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

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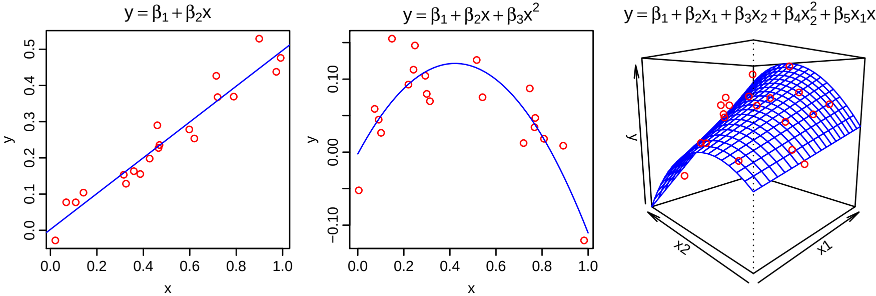
Outline

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

- Which of these are Linear Models (fitted to data)?



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Go to `www.menti.com` *and enter code shown (phone or laptop)*

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- Linear models can *include curved responses* (e.g. polynomial regression)

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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:
  $f(x_i, \boldsymbol{\beta}) + \varepsilon_i$
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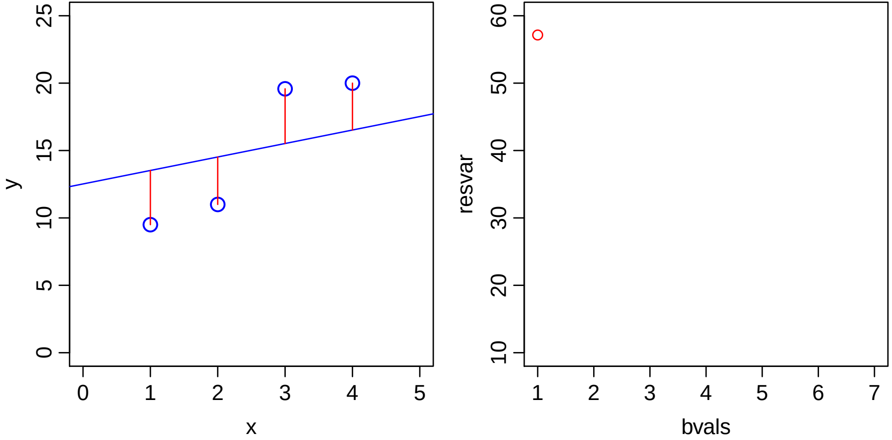
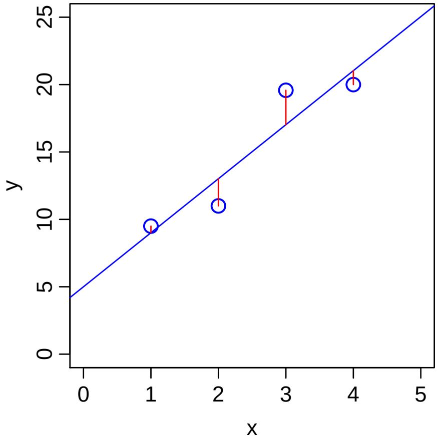
- The objective is to find estimates of values of the k parameters ($\hat{\beta}_j$) that minimize the sum (S) of squared residuals (r_i) (AKA RSS):
  $S = \sum_{i=1}^{n} [y_i - f(x_i, \boldsymbol{\beta})]^2 = \sum_{i=1}^{n} r_i^2$

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



If the model is linear, the solution is easy using algebra



$$y_1 = \beta_0 + \beta_1 x_1 + \varepsilon_i$$

$$\begin{aligned} 9.50 &= 5 + 4 \times 1 + 0.50 \\ 11.00 &= 5 + 4 \times 2 - 2.00 \\ 19.58 &= 5 + 4 \times 3 + 2.58 \\ 20.00 &= 5 + 4 \times 4 - 1.00 \end{aligned}$$

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

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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 $\mathbf{Y} = \mathbf{X}\boldsymbol{\beta} + \boldsymbol{\varepsilon}$ is impossible *mathematically*

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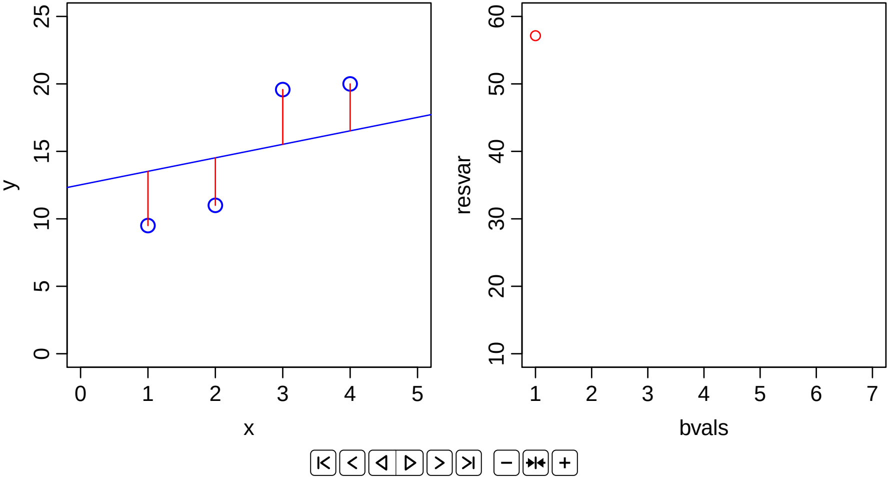
- Whether a refinement has taken place in any step of the iteration is determined by re-calculating the residuals at that step
- Eventually, if it all goes well, we find a combination of β_j's that is *very close* to the desired solution $\frac{\partial S}{\partial \beta_j} = 0, j = 0, 1, 2, \ldots,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



y
x
resvar
bvals

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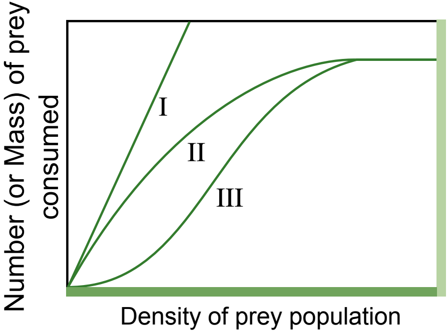
- *Can you think of some examples?*

Example: Functional responses

$$f(x_R) = \frac{a x_R^{q+1}}{1 + h a x_R^{q+1}}$$ (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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6. Repeat 4–5
7. 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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- 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-Marqualdt 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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- That is, our model is $y_i = \beta_0 + \beta_1 x_i + \varepsilon_i$ (Linear Regression)
- Then we want to solve
  $\frac{\partial S}{\partial \beta_0} = \sum_{i=1}^{n} \frac{\partial [y_i - (\beta_0 + \beta_1 x_i)]^2}{\partial \beta_0} = 0$
  $\frac{\partial S}{\partial \beta_1} = \sum_{i=1}^{n} \frac{\partial [y_i - (\beta_0 + \beta_1 x_i)]^2}{\partial \beta_1} = 0$

Why is intrinsic non-linearity a problem?

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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 $\mathbf{Y} = \mathbf{X}\boldsymbol{\beta} + \boldsymbol{\varepsilon}$ (*this is what R solves when you use* `lm()`)