THE STANDARD ERROR OF THE LAB SCIENTIST

. . . and other common statistical misconceptions in the scientific literature.

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Some Quotes

Instead of an outline, here are some quotes from scientific publications that we will have a closer look at:

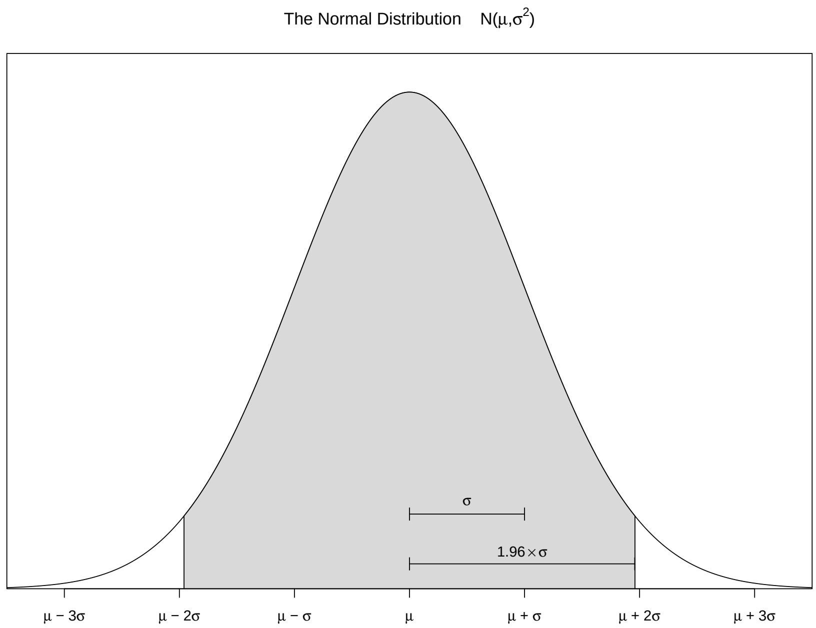
“ . . . 95% confidence intervals (mean plus minus two standard deviations) . . . ”

“ . . . the model predicted the data well (correlation coefficient R^2 = 0.85) . . . ”

“ . . . we used the jackknife to estimate the error for future predictions . . . ”

Quote #1

" . . . 95% confidence intervals (mean plus minus two standard deviations) . . . "



Parameters and Statistics

A statistic is a numerical quantity derived from a sample to estimate an unknown parameter that describes some feature of the entire population.

For example, assume that the measurements taken in an experiment follow a normal distribution $X \sim N(\mu, \sigma^2)$, and assume that we carry out n independent experiments, i. e. let $X_1, \ldots, X_n$ be a random sample from X.

$\longrightarrow$ μ is the unknown population mean (a parameter).

$\bar{X} = \sum_i X_i/n$ is the sample mean (a statistic).

$\longrightarrow$ σ is the standard deviation of X.

$\hat{\sigma} = \sqrt{S^2/(n-1)}$ is the sample standard deviation, where $S^2 = \sum_i (X_i - \bar{X})^2$.

Note that $\hat{\sigma}$ is not a standard error!

The Standard Error

The standard error of a statistic is the standard deviation of its sampling distribution.

For example: $X \sim N(\mu, \sigma^2)$, hence $\bar{X} \sim N(\mu, \sigma^2/n)$, and therefore the standard error of $\bar{X}$ is $\sigma/\sqrt{n}$.

A standard error itself is a parameter, not a statistic!

As the standard deviation of X is often unknown, so is the standard error of $\bar{X}$, but in practice we can estimate it, for example by $\widehat{\text{se}}(\bar{X}) = \hat{\sigma}/\sqrt{n}$.

In general, the standard error depends on the sample size: the larger the sample size, the smaller the standard error.

This means that the term *standard deviation* in " ... 95% confidence intervals (mean plus minus two standard deviations) ... " better be referring to the sampling distribution, not the population.

But what about that factor 2?

Confidence Intervals

If the standard deviation σ of X is known, then $\frac{\bar{X}-\mu}{\sigma/\sqrt{n}} \sim N(0,1)$.

We can obtain a 95% confidence interval for the population mean μ as

$$I \;=\; [\bar{X} - z_{0.975} \times \sigma/\sqrt{n}\;;\;\bar{X} + z_{0.975} \times \sigma/\sqrt{n}]$$

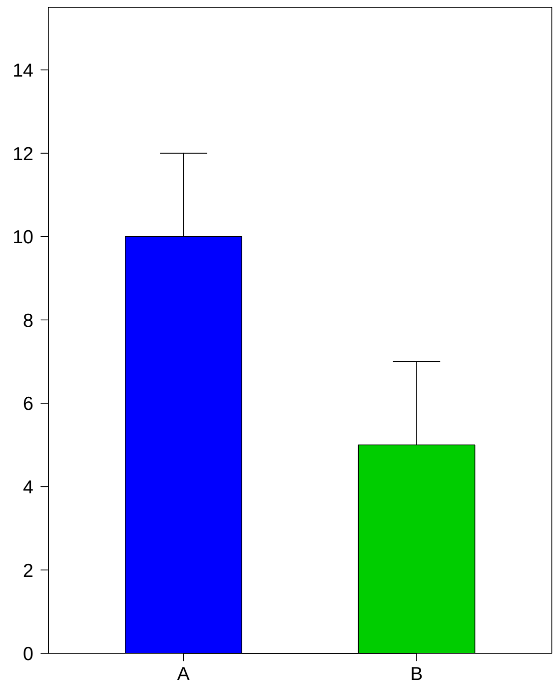
If σ is unknown and we have to estimate it from the data as well, then $\frac{\bar{X}-\mu}{\hat{\sigma}/\sqrt{n}} \sim t_{n-1}$.

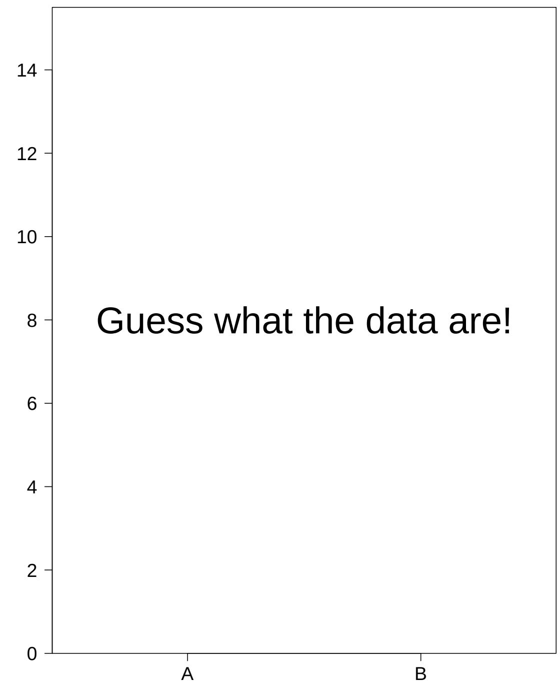
The 95% confidence interval for μ is now

$$I \;=\; [\bar{X} - t^{n-1}_{0.975} \times \hat{\sigma}/\sqrt{n}\;;\;\bar{X} + t^{n-1}_{0.975} \times \hat{\sigma}/\sqrt{n}]$$

n	3	4	5	6	7	8	9	10
$t^{n-1}_{0.975}$	4.30	3.18	2.78	2.57	2.45	2.36	2.31	2.26

Plotting Data (Confusion Part 1)





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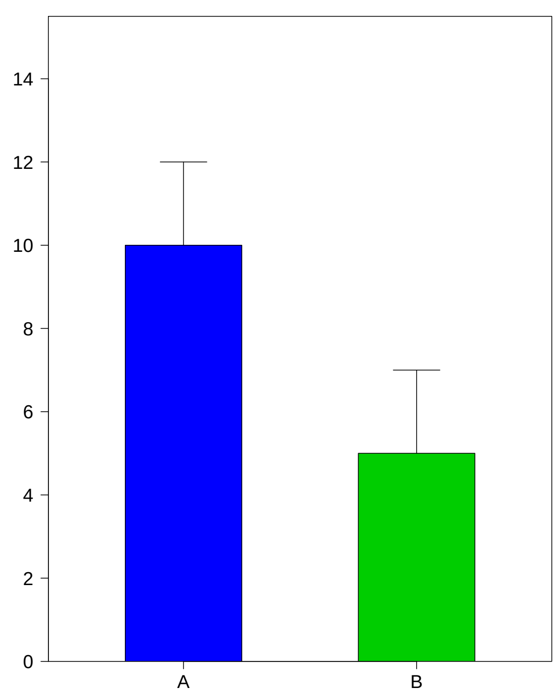

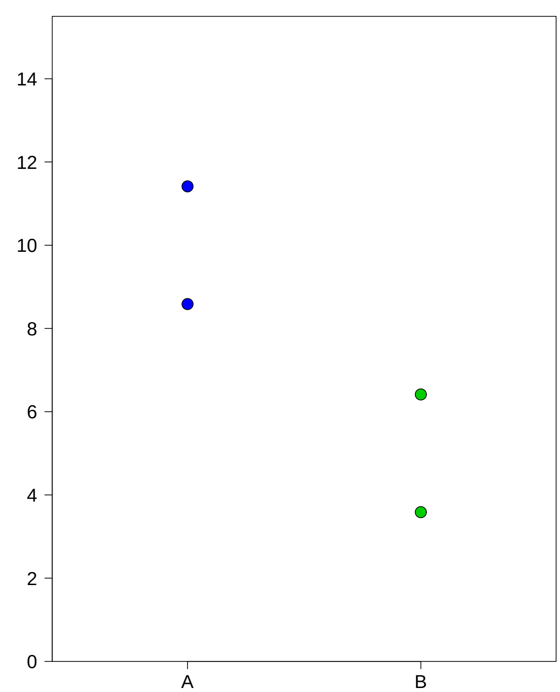

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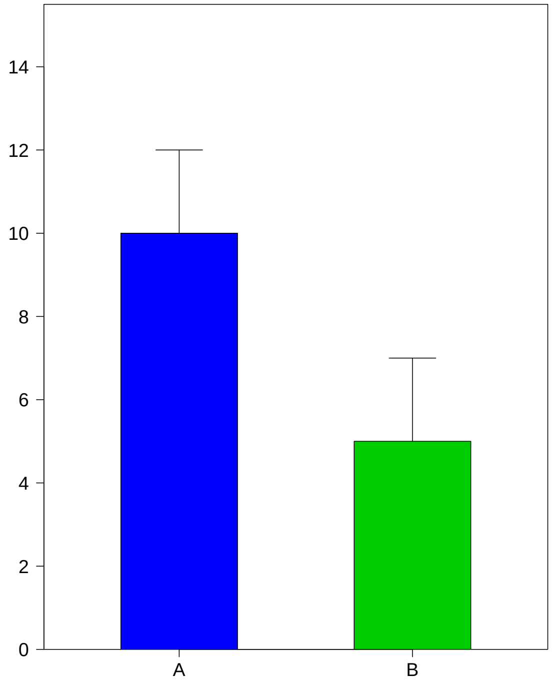

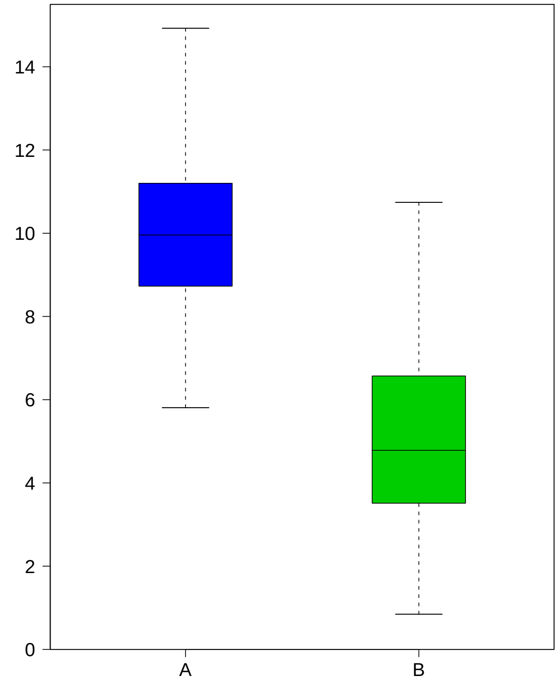

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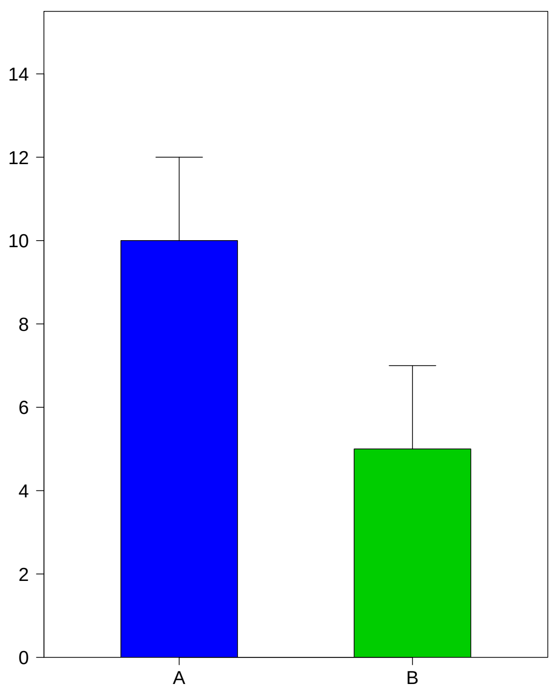
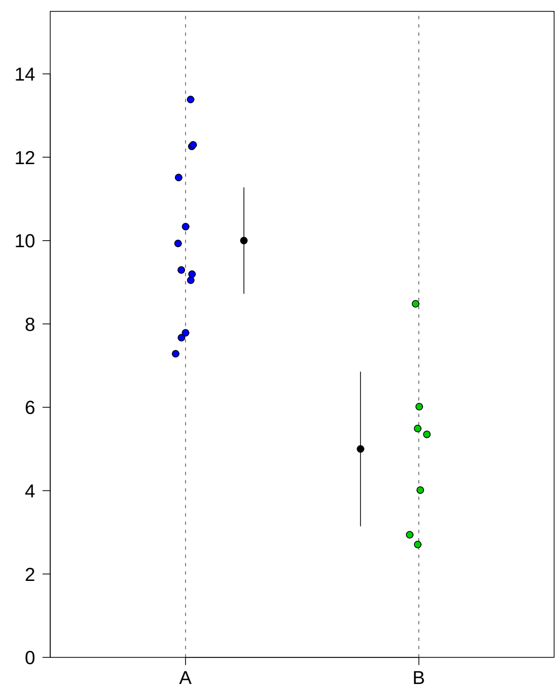




Reporting Uncertainty (Confusion Part 2)

- Results are frequently reported in the form 'mean plus minus standard error', such as 7.4 ($\pm$1.3).
- What is reported as the (estimated) standard error is often the sample standard deviation ($\hat{\sigma}$, not $\hat{\sigma}/\sqrt{n}$).
- The plus/minus notation can also mislead readers to believe 7.4 ($\pm$1.3) is a confidence interval.
- To allow others to correctly quantify uncertainty, it is also necessary to report the number of experiments that have been performed (for the t-quantile and to calculate an estimate for the standard error, if necessary).

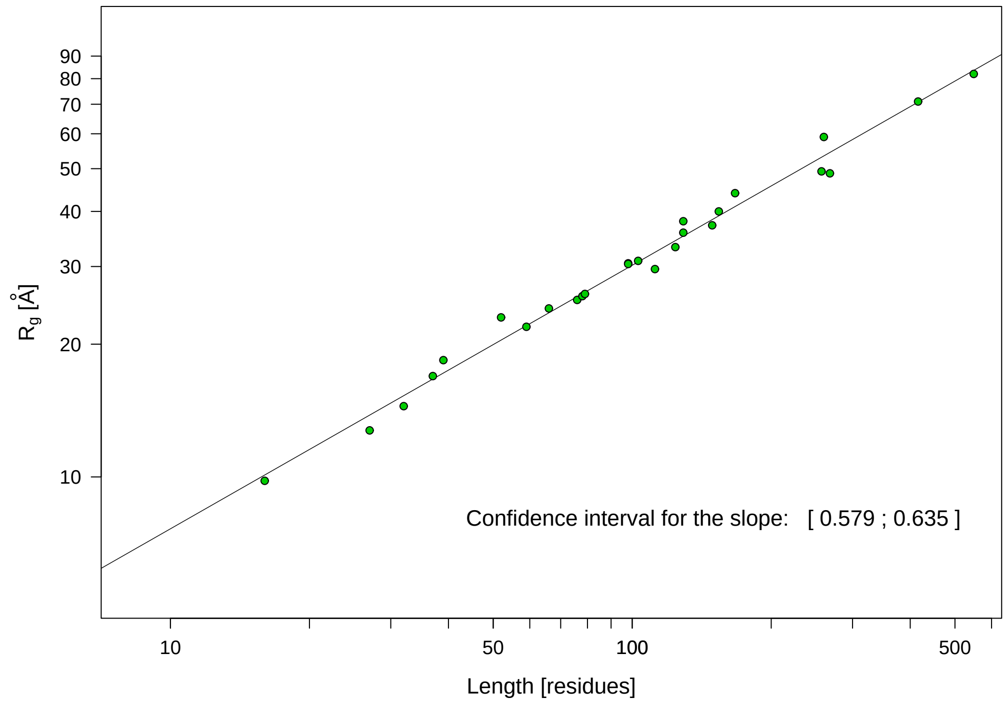
An Example

Do chemically denatured proteins behave as random coils?

- The radius of gyration R_g of a protein is defined as the root mean square distance from each atom of the protein to their centroid.
- For an ideal (infinitely thin) random-coil chain in a solvent, the average radius of gyration of a random coil is a simple function of its length n: $R_g \propto n^{0.5}$.
- For an excluded volume polymer (a polymer with non-zero thickness and non-trivial interactions between monomers) in a solvent, the average radius of gyration, we have $R_g \propto n^{0.588}$ (Flory 1953).

$\longrightarrow$ The radius of gyration can be measured using small angle x-ray scattering.

An Example



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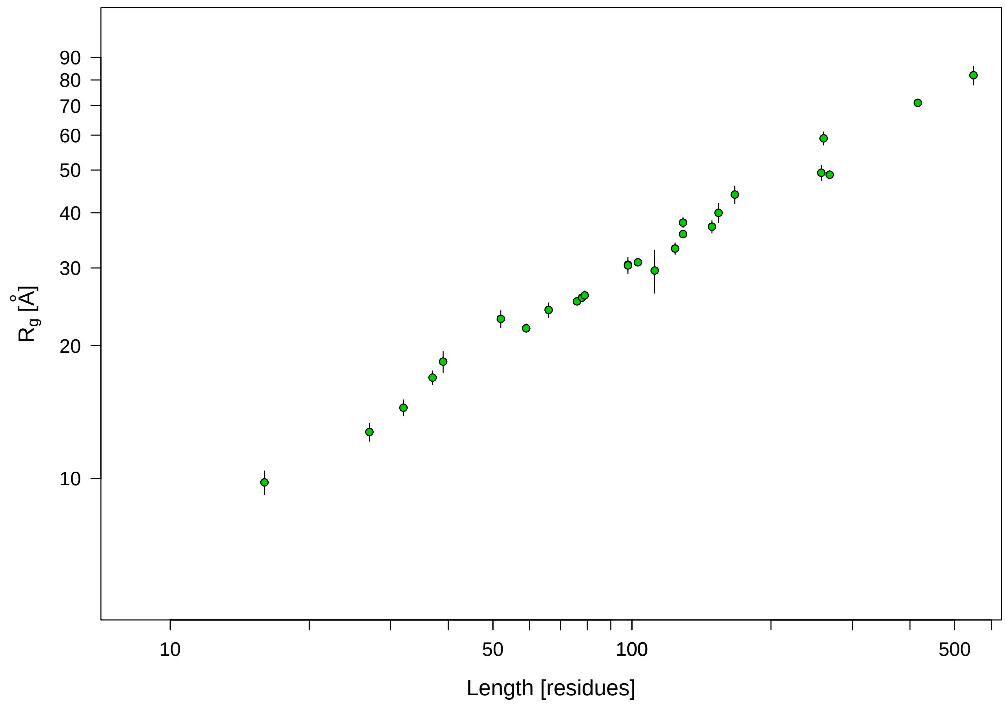
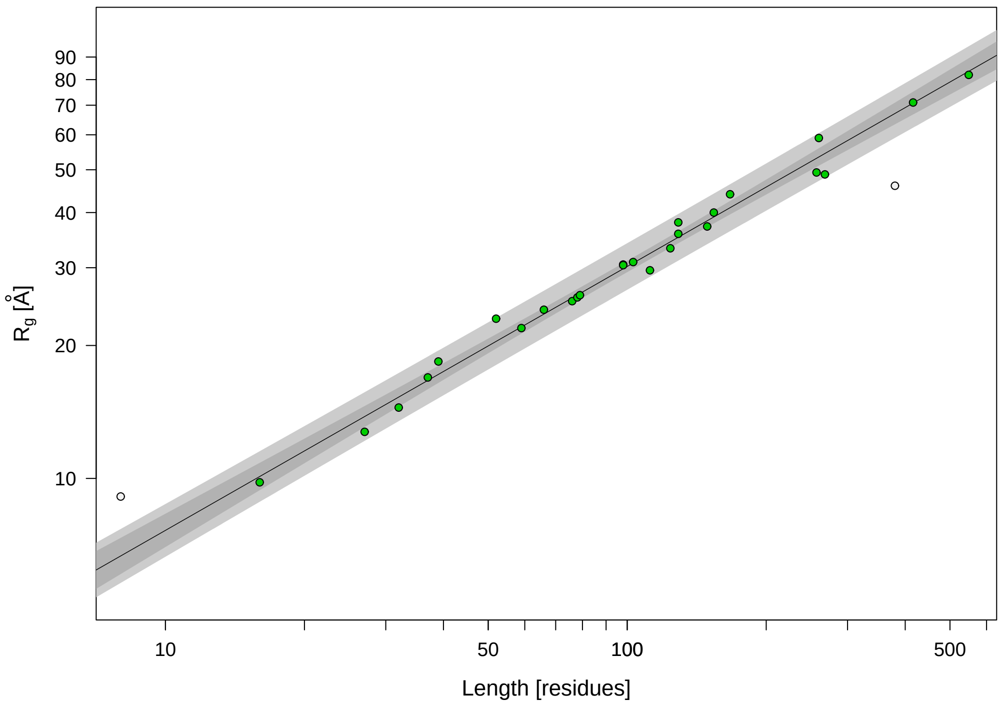
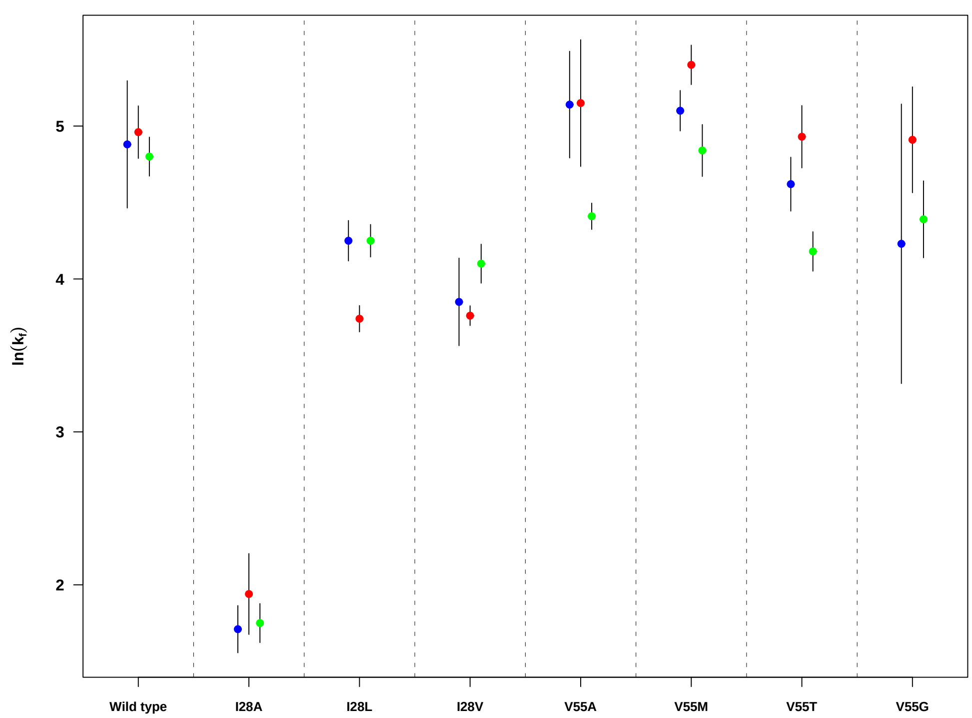


Variability



Variance Components



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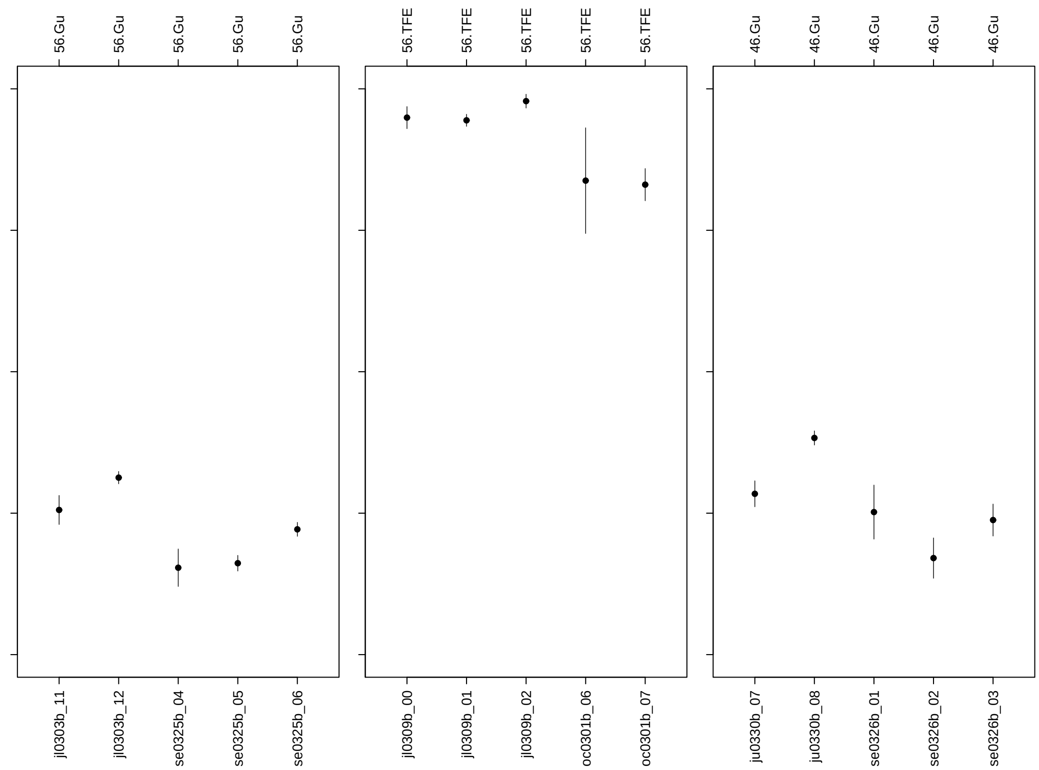

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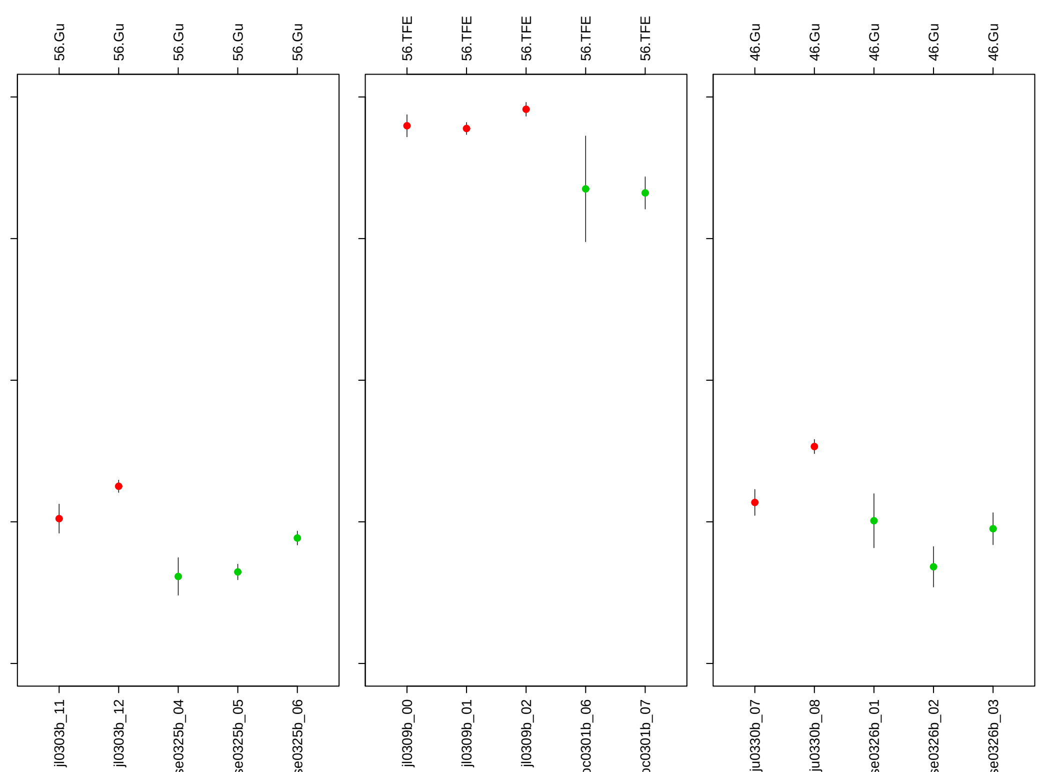
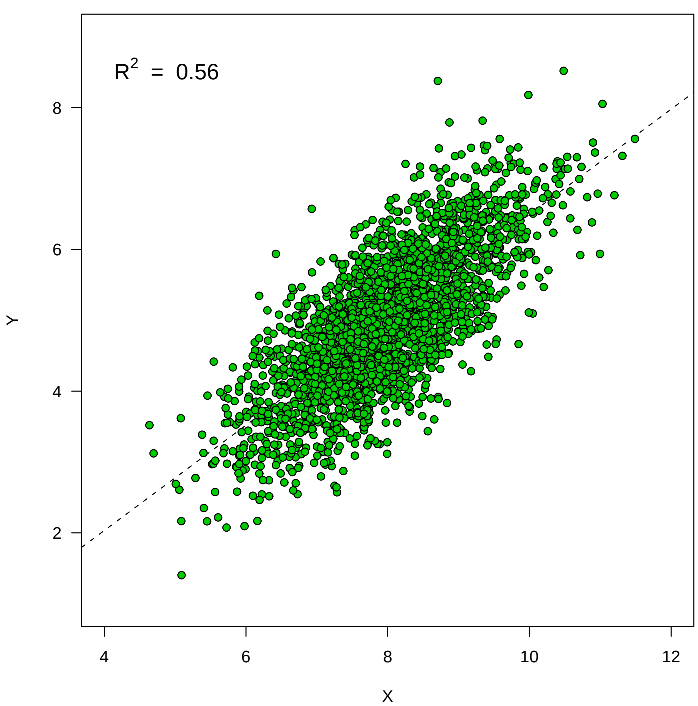


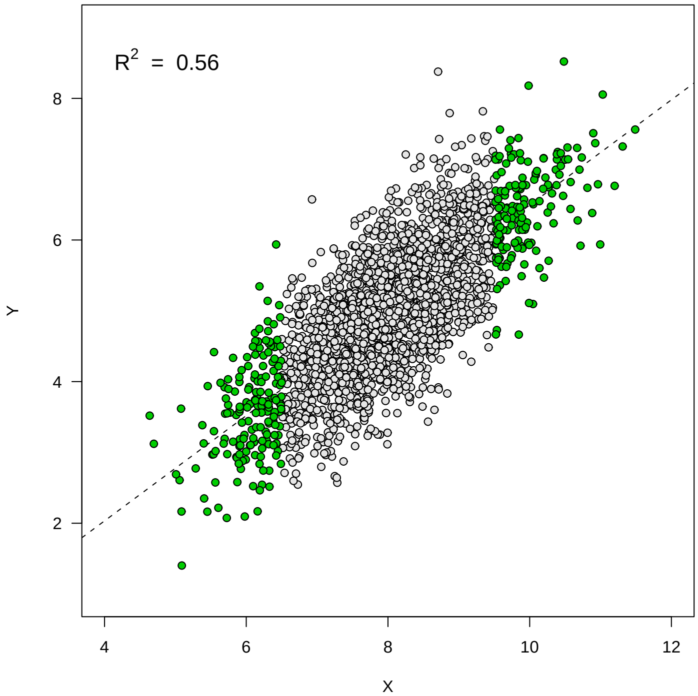
Quote #2

" . . . the model predicted the data well (correlation coefficient $R^2 = 0.85$) . . . "

Correlation



Correlation



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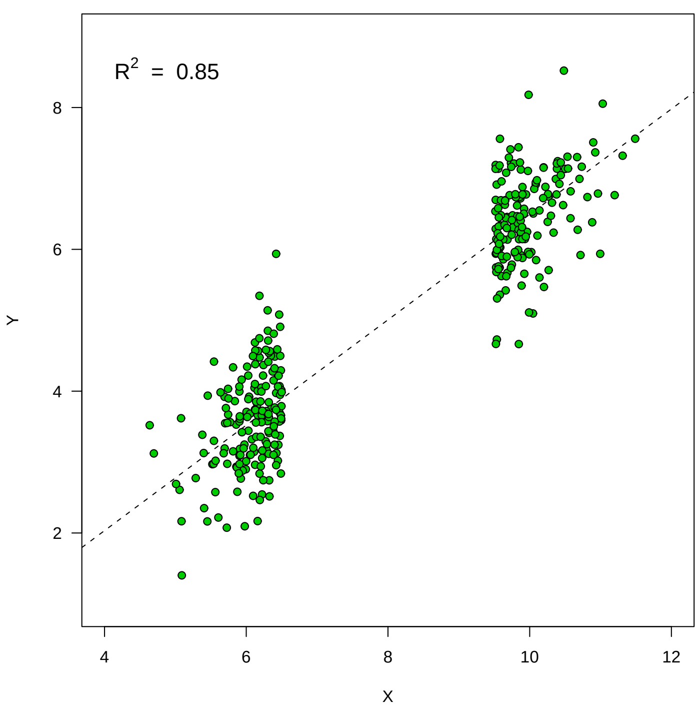


Correlation vs Regression

- In a correlation setting we try to determine whether two random variables vary together (covary).
- There is no ordering between those variables, and we do not try to explain one of the variables as a function of the other.

- In regression settings we describe the dependence of one variable on the other variable.
- There is an ordering of the variables, often called the dependent variable and the independent variable.

Correlation vs Regression

The correlation coefficient of two jointly distributed random variables X and Y is defined as

$$\rho = \frac{\text{cov}(X,Y)}{\sigma_X \sigma_Y}$$

where cov(X,Y) is the covariance between X and Y, and σ_X and σ_Y are their respective standard deviations.

If X and Y follow a bivariate normal distribution with correlation ρ

$$\begin{pmatrix} x_i \\ y_i \end{pmatrix} \sim N\left(\begin{pmatrix} \mu_X \\ \mu_Y \end{pmatrix}, \begin{pmatrix} \sigma_X^2 & \rho\sigma_X\sigma_Y \\ \rho\sigma_X\sigma_Y & \sigma_Y^2 \end{pmatrix} \right)$$

then

$$y_i | x_i \sim N\left(\beta_0 + \beta_1 x_i, \sigma^2\right)$$

where $\beta_0 = \mu_Y - \beta_1\mu_X,\ \beta_1 = \rho\sigma_Y/\sigma_X,$ and $\sigma^2 = \sigma_Y^2(1-\rho^2)$.

Some Comments

- The sample (multiple) correlation coefficient in a regression setting is defined as the correlation between the observed values Y and the fitted values $\hat{Y}$ from the regression model: R = cor($Y, \hat{Y}$)

- R^2 is called the coefficient of determination: it is equal to the proportion of the variability in Y explained by the regression model.

- The notion "the higher R^2, the better the model" is simply wrong.

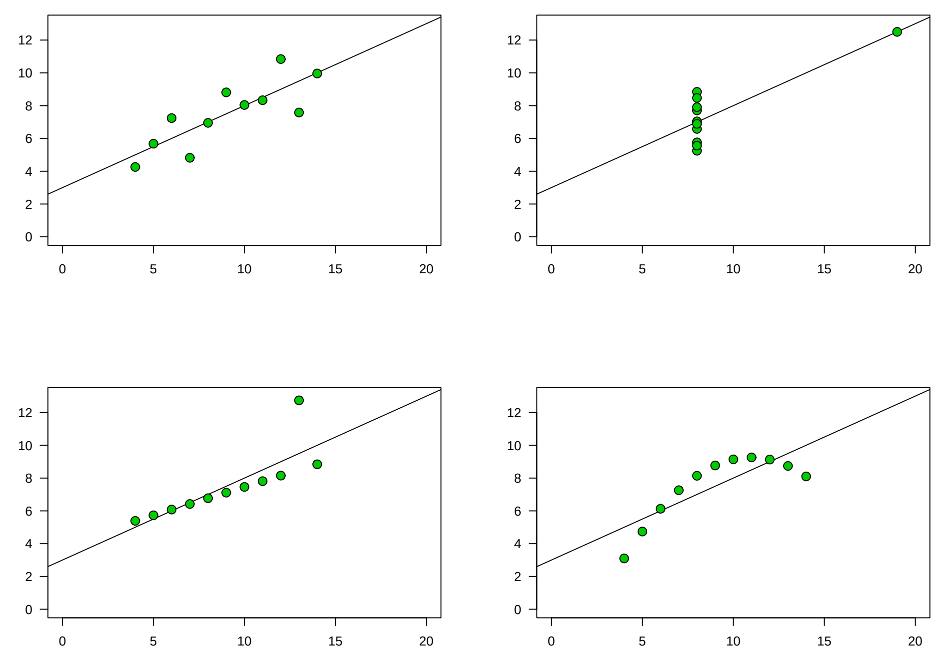
- Assuming we have an intercept in the (linear regression) model, the more predictors we include in the model, the higher R^2.

- However, there is a test for "significant" reductions in R^2 (there is a one-to-one correspondence to the usual t and F statistics).

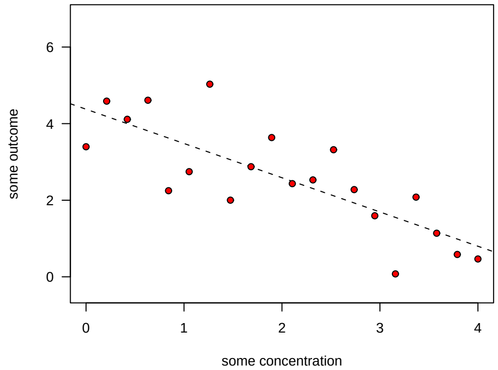
- R^2 tells us nothing about model violations.

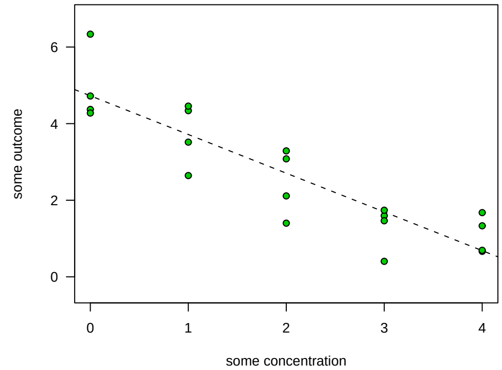
Model Fit

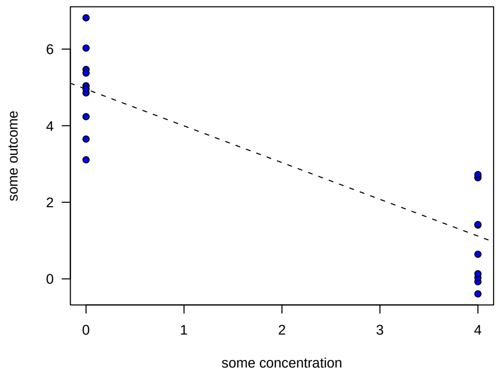
$\hat{\beta}_0 = 3.0$, $\hat{\beta}_1 = 0.5$, p-value (slope) = 0.002, $R^2 = 0.67$, RSE = 1.24 (9 df).



Experimental Design







Standard error ratios
for the slope:

1.65 : 1.41 : 1.00

In Conclusion: A Few Suggestions

- Take Karl Broman's course "Statistics for Laboratory Scientists" (140.615/616).
- For your analysis, use tools that help you understand the data, and try to get an idea what all that statistical output from your program means.
- Avoid "black boxes" as much as possible. Plot the data.
- For more complicated quantitative projects, adopt a biostatistician.
- Keep recruiting people like Ray and Matthew. Cheers!