

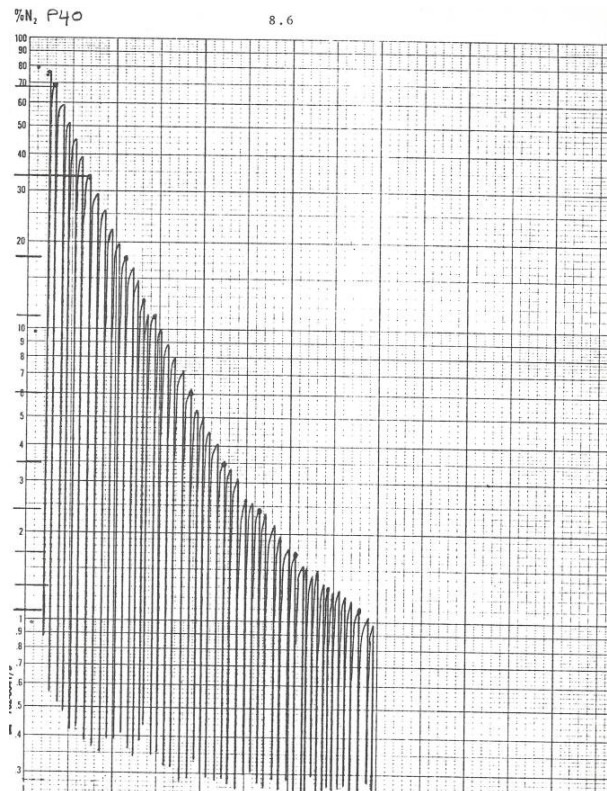
Monomolecular curve for nitrogen washout data

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1. Introduction

Data for this example contains information on the percentage nitrogen washout during pure oxygen breathing by 32 scoliosis patients. During the process, nose breathing is prevented by using a nose clamp. The patient is connected to a nitrogen analyzer while pure oxygen is administered. When the patient exhales, an x-y writer is set in motion, recording the percentage of nitrogen still present is measured in the lungs. An example of such a graph for one of the patients is given below.

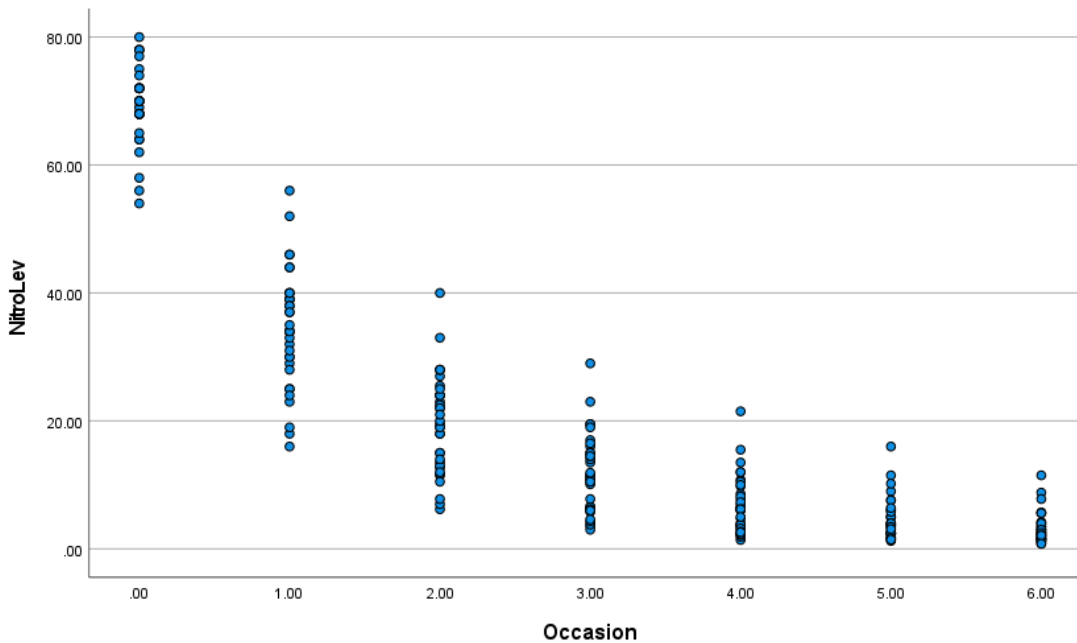


Seven measurements are available for each patient, corresponding to the 1st, 6th, 11th, and 31st exhalation. In healthy young subjects, nitrogen is almost completely washed out after two minutes.

Data are contained in **nitrogen35.lsf**. Data for the first 3 patients are shown below. In this file, Patient_no indicates the individual patient and serves as our level-2 ID; Occasion indicates the order of the 7 selected measurements, and Nitro_Lev the nitrogen remaining in the lungs as measured on each occasion. Note that a logarithmic scale is used for the nitrogen levels.

	Patient_no	Occasion	NitroLev
1	1.00	0.00	72.00
2	1.00	1.00	37.00
3	1.00	2.00	22.00
4	1.00	3.00	13.50
5	1.00	4.00	8.60
6	1.00	5.00	6.00
7	1.00	6.00	4.20
8	2.00	0.00	68.00
9	2.00	1.00	40.00
10	2.00	2.00	24.00
11	2.00	3.00	17.00
12	2.00	4.00	10.80
13	2.00	5.00	9.00
14	2.00	6.00	5.70
15	3.00	0.00	58.00
16	3.00	1.00	30.00
17	3.00	2.00	15.00
18	3.00	3.00	6.20
19	3.00	4.00	3.20
20	3.00	5.00	2.25
21	3.00	6.00	1.60

A scatterplot of all observed values over the measurements is given below.



The shape of the curve indicates that a nonlinear model is required to describe these data.

2. Monomolecular model

The monomolecular function we intend to fit to the model is defined as

$$\text{NitroLev}_{ij} = b_1[1 + \exp(b_2 - b_3 * \text{Occasion}_{ij})] + e_{ij}$$

where

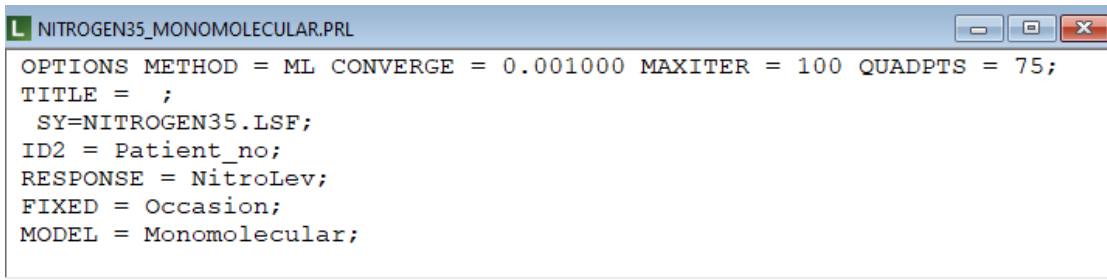
$$b_{1i} = \beta_1 + u_{1i}$$

$$b_{2i} = \beta_2 + u_{2i}$$

$$b_{3i} = \beta_3 + u_{3i}$$

The monomolecular curve has no point of inflection. The parameter b_1 represents the time-asymptotic value of the nitrogen levels remaining in the lungs.

To fit this model, we use the syntax in **NITROGEN35_MONOMOLECULAR.PRL**:



```
NITROGEN35_MONOMOLECULAR.PRL
OPTIONS METHOD = ML CONVERGE = 0.001000 MAXITER = 100 QUADPTS = 75;
TITLE = ;
SY=NITROGEN35.LSF;
ID2 = Patient_no;
RESPONSE = NitroLev;
FIXED = Occasion;
MODEL = Monomolecular;
```

For this model, the maximum likelihood solution is as follows. All three estimated fixed effects are highly significant, as is the case for the estimate of $\text{var}(u_3, u_3)$.

NITROGEN35_MONOMOLECULAR.OUT

Coefficients	Beta	Std.Err.	Z-value	P > z

b1	1.78294	0.08124	21.94772	0.00000
b2	3.66100	0.04465	82.00246	0.00000
b3	0.73479	0.02777	26.45529	0.00000

Variance estimate	Level 1	Std.Err.	Z-value	P > z

Sigma**2	1.26383	0.08134	15.53698	0.00000

Covariances	Level 2	Std.Err.	Z-value	P > z

u1,u1	0.19165	0.06958	2.75424	0.00588
u2,u1	-0.09525	0.03806	-2.50239	0.01234
u2,u2	0.05087	0.02110	2.41132	0.01589
u3,u1	-0.04479	0.01934	-2.31591	0.02056
u3,u2	0.01796	0.01047	1.71509	0.08633
u3,u3	0.05290	0.00913	5.79599	0.00000

Note: ML estimates of individual coefficients written to file THETA1.EST

The average expected remaining nitrogen can thus be calculated as

$$\text{Predicted}(\text{Nitrolev}_{ij}) = 1.78294[1 + \exp(3.66100 - 0.73479 * \text{Occasion}_{ij})]$$

3. Plots of the individual coefficients

Maximum likelihood estimates of the individual coefficients are also written to an external file named **thetai.est** or, in the case of MAP estimation, to **thetai.map**. The first few lines of the file **thetai.est** are shown below.

thetai.est - Notepad

File	Edit	Format	View	Help
2.12158		3.49594		0.629569
2.31073		3.35859		0.522101
1.08234		3.98612		0.733095
1.90386		3.61583		0.611129
1.78947		3.63615		0.569072
1.91858		3.68662		0.556430
2.02318		3.55431		0.489242
1.04913		3.97380		0.869409
2.02318		3.55431		0.489242
1.82394		3.71201		0.582527
1.87060		3.59412		0.690907
2.07645		3.60373		0.428830

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When the observed nitrogen levels for each patient is plotted against occasion along with the predicted levels using the individual coefficients, we note the same close correspondence between observed and predicted values. The plots for the first 3 cases below serve to illustrate this.

