Experimental Design and Data Analysis, Lecture 10

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Lecture Overview

1. generalized linear models
   - logistic regression
   - Poisson regression

generalized linear models

Setting

An experiment with:

- an outcome Y that is has a different nature than in ANOVA or linear regression;
- one or more numerical explanatory variables $X_1, \ldots, X_p$.
- one or more factor explanatory variables. ("independent variable").

The purpose is to explain Y by a linear function of X.

EXAMPLE Educational study with outcome passed the exam or not and explanatory variable number of pupils per teacher. Y is binary.

EXAMPLE The number of plant species on a Galapagos Island, with explanatory variables area, highest elevation, distance to nearest island, distance to Santa Cruz island and area of adjancent island. Y is a count.

EXAMPLE Political study with outcome party identification with explanatory variables age, education level and income. Y is multinomial (categorical).

Different models

For each of the three examples a different model applies.

- For binary responses, the logistic regression model assumes:

$$\log\left(\frac{\Pr(Y=1)}{\Pr(Y=0))}\right) = \beta_0 + \beta_1 X_1 + \ldots \beta_p X_p.$$

- For multinomial responses, the multinomial logit model assumes:

$$\log\left(\frac{\Pr(Y=C_i)}{\Pr(Y=C_1))}\right) = \beta_0^i + \beta_1^i X_1 + \ldots \beta_p^i X_p,$$

  where C_1 is the reference class of the categorical responses.

- For count responses, the Poisson regression model assumes:

$$\log \mathrm{E}(Y) = \beta_0 + \beta_1 X_1 + \ldots \beta_p X_p.$$

logistic regression

Setting

An experiment with:

- an outcome Y that is 0 or 1 ("binary dependent variable");
- one or more numerical explanatory variables $X_1, \ldots, X_p$.
- one or more factor explanatory variables $F_1, \ldots, F_m$.

The purpose is to explain Y by a function of X's and F's .

EXAMPLE A subject participates or not in an internet survey presented in 3 formats at 3 different days of the week.

EXAMPLE Educational study with outcome passed the exam or not and explanatory variable number of pupils per teacher.

EXAMPLE Medical study with outcome patient died or not with explanatory variables type of treatment, sex and age.

Design

Logistic regression can be used for factorial experiments, in a regression setting, for ANCOVA, and for experiments with blocks.

- The design is the same as for the corresponding experiment.

Logistic regression is also used in a case-control setting.

- Consider a population consisting of 2 subpopulations of units with outcome 0 and with outcome 1, respectively ("controls" and "cases").
- Independently choose random samples of units from the two subpopulations.
- Measure the explanatory variables for these units.

The case-control design has the advantage that the numbers of cases and controls in the samples can be fixed in advance (and made approx. equal).

Logistic regression model

- Response Y is categorical (0-1) $\rightarrow$ cannot use lin.regr./anova/ancova.
- In this case, we model $\Pr(Y = 1)$ as a function of explanatory variables.
- The logistic regression model assumes that outcome $Y_k \in \{0, 1\}$ satisfies

$$\Pr(Y_k = 1) = \Psi(\boldsymbol{x}_k^T \theta) = \frac{1}{1 + e^{-\boldsymbol{x}_k^T \theta}}, \quad \Pr(Y_k = 0) = 1 - \Pr(Y_k = 1),$$

  $\boldsymbol{x}_k^T \theta = \mu + \alpha_{f(k)} + \ldots + \beta_1 x_{k1} + \ldots$, $f(k) \in \{1, \ldots, I\}$ is the factor level of observation Y_k, $\boldsymbol{x}_k = (1, \ldots, 0, 1, 0, \ldots, x_{k1}, \ldots)^T$ is the k-th vector of predictor values, $\theta = (\mu, \alpha_1, \ldots, \beta_1, \ldots)^T$ is the parameter vector.
- $\Psi(x) = 1/(1 + e^{-x})$, $\Psi : \mathbb{R} \mapsto [0, 1]$, is called logistic function.
- The explanatory variables can be either numerical or categorical, or a mix.
- As in lin.regr./anova/ancova, we can test for factors/variables, their interactions, estimate the parameters, and predict future observations.
- In R: `glm(y~f1+...+x1+...,family=binomial,data=mydata)`

If the categorical response variable has more than 2 values, one extends the usual logistic regression to multinomial logistic regression (implem. in R by special packages).

Example: logistic regression with one factor and one contin. predictor

- For example, for a single factor with I levels and a single numerical explanatory variable the logistic regression model assumes that the outcome Y_{in} of a unit measured at level i of the factor and having explanatory variable X_{in} satisfies

$$\Pr(Y_{in} = 1) = \Psi\big(\mu + \alpha_i + \beta X_{in}\big), \quad i = 1, \ldots, I, \quad n = 1, \ldots, N,$$

- Want to tests the null hypotheses $H_0 : \alpha_1 = \ldots = \alpha_I$, and $H_0 : \beta = 0$, i.e., the factor and/or explanatory variable do not influence the outcome.
- Also estimate the factor effects $\alpha_1, \ldots, \alpha_I$ and the regression parameter β.

The outcome Y is like a coin-toss; the probability $\Pr(Y = 1)$ of "heads" is modelled. The linear predictor $\mu + \alpha_i + \beta X_{in}$ can take any real value. The logistic function maps this into a probability: a number between 0 and 1. A bigger linear predictor gives a probability of heads closer to 1.

Logistic regression — odds

- The odds is $o = \frac{\Pr(Y=1)}{\Pr(Y=0)}$. This means that the probability of "success" $\Pr(Y=1)$ is o times as big as the probability of "failure" $\Pr(Y=0)$.
- One can show that the logistic regression is a linear model for the log odds: $\log o_k = \boldsymbol{x}_k^T \theta$ or $o_k = e^{\boldsymbol{x}_k^T \theta}$.
- For example, for the logistic regression with one factor and one contin. predictor,

$$\log o_{in} = \log \frac{\Pr(Y_{in}=1)}{\Pr(Y_{in}=0)} = \mu + \alpha_i + \beta X_{in}, \quad \text{or} \quad o_{in} = e^{\mu+\alpha_i+\beta X_{in}}.$$

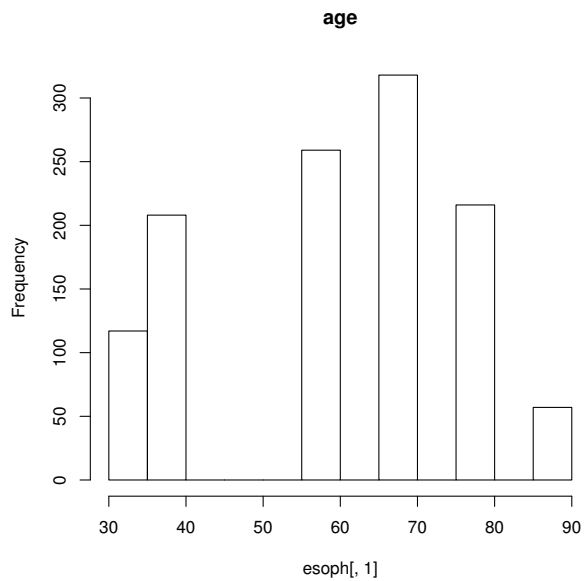
- A change Δ in the linear predictor $\mu + \alpha_i + \beta X_{in}$ multiplies the odds by e^{Δ}. For example,
  - an increase of predictor X by one unit multiplies the odds by e^{β}.
  - a change from level i to level i' multiplies the odds by $e^{\alpha_{i'} - \alpha_i}$.

Analysis in R — data input, graphics

In the data set `esoph.txt`, the column `cancer` indicates whether the individual (1–1175) suffers from cancer of the esophagus (gullet). The first three columns give the age rounded to a multiple of 10, alcohol consumption, and tobacco use.

```
> esoph=read.table("esoph.txt",h=T)
> esoph
     age alc tob cancer
1     30  20   5      0
2     30  20   5      0
3     30  20   5      0
[ a lot of output deleted ]
1173  90 140   5      0
1174  90 140  15      1
1175  90 140  15      0
```

```
> hist(esoph[,1],main="age")
```



The histogram shows the age distribution.

Analysis in R — summary

```
> tot=xtabs(~alc+tob,data=esoph)
> tot
     tob
alc    5  15  25  35
  20 270  94  47  33
  60 213 102  77  38
  100 80  68  22  19
  140 40  30  19  23
```

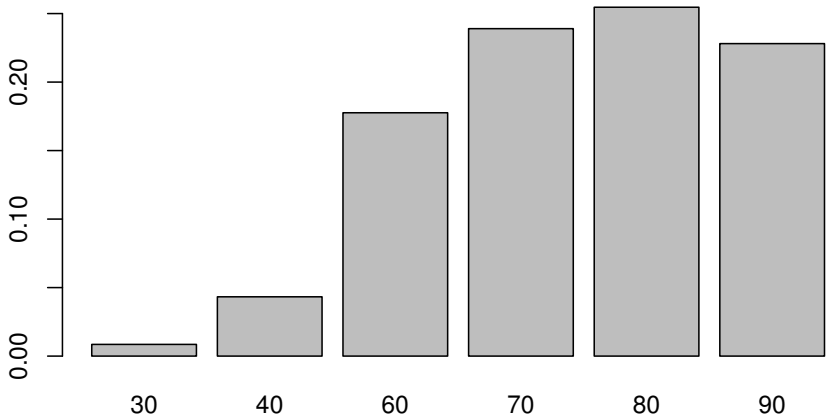
The table shows the total numbers of individuals for each combination of levels of alcohol and tobacco use.

```
> tot.c=xtabs(cancer~alc+tob,data=esoph)
> round (tot.c/tot,2)
     tob
alc     5   15   25   35
  20  0.03 0.11 0.11 0.15
  60  0.16 0.17 0.19 0.24
  100 0.24 0.28 0.27 0.37
  140 0.40 0.40 0.37 0.43
```

The table shows the percentage of individuals with cancer for every combination of levels of alcohol and tobacco use.

Analysis in R — graphics

```
> totage=xtabs(~age,data=esoph)
> barplot(xtabs(cancer~age,data=esoph)/totage)
```



The barplot shows the percentage per age-group. Since it doesn't look very linear, we will add age^2 as an explanatory variable in the next slide.

Analysis in R — estimation and testing

```
> esoph$age2=esoph$age^2
> esophglm=glm(cancer~age+age2+alc+tob,data=esoph,family=binomial)
> summary(esophglm)
             Estimate Std. Error z value Pr(>|z|)
(Intercept) -9.8072283  1.5850673  -6.187 6.12e-10 ***
age          0.1688542  0.0491991   3.432 0.000599 ***
age2        -0.0009608  0.0003776  -2.545 0.010934 *
alc          0.0162614  0.0021092   7.710 1.26e-14 ***
tob          0.0256080  0.0081412   3.145 0.001658 **
```

The function `glm` ("generalized linear model") is used instead of `lm` to create the glm object in R. The option `family=binomial` overrules the default normal model (which gives `lm`). The 4 explanatory variables are inserted as numerical. The estimated odds is $\hat{o}_k = \frac{\widehat{\Pr(Y_k=1)}}{\widehat{\Pr(Y_k=0)}} \approx \exp\{-9.8 + 0.17\text{age}_k - 0.00096\text{age2}_k + 0.016\text{alc}_k + 0.026\text{tob}_k\}$.
The positive signs of the parameter estimates mean that higher values of these variables give higher probability of cancer. For instance, raising `tobacco` by 1 increases the linear predictor by 0.0256080 and increases the odds of cancer by a factor $e^{0.0256080} = 1.026$. For age the dependence is parabolic: from 25 to 30 years the odds increase by $\exp\{0.17 \cdot (30 - 25) - 0.00096 \cdot (30^2 - 25^2)\} = 1.786932$.

Analysis in R — `glm` instead of `lm`

- Once a `glm` object is created one can access the various components of the results in the same way as for any other linear model R-object, using functions such as `summary`, `anova`, `drop1`, `coef`, `residuals`, etc.
- For example, `mod=glm(y~x1+x2,data,family=binomial)`, and the command `summary(mod)` displays the (MLE) estimates of the model coefficients and individual tests that these coefficients are zero.
- Pay attention to the parametrization (in case of factors) and to the order of the variables in the model formula. Need to specify the test (for logistic model, always "Chisq") in testing commands, e.g, `drop1(mod,test="Chisq")`.
- Instead of anova table, `anova(mod,test="Chisq")` yields the so called deviance tables, which are used to examine the progressive fit of the model as each covariate/factor is added to the model.
- The safest way (and to have the full control of what you test) is to use `anova(mod1,mod2,test="Chisq")` or `drop1(mod,test="Chisq")`.
- Diagnostics for GLM's is not as straightforward as for linear models, and will not be treated in this course. For example, there are at least 5 types of residuals and 2 types of fitted values for GLM's.

Analysis in R — estimation and testing (1)

```
> esoph$age=factor(esoph$age); esoph$alc=factor(esoph$alc)
> esoph$tob=factor(esoph$tob) # note: the variables are factors now
> glm2=glm(cancer~age+alc+tob,data=esoph,family=binomial); summary(glm2)
[ some output deleted ]
            Estimate Std. Error z value Pr(>|z|)
(Intercept)  -5.9108     1.0302  -5.738 9.59e-09 ***
age40         1.6095     1.0675   1.508 0.131631
age60         2.9752     1.0242   2.905 0.003673 **
age70         3.3584     1.0198   3.293 0.000991 ***
age80         3.7270     1.0252   3.635 0.000278 ***
age90         3.6818     1.0644   3.459 0.000542 ***
alc60         1.1216     0.2384   4.704 2.55e-06 ***
alc100        1.4471     0.2628   5.506 3.68e-08 ***
alc140        2.1154     0.2876   7.356 1.90e-13 ***
tob15         0.3407     0.2054   1.659 0.097159 .
tob25         0.3962     0.2456   1.613 0.106708
tob35         0.8677     0.2765   3.138 0.001701 **
```

In the previous model, `tob`, `alc` and age were numeric, here they are categorical, treated as `factor`. The variable age2 is dropped. For example, the estimated odds for the group (age70, `alc20`, `tob35`) is $\hat{o} \approx \exp\{-5.91 + 3.36 + 0 + 0.87\}$.

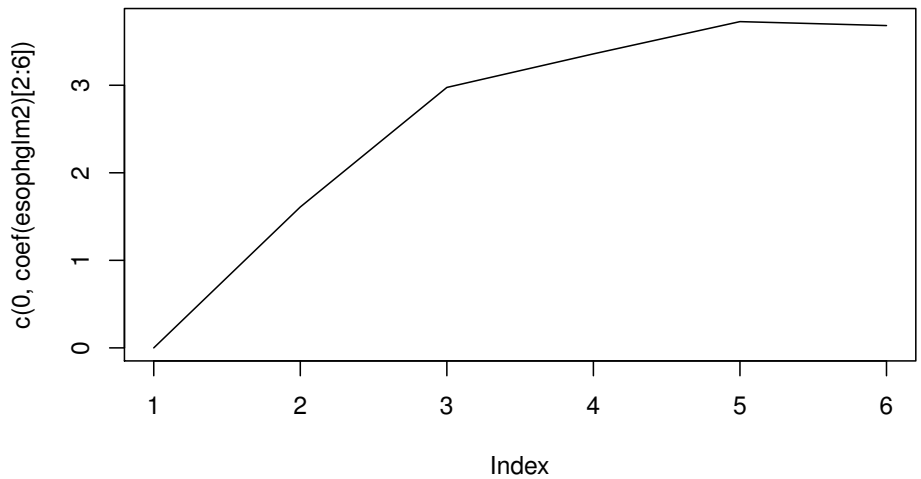
Analysis in R — estimation and testing (2)

Recall that $\widehat{\Pr(Y_k = 1)} = \Psi(\boldsymbol{x}_k^T \hat{\theta})$. For example, the estimate of the probability of cancer for the group (age70, alc20, tob35) is computed as $\Psi(\text{Intercept} + \text{age70} + \text{alc20} + \text{tob35}) = 0.1564698$.

In R, all $\widehat{\Pr(Y_k = 1)}$ are obtained by `fitted(glm2)`. To predict the probability of cancer for `newdata`, use `predict(glm2,newdata,type="response")`, for example, `newdata=data.frame(age="70",alc="20",tob="35")`.

Make a graph of the coefficients for the different age categories:

```
> plot(c(0,coef(glm2)[2:6]),type="l")
```



By inserting the variables as factors each level gets its own parameter, and we can look at the dependence on levels. Disadvantage: (too) many parameters.

Analysis in R — estimation and testing (3)

```
> drop1(glm2,test="Chisq")
Single term deletions
       Df Deviance    AIC    LRT   Pr(Chi)
<none>      898.86 922.86
age     5   976.37 990.37 77.511 2.782e-15 ***
alc     3   964.91 982.91 66.054 2.984e-14 ***
tob     3   909.46 927.46 10.599   0.01411 *
```

As the variables are factors now, the `drop1` command reduces the list of the p-values to one p-value per variable, for testing the null hypothesis that the factor has no effect. All three factors are significant. The `anova` command works too, but gives "sequential" tests, which are hard to interpret (only the last p-value can be well interpreted). Another (and the best) way to get correct p-values, for example, for the factor `alc`: `glm3=glm(cancer~age+tob,data=esoph,family=binomial)`, then `anova(glm3,glm2)` will give the right p-values for the factor `alc`.

Aggregated data format (1)

- Measurements with the same values of all explanatory variables need not be represented by separate lines in the data matrix.
- Instead we can count for every combination of explanatory variables the total numbers of 0's and 1's.
- One line in dataset `esophshort.txt` contains the aggregated data of lines with equal values of the explanatory variables (factors) in the dataset.

```
> esophshort=read.table("esophshort.txt",header=TRUE)
> esophshort$age2=esophshort$age^2
> head(esophshort)
  age alc tob ncases ncontrols
1  30  20   5      0        40
2  30  20  15      0        10
3  30  20  25      0         6
4  30  20  35      0         5
5  30  60   5      0        27
6  30  60  15      0         7
```

Aggregated data format (2)

```
> shortglm=glm(cbind(ncases,ncontrols)~age+age2+alc+tob,
+          data=esophshort,family=binomial)
> summary(shortglm)
[ some output deleted ]
             Estimate Std. Error z value Pr(>|z|)
(Intercept) -9.8072283  1.5850903  -6.187 6.13e-10 ***
age          0.1688542  0.0491997   3.432 0.000599 ***
age2        -0.0009608  0.0003776  -2.545 0.010935 *
alc          0.0162614  0.0021092   7.710 1.26e-14 ***
tob          0.0256080  0.0081413   3.145 0.001658 **
```

The output is identical to that of the earlier analysis with the "long" data, using the explanatory variables as `numeric` variables.

This aggregated format in the form of pair `(success,failure)`, the counts of successes and failures for each combination of levels of the factors (or values of numeric variables), is one of 3 possible ways to specify the responses in `R` for the logistic model. This format is not useful if there is a continuous predictor in the model that is different for different individuals (e.g., different ages for different individuals).

Testing interaction between factor and contin. predictor (1)

Condsider a model with one factor `alc` and one contin. predictor age.

```
> esoph$age=as.numeric(esoph$age)
> glm3=glm(cancer~age+alc,data=esoph,family=binomial)
      Df Deviance     AIC    LRT  Pr(>Chi)
<none>      925.23  935.23
age    1   983.67  991.67 58.440 2.096e-14 ***
alc    3  1012.48 1016.48 87.244 < 2.2e-16 ***
```

Recall the model we are actually studying

$$\Pr(Y_{in} = 1) = \Psi(\mu + \alpha_i + \beta X_{in}) = 1/\left(1 + e^{-(\mu+\alpha_i+\beta X_{in})}\right),$$

both the factor and contin. predictor are in the model (as in ancova).

However, the coefficient(s) β (reflecting the influence of the continuous predictor) may depend on the level of the factor, i.e.,

$$\Pr(Y_{in} = 1) = \Psi(\mu + \alpha_i + \beta_i X_{in}) = 1/\left(1 + e^{-(\mu+\alpha_i+\beta_i X_{in})}\right).$$

In this case we say that the corresponding factor and variable interact.

Testing interaction between factor and contin. predictor (2)

Testing for no interaction between the factor and predictor:

$$H_0 : \beta_1 = \ldots = \beta_I.$$

In R, to test for interaction (in logistic model and ANCOVA) between factor and contin. predictor, simply include the interaction term in the model formula, e.g., y∼f+x+f:x or y∼f*x.

Testing for the interaction between factor alc and predictor age:

```
> glm4=glm(cancer~age*alc,data=esoph,family=binomial)
> anova(glm4,test="Chisq") # only the last p-value is relevant
[  some output deleted ]
         Df Deviance Resid. Df Resid. Dev  Pr(>Chi)
NULL                      1174    1072.13
age       1   59.647      1173    1012.48 1.135e-14 ***
alc       3   87.244      1170     925.23 < 2.2e-16 ***
age:alc   3    4.549      1167     920.68     0.208
```

Only the last p-value is relevant which always concerns interaction for models with interaction. We conclude from it that $H_0 : \beta_1 = \beta_2$ is not rejected, i.e., there is no interaction between factor alc and predictor age.

Testing for interaction between factors and contin. variables in ANCOVA is the same.

From logistic regression to machine learning prediction

- Fitting the observed data $(X_1, Y_1), \ldots, (X_N, Y_N)$ in logistic regression

$$\Pr(Y_k = 1) = \frac{1}{1 + e^{-\boldsymbol{x}_k^T \theta}}, \quad k = 1, \ldots, N,$$

  we obtain (by the maximum likelihood) an estimate $\hat{\theta}$ of the parameter θ.

- For a new predictor vector X_{new}, we can predict its success probability

$$\hat{P}_{new} = \frac{1}{1 + e^{-\boldsymbol{x}_{new}^T \hat{\theta}}}.$$

- Now use $\hat{P}_{new}$ to predict the new label $\hat{Y}_{new}$ as

$$\hat{Y}_{new} = \begin{cases} 1, & \text{if} \quad \hat{P}_{new} \geq p_0 \\ 0, & \text{if} \quad \hat{P}_{new} < p_0 \end{cases} \quad \text{for some threshold} \quad p_0 \in [0, 1].$$

- This yields one of the commonly used prediction methods in machine learning, which you may have had in one of you machine learning courses.

Poisson regression

Setting and design

An experiment with:

- an outcome Y that is a count;
- one or more numerical explanatory variables $X_1, \ldots, X_p$.
- one or more factor explanatory variables. ("independent variable").

The purpose is to explain Y by a function of X.

EXAMPLE The number of plant species on a Galapagos Island, with explanatory variables area, highest elevation, distance to nearest island, distance to Santa Cruz island and area of adjancent island.

EXAMPLE The number of military coups in Sub Saharan Africa countries with explanatory variables number of years country ruled by military oligarchy, number of political parties and population size.

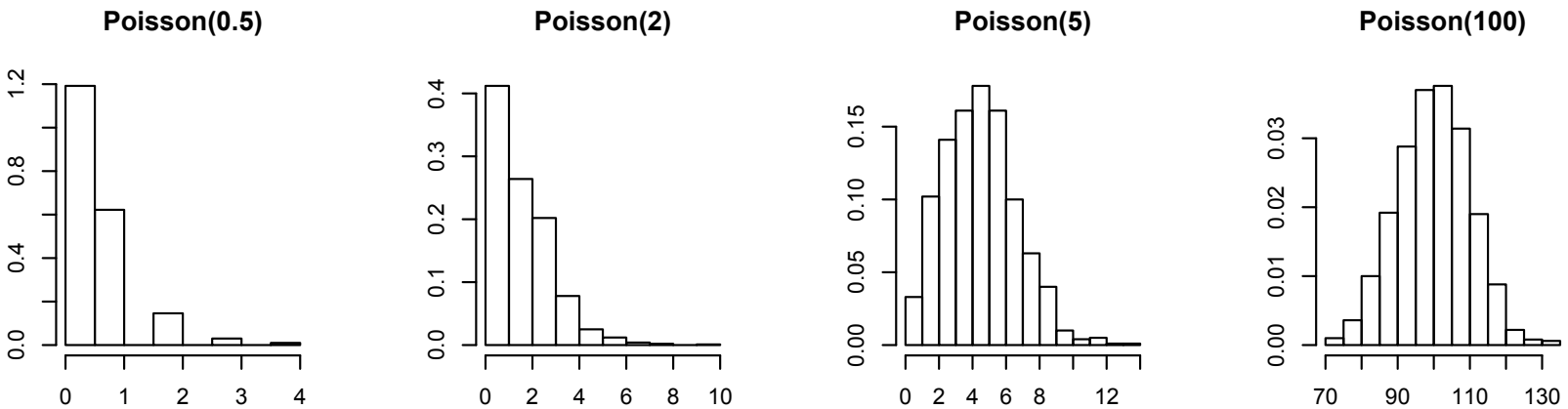
Design. Poisson regression can be used for factorial experiments, in a regression setting, for ANCOVA, and for experiments with blocks. The design is the same as for the corresponding experiment.

The Poisson distribution

- A random variable Y is said to have the Poisson(λ)-distribution, $\lambda > 0$, if

$$\Pr(Y = k) = \frac{\lambda^k}{k!} e^{-\lambda}, \quad k = 0, 1, 2, \ldots.$$

- If $Y \sim \text{Poisson}(\lambda)$, then $\text{E}(Y) = \text{Var}(Y) = \lambda$.
- Hence, the larger the parameter, the larger the values of Y on average and the larger the spread in the values of Y.
- For very large λ, the Poisson(λ)-distribution is approximately equal to a normal distribution with mean $\mu = \lambda$ and variance $\sigma^2 = \lambda$.



Analysis

- In Poisson-regression, the parameter λ is modelled as:

$$\log \lambda = \mu + \alpha_i + \ldots + \beta_1 X_1 + \ldots, \quad \text{or} \quad \lambda = e^{\mu+\alpha_i+\ldots+\beta_1 X_1+\ldots},$$

  on the right: the combination of (numerical and/or categorical) variables.
- For each Y_k the parameter λ_k is modelled differently, since the values of involved factors/predictors will differ for diff. observations: $\lambda_k = e^{\boldsymbol{x}_k^T \theta}$.
- For example, for the Poisson regression with one factor (with I levels) and one continuous predictor X,

$$Y_{in} \sim \text{Poisson}(\lambda_{in}), \quad \lambda_{in} = e^{\mu+\alpha_i+\beta X_{in}}, \quad i = 1, \ldots, I, \; n = 1, \ldots, N.$$

- Hence, the variances are different as well. This means that the response residuals $Y_{in} - \hat{Y}_{in} = Y_{in} - e^{\hat{\mu}+\hat{\alpha}_i+\hat{\beta} X_{in}}$ are not from one fixed distribution, hence a normal QQ-plot of these response residuals is not useful!

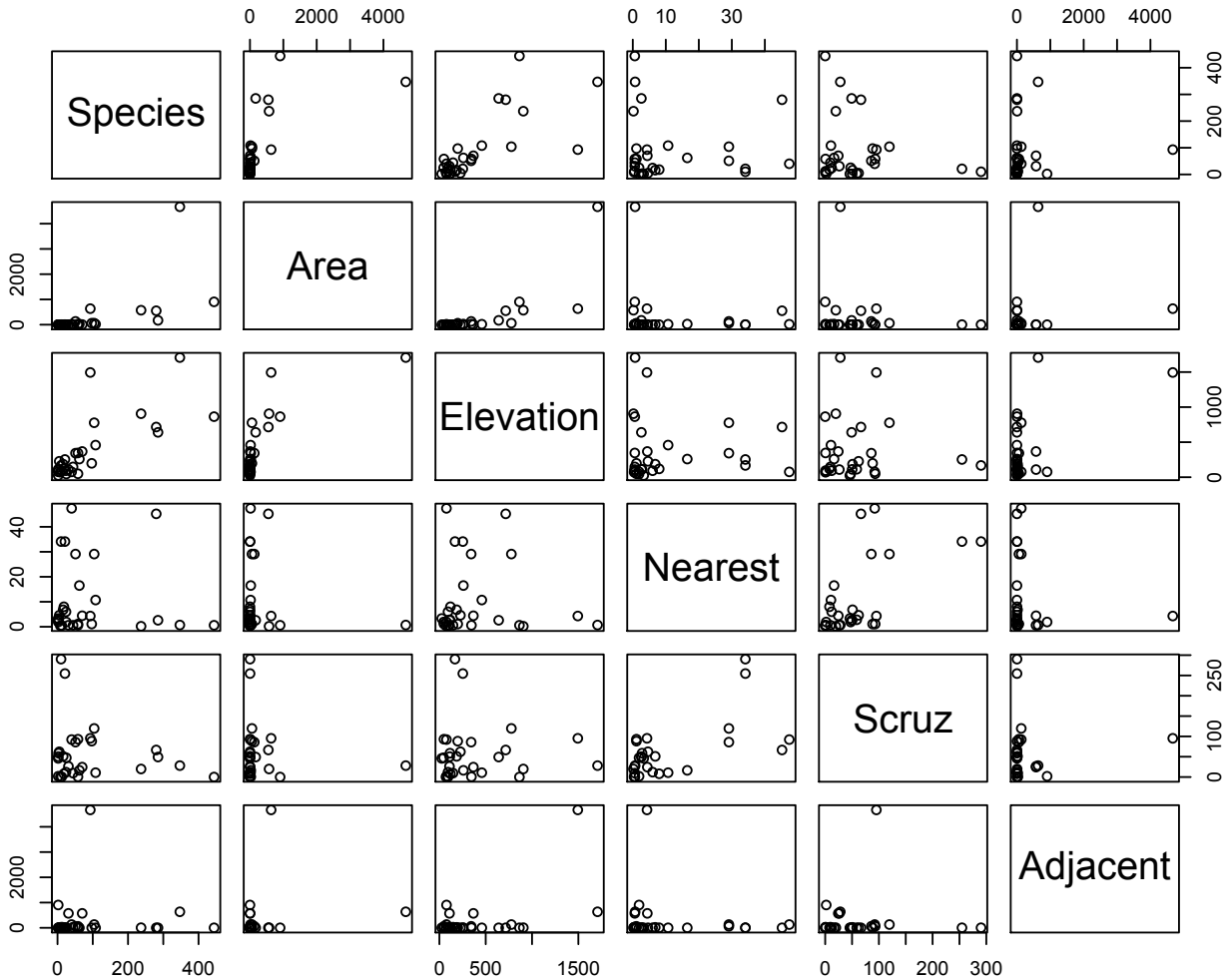
Instead, the deviance residuals are useful for diagnostic plots. Deviance is a measure of the discrepancy between the full model and the model under consideration. Deviance residuals are response residuals scaled by the deviance of that observation.

Analysis in R — data input

The column `Species` of the data set `gala.txt` indicates the number of different plant species on the Galapagos island. The explanatory variables are `Area` (area of island), `Elevation` (highest elevation of island), `Nearest` (distance to nearest island), `Scruz` (distance to Santa Cruz) and `Adjacent` (area of adjacent island). All explanatory variables are numeric.

```
> gala=read.table("gala.txt",header=TRUE); gala
             Species  Area Elevation Nearest Scruz Adjacent
Baltra            58 25.09       346     0.6   0.6     1.84
Bartolome         31  1.24       109     0.6  26.3   572.33
Caldwell           3  0.21       114     2.8  58.7     0.78
Champion          25  0.10        46     1.9  47.4     0.18
Coamano            2  0.05        77     1.9   1.9   903.82
Daphne.Major      18  0.34       119     8.0   8.0     1.84
[ some output deleted ]
```

Analysis in R — graphics



The problem of collinearity amongst explanatory variables is similar in nature as in the linear models case.

Analysis in R — estimation and testing

```
> galaglm=glm(Species~Area+Elevation+Nearest+Scruz+Adjacent,
+ family=poisson,data=gala)
> summary(galaglm)
[some output deleted ]
Coefficients:
             Estimate Std. Error z value Pr(>|z|)
(Intercept)  3.155e+00  5.175e-02  60.963  < 2e-16 ***
Area        -5.799e-04  2.627e-05 -22.074  < 2e-16 ***
Elevation    3.541e-03  8.741e-05  40.507  < 2e-16 ***
Nearest      8.826e-03  1.821e-03   4.846 1.26e-06 ***
Scruz       -5.709e-03  6.256e-04  -9.126  < 2e-16 ***
Adjacent    -6.630e-04  2.933e-05 -22.608  < 2e-16 ***
```

The output of the function `glm` is an object of type`glm`, to which functions as `anova`, `drop1`, `summary`, `coef`, `fitted`, `predict`, `confint`, etc. can be applied, in the same way as for the logistic regression. Remember that the interpretation of the predicted responses is of course different: for example, the predicted responses or the Poisson regression with one factor (with I levels) and one contin. predictor X are $\hat{Y}_{in} = \hat{\lambda}_{in} = e^{\hat{\mu}+\hat{\alpha}_i+\hat{\beta}x_{in}}$.

further designs

Further designs

- Other GLM's for non-normal outcomes. Besides binomial and count data the `glm` function can also model multinomial, negative binomial, Gamma.
- Longitudinal analysis. In longitudinal experiments one is interested in the development of individuals or other experimental units over time. This typically leads to multiple measurements per individual, taken at different time points (and often modeled with mixed effects models).
- Mixed models. Mixed models define outcomes in terms of parameters, (random) errors and additional random effects. This allows to model variation due to the selection of experimental units, fluctuations over time, extraneous variables that influence some measurements, etc.

To finish

Today we discussed

1. generalized linear models
    1. logistic regression
    2. Poisson regression