

WinNonlin Compartmental Modeling Analysis

Version 4.0.1 Build 200210171634

User-defined ASCII model:

```
MODEL
remark *****
remark Developer:
remark Model Date:      08-14-2006
remark Model Version:   1.0
remark *****
remark
remark - define model-specific commands
COMMANDS
NFUNCTIONS 1
NDERIVATIVES 5
NPARAMETERS 3
PNames 'EMAX', 'EC50', 'TAU'
END
remark - define temporary variables
TEMPORARY
T=X
E0=0.09
D=100
V=2.41
CL=1.3
C=D/V*EXP(-CL/V*T)
END
remark - define differential equations starting values
START
Z(1) = 0
Z(2) = 0
Z(3) = 0
Z(4) = 0
Z(5) = 0
END
remark - define differential equations
DIFFERENTIAL
DZ(1) = 1/TAU*(EMAX*C/(EC50+C) - Z(1))
DZ(2) = (Z(1)-Z(2))/TAU
DZ(3) = (Z(2)-Z(3))/TAU
DZ(4) = (Z(3)-Z(4))/TAU
DZ(5) = (Z(4)-Z(5))/TAU
END
remark - define algebraic functions
FUNCTION 1
F= E0+Z(5)
END
remark - define any secondary parameters
remark - end of model
EOM
```

Settings for analysis:

Input Workbook: [Untitled12]

Input Worksheet: Sheet1

Input Sort Keys: [none]

Gauss-Newton (Levenberg and Hartley) method used
Iterative reweighting used during minimization process
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)	Concentration (mg/L)	Activity
0	41.5	0.092
0.25	36.28	0.076
0.5	31.685	0.087
0.75	27.658	0.098
1	24.22	0.112
2	14.113	0.285
3	8.252	0.523
4	4.971	0.798
5	2.803	1.225
6	1.639	1.348
8	0.551	1.332
10	0.182	1.102
15	0.012	0.318
20		0.131
30		0.102
40	?	0.096

Output data:

Initial Parameters

Parameter	Value	Lower	Upper
EMAX	1.5	0	15
EC50	1	0	10
TAU	1	0	10

Minimization Process

Iteration	Weighted_SS	EMAX	EC50	TAU
0	0.454542	1.5	1	1
1	3.39E-02	1.528	0.7776	0.8145
2	3.14E-02	1.623	0.9532	0.8402
3	3.13E-02	1.627	0.9682	0.8393
3	3.13E-02	1.627	0.9682	0.8391

Final Parameters

E	E	E	E	E	E	E	EC	EC	EC	EC	EC	EC	EC	TA	TA	TA	TA	TA	TA	TA
M	M	M	M	M	M	M	50	50	50	50	50	50	50	U	U	U	U	U	U	U
AX	AX	AX	AX	AX	AX	AX	_S	_C	_U	_U	_P	_P	_P	St	CV	Un	Un	PI	PI	PI
	_S	_C	_U	_U	_P	_P	td	V	ni	ni	la	la	la	dE	%	iva	iva	an	an	an
	td	V	ni	ni	la	la	Er	%	va	va	na	na	na	rro		rCl	rCl	ar	ar	ar
	Er	%	va	va	na	na	ror		rCl	rCl	rCl	rCl	rCl	r		_L	_U	Cl	Cl	Cl
	ror		rCl	rCl	rCl	rCl			_L	_U	_L	_U	_L	_U		ow	pp	_L	_U	_U
			ow	pp	ow	pp			ow	pp	ow	pp	ow	pp		er	er	ow	pp	pp
			er	er	er	er			er	er	er	er	er	er				er	er	er

1.6	0.1	7.2	1.3	1.8	1.2	2.0	0.9	0.2	30.	0.3	1.5	0.0	1.9	0.8	0.0	4.2	0.7	0.9	0.7	0.9
272	177	4	728	816	445	099	682	920	16	373	991	192	172	390	357	6	618	162	229	551
41	66		23	59	70	11	44	47		16	72	64	24	72	23		97	47	92	51

Correlation Matrix

Parameter	EMAX	EC50	TAU
EMAX	1		
EC50	0.943434	1	
TAU	0.90801	0.877612	1

Eigenvalues

Number	Value
1	11.64
2	1.735
3	2.44E-02

Condition Numbers

Iteration	Rank	Condition
0	3	26.340803
1	3	17.686092
2	3	20.288004
3	3	20.428404

Variance-Covariance Matrix

Parameter	EMAX	EC50	TAU
EMAX	1.39E-02		
EC50	3.24E-02	8.53E-02	
TAU	3.82E-03	9.16E-03	1.28E-03

Summary Table

Concentration (mg/L)	Time_obs (hr)	Activity_obs	Time (hr)	Activity_y	Predicted	Residual	Weight	SE_Yhat	Standard_Res
41.5	0	0.092	0.0000	0.0920	0.0900	0.0020	11.1111	Missing	Missing
36.28	0.25	0.076	0.2500	0.0760	0.0900	-0.0140	11.1081	0.0000	-0.9519
31.685	0.5	0.087	0.5000	0.0870	0.0906	-0.0036	11.0364	0.0001	-0.2442
27.658	0.75	0.098	0.7500	0.0980	0.0936	0.0044	10.6822	0.0005	0.2921
24.22	1	0.112	1.0000	0.1120	0.1019	0.0101	9.8088	0.0014	0.6436
14.113	2	0.285	2.0000	0.2850	0.2382	0.0468	4.1983	0.0120	2.2535
8.252	3	0.523	3.0000	0.5230	0.5432	-0.0202	1.8410	0.0233	-0.7283
4.971	4	0.798	4.0000	0.7980	0.8932	-0.0952	1.1196	0.0250	-2.4359
2.803	5	1.225	5.0000	1.2250	1.1701	0.0549	0.8547	0.0265	1.1944
1.639	6	1.348	6.0000	1.3480	1.3304	0.0176	0.7516	0.0335	0.3847
0.551	8	1.332	8.0000	1.3320	1.3416	-0.0096	0.7454	0.0351	-0.2156

0.182	10	1.102	10.0000	1.1020	1.0863	0.0157	0.9205	0.0326	0.3973
0.012	15	0.318	15.0000	0.3180	0.3313	-0.0133	3.0182	0.0222	-0.7622
	20	0.131	20.0000	0.1310	0.1155	0.0155	8.6561	0.0030	0.9428
	30	0.102	30.0000	0.1020	0.0901	0.0119	11.0950	0.0000	0.8052
?	40	0.096	40.0000	0.0960	0.0900	0.0060	11.1110	0.0000	0.4072

Diagnostics

Function	Item	Value
1	CSS	3.75005
1	WCSS	5.0475
1	SSR	1.63E-02
1	WSSR	3.13E-02
1	S	4.91E-02
1	DF	13
1	CORR_(OBS,PRED)	0.9978
1	AIC	-49.40291
1	SBC	-47.08515

Differential Equations

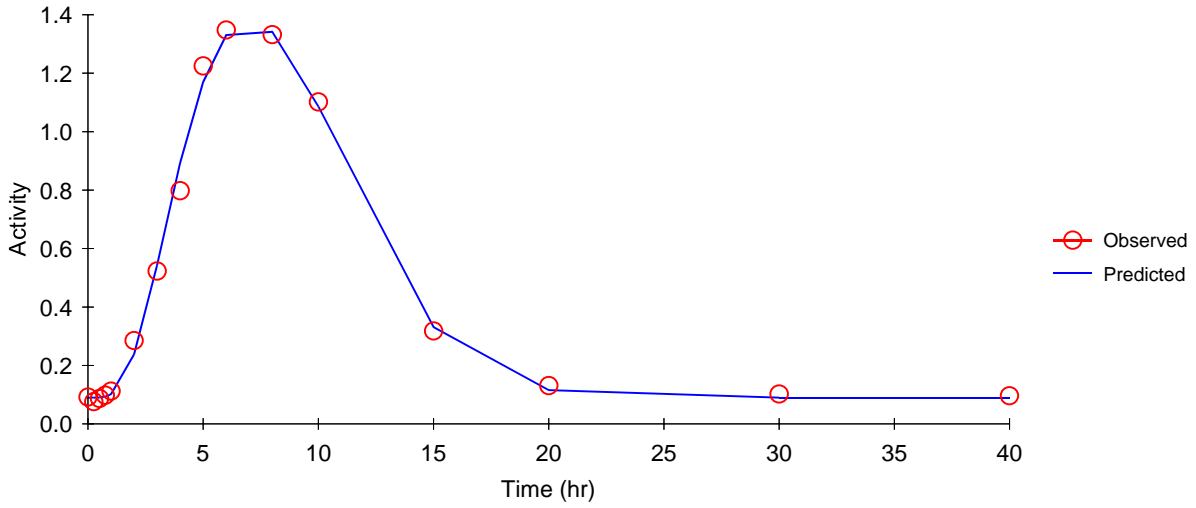
Time	Z[1]	Z[2]	Z[3]	Z[4]	Z[5]
0	0.000000	0.000000	0.000000	0.000000	0.000000
0.25	0.409024	0.057946	0.005611	0.000411	0.000024
0.5	0.711220	0.191226	0.036057	0.005200	0.000609
0.75	0.933918	0.356780	0.098070	0.020870	0.003614
1	1.097382	0.528677	0.188034	0.052401	0.011949
2	1.406477	1.075857	0.669600	0.343459	0.148189
3	1.461348	1.336790	1.074763	0.749076	0.453192
4	1.417436	1.409099	1.294988	1.077395	0.803199
5	1.315428	1.375392	1.364982	1.264939	1.080050
6	1.165227	1.273725	1.333225	1.326069	1.240443
8	0.768076	0.934127	1.078193	1.188253	1.251643
10	0.394033	0.543514	0.702225	0.857492	0.996333
15	0.037321	0.063925	0.104741	0.163212	0.241325
20	0.002616	0.004745	0.008488	0.014914	0.025525
30	0.000012	0.000021	0.000040	0.000073	0.000130
40	0.000000	0.000000	0.000000	0.000000	0.000001

Partial Derivatives

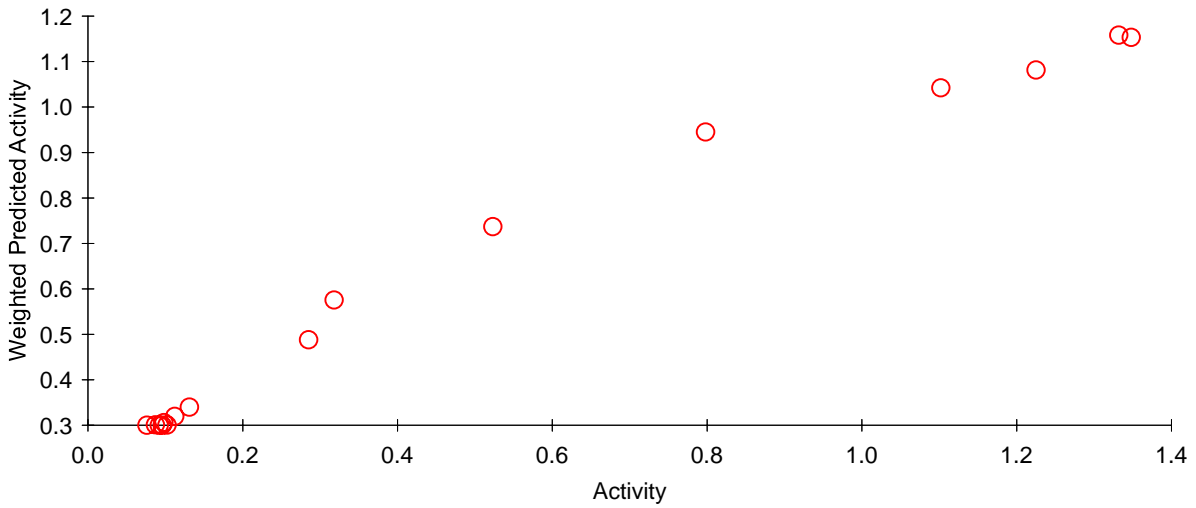
Function	Time (hr)	EMAX	EC50	TAU
1	0	0.00000000	0.00000000	0.00000000
1	0.25	0.00004991	-0.00000196	-0.00045904
1	0.5	0.00124311	-0.00004997	-0.01084462
1	0.75	0.00725803	-0.00029983	-0.05996786
1	1	0.02299751	-0.00097854	-0.17962909
1	2	0.18659872	-0.00918810	-1.13743236
1	3	0.37787931	-0.02269593	-1.72206355
1	4	0.52227249	-0.04057522	-1.68609694
1	5	0.61360648	-0.06509464	-1.30496160
1	6	0.66088658	-0.09936614	-0.82176381
1	8	0.66406469	-0.20284821	0.02578684
1	10	0.58745070	-0.32334784	0.62670648
1	15	0.25764659	-0.30988309	1.00963946
1	20	0.04615140	-0.07118187	0.29448307

1	30	0.00026657	-0.00044644	0.00218423
1	40	0.00000221	-0.00000376	-0.00002520

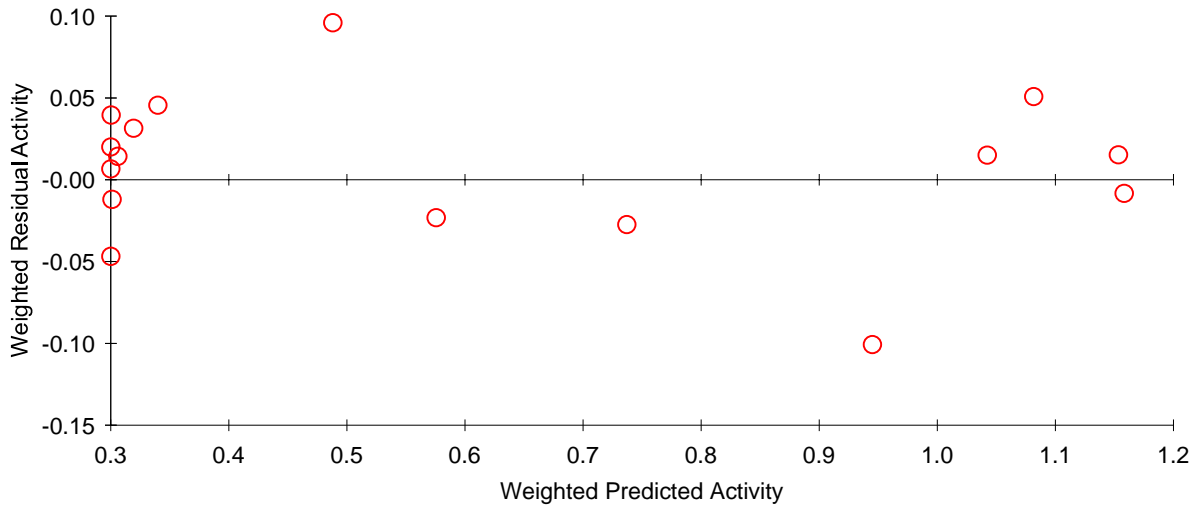
X vs. Observed Y and Predicted Y



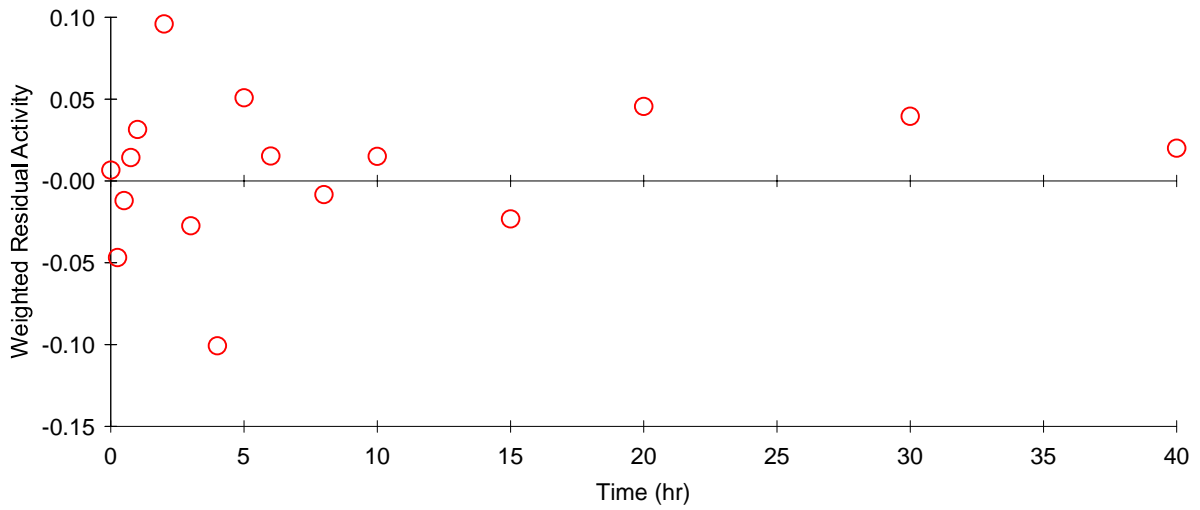
Observed Y vs. Weighted Predicted Y



Weighted Predicted Y vs. Weighted Residual Y



X vs. Weighted Residual Y



Partial Derivatives

