Nonlinear curves for the weights of male mice

Contents

1. Introduction

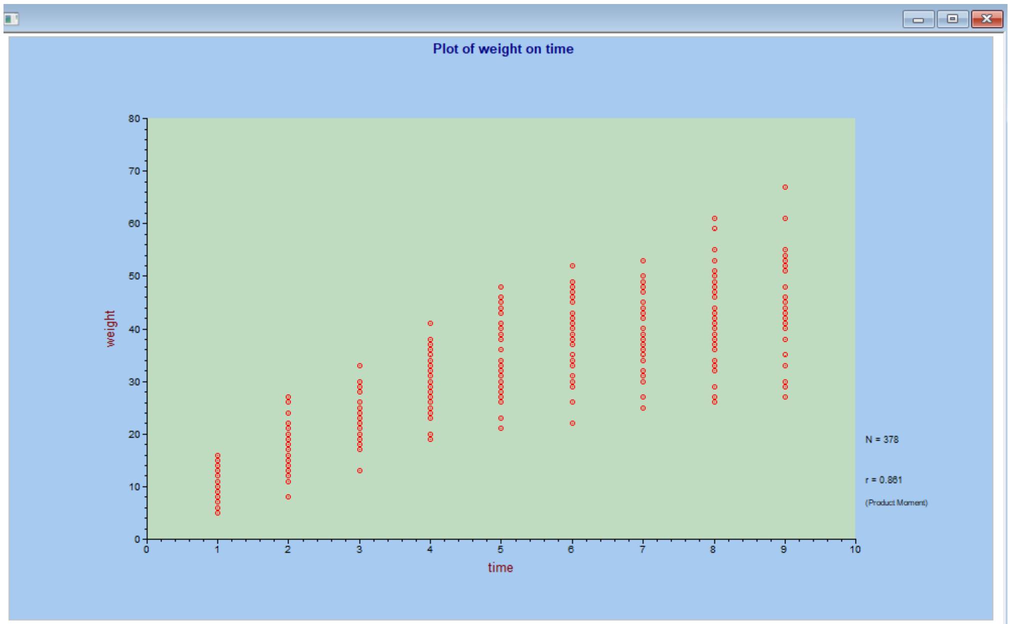
The data for this example contain repeated measurements on 82 striped mice and were obtained from the Department of Zoology at the University of Pretoria, South Africa (Du Toit, 1979). A number of male and female mice were released in an outdoor enclosure with nest boxes and sufficient food and water. They were allowed to multiply freely. Occurrence of birth was recorded daily and newborn mice were weighed weekly, from the end of the second week after birth until physical maturity was reached. To illustrate the use of a Gompertz curve for describing the growth of mice, a subset of the data is used. The data set consists of the weights of 42 male mice, measured at nine. The data are in the file **malemice.lsf**. The image below shows the data for the first two mice:

1	1.00	1.00	15.00	1.00	1.00	1.00	0.00
2	1.00	2.00	17.00	1.00	2.00	4.00	0.00
3	1.00	3.00	23.00	1.00	3.00	9.00	0.00
4	1.00	4.00	24.00	1.00	4.00	16.00	0.00
5	1.00	5.00	26.00	1.00	5.00	25.00	0.00
6	1.00	6.00	31.00	1.00	6.00	36.00	0.00
7	1.00	7.00	37.00	1.00	7.00	49.00	0.00
8	1.00	8.00	42.00	1.00	8.00	64.00	0.00
9	1.00	9.00	46.00	1.00	9.00	81.00	0.00
10	2.00	1.00	11.00	1.00	1.00	1.00	0.00
11	2.00	2.00	14.00	1.00	2.00	4.00	0.00
12	2.00	3.00	20.00	1.00	3.00	9.00	0.00
13	2.00	4.00	24.00	1.00	4.00	16.00	0.00
14	2.00	5.00	29.00	1.00	5.00	25.00	0.00
15	2.00	6.00	35.00	1.00	6.00	36.00	0.00
16	2.00	7.00	36.00	1.00	7.00	49.00	0.00
17	2.00	8.00	41.00	1.00	8.00	64.00	0.00
18	2.00	9.00	43.00	1.00	9.00	81.00	0.00

The data set contains the following variables:

- ID2: Mouse identifier
- ID1: Measurement occasion identification
- Weight: weight in grams
- Intcept: A column of 1's that can be used to represent an intercept term
- Time: Time of measurement in
- Timesq: Time * Time

A scatter plot of the observed weights over the period of measurement is shown below. The variation in observed weight increases over the measurement period.



2. An unrestricted model

We first fit an unrestricted or baseline model to these data. The syntax for this model can be found in **malemice_saturated.prl**:

malemice_saturated.prl

```
!------------------------------------------------------------
! Repeated weight  measurements on 42 striped male mice
! Data is contained in male_mice.lsf which is a subset
! of mouse.lsf
!
! ! The syntax below illustrates how to fit an unrestricted
! or "baseline" model to the data.
! Denote the  -2Ln(L) value reported in the output by F1.
! and the -2Ln(L) value reported in when running
! malemice_Gompertz.prl by F2
! F2-F1 has a chi-square distribution with k degrees
! of freedom, where k = 54 - 10 =44
! It is interesting to note the change in F2 if one replace
! the Gompertz function with the logistic function
!
!------------------------------------------------------------
 OPTIONS OLS=YES CONVERGE=0.0000010 MAXITER=10 OUTPUT=STANDARD ;
 TITLE=Weight measurements 42 male mice- Saturated model;
 SY=malemice.LSF;
 ID2=id2;
 RESPONSE=weight;
 DUMMY=time ;
 FIXED= dummy1:dummy9 ;
 RANDOM2=dummy1:dummy9;
```

Under this model, the relationship between weight and time of measurement is explored, and a full variance-covariance matrix for all measurement occasions is fitted.

For this model, the following estimates are obtained:

```
 o--------------------o
 | FIXED PART OF MODEL |
 o--------------------o
```

COEFFICIENTS	BETA-HAT	STD.ERR.	Z-VALUE	PR > |Z|
dummy1	11.33333	0.40917	27.69814	0.00000
dummy2	17.00000	0.63532	26.75828	0.00000
dummy3	23.00000	0.61721	37.26425	0.00000
dummy4	28.52381	0.77169	36.96270	0.00000
dummy5	33.33333	1.02832	32.41528	0.00000
dummy6	37.90476	1.05076	36.07373	0.00000
dummy7	40.47619	1.05905	38.21937	0.00000
dummy8	42.40476	1.22199	34.70134	0.00000
dummy9	44.42857	1.26264	35.18697	0.00000

All the fixed effects are highly significant. For this model, a $-2\ln(L)$ of 1773 was obtained, with 54 parameters estimated.

```
 o------------------o
 | -2 LOG-LIKELIHOOD |
 o------------------o
  DEVIANCE= -2*LOG(LIKELIHOOD) =     1773.46967142625
  NUMBER OF FREE PARAMETERS =              54
```

Most of the estimated variance and covariance components are highly significant too.

```
o---------------------o
| RANDOM PART OF MODEL |
o---------------------o
```

LEVEL 2		TAU-HAT	STD.ERR.	Z-VALUE	PR > |Z|
dummy1	/dummy1	7.0317	1.5345	4.5826	0.0000
dummy2	/dummy1	7.5714	2.0502	3.6931	0.0002
dummy2	/dummy2	16.9524	3.6993	4.5826	0.0000
dummy3	/dummy1	5.9762	1.8786	3.1812	0.0015
dummy3	/dummy2	13.4048	3.2766	4.0910	0.0000
dummy3	/dummy3	16.0000	3.4915	4.5826	0.0000
dummy4	/dummy1	4.9444	2.1839	2.2640	0.0236
dummy4	/dummy2	13.1905	3.7733	3.4957	0.0005
dummy4	/dummy3	16.8810	4.0389	4.1795	0.0000
dummy4	/dummy4	25.0113	5.4579	4.5826	0.0000
dummy5	/dummy1	5.3889	2.8508	1.8903	0.0587
dummy5	/dummy2	16.8810	4.9710	3.3959	0.0007
dummy5	/dummy3	21.1190	5.2477	4.0244	0.0001
dummy5	/dummy4	30.8254	7.0051	4.4004	0.0000
dummy5	/dummy5	44.4127	9.6916	4.5826	0.0000
dummy6	/dummy1	1.8651	2.8012	0.6658	0.5055
dummy6	/dummy2	11.0000	4.6474	2.3669	0.0179
dummy6	/dummy3	16.4762	4.9121	3.3542	0.0008
dummy6	/dummy4	26.6927	6.6768	3.9979	0.0001
dummy6	/dummy5	40.7222	9.4085	4.3283	0.0000
dummy6	/dummy6	46.3719	10.1192	4.5826	0.0000
dummy7	/dummy1	0.7460	2.8107	0.2654	0.7907
dummy7	/dummy2	8.0714	4.5348	1.7799	0.0751
dummy7	/dummy3	12.5714	4.6592	2.6982	0.0070
dummy7	/dummy4	21.1553	6.2216	3.4003	0.0007
dummy7	/dummy5	36.0556	8.9869	4.0120	0.0001
dummy7	/dummy6	41.4501	9.6394	4.3001	0.0000
dummy7	/dummy7	47.1066	10.2795	4.5826	0.0000
dummy8	/dummy1	-0.5635	3.2416	-0.1738	0.8620
dummy8	/dummy2	6.3333	5.1254	1.2357	0.2166
dummy8	/dummy3	9.7619	5.1148	1.9086	0.0563
dummy8	/dummy4	18.6689	6.7562	2.7632	0.0057
dummy8	/dummy5	35.0794	9.7785	3.5874	0.0003
dummy8	/dummy6	42.8005	10.6236	4.0288	0.0001
dummy8	/dummy7	51.1882	11.5208	4.4431	0.0000
dummy8	/dummy8	62.7171	13.6860	4.5826	0.0000
dummy9	/dummy1	-0.7619	3.3503	-0.2274	0.8201
dummy9	/dummy2	4.5714	5.2463	0.8714	0.3836
dummy9	/dummy3	8.3810	5.2135	1.6075	0.1079
dummy9	/dummy4	15.8707	6.7729	2.3433	0.0191
dummy9	/dummy5	31.9048	9.7489	3.2726	0.0011
dummy9	/dummy6	40.5884	10.6374	3.8156	0.0001
dummy9	/dummy7	50.2245	11.6258	4.3201	0.0000
dummy9	/dummy8	62.4456	13.8864	4.4969	0.0000
dummy9	/dummy9	66.9592	14.6117	4.5826	0.0000

3. Gompertz curve

As a second model, we fit a Gompertz curve to these data.

malemice_Gompertz.prl

```
!------------------------------------------------------------------
OPTIONS METHOD = ML CONVERGE = 0.0000010 MAXITER = 30 QUADPTS = 20;
TITLE = Weights of 42 Male mice - Gompertz growth curve;
SY=malemice.LSF;
ID1 = id1;
ID2 = id2;
RESPONSE = weight;
FIXED = time;
MODEL = Gompertz;
```

The model to be fitted can be expressed as

$$
\begin{aligned}
y &= b_1 * \exp[-b_2(\exp(-s * b_3 * time))] + e \\
b_1 &= \beta_1 + u_1 \\
b_2 &= \beta_2 + u_2 \\
b_3 &= \beta_3 + u_3
\end{aligned}
$$

As we have a monotonic increase in function values over time, $s = 1$. The maximum likelihood solution is given below:

Coefficients	Beta	Std.Err.	Z-value	P > |z|
b1	52.24344	1.66084	31.45607	0.00000
b2	2.23816	0.05551	40.31933	0.00000
b3	0.37218	0.01581	23.54733	0.00000

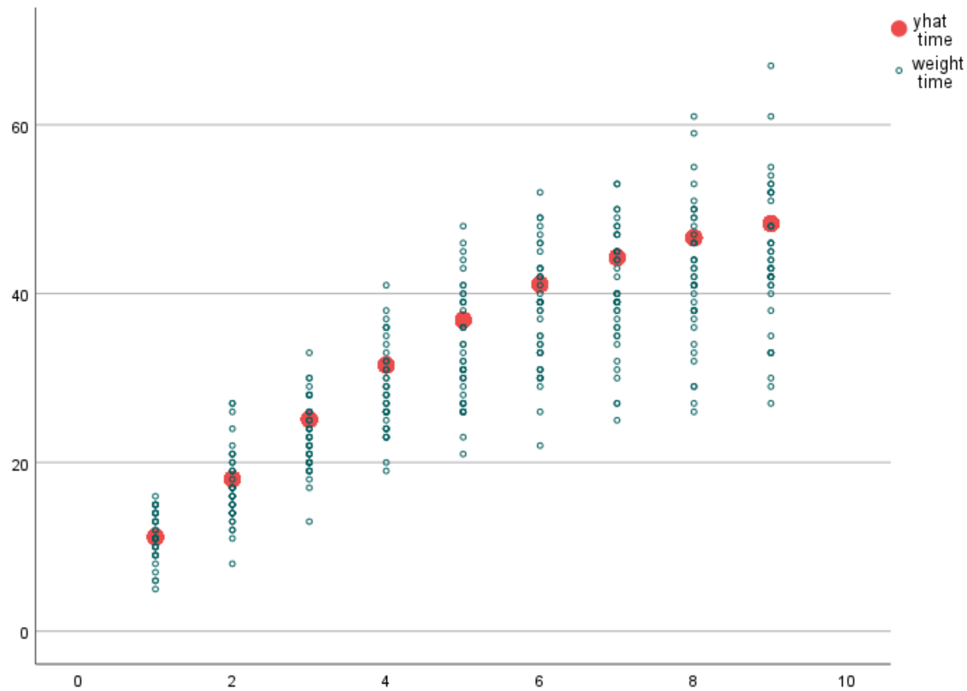
Variance estimate	Level 1	Std.Err.	Z-value	P > |z|
Sigma**2	3.36568	0.17555	19.17226	0.00000

Covariances	Level 2	Std.Err.	Z-value	P > |z|
u1,u1	199.88688	34.90605	5.72642	0.00000
u2,u1	3.44161	0.91751	3.75102	0.00018
u2,u2	0.19754	0.03973	4.97188	0.00000
u3,u1	-1.21146	0.28399	-4.26579	0.00002
u3,u2	-0.00604	0.00794	-0.75971	0.44743
u3,u3	0.01608	0.00312	5.15733	0.00000

The expected weight under this model is calculated as

$$\hat{y} = \hat{\beta}_1 * \exp[-\hat{\beta}_2(\exp(-\hat{\beta}_3 * time))]$$
$$= 52.24344 * \exp[-2.23816(\exp(-0.37218 * time))]$$

A plot of the fitted curve and the observed data is shown below.



4. Logistic curve

As a final model, we fit a logistic curve to these data. Using the syntax for the Gompertz curve, we modify the Model statement to read

```
MODEL = Logistic;
```

Doing so corresponds to fitting the model

$$y = b_1 / (1 + s * \exp(b_2 - b_3 * Time)) + e$$

where

$$b_1 = \beta_1 + u_1$$
$$b_2 = \beta_2 + u_2$$
$$b_3 = \beta_3 + u_3$$

to the data. The maximum likelihood solution obtained is given below.

Coefficients	Beta	Std.Err.	Z-value	P > |z|
b1	48.43233	1.32011	36.68819	0.00000
b2	1.69334	0.04755	35.61446	0.00000
b3	0.56000	0.01984	28.22879	0.00000

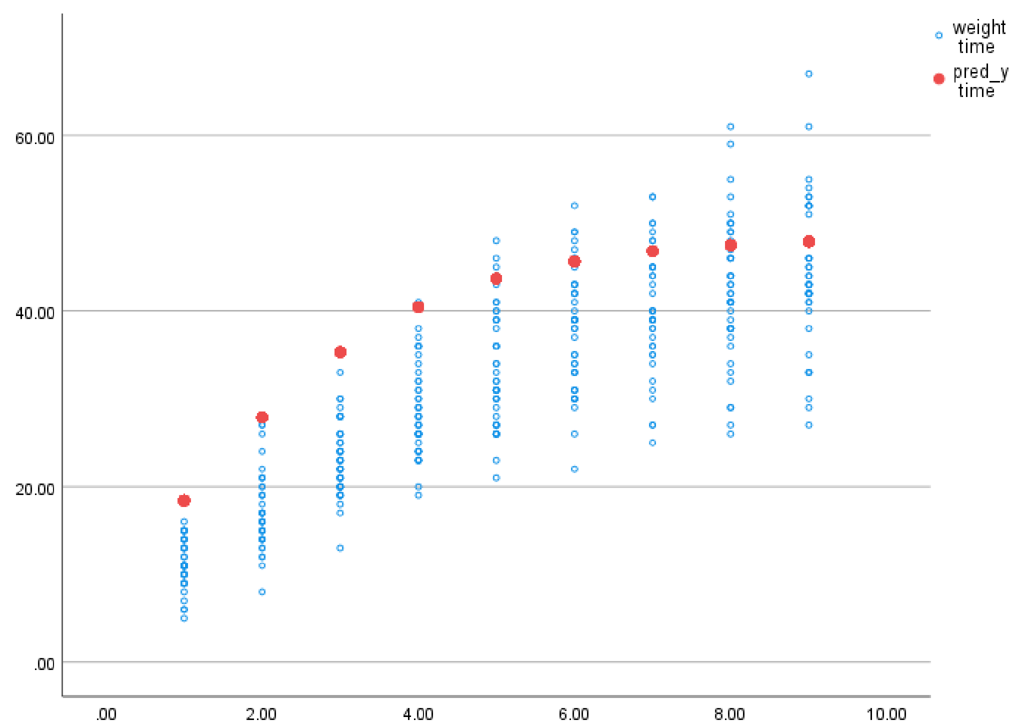
Variance estimate	Level 1	Std.Err.	Z-value	P > |z|
Sigma**2	2.82371	0.14682	19.23232	0.00000

Covariances	Level 2	Std.Err.	Z-value	P > |z|
u1,u1	131.30551	22.23709	5.90480	0.00000
u2,u1	2.53314	0.63618	3.98183	0.00007
u2,u2	0.15812	0.02922	5.41141	0.00000
u3,u1	-0.92874	0.26618	-3.48911	0.00048
u3,u2	0.00589	0.00872	0.67494	0.49972
u3,u3	0.02630	0.00500	5.25663	0.00000

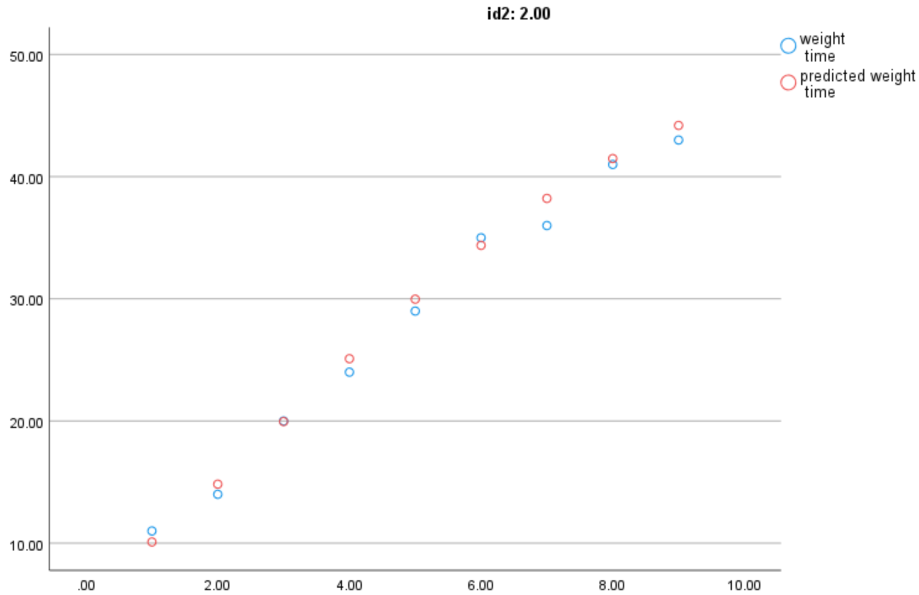
We can calculate the predicted weight by using the formula

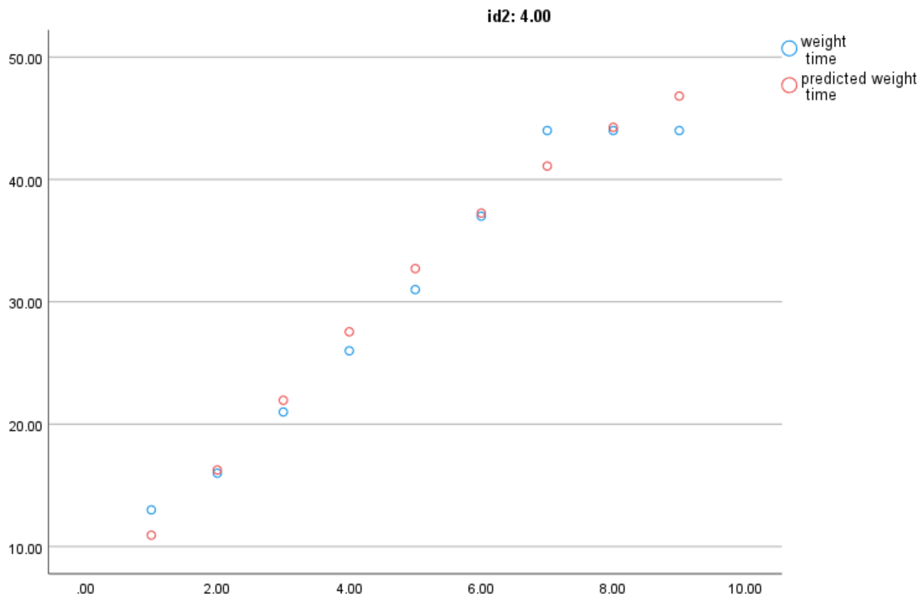
$$\hat{y} = \hat{b}_1 * \exp[-\hat{b}_2 * (\exp - \hat{b}_3 * Time)]$$

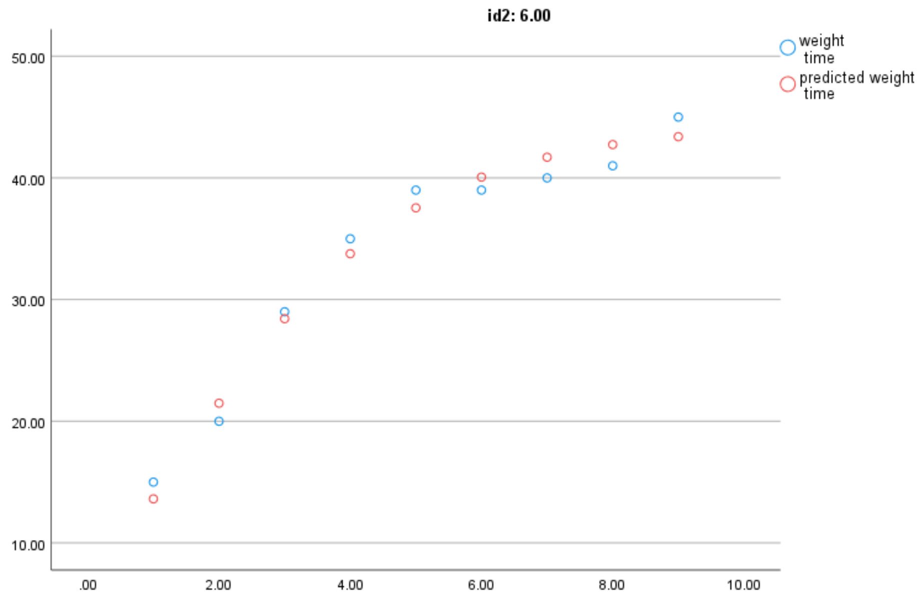
A plot of predicted average and observed weight is given below. When compared to the similar graphs for the Gompertz curve, we note that the logistic curve overestimates the weight, especially at the beginning of the measurement period.

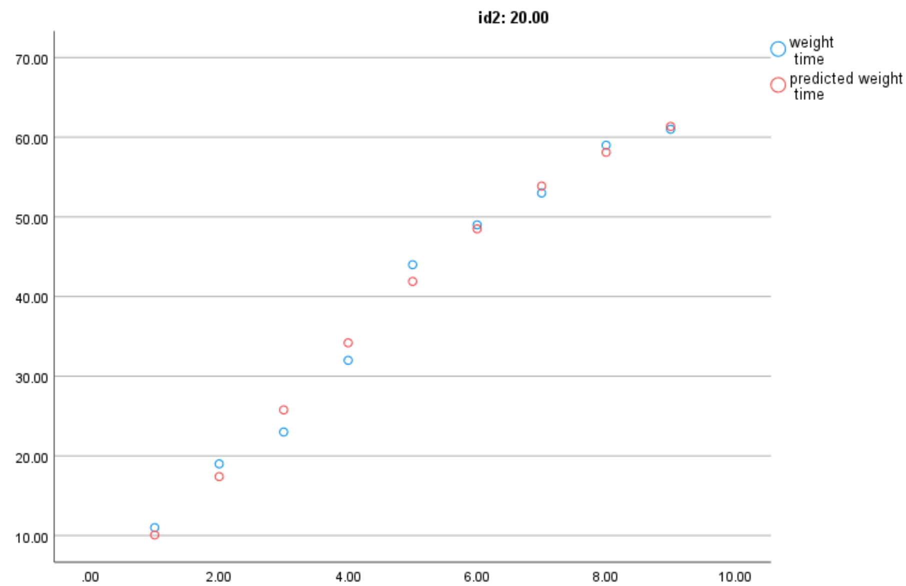


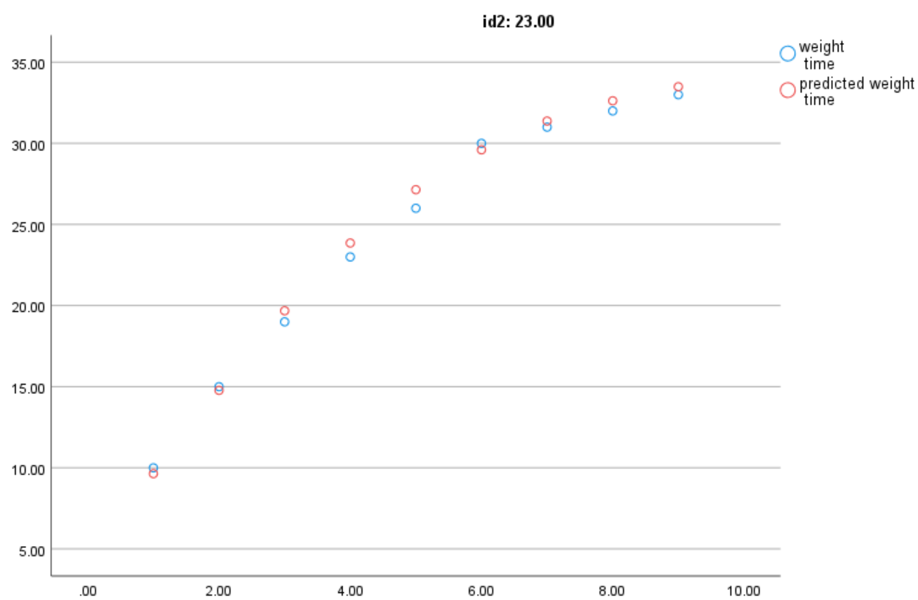
The program also writes the estimated parameters for each level-2 unit to an external text file named **thetai.est**. Using these results, we can obtain predicted outcome at each time point for each level-2 unit, *i.e.* each mouse. A few of these graphs are shown below.






id2: 6.00
weight
time
predicted weight
time
50.00
40.00
30.00
20.00
10.00
.00
2.00
4.00
6.00
8.00
10.00


id2: 20.00
weight
time
predicted weight
time
70.00
60.00
50.00
40.00
30.00
20.00
10.00
.00
2.00
4.00
6.00
8.00
10.00


id2: 23.00
weight
time
predicted weight
time
35.00
30.00
25.00
20.00
15.00
10.00
5.00
.00
2.00
4.00
6.00
8.00
10.00