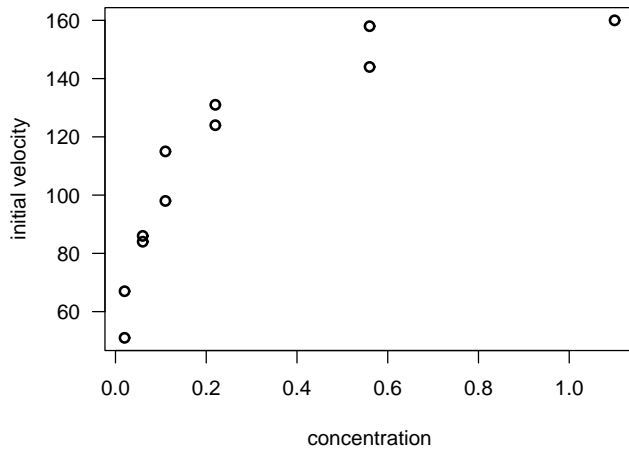


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A biochemical experiment



Michaelis-Menten equation

$$V = \frac{V_{\max} \times C}{K + C}$$

V = initial velocity

C = concentration

V_{\max} = maximum velocity

K = rate constant

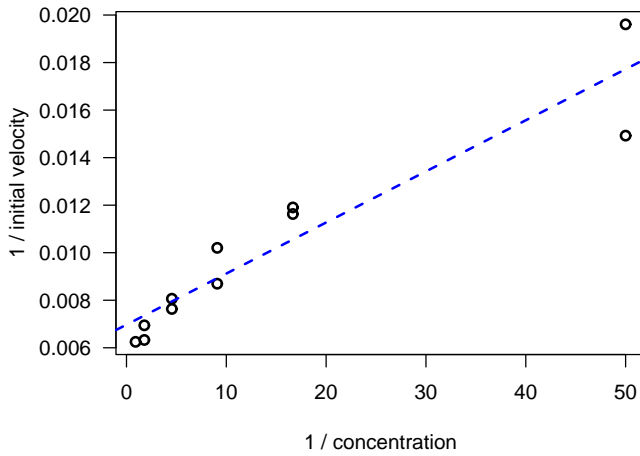
Linearize

$$V = \frac{V_{\max} \times C}{K + C}$$

$$\begin{aligned} \Rightarrow \frac{1}{V} &= \frac{K + C}{V_{\max} \times C} \\ &= \frac{K}{V_{\max} \times C} + \frac{1}{V_{\max}} \end{aligned}$$

$$\Rightarrow \frac{1}{V} = \left(\frac{1}{V_{\max}} \right) + \left(\frac{K}{V_{\max}} \right) \times \left(\frac{1}{C} \right)$$

Fit the line



Model:

$$\frac{1}{V} = \beta_0 + \beta_1 \left(\frac{1}{C} \right) + \text{error}$$

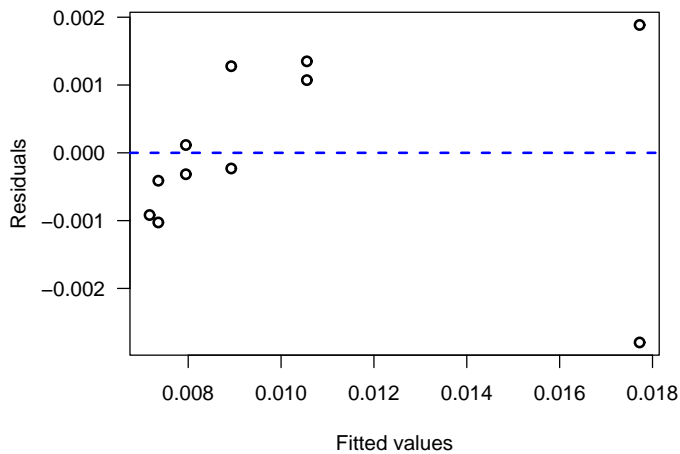
Intercept 0.00697

Slope 0.00022

$$\hat{V}_{\max} = 1/\text{Intercept} = 1/0.00697 \\ = 143$$

$$\hat{K} = \text{Slope} \times \hat{V}_{\max} = 0.031$$

Residuals vs fitted values



Which is more reasonable?

$$\frac{1}{V} = \beta_0 + \beta_1 \left(\frac{1}{C} \right) + \text{error}$$

$$V = \frac{V_{\max} \times C}{K + C} + \text{error}$$

Nonlinear regression

We imagine that

$$V_i = \frac{V_{\max} \times C_i}{K + C_i} + \epsilon, \quad \epsilon \sim \text{iid normal}(0, \sigma^2)$$

We estimate V_{\max} and K by the values for which

$$\text{RSS} = \sum_i \left(V_i - \frac{\hat{V}_{\max} \times C_i}{\hat{K} + C_i} \right)^2$$

is minimized.

→ An iterative method; need “starting values”.

Nonlinear regression in R

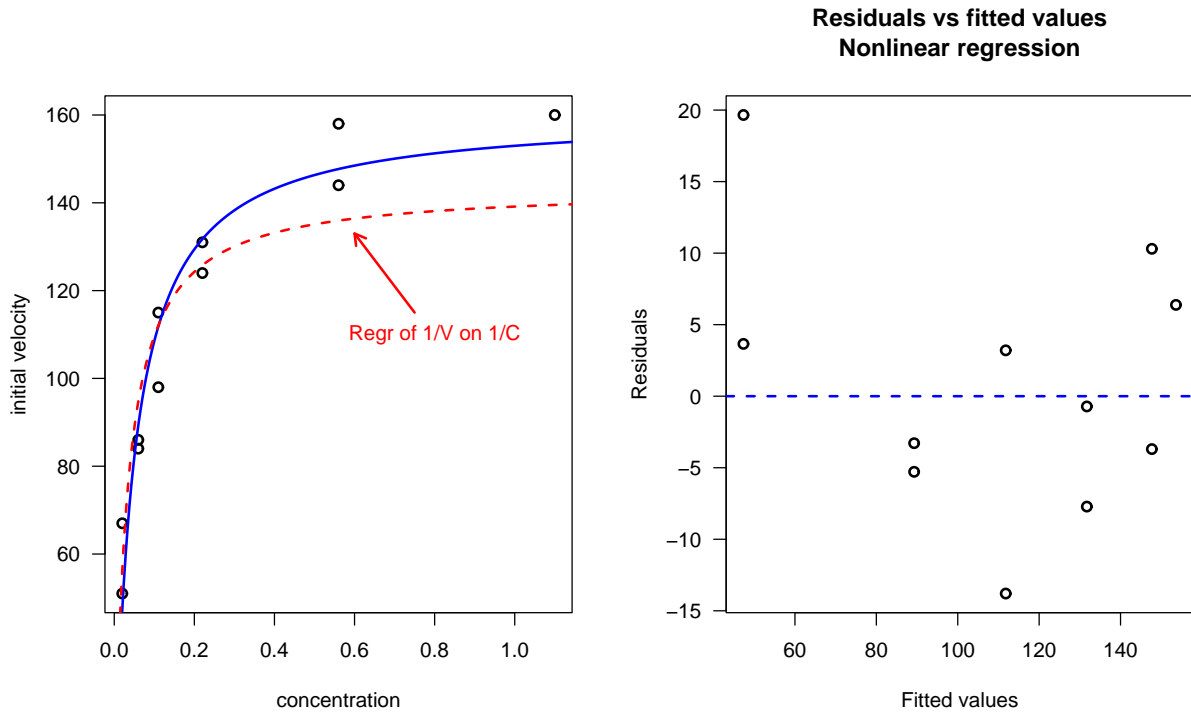
```
> library(nls)

> nls.out <- nls(vel ~ (Vm * conc) / (K + conc),
               data=mydata,
               start = c(Vm=143, K=0.031))

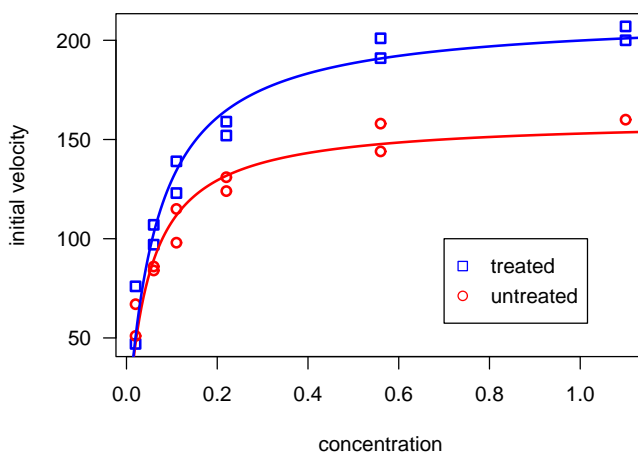
> summary(nls.out)$param
```

	Est	SE	t-val	P-val
Vm	160.28	6.48	24.7	1.4e-09
K	0.048	0.008	6.1	1.7e-04

The fit



A second set of data



$$V = \frac{(V_{\max} + \Delta V_{\max} x) \times C}{(K + \Delta K x) + C} + \text{error}$$

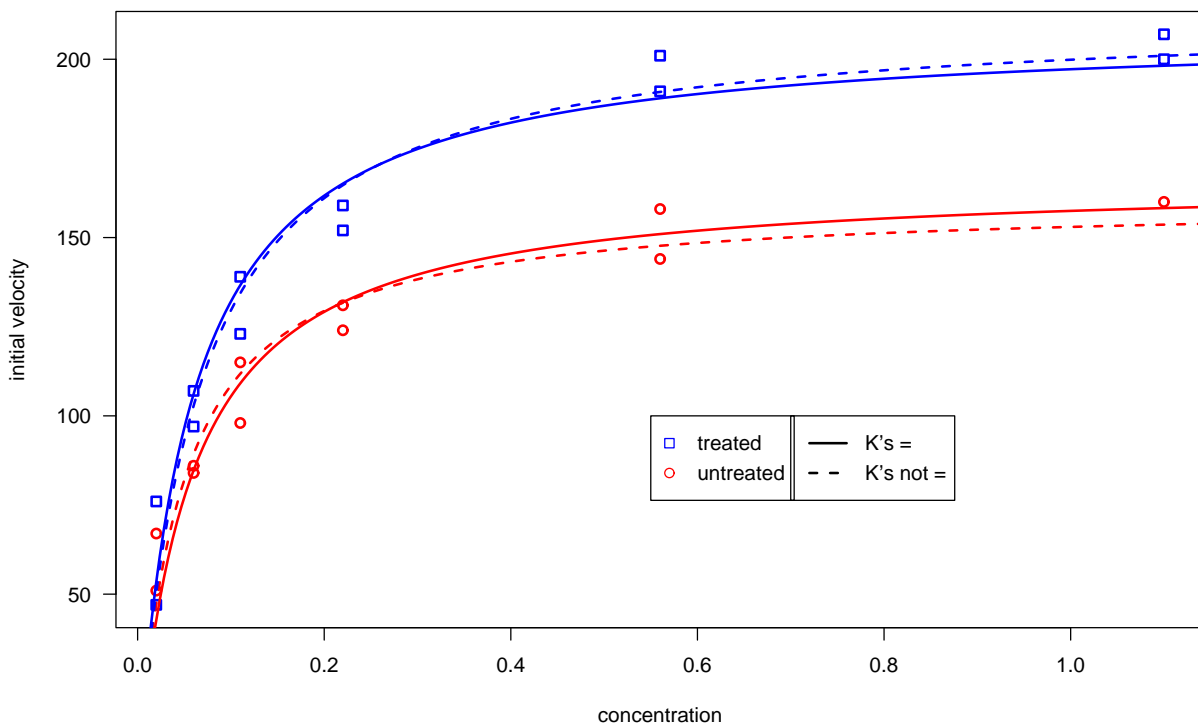
$x = 0/1$ if cells were
untreated/treated.

Estimation in R

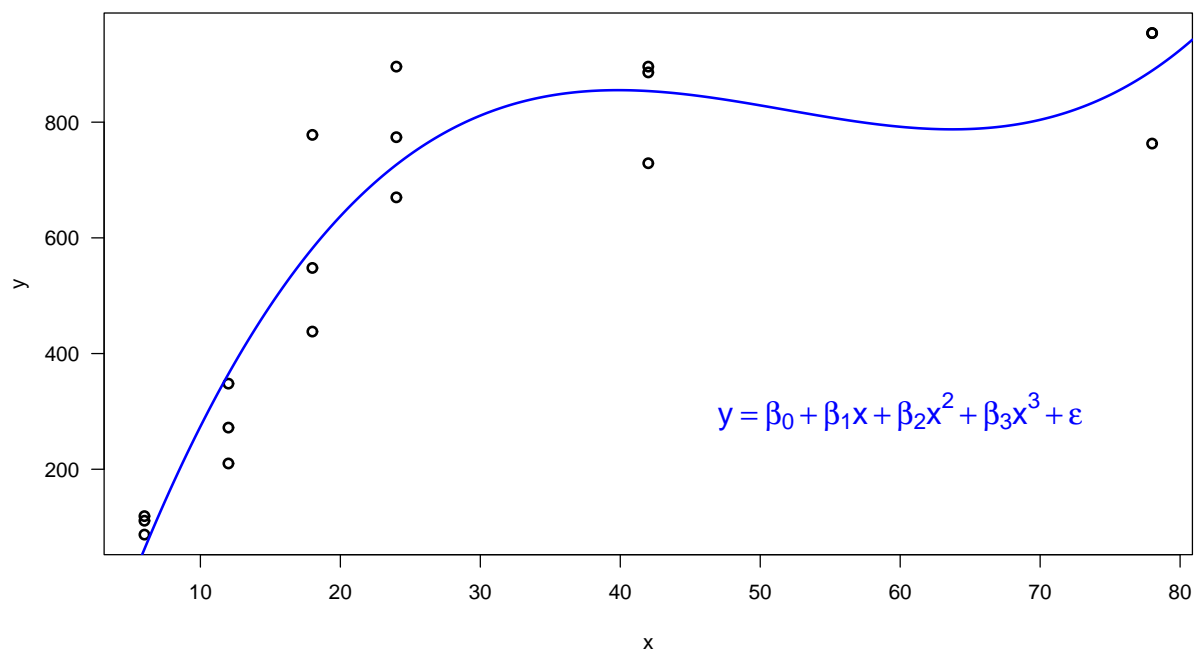
```
> nls.outC <- nls(vel ~ ((Vm +dV * x) * conc)/  
                  (K + dK*x + conc),  
                  data=puro,  
                  start=c(Vm=160, K=0.048, dV=0, dK=0))  
  
> summary(nls.outC)$param
```

	Est	SE	t-val	P-val
Vm	160.28	6.90	23.2	2.0e-15
K	0.048	0.008	5.8	1.5e-05
dV	52.40	9.55	5.5	2.7e-05
dK	0.016	0.011	1.4	1.7e-01

K's equal vs not



From last time...



An alternative model

Linear “spline”

$$y = \begin{cases} \beta_0 + \beta_1 x + \epsilon & \text{if } x \leq x_0 \\ \beta_0 + \beta_1 x_0 + \epsilon & \text{if } x \geq x_0 \end{cases}$$

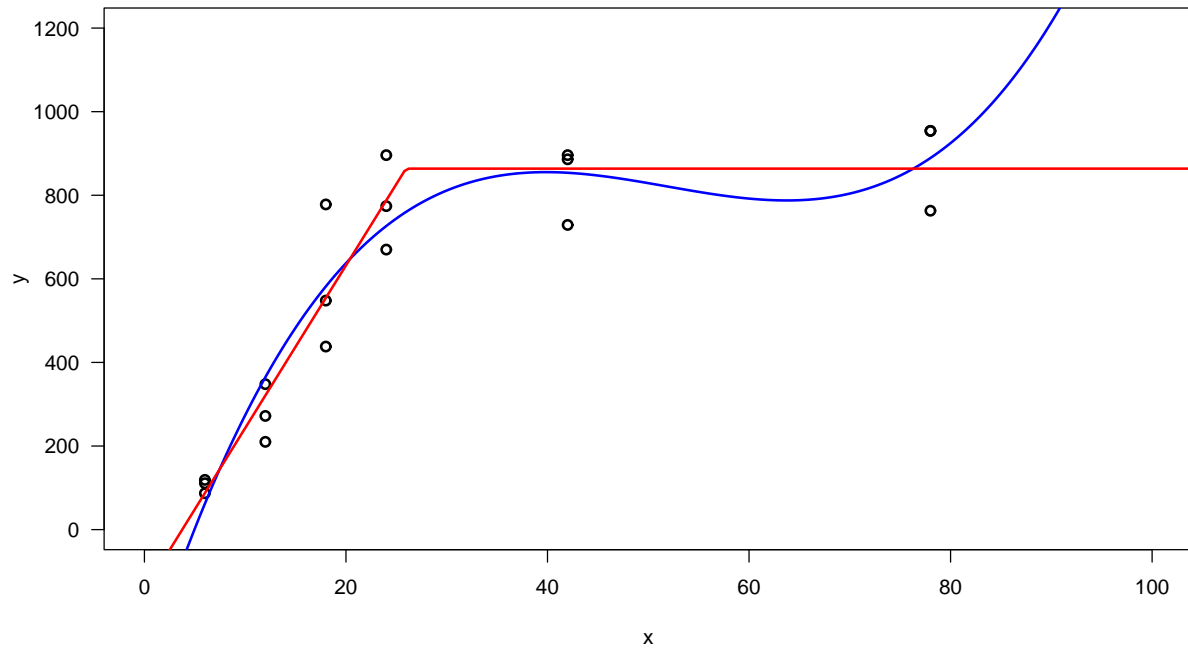
R code:

```
> f <- function(x,b0,b1,x0)
  ifelse(x<x0, b0+b1*x, b0+b1*x0)

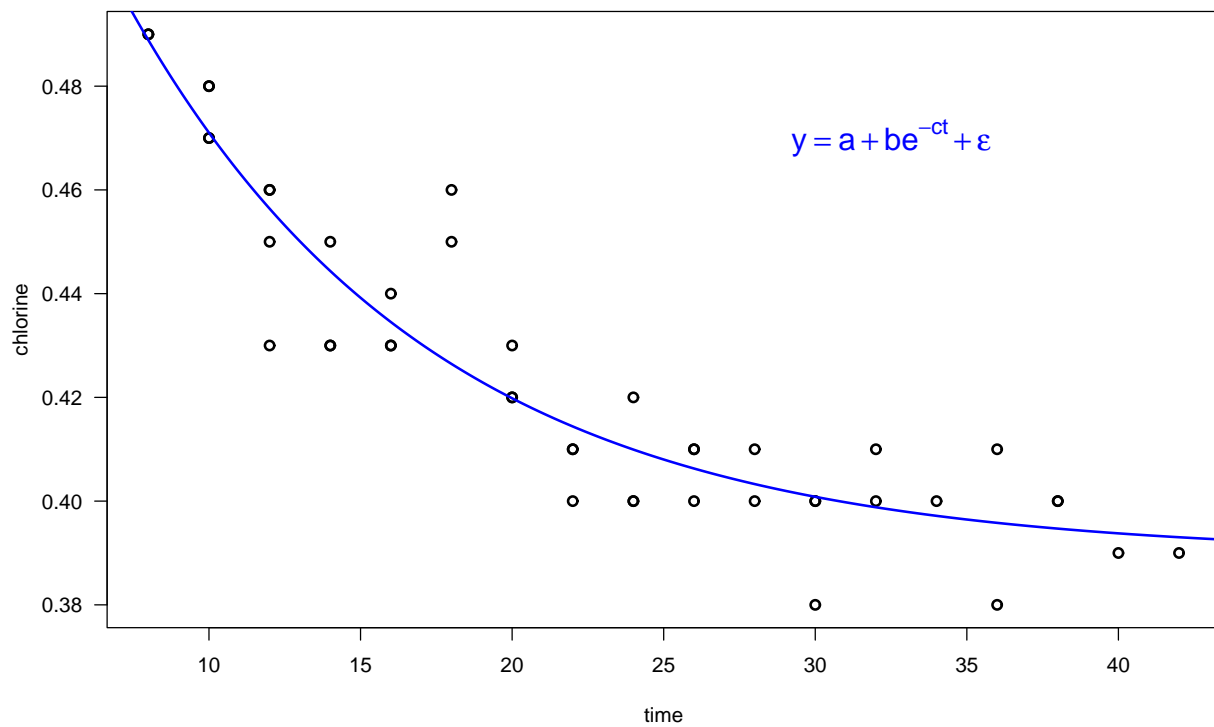
> nls.out <- nls(y ~ f(time,b0,b1,x0), data=mydata,
  start=c(b0=200, b1=100, x0=30))

> summary(nls.out)$param
      Est      SE  t-val    P-val
b0    -146   71.3   -2.0   5.8e-02
b1      39    4.3    9.0   2.1e-07
x0      26    1.8   14.6   2.9e-10
```

Results



One last example...



R code

```
> nls.out <- nls(chlorine ~ a + b*exp(-c*time), data=cl,  
                start=c(a=0.05, b=0.49, c=0.1))
```

```
> summary(nls.out)$param
```

	Est	SE	t-val	P-val
a	0.390	0.006	66.7	1.9e-43
b	0.219	0.031	7.0	1.7e-08
c	0.099	0.018	5.5	2.4e-06