Nonlinear Regression Programs

Model Specification
Program Set-up

Objectives

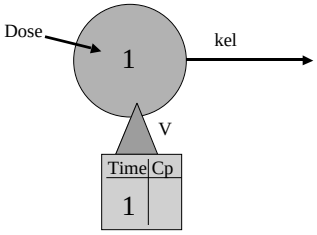
- To understand the steps required to input a model into various programs
  - Boomer, SAAM II, WinNONLIN, and ADAPT II
- To understand how to complete a nonlinear regression problem using each of these programs

General Approaches

- Draw/Sketch Diagram of Model
- Derive Equation - Differential or Integrated
- Define Model in the Program
  - Selection of Model from Library (WinNONLIN)
  - Selection of Parameters of Model (Boomer, SAAM II)
  - Describe Model using Computer Language (ADAPT II, WinNONLIN, SAAM II)

Using Boomer - Macintosh/Windows

- Draw Diagram of the Model



Boomer - Define the Model

Parameter Name	Parameter Type	Direction
Dose	1 Initial Value	Into 1
kel	2 First Order	From 1 To 0
V	18 Volume	From 1 To 1

Boomer - Running the Problem

- Start Boomer
- Select Input/Output option and Normal Fitting
- Describe Model
- Select Algorithms
- Enter Data
- Run the Analysis
- Read the Output

Using SAAM II - Macintosh/Windows

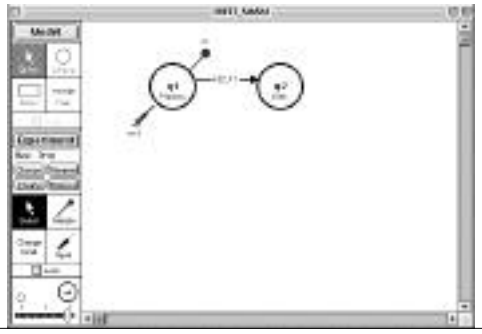
- Graphical User Interface to Define the Model by Parameter Selection

SAAM II - Running the Problem

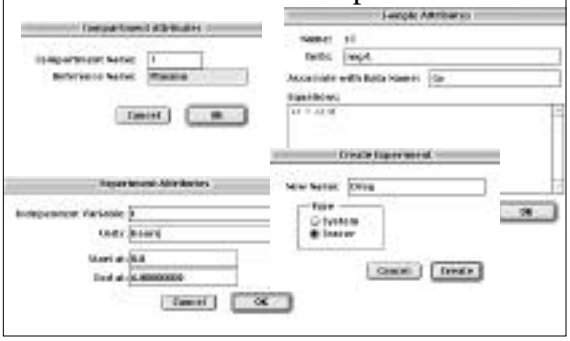
- Start SAAM II
- Describe Model
- Describe Experiment
- Enter Data
- Run the Analysis
- Read the Output

SAAM II - First Window

SAAM II - Model Defined



Define Model - Experiment



Add Data and Parameter Estimates

Using WinNONLIN Pro - Windows

- Model Selected from Library

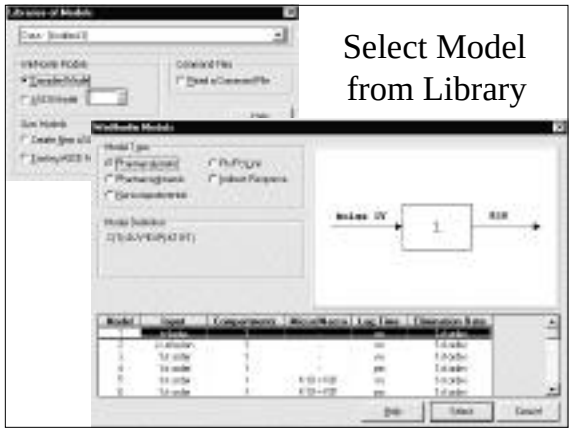
Model	Input	# Compart	micro/macro	Lag	Elimin
1	iv-bolus	1	-	no	1st ord
2	iv-infus	1	-	no	1st ord
3	1st ord	1	-	no	1st ord
4	1st ord	1	-	yes	1st ord
5	1st ord	1	k10=k01	no	1st ord
6	1st ord	1	k10=k01	yes	1st ord
7	iv-bolus	2	micro	no	1st ord

WinNONLIN Pro - Running the Problem

- Start WinNONLIN Pro
- Enter Data
- Select Model
- Enter Parameters
- Run the Analysis
- Read the Output

WinNONLIN Pro - Enter Data

Select Model from Library



WinNONLIN Pro - Data Defined

Add Parameter Estimates and Dose

Using ADAPT II - VAX VMS / Windows

- Model Defined by Subroutine

```
C-------- in DIFFEQ ----------------------------------------------C
C 1.  Enter Differential Equations Below
C      {e.g.  XP(1) = -P(1)*X(1) }  C
C----c-----------------------------------------------------------------C
       xp(1) = -p(1)*x(1)            P(1) = kel
C----------------------------------------------------------------------C
C 3.  Enter Output Equations Below   {e.g.  Y(1) = X(1)/P(2) }
C----c-----------------------------------------------------------------C
       Y(1) = x(1)/p(2)              P(2) = V
```

ADAPT II - Running the Problem

- Set up class directory, copy files
- Start ADAPT II
- Enter Options
- Edit Model (in subroutine as needed)
- Enter Doses, Data, and Parameters
- Run the Analysis
- Read the Output

ADAPT II - Dose Information Entered

```
----- SUPPLY MODEL INPUT INFORMATION -----

Enter the number of model inputs: 0
Enter the number of bolus inputs: 1
Enter the compartment number for each bolus input (e.g. 1,3,...): 1
Enter the number of input event times: 1
For each input event enter as required:
        Time    Value for all Inputs
Event     Units,       B(1)
 1.       0,250
```

ADAPT II - Enter Data

----- SUPPLY MODEL OUTPUT INFORMATION -----

Enter the number of model output equations: 1
Enter the number of observation times: 5
For each observation enter as required:
Time Measured Value For Each Output
Observation Units , Y(1)
1. 1,8
2. 2,5
3. 3,2.6
4. 5,0.9
5. 6,0.56

Add Parameter Estimates

----- INITIALIZE ESTIMATION PROCEDURE -----

Read parameter values from a file (Y/N)? n
Enter initial values for parameters & specify those to be estimated:
Value Estimate (Y/N)?
kel .5,y
V 20,y
IC(1) 0,n

Comparison of Results

Parameter	Boomer	SAAM	WinNONLIN	ADAPT
kel	0.5407	0.5406	0.5406	0.5407
V	18.06	18.07	18.07	18.06