Statistical methods in genetic relatedness and pedigree analysis

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Exercise set III. Coefficients of relatedness

```
library(pedsuite)
```

The main package today is **ribd**, which you can read more about here: https://github.com/magnusdv/ribd.

In some of the exercises you may use QuickPed instead of R: https://magnusdv.shinyapps.io/quickped/.

Exercise III-1

Use Wright's path formula to compute the kinship coefficient of

a) Uncle – niece.
b) Half first cousins.

Exercise III-2

Use R or QuickPed to compute the inbreeding coefficient of a child whose parents are

a) Uncle – niece.
b) Half first cousins.

Check that the answers agree with the kinship coefficients in the previous exercise. (Why should they?)

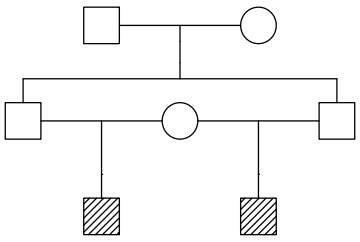
Exercise III-3

In a case of incest a man had a child by his own granddaughter.

a) Create the pedigree in R or QuickPed.
b) Compute the inbreeding coefficient of the child.

Exercise III-4

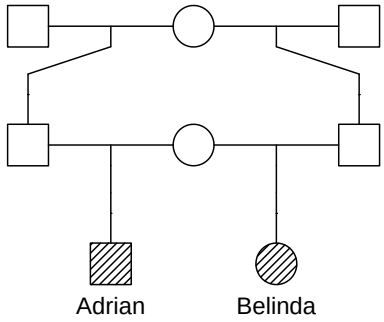
Consider the following pedigree:



a) Describe the relationship between the children. Are they inbred?
b) Use Wright's path formula to compute the kinship coefficient between the children.
c) Show that their IBD coefficients are $\kappa = (\frac{3}{8}, \frac{1}{2}, \frac{1}{8})$. (Hint: Do κ_2 first, then κ_0, and then κ_1.)
d) Verify that the formula $\varphi = \frac{1}{4}\kappa_1 + \frac{1}{2}\kappa_2$ holds in this case.
e) Place the relation in the IBD triangle. (Use the triangle on page 5, or draw your own.)
f) This relationship is sometimes called *3/4-siblings*. Why?

Exercise III-5

Consider the relationship between Adrian and Belinda:



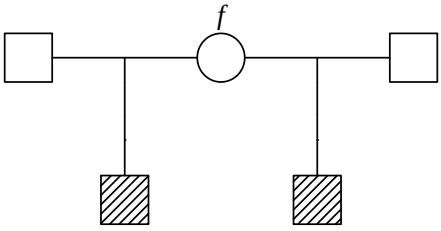
a) Create and plot the pedigree in R. (Hint: `x = halfSibStack(2)`.)
b) Compute the kinship coefficient between Adrian and Belinda.
c) Compute their IBD coefficients $(\kappa_0, \kappa_1, \kappa_2)$.
d) Plot the corresponding point in the IBD triangle.
e) (For the mathematically inclined) Explain why Adrian and Belinda may be called *5/8-siblings*.

Exercise III-6

a) What is the kinship coefficient between monozygotic twins?
b) Can you think of a relationship with kinship coefficient $\varphi = 1$?

Exercise III-7 (Founder inbreeding)

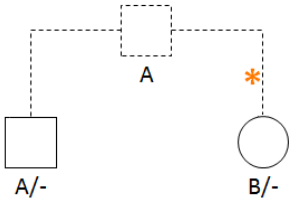
The pedigree shows two half siblings whose mother has inbreeding coefficient f.



a) Show that the IBD coefficients of the half siblings are $\kappa_0 = \frac{1}{2}(1-f)$, $\kappa_1 = \frac{1}{2}(1+f)$ and $\kappa_2 = 0$.
b) Where in the IBD triangle do such relationships belong?
c) Suppose the mother is 100% inbred (e.g. from an inbred mouse strain). Place the resulting half-sibling relationship in the IBD triangle, and comment on the result.

Exercise III-8 (IBD versus mutations)

In the pedigree below the alleles have the same origin, but a mutation event has occurred on the right hand side, turning the A allele into a B. Two scientists argue about the IBD status of the alleles in this case.



Scientist 1: *The alleles are clearly not IBD. They aren't even IBS!*

Scientist 2: *You are deceived by appearance. IBD is not defined pointwise, but for segments! Since the alleles have the same origin, their immediate surroundings are IBD, and that's what counts. Mutations are just noise.*

Discuss the statements. Scientist 1 is a medical geneticist, while Scientist 2 works with kinship analysis. How is this reflected in their point-of-views?

Exercise III-9 (Full sib mating)

Consider the relationship between a pair of siblings whose parents are full siblings.

a) Use R or QuickPed to find the identity coefficients of the relationship.
Hint if you use R: `fullSibMating(1)`.
b) Verify that all 9 coefficients are non-zero. (This is the simplest example of a relationship with this property!)
c) Compare Δ_9 ("no IBD") with the value of κ_0 for outbred siblings. Comment the result.

Exercise III-10

Consider the relationship between a pair of siblings whose parents are first cousins.

a) Create the pedigree in R or QuickPed, and calculate the identity coefficients.
b) Exactly one of the nine identity states is impossible – which? Explain in words why this state is impossible.

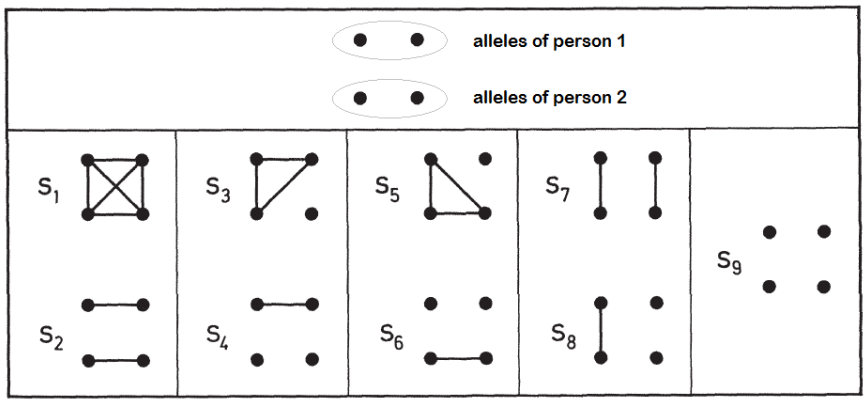


Figure 1: Jacquard's 9 condensed identity states

Bonus exercises

Exercise III-11 (Double second cousins)

a) In QuickPed, load the built-in pedigree "Double 2nd cousins - A". Verify that the fathers, and also the mothers, are first cousins.

b) Compute the IBD coefficients $(\kappa_0, \kappa_1, \kappa_2)$ and plot the corresponding point in the IBD triangle.

c) Prove that the point lies on the border of the inadmissible region.
Hint: You must show that $\kappa_1^2 = 4\kappa_0\kappa_2$. For higher numerical accuracy, you can obtain the coefficients in R as follows.

```
x = doubleCousins(2,2)
k = kappaIBD(x, 17:18)
```

d) Now load the built-in pedigree "Double 2nd cousins - B". Describe the structure of the pedigree.

e) Compute and plot the IBD coefficients, and compare with the previous.

f) (Challenge!) There exists a third type of double second cousins. Can you construct it? What are its IBD coefficients?

Exercise III-12 (IBD vs. IBS)

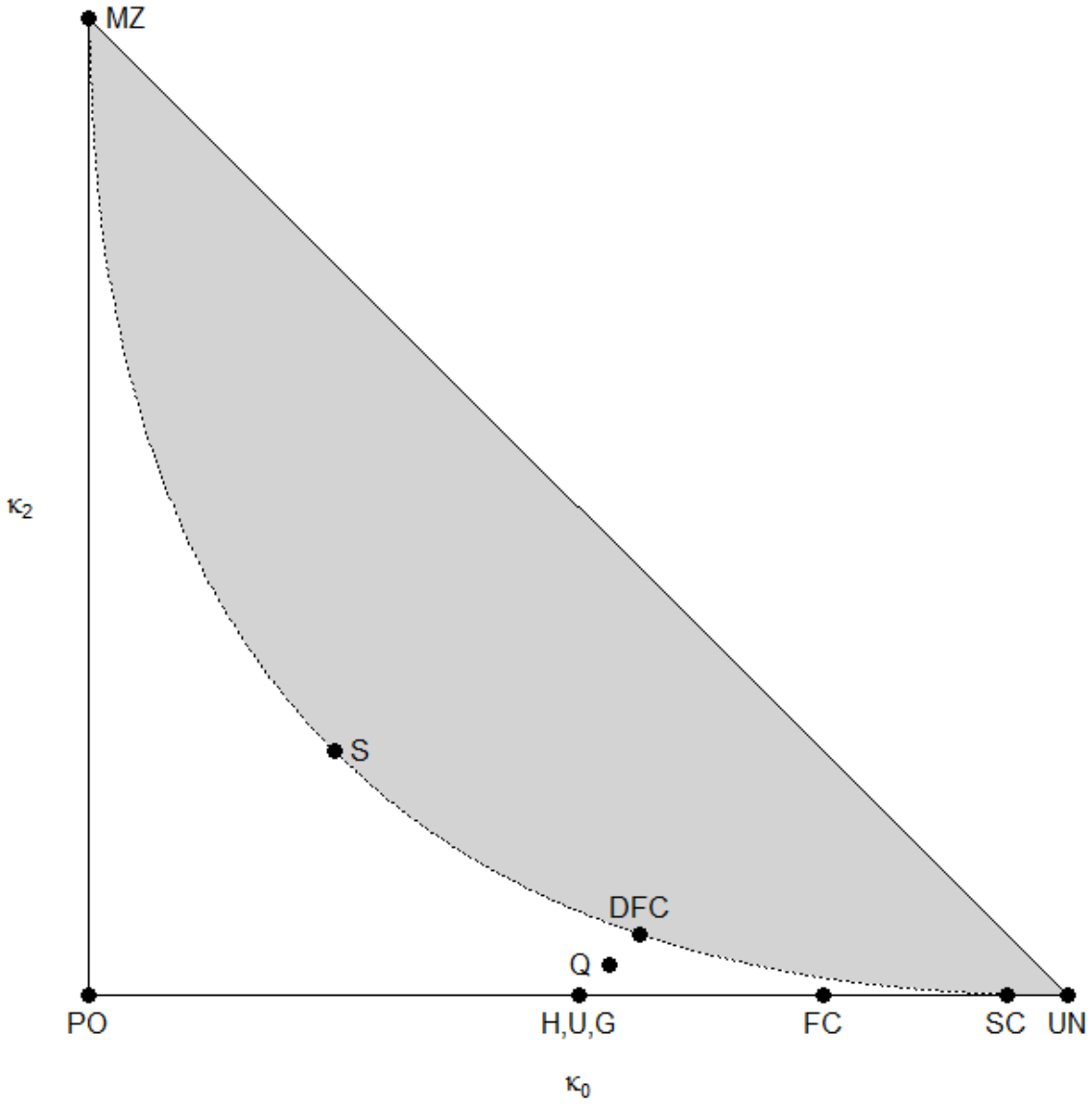
Recall Figure 1, which shows the nine possible identity states for pairwise relatedness. For each pair of marker genotypes below, what are the *possible* states? We assume no mutations.
Hint: Remember that IBS is not the same as IBD. For example, this implies that state 9 is always possible.

a) A/B and A/B
b) A/A and A/B
c) 13/17 and 15/15
d) C/D and A/B

Exercise III-13 (Parent-child relationships with inbreeding)

This exercise examines the identity coefficients of various types of parent-child relationships. For simplicity they are stated as mother–son, but the sexes are irrelevant for the calculations.

a) Warm-up: What are the identity coefficients between mother and son in the absence of inbreeding?
b) Suppose the parents of a boy are related, but not themselves inbred. Which of the nine identity states are possible between mother and son? (Hint: No calculations are needed. For each state, either show how it may occur, or find a simple argument that it cannot.)
c) In a case of incest, a man has a son by his own daughter. Compute the identity coefficients of the relationship between mother and son.
d) Suppose a woman has inbreeding coefficient f and has a son with a man unrelated to her. Is the child inbred? What are the identity coefficients between mother and son?


MZ
κ2
S
DFC
Q
PO
H,U,G
FC
SC
UN
κ0