Statistical methods in genetic relatedness and pedigree analysis

NORBIS course, Oslo, June 2022
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Solutions for exercise set II

Note: Some answers are given in the exercise and therefore omitted here.

Exercise II-1 (Getting started)

(Answer omitted.)

Exercise II-2 (Building pedigrees)

c) To add a child, use e.g., `x = addSon(x, parents = c(8,9))`.

Exercise II-3 (Built-in basic pedigrees)

The pedigrees can be made with the following commands. (Plots not shown.)

a)
```
x = avuncularPed("aunt", "nephew")
```

b)
```
x = linearPed(n = 4)
```

c)
```
x = cousinPed(degree = 1, removal = 1)
```

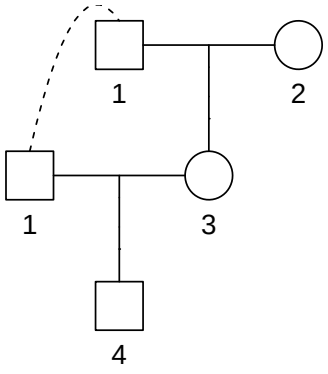
d)
```
x = cousinPed(degree = 2, half = TRUE)
```

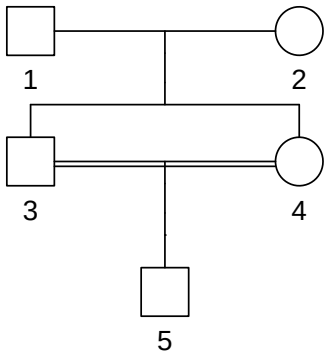
Exercise II-4 (Inbred pedigrees)

The pedigrees are shown below.

a)
```
x = nuclearPed(1, sex = 2) |> addSon(parents = c(1,3))
plot(x)
```

b)
```
x = nuclearPed(2, sex = 1:2) |> addSon(parents = c(3,4))
plot(x)
```





Exercise II-5 (Genotypes and plot options)

(Answer omitted.)

Exercise II-6 (Pedigree likelihood)

a)
```
x = nuclearPed(3) |>
  addMarker(geno = c("A/A", NA, "A/B", "A/B", "A/B"))

afreq(x, marker = 1)
```

```
##   A   B
## 0.5 0.5
```

b)
```
x = setAfreq(x, marker = 1, afreq = c(A = 0.9, B = 0.1))
likelihood(x, marker = 1)
```

```
## [1] 0.026325
```

Exercise II-7 (More likelihoods)

a)
```
x1 = nuclearPed(sex = 2) |>
  addMarker(geno = c("A/A", "A/B", "A/A"), afreq = c(A = 0.5, B = 0.5))
likelihood(x1, marker = 1)
```

```
## [1] 0.0625
```

b)
```
x2 = linearPed(2) |>
  addMarker(geno = c("A/A", NA, "A/B", NA, "A/A"), afreq = c(A = 0.9, B = 0.1))
likelihood(x2, marker = 1)
```

```
## [1] 0.03645
```

Exercise II-8 (Creating and loading a ped file)

c) 6 is both an uncle and half-uncle of 7, as shown by this command:

```
verbalise(x, ids = c(6,7))
```

```
## Avuncular: 6 is an uncle of 7
##    6-[2,3]-5-7
## Half-avuncular: 6 is a half-uncle of 7
##    6-[2]-4-7
```

Exercise II-9 (X-linked recessive inheritance)

a) The affected male (7) has genotype D; the unaffected males (1,4,6) are N. The females 2 and 3 are obligate carriers with genotype D/N, while 5 and 8 are uncertain.

b) 0.25. The grandmother (2) has genotype D/N, and therefore probability $\frac{1}{2}$ of passing on the disease allele to her daughter 5, who in turn has probability $\frac{1}{2}$ of transmitting it to 8. No assumptions about frequencies or HWE were needed for this calculation.

c) If the grandfather (1) may have been affected, we don't know which of the grandparents are the source of disease allele. In fact three possibilities must be considered for the genotypes of 1 and 2: $(G_1, G_2) = (D, N/N)$, $(G_1, G_2) = (N, D/N)$ and $(G_1, G_2) = (D, D/N)$.

d) The probability that 8 is a carrier is ≈ 0.376, as seen by the `D/N` entry in the following output.

```
oneMarkerDistribution(ped, id = 8, partialmarker = 1, verbose = FALSE)
```

```
##          D/D          D/N          N/N
## 0.000375625 0.375873750 0.623750625
```

One (slight) weakness of the calculation as given is that it does not account for the fact that she is unaffected. This could be done by giving her a partial genotype:

```
ped = setGenotype(ped, 1, id = 8, geno = "N/-")
```

Finally, as in all cases involving disease segregation, one may question the validity of HWE at the disease locus, and also the assumption of no *de novo* mutations.

Bonus exercises

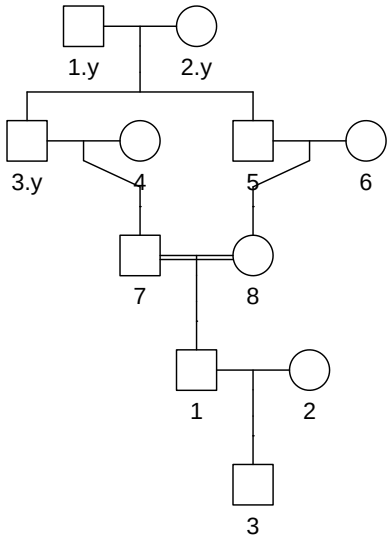
Exercise II-10 (Merging pedigrees)

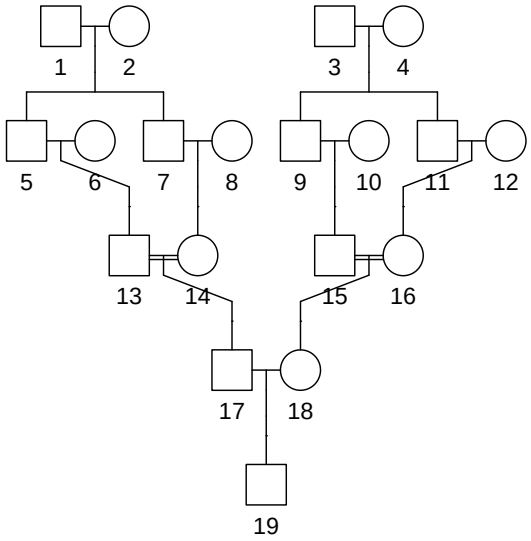
c) The plot is shown to the left below. Labels are changed when needed to avoid repeated names.

```
x2 = mergePed(x, fa, by = c("1" = "9"))
plot(x2)
```

d) The final pedigree is shown to the right below.

```
x3 = mergePed(x2, mo, by = c("2" = "9"), relabel = TRUE)
plot(x3)
```





e) With piping, the entire pedigree can be made as follows:

```
fa = cousinPed(1, child = T)
mo = swapSex(fa, 9)

x = nuclearPed(1) |>
  mergePed(fa, by = c("1" = "9")) |>
  mergePed(mo, by = c("2" = "9"), relabel = TRUE)
```

Exercise II-11 (Quadruple second cousins)

Here is one way to do it:

```
# Fathers: double cousins
fa = doubleCousins(1, 1)

# Mothers: double cousins
mo = doubleCousins(1, 1) |> swapSex(9:10)

# Add a child to each father
x = fa |> addSon(9) |> addSon(10)

# Merge with mothers
x = mergePed(x, mo, by = c("11" = "9", "13" = 10), relabel = TRUE)

# Plot (confusing)
plot(x)

# Check that bottom individuals are quad 2nd cousins
verbalise(x)
```

```
## Quadruple second cousins
##    21-17-9-[1,2]-11-19-22
##    21-17-10-[3,4]-12-19-22
##    21-18-13-[5,6]-14-20-22
##    21-18-16-[7,8]-15-20-22
```