

Statistical methods in genetic relatedness and pedigree analysis

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Exercise set III. Coefficients of pairwise relatedness

The packages `ribd` and `forrel` are used in many of the following exercises, so we start by loading these. Note that each of these automatically loads `pedtools` as well, so you don't have to do that explicitly.

```
library(ribd)
library(forrel)
```

Exercise III-1

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

- Uncle - niece
- First cousins once removed

Exercise III-2

Use the `ribd` function `inbreeding()` to compute the inbreeding coefficient of a child whose parents are

- Uncle - niece.
- First cousins once removed. (Hint: `cousinPed(degree = 1, removal = 1, child = T)`.)

Check that the answers agree with the kinship coefficients you computed in Exercise 1. (Why should they?)

Exercise III-3

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

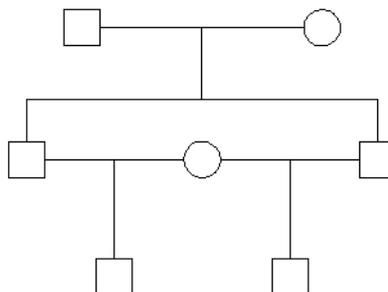
- Plot the pedigree in R.
- Compute the inbreeding coefficient of the child.

Exercise III-4

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

Exercise III-5 (3/4 siblings)

Consider the following pedigree:

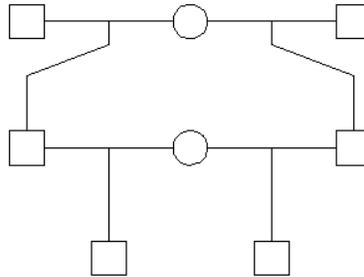


- Describe the relationship between the children in the last generation. Are the children inbred?

- b) Use Wright's path formula to compute the kinship coefficient between the children.
- c) Show that the IBD coefficients between the children are $\kappa = (\frac{3}{8}, \frac{1}{2}, \frac{1}{8})$.
(Hint: Do κ_2 first, then κ_0 , and finally κ_1 .)
- d) Use part c) and the formula $\varphi = \frac{1}{4}\kappa_1 + \frac{1}{2}\kappa_2$ to check your answer in b).
- e) Place the relation in the IBD triangle. (You can use the big triangle on page 5, or draw your own.)

Exercise III-6

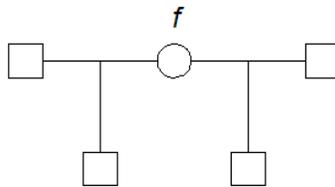
Consider the following pedigree:



- a) Describe the relationship between the children in the last generation.
- b) Use Wright's path formula to compute the kinship coefficient between the children.
- c) One can show that the IBD coefficients between the children are $\kappa = (\frac{7}{16}, \frac{1}{2}, \frac{1}{16})$. Place the relation in the IBD triangle.

Exercise III-7 (Founder inbreeding)

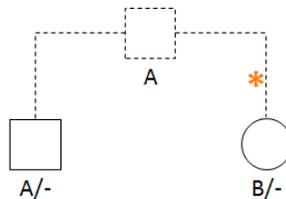
The pedigree shows two half siblings whose mother has inbreeding coefficient f .



- a) Show that the IBD coefficients of the half siblings are $\kappa = (\frac{1}{2}(1 - f), \frac{1}{2}(1 + f), 0)$.
- 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 has happened 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 are 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 (Double second cousins)

- Draw (by hand) a pedigree connecting double second cousins.
- Use the following code to compute the IBD coefficients of double second cousins:

```
x = doubleCousins(2, 2)
ids = c(7, 12)
plot(x, shaded = ids) # Unfortunately R cannot plot this nicely
k = kappaIBD(x, ids)
k
```

- Also compute the Jacquard coefficients of the same pair:

```
condensedIdentity(x, ids)
```

Compare with the κ coefficients above and comment on the result.

- Plot the point in the IBD triangle:

```
showInTriangle(k[1], k[3], label = "double 2nd cousins", pos = 3)
```

- Prove that the point lies on the border of the unattainable region.
(Hint: You must show that $\kappa_1^2 = 4\kappa_0\kappa_2$.)

Exercise III-10

Figure 1 shows the nine possible identity states for pairwise relatedness. For each pair of genotypes below, what are the possible Jacquard states?

Hint: Remember that IBS is not the same as IBD. For example, this implies that state 9 is always possible. (Make sure you understand this!)

- A/B and A/B
- A/A and A/B
- $13/17$ and $15/15$
- C/D and A/B

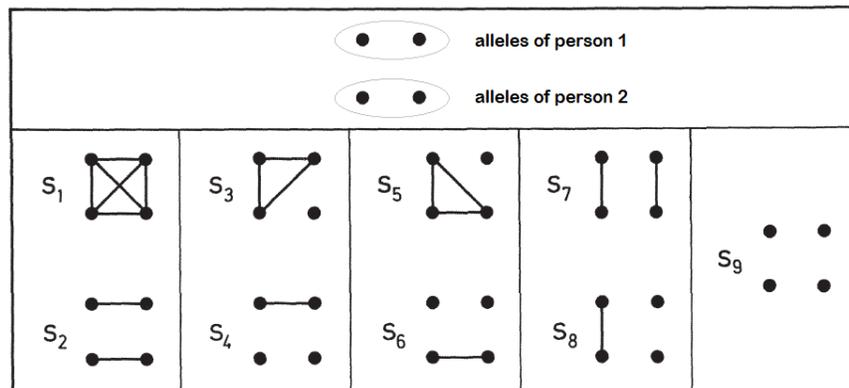


Figure 1: Jacquard's 9 condensed identity states

Exercise III-11 (Full sib mating)

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

- a) Use `ribd` to find the Jacquard coefficients of the relationship. (Hint: `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-12

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

- a) Create the pedigree in R and compute the Jacquard coefficients with `ribd`.
- b) Exactly one of the nine identity states is impossible - which is it? Try to explain in words why this state is impossible.

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

This exercise examines the Jacquard coefficients of various parent-child relationships.

- a) Recall the Jacquard coefficients between a parent and his/her child, in the absence of inbreeding.
- b) Suppose a child is inbred (i.e. the parents are related), but the parents are not themselves inbred. Which of the nine identity states are now possible between either parent and the child?
(Hint: No calculations are needed. For each of the nine states, either show that it is possible, or find a simple argument that it is not.)
- c) A man has a child by his own daughter. Compute the Jacquard coefficients of the relationship between the mother and the child.
- d) Suppose a woman has inbreeding coefficient f and has a child with a man unrelated to her. Is the child inbred? What are the Jacquard coefficients between the mother and child?

