

Fitting Mathematical Models to Biological Data using Non-Linear Least-Squares Minimization (NLLS)

Samraat Pawar

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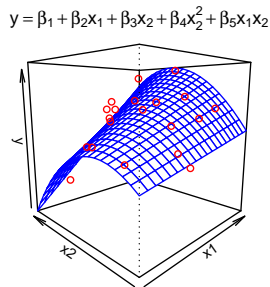
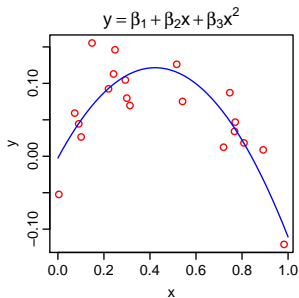
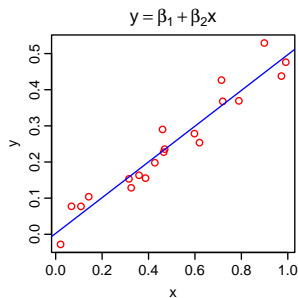
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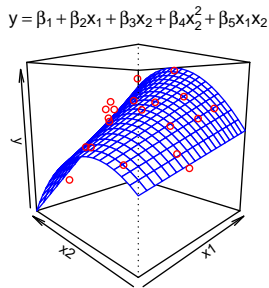
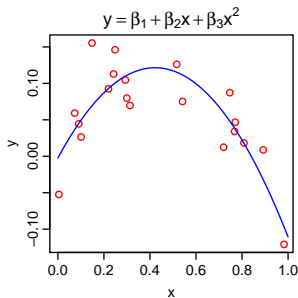
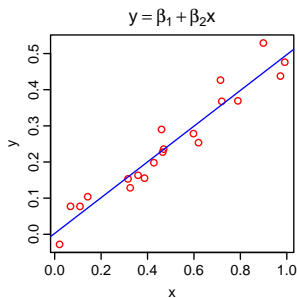
OUTLINE

- Why Non-Linear Least Squares regression / fitting?
- The NLLS fitting method
- NLLS in R
- Practicals overview

LINEAR MODELS ARE GREAT

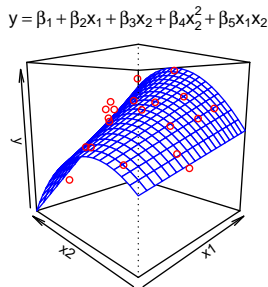
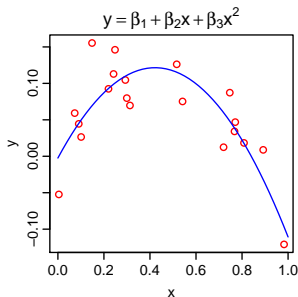
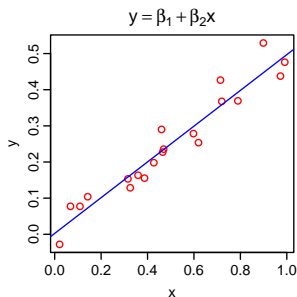


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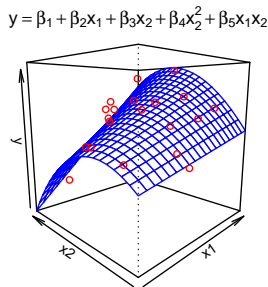
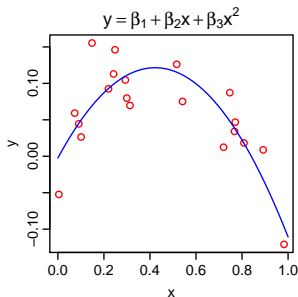
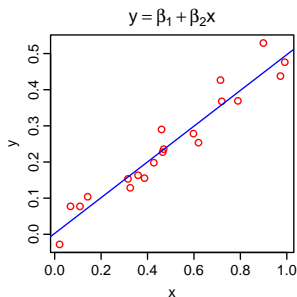
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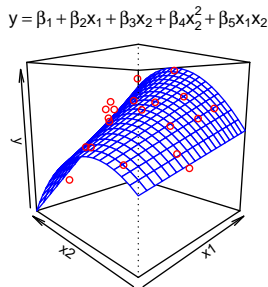
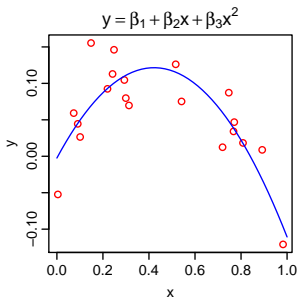
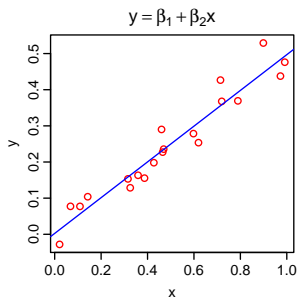
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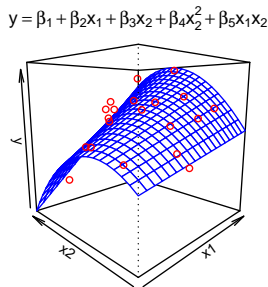
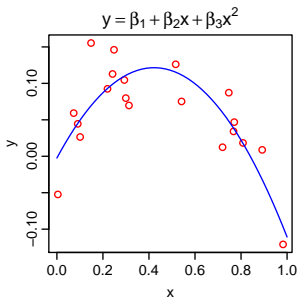
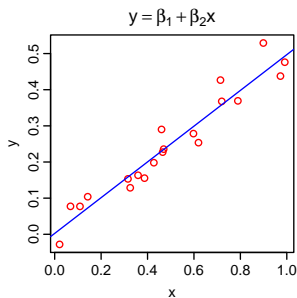
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- OK, so then *why Non-Linear Least Squares (NLLS) fitting?*

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NO!

SO WHAT — WHY IS INTRINSIC NON-LINEARITY A PROBLEM?

Recall what the Least Squares method does:

- Consider a predictor x , data y , n observations, and a model that we want to fit to the data:

$$f(x_i, \beta) + \varepsilon_i$$

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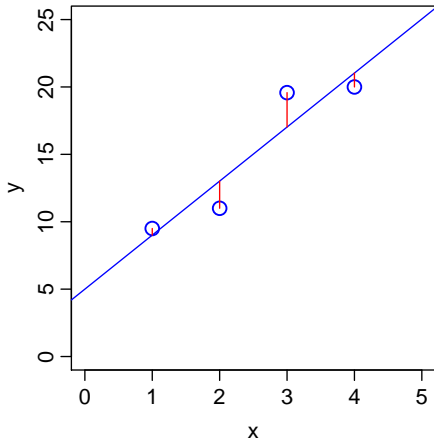
- The objective is to find estimates of values of the k parameters ($\hat{\beta}_j$) that minimize the sum (S) of squared residuals (r_i) (AKA RSS):

$$S = \sum_{i=1}^n [y_i - f(x_i, \beta)]^2 = \sum_{i=1}^n r_i^2$$

THE LEAST-SQUARES SOLUTION

OLS minimizes the *sum* of the *squared* residuals

IF THE MODEL IS LINEAR, THE SOLUTION IS EASY USING ALGEBRA



$$y_i = \beta_0 + \beta_1 x_i + \varepsilon_i$$

$$9.50 = 5 + 4 \times 1 + 0.50$$

$$11.00 = 5 + 4 \times 2 - 2.00$$

$$19.58 = 5 + 4 \times 3 + 2.58$$

$$20.00 = 5 + 4 \times 4 - 1.00$$

$$\beta_0 = 5; \beta_1 = 4$$

INTRINSIC NON-LINEARITY DOES NOT ALLOW A ALGEBRAIC SOLUTION

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- That is, they are functions of both x and the parameters β_j , so the gradient equations do not have a solution like the OLS case
- So the nice trick of solving $\mathbf{Y} = \mathbf{X}\beta + \varepsilon$ is impossible *mathematically*

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- Whether a refinement has taken place in any step of the iteration is determined by re-calculating the residuals at that step
- Eventually, if it all goes well, we find a combination of β_j 's that is *very close* to the desired solution $\frac{\partial S}{\partial \beta_j} = 0, j = 0, 1, 2, \dots, k$

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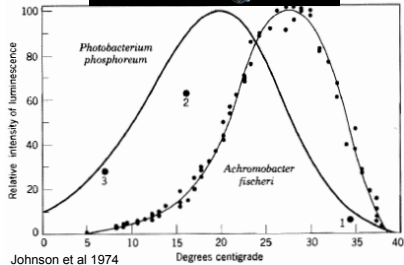
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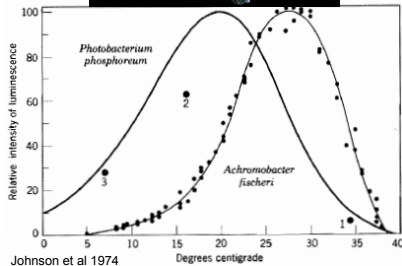
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- *Can you think of some examples?*

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k = Boltzmann constant (eV K^{-1})

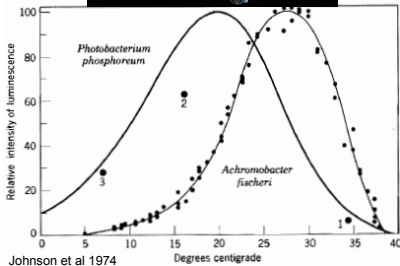
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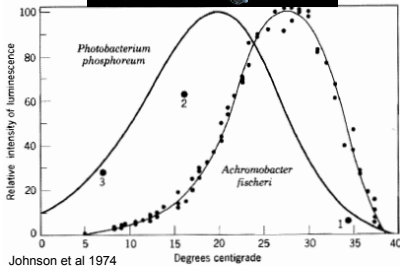
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- *What about alternative models?*

EXAMPLE: FUNCTIONAL RESPONSES

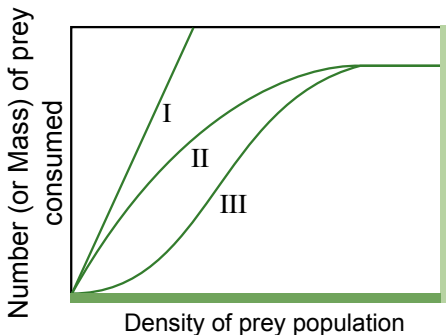
$$f(x_R) = \frac{ax_R^{q+1}}{1+hax_R^{q+1}} \text{ (Holling, 1959)}$$

x_R = Resource density (Mass / Area or Volume)

a = Search rate (Area or Volume / Time)

h = Handling time

q = Shape parameter (dimensionless)



Note that:

- NLLS fitting can yield $h < 0$, $q < 0$, or both
- $h < 0$ is biologically impossible but indicates an upward curving response
- $q < 0$ is biologically unlikely as it indicates a decline in search rate with resource density (but is useful as a measure of deviation away from a type III response)

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- ➏ Repeat 4–5
- ➐ Stop simulations when the adjustments make virtually no difference to the rss

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The *tricky part* — *adjust parameters to make curve come closer to the data points* (step 4) has two main algorithms that you can choose between:

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- The command is `nlsLM`

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- You may also want to compare multiple models.

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- What if the errors are not normal? — use Maximum Likelihood or Bayesian methods instead.

MORE NLLS TIPS

- You can use mixed-effects modelling with NLLS in R; the package is `nlme` <https://stat.ethz.ch/R-manual/R-devel/library/nlme/html/nlme.html> (You are probably stuck with the Gauss-Newton algorithm with `nlme` though)

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- You can also use Python — look up `lmfit` <https://lmfit.github.io/lmfit-py/index.html>. `python` seems to have a better Levenberg-Marquardt implementation than R

READINGS AND RESOURCES

- Motulsky, Harvey, and Arthur Christopoulos. Fitting models to biological data using linear and nonlinear regression: a practical guide to curve fitting. OUP USA, 2004.
- Johnson, J. B. & Omland, K. S. 2004 Model selection in ecology and evolution. *Trends Ecol. Evol.* 19, 101–108.

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- That is, the solution of $\frac{\partial r_i}{\partial \beta_j}$ is simple (enough)

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- Then we want to solve
$$\frac{\partial S}{\partial \beta_0} = \sum_{i=1}^n \frac{\partial [y_i - (\beta_0 + \beta_1 x_i)]^2}{\partial \beta_0} = 0$$
$$\frac{\partial S}{\partial \beta_1} = \sum_{i=1}^n \frac{\partial [y_i - (\beta_0 + \beta_1 x_i)]^2}{\partial \beta_1} = 0$$

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just boils down to solving two simultaneous equations because $\frac{\partial r_i}{\partial \beta_j}$ is simple *because* the model is intrinsically linear:

$$-n\beta_0 + \sum_{i=1}^n y_i + \beta_1 \sum_{i=1}^n x_i = 0$$

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- That is, we need to solve $\mathbf{Y} = \mathbf{X}\beta + \varepsilon$ (*this is what R solves when you use `lm()`*)