Kurs Bio144:

Datenanalyse in der Biologie

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Week 4: Multiple linear regression (finalize) / Residual analysis / Checking modelling assumptions

16./17. March 2017

Overview (todo: check)

- Interactions between covariates
- Multiple vs. many single regressions
- Checking assumptions / Model validation
- What to do when things go wrong?
- Transformation of variables/the response
- Handling of outliers

Course material covered today

- Chapter 3.3 in *Lineare Regression*
- To do

Recap of last week I

to do

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Last week we introduced binary and factor covariates that allowed for group-specific intercepts.

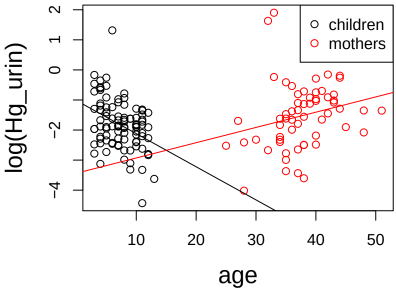
Group-specific slopes / Interactions

It may happen that groups do not only differ in their intercept (β_0), but also in their slopes (β_x).

For simplicity, let us look at a binary covariate ($x_i \in \{0, 1\}$).

Remember the mercury (Hg) example from last week. We now extended the dataset and include mothers *and* children ($\leq$ 11 years).

It is known that Hg concentrations may change over the lifetime of humans. So let us look at `log(Hg`$_{\texttt{urin}}$`)` depending on the participants age:



An important observation is that children and mothers show different dependencies of age!

It is therefore crucial to formulate a model that allows for different intercepts *and* slopes, depending on group membership (mother/child).

The smallest possible model is then given as

$$y_i = \beta_0 + \beta_1 \text{mother}_i + \beta_2 \text{age}_i + \beta_3 \text{age}_i \cdot \text{mother}_i + e_i \ , \tag{1}$$

where $y_i = \log(Hg_{\text{urin}})_i$, and `mother` is a binary "dummy" variable that indicates if the person is a mother (1) or a child (0).

This results in essentially **two** models with group specific intercept and slope:

Mothers ($x_i = 1$): $\hat{y}_i = \beta_0 + \beta_1 + (\beta_2 + \beta_3)\text{age}_i + e_i$

Children ($x_i = 0$): $\hat{y}_i = \beta_0 + \beta_2 \text{age}_i + e_i$

Fitting model (1) in R is done as follows, where `age:mother` denotes the interaction term $(\text{age}_i \cdot \text{mother}_i)$:

```
> r.hg <- lm(log(Hg_urin)~  mother + age + age:mother,d.hg)
> summary(r.hg)$coef
```

```
              Estimate Std. Error   t value     Pr(>|t|)
(Intercept) -1.0188317 0.25250071 -4.034966 8.624100e-05
mother      -2.4176907 0.91198012 -2.651034 8.874694e-03
age         -0.1101447 0.03225589 -3.414715 8.188542e-04
mother:age   0.1609032 0.03965739  4.057333 7.912112e-05
```

Interpretation:

Mothers: $\hat{y}_i = -1.02 + (-2.42) + (-0.11 + 0.16) \cdot \text{age}_i$

Children: $\hat{y}_i = -1.02 + (-0.11) \cdot \text{age}$

- The Hg level drops in young children.
- The Hg level increases in adults (mothers).

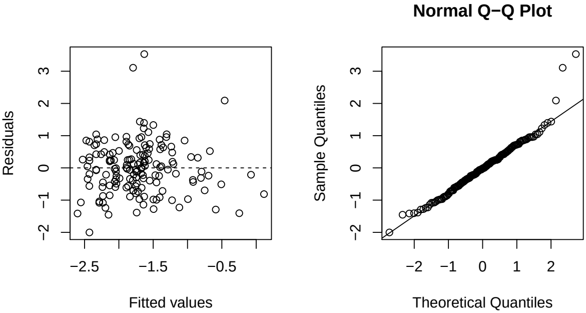
Remember (from last week), however, that the Hg model also included smoking status, amalgam fillings and fish consumption as important predictors. It is very straightforward to just include these predictors in model (1), which leads to the following model

```
> r.hg <- lm(log(Hg_urin)~  mother * age + smoking + amalgam + fish,d.hg)
```

	Coefficent	95%-confidence interval	*p*-value
Intercept	-1.35	from -1.82 to -0.87	< 0.0001
mother	-2.66	from -4.38 to -0.94	0.003
age	-0.098	from -0.16 to -0.04	0.001
smoking	0.60	from 0.06 to 1.15	0.03
amalgam	0.19	from 0.10 to 0.28	< 0.0001
fish	0.072	from 0.04 to 0.10	< 0.0001
mother:age	0.14	from 0.07 to 0.22	0.0001

(Note that `mother*age` in R encodes for `mother` + `age` + `mother:age`.)

Again, for completeness, some model checking:



Multiple vs. many single regressions

Question: I find group-specific intercepts and interactions too complicated. Could I simply fit separate models for each variable?

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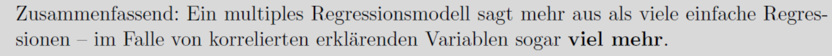
Answer (Stahel 3.3o):



Zusammenfassend: Ein multiples Regressionsmodell sagt mehr aus als viele einfache Regressionen – im Falle von korrelierten erklärenden Variablen sogar **viel mehr.**

Why?

Illustration

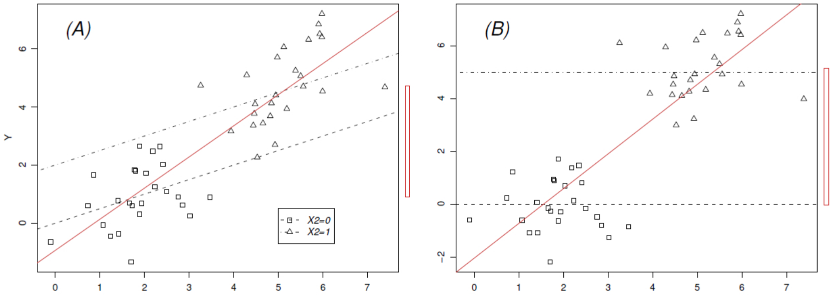
Chapter 3.3c in the Stahel script illustrates the point on four artificial examples. The model is always given as

$$y_i = \beta_0 + \beta_1 x_i^{(1)} + \beta_2 x_i^{(2)} + e_i \ ,$$

where $\mathbf{x}^{(1)}$ is a continuous variable, and $\mathbf{x}^{(2)}$ is a binary grouping variable (thus taking values 0 for group 0 and 1 for group 1).

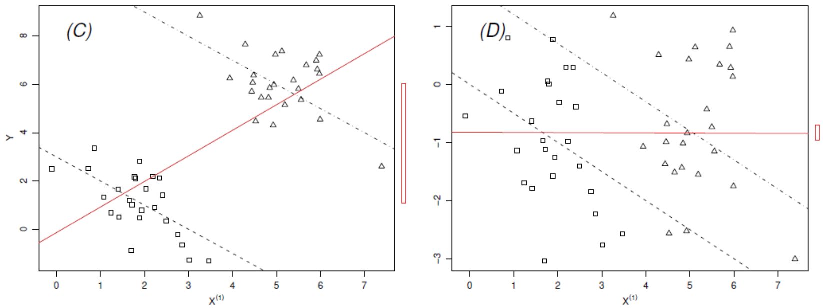
Thus the model is

$$\begin{aligned} \hat{y}_i &= \beta_0 + \beta_1 x_i^{(1)} && \text{if } x_i^{(2)} = 0. \\ \hat{y}_i &= \beta_0 + \beta_2 + \beta_1 x_i^{(1)} && \text{if } x_i^{(2)} = 1. \end{aligned}$$



Example A: Within-group slope is > 0. Fitting $y \sim x$ leads to an overestimated slope when group-variable is not included in the model.

Example B: Within-group slope is 0, but fitting $y \sim x$ leads to a slope estimate > 0, wich is only an artefact of not accounting for the group variable $x^{(2)}$.



Example C: Within-group slope is < 0, but fitting $y \sim x$ leads to an estimated slope of > 0!

Example D: Within-group slope is < 0, but fitting $y \sim x$ leads to a slope estimate of 0.

Another interpretation of multiple regression

In multiple regression, the coefficient β_x of a covariate x can be interpreted as follows:

β_x explains how the response changes with x, while holding all the other variables constant.

This idea is similar in spirit to an experimental design, where the influence of a covariate of interest on the response is investigated in various environments[1]. Clayton and Hills (1993) continue (p.273):

> *To extend our analogy, the data analyst is in a position like that of an experimental scientist who has the capability to plan and carry out many experiments within a single day. Not surprisingly, a cool head is required!*

[1] Clayton, D. and M. Hills (1993). Statistical Models in Epidemiology. Oxford: Oxford University Press.

Checking modelling assumptions

Remember from week 2, that in linear regression the modelling assumption is that the residuals e_i are independently normally distributed around zero, that is, $e_i \sim \mathrm{N}(0, \sigma_e^2)$. This implies four things:

a) The expected value of e_i is 0: $\mathrm{E}(e_i) = 0$.

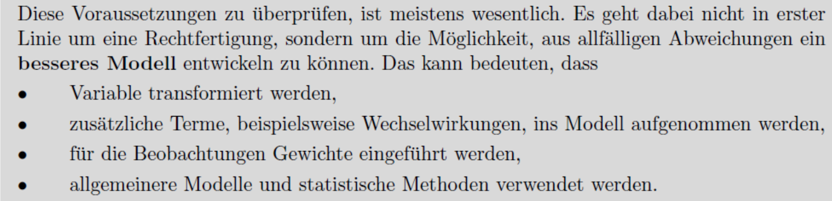
b) All e_i have the same variance: $\mathrm{Var}(e_i) = \sigma_e^2$.

c) The e_i are normally distributed.

d) The e_i are independent of each other.

So far, we have discussed the Tukey-Anscombe plot and the QQ-plot.

Stahel 4.1b:



Diese Voraussetzungen zu überprüfen, ist meistens wesentlich. Es geht dabei nicht in erster Linie um eine Rechtfertigung, sondern um die Möglichkeit, aus allfälligen Abweichungen ein **besseres Modell** entwickeln zu können. Das kann bedeuten, dass

- Variable transformiert werden,
- zusätzliche Terme, beispielsweise Wechselwirkungen, ins Modell aufgenommen werden,
- für die Beobachtungen Gewichte eingeführt werden,
- allgemeinere Modelle und statistische Methoden verwendet werden.

The aim is to find a model that describes the data well. But always keep in mind the following statement from a wise man:

> All models are wrong, but some are useful.
> (Box 1978)

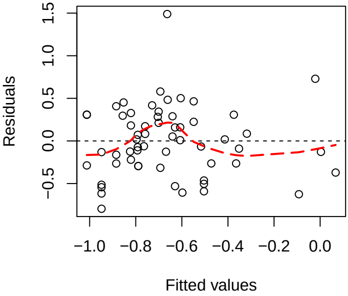
Overview of model-checking tools

Those used in this course are:

- Tukey-Anscombe plot (see weeks 2 and 3)
  $\Rightarrow$ To check assumptions a), b) and d)
- Quantile-quantile (QQ) plot (see weeks 2 and 3)
  $\Rightarrow$ To check assumption c)
- Scale-location plot (Streuungs-Diagramm)
  $\Rightarrow$ To check assumption b)
- Leverage plot (Hebelarm-Diagramm)
  $\Rightarrow$ To find influential observations

Tukey-Anscombe plot

It is useful to enrich the TA-plot by adding a “running mean” or a “smoothed mean”, which can give hints on the trend of the residuals. For the mercury example where $\log(Hg_{\text{urin}})$ is regressed on smoking, amalgam and fish consumption (slides 33-35 or week 3):



The TA plot (again) indicates that there is a small problem in the range of -0.7 to -0.6, namely due to an outlier...

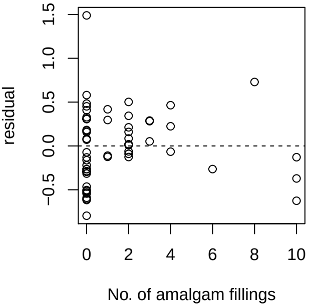
We claimed that the TA plot is also able to check the *independence assumption* d). But how?

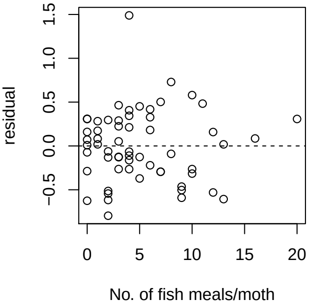
A dependency would be reflected by some kind of trend.

Other ideas to plot residuals to check for a dependency? Please discuss!

The dependency is not necessarily on the fitted values (x-axis of TA plot). Ideas:

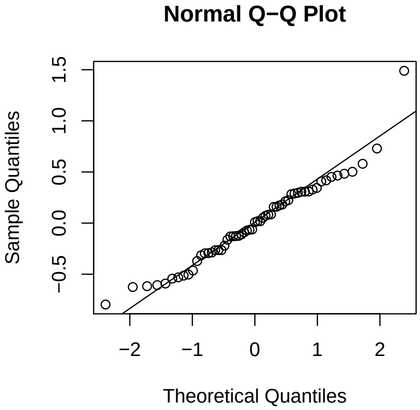
- Plot in dependency of time (if available) or sequence of obervations.
- Plot against the covariates.





QQ-plot

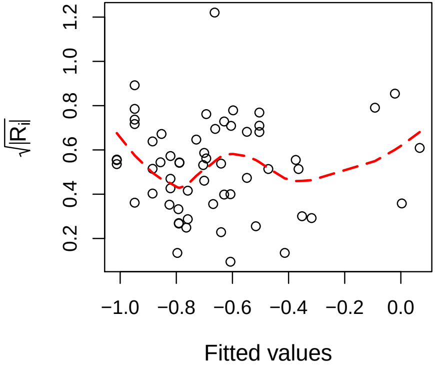
The outlier recorded above is also visible in the (well-known) QQ-plot, which is useful to check normal distribution of residuals (assumption c):



Scale-location plot (Streuungs-Diagramm)

The scale-location plot is particularly suited to check the assumption of equal variances (**homoscedasticiy / Homoskedasdizität**).

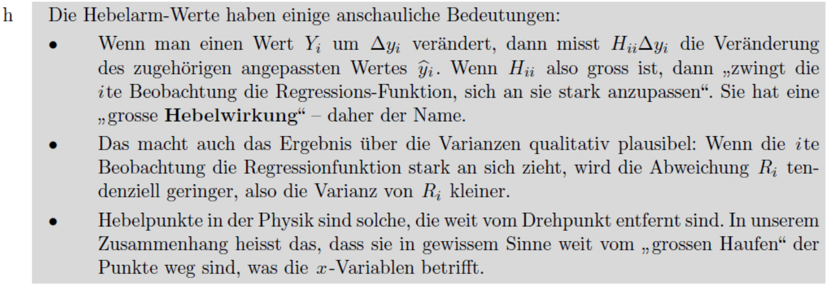
The idea is to plot the squared residuals $\sqrt{|R_i|}$ against the fitted values $\hat{y}_i$:



Leverages

To understand the leverage plot, we need to introduce the idea of the *leverage* (“Hebel”), see Stahel 4.3 h).

The leverage of individual i is defined as $H_{ii} = (1/n) + (x_i - \overline{x})^2 SSQ^{(X)}$, which becomes larger the further away from the mean...

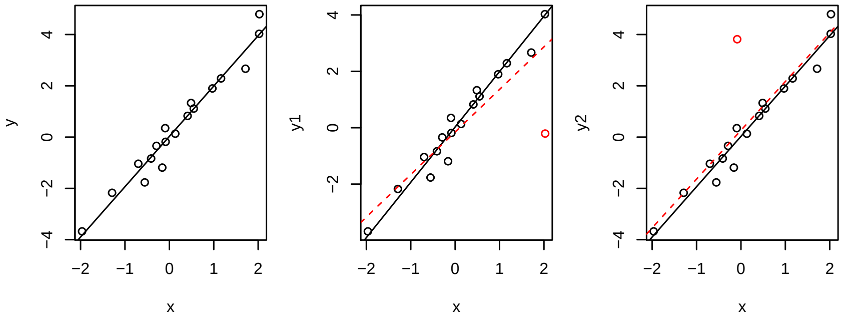


h Die Hebelarm-Werte haben einige anschauliche Bedeutungen:

- Wenn man einen Wert Y_i um Δy_i verändert, dann misst $H_{ii}\Delta y_i$ die Veränderung des zugehörigen angepassten Wertes $\widehat{y}_i$. Wenn H_{ii} also gross ist, dann „zwingt die $i$te Beobachtung die Regressions-Funktion, sich an sie stark anzupassen“. Sie hat eine „grosse **Hebelwirkung**“ – daher der Name.
- Das macht auch das Ergebnis über die Varianzen qualitativ plausibel: Wenn die $i$te Beobachtung die Regressionfunktion stark an sich zieht, wird die Abweichung R_i tendenziell geringer, also die Varianz von R_i kleiner.
- Hebelpunkte in der Physik sind solche, die weit vom Drehpunkt entfernt sind. In unserem Zusammenhang heisst das, dass sie in gewissem Sinne weit vom „grossen Haufen“ der Punkte weg sind, was die x-Variablen betrifft.

Graphical illustration of the leverage effect

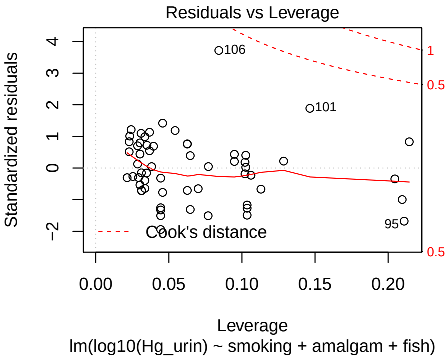
Data points with x_i values far from the mean have a stronger leverage effect than when $x_i \approx \overline{x}$:



The outlier in the middle plot "pulls" the regression line in its direction and biases the slope.

Leverage plot (Hebelarm-Diagramm)

In the leverage plot, (standardized) residuals $\tilde{R}_i$ are plotted against the leverage H_{ii}:



Note: Cook's distance measures how much the regression changes when the ith observation is omitted.

What can go “wrong” during the modelling process?

- …

What to do when things go wrong?

(i) Transform the outcome or the covariables.

(ii) Take care of outliers.

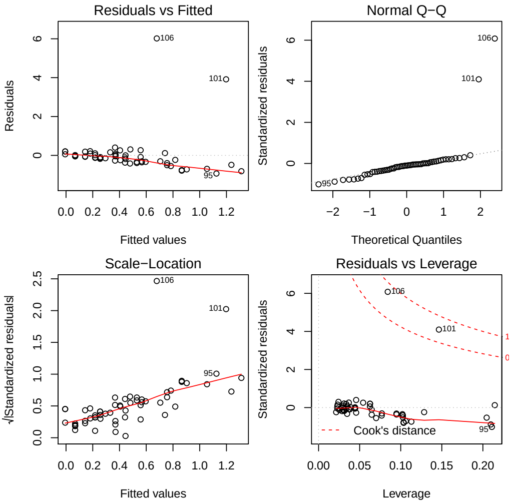
(iii) Use weighted regression (not discussed here; todo: check).

(iv) Improve the model, e.g., by adding additional terms or interactions (see “model selection” in week 7).

(v) Use another model family (generalized or nonlinear regression model).

Transformation of the response?

```
> r2.urin.mother <- lm(Hg_urin ~  smoking  + amalgam + fish,data=d.hg)
```

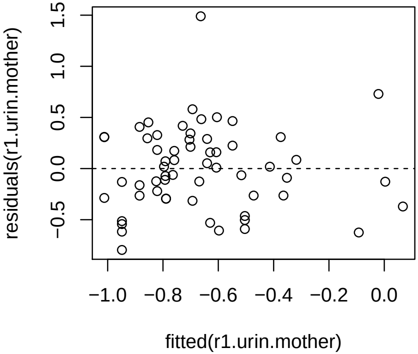


Outliers

Mention that leverage plot is good to find influential observations.

Outliers also graphically visible in TA and QQ plots

```
> plot(fitted(r1.urin.mother),residuals(r1.urin.mother))
> abline(h=0,lty=2)
> qqnorm(fitted(r1.urin.mother))
> qqline(fitted(r1.urin.mother))
```


residuals(r1.urin.mother)
fitted(r1.urin.mother)