A growth curve for the Vonesh hemodialyzer data

Contents

1. Introduction

Vonesh and Carter (1992) describe data measured on high-flux hemodialyzers to assess their *in vivo* ultrafiltration characteristics. The ultrafiltration rates (in mL/hr) of 20 high-flux dialyzers were measured at seven different transmembrane pressures (in dmHg). The *in vitro* evaluation of the dialyzers used bovine blood at flow rates of either 200~dl/min or 300~dl/min. The data are also analyzed in Littell, Milliken, Stroup, and Wolfinger (1996). The first 20 records of this data are shown below.

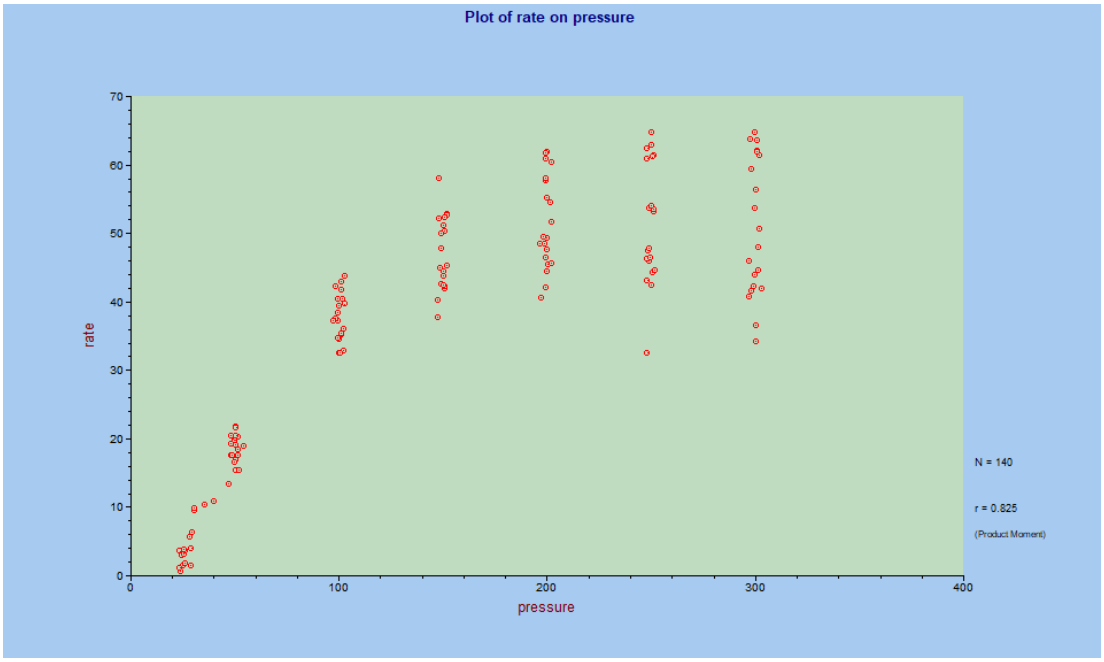
Vonesh.lsf

	device	occasion	supply	pressure	rate	sup_pres
1	1.00	1.00	0.00	23.50	1.23	0.00
2	1.00	2.00	0.00	50.50	15.38	0.00
3	1.00	3.00	0.00	102.00	32.83	0.00
4	1.00	4.00	0.00	147.50	37.83	0.00
5	1.00	5.00	0.00	197.00	40.59	0.00
6	1.00	6.00	0.00	248.00	32.55	0.00
7	1.00	7.00	0.00	300.00	34.30	0.00
8	2.00	1.00	0.00	30.50	9.48	0.00
9	2.00	2.00	0.00	50.50	21.75	0.00
10	2.00	3.00	0.00	99.50	37.23	0.00
11	2.00	4.00	0.00	150.00	44.43	0.00
12	2.00	5.00	0.00	199.00	42.16	0.00
13	2.00	6.00	0.00	248.00	43.06	0.00
14	2.00	7.00	0.00	300.00	36.62	0.00
15	3.00	1.00	0.00	25.50	3.93	0.00
16	3.00	2.00	0.00	49.50	19.83	0.00
17	3.00	3.00	0.00	99.50	40.42	0.00
18	3.00	4.00	0.00	148.00	52.26	0.00
19	3.00	5.00	0.00	199.50	49.40	0.00
20	3.00	6.00	0.00	249.00	45.98	0.00

The data set contains the following variables:

- device: Dialyzer identifier
- occasion: Measurement occasion identification
- supply: weight in grams
- pressure: Transmembrane pressure
- Rate: Blood flow rate
- sup_pres: Interaction between supply and pressure

A scatter plot of the observed blood flow rate at different levels of transmembrane pressuse is shown below. From the graph, we can see that a suitable model would be nonlinear.



1. Quadratic model with interaction term

As a first step, we fit a quadratic model to the data. We include a possible interaction between Supply and Pressure as a fixed effect and allow both pressure and the quadratic pressure to vary randomly between dialyzers. Within a dialyzer, we allow pressure to vary randomly.

Voneshl.prl

```
! The level 2 units are dialyzers, machines for filtering impurities from blood
! 7 repeated measures
!
!
!-----------------------------------------------------------------
OPTIONS METHOD = ML CONVERGE = 0.0000010 MAXITER =30 QUADPTS =35;
TITLE = Filtering impurities from blood, 7 repeated measures ;
SY=Vonesh.LSF;
ID1 = occasion;
ID2 = device;
RESPONSE = rate;
FIXED = supply pressure press_sq sup_pres ;
RANDOM1=pressure;
random2 = intcept pressure press_sq;
```

For this model, we obtain the following results. All fixed effects are highly significant. While both the intercept and the pressure slope vary significantly over the dialyzers, there is no evidence of random variation on the squared pressure at this level.

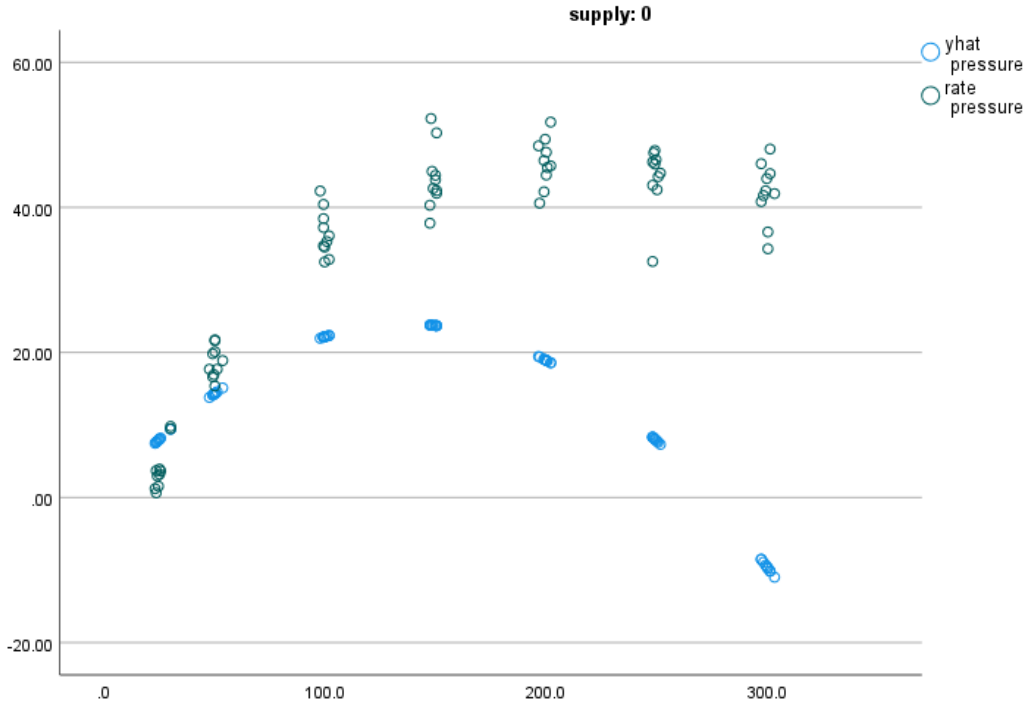
Voneshl.OUT

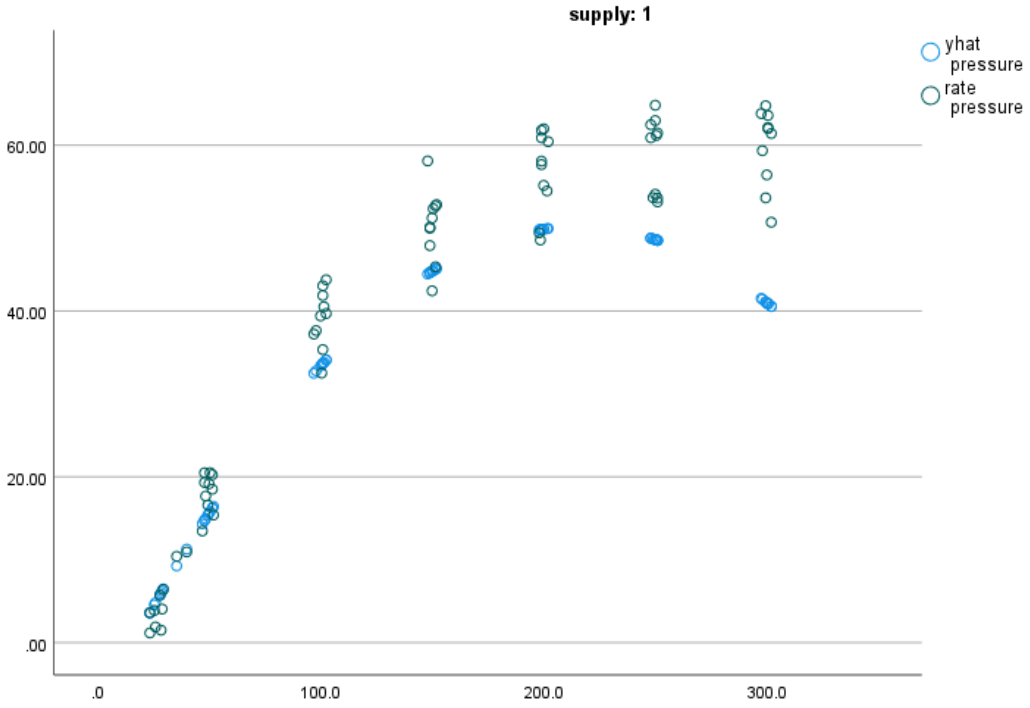
```
                        +------------------------+
                        | FIXED PART OF MODEL    |
                        +------------------------+


-------------------------------------------------------------------------------
  COEFFICIENTS              BETA-HAT      STD.ERR.       Z-VALUE       PR > |Z|
-------------------------------------------------------------------------------
  supply                   -8.53286       1.82823       -4.66728       0.00000
  pressure                  0.34856       0.01667       20.91023       0.00000
  press_sq                 -0.00127       0.00005      -23.89528       0.00000
  sup_pres                  0.19754       0.04159        4.74961       0.00000


                        +------------------------+
                        |   -2 LOG-LIKELIHOOD    |
                        +------------------------+

  DEVIANCE= -2*LOG(LIKELIHOOD) =    917.089399480477
  NUMBER OF FREE PARAMETERS =              11


                        +------------------------+
                        | RANDOM PART OF MODEL   |
                        +------------------------+


-------------------------------------------------------------------------------
  LEVEL 2                        TAU-HAT      STD.ERR.      Z-VALUE   PR > |Z|
-------------------------------------------------------------------------------
  intcept /intcept               0.00000       0.00000       0.00000   0.00000
  pressure/intcept               0.00000       0.00000       0.00000   0.00000
  pressure/pressure              0.00218       0.00096       2.27394   0.02297
  press_sq/intcept              -0.00015       0.00029      -0.51490   0.60662
  press_sq/pressure             -0.00000       0.00001      -0.08795   0.92991
  press_sq/press_sq             -0.00000       0.00000      -0.38074   0.70339

-------------------------------------------------------------------------------
  LEVEL 1                        TAU-HAT      STD.ERR.      Z-VALUE   PR > |Z|
-------------------------------------------------------------------------------
  pressure/pressure              0.00086       0.00005      16.38649   0.00000
```

Under this model the expected rate can be calculated as:

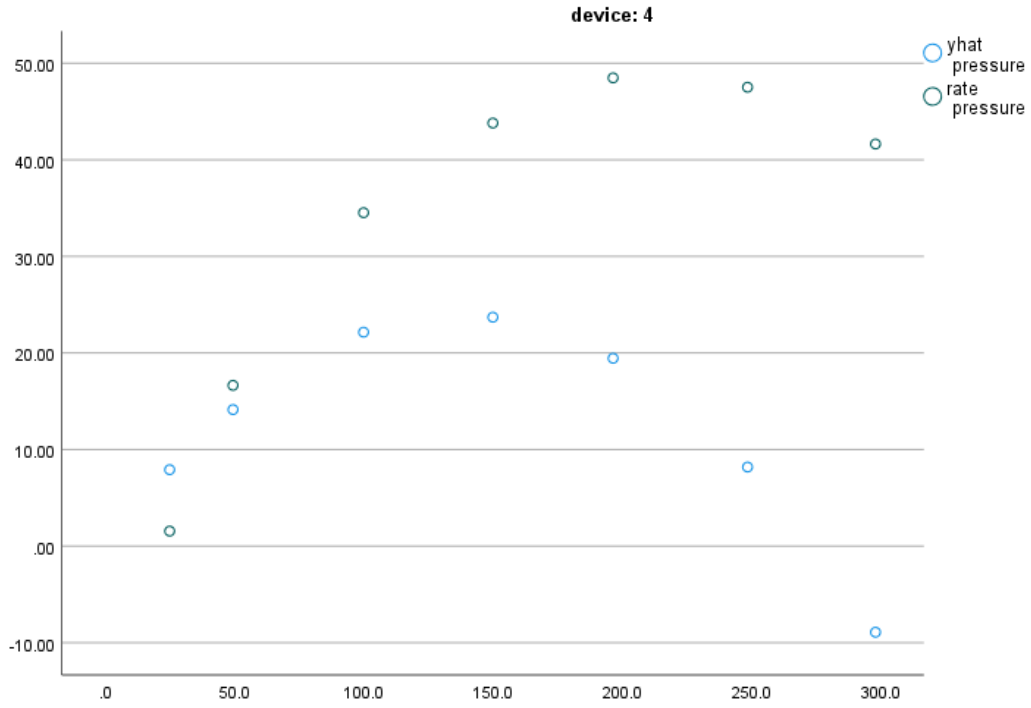
$$y_{ij} = \beta_0\left(Supply_j\right) + \beta_1\left(Pressure_{ij}\right) + \beta_2\left(Press\_sq_{ij}\right) + \beta_3\left(Supply_j\right)\left(Pressure_{ij}\right)$$

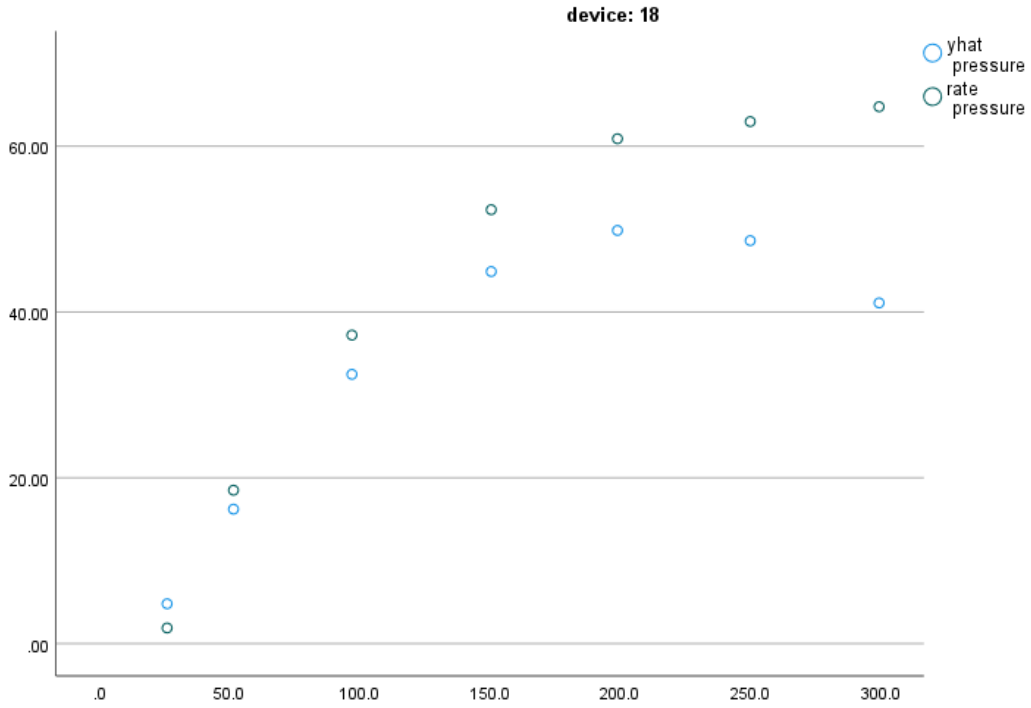
When the expected and observed values are plotted again pressure, we note that the expected values do not follow the same trend as the observed. The fitted model does a better job when Supply = 1 than when Supply = 0 as illustrated by the graphs below, but consistently underestimates the rate at higher pressures.



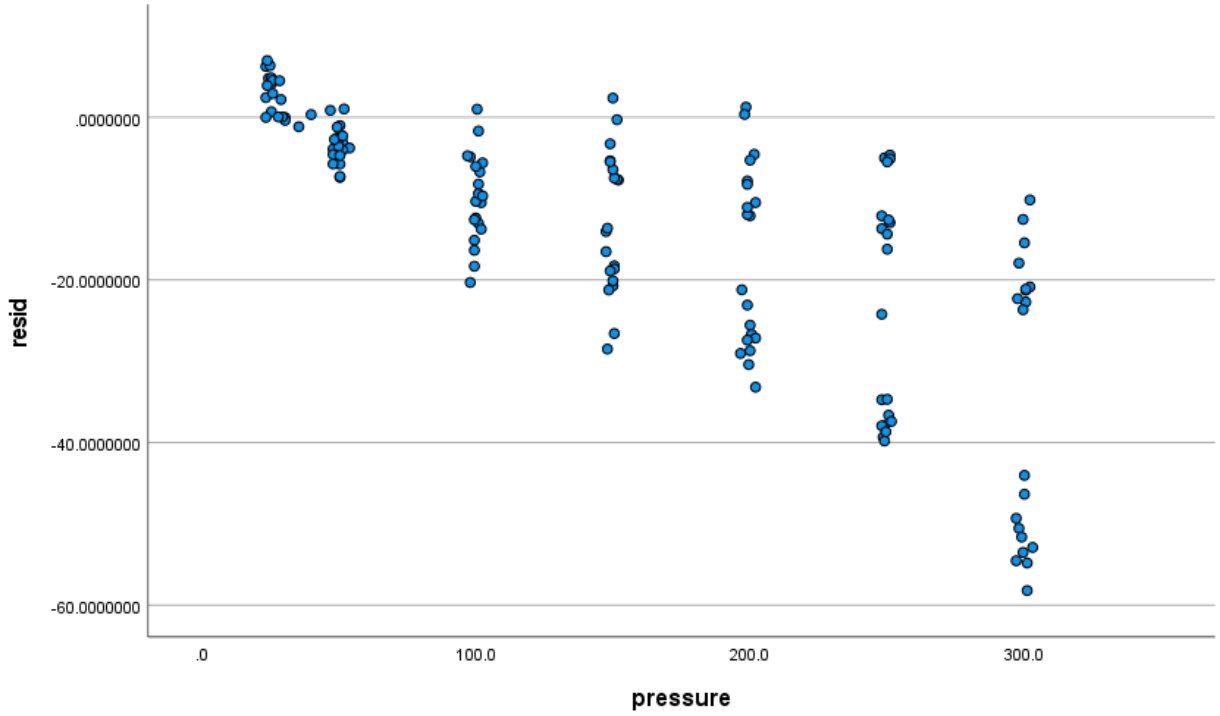


Similar graphs for a few individual devices are shown below. Arguably the only place where the model does an adequate job of describing the data is at the lower end of the pressure range (below 100).





The plot of residuals shown below indicates a trend towards more negative residuals with increased pressure.



2. Logistic model

As an alternative, we fit a logistic model to the data. The model fitted is

$$y = b_1 / [1 + \exp(b_2 - b_3 * Pressure)] + e$$
$$b_1 = \beta_1 + \gamma_1 * Supply + u_1$$
$$b_2 = \beta_2 + \gamma_2 * Supply + u_2$$
$$b_3 = \beta_3 + \gamma_3 * Supply + u_3$$

The syntax for this model is shown below.

Voneshlg.prl

```
!-----------------------------------------------------------------
! Vonesh & Carter: Ultrafiltration Data (Biometrics, 1992, 1-17)
!
! The level 2 units are dialyzers, machines for filtering impurities from blood
! 7 repeated measures
!
! Group 1:   Qb = 200 dl/min   (cases  1 - 10)
! Group 2:   Qb = 300 dl/min   (cases 11 - 20)
!
! rate = Filtration Rate
! pressure = Source Pressure
!
!-----------------------------------------------------------------
OPTIONS METHOD = ML CONVERGE = 0.0000010 MAXITER =30 QUADPTS =85;
TITLE = Filtering impurities from blood, 7 repeated measures ;
SY=Vonesh.LSF;
ID1 = occasion;
ID2 = device;
RESPONSE = rate;
FIXED = pressure;
MODEL = Logistic;
COVARIATES b1 = supply
           b2 = supply
           b3=supply;
```

For this model, we obtain the following output:

Voneshlg.OUT

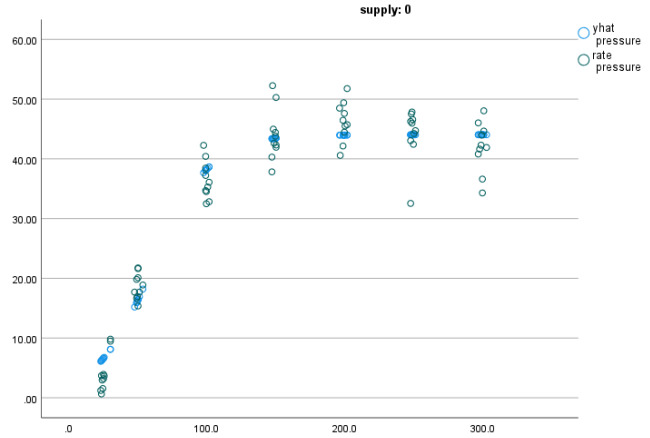
Coefficients	Beta	Std.Err.	Z-value	P > |z|
b1	44.04093	0.78525	56.08523	0.00000
b2	2.96278	0.04468	66.30621	0.00000
b3	0.04838	0.00150	32.17803	0.00000

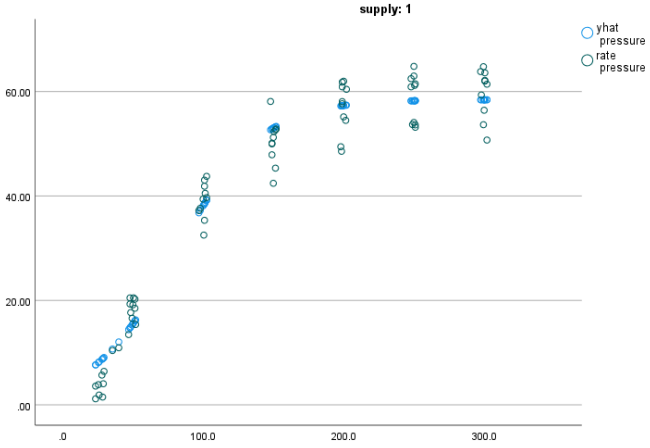
Covariate Names	Gamma	Std.Err.	Z-value	P > |z|
supply	14.42944	1.13875	12.67131	0.00000
supply	-0.29743	0.06946	-4.28183	0.00002
supply	-0.01545	0.00183	-8.43802	0.00000

Variance estimate	Level 1	Std.Err.	Z-value	P > |z|
Sigma**2	10.41698	0.89086	11.69323	0.00000

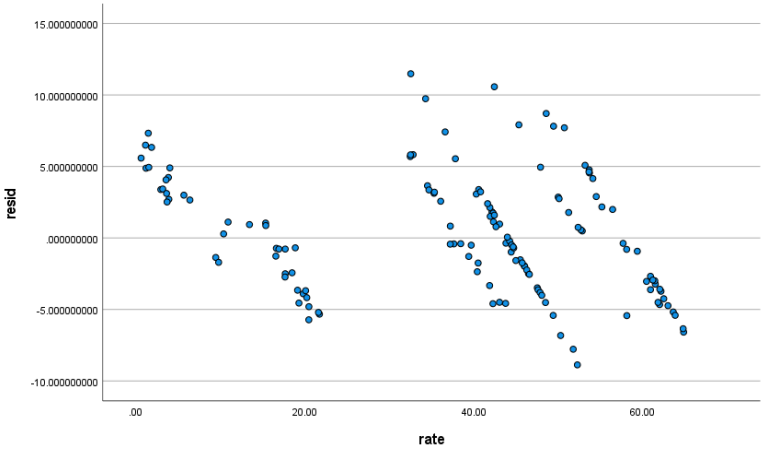
Covariances	Level 2	Std.Err.	Z-value	P > |z|
u1,u1	8.93328	2.88639	3.09496	0.00197
u2,u1	0.05439	0.12196	0.44597	0.65562
u2,u2	0.00035	0.00412	0.08382	0.93320
u3,u1	0.00057	0.00305	0.18691	0.85173
u3,u2	0.00002	0.00017	0.11170	0.91106
u3,u3	0.00002	0.00001	4.01195	0.00006

When we make a graphical display of the expected rates of transfer under this model and the observed measurements for the two Supply groups, we see that this model does a much better job describing the data.

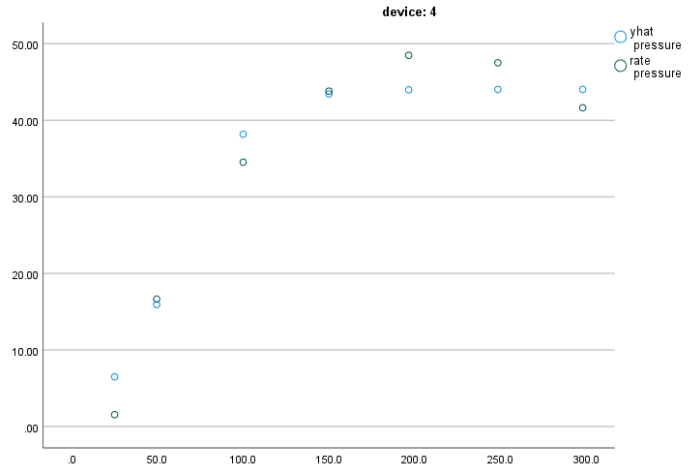


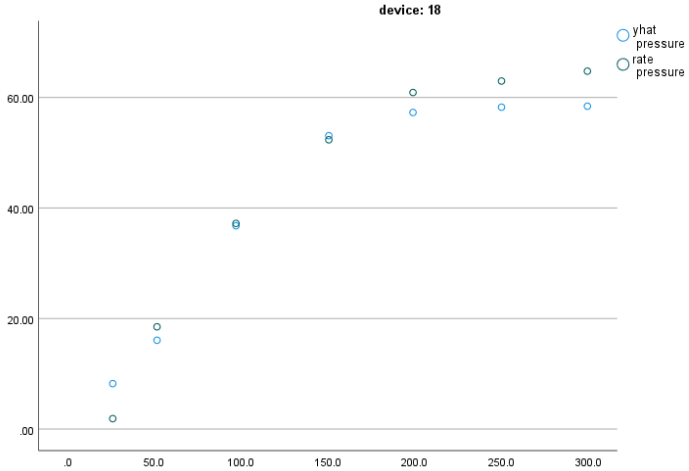


A plot of the residuals is given below.



The model describes the data for individual machines reasonably well, as can be seen from the two graphs below, especially when compared to the graphs for the same two devices using the results from the previous model. For this model, the squared sum of residuals is 30.393.





3. Monomolecular

In this section, we fit a monomolecular model to these data. The monomolecular model was originally derived from physical chemistry, where it describes the progress of first-order chemical reactions. The monomolecular model has no inflection point; and unlike other asymptotic forms it is always concave-down.

The model fitted to the data is:

$$y = b_1 * [1 - \exp(b_2 - b_3 * Pressure)] + e$$
$$b_1 = \beta_1 + \gamma_1 * Supply + u_1$$
$$b_2 = \beta_2 + \gamma_2 * Supply + u_2$$
$$b_3 = \beta_3 + \gamma_3 * Supply + u_3$$

Note that in this model, the traditional “s” term in the monomolecular model is set to -1. Syntax for this model is shown below.

Voneshm.prl

```
!-------------------------------------------------------------
! Vonesh & Carter: Ultrafiltration Data (Biometrics, 1992, 1-17)
!
! The level 2 units are dialyzers, machines for filtering impurities from blood
! 7 repeated measures
!
! Group 1:   Qb = 200 dl/min   (cases  1 - 10)
! Group 2:   Qb = 300 dl/min   (cases 11 - 20)
!
! rate = Filtration Rate
! pressure = Source Pressure
! The selected model is the Monomolecular function
!
!    Level 1 model:
!       rate= b1*[1+s*exp(b2-b3*pressure)]+ e
!       note: s= -1
!
!    Level 2 model:
!       b1= beta1+ gamma1*supply+ u1
!       b2= beta2+ gamma2*supply+ u2
!       b3= beta3+ gamma3*supply+ u3
!-------------------------------------------------------------
OPTIONS METHOD = ML CONVERGE = 0.0000010 MAXITER =30 QUADPTS =35;
TITLE = Filtering impurities from blood, 7 repeated measures ;
SY=Vonesh.LSF;
ID1 = occasion;
ID2 = device;
RESPONSE = rate;
FIXED = pressure;
MODEL = Monomolecular;
COVARIATES b1 = supply
           b2 = supply
           b3 = supply;
```

The output file contains three estimates of beta, and three of gamma, as shown below.

Voneshm.OUT

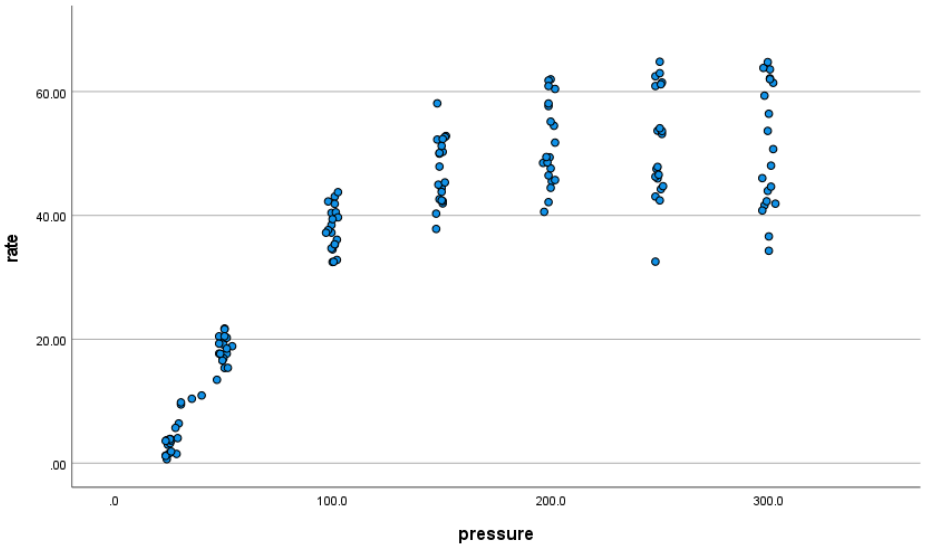
Coefficients	Beta	Std.Err.	Z-value	P > |z|
b1	45.15021	0.97957	46.09199	0.00000
b2	0.47107	0.01590	29.63092	0.00000
b3	0.02130	0.00079	27.01681	0.00000

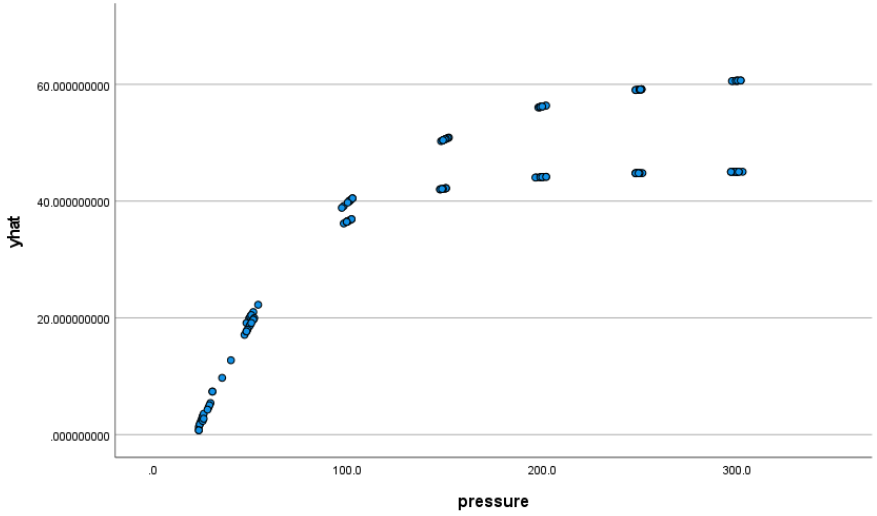
Covariate Names	Gamma	Std.Err.	Z-value	P > |z|
supply	17.09886	1.44390	11.84212	0.00000
supply	-0.17428	0.02119	-8.22603	0.00000
supply	-0.00815	0.00105	-7.77466	0.00000

Variance estimate	Level 1	Std.Err.	Z-value	P > |z|
Sigma**2	6.53854	0.55708	11.73714	0.00000

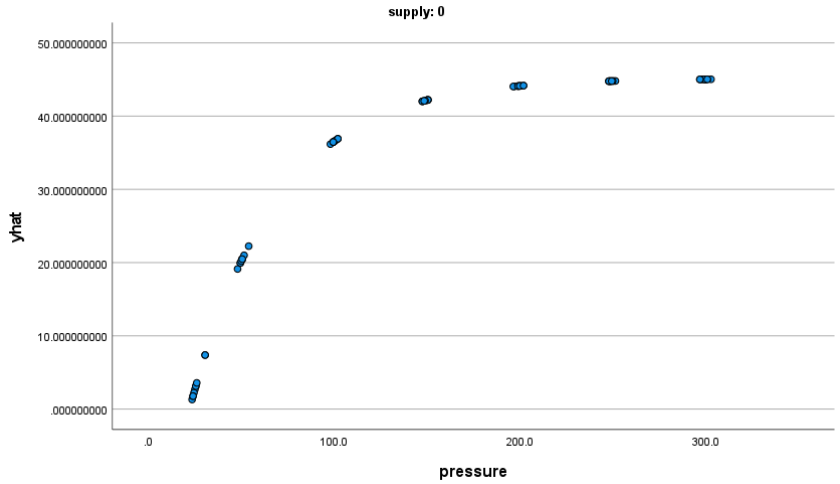
Covariances	Level 2	Std.Err.	Z-value	P > |z|
u1,u1	17.11257	4.60511	3.71600	0.00020
u2,u1	-0.06420	0.05011	-1.28119	0.20013
u2,u2	0.00025	0.00064	0.39737	0.69110
u3,u1	-0.00384	0.00255	-1.50713	0.13178
u3,u2	0.00001	0.00003	0.43368	0.66452
u3,u3	0.00001	0.00000	2.99799	0.00272

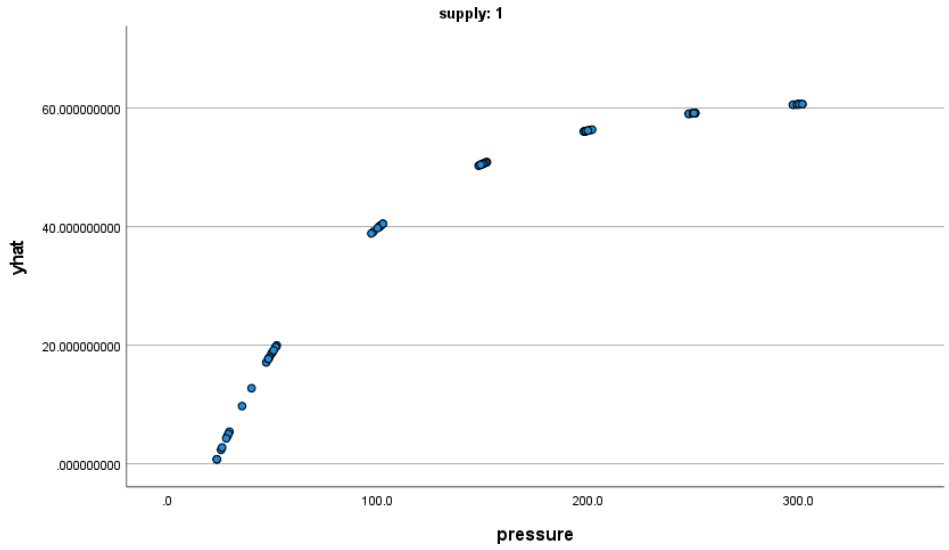
From the graphs of the observed rate against transmembrane pressure and expected rate against the same as shown below, we conclude that the fitted model describes the data reasonably well.



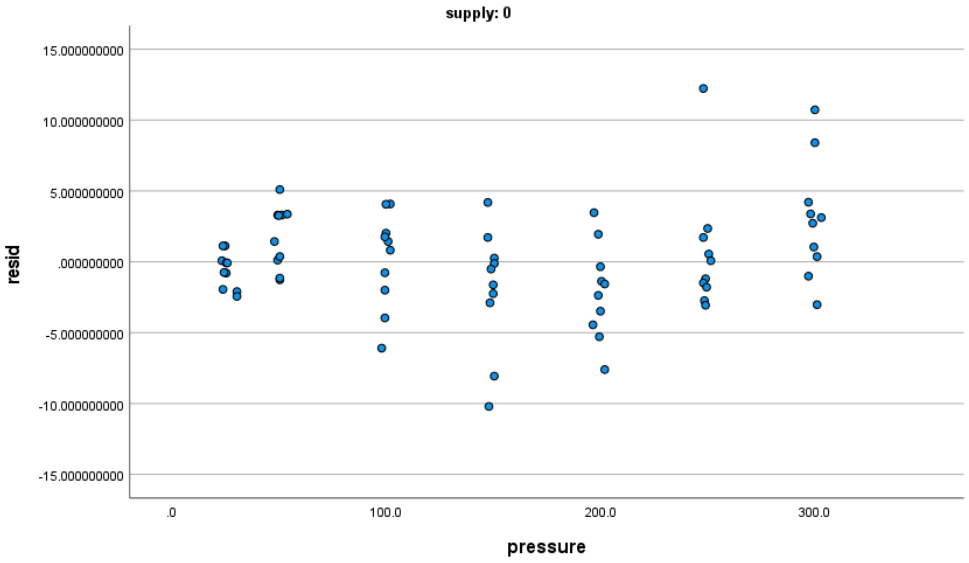


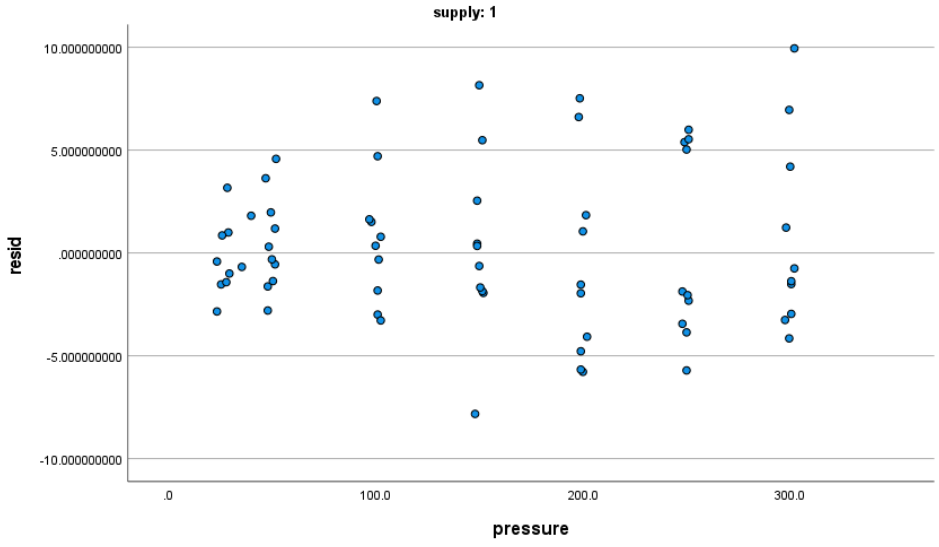
The expected values are plotted against pressure for the two groups of Supply. A clear supply effect is noted.





Residuals for the two groups of devices are shown below.





Residuals are reasonably evenly distributed around zero, and no marked change is observed with increased pressure. This is a contrast to the residual plot obtained under the quadratic model, where there was a clear trend towards larger negative residuals with increased pressure. The squared sum of residuals for this model is calculated as 28.93686, this model compared to 30.393 for the logistic model.

Revisiting the two dialyzers we produced individual graphs for previously, it is clear that the expected outcome under the current model is much closer to the observed data. We conclude that the monomolecular model fits the data best in terms of the three models considered here.