



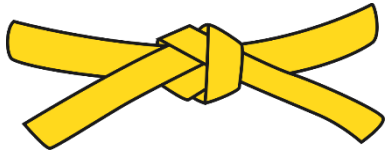
Lecture 2: Measures of relatedness

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ISFG-GHEP Online School 2024

Kinship and pedigree analysis: Methods and applications

Plan



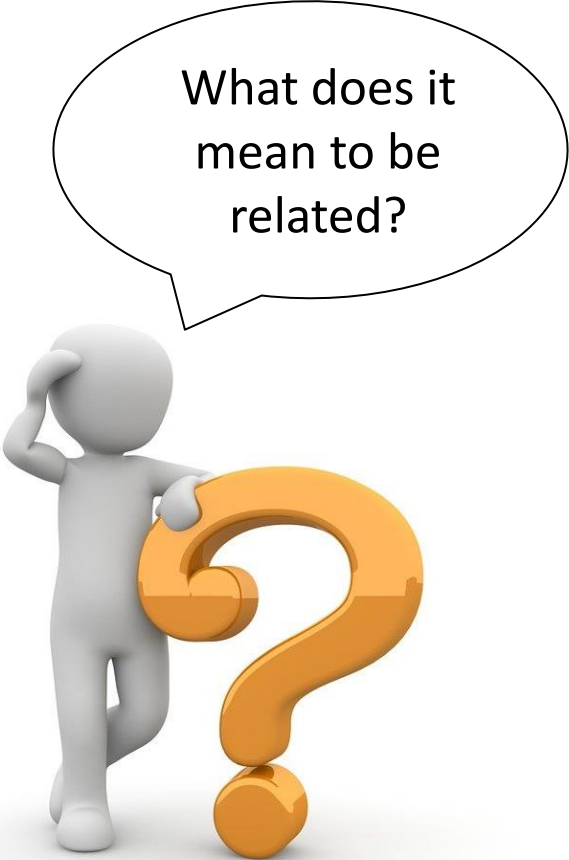
Kinship/inbreeding coefficient



IBD coefficients & IBD triangle



Jacquard's identity coefficients

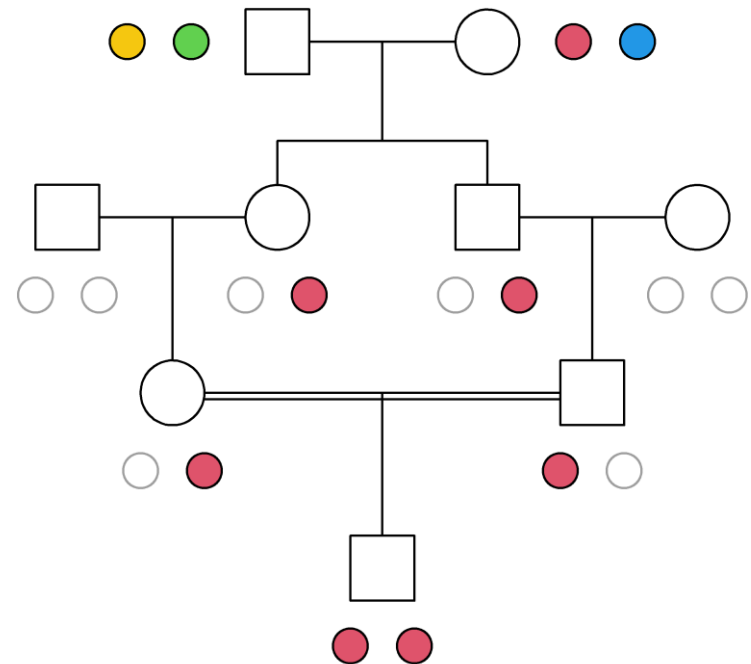


What does it
mean to be
related?

- Attempt 1
 - being connected through a pedigree
 - having a common ancestor...not too far back
- Attempt 2 - genetic
 - sharing DNA?
 - (more than unrelated people)
- To make this precise, we need some terminology!

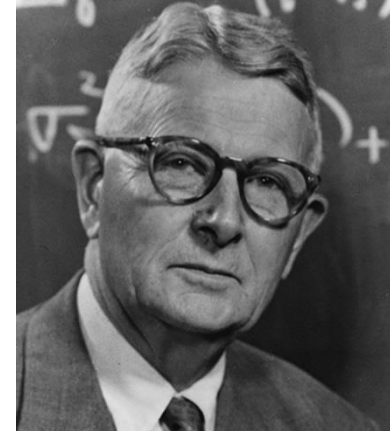
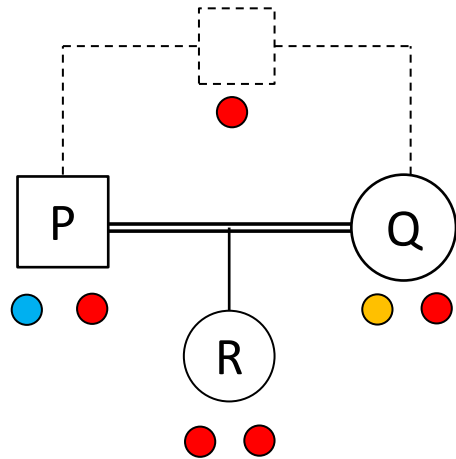
IBD and autozygosity

- IBD = **Identical by descent**
= identical alleles with a common origin **in the given pedigree**
- autozygous = homozygous + IBD



Inbreeding coefficient
 $f = P(\text{autozygosity})$

Coefficient of kinship/inbreeding



Sewall Wright
(1889 - 1988)

- Wright (1921): The kinship coefficient φ between P and Q

$$\varphi_{P,Q} = P(\text{random allele of P is IBD with random allele of Q})$$

$$= P(\text{R receive IBD alleles from her parents})$$

$$= P(\text{R is autozygous})$$

$$= f_R$$

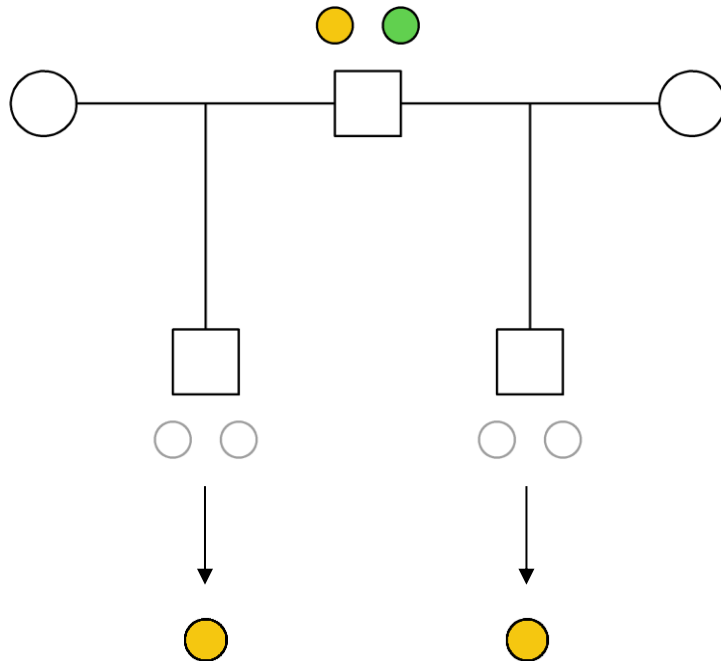
the inbreeding coefficient of R

P and Q related



$$\varphi_{P,Q} > 0$$

Example: Kinship coefficient of half siblings



Kinship coefficient

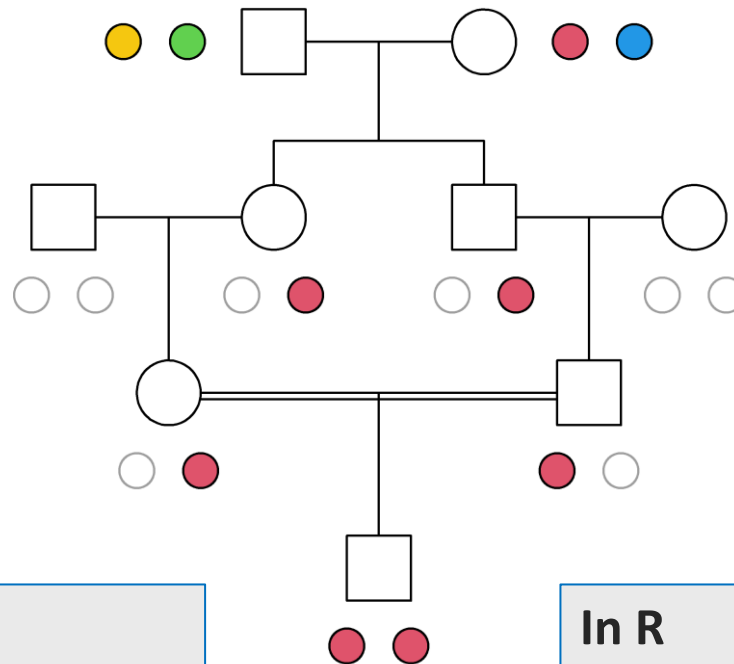
$$\begin{aligned}\varphi &= P(\text{yellow circle from both}) \cdot 2 \\ &= 0.5^4 \cdot 2 \\ &= 1/8\end{aligned}$$

↑
green

Inbreeding coefficient: Example

Wright's path formula:

$$\varphi_{P,Q} = \sum_A \sum_v \left(\frac{1}{2}\right)^{|v|+1} (1 + f_A)$$



By hand

$$\begin{aligned} f &= P(\text{red autozygous}) \cdot 4 \\ &= 0.5^6 \cdot 4 \\ &= 1/16 \end{aligned}$$

↑
other colors

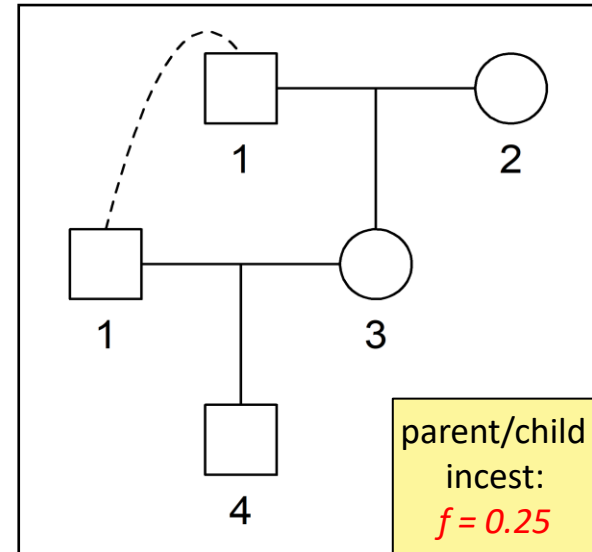
In R

```
> library(pedsuite)
> x = cousinPed(1, child = T)
> inbreeding(x, ids = 9)
[1] 0.0625
```

More kinship & inbreeding coefficients

Relationship	kinship ϕ = f of child
Parent-child	1/4
Full siblings	1/4
Half siblings	1/8
Grandparent-grandchild	1/8
Avuncular (uncle/aunt)	1/8
1st cousins	1/16
2nd cousins	1/64
3rd cousins	1/256

Challenge
Different relationships
with the same kinship!



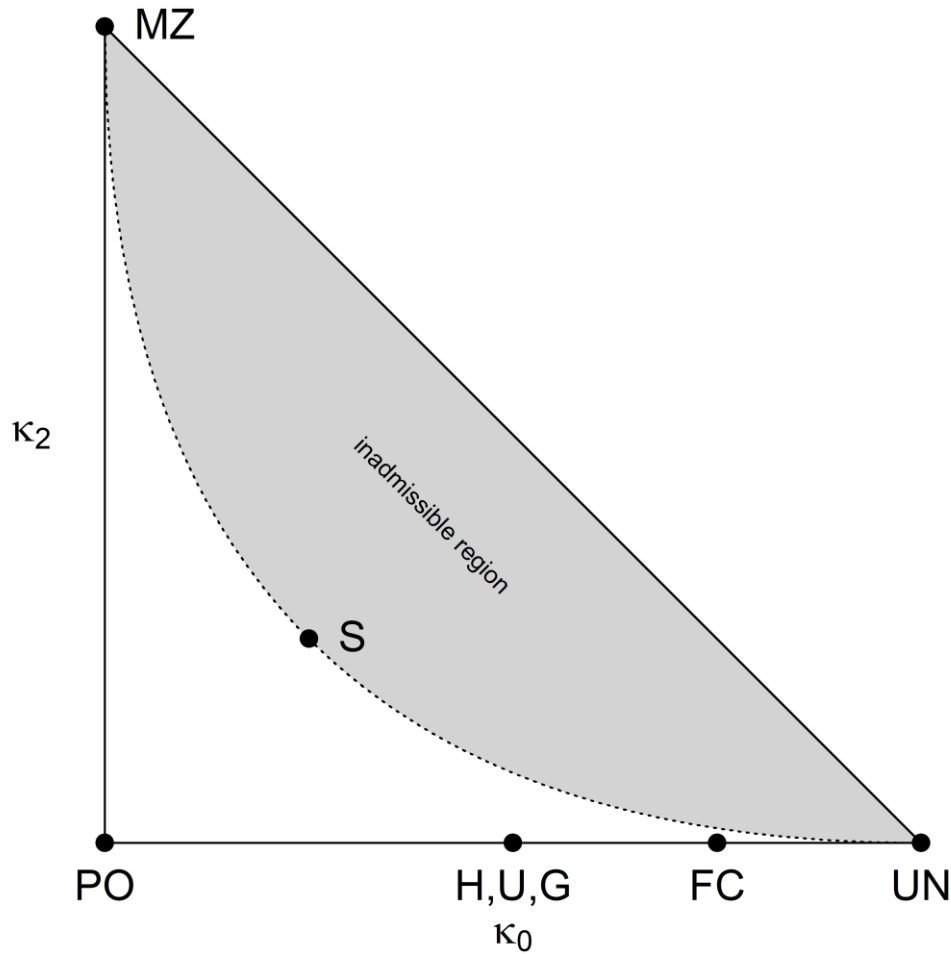
```
> x = nuclearPed(1, sex = 2) |>
  addSon(parents = c(1, 3))

> kinship(x, ids = c(1, 3))
[1] 0.25

> inbreeding(x, id = 4)
[1] 0.25
```




The IBD triangle



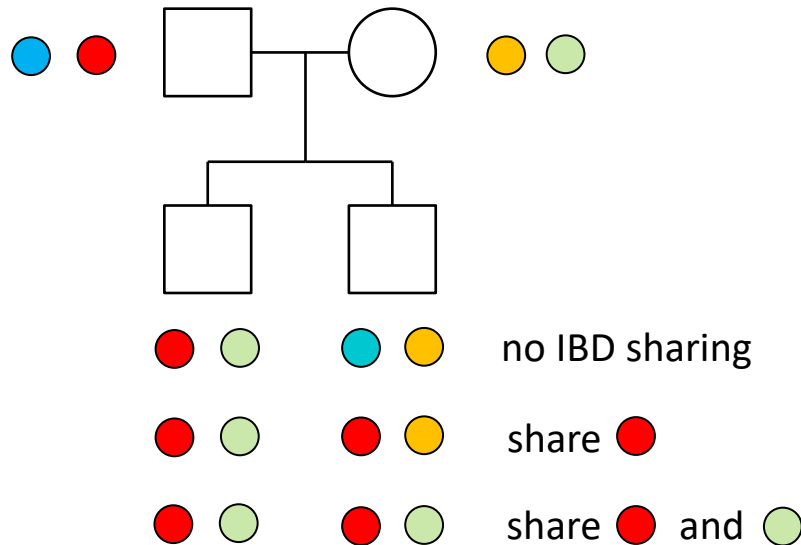
Charles Cotterman
(1914-1989)



Elisabeth Thompson
(1949 -)

IBD coefficients

- Summary so far:
 - Two individuals are related if they can have IBD alleles
 - Their kinship coefficient measures the amount of IBD sharing
- Natural generalisation:
 - How *many* alleles are IBD in each locus?

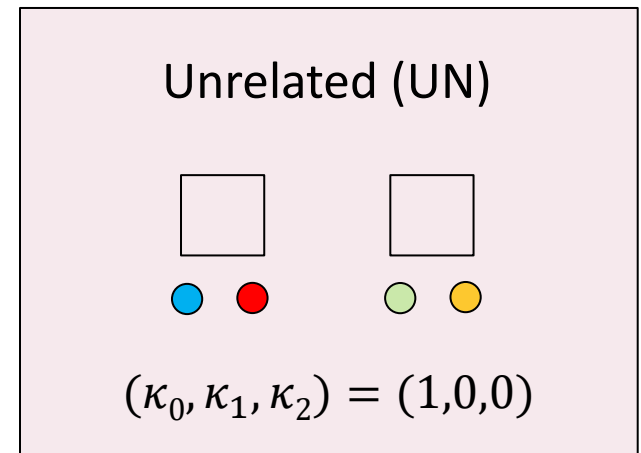
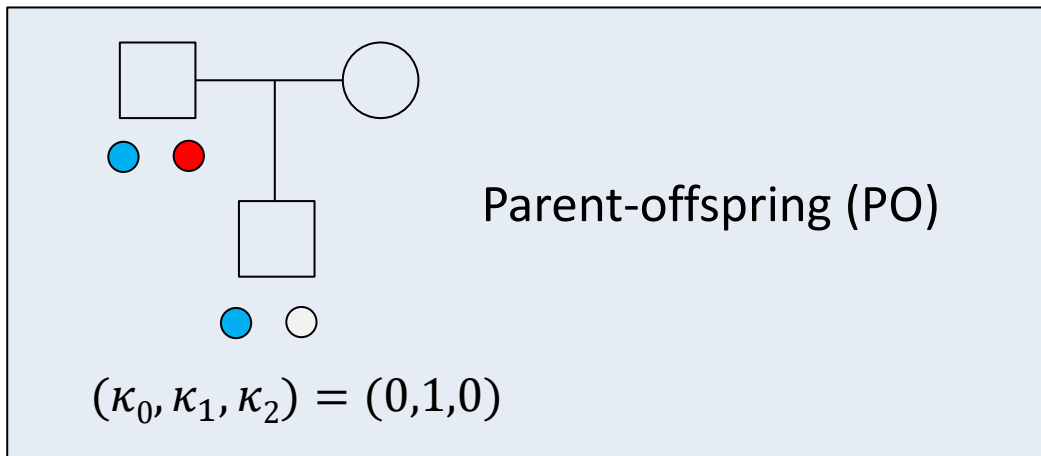
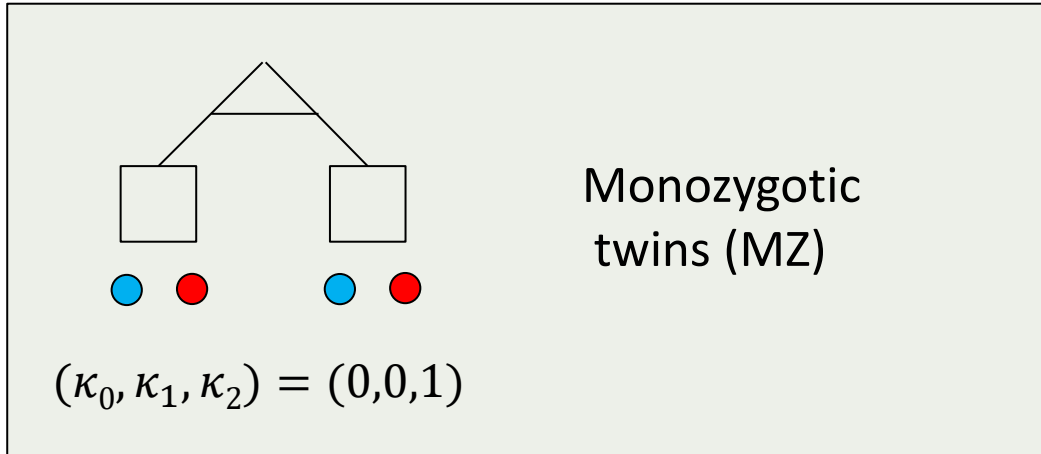


Definition

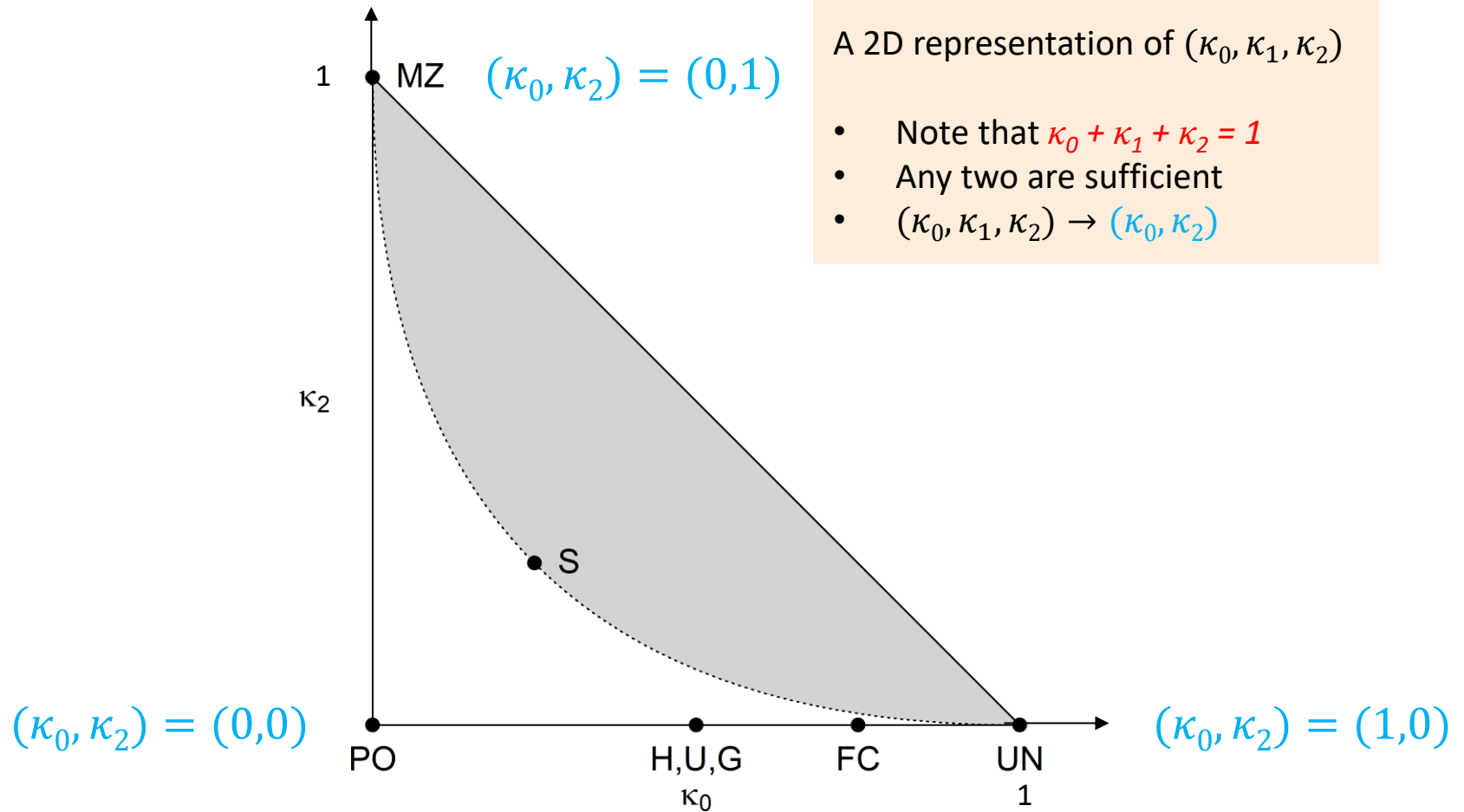
- $\kappa_0 = Pr(0 \text{ alleles IBD})$
- $\kappa_1 = Pr(1 \text{ alleles IBD})$
- $\kappa_2 = Pr(2 \text{ alleles IBD})$

(at random autosomal locus)

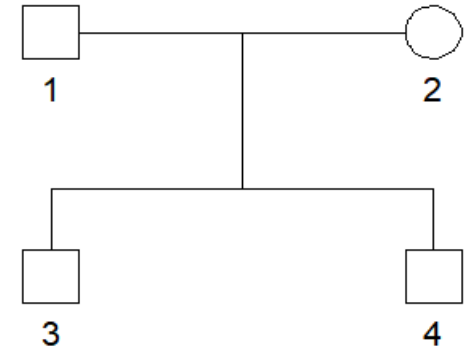
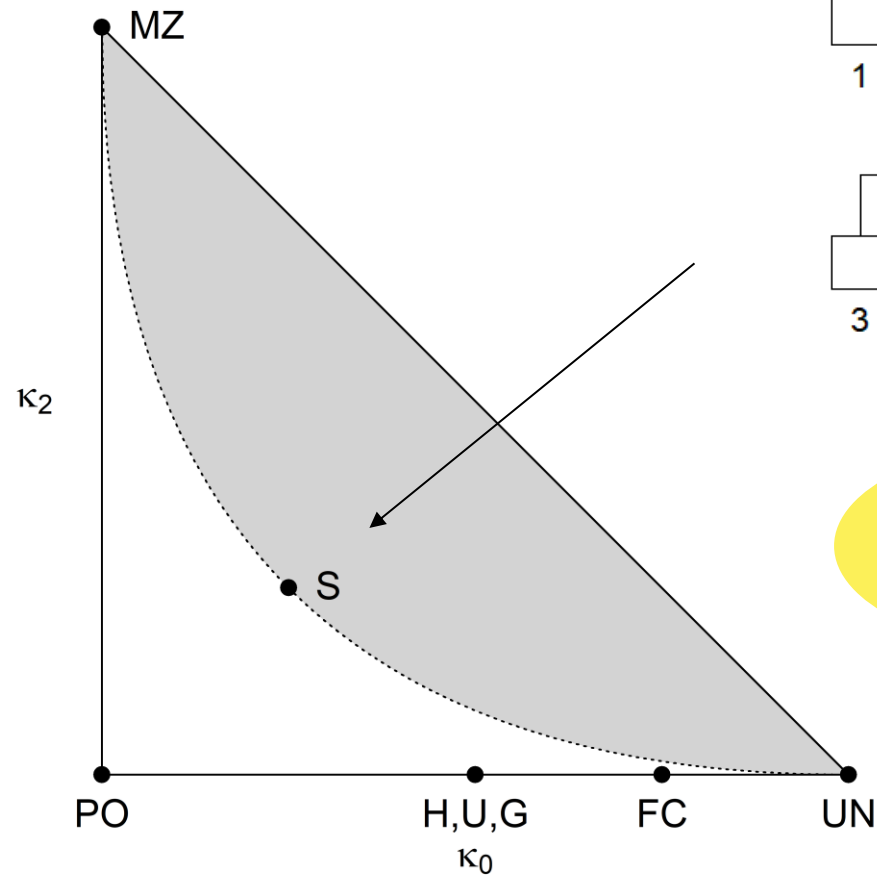
Three trivial relationships



The relatedness triangle

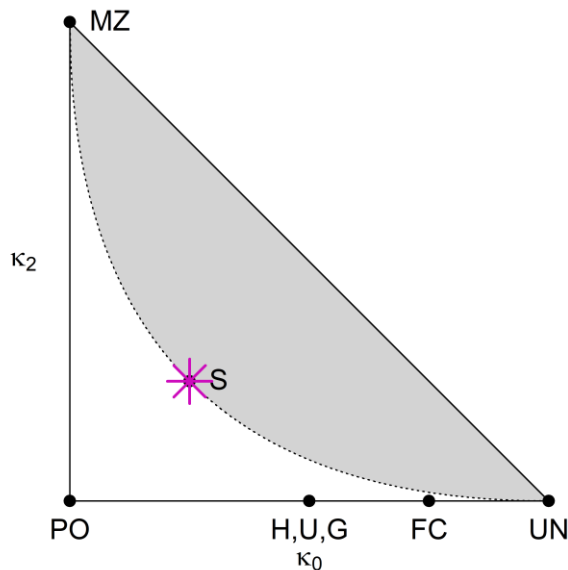
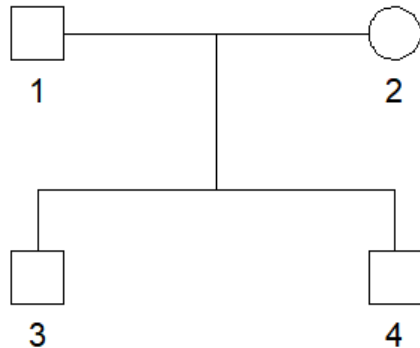
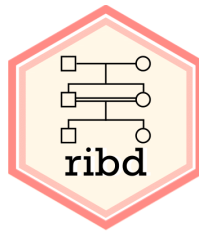


What are the coefficients of full sibs



Let's do this
in R!

ribd: Pedigree-based relatedness coefficients



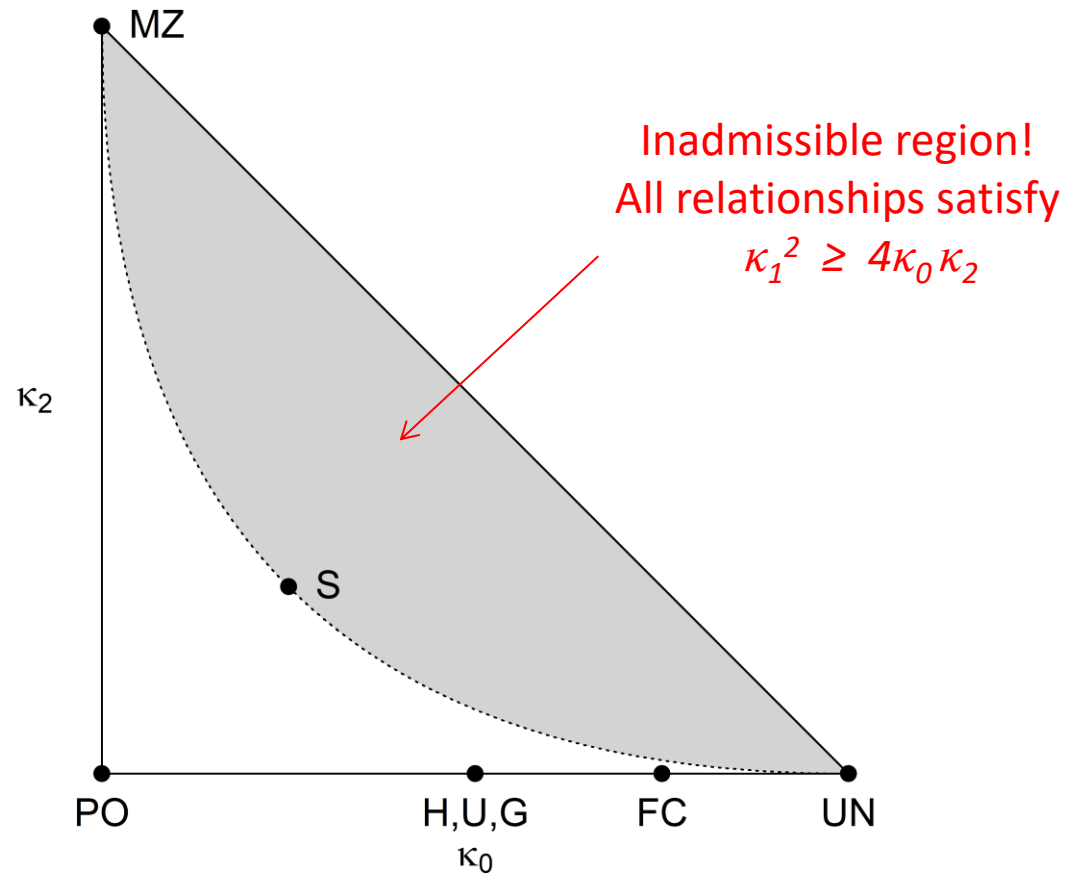
```
> library(pedsuite)
> x = nuclearPed(2)

> kinship(x, ids = 3:4)
[1] 0.25

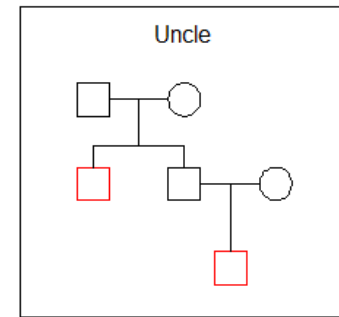
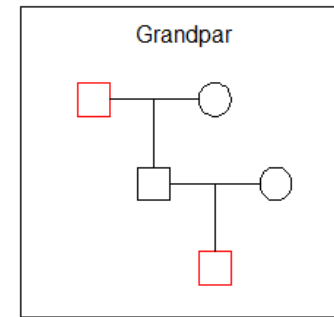
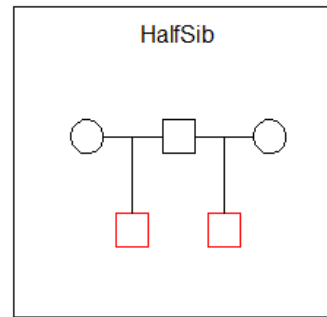
> kappaIBD(x)
id1 id2 kappa0 kappa1 kappa2
1 2 1.00 0.0 0.00
1 3 0.00 1.0 0.00
1 4 0.00 1.0 0.00
2 3 0.00 1.0 0.00
2 4 0.00 1.0 0.00
3 4 0.25 0.5 0.25

> k = kappaIBD(x, ids = 3:4)
> showInTriangle(k)
```

The relatedness triangle

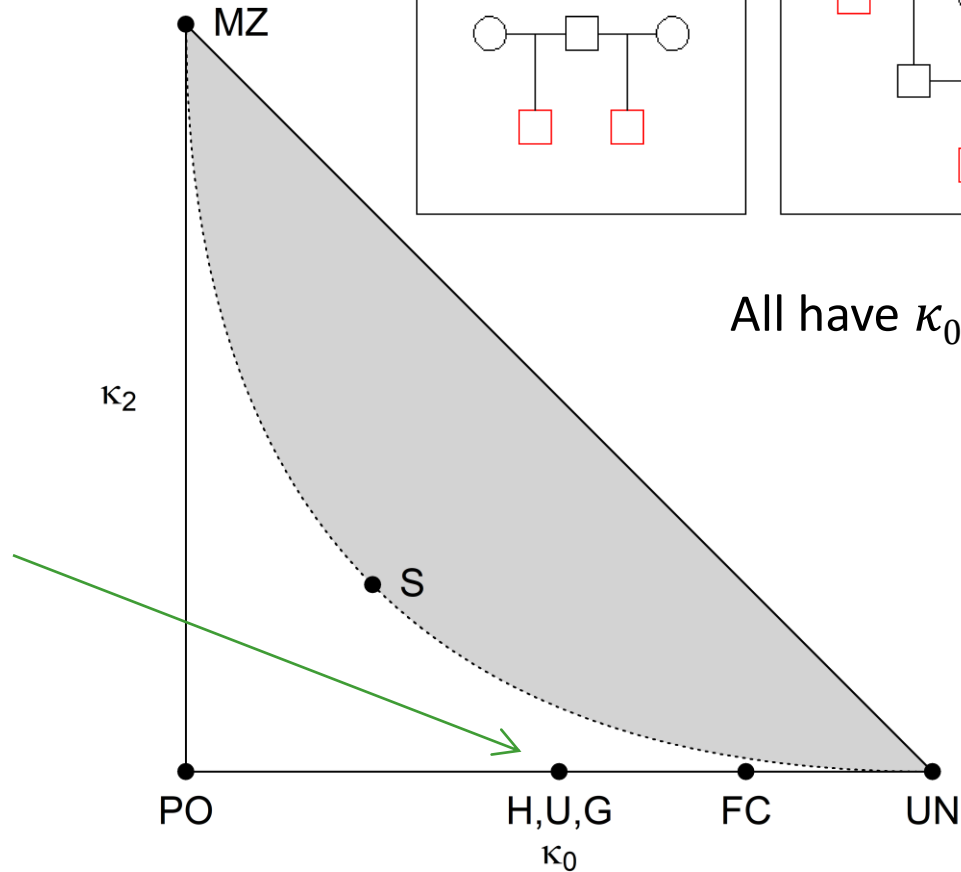


The relatedness triangle



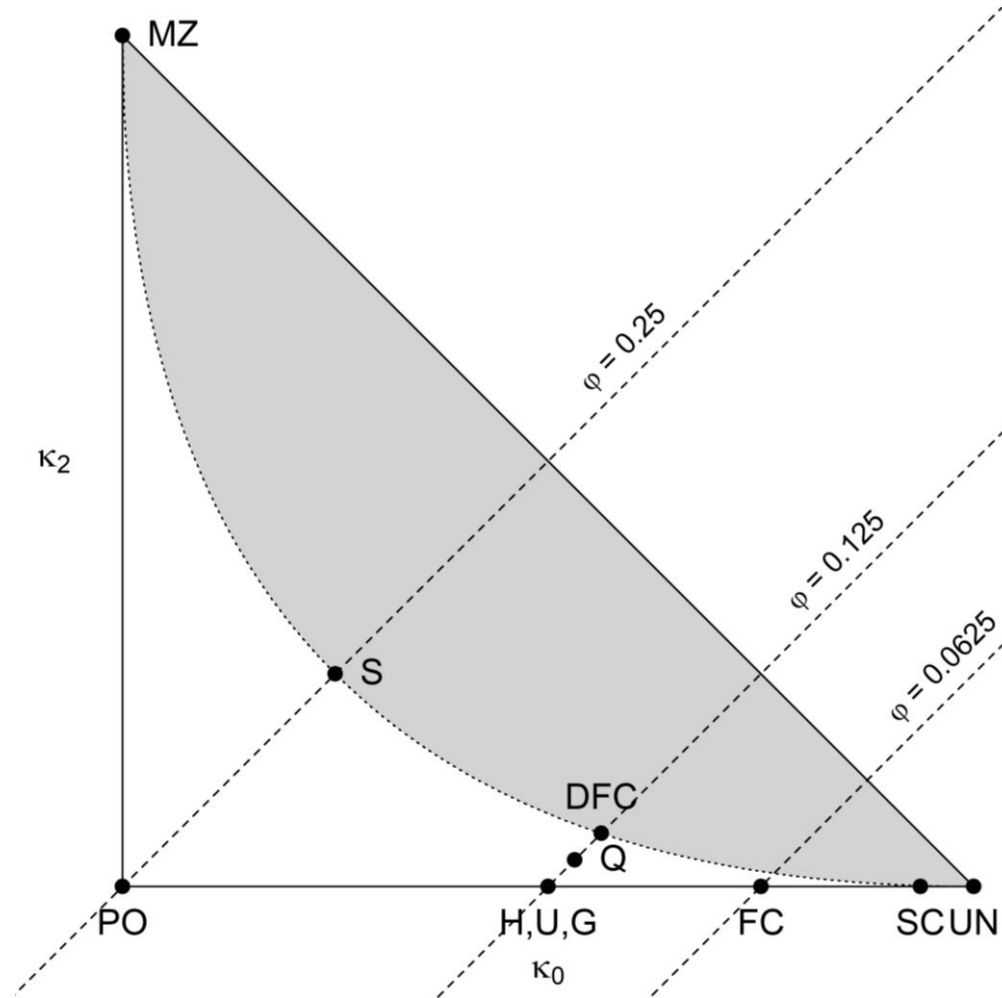
All have $\kappa_0 = \kappa_1 = \frac{1}{2}$

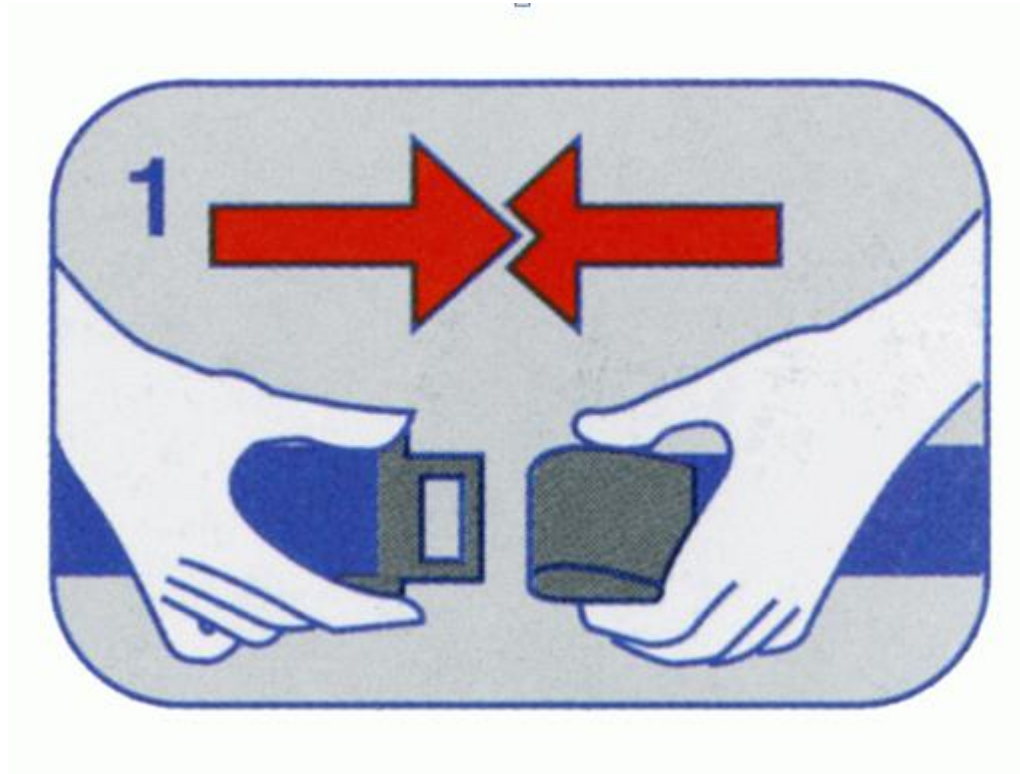
Some relationships coincide!



An important identity:

$$\varphi = \frac{1}{4}\kappa_1 + \frac{1}{2}\kappa_2$$

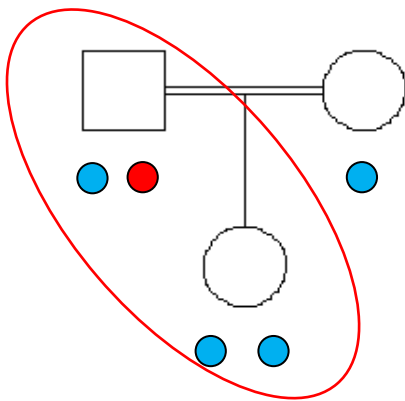




Jacquard's identity coefficients

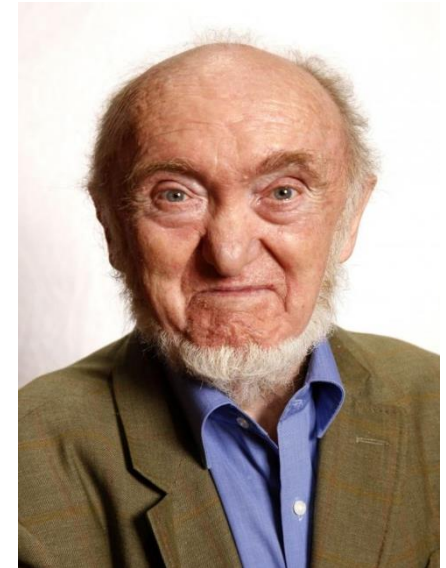
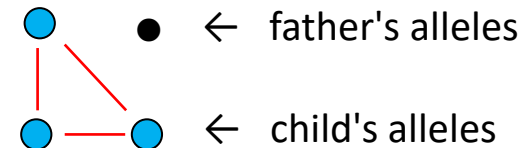


- Jacquard (1970):
 - Structures Génétiques des Populations
- Motivation: Inbred relationships
 - $\kappa_0, \kappa_1, \kappa_2$ are not well defined
- Example:



What's the IBD status here? 1 or 2?
Cannot be summarised in one number!

Configuration:

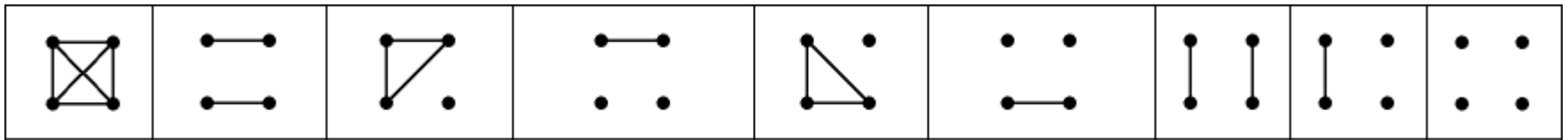


Albert Jacquard
(1925 - 2013)

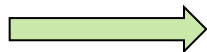
Jacquard's 9 coefficients

- Two individuals, two alleles each:
 - • ← alleles of individual 1
 - • ← alleles of individual 2

9 possible IBD configurations:



- Any pairwise relationship can be summarised by the relative frequencies of these



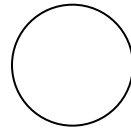
Jacquard's *condensed identity coefficients*:

$$\Delta_1, \Delta_2, \dots, \Delta_9$$

If no inbreeding: kappa!



A/B



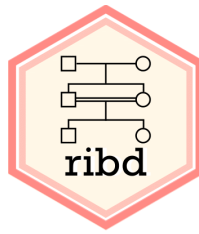
C/D

0	0	0	0	0	0	κ_2	κ_1	κ_0

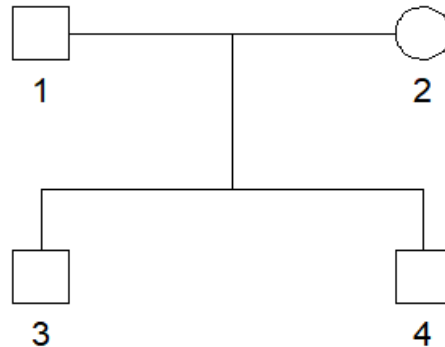


- • ← alleles of individual 1
- • ← alleles of individual 2

Try it out!



```
> library(pedsuite)
> x = nuclearPed(2)
> plot(x)
```



```
> inbreeding(x)
  1  2  3  4
  0  0  0  0
```

```
> kinship(x)
      1  2  3  4
1  0.50 0.00 0.25 0.25
2  0.00 0.50 0.25 0.25
3  0.25 0.25 0.50 0.25
4  0.25 0.25 0.25 0.50
```

```
> kappaIBD(x)
id1 id2 kappa0 kappa1 kappa2
  1  2  1.00  0.0  0.00
  1  3  0.00  1.0  0.00
  1  4  0.00  1.0  0.00
  2  3  0.00  1.0  0.00
  2  4  0.00  1.0  0.00
  3  4  0.25  0.5  0.25
```


```
> identityCoefs(x)
id1 id2 D1 D2 D3 D4 D5 D6 D7 D8 D9
  1  2  0  0  0  0  0  0  0.00 0.0 1.00
  1  3  0  0  0  0  0  0  0.00 1.0 0.00
  1  4  0  0  0  0  0  0  0.00 1.0 0.00
  2  3  0  0  0  0  0  0  0.00 1.0 0.00
  2  4  0  0  0  0  0  0  0.00 1.0 0.00
  3  4  0  0  0  0  0  0  0.25 0.5 0.25
```

QuickPed: An Interactive Pedigree Creator

New app design!

Discover the **new features**
Or stay with the old version: QuickPed3

Purpose: QuickPed lets you rapidly create attractive pedigree plots, save them as images or text files, and analyse the relationships within them.

Instructions: Choose a suitable start pedigree and modify it by clicking on individuals and using appropriate buttons. For example, to add a male child, select the parent(s) and press the  icon. Check out the [online user manual](#) for various tips and tricks, including an introduction to relatedness coefficients.

Citation: If you use QuickPed in a publication, please cite this paper: Vigeland MD (2022). QuickPed: an online tool for drawing pedigrees and analysing relatedness. *BMC Bioinformatics*, 23. DOI:10.1186/s12859-022-04759-y.


Quick start

Built-in pedigree

Trio ▼

or

Load a ped file



or

Random pedigree

Reset all

Modify

Add



Sex



Style



Fill



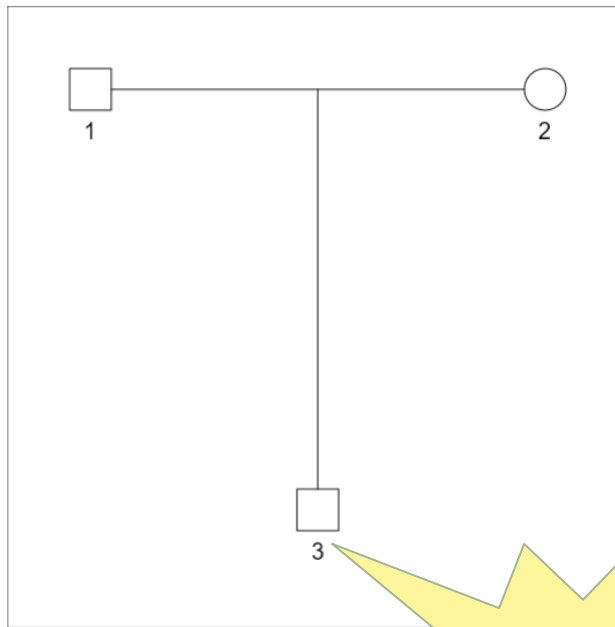
Twins

MZ / DZ

Remove



Undo



Double-click on an individual to add text



Labels

1, 2, 3, .. I-1, I-2, ..

Show all Hide all

1

2

3

Update

Plot settings

Width Height

430 430

Cex Symbols

1,4 1

Margins

3

Other options (beta)

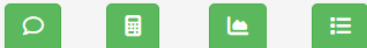
- Straight legs
- Arrows

R code

 PNG

 PDF

Relationships



Coefficients!

Ped file

Include

- Headers
- Family ID
- Affection status

 Save ped file