MUNI
PHARM

Statistical methods

Biophysics

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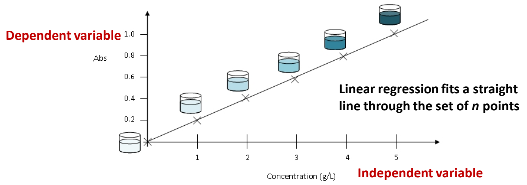
Linear regression

- In experiments we are looking for dependences between two variables (measured and set variable).
- An example can be influence of concentration (independent variable) to absorbance in solution (dependent variable).

- Absorbance is a function of concentration, A= f (c)



Linear regression fits a straight line through the set of *n* points

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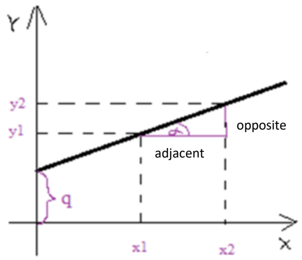
Data dependencies

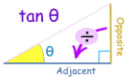
Equation of the line

$$y = k \times x + q$$



q =constant=shift on ***y*** axis (intercept)

k = slope= tg α= $(y_2\text{-}y_1)/(x_2\text{-}x_1)$



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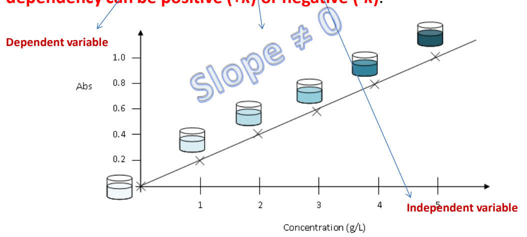
Data dependencies

$$A = k \times c + 0$$

In the case of the absorbance, the line goes through the zero point, it means zero concentration = zero absorbance, therefore **intercept *q***, or shift of the *y* axis is 0. **Slope *k***, describes the rate of change between the independent and dependent variables - **data dependency can be positive (+*k*) or negative (-*k*)**.



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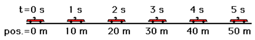
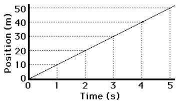
Equation of the line

Sample Problem: Consider a car moving with a constant velocity of 10 m/s for 5 seconds.





What is the meaning of the slope *k*?

***k* = slope= $(y_2\text{-}y_1)/(x_2\text{-}x_1)$**

The slope of the line is 10 meter/1 second = the slope of the line (10 m/s) is equal to the velocity of the car.

The slope express the rate of the examined process (e.g. in chemical kinetics the slope express the rate of the chemical reactions).

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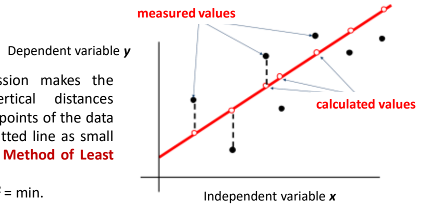
Method of Least Squares

The purpose of regression analysis is to analyze relationships among variables. We are trying to replace

each measured (experimental) value of the dependent variable y_{exp}

by value calculated (predicted) y_{pred}



Linear regression makes the sum of vertical distances between the points of the data set and the fitted line as small as possible – **Method of Least Squares**

$\Sigma\ (y_{exp} - y_{pred})^2$ = min.

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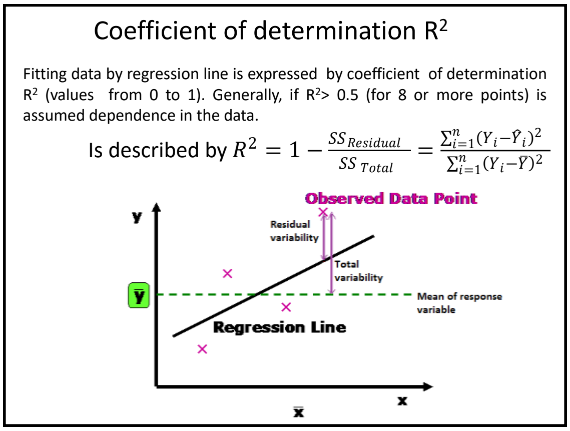

Coefficient of determination R^2

Fitting data by regression line is expressed by coefficient of determination R^2 (values from 0 to 1). Generally, if R^2> 0.5 (for 8 or more points) is assumed dependence in the data.

Is described by $R^2 = 1 - \frac{SS_{Residual}}{SS_{Total}} = \frac{\sum_{i=1}^{n}(Y_i - \hat{Y}_i)^2}{\sum_{i=1}^{n}(Y_i - \bar{Y})^2}$

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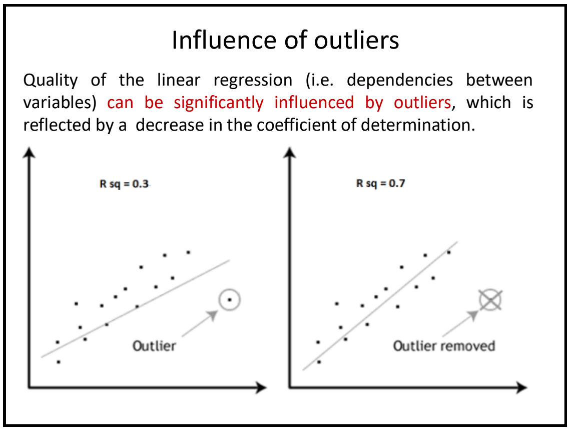

Influence of outliers

Quality of the linear regression (i.e. dependencies between variables) can be significantly influenced by outliers, which is reflected by a decrease in the coefficient of determination.

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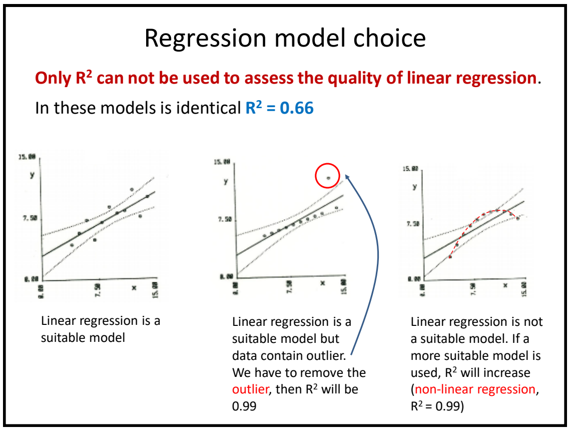

Regression model choice

Only R^2 can not be used to assess the quality of linear regression.

In these models is identical **R^2 = 0.66**

Linear regression is a suitable model

Linear regression is a suitable model but data contain outlier. We have to remove the outlier, then R^2 will be 0.99

Linear regression is not a suitable model. If a more suitable model is used, R^2 will increase (non-linear regression, R^2 = 0.99)

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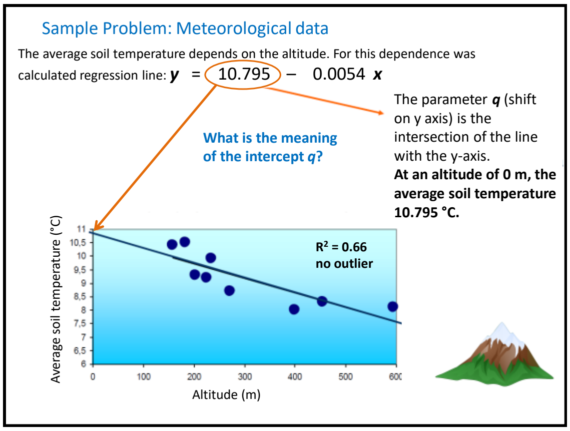

Sample Problem: Meteorological data

The average soil temperature depends on the altitude. For this dependence was calculated regression line: ***y*** = 10.795 – 0.0054 ***x***

What is the meaning of the intercept *q*?

The parameter ***q*** (shift on y axis) is the intersection of the line with the y-axis. **At an altitude of 0 m, the average soil temperature 10.795 °C.**

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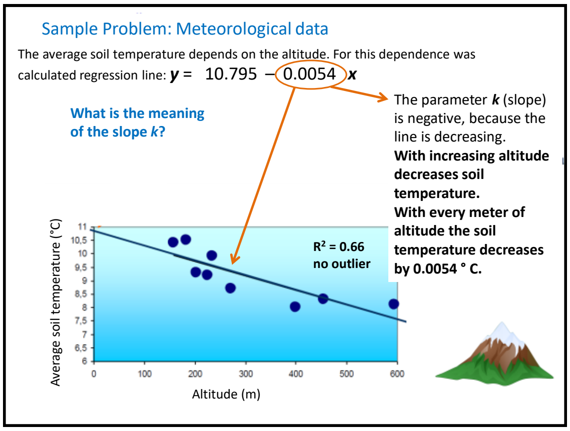

Sample Problem: Meteorological data

The average soil temperature depends on the altitude. For this dependence was calculated regression line: ***y*** = 10.795 – 0.0054 ***x***

What is the meaning of the slope *k*?

The parameter ***k*** (slope) is negative, because the line is decreasing. **With increasing altitude decreases soil temperature. With every meter of altitude the soil temperature decreases by 0.0054 ° C.**

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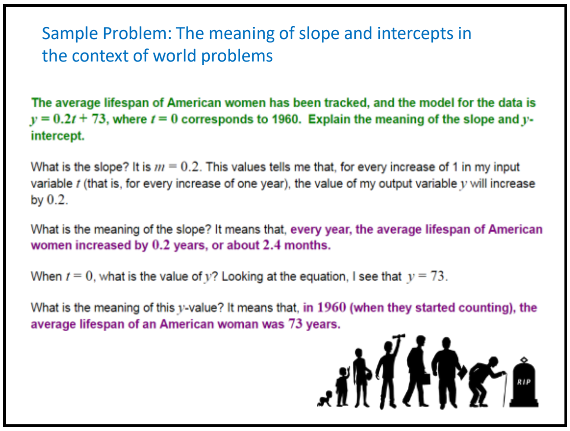

Sample Problem: The meaning of slope and intercepts in the context of world problems

The average lifespan of American women has been tracked, and the model for the data is $y = 0.2t + 73$, where $t = 0$ corresponds to 1960. Explain the meaning of the slope and y-intercept.

What is the slope? It is $m = 0.2$. This values tells me that, for every increase of 1 in my input variable t (that is, for every increase of one year), the value of my output variable y will increase by 0.2.

What is the meaning of the slope? It means that, **every year, the average lifespan of American women increased by 0.2 years, or about 2.4 months.**

When $t = 0$, what is the value of y? Looking at the equation, I see that $y = 73$.

What is the meaning of this y-value? It means that, **in 1960 (when they started counting), the average lifespan of an American woman was 73 years.**

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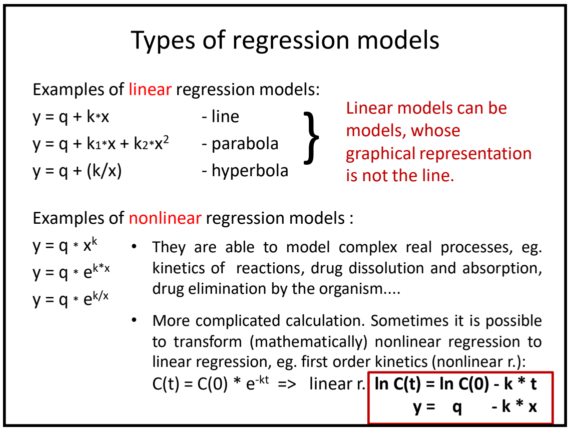

Types of regression models

Examples of linear regression models:

$y = q + k * x$ - line

$y = q + k_1 * x + k_2 * x^2$ - parabola

$y = q + (k/x)$ - hyperbola

Linear models can be models, whose graphical representation is not the line.

Examples of nonlinear regression models :

$y = q * x^k$

$y = q * e^{k*x}$

$y = q * e^{k/x}$

- They are able to model complex real processes, eg. kinetics of reactions, drug dissolution and absorption, drug elimination by the organism....
- More complicated calculation. Sometimes it is possible to transform (mathematically) nonlinear regression to linear regression, eg. first order kinetics (nonlinear r.): $C(t) = C(0) * e^{-kt}$ => linear r. $\boxed{\begin{array}{l} \ln C(t) = \ln C(0) - k * t \\ \quad y = \quad q \quad - k * x \end{array}}$

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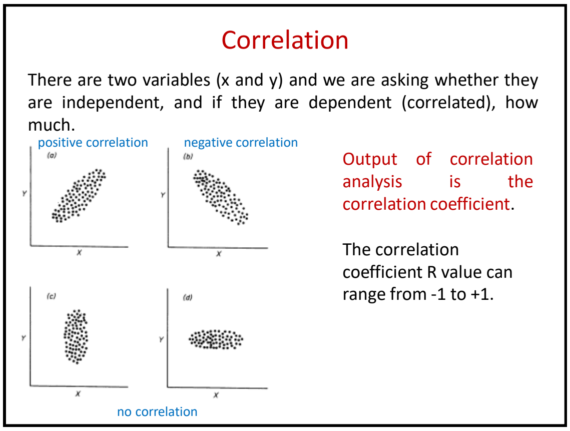

Correlation

There are two variables (x and y) and we are asking whether they are independent, and if they are dependent (correlated), how much.

Output of correlation analysis is the correlation coefficient.

The correlation coefficient R value can range from -1 to +1.

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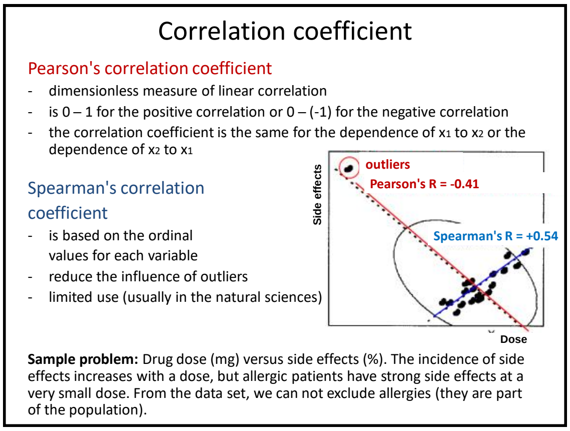

Correlation coefficient

Pearson's correlation coefficient

- dimensionless measure of linear correlation
- is 0 – 1 for the positive correlation or 0 – (-1) for the negative correlation
- the correlation coefficient is the same for the dependence of x_1 to x_2 or the dependence of x_2 to x_1

Spearman's correlation coefficient

- is based on the ordinal values for each variable
- reduce the influence of outliers
- limited use (usually in the natural sciences)

Sample problem: Drug dose (mg) versus side effects (%). The incidence of side effects increases with a dose, but allergic patients have strong side effects at a very small dose. From the data set, we can not exclude allergies (they are part of the population).

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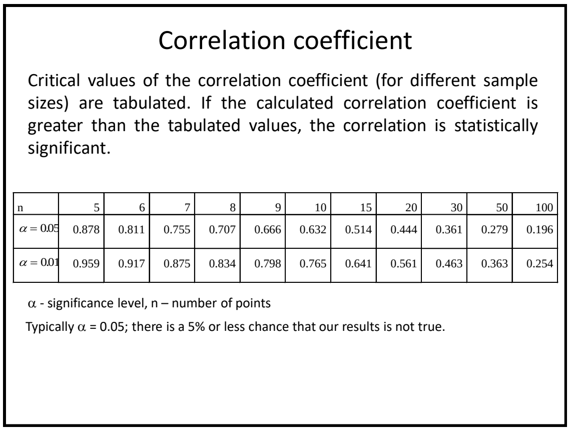

Correlation coefficient

Critical values of the correlation coefficient (for different sample sizes) are tabulated. If the calculated correlation coefficient is greater than the tabulated values, the correlation is statistically significant.

n	5	6	7	8	9	10	15	20	30	50	100
$\alpha = 0.05$	0.878	0.811	0.755	0.707	0.666	0.632	0.514	0.444	0.361	0.279	0.196
$\alpha = 0.01$	0.959	0.917	0.875	0.834	0.798	0.765	0.641	0.561	0.463	0.363	0.254

α - significance level, n – number of points

Typically $\alpha = 0.05$; there is a 5% or less chance that our results is not true.

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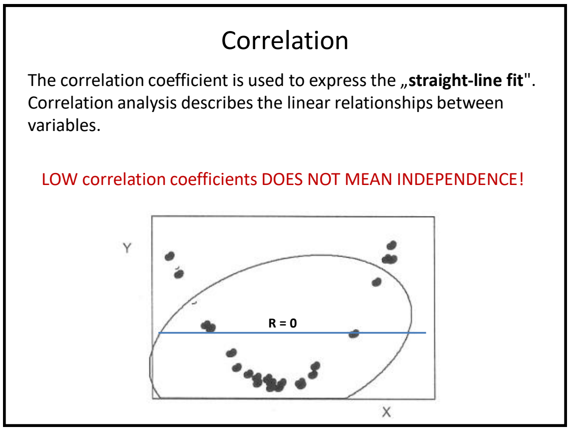

Correlation

The correlation coefficient is used to express the „**straight-line fit**". Correlation analysis describes the linear relationships between variables.

LOW correlation coefficients DOES NOT MEAN INDEPENDENCE!

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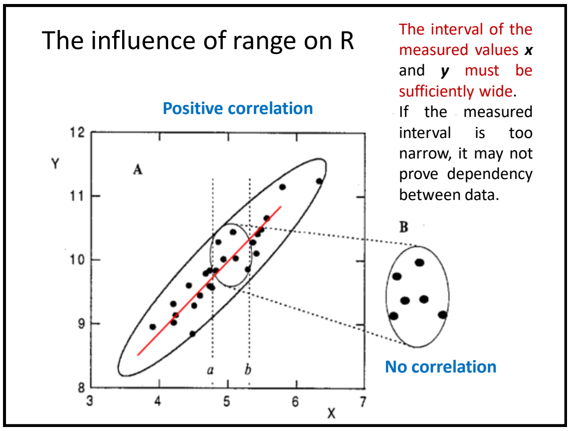

The influence of range on R

The interval of the measured values ***x*** and ***y*** must be sufficiently wide. If the measured interval is too narrow, it may not prove dependency between data.

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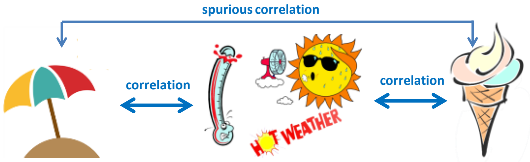
Spurious correlation

Correlation don't expresses cause and effect!!!

Sample problem:
The ice cream sales are mutually correlated with the number of beach umbrellas sales. In fact, the sales of ice cream don't affects the sales of beach umbrellas = spurious correlation.

Spurious correlation occurs when the other unobserved or not analyzed variable/s affects both variables that we study.



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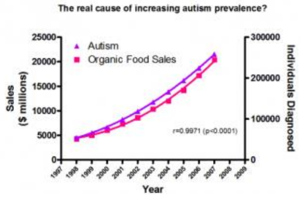
Spurious correlation

Correlation don't expresses cause and effect!!!

Spurious correlation occurs when the other unobserved or not analyzed variable/s affects both variables that we study.

Sample Problem: Factors related to the increasing incidence of autism



Higher incidence of autism: better diagnosis, broader criteria for classification as autistic, changes in diagnosis due to better diagnosis (some autistic people were previously included in the group of mentally retarded).

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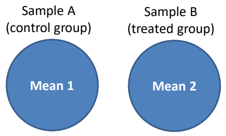
Two-sample t-tests

Independent (unpaired) t-test

The unpaired t-test is useful for comparing the means of two independent samples.

Sample problem: We are evaluating the effect of a medical treatment, and we enroll 100 subjects into our study, then randomly assign 50 subjects to the treatment group and 50 subjects to the control group.



Is the mean of the control group significantly different from the the mean of treated group?

Note – it is need two independent samples and one dependent variable.

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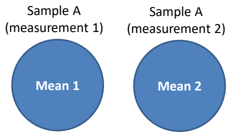
Two-sample t-tests

Paired t-test

The paired t-test is useful for comparing the means when both samples consist of the same test subjects.

Sample problem: Subjects are tested prior to a treatment (e.g. high blood pressure treatment) and the same subjects are tested after treatment again.



Is the mean of measurment 1 significantly different from the mean of measurement 2?

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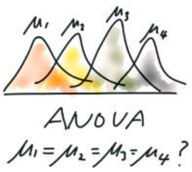
ANOVA

Analysis of variance (ANOVA) provides a statistical test of whether or not the means of several groups are equal, and therefore generalizes the t-test to more than two groups.

ANOVAs are useful for comparing (testing) three or more means (groups or variables) for statistical significance.

- One-way ANOVA: we analyze the effect of **one factor** (e.g. dose) on the examined dependent variable (e.g. blood pressure).
- Two-way ANOVA: we analyze the effect of **multiple factors** (e.g. different drug a their dose) on the examined dependent variable (e.g. blood pressure).



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