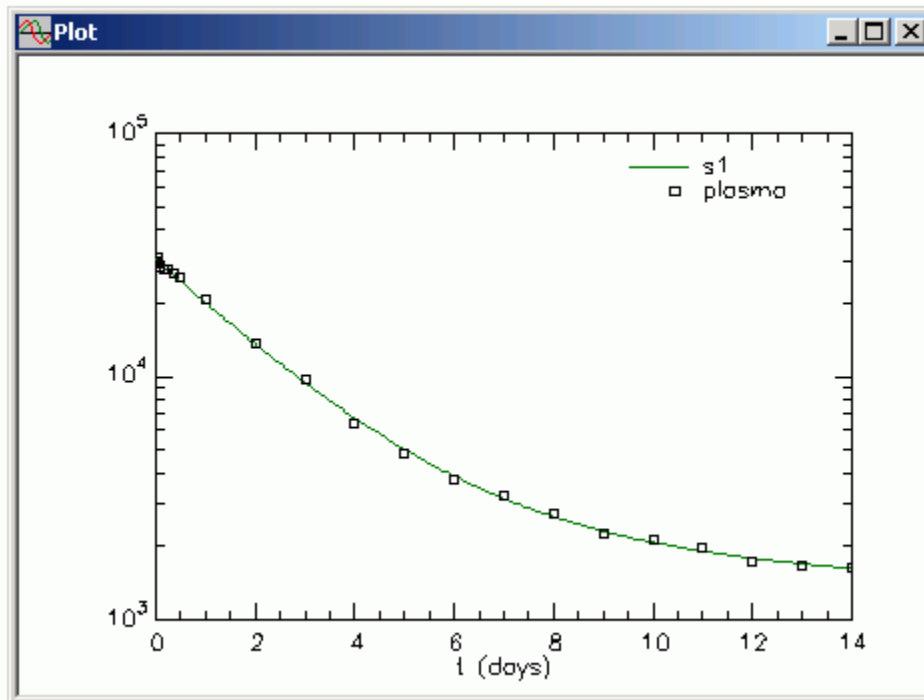


In the linear mode, the plot will appear (the **Y Axis** minimum has been set equal to zero):



Here you can see that **q23** has been reset to zero at the appropriate times.

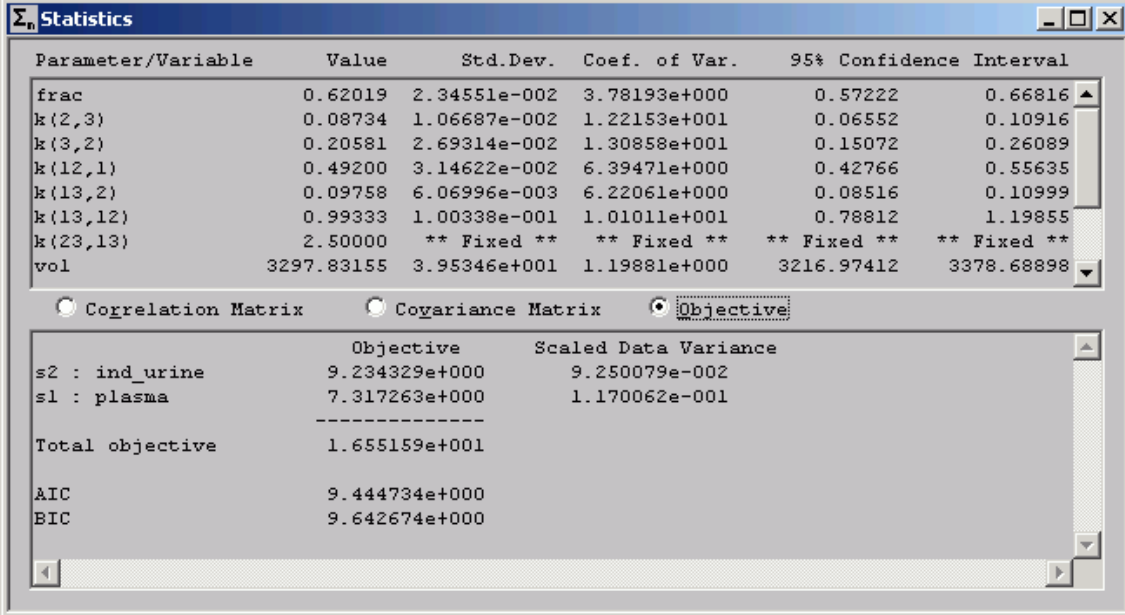
- b. Plot **s1:plasma**. The plot will appear as follows (the **Y Axis** scale has been set to autoscale):



You can see that the model describes the data quite well.

Close the **Plot** window.

- c. View the statistics. The **Statistics** window will appear as follows:



Parameter/Variable	Value	Std.Dev.	Coef. of Var.	95% Confidence Interval	
frac	0.62019	2.34551e-002	3.78193e+000	0.57222	0.66816
k(2,3)	0.08734	1.06687e-002	1.22153e+001	0.06552	0.10916
k(3,2)	0.20581	2.69314e-002	1.30858e+001	0.15072	0.26089
k(12,1)	0.49200	3.14622e-002	6.39471e+000	0.42766	0.55635
k(13,2)	0.09758	6.06996e-003	6.22061e+000	0.08516	0.10999
k(13,12)	0.99333	1.00338e-001	1.01011e+001	0.78812	1.19855
k(23,13)	2.50000	** Fixed **	** Fixed **	** Fixed **	** Fixed **
vol	3297.83155	3.95346e+001	1.19881e+000	3216.97412	3378.68898

Correlation Matrix
 Covariance Matrix
 Objective

	Objective	Scaled Data Variance
s2 : ind_urine	9.234329e+000	9.250079e-002
s1 : plasma	7.317263e+000	1.170062e-001

Total objective	1.655159e+001	
AIC	9.444734e+000	
BIC	9.642674e+000	

The statistical information supports the model quite well also.

Close the **Statistics** window.

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