Regression analysis (in R)

Catalina Vallejos (The Alan Turing Institute and UCL) Aaron Lun (Cancer Research UK - Cambridge Institute)

April 5th, 2017

Outline for the course

- Introduction to statistics
- Hypothesis testing (in R)
- Regression analysis (in R)
- Multiple testing (in R)

In statistics, **regression analysis** is a tool to quantify relationships between 2 or more variables

In statistics, **regression analysis** is a tool to quantify relationships between 2 or more variables

In regression, variables are clasified as

- ▶ **Response**: outcome variable of interest (dependent)
- **Explanatory**: covariate(s) to explain the response (independent)

Examples?

There are different types of regression models, which one to use depends on the properties of the analysed variables. For example,

► For a binary response (e.g. failure/success), a common choice is **logistic regression**

There are different types of regression models, which one to use depends on the properties of the analysed variables. For example,

- For a binary response (e.g. failure/success), a common choice is logistic regression
- ► For a continuous response (e.g. blood sugar level), a typical choice is **linear regression**

There are different types of regression models, which one to use depends on the properties of the analysed variables. For example,

- For a binary response (e.g. failure/success), a common choice is logistic regression
- ► For a continuous response (e.g. blood sugar level), a typical choice is **linear regression**

Today, we will focus on linear regression

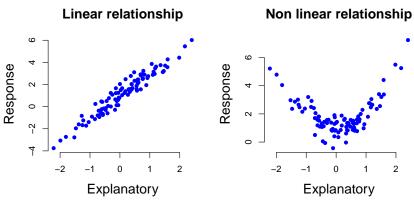
Linear regression

Linear regression

Linear regression is a statistical tool to capture **linear** relationships between a single **continuous** response variable and one or more explanatory variables (may be discrete or continuous)

Linear regression

Linear regression is a statistical tool to capture **linear** relationships between a single **continuous** response variable and one or more explanatory variables (may be discrete or continuous)



In **simple linear regression**, the aim is to capture a linear relationship between a response (y) and a **single** covariate (x)

The simple linear regression model is writen as

$$y_i = \beta_0 + \beta_1 x_i + \epsilon_i, \qquad i = 1, \dots, n$$

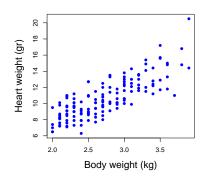
$$\beta_0 \text{ is the intercept}$$

$$\beta_1 \text{ is the slope (gradient)}$$

$$\epsilon_i \text{ is the error term}$$

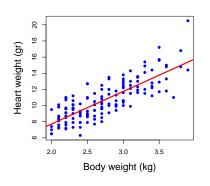
(*) Plot the response on the vertical axis and the covariate on the horizontal axis

The data in Fisher (1947) shows heart and body weights for 144 cats



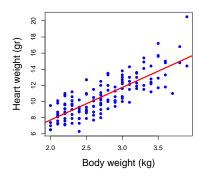
Is there a relationship between heart and body weight?

The data in Fisher (1947) shows heart and body weights for 144 cats



Is there a linear relationship between heart and body weight?

The data in Fisher (1947) shows heart and body weights for 144 cats



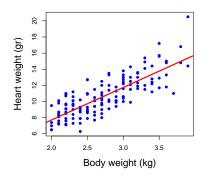
We can fit a simple linear regression

$$y_i = \beta_0 + \beta_1 x_i + \epsilon_i$$

where

- y_i = heart weight of cat i
- $> x_i = body weight of cat i$

The data in Fisher (1947) shows heart and body weights for 144 cats



We can fit a simple linear regression

$$y_i = \beta_0 + \beta_1 x_i + \epsilon_i$$

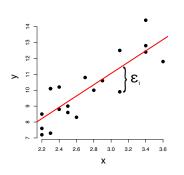
where

- \triangleright y_i = heart weight of cat i
- $> x_i = body weight of cat i$

How to estimate β_0 and β_1 ?

Idea: find β_0 and β_1 such that the line is a good fit for the data

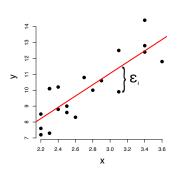
Idea: find β_0 and β_1 such that the line is a good fit for the data



For example, by minimizing the **residuals** of the regression

$$\epsilon_i = Y_i - (\beta_0 + \beta_1 x_i) \equiv Y_i - \hat{Y}_i$$

Idea: find β_0 and β_1 such that the line is a good fit for the data



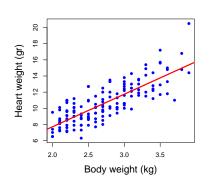
For example, by minimizing the **residuals** of the regression

$$\epsilon_i = Y_i - (\beta_0 + \beta_1 x_i) \equiv Y_i - \hat{Y}_i$$

Typically, this is done by minimizing the **Sum of Square Errors (SSE)**

$$SSE = \sum_{i=1}^{n} \epsilon_i^2$$

The data in Fisher (1947) shows heart and body weights for 144 cats

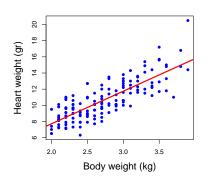


In this example we have

- $\beta_0 = -0.36$
- $\beta_1 = 4.03$

How to interpret this?

The data in Fisher (1947) shows heart and body weights for 144 cats



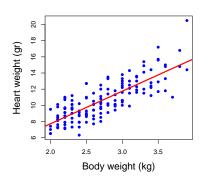
In this example we have

- $\beta_0 = -0.36$
- $\beta_1 = 4.03$

How to interpret this?

For a 1kg increase in body weight, we expect heart weight to increase by $4.03 \mathrm{gr}$

The data in Fisher (1947) shows heart and body weights for 144 cats



In this example we have

- $\beta_0 = -0.36$
- $\beta_1 = 4.03$

How to interpret this?

For a 1kg increase in body weight, we expect heart weight to increase by 4.03gr

Is this increase statistically significant?

We can answer this using hypothesis testing:

$$H_0: \beta_1 = 0$$
 vs $H_1: \beta_1 \neq 0$

Recall:
$$y_i = \beta_0 + \beta_1 x_i + \epsilon_i$$

 \rightarrow if $\beta_1 = 0$, y_i and x_i are not (linearly) dependent

We can answer this using hypothesis testing:

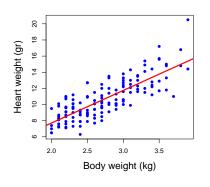
$$H_0: \beta_1 = 0$$
 vs $H_1: \beta_1 \neq 0$

Recall:
$$y_i = \beta_0 + \beta_1 x_i + \epsilon_i$$

 \rightarrow if $\beta_1 = 0$, y_i and x_i are not (linearly) dependent

Assumming $\epsilon_i \sim \text{Normal}(0, \sigma^2)$, we can derive a *t*-test for β_1

The data in Fisher (1947) shows heart and body weights for 144 cats

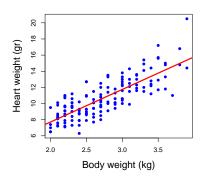


In this example we have

$$\beta_1 = 4.03$$

The *p*-value is $< 2 \times 10^{-16}$

The data in Fisher (1947) shows heart and body weights for 144 cats



In this example we have

$$\beta_1 = 4.03$$

The *p*-value is $< 2 \times 10^{-16}$

We reject H_0 , i.e. we conclude that the linear relationship between heart and body weight is statistically significant ($\alpha=0.05$)

Simple linear regression: Analysis of Variance (ANOVA)

ANOVA aims to decompose the total variance of y

Recall: Var(y) =
$$\sum_{i=1}^{n} (y_i - \bar{y})^2/(n-1)$$
, with $\bar{y} = (\sum_{i=1}^{n} y_i)/n$

Simple linear regression: Analysis of Variance (ANOVA)

ANOVA aims to decompose the total variance of y

Recall:
$$Var(y) = \sum_{i=1}^{n} (y_i - \bar{y})^2/(n-1)$$
, with $\bar{y} = (\sum_{i=1}^{n} y_i)/n$

$$\sum_{i=1}^{n} (\hat{y}_i - \bar{y})^2 = \sum_{i=1}^{n} (y_i - \bar{y})^2 - \sum_{i=1}^{n} (y_i - \hat{y}_i)^2$$
SSR (Regression) SST (Total) SSE (Error)

- SST quantifies the total variability of y
- SSE quantifies residual variability of y (unexplained by x)
- SSR quantifies how much of the variability of y is explained by x

Simple linear regression: Analysis of Variance (ANOVA)

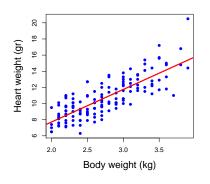
The **coefficient of determination** R^2 is defined as the proportion of total variability of y that is explained by x

$$R^2 = \frac{\text{SSR}}{\text{SST}} = 1 - \frac{\text{SSE}}{\text{SST}}$$

- ▶ $0 \le R^2 \le 1$
- ▶ If $R^2 = 0$, x explains none of the variability of y
- ▶ If $R^2 = 1$, x explains all of the variability of y (perfect fit!)

Warning: this assumes the relationship between x and y is linear

The data in Fisher (1947) shows heart and body weights for 144 cats



In this example we have

$$R^2 = 0.65$$

Body weight explains 65% of the variability of a cat's heart weight

Pearson's correlation $(\rho_{x,y})$ quantifies linear dependency between variables x and y

Pearson's correlation $(\rho_{x,y})$ quantifies linear dependency between variables x and y

How does this relate to simple linear regression?

Pearson's correlation $(\rho_{x,y})$ quantifies linear dependency between variables x and y

How does this relate to simple linear regression?

Both methods are closely related:

$$\rho_{xy} = \sqrt{R^2}$$

Pearson's correlation $(\rho_{x,y})$ quantifies linear dependency between variables x and y

How does this relate to simple linear regression?

Both methods are closely related:

$$\rho_{xy} = \sqrt{R^2}$$

However,

- ▶ in linear regression, x and y receive an asymmetric treatment
- ▶ in correlation, x and y receive a **symmetric** treatment

Pearson's correlation $(\rho_{x,y})$ quantifies linear dependency between variables x and y

How does this relate to simple linear regression?

Both methods are closely related:

$$\rho_{xy} = \sqrt{R^2}$$

However,

- ▶ in linear regression, x and y receive an asymmetric treatment
- ▶ in correlation, x and y receive a **symmetric** treatment

Examples?

Pearson's correlation $(\rho_{x,y})$ quantifies linear dependency between variables x and y

How does this relate to simple linear regression?

Both methods are closely related:

$$\rho_{xy} = \sqrt{R^2}$$

However,

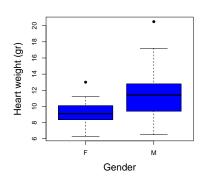
- ▶ in linear regression, x and y receive an asymmetric treatment
- ▶ in correlation, x and y receive a **symmetric** treatment

Examples?

Let's play: http://guessthecorrelation.com

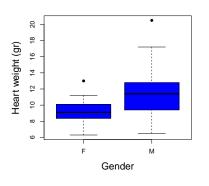


The data in Fisher (1947) also contains gender information



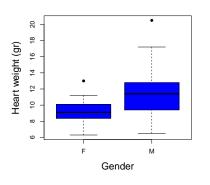
Is there a relationship between gender and a cat's heart weight?

The data in Fisher (1947) also contains gender information



In principle, we can answer this question using a *t*-test

The data in Fisher (1947) also contains gender information

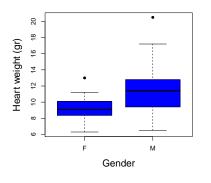


In principle, we can answer this question using a *t*-test

In this example we have:

$$t = -5.35$$
 p-value = 3.38×10^{-7}

The data in Fisher (1947) also contains gender information



In principle, we can answer this question using a *t*-test

In this example we have:

$$t = -5.35$$
 p-value = 3.38×10^{-7}

Can we answer the same question using linear regression?

Linear regression also allows us to answer this question by treating the grouping variable (e.g. gender) as a **categorical covariate**

Linear regression also allows us to answer this question by treating the grouping variable (e.g. gender) as a **categorical covariate**

However, categorical covariates require an special treatment . . .

Recall:
$$y_i = \beta_0 + \beta_1 x_i + \epsilon_i$$

Instead of defining a single regression effect β_1 , we need to estimate an effect for **each level** of the categorical covariate

Linear regression also allows us to answer this question by treating the grouping variable (e.g. gender) as a **categorical covariate**

However, categorical covariates require an special treatment . . .

Recall:
$$y_i = \beta_0 + \beta_1 x_i + \epsilon_i$$

Instead of defining a single regression effect β_1 , we need to estimate an effect for **each level** of the categorical covariate

This can be done using dummy variables

In this context, **dummy variables** are used as **binary** indicators associated to particular levels of a categorical covariate

In this context, **dummy variables** are used as **binary** indicators associated to particular levels of a categorical covariate

For example,

$$D_i = \begin{cases} 1, \text{if cat } i \text{ is male;} \\ 0, \text{if cat } i \text{ is female.} \end{cases}$$

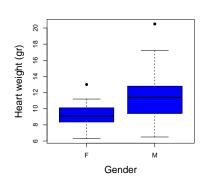
In this context, **dummy variables** are used as **binary** indicators associated to particular levels of a categorical covariate

For example,

$$D_i = \begin{cases} 1, \text{ if cat } i \text{ is male;} \\ 0, \text{ if cat } i \text{ is female.} \end{cases}$$

Note: gender has **two** levels, but we only define **one** dummy variable (here we left *female* as a **reference category**)

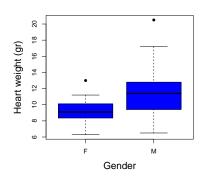
The data in Fisher (1947) also contains gender information



In this example we have

$$y_i = \beta_0 + \beta_1 D_i + \epsilon_i$$

The data in Fisher (1947) also contains gender information

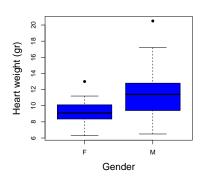


In this example we have

$$y_i = \beta_0 + \beta_1 D_i + \epsilon_i$$

- ▶ For a male cat: $\hat{y}_i = \beta_0 + \beta_1$
- ▶ For a female cat: $\hat{y}_i = \beta_0$

The data in Fisher (1947) also contains gender information



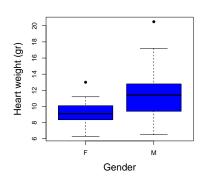
In this example we have

$$y_i = \beta_0 + \beta_1 D_i + \epsilon_i$$

- ▶ For a male cat: $\hat{y}_i = \beta_0 + \beta_1$
- ▶ For a female cat: $\hat{y}_i = \beta_0$

 $\Rightarrow \beta_1$ quantifies the difference between female and male cats

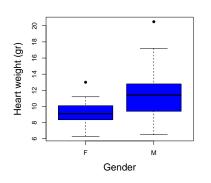
Is there a relationship between gender and a cat's heart weight?



We can answer this using the test

$$H_0: \beta_1 = 0$$
 vs $H_1: \beta_1 \neq 0$

Is there a relationship between gender and a cat's heart weight?



We can answer this using the test

$$H_0: \beta_1 = 0$$
 vs $H_1: \beta_1 \neq 0$

Assuming $\epsilon_i \sim \text{Normal}(0, \sigma^2)$, we derive a t-test:

$$eta_1 = 2.12 \ t = 5.35 \ p ext{-value} = 3.38 imes 10^{-7}$$

Multiple linear regression is an extension of simple linear regression that allows more than 1 covariate

Multiple linear regression is an extension of simple linear regression that allows more than 1 covariate

$$y_i = \beta_0 + \beta_1 x_{i1} + \beta_2 x_{i2} + \cdots + \beta_p x_{ip} + \epsilon_i$$

For example, with 2 continuous covariates:

$$y_i = \beta_0 + \beta_1 x_{i1} + \beta_2 x_{i2} + \epsilon_i,$$

where

- ▶ y_i: heart weight for cat i
- ► x_{i1}: body weight for cat i
- ► x_{i2}: age for cat i

In multiple linear regression, there are 2 types of **hypothesis**:

In multiple linear regression, there are 2 types of **hypothesis**:

► Marginal: to assess the significance of a single covariate

$$H_0: \beta_j = 0 \text{ vs } H_1: \beta_j \neq 0$$

In multiple linear regression, there are 2 types of **hypothesis**:

Marginal: to assess the significance of a single covariate

$$H_0: \beta_j = 0$$
 vs $H_1: \beta_j \neq 0$

Global: to assess the joint effect of all covariates

$$H_0: \beta_1 = \cdots = \beta_p = 0$$
 vs $H_1:$ at least one $\beta_j \neq 0$

In multiple linear regression, there are 2 types of hypothesis:

Marginal: to assess the significance of a single covariate

$$H_0: \beta_j = 0$$
 vs $H_1: \beta_j \neq 0$

Assuming $\epsilon_i \sim N(0, \sigma^2)$, we can use a *t*-test

Global: to assess the joint effect of all covariates

$$H_0: \beta_1 = \cdots = \beta_p = 0$$
 vs $H_1:$ at least one $\beta_j \neq 0$

In multiple linear regression, there are 2 types of **hypothesis**:

Marginal: to assess the significance of a single covariate

$$H_0: \beta_j = 0 \text{ vs } H_1: \beta_j \neq 0$$

Assuming $\epsilon_i \sim N(0, \sigma^2)$, we can use a *t*-test

Global: to assess the joint effect of all covariates

$$H_0: \beta_1 = \cdots = \beta_p = 0$$
 vs $H_1:$ at least one $\beta_j \neq 0$

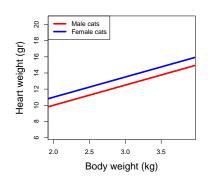
Assuming $\epsilon_i \sim N(0, \sigma^2)$, we can use an *F*-test (from ANOVA table)

... or mixing a continuous and a categorical covariate

$$y_i = \beta_0 + \beta_1 x_{i1} + \beta_2 x_{i2} + \epsilon_i,$$

where

- ▶ y_i: heart weight for cat i
- ▶ x_{i1}: body weight for cat i

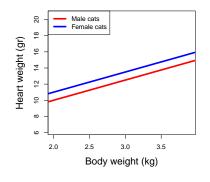


For a male cat:

$$\hat{y}_i = \beta_0 + \beta_1 x_{i1} + \beta_2$$

For a female cat:

$$\hat{y}_i = \beta_0 + \beta_1 x_{i1}$$



For a male cat:

$$\hat{y}_i = \beta_0 + \beta_1 x_{i1} + \beta_2$$

For a female cat:

$$\hat{y}_i = \beta_0 + \beta_1 x_{i1}$$

 \Rightarrow parallel lines, effect of body weight is independent of gender

 $\Rightarrow \beta_2$ quantifies a global difference between female and male cats





Recall: the multiple linear regression model is written as

$$y_i = \beta_0 + \beta_1 x_{i1} + \beta_2 x_{i2} + \cdots + \beta_p x_{ip} + \epsilon_i$$

What assumptions underlie this model?

▶ Firstly, we need more observations than variables (n > p)

▶ Firstly, we need more observations than variables (n > p)

This might not hold in some genomics applications ...
... but that's outside the scope of this course!

▶ Firstly, we need more observations than variables (n > p)

This might not hold in some genomics applications ...
... but that's outside the scope of this course!

▶ Secondly, we assume that residuals ϵ_i are **independent** and **identically distributed** with

$$\epsilon_i \sim \mathsf{N}(0, \sigma^2)$$

▶ Firstly, we need more observations than variables (n > p)

This might not hold in some genomics applications ...
... but that's outside the scope of this course!

▶ Secondly, we assume that residuals ϵ_i are **independent** and **identically distributed** with

$$\epsilon_i \sim \mathsf{N}(0, \sigma^2)$$

How can we assess this?

Idea: after estimating the regression coefficients, define residuals as

$$\epsilon_i = y_i - \hat{y}_i$$

Use these estimated residuals to diagnose model quality

Idea: after estimating the regression coefficients, define residuals as

$$\epsilon_i = y_i - \hat{y}_i$$

Use these estimated residuals to diagnose model quality

For example, we can prepare a $_$ $_$ $_$ to see if residuals are normally distributed

Idea: after estimating the regression coefficients, define residuals as

$$\epsilon_i = y_i - \hat{y}_i$$

Use these estimated residuals to diagnose model quality

For example, we can prepare a _____ to see if residuals are normally distributed

More about this in the practical ...

What if things go wrong?

What if things go wrong?

If the residuals are not good enough to pass the diagnostic criteria, we need to revisit the model. For example

- We can transform some of the covariates or
- We can transform the response variable

Suppose a simple linear regression model

$$y_i = \beta_0 + \beta_1 x_i + \epsilon_i$$

Covariate transformation can be useful in situations where the relationship between y and x is **not linear**

Suppose a simple linear regression model

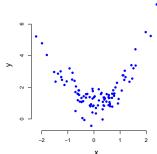
$$y_i = \beta_0 + \beta_1 x_i + \epsilon_i$$

Covariate transformation can be useful in situations where the relationship between y and x is **not linear**

Idea: replace x_i by a transformed version of x_i (e.g. $x_i^* = x_i^2$)

$$y_i = \beta_0 + \beta_1 x_i + \epsilon_i$$

Non linear relationship



$$y_i = \beta_0 + \beta_1 x_i + \epsilon_i \qquad \qquad y_i = \beta_0 + \beta_1 x_i^2 + \epsilon_i$$
 Non linear relationship Linear relationship

Suppose a simple linear regression model

$$y_i = \beta_0 + \beta_1 x_i + \epsilon_i$$

Response transformation can be useful in situations where the variance of y is not constant as a function of x

We refer to this as **heteroskedastic** errors

Suppose a simple linear regression model

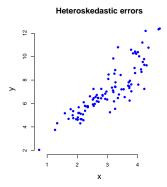
$$y_i = \beta_0 + \beta_1 x_i + \epsilon_i$$

Response transformation can be useful in situations where the variance of y is not constant as a function of x

We refer to this as **heteroskedastic** errors

Idea: replace y_i by a transformed version of y_i (e.g. $y_i^* = \log(y_i)$)

$$y_i = \beta_0 + \beta_1 x_i + \epsilon_i$$



$$y_i = \beta_0 + \beta_1 x_i + \epsilon_i$$

$$\log(y_i) = \beta_0 + \beta_1 x_i + \epsilon_i$$

