Fitting mathematical models to biological data using least-squares minimization

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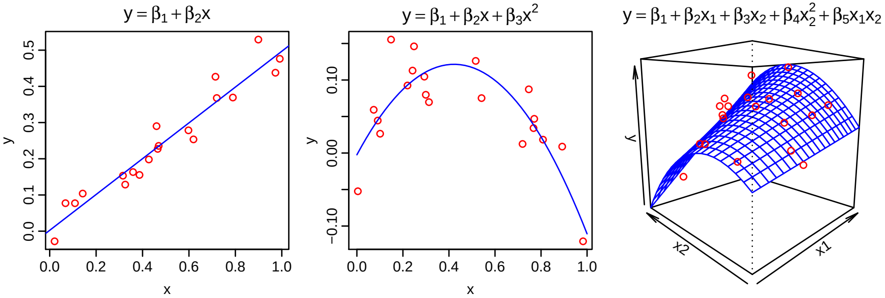
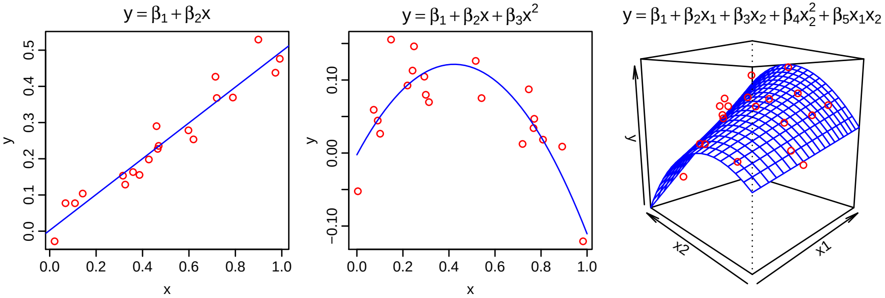
Outline

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



$y = \beta_1 + \beta_2 x$
$y = \beta_1 + \beta_2 x + \beta_3 x^2$
$y = \beta_1 + \beta_2 x_1 + \beta_3 x_2 + \beta_4 x_2^2 + \beta_5 x_1 x_2$
x
y
0.0 0.2 0.4 0.6 0.8 1.0
0.0 0.1 0.2 0.3 0.4 0.5
−0.10 0.00 0.10
x1
x2



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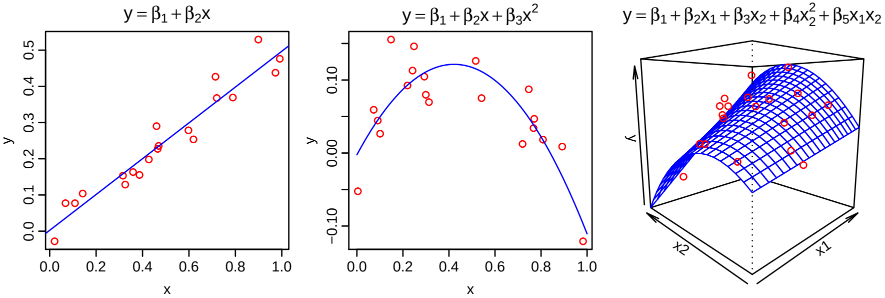

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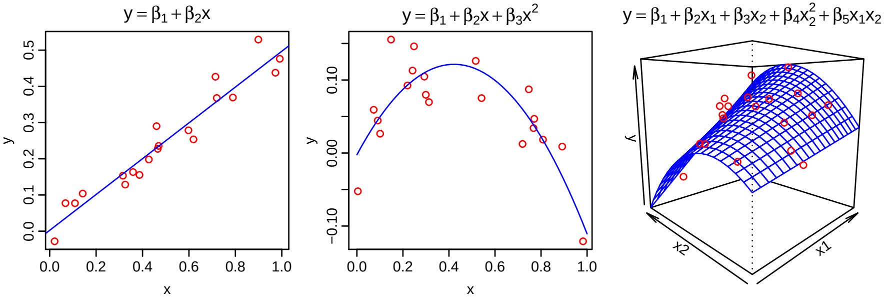

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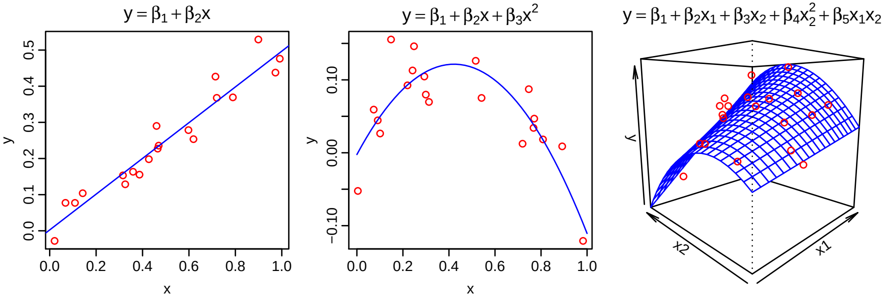

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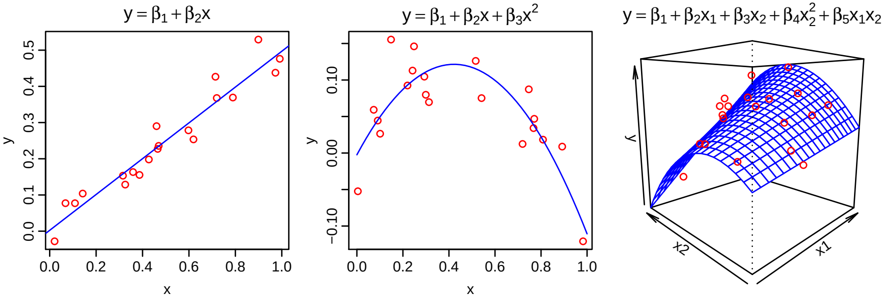

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- Linear models can *include curved responses* (e.g. polynomial regression)
- OK, so then *why Non-Linear Least Squares (NLLS) fitting?*

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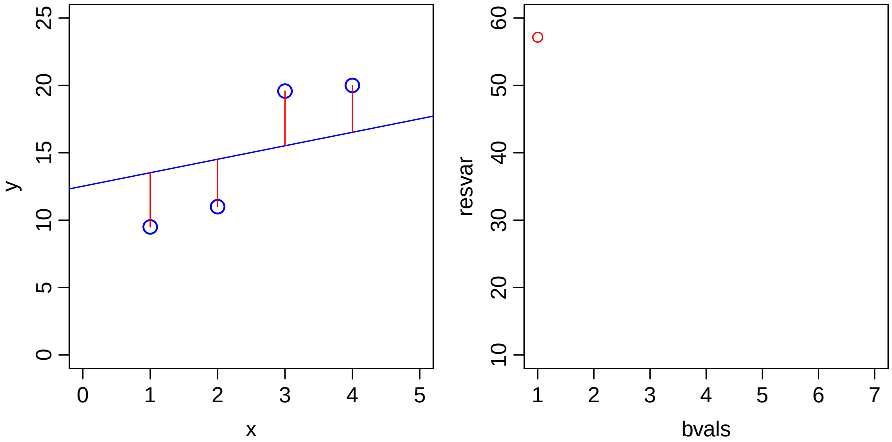
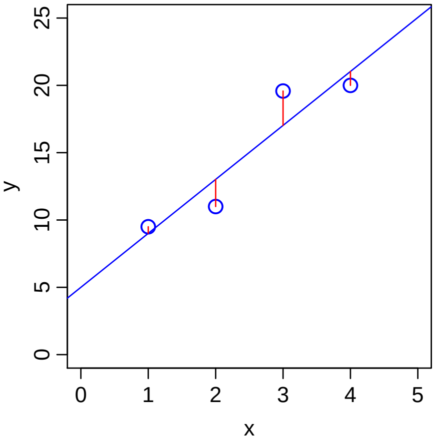
- The objective is to find estimates of values of the k parameters ($\hat{\beta}_j$) that minimize the sum (S) of squared residuals (r_i) (AKA RSS):
  $S = \sum_{i=1}^{n} [y_i - f(x_i, \boldsymbol{\beta})]^2 = \sum_{i=1}^{n} r_i^2$

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



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



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

$$9.50 = 5 + 4 \times 1 + 0.50$$
$$11.00 = 5 + 4 \times 2 - 2.00$$
$$19.58 = 5 + 4 \times 3 + 2.58$$
$$20.00 = 5 + 4 \times 4 - 1.00$$

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

Intrinsic non-linearity does not allow a algebraic solution

- So, then, in an intrinsically non-linear model such as $y_i = \beta_0 e^{\beta_2 x_i} + \varepsilon_i$ the derivatives $\frac{\partial r_i}{\partial \beta_j}$ are naughty

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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*

So — Enter NLLS

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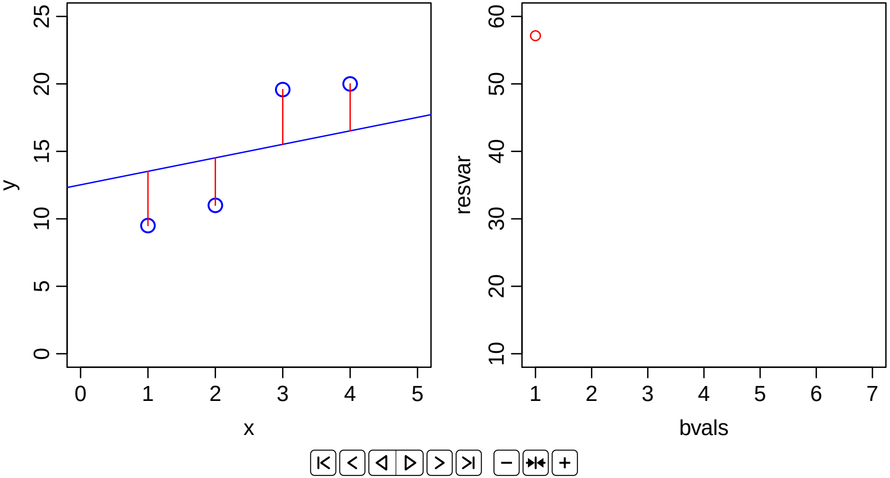
- Whether a refinement has taken place in any step of the iteration is determined by re-calculating the residuals at that step
- Eventually, if it all goes well, we find a combination of β_j's that is *very close* to the desired solution $\frac{\partial S}{\partial \beta_j} = 0, j = 0, 1, 2, \ldots,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


y
x
resvar
bvals

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- *Can you think of some examples?*

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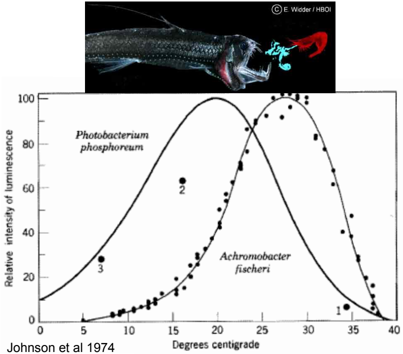

Johnson et al 1974

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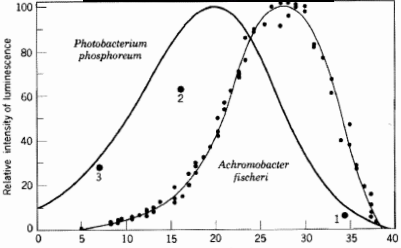

Johnson et al 1974

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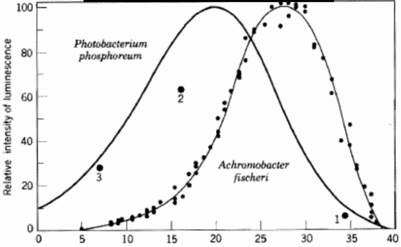

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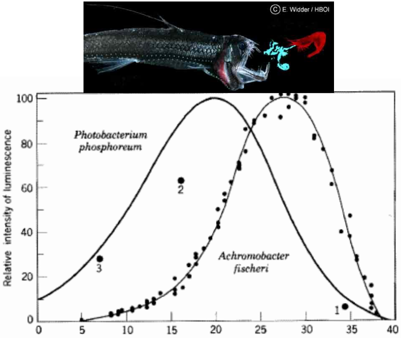

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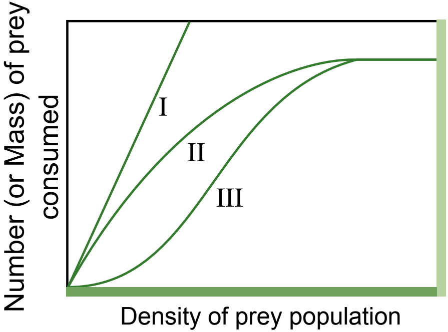
- *What about alternative models?*

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:

- The Gauss-Newton algorithm is the default in the `nls` package (part of the `stats` base package) — good in many cases, but doesn't work very well if the model is mathematically weird (the optimization landscape is difficult) and the starting values for parameters are far-off-optimal

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  - R^2

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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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- Then we want to solve
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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:

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

  $\sum_{i=1}^{n} x_i y_i - \beta_0 \sum_{i=1}^{n} x_i + \beta_1 \sum_{i=1}^{n} x_i^2 = 0$

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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()`)