

# Kurs Bio144:

# Datenanalyse in der Biologie

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Lecture 3: Simple linear regression  
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# Overview

- Introduction of the linear regression model
- Parameter estimation
- Simple model checking
- Goodness of the model: Correlation and  $R^2$
- Tests and confidence intervals
- Confidence and prediction ranges

# Course material covered today

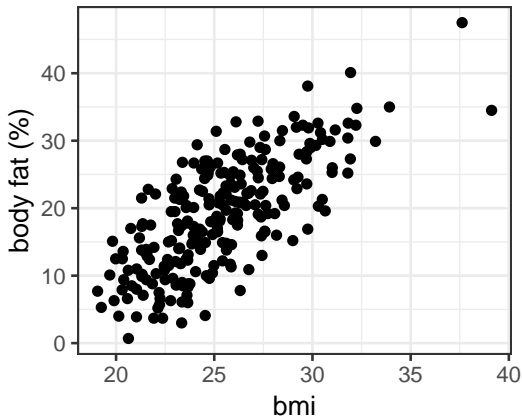
The lecture material of today is based on the following literature:

- Chapter 2 of *Lineare Regression*, p.7-20 (Stahel script),
- Alternatively, chapters 13.1 - 13.4 in the Stahel book "Statistische Datenanalyse".

## The body fat example

Remember: Aim is to find prognostic factors for body fat, without actually measuring it.

Even simpler question: How good is BMI as a predictor for body fat?



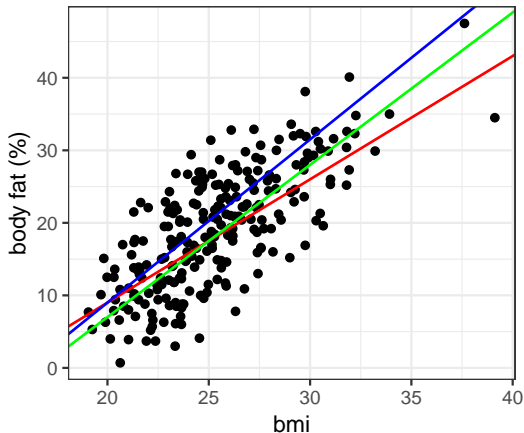
## Linear relationship

- The most simple relationship between an *explanatory variable* ( $X$ ) and a *target/outcome variable* ( $Y$ ) is a linear relationship. All points  $(x_i, y_i)$ ,  $i = 1, \dots, n$ , on a straight line follow the equation

$$y_i = \alpha + \beta x_i .$$

- Here,  $\alpha$  is the **axis intercept** and  $\beta$  the **slope** of the line.  $\beta$  is also denoted as the regression coefficient of  $X$ .
- If  $\alpha = 0$  the line goes through the origin  $(x, y) = (0, 0)$ .
- **Interpretation** of linear dependency: proportional increase in  $y$  with increase (decrease) in  $x$ .

But which is the “true” or “best” line?



**Task:** Estimate the regression parameters  $\alpha$  and  $\beta$  (by “eye”) and write them down.

It is obvious that

- the linear relationship does not describe the data perfectly.
- another realization of the data (other 243 males) would lead to a slightly different picture.

⇒ We need a **model** that describes the relationship between BMI and bodyfat.

# The simple linear regression model

In the linear regression model the dependent variable  $Y$  is related to the independent variable  $x$  as

$$Y = \alpha + \beta x + \epsilon, \quad \epsilon \sim N(0, \sigma^2).$$

In this formulation  $Y$  is a random variable  $Y \sim N(\alpha + \beta x, \sigma^2)$  where

$$Y = \underbrace{\text{expected value}}_{E(Y)=\alpha+\beta x} + \underbrace{\text{random error}}_{\epsilon}.$$

Note:

- The model for  $Y$  given  $x$  has **three parameters**:  $\alpha$ ,  $\beta$  and  $\sigma^2$ .
- $x$  is the **independent** / **explanatory** / **regressor** variable.
- $Y$  is the **dependent** / **outcome** / **response** variable.



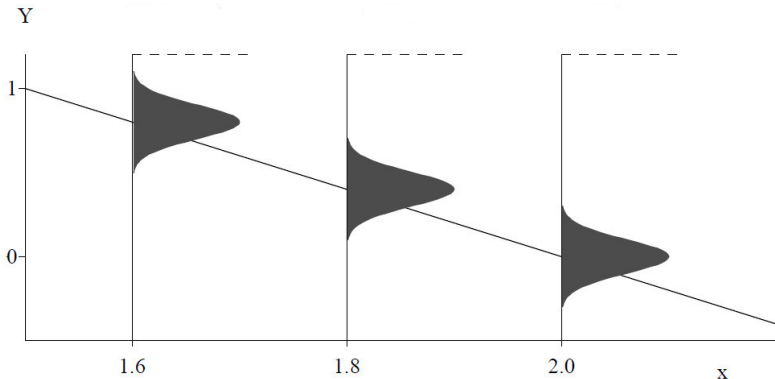
## Note:

- The linear model propagates the most simple relationship between two variables. When using it, please always think if such a relationship is meaningful/reasonable/plausible.
- Always look at the data **before** you start with model fitting.

## Visualization of the regression assumptions

The assumptions about the linear regression model lie in the error term

$$\epsilon \sim N(0, \sigma^2) .$$



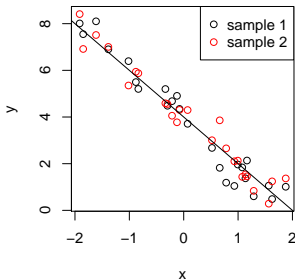
Note: The true regression line goes through  $E(Y)$ .

# Insight from data simulation

(Simulation are *always* a great way to understand statistics!!)

Generate an independent (explanatory) variable **x** and **two** samples of a dependent variable **y** assuming that

$$y_i = 4 - 2x_i + \epsilon_i, \quad \epsilon_i \sim N(0, 0.5^2).$$



→ Random variation is always present. This leads us to the next question.

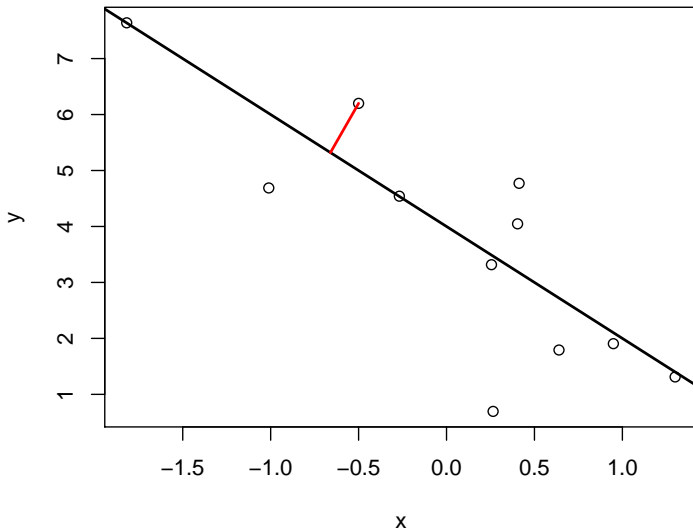
# Parameter estimation

In a regression analysis, the task is to estimate the **regression coefficients**  $\alpha$ ,  $\beta$  and the **residual variance**  $\sigma^2$  for a given set of  $(x, y)$  data.

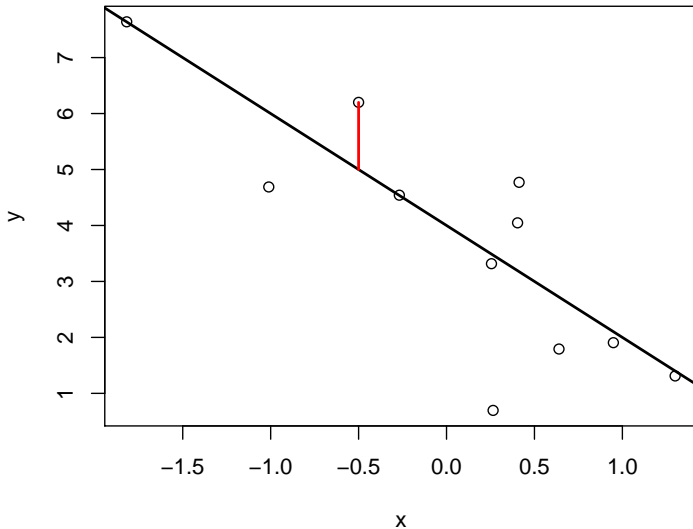
- **Problem:** For more than two points  $(x_i, y_i)$ ,  $i = 1, \dots, n$ , there is generally no perfectly fitting line.
- **Aim:** We want to find the parameters  $(a, b)$  of the best fitting line  $Y = a + bx$ .
- **Idea:** Minimize the deviations between the data points  $(x_i, y_i)$  and the regression line.

But how?

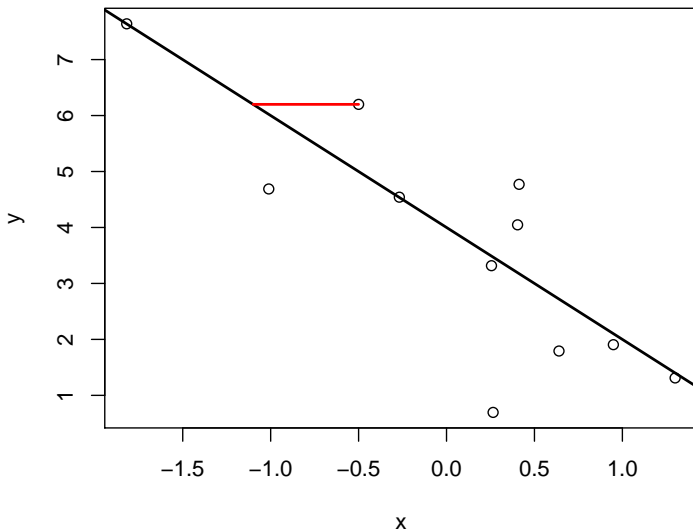
## Should we minimize these distances...



... or these?



Or maybe even these?



# Least squares

For multiple reasons (theoretical aspects and mathematical convenience), the parameters are estimated using the **least squares** approach. In this, yet something else is minimized:

The parameters  $\alpha$  and  $\beta$  are estimated such that the sum of **squared vertical distances** (sum of squared residuals)

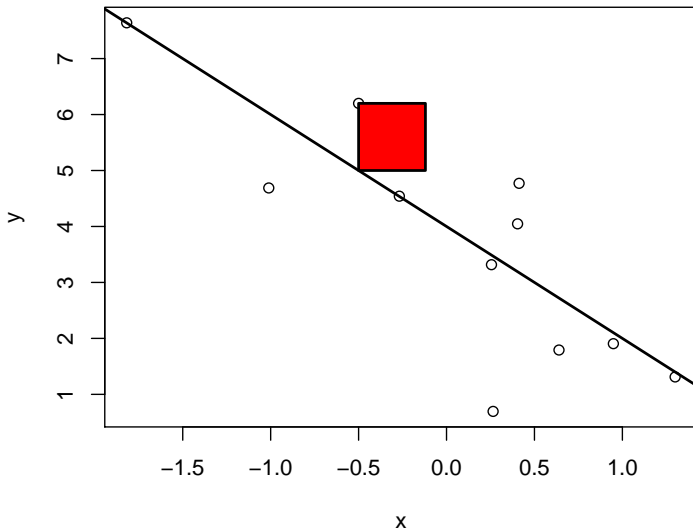
$$SSE = \sum_{i=1}^n e_i^2, \quad \text{where} \quad e_i = y_i - \underbrace{(a + bx_i)}_{=\hat{y}_i}$$

is being minimized.

**Note:**  $\hat{y}_i = a + bx_i$  are the **predicted values**.



So we minimize the sum of these areas!



## Least squares estimates

For a given sample  $(x_i, y_i), i = 1, \dots, n$ , with mean values  $\bar{x}$  and  $\bar{y}$ , the least squares estimates  $\hat{\alpha}$  and  $\hat{\beta}$  are computed as

$$\hat{\beta} = \frac{\sum_{i=1}^n (y_i - \bar{y})(x_i - \bar{x})}{\sum_{i=1}^n (x_i - \bar{x})^2} = \frac{\text{cov}(x, y)}{\text{var}(x)},$$

$$\hat{\alpha} = \bar{y} - \hat{\beta}\bar{x}.$$

Moreover,

$$\hat{\sigma}^2 = \frac{1}{n-2} \sum_{i=1}^n e_i^2 \quad \text{with residuals } e_i = y_i - (\hat{\alpha} + \hat{\beta}x_i)$$

is an unbiased estimate of the residual variance  $\sigma^2$ .

(The derivation of the parameters can be looked up in the Stahel script 2.A b.

Idea: Minimization through derivating equations and setting them =0.)

## Do-it-yourself “by hand”

Go to the Shiny gallery and try to “estimate” the correct parameters.

You can do this here:

[https://gallery.shinyapps.io/simple\\_regression/](https://gallery.shinyapps.io/simple_regression/)

# Estimation using R

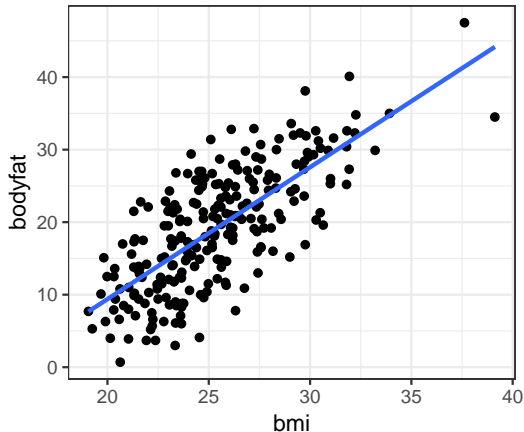
Let's estimate the regression parameters from the bodyfat example

```
r.bodyfat <- lm(bodyfat ~ bmi,d.bodyfat)

summary(r.bodyfat)

##
## Call:
## lm(formula = bodyfat ~ bmi, data = d.bodyfat)
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -13.5485  -3.5583   0.0785   4.0384  12.7330
##
## Coefficients:
##              Estimate Std. Error t value Pr(>|t|)
## (Intercept)  -26.9844     2.7689  -9.746  <2e-16 ***
## bmi           1.8188     0.1083  16.788  <2e-16 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 5.573 on 241 degrees of freedom
## Multiple R-squared:  0.539, Adjusted R-squared:  0.5371
## F-statistic: 281.8 on 1 and 241 DF, p-value: < 2.2e-16
```

The resulting line can be added to the scatterplot:



Interpretation: for an increase in the BMI by one index point, we roughly expect a 1.82% percentage increase in bodyfat.

## Uncertainty in the estimates $\hat{\alpha}$ and $\hat{\beta}$

Important:  $\hat{\alpha}$  and  $\hat{\beta}$  are themselves **random variables** and as such contain **uncertainty!**

Let us look again at the regression output, this time only for the coefficients. The second column shows the standard error of the estimate:

```
summary(r.bodyfat)$coef
```

	Estimate	Std. Error	t value	Pr(> t )
## (Intercept)	-26.984368	2.7689004	-9.745518	3.921511e-19
## bmi	1.818778	0.1083411	16.787522	2.063854e-42

→ The logical next question is: what is the distribution of the estimates?

## Distribution of the estimators for $\hat{\alpha}$ and $\hat{\beta}$

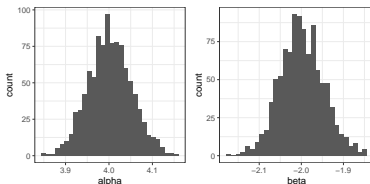
To obtain an idea, we generate data points according to model

$$y_i = 4 - 2x_i + \epsilon_i, \quad \epsilon_i \sim N(0, 0.5^2).$$

In each round, we estimate the parameters and store them:

```
niter <- 1000
pars <- matrix(NA, nrow=niter, ncol=2)
for (ii in 1:niter){
  x <- rnorm(100)
  y <- 4 - 2*x + rnorm(100, 0, sd=0.5)
  pars[ii,] <- lm(y~x)$coef
}
```

Doing it 1 000 times, we obtain the following distributions for  $\hat{\alpha}$  and  $\hat{\beta}$ :



This looks suspiciously normal!

In fact, from theory it is known that

$$\hat{\beta} \sim N(\beta, \sigma^{(\beta)2}) \quad \text{and} \quad \hat{\alpha} \sim N(\alpha, \sigma^{(\alpha)2})$$

For formulas of the standard deviations  $\sigma^{(\beta)2}$  and  $\sigma^{(\alpha)2}$ , please consult Stahel 2.2.h.

**To remember:**

- $\hat{\alpha}$  and  $\hat{\beta}$  are **unbiased estimators** of  $\alpha$  and  $\beta$ .
- the parameters estimates  $\hat{\alpha}$  and  $\hat{\beta}$  are **normally distributed**.
- the formulas for the variances depend on the residual variance  $\sigma^2$ , the sample size  $n$  and the variability of  $X$  ( $SSQ^{(X)(*)}$ ).

$$(*) \quad SSQ^{(X)} = \sum_{i=1}^n (x_i - \bar{x})^2$$



## Are the modelling assumptions met?

In practice, it is advisable to check if all our **modelling assumptions are met**.

→ Otherwise we might draw invalid conclusions from the results.

Remember: Our assumption is that  $\epsilon_i \sim N(0, \sigma^2)$ . This implies

- a) The expected value of  $\epsilon_i$  is 0:  $E(\epsilon_i) = 0$ .
- b) All  $\epsilon_i$  have the same variance:  $\text{Var}(\epsilon_i) = \sigma^2$ .
- c) All  $\epsilon_i$  are normally distributed.

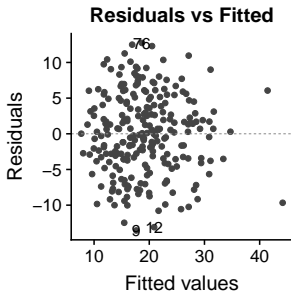
In addition, it is assumed that

- d)  $\epsilon_1, \epsilon_2, \dots, \epsilon_n$  are independent.

**Note:** We do not actually observe  $\epsilon_i$ , but only the residuals  $e_i$ . Let us introduce two simple graphical model checking tools for our residuals  $e_i$ .

## Model checking tool I: Tukey-Anscombe diagram

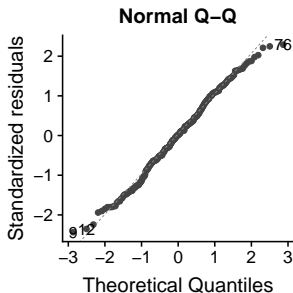
The **Tukey-Anscombe** diagram plots the residuals against the fitted values. For the bodyfat data it looks like this:



This plot is ideal to check if assumptions a) and b) (and partially d)) are met. Here, this seems fine.

## Model checking tool II: Quantile-quantile diagram

Remember the QQ-plot from Section 8.8. We can generate the respective plot for the residuals:



If the residuals are normally distributed, they should approximately lie on a straight line. → Assumption (c) seems ok here.

# How good is the regression model?

This is, per se, a difficult question....

One often considered index is the **coefficient of determination** (**Bestimmtheitsmass**)  $R^2$ . Let us again look at the regression output from the bodyfat example:

```
summary(r.bodyfat)$r.squared
```

```
## [1] 0.5390391
```

Compare this to the squared correlation between the two variables:

```
cor(d.bodyfat$bodyfat,d.bodyfat$bmi)^2
```

```
## [1] 0.5390391
```

→ In simple linear regression,  $R^2$  is the squared correlation between the independent and the dependent variable.

- $R^2$  indicates the proportion of variability of the response variable  $y$  that is **explained by the ensemble of all covariates**.
- Its value lies between 0 and 1.

The **larger**  $R^2$

⇒ the **more** variability of  $y$  is captured (“explained”) by the covariate

⇒ the **“better”** is the model.

(However, we will qualify this statement later in the course...)

# Testing and Confidence Intervals

After the regression parameters and their uncertainties have been estimated, there are typically two fundamental questions:

① **"Are the parameters compatible with some specific value?"**

Typically, the question is whether the slope  $\beta$  might be 0 or not, that is: "Is there an effect of the covariate  $x$  or not?"

⇒ This leads to a **statistical test**.

② **"Which values of the parameters are compatible with the data?"**

⇒ This leads us to determine **confidence intervals**.

Let's first go back to the output from the bodyfat example:

```
summary(r.bodyfat)$coef
```

##	Estimate	Std. Error	t value	Pr(> t )
## (Intercept)	-26.984368	2.7689004	-9.745518	3.921511e-19
## bmi	1.818778	0.1083411	16.787522	2.063854e-42

Besides the estimate and the standard error (which we discussed before), there is a **t value** and a probability **Pr(>|t|)** that we need to understand.

How do these things help us to answer the two questions above?

## Testing the effect of a covariate

Remember: in a statistical test you first need to specify the *null hypothesis*. Here, typically, the null hypothesis is

$$H_0 : \beta = \beta_0 = 0 .$$

In words:  $H_0$  = “no effect”

(Included in  $H_0$  is the assumption that the data follow the simple linear regression model!)

Here, the *alternative hypothesis* is given by

$$H_A : \beta \neq 0$$



Remember: To carry out a statistical test, we need a *test statistic*.

What is a test statistic?

→ It is some type of **summary statistic** that follows a known distribution under  $H_0$ . For our purpose, we use the so-called  **$T$ -statistic**

$$T = \frac{\hat{\beta} - \beta_0}{se(\hat{\beta})} . \quad (1)$$

Again: typically,  $\beta_0 = 0$ , so the formula simplifies to.... (please think:-))

Under  $H_0$ ,  $T$  has a  $t$ -distribution with  $n - 2$  degrees of freedom ( $n$  = number of data points).

(You should try to recall the  $t$ -distribution. Check Mat183, keyword:  $t$ -test.)

So let's again go back to the bodyfat regression output:

```
summary(r.bodyfat)$coef
```

##	Estimate	Std. Error	t value	Pr(> t )
## (Intercept)	-26.984368	2.7689004	-9.745518	3.921511e-19
## bmi	1.818778	0.1083411	16.787522	2.063854e-42

Task:

→ Please use equation (1) to find out how the first three columns (Estimate, Std. Error and t value) are related! Check your ideas by doing some calculations...

Note: The last column contains the **p-value** of the test  $\beta = 0$ .

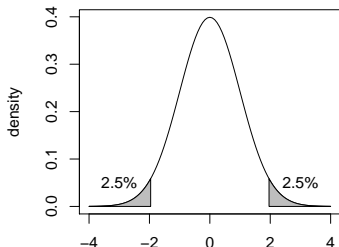
## Recap: Formal definition of the $p$ -value

The **formal definition of  $p$ -value** is the probability to observe a data summary (e.g., an average) that is at least as extreme as the one observed, given that the Null Hypothesis is correct.

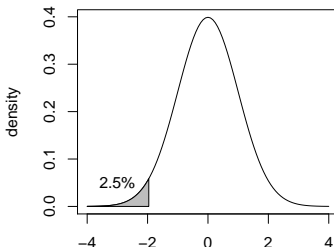
Example (normal distribution): Assume the observed test-statistic leads to a  $z$ -value  $= -1.96$

$$\Rightarrow \Pr(|z| \geq 1.96) = 0.05 \text{ and } \Pr(z \leq -1.96) = 0.025 .$$

**Two-sided p-value (0.05)**



**One-sided p-value (0.025)**



The regression output on slide 34 indicates that the  $p$ -value for BMI is very small ( $p < 0.0001$ ).

Conclusion: there is **very strong evidence** that the BMI is associated with bodyfat, because  $p$  is extremely small (thus it is very unlikely that such a slope  $\hat{\beta}$  would be seen if there was no effect of BMI on body fat).

This basically answers question 1 from slide 30.

## A cautionary note on the use of $p$ -values

Maybe you have seen that in statistical testing, often the criterion  $p \leq 0.05$  is used to test whether  $H_0$  should be rejected. This is often done in a black-or-white manner.

However, we will put a lot of attention to a more reasonable and cautionary interpretation of  $p$ -values in this course!

# Confidence intervals of regression parameters

Question 2 from slide 30:

“Which values of the parameters are compatible with the data?”

To answer this question, we can determine the confidence intervals of the regression parameters.

**Facts we know about  $\hat{\beta}$ :**

- $\hat{\beta}$  is estimated with a standard error of  $\sigma^{(\beta)}$ .
- The distribution of  $\hat{\beta}$  is normal, namely  $\hat{\beta} \sim N(\beta, \sigma^{(\beta)2})$ .
- However, since we need to estimate  $\sigma^{(\beta)2}$  from the data, we have a  $t$ -distribution.

Doing some calculations (similar to those in chapter 8.2.2 of Mat183 script) leads us to the 95% confidence interval

$$[\hat{\beta} - c \cdot \hat{\sigma}^{(\beta)}; \hat{\beta} + c \cdot \hat{\sigma}^{(\beta)}] ,$$

where  $c$  is the 97.5% quantile of the  $t$ -distribution with  $n - 2$  degrees of freedom.

Doing this for the bodfat example “by hand” is not hard. We have 241 degrees of freedom:

```
coefs <- summary(r.bodyfat)$coef
beta <- coefs[2,1]
sdbeta <- coefs[2,2]
beta + c(-1,1) * qt(0.975,241) * sdbeta

## [1] 1.605362 2.032195
```

Even easier: directly ask R to give you the CIs.

```
confint(r.bodyfat,level=c(0.95))

##              2.5 %      97.5 %
## (Intercept) -32.438703 -21.530032
## bmi         1.605362   2.032195
```

In summary,

	Coefficient	95%-confidence interval	p-value
Intercept	-26.98	from -32.44 to -21.53	< 0.0001
bmi	1.82	from 1.61 to 2.03	< 0.0001

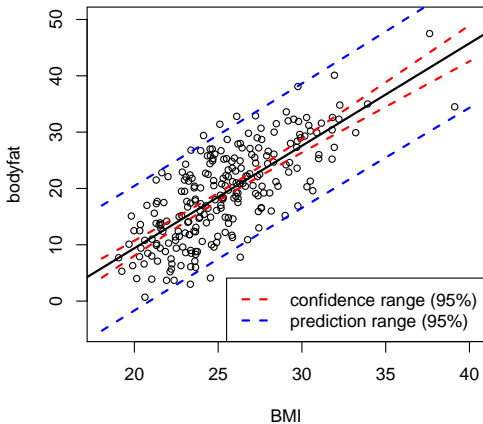
Interpretation: for an increase in the bmi by one index point, roughly 1.82% percentage points more bodyfat are expected, and all true values for  $\beta$  between 1.61 and 2.03 are compatible with the observed data.



# Confidence and Prediction Ranges

- Remember: When another sample from the same population was taken, the regression line would look slightly different.
- There are two questions to be asked:
  - 1 Which other regression lines are compatible with the observed data?  
⇒ This leads to the **confidence range**.
  - 2 Where do future observations with a given  $x$  coordinate lie?  
⇒ This leads to the **prediction range**.

## Bodyfat example



Note: The prediction range is much broader than the confidence range.

## Calculation of the confidence range

Given a fixed value of  $x$ , say  $x_0$ . The question is:

Where does  $\hat{y}_0 = \hat{\alpha} + \hat{\beta}x_0$  lie with a certain confidence (i.e., 95%)?

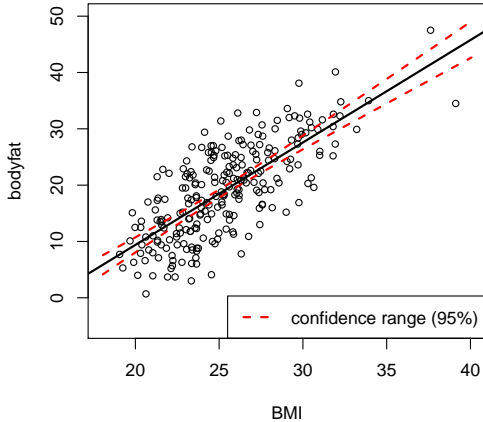
This question is not trivial, because both  $\hat{\alpha}$  and  $\hat{\beta}$  are estimates from the data and contain uncertainty.

The details of the calculation are given in Stahel 2.4b.

Plotting the confidence interval around all  $\hat{y}_0$  values one obtains the **confidence range** or **confidence band for the expected values** of  $y$ .

Note: For the confidence range, only the uncertainty in the estimates  $\hat{\alpha}$  and  $\hat{\beta}$  are decisive.

## Confidence range



## Calculation of the prediction range

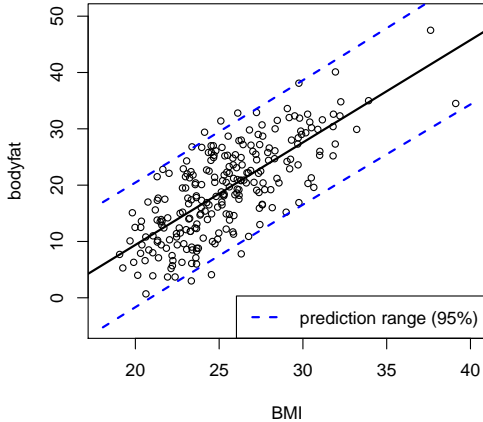
Given a fixed value of  $x$ , say  $x_0$ . The question is:

Where does a **future observation** lie with a certain confidence (i.e., 95%)?

To answer this question, we have to **consider not only the uncertainty in the predicted value**  $\hat{y}_0 = \hat{\alpha} + \hat{\beta}x_0$ , but also the **error in the equation**  $e_i \sim N(0, \sigma_e^2)$ .

This is the reason why the **prediction range is always wider than the confidence range**.

## Prediction range



## Tasks until the next practical (Thu/Fri)

The idea of the course is that as a preparation for the practical part you will do the following:

- Understand what today's lecture was about. You will certainly need to click through it again.
- Go to openedX and do all the "Before class (BC)" tasks.

→ **The same procedure applies to all course weeks.**