

# WinNonlin Compartmental Modeling Analysis

Version 4.0.1 Build 200210171634

## User-defined ASCII model:

```
MODEL
Remark *****
remark   Developer: TA
remark   Model Date:03-23-2006
remark   Model Version: 1.0
remark   *****
commands
COMMANDS
NFUNCTIONS 1
NDERIVATIVES 1
NPARAMETERS 4
PNAME$ 'kout','Ro','IC50','Imax'
NSECONDARY 1
SNAMES 'kin'
END
TEMPORARY
T=X
D1= 250000
V= 84
CL=46
kin=Ro*Kout
C1 = D1/V*exp(-CL/V*T)
IHF1 = Imax*C1/(C1+IC50)
END
START
Z(1) = Ro
END
DIFFERENTIAL
DZ(1) = kin*(1-IHF1)-kout*Z(1)
END
FUNCTION 1
F= Z(1)
END
remark - define any secondary
SECONDARY
kin=Ro*kout
END
remark - end of model
EOM
```

## Settings for analysis:

Input Workbook: C:\Data\misc\ACCP\_2006\Data\WNLdata\NizatidineOneD.pwo

Input Worksheet: Sheet1

Input Sort Keys: [none]

Gauss-Newton (Levenberg and Hartley) method used

Convergence criteria of 0.0001 used during minimization process

50 maximum iterations allowed during minimization process

0.001 value used in estimation of partial derivatives

**Input data:**

| Time (hr) | Acid_Secretion ({mEq/hr}) |
|-----------|---------------------------|
| 0         | 31.67                     |
| 0.25      | 15.71                     |
| 0.5       | 2.14                      |
| 0.75      | 0.95                      |
| 1         | 0.83                      |
| 1.25      | 1.31                      |
| 1.5       | 3.33                      |
| 1.75      | 3.93                      |
| 2         | 3.93                      |
| 2.25      | 5.95                      |
| 2.5       | 6.19                      |
| 2.75      | 7.02                      |
| 3         | 10.12                     |
| 3.25      | 9.64                      |
| 3.5       | 12.74                     |

**Output data:**

WARNING: Possible inaccuracies in output.  
See ASCII output file for details.

**Initial Parameters**

| Parameter | Value | Lower | Upper |
|-----------|-------|-------|-------|
| KOUT      | 5     | 0     | 50    |
| RO        | 30    | 0     | 100   |
| IC50      | 190   | 0     | 500   |
| IMAX      | 0.9   | 0     | 1     |

**Minimization Process**

| Iteration | Weighted_SS | kout  | Ro    | IC50  | Imax   |
|-----------|-------------|-------|-------|-------|--------|
| 0         | 143.581     | 5     | 30    | 190   | 0.9    |
| 1         | 82.0875     | 4.324 | 32.36 | 198.6 | 0.9703 |
| 2         | 72.4254     | 4.852 | 32.46 | 194.2 | 0.9833 |
| 3         | 68.1613     | 4.372 | 32.52 | 209   | 0.9937 |
| 4         | 65.6048     | 4.616 | 32.67 | 213.3 | 0.9987 |
| 5         | 65.3496     | 4.525 | 32.61 | 209.2 | 0.9989 |
| 6         | 65.1221     | 4.609 | 32.68 | 210.7 | 0.9996 |
| 7         | 64.9475     | 4.526 | 32.62 | 211   | 0.9999 |
| 8         | 64.915      | 4.559 | 32.65 | 210.7 | 1      |
| 8         | 64.9116     | 4.549 | 32.64 | 210.6 | 1      |

**Final Parameters**

|    |    |    |    |    |    |    |    |   |   |   |    |    |   |    |    |    |    |    |    |   |   |   |   |   |   |   |
|----|----|----|----|----|----|----|----|---|---|---|----|----|---|----|----|----|----|----|----|---|---|---|---|---|---|---|
| k  | k  | k  | k  | k  | k  | k  | R  | R | R | R | R  | R  | R | IC | IC | IC | IC | IC | IC | I | I | I | I | I | I | I |
| o  | o  | o  | o  | o  | o  | o  | o  | o | o | o | o  | o  | o | 5  | 5  | 5  | 5  | 5  | 5  | m | m | m | m | m | m | m |
| ut | ut | ut | ut | ut | ut | ut |    |   |   |   |    |    |   | 0  | 0  | 0  | 0  | 0  | 0  | a | a | a | a | a | a | a |
|    |    |    |    |    |    |    | St | C | U | U | PI | PI |   |    |    |    |    |    |    | x | x | x | x | x | x | x |



|      |           |           |         |          |  |
|------|-----------|-----------|---------|----------|--|
| KOUT | 1.22587   |           |         |          |  |
| RO   | 0.751779  | 5.86392   |         |          |  |
| IC50 | -69.359   | -72.3322  | 10059.4 |          |  |
| IMAX | -5.81E-02 | -1.96E-02 | 7.64737 | 6.72E-03 |  |

## Summary Table

| Time_obs (hr) | Acid_Secretion_obs ({mEq/hr}) | Time (hr) | Acid_Secretion ({mEq/hr}) | Predicted ({mEq/hr}) | Residual ({mEq/hr}) | Weight | SE_Yhat | Standard_Res |
|---------------|-------------------------------|-----------|---------------------------|----------------------|---------------------|--------|---------|--------------|
| 0             | 31.67                         | 0.0000    | 31.6700                   | 32.6416              | -0.9716             | 1.0000 | 2.4216  | -5.0419      |
| 0.25          | 15.71                         | 0.2500    | 15.7100                   | 12.0481              | 3.6619              | 1.0000 | 2.0681  | 2.8735       |
| 0.5           | 2.14                          | 0.5000    | 2.1400                    | 5.6578               | -3.5178             | 1.0000 | 1.2927  | -1.7104      |
| 0.75          | 0.95                          | 0.7500    | 0.9500                    | 3.8477               | -2.8977             | 1.0000 | 1.0231  | -1.3152      |
| 1             | 0.83                          | 1.0000    | 0.8300                    | 3.5346               | -2.7046             | 1.0000 | 1.0629  | -1.2382      |
| 1.25          | 1.31                          | 1.2500    | 1.3100                    | 3.7322               | -2.4222             | 1.0000 | 1.0456  | -1.1047      |
| 1.5           | 3.33                          | 1.5000    | 3.3300                    | 4.1264               | -0.7964             | 1.0000 | 0.9632  | -0.3571      |
| 1.75          | 3.93                          | 1.7500    | 3.9300                    | 4.6187               | -0.6887             | 1.0000 | 0.8596  | -0.3031      |
| 2             | 3.93                          | 2.0000    | 3.9300                    | 5.1793               | -1.2493             | 1.0000 | 0.7719  | -0.5424      |
| 2.25          | 5.95                          | 2.2500    | 5.9500                    | 5.8003               | 0.1497              | 1.0000 | 0.7323  | 0.0646       |
| 2.5           | 6.19                          | 2.5000    | 6.1900                    | 6.4801               | -0.2901             | 1.0000 | 0.7627  | -0.1258      |
| 2.75          | 7.02                          | 2.7500    | 7.0200                    | 7.2187               | -0.1987             | 1.0000 | 0.8628  | -0.0875      |
| 3             | 10.12                         | 3.0000    | 10.1200                   | 8.0157               | 2.1043              | 1.0000 | 1.0143  | 0.9533       |
| 3.25          | 9.64                          | 3.2500    | 9.6400                    | 8.8699               | 0.7701              | 1.0000 | 1.1963  | 0.3643       |
| 3.5           | 12.74                         | 3.5000    | 12.7400                   | 9.7788               | 2.9612              | 1.0000 | 1.3921  | 1.4875       |

## Diagnostics

| Function | Item            | Value    |
|----------|-----------------|----------|
| 1        | CSS             | 891.575  |
| 1        | WCSS            | 891.575  |
| 1        | SSR             | 64.9116  |
| 1        | WSSR            | 64.9116  |
| 1        | S               | 2.42921  |
| 1        | DF              | 11       |
| 1        | CORR_(OBS,PRED) | 0.9663   |
| 1        | AIC             | 70.59539 |
| 1        | SBC             | 73.42759 |

## Differential Equations

| Time | Z[1]      |
|------|-----------|
| 0    | 32.641570 |
| 0.25 | 12.048131 |
| 0.5  | 5.657757  |
| 0.75 | 3.847685  |
| 1    | 3.534614  |
| 1.25 | 3.732180  |
| 1.5  | 4.126392  |
| 1.75 | 4.618683  |
| 2    | 5.179328  |
| 2.25 | 5.800319  |
| 2.5  | 6.480126  |

2.75 7.218690  
 3 8.015691  
 3.25 8.869886  
 3.5 9.778808

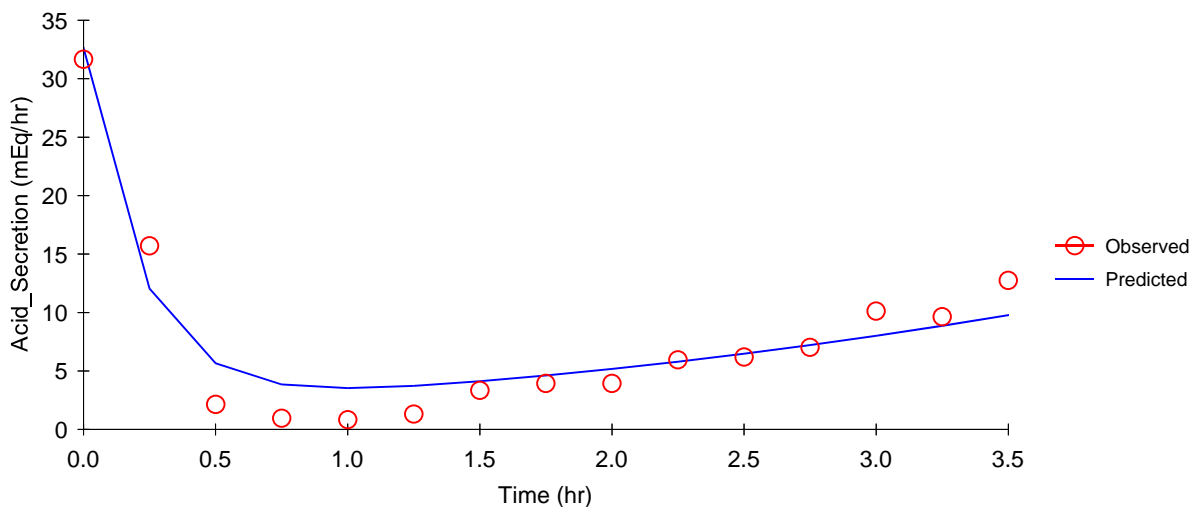
### Partial Derivatives

| Function | Time (hr) | kout        | Ro         | IC50       | Imax         |
|----------|-----------|-------------|------------|------------|--------------|
| 1        | 0         | 0.00000000  | 1.00000000 | 0.00000000 | 0.00000000   |
| 1        | 0.25      | -2.42489450 | 0.36910388 | 0.00697247 | -20.59347729 |
| 1        | 0.5       | -1.52597991 | 0.17333009 | 0.01006632 | -26.98384927 |
| 1        | 0.75      | -0.69733808 | 0.11787703 | 0.01199749 | -28.79392845 |
| 1        | 1         | -0.25479078 | 0.10828595 | 0.01363779 | -29.10699598 |
| 1        | 1.25      | -0.05220287 | 0.11433833 | 0.01526560 | -28.90943845 |
| 1        | 1.5       | 0.03654209  | 0.12641528 | 0.01696642 | -28.51522792 |
| 1        | 1.75      | 0.07723660  | 0.14149696 | 0.01876080 | -28.02293764 |
| 1        | 2         | 0.09906912  | 0.15867275 | 0.02064481 | -27.46229173 |
| 1        | 2.25      | 0.11394166  | 0.17769729 | 0.02260258 | -26.84129979 |
| 1        | 2.5       | 0.12642011  | 0.19852372 | 0.02461013 | -26.16149119 |
| 1        | 2.75      | 0.13812721  | 0.22115021 | 0.02663649 | -25.42292576 |
| 1        | 3         | 0.14953674  | 0.24556696 | 0.02864435 | -24.62592315 |
| 1        | 3.25      | 0.16067417  | 0.27173588 | 0.03059095 | -23.77172705 |
| 1        | 3.5       | 0.17138477  | 0.29958141 | 0.03242934 | -22.86280372 |

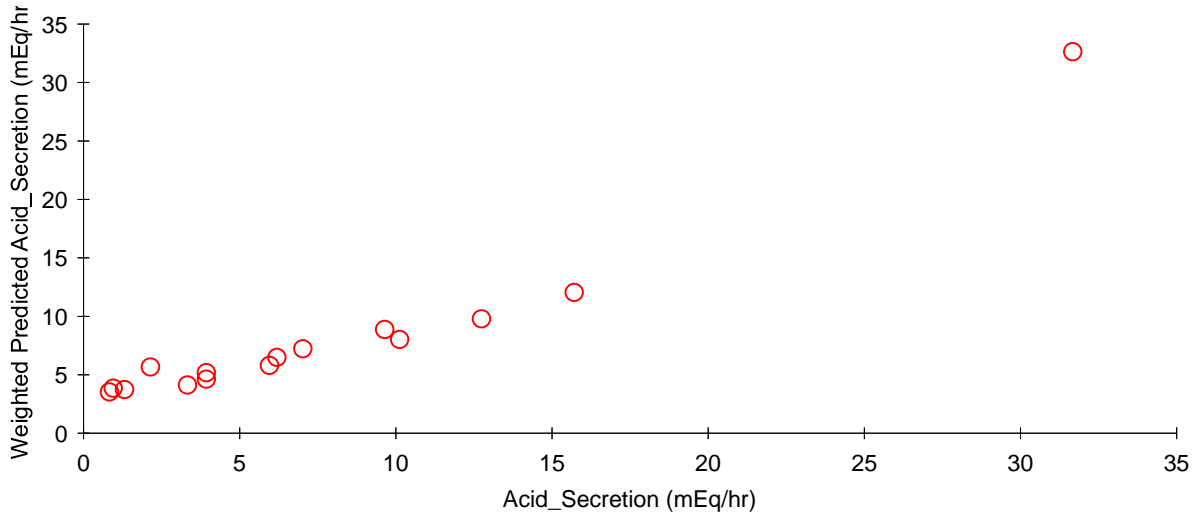
### Secondary Parameters

| KIN        | KIN_StdError |
|------------|--------------|
| 148.501059 | 40.62978571  |

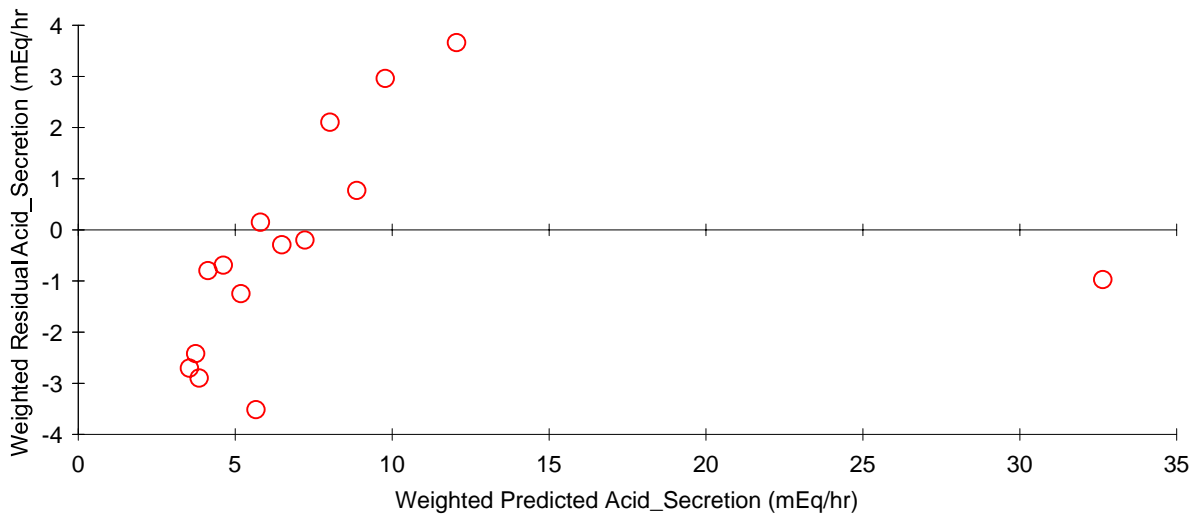
### X vs. Observed Y and Predicted Y



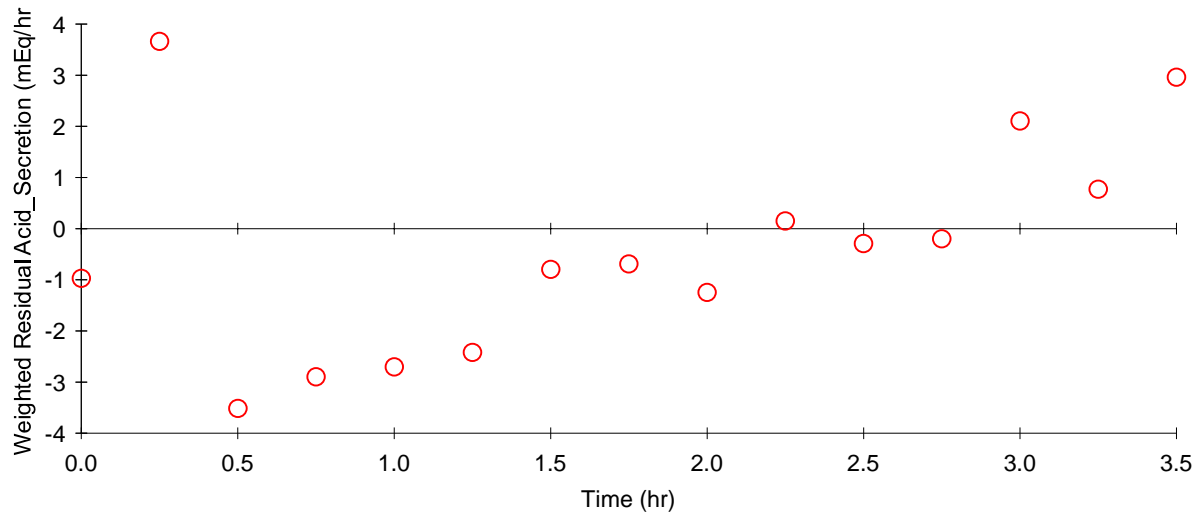
### Observed Y vs. Weighted Predicted Y



### Weighted Predicted Y vs. Weighted Residual Y



## X vs. Weighted Residual Y



## Partial Derivatives

