Lecture 2

Introduction II
Pedigree analysis in R with the *ped suite*

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Statistical methods in genetic relatedness and pedigree analysis

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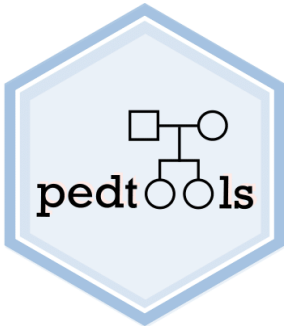
Plan

- What is **R**?

- Your first R session?
  - basic functionality
  - plotting
  - installing packages

- The *ped suite* packagers **pedtools** and **pedprobr**
  - creating and plotting pedigrees
  - marker genotypes
  - likelihoods



What is R?

- A framework for statistical and numerical computing
  - calculator
  - flexible plotting
  - large core of functions for data handling and numerical analysis
  - programming language
  - external packages
    - anyone can make one
    - thousands!

- About R:
  - it's free!
  - it's widely used
  - it *can* do anything (but it may not be easy)
  - challenging for beginners *(unless they have good teachers!)*

Time to get your hands dirty: Your first R session

Using R as a basic calculator

```
>   2 + 3
[1] 5
>   1+2     * 3
[1] 7
>   (1 + 2) * 3
[1] 9
>   4^2
[1] 16
>   exp(1)
[1] 2.718282
>   log(100)
[1] 4.60517
>   log(100, base = 10)
[1] 2
>   log10(100)
[1] 2
```

Variables

For assignments, you have two choices: = or <-

```
>   a = 5      or   a <- 5
>   b = 3      or   b <- 3
>   a
[1] 5
>   a - 2*b
[1] -1
```

Changing a variable:

```
>   a = a+1
>   a
[1] 6
```

Creating new variables from old:

```
>   myVariable_name = a^(b - 1)
>   myVariable_name
[1] 36
```


Vectors

```
>   c(3, 2, 6, -1)
[1]  3  2  6 -1
>   4:20
[1]  4  5  6  7  8  9 10 11 12
[10] 13 14 15 16 17 18 19 20
>   5:7 - 4
[1] 1  2  3
>   c(10,20,30,40) + c(1,3,8,0)
[1] 11 23 38 40
>   seq(from = 2, to = 15, by = 3)
[1]  2  5  8 11 14
```

There is a help page for every function!

```
> ?seq
```

Try some variations:

```
>   seq(10, by = 2, length = 5)
>   seq(10, 0, by = -2)
>   5:(-5)
```


Matrix-like containers

Data frames: Each vector becomes a column

```
>   x = data.frame(Name = c("Ali", "Bob", "Joe"), Weight = c(75, 81, 70))
>   x
  Name Weight
1  Ali     75
2  Bob     81
3  Joe     70
```

Matrices:

```
>   x = matrix(1:12, nrow = 3, ncol = 4)
>   x
     [,1] [,2] [,3] [,4]
[1,]    1    4    7   10
[2,]    2    5    8   11
[3,]    3    6    9   12
```

Faster, but less flexible. Good for all-numeric data

Lists

```
>   a = list(good = 1:3, bad = 0)
>   a
$good
[1] 1  2  3

$bad
[1] 0
>   a$good
[1] 1  2  3
```

The dollar operator:
Extracts a named list element

Easy to change lists:

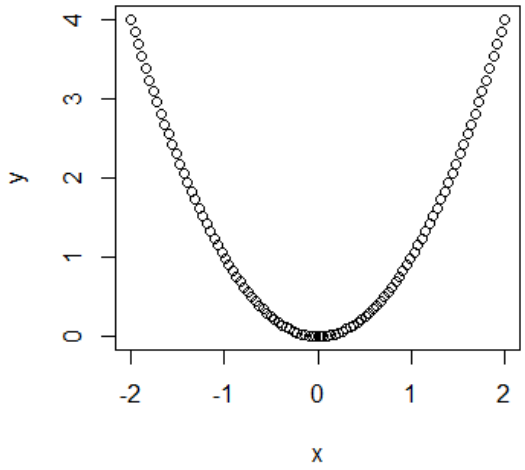
```
>   a$bad = NULL                (delete item)
>   a$ok = -1                   (add new item)
>   a$good = c(a$good, 10)      (modify item)
>   a
$good
[1] 1  2  3  10

$ok
[1] -1
```


Basic plotting

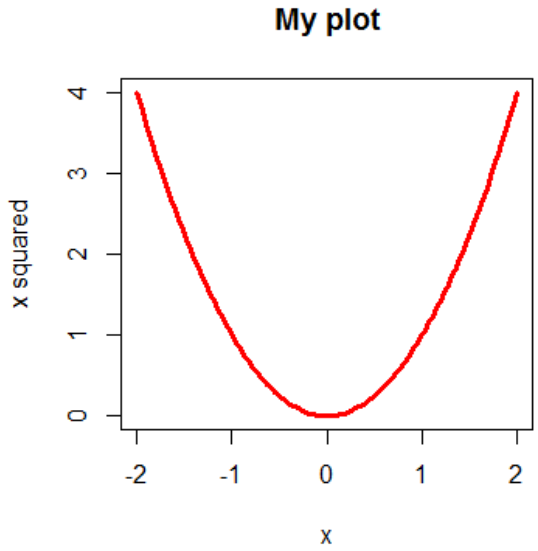
Let's plot the graph of $y = x^2$!

```
>   x = seq(-2, 2, length = 100)
>   y = x^2
>   plot(x, y)
```



Many options to play with...

```
>   plot(x, y, type="l", lwd = 3, col = "red",
         ylab = "x squared", main = "My plot!")
```



Basic R stuff that we skip in this brief introduction

- User-defined functions
- Non-numerical objects (character strings, boolean, ++)
- Random numbers / simulation
- Statistics (summary stats, hypothesis testing, regression analysis ++)
- ... and LOTS of other things...

Installing packages

To access the functions of an external package, you must:

- install the package
  - downloads it to your computer
  - this is done only once
  - **install.packages()** (needs internet connection - or local zip file)
- load it into R
  - every new session
  - **library()** or **require()**

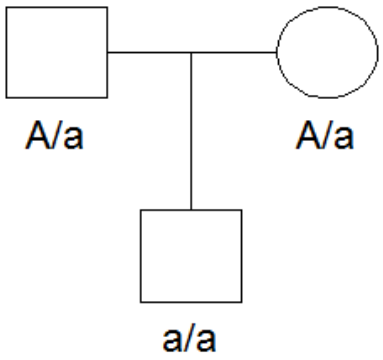
To check if a package is installed, simply try to load it:

```
> library(pedtools)
```

If you get an error, do:

```
> install.packages("pedtools")
```


pedtools: Tools for working with pedigrees in R



What it contains

pedigrees

markers

What it does

- Create
- Manipulate
- Understand
- Plot

kinship2

pedtools

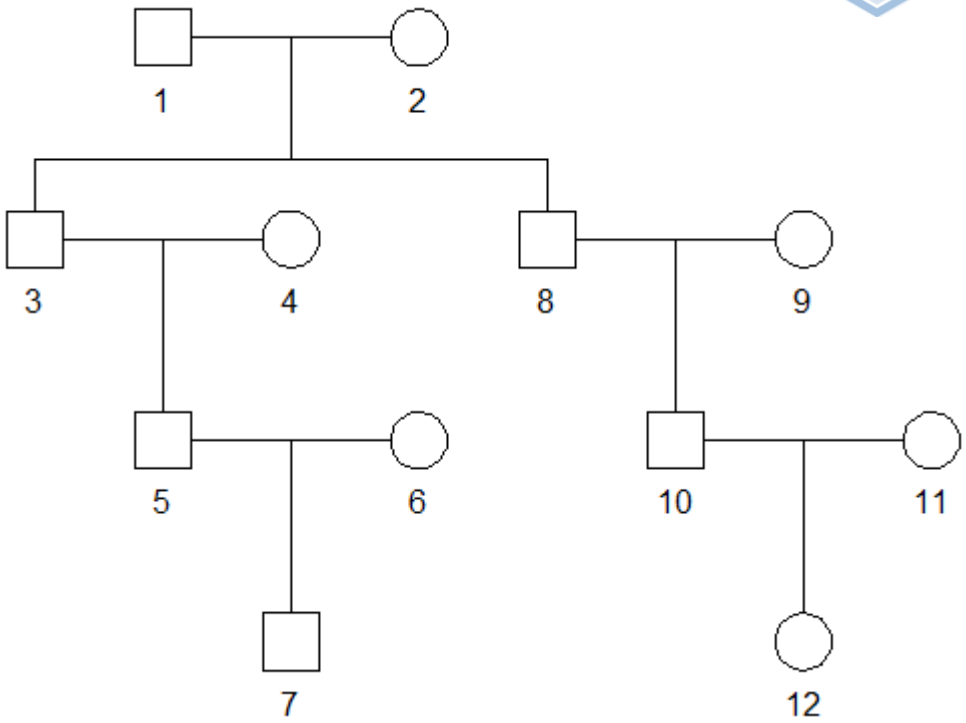
```
> library(pedtools)
> x = cousinPed(2)
> plot(x)
```

Changing genders:

```
> x2 = swapSex(x, 7)
```

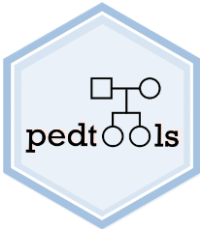
Or several at once:

```
> x3 = swapSex(x, c(3,5,7))
> plot(x3)
```



When changing an R object, always store the result back in a variable, with:

- a different name, or
- the same name (if you don't need the old)



Create: basic

- nuclearPed
- linearPed
- cousinPed
- halfSibPed
- halfCousinPed

Create: complex

- doubleCousins
- quadHalfFirstCousins
- fullSibMating
- halfSibStack
- randomPed

Manipulate

- addChildren
- addParents
- removeIndividuals
- branch
- mergePed
- breakLoops
- reorderPed
- relabel

Member subsets

- founders
- nonfounders
- leaves
- males
- females
- typedMembers
- untypedMembers

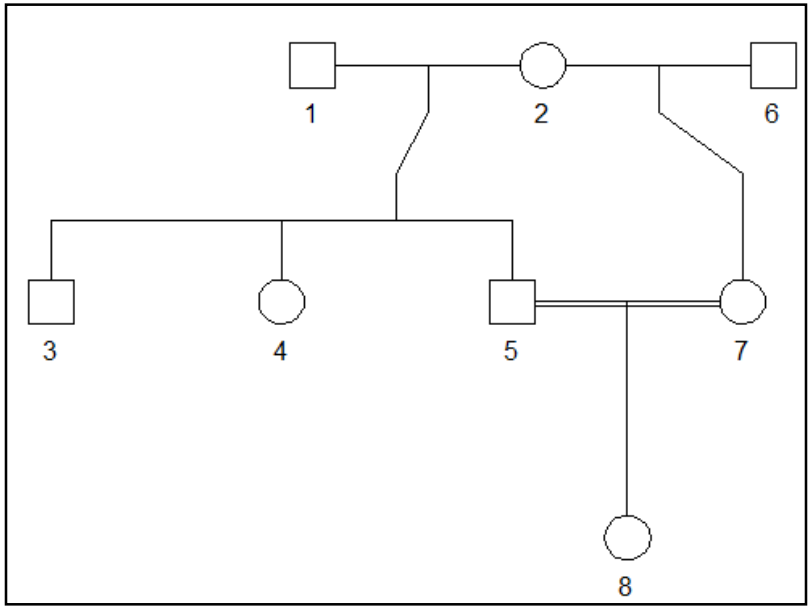
Relatives

- father
- mother
- children
- siblings
- grandparents
- cousins
- spouses

- ancestors
- descendants
- unrelated

Now try this!

```
>   x = nuclearPed(3, sex = c(1, 2, 1))
>   plot(x)
>   x = addDaughter(x, 2)
>   plot(x)
>   x = addChildren(x, father = 5, mother = 7, nch = 1, sex = 2)
>   plot(x)
```



Tip: Plot after each step to keep track of what's going on!

Alternative creation process: Using pedigree files

- Pedigree file:
  - Text file describing the family structure
  - Extension **.ped** (by convention)

- Format: Compulsory columns (usually in this order):
  - (Family ID)
  - Individual ID
  - ID of father
  - ID of mother
  - Gender (1 = male, 2 = female, 0 = unknown)

For (old) experts: This is «pre-makeped format»

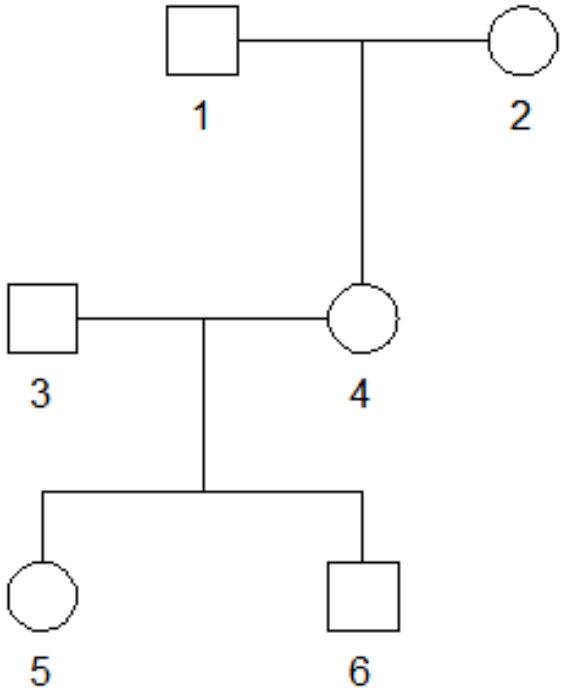
Example: pedigree file

Contents of *example.ped*:

FAMID	ID	FID	MID	SEX
1	1	0	0	1
1	2	0	0	2
1	3	0	0	1
1	4	1	2	2
1	5	3	4	2
1	6	3	4	1

0's if founder

1 = male
2 = female

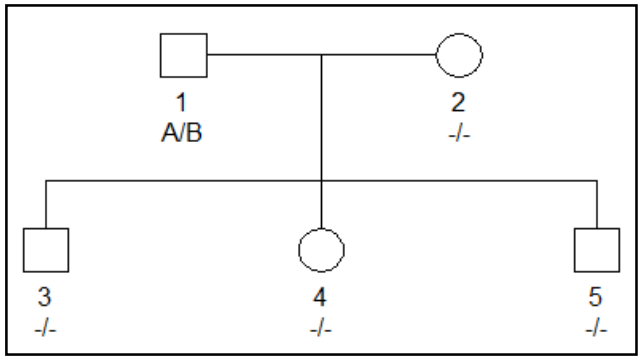


In pedtools:

```
> x = readPed("example.ped")
> plot(x)
```

Adding marker data

```
>   x = nuclearPed(3, sex = c(1, 2, 1))
>   m = marker(x, "1" = c("A", "B"))
>   plot(x, m)
```

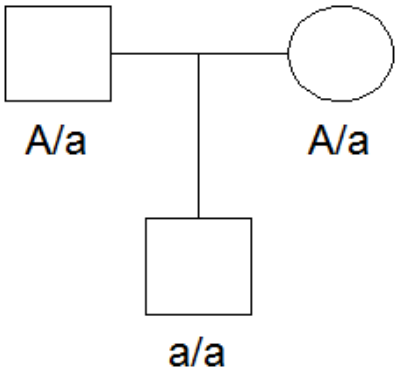


What is m??

```
>   m
      [,1] [,2]
[1,]    1    2
[2,]    0    0
[3,]    0    0
[4,]    0    0
[5,]    0    0
attr(,"missing")
[1] 0
attr(,"alleles")
[1] "A" "B"
attr(,"nalleles")
[1] 2
attr(,"afreq")
[1] 0.5 0.5
attr(,"chrom")
[1] NA
```

Answer:
A matrix with *attributes*

pedprobr: Pedigree probabilities in R



What it does

Compute the probability

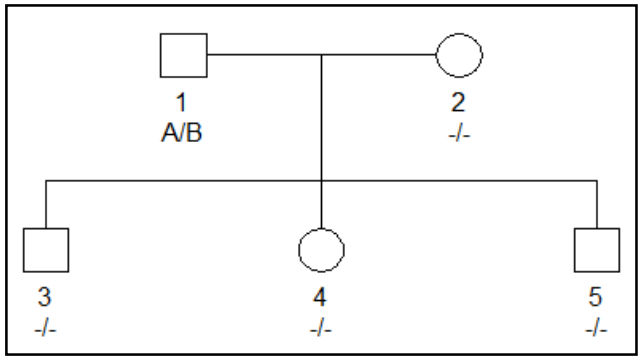
$$\mathcal{P}(genotypes \mid pedigree;\ params)$$

Features

- arbitrary inbreeding
- autosomal & X-linked
- linked markers
- mutation models
- Elston-Stewart algorithm

Adding marker data

```
>   x = nuclearPed(3, sex = c(1, 2, 1))
>   m = marker(x, "1" = c("A", "B"))
>   plot(x, m)
```



Compute the pedigree likelihood:

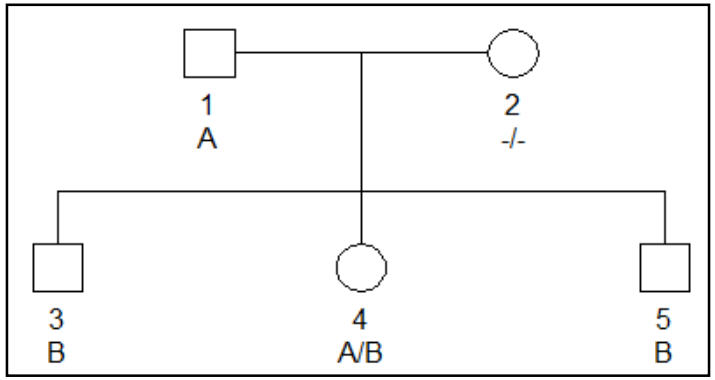
```
> library(pedprobr)
> likelihood(x, m)
[1] 0.5
```

Control:
HWE implies P(A/B) = 2pq

```
> 2 * 0.5 * 0.5
[1] 0.5
```

Adding X-linked marker data

```
>   m2 = marker(x, alleles = c("A", "B"), chrom = "X")
>   genotype(m2, 1) = "A"
>   genotype(m2, 4) = c("A", "B")
>   genotype(m2, c(3, 5)) = "B"
>   plot(x, m2)
```

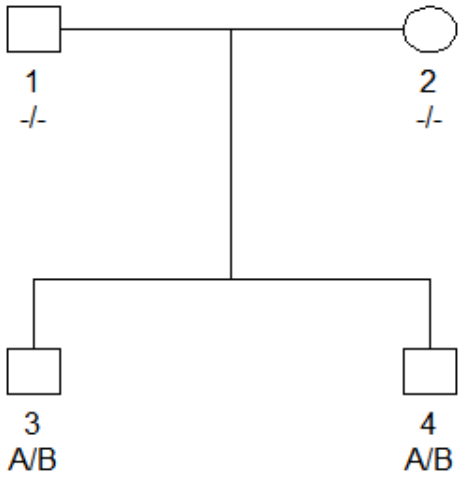



```
>   likelihood(x, m2)
[1] 0.15625
```

oneMarkerDistribution

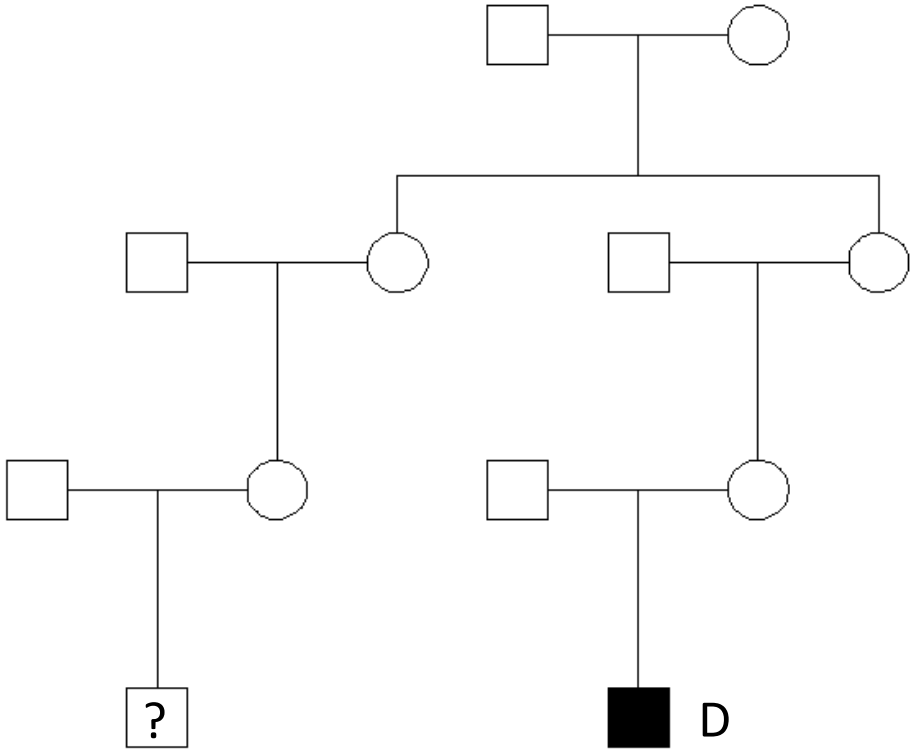
Computes the genotype distribution for one or several pedigree members, conditional on the observed genotypes

```
>   x = nuclearPed(2)
>   m = marker(x, afreq = c(A = 0.5, B = 0.5))
>   genotype(m, id = 3:4) = c("A", "B")
>   plot(x,m)
```




```
>   oneMarkerDistribution(x, partial = m, id = 1:2)
Joint genotype probability distribution for individuals 1 and 2:
    A/A B/B A/B
A/A 0.0 0.2 0.1
B/B 0.2 0.0 0.1
A/B 0.1 0.1 0.2
```

Practical example with oneMarkerDistribution



Will my child have the disease?

Summary

- Basic **R**
  - arithmetic
  - variables
  - vectors
  - lists
  - plots

- Ped suite packages **pedtools** + **pedprobr**
  - create pedigrees
  - modify pedigrees
  - markers
  - likelihoods
  - genotype distributions