<u>Directions</u>: Answer each of the four exercises below showing all relevant work. Conclusions and justifications are to be given in clear detailed English. Please type up your solutions or write very neatly.

1. Huet, Bouvier, et al (*Statistical Tools for Nonlinear Regression*, p.2) use the *Pasture Regrowth* dataset from Ratkowsky (*Nonlinear Regression*, p.88) to fit a certain four-parameter sigmoidal growth model. In the dataset, $Y =$ pasture regrowth since last grazing, and $X =$ time, and for our present purposes, let’s assume that the data are independent measurements. The nonlinear model function that these authors used to fit the data is somewhat complicated – and coming up with starting values for the model parameters is not easy and comes only come after we understand the roles these parameters play. These data are given, plotted, and analyzed in the Appendix.
   (a) List all the needed assumptions for the given **`proc nlin`** analysis. Give an example of conditions where – in the context of this situation – the above required independent-measurements assumption would <u>*not*</u> be met.
   (b) After examining SAS Program B (**`proc nlin`**), write down the assumed 4-parameter model function that the researchers fit to the data; see the right-hand side of the **`model`** statement.
   (c) Assuming that θ_4 is positive and using algebra and one ‘limit’, clearly give the roles of the θ_1 and θ_2 parameters. (Hint: Which parameters – or functions of parameters – are the upper and lower asymptotes for this model?) Upon examining the graph of the data below, what are your “eyeball estimates” of these two parameter values?
   (d) To obtain NLIN starting values for θ_3 and θ_4, we use the following approach: write down the expression with ‘y’ on the left-hand side and the above assumed nonlinear model function on the right-hand side (with no error term for now), substitute in our eyeball estimates for the upper and lower asymptotes and solve so that the new right-hand expression is a linear model in $log(x)$. Next, relate what you have found above to the simple linear regression (**`proc reg`**) performed in SAS Program A, and use SAS Output A to report the starting values for θ_3 and θ_4. Verify that these starting values (or approximations to these) are used in SAS Program B.
   (e) Using SAS Output B (**`proc nlin`**), report the estimate of σ^2 here.
   (f) Using SAS Output B (**`proc nlin`**), do a two-sided Wald test that $\theta_4 = 3$ using $\alpha = 1\%$. Redo this two-sided Wald test using $\alpha = 5\%$. Clearly report your test statistics, p-values, and conclusions in both cases.
   (g) Repeat both tests done in part (f) but using Likelihood Ratio tests instead.
   (h) In examining the listing of the residuals in Output C and the Residual Plot, it is apparent that one of the residuals (at $x = 21$) may be ‘large’. If the **`proc nlin`** were to be rerun with this potential outlier removed, would the estimate of the lower asymptote increase or decrease?

2. In *Nonlinear Regression Analysis and its Applications* (1988, p.269), Bates and Watts report data from Treloar (1974) regarding the "velocity" of an enzymatic reaction. The number of counts per minute of radioactive product from the reaction was measured as a function of substrate concentration (in ppm), and from these counts the initial rate, or "velocity," of the reaction was calculated (in counts/min^2). The experiment was conducted with the enzyme treated with puromycin (variable ‘treat’ = "yes") and again with the enzyme untreated (‘treat’ = "no"). The velocity is assumed to depend on the substrate concentration according to the usual Michaelis-Menton (MM_2) equation. In the word of the authors, it has been hypothesized that the “ultimate velocity parameter" (θ_1) should be affected by introduction of the Puromycin, but not necessarily the "half-velocity parameter” (θ_2). Here, $Y =$ velocity and $X =$ concentration.

(a) Clearly list all the needed assumptions for the given `proc nlin` analyses (see the Appendix) in the context of this situation/exercise.
(b) Write down the model function which is fit in SAS Program A. Clearly indicate the roles of θ_3 and θ_4 used in this model function.
(c) Based on the output, give estimates for the MM_2 model parameters (upper asymptote and LD_{50}) for both the treated and untreated curves. Report these estimates in a 2×2 table.
(d) Test both hypotheses indicated by the authors' claims (above) using one-at-a-time Wald hypothesis tests. In both cases – and using the model in SAS Program A – report the hypotheses, test statistics, degrees of freedom, p-values, and conclusions.
(e) Using the full-and-reduced (likelihood-based) F-test, test whether the half-velocity parameters are equal, reporting the calculated test statistic, degrees of freedom, p-value, and your conclusion.
(f) Using the full-and-reduced (likelihood-based) F-test – and assuming the half-velocity parameters are indeed the same – test whether the ultimate velocity parameters are equal, reporting the calculated test statistic, degrees of freedom, p-value, and your conclusion.
(g) Finally, compare the model function in Program/Output A with that in Program/Output D – are they equivalent? Why/why not? In what way are the approaches different? In which situation(s) is Program/Output A preferred, and in which situation(s) is Program/Output D preferred? Be clear in your explanation.

3. In "Calibration and assay development using the four-parameter logistic curve" (*Chem. Intell. Lab. Systems*, 1993, p.97), O'Connell *et al* fit the four-parameter log-logistic (LL4) model function to their radioimmunoassay (RIA) data. The data are analyzed in SAS in the Appendix using one run of `proc nlin` and then three runs of `proc nlmixed`.
   (a) Clearly list all the needed assumptions for the run of `proc nlin` and the three runs of `proc nlmixed` in the context of this exercise/situation.
   (b) Looking at the residual plot of the `proc nlin` fit in Output A, comment on whether all necessary assumptions appear to be met. (Note that the `proc nlmixed` fit in Output C fits this same homoskedastic or constant variance nonlinear model as in this `proc nlin`).
   (c) In Output B, researchers are trying to obtain a good model for the model variance for these data. Explain what is being done in the `proc nlmixed` run in Output D: what is the 'model' and what are the roles of the new parameter(s). Perform a likelihood-based test of whether the extra parameter (rho $= \rho$) in the variance is need, writing out your hypotheses, test statistic, degrees of freedom, p-value, and clear conclusion. Does this conclusion seem sensible considering the residual plot on p.3?
   (d) It turns out that the `proc nlmixed` in Output E involves another – potentially more appropriate but also more complicated – way of modeling the variance for these data. Comparing Outputs C and E, perform a likelihood-based hypothesis test testing for homoskedasticity, again writing out your hypotheses, test statistic, degrees of freedom, p-value, and clear conclusion.
   (e) Compare the parameter estimates for the model parameters (the θs) and – more importantly – the associated standard errors for Outputs C and E. What has changed and how?

4. Simulated data are graphed and examined in the Appendix starting on p.18 using two runs of `proc nlin`.
   (a) Clearly list all the needed assumptions for the first `proc nlin` analysis.

(b) Write down the model function being fit in Output A. What is the precise relevance/function of the parameter named 'phi' (denoted ϕ)?

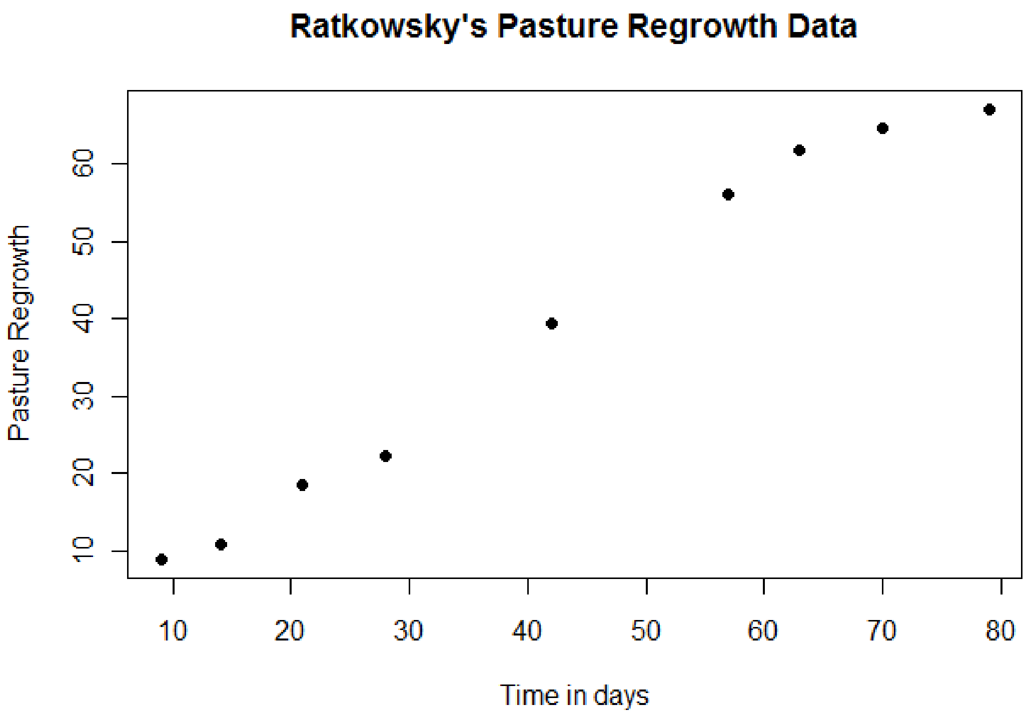
(c) Write down the OLS estimate of 'phi'. Also, perform a two-sided WALD test that the true value of 'phi' is equal to -0.40 (using $\alpha = 5\%$), and clearly indicate the 95 % Wald Confidence Interval (WCI) for this parameter. For the test, give the hypotheses, test statistic, p-value, and degrees of freedom.

(d) Repeat part (c) using the likelihood test. Remember to give the hypotheses, test statistic, p-value, and degrees of freedom.

(e) It turns out that the 95% likelihood-based confidence interval for 'phi' for these data is very different from the reported 95% WCI. In your opinion, is this true CI shifted to the right or to the left of the WCI? Clearly and succinctly explain your answer, making reference to the plot of the data and fitted curve.

Homework 3 Appendix

Exercise 1 Graph



Exercise 1 SAS Program/Output A

```
data one;
  do x=9,14,21,28,42,57,63,70,79;
    input y @@;
    y=y/100;
    output;
  end;
datalines;
893 1080 1859 2233 3935 5611 6173 6462 6708
;
data two;
  set one;
  ny=log(-log((70-y)/65));
  nx=log(x);
proc reg data=two;
  model ny=nx;
run;
```

```
                    The REG Procedure
                      Model: MODEL1
                Dependent Variable: ny

        Number of Observations Read          9
        Number of Observations Used          9
```

```
                         Analysis of Variance
                                    Sum of           Mean
Source                   DF        Squares         Square    F Value    Pr > F
Model                     1       16.87291       16.87291     550.90    <.0001
Error                     7        0.21439        0.03063
Corrected Total           8       17.08730

             Root MSE              0.17501    R-Square     0.9875
             Dependent Mean       -0.53872    Adj R-Sq     0.9857
             Coeff Var           -32.48571

                            Parameter Estimates
                           Parameter       Standard
     Variable     DF        Estimate          Error    t Value    Pr > |t|
     Intercept     1        -7.18999        0.28932     -24.85      <.0001
     nx            1         1.88511        0.08032      23.47      <.0001
```

Exercise 1 SAS Program/Output B

```
proc nlin data=one;
  parms th1=70 th2=65 th3=-7 th4=2;
  model y=th1-th2*exp(-exp(th3)*(x**th4));
  output out=three r=resids p=preds;
run;
```

```
                          The NLIN Procedure
                         Dependent Variable y
                        Method: Gauss-Newton
                           Iterative Phase
                                                                   Sum of
       Iter         th1          th2          th3          th4     Squares
          0     70.0000      65.0000      -7.0000       2.0000       832.1
          1     68.9082      64.3067      -6.1978       1.5712       276.5
          2     63.5647      52.7166      -9.3162       2.4354     85.3555
          3     69.8974      61.6943      -9.0989       2.3440      9.7022
          4     69.9211      61.6539      -9.2072       2.3777      8.3768
          5     69.9575      61.6846      -9.2082       2.3776      8.3759
          6     69.9552      61.6815      -9.2089       2.3778      8.3759
          7     69.9552      61.6815      -9.2089       2.3778      8.3759
       NOTE: Convergence criterion met.

                          Estimation Summary
                  Method                    Gauss-Newton
                  Iterations                           7
                  Observations Read                    9
                  Observations Used                    9
                  Observations Missing                 0

                                  Sum of         Mean                Approx
  Source                   DF    Squares       Square    F Value     Pr > F
```

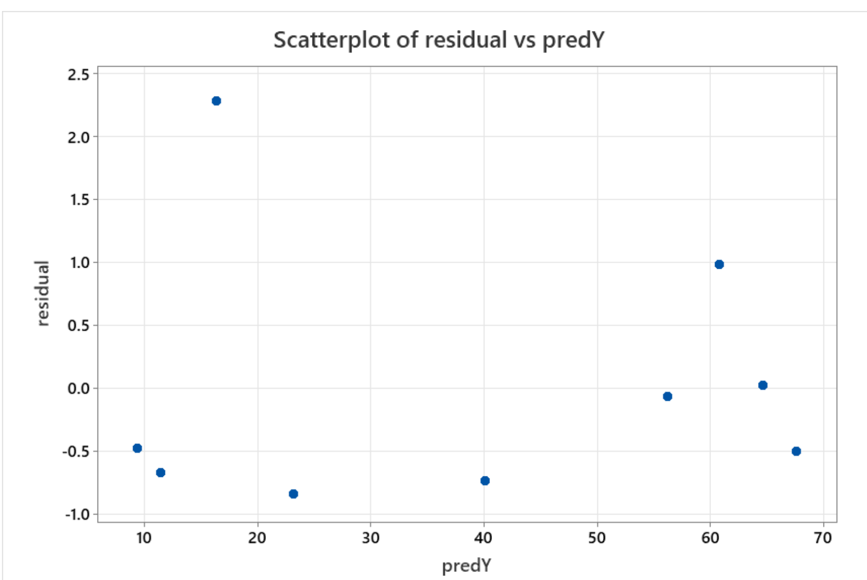
```
Model                        3       4639.7       1546.6      923.22     <.0001
Error                        5       8.3759       1.6752
Corrected Total              8       4648.1

                                      Approx
       Parameter        Estimate    Std Error    Approximate 95% Confidence Limits
       th1               69.9552       2.3620      63.8835      76.0269
       th2               61.6815       3.1927      53.4744      69.8885
       th3               -9.2089       0.8173     -11.3098      -7.1080
       th4                2.3778       0.2210       1.8098       2.9459

                        Approximate Correlation Matrix
                    th1               th2               th3               th4
   th1        1.0000000         0.9251613         0.7095438        -0.7658736
   th2        0.9251613         1.0000000         0.8615146        -0.8906628
   th3        0.7095438         0.8615146         1.0000000        -0.9955752
   th4       -0.7658736        -0.8906628        -0.9955752         1.0000000
```

Exercise 1 SAS Program and Output C

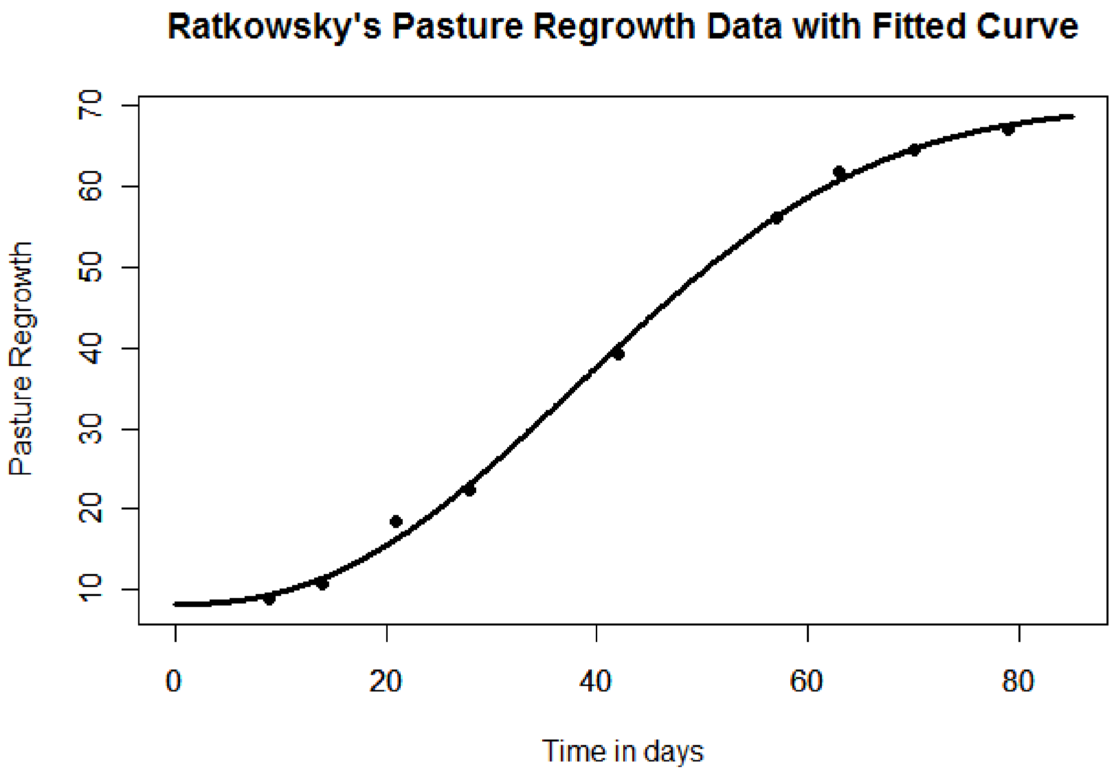
```
proc print noobs;
run;
```

x	y	preds	resids
9	8.93	9.4107	-0.48069
14	10.80	11.4693	-0.66931
21	18.59	16.3057	2.28432
28	22.33	23.1737	-0.84374
42	39.35	40.0846	-0.73458
57	56.11	56.1766	-0.06655
63	61.73	60.7442	0.98581
70	64.62	64.5949	0.02506
79	67.08	67.5803	-0.50032

Exercise 1 SAS Residual Plot



Exercise 1 Fitted Nonlinear Model and Data



Exercise 1 SAS Program/Output D

```
proc nlin data=one;
  parms th1=70 th2=55 th3=-12;
  th4=3;
  model y=th1-th2*exp(-exp(th3)*(x**th4));
run;
```

```
                          The NLIN Procedure
                         Dependent Variable y
                        Method: Gauss-Newton

                           Iterative Phase
                                                          Sum of
            Iter          th1          th2          th3   Squares
               0      70.0000      55.0000     -12.0000    112.9
               1      64.8344      53.7243     -11.5162   28.9029
               2      66.7202      56.0710     -11.5451   19.2408
               3      66.7573      56.0959     -11.5467   19.2384
               4      66.7590      56.0969     -11.5469   19.2384
               5      66.7592      56.0969     -11.5469   19.2384
       NOTE: Convergence criterion met.

                          Estimation Summary
```

Method	Gauss-Newton
Iterations	5
Observations Read	9
Observations Used	9
Observations Missing	0

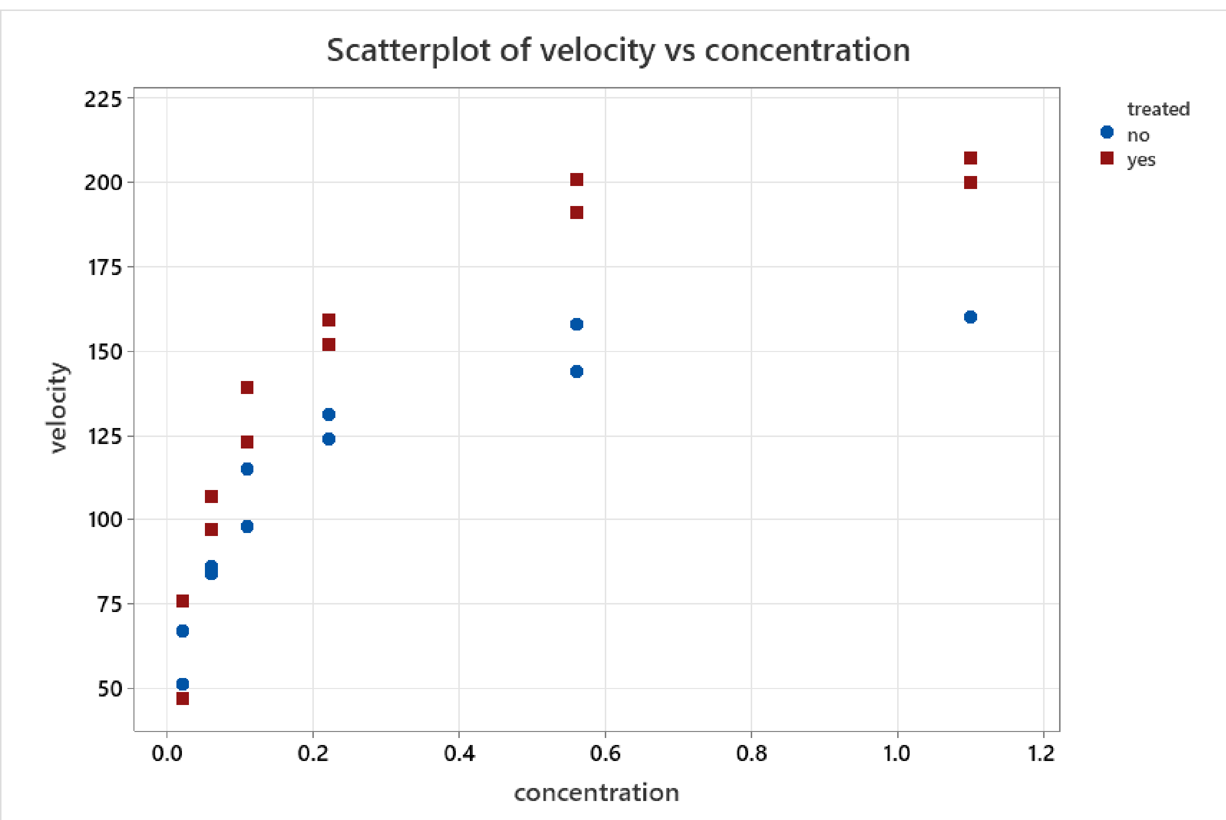
Source	DF	Sum of Squares	Mean Square	F Value	Approx Pr > F
Model	2	4628.8	2314.4	721.81	<.0001
Error	6	19.2384	3.2064		
Corrected Total	8	4648.1			

Parameter	Estimate	Approx Std Error	Approximate 95% Confidence Limits	
th1	66.7592	1.4695	63.1633	70.3550
th2	56.0969	1.6005	52.1806	60.0133
th3	-11.5469	0.0999	-11.7912	-11.3026

Approximate Correlation Matrix

	th1	th2	th3
th1	1.0000000	0.7565905	-0.7648290
th2	0.7565905	1.0000000	-0.3861020
th3	-0.7648290	-0.3861020	1.0000000

Exercise 2 Graph and Listing of Data



conc	treat	dummy	dumyes	dumno	velocity
0.02	no	0	0	1	67
0.02	no	0	0	1	51
0.06	no	0	0	1	84
0.06	no	0	0	1	86
0.11	no	0	0	1	98
0.11	no	0	0	1	115
0.22	no	0	0	1	131
0.22	no	0	0	1	124
0.56	no	0	0	1	144
0.56	no	0	0	1	158
1.10	no	0	0	1	160
0.02	yes	1	1	0	76
0.02	yes	1	1	0	47
0.06	yes	1	1	0	97
0.06	yes	1	1	0	107
0.11	yes	1	1	0	123
0.11	yes	1	1	0	139
0.22	yes	1	1	0	159
0.22	yes	1	1	0	152
0.56	yes	1	1	0	191
0.56	yes	1	1	0	201
1.10	yes	1	1	0	207
1.10	yes	1	1	0	200

Exercise 2 SAS Program and Output A

```
proc nlin data=one;
  parms th1=150 th2=0.10 th3=0 th4=0;
  model velocity=((th1+th3*dummy)*conc)/(th2+th4*dummy+conc);
run;
```

The NLIN Procedure
Dependent Variable velocity
Method: Gauss-Newton

Iterative Phase

Iter	th1	th2	th3	th4	Sum of Squares
0	150.0	0.1000	0	0	45433.4
1	158.5	0.0239	53.5635	0.0151	8794.1
2	155.1	0.0376	53.7329	0.0182	2379.9
3	158.9	0.0453	53.0719	0.0175	2066.1
4	160.0	0.0473	52.5673	0.0167	2055.3
5	160.2	0.0476	52.4332	0.0165	2055.1
6	160.3	0.0477	52.4085	0.0164	2055.1
7	160.3	0.0477	52.4044	0.0164	2055.1
8	160.3	0.0477	52.4038	0.0164	2055.1

```
NOTE: Convergence criterion met.

                    Estimation Summary
        Method                       Gauss-Newton
        Iterations                              8
        Observations Read                      23
        Observations Used                      23
        Observations Missing                    0
    NOTE: An intercept was not specified for this model.

                               Sum of        Mean               Approx
Source                   DF   Squares      Square    F Value    Pr > F
Model                     4    417562      104390     965.14    <.0001
Error                    19    2055.1       108.2
Uncorrected Total        23    419617

                            Approx
Parameter      Estimate    Std Error    Approximate 95% Confidence Limits
th1               160.3       6.8960       145.8       174.7
th2              0.0477      0.00828      0.0304      0.0650
th3             52.4038       9.5510     32.4135     72.3942
th4              0.0164       0.0114    -0.00751      0.0403

                   Approximate Correlation Matrix
                 th1            th2            th3            th4
   th1     1.0000000      0.7768268     -0.7220184     -0.5628691
   th2     0.7768268      1.0000000     -0.5608833     -0.7245748
   th3    -0.7220184     -0.5608833      1.0000000      0.7712219
   th4    -0.5628691     -0.7245748      0.7712219      1.0000000
```

Exercise 2 SAS Program and Output B

```
proc nlin data=one;
  parms th1=150 th2=0.10 th3=0;
  th4=0;
  model velocity=((th1+th3*dummy)*conc)/(th2+th4+conc);
run;
```

```
                     The NLIN Procedure
                 Dependent Variable velocity
                   Method: Gauss-Newton

                     Iterative Phase
                                                     Sum of
        Iter        th1         th2         th3     Squares
           0      150.0      0.1000           0     45433.4
           1      161.6      0.0321     47.9824      9612.9
           2      162.3      0.0482     41.2622      2595.2
           3      165.7      0.0561     41.6938      2251.4
           4      166.5      0.0577     41.9696      2241.1
```

```
              5       166.6      0.0579     42.0189      2240.9
              6       166.6      0.0580     42.0251      2240.9
              7       166.6      0.0580     42.0259      2240.9
              8       166.6      0.0580     42.0260      2240.9
      NOTE: Convergence criterion met.

                         Estimation Summary
                  Method                    Gauss-Newton
                  Iterations                           8
                  Observations Read                   23
                  Observations Used                   23
                  Observations Missing                 0
            NOTE: An intercept was not specified for this model.

                                     Sum of        Mean               Approx
  Source                    DF      Squares      Square    F Value    Pr > F
  Model                      3       417376      139125    1241.70    <.0001
  Error                     20       2240.9       112.0
  Uncorrected Total         23       419617

                                   Approx
  Parameter      Estimate       Std Error    Approximate 95% Confidence Limits
  th1               166.6          5.8074        154.5        178.7
  th2              0.0580         0.00591       0.0456       0.0703
  th3             42.0260          6.2721      28.9426      55.1093

                    Approximate Correlation Matrix
                            th1              th2              th3
            th1       1.0000000        0.6112817       -0.5405580
            th2       0.6112817        1.0000000        0.0644066
            th3      -0.5405580        0.0644066        1.0000000
```

Exercise 2 SAS Program and Output C

```
proc nlin data=one;
  parms th1=150 th2=0.10;
  th3=0;
  model velocity=((th1+th3*dummy)*conc)/(th2+conc);
run;
```

```
                         The NLIN Procedure
                     Dependent Variable velocity
                        Method: Gauss-Newton

                           Iterative Phase
                                                  Sum of
                  Iter         th1         th2     Squares
                     0       150.0      0.1000     45433.4
                     1       190.7      0.0398     11454.1
                     2       187.5      0.0536      7424.5
                     3       190.1      0.0591      7280.7
```

```
                 4       190.7      0.0602      7276.6
                 5       190.8      0.0604      7276.5
                 6       190.8      0.0604      7276.5
                 7       190.8      0.0604      7276.5
    NOTE: Convergence criterion met.

                                  Sum of        Mean               Approx
 Source                   DF     Squares      Square    F Value    Pr > F
 Model                     2      412340      206170     595.00    <.0001
 Error                    21      7276.5       346.5
 Uncorrected Total        23      419617

                                                Approx
 Parameter      Estimate    Std Error    Approximate 95% Confidence Limits
 th1               190.8       8.7646       172.6       209.0
 th2              0.0604       0.0108      0.0380      0.0828

                    Approximate Correlation Matrix
                                  th1             th2
                  th1       1.0000000       0.7757154
                  th2       0.7757154       1.0000000
```

Exercise 2 SAS Program and Output D (after introducing TWO dummy variables in the dataset for puromycin YES called 'dumyes' and for puromycin NO called 'dumno')

```
proc nlin data=one;
  parms th1yes=150 th1no=150 th2yes=0.10 th2no=0.10;
  th1=th1yes*dumyes+th1no*dumno;
  th2=th2yes*dumyes+th2no*dumno;
  model velocity=(th1*conc)/(th2+conc);
run;
```

```
                         The NLIN Procedure
                     Dependent Variable velocity
                        Method: Gauss-Newton

                          Iterative Phase
                                                                Sum of
    Iter      th1yes       th1no      th2yes       th2no       Squares
       0       150.0       150.0      0.1000      0.1000       45433.4
       1       212.0       158.5      0.0390      0.0239        8794.1
       2       208.8       155.1      0.0558      0.0376        2379.9
       3       212.0       158.9      0.0628      0.0453        2066.1
       4       212.6       160.0      0.0640      0.0473        2055.3
       5       212.7       160.2      0.0641      0.0476        2055.1
       6       212.7       160.3      0.0641      0.0477        2055.1
       7       212.7       160.3      0.0641      0.0477        2055.1
       8       212.7       160.3      0.0641      0.0477        2055.1
    NOTE: Convergence criterion met.
```

Estimation Summary

Method	Gauss-Newton
Iterations	8
Observations Read	23
Observations Used	23
Observations Missing	0

NOTE: An intercept was not specified for this model.

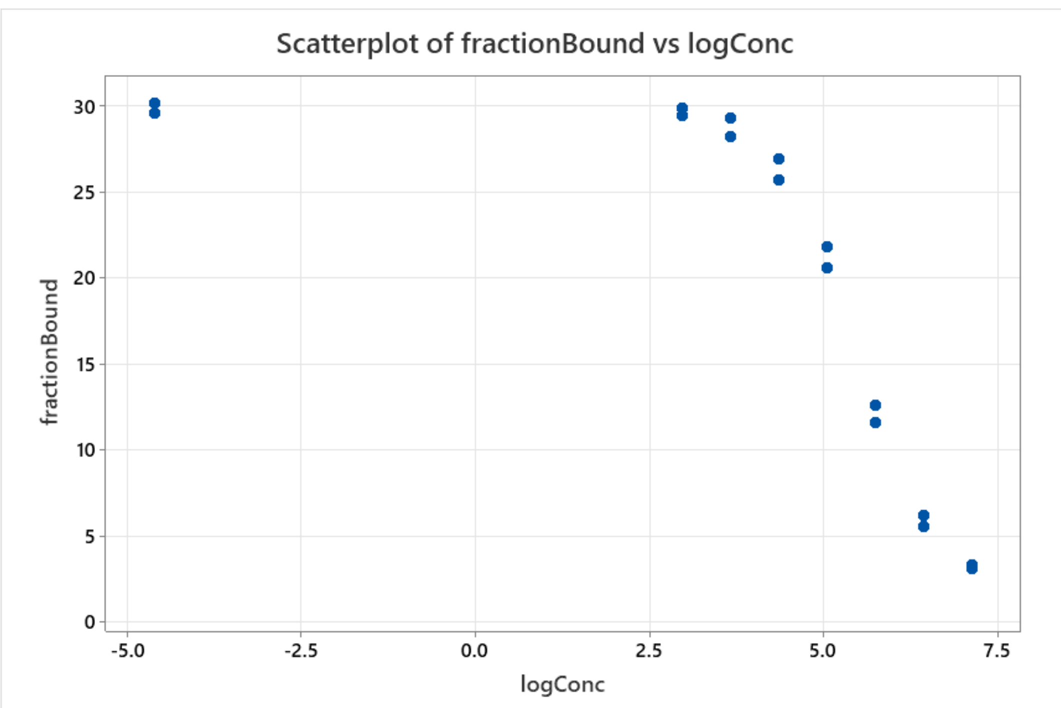
Source	DF	Sum of Squares	Mean Square	F Value	Approx Pr > F
Model	4	417562	104390	965.14	<.0001
Error	19	2055.1	108.2		
Uncorrected Total	23	419617			

Parameter	Estimate	Approx Std Error	Approximate 95% Confidence Limits	
th1yes	212.7	6.6081	198.9	226.5
th1no	160.3	6.8960	145.8	174.7
th2yes	0.0641	0.00788	0.0476	0.0806
th2no	0.0477	0.00828	0.0304	0.0650

Approximate Correlation Matrix

	th1yes	th1no	th2yes	th2no
th1yes	1.0000000	0.0000000	0.7650837	0.0000000
th1no	0.0000000	1.0000000	0.0000000	0.7768268
th2yes	0.7650837	0.0000000	1.0000000	0.0000000
th2no	0.0000000	0.7768268	0.0000000	1.0000000

Exercise 3 Graph and Data Listing



conc	fraction_bound	log_conc
0.0	30.16	-4.60517
0.0	29.58	-4.60517
19.4	29.87	2.96579
19.4	29.43	2.96579
38.8	28.19	3.65868
38.8	29.33	3.65868
77.5	26.96	4.35041
77.5	25.72	4.35041
155.0	21.82	5.04349
155.0	20.59	5.04349
310.0	12.62	5.73660
310.0	11.57	5.73660
620.0	5.56	6.42974
620.0	6.17	6.42974
1240.0	3.33	7.12287
1240.0	3.07	7.12287

Exercise 3 SAS Program/Output A (NLIN)

```
proc nlin data=one;
  parms th1=30 th2=0 th3=300 th4=2;
  if conc=0 then do;
    mean=th1;
  end;
  else do;
    t=(conc/th3)**th4;
    mean=th2+(th1-th2)/(1+t);
  end;
  model fraction_bound=mean;
  output out=two r=residual p=predicted_value;
run;
proc print noobs;
  var residual predicted_value;
run;
```

The NLIN Procedure
Dependent Variable fraction_bound

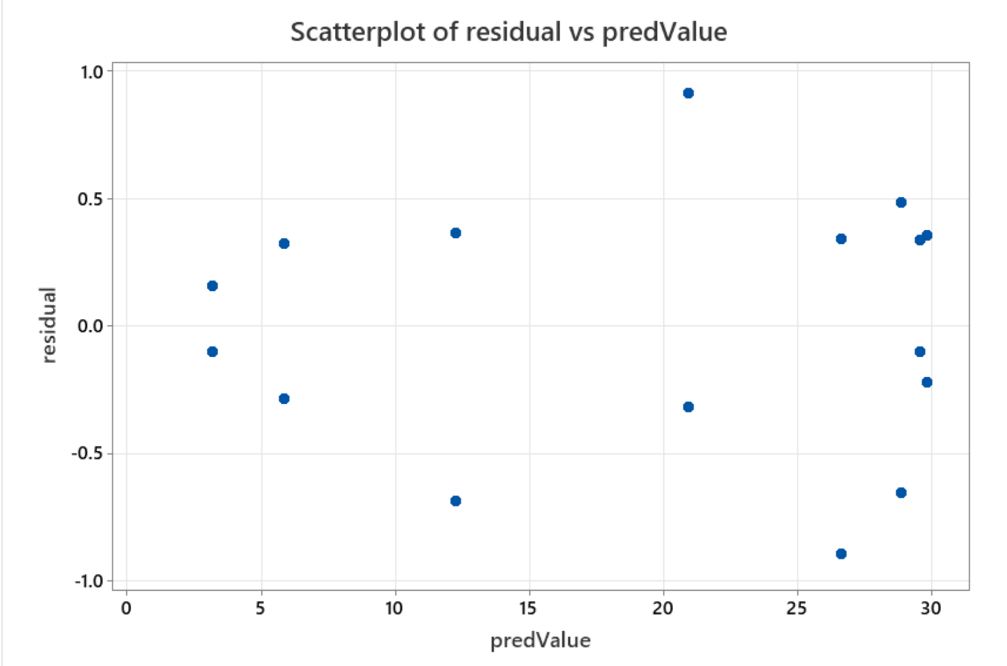
Source	DF	Sum of Squares	Mean Square	F Value	Approx Pr > F
Model	3	1704.2	568.1	1869.08	<.0001
Error	12	3.6471	0.3039		
Corrected Total	15	1707.8			

Parameter	Estimate	Approx Std Error	Approximate 95% Confidence Limits	
th1	29.8033	0.2658	29.2242	30.3823
th2	1.9929	0.5667	0.7582	3.2276

th3	232.4	8.6272	213.6	251.2
th4	1.8619	0.1122	1.6174	2.1065

Exercise 3 NLIN Residuals and Residual Plot

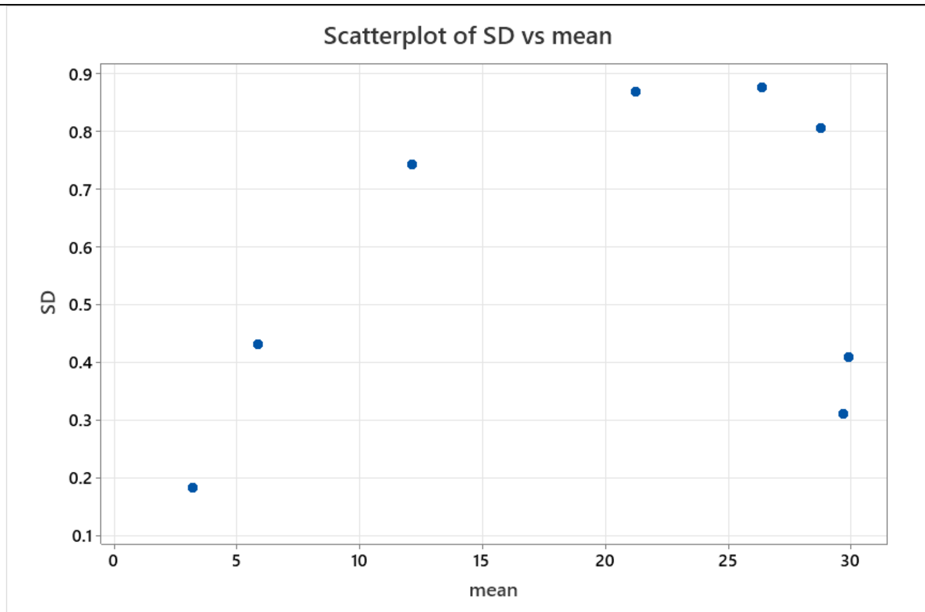
residual	predValue
0.35675	29.8033
-0.22325	29.8033
0.33705	29.5329
-0.10295	29.5329
-0.65525	28.8452
0.48475	28.8452
0.34247	26.6175
-0.89753	26.6175
0.91179	20.9082
-0.31821	20.9082
0.36251	12.2575
-0.68749	12.2575
-0.28828	5.8483
0.32172	5.8483
0.15796	3.1720
-0.10204	3.1720



Exercise 3 SAS Program/Output B

```
proc sort data=one;
  by conc; run;
proc means noprint;
  var fraction_bound;
  by conc;
  output out=three
   mean=mean stddev=sd;
run;
proc print; run;
```

Obs	conc	mean	sd
1	0.0	29.870	0.41012
2	19.4	29.650	0.31113
3	38.8	28.760	0.80610
4	77.5	26.340	0.87681
5	155.0	21.205	0.86974
6	310.0	12.095	0.74246
7	620.0	5.865	0.43134
8	1240.0	3.200	0.18385



Exercise 3 SAS Program and Output C

```
proc nlmixed data=one;
  parms th1=30 th2=0 th3=300 th4=2 sigma=1;
  if conc=0 then do;
    mean=th1;
  end;
  else do;
    t=(conc/th3)**th4; den=1+t;
    mean=th2+(th1-th2)/den;
  end;
  var=sigma*sigma;
  model fraction_bound ~ normal(mean,var);
run;
```

```
                              The NLMIXED Procedure

                                  Fit Statistics
                        -2 Log Likelihood                    21.7
                        AIC (smaller is better)              31.7
                        AICC (smaller is better)             37.7
                        BIC (smaller is better)              35.6
```

Parameter Estimates

Parameter	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper
th1	29.8033	0.2329	16	127.97	<.0001	0.05	29.3095	30.2970
th2	1.9929	0.4927	16	4.04	0.0009	0.05	0.9484	3.0374
th3	232.44	7.4175	16	31.34	<.0001	0.05	216.72	248.17
th4	1.8619	0.09942	16	18.73	<.0001	0.05	1.6512	2.0727
sigma	0.4774	0.08440	16	5.66	<.0001	0.05	0.2985	0.6564

Exercise 3 SAS Program and Output D

```
proc nlmixed data=one;
  parms th1=30 th2=0 th3=300 th4=2 sigma=0.01 rho=0;
  if conc=0 then do;
    mean=th1;
  end;
  else do;
    t=(conc/th3)**th4; den=1+t;
    mean=th2+(th1-th2)/den;
  end;
  var=sigma*sigma*(mean)**rho;
  model fraction_bound ~ normal(mean,var);
run;
```

```
                              The NLMIXED Procedure

                                  Fit Statistics
                        -2 Log Likelihood                    19.4
```

```
                    AIC (smaller is better)          31.4
                    AICC (smaller is better)         40.7
                    BIC (smaller is better)          36.0
```

Parameter Estimates

Parameter	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper
th1	29.7840	0.2777	16	107.24	<.0001	0.05	29.1952	30.3728
th2	2.0618	0.2811	16	7.33	<.0001	0.05	1.4659	2.6577
th3	231.74	5.6829	16	40.78	<.0001	0.05	219.69	243.79
th4	1.8784	0.08705	16	21.58	<.0001	0.05	1.6939	2.0629
sigma	0.1223	0.09460	16	1.29	0.2144	0.05	-0.07822	0.3229
rho	0.9410	0.5501	16	1.71	0.1065	0.05	-0.2252	2.1071

Exercise 3 SAS Program and Output E

```
proc nlmixed data=one;
  parms th1=30 th2=2 th3=250 th4=2 sigma=0.01 rho1=5 rho2=4;
  if conc=0 then do;
    mean=th1;
  end;
  else do;
    t=(conc/th3)**th4; den=1+t;
    mean=th2+(th1-th2)/den;
  end;
  var=.00001*sigma*sigma*((mean)**rho1)*((1.1*th1-mean)**rho2);
  model fraction_bound ~ normal(mean,var);
run;
```

The NLMIXED Procedure

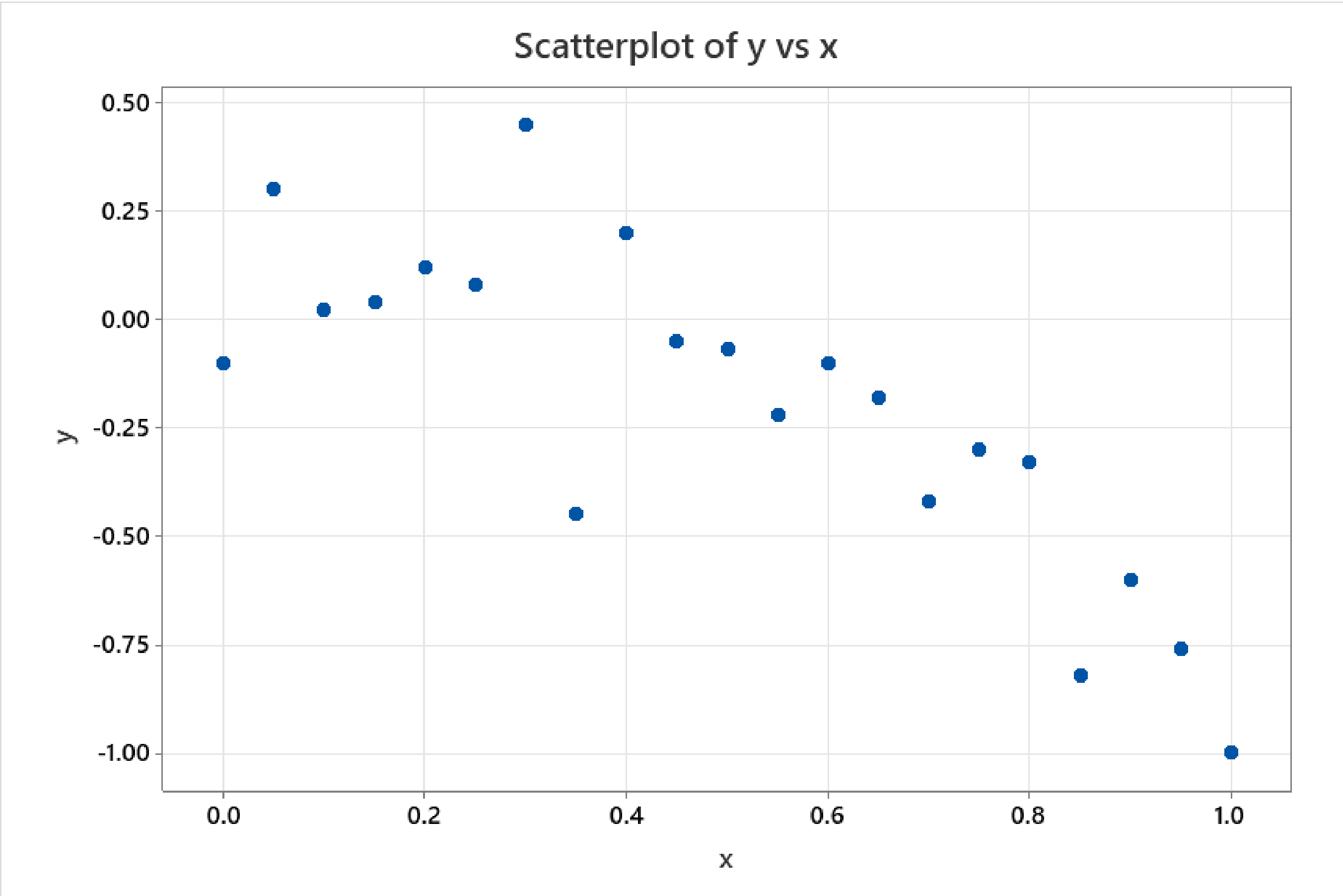
Fit Statistics

-2 Log Likelihood	15.4
AIC (smaller is better)	29.4
AICC (smaller is better)	43.4
BIC (smaller is better)	34.8

Parameter Estimates

Parameter	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper
th1	29.8710	0.1771	16	168.64	<.0001	0.05	29.4955	30.2464
th2	1.9814	0.2295	16	8.63	<.0001	0.05	1.4948	2.4680
th3	230.04	6.7797	16	33.93	<.0001	0.05	215.67	244.42
th4	1.8332	0.08383	16	21.87	<.0001	0.05	1.6555	2.0109
sigma	0.2476	0.6171	16	0.40	0.6936	0.05	-1.0606	1.5557
rho1	2.9106	1.0545	16	2.76	0.0139	0.05	0.6751	5.1461
rho2	2.0161	0.9914	16	2.03	0.0589	0.05	-0.08554	4.1176

Exercise 4 Scatterplot of Data



Exercise 4 SAS Program/Output A

```
proc nlin;
  parms b0=0 b2=-0.5 phi=0.25;
  model y=b0-2*phi*b2*x+b2*x*x;
run;
```

```
                     The NLIN Procedure
                        Dependent Variable y
                        Method: Gauss-Newton

                          Iterative Phase
                                                          Sum of
           Iter          b0           b2          phi     Squares
              0           0      -0.5000       0.2500      2.3100
              1      0.0424      -1.5529       0.0508      1.9069
              2      0.0424      -1.5529       0.1859      0.6451
      NOTE: Convergence criterion met.

                          Estimation Summary
```

```
                     Method                     Gauss-Newton
                     Iterations                            2
                     Observations Read                    21
                     Observations Used                    21
                     Observations Missing                  0

                                      Sum of        Mean                Approx
Source                     DF        Squares      Square    F Value    Pr > F
Model                       2         2.1702      1.0851      30.28    <.0001
Error                      18         0.6451      0.0358
Corrected Total            20         2.8153

                                  Approx
Parameter      Estimate       Std Error    Approximate 95% Confidence Limits
b0               0.0424          0.1130      -0.1950       0.2798
b2              -1.5529          0.5056      -2.6150      -0.4907
phi              0.1859          0.1113      -0.0480       0.4197

                       Approximate Correlation Matrix
                           b0              b2              phi
           b0        1.0000000       0.7084130      -0.8891903
           b2        0.7084130       1.0000000      -0.9188135
           phi      -0.8891903      -0.9188135       1.0000000
```

Exercise 4 SAS Program/Output B

```
proc nlin;
  parms b0=0 b2=-0.5;
  phi=-0.40;
  model y=b0-2*phi*b2*x+b2*x*x;
run;
```

```
                              The NLIN Procedure
                             Dependent Variable y
                             Method: Gauss-Newton

                               Iterative Phase
                                                        Sum of
                     Iter          b0           b2     Squares
                        0           0      -0.5000      1.4278
                        1      0.2189      -0.5642      0.7852
       NOTE: Convergence criterion met.

                              Estimation Summary
                     Method                     Gauss-Newton
                     Iterations                            1
                     Observations Read                    21
                     Observations Used                    21
                     Observations Missing                  0
```

Source	DF	Sum of Squares	Mean Square	F Value	Approx Pr > F
Model	1	2.0301	2.0301	49.13	<.0001
Error	19	0.7852	0.0413		
Corrected Total	20	2.8153			

Parameter	Estimate	Approx Std Error	Approximate 95% Confidence Limits	
b0	0.2189	0.0744	0.0633	0.3746
b2	-0.5642	0.0805	-0.7327	-0.3957

Approximate Correlation Matrix

	b0	b2
b0	1.0000000	-0.8026837
b2	-0.8026837	1.0000000