ISFG-GHEP Online School 2024
October 7, 14, **21**, 28

Kinship and pedigree analysis: Methods and applications

Teachers

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Schedule

The course runs each Monday of October 2024, from 16 to 20 (CEST). The following schedule is tentative:

Oct 7: Theory of relatedness

- 16:00–17:00 **Introduction to pedigrees, QuickPed and R** (MDV)
- 17:00–17:45 Exercises I. (Solutions)
- 17:45–18:00 *Break*
- 18:00–19:00 **Measures of relatedness** (MDV)
- 19:00–19:45 Exercises II. (Solutions)
- 19:45–20:00 Wrap-up

Oct 14: Kinship testing

- 16:00–17:00 **Introduction to forensic kinship testing** (TE)
- 17:00–17:45 Exercises III. (Solutions)
- 17:45–18:00 *Break*
- 18:00–19:00 **Kinship testing with Familias** (TE)
- 19:00–19:45 Exercises IV. File needed: kinship-riddle.fam. (Solutions)
- 19:45–20:00 Wrap-up

Oct 21: Relatedness inference

- 16:00–17:00 **Realised relatedness: Why are some siblings more alike than others?** (MDV)
- 17:00–17:45 Exercises V
- 17:45–18:00 *Break*
- 18:00–19:00 **Pedigree reconstruction** (MDV)
- 19:00–19:45 Exercises VI
- 19:45–20:00 Wrap-up

Oct 28: Disaster victim identification

- 16:00–17:00 **DNA-based disaster victim identification** (TE)
- 17:00–17:45 Exercises VII
- 17:45–18:00 *Break*
- 18:00–19:00 **Practical DVI with Diviana** (MDV)
- 19:00–19:45 Exercises VIII
- 19:45–20:00 Wrap-up

Home page
https://magnusdv.github.io/pedsuite/articles/web_only/course-ghep2024.html
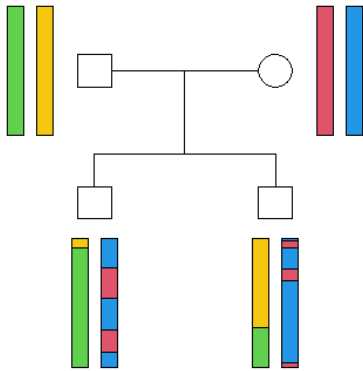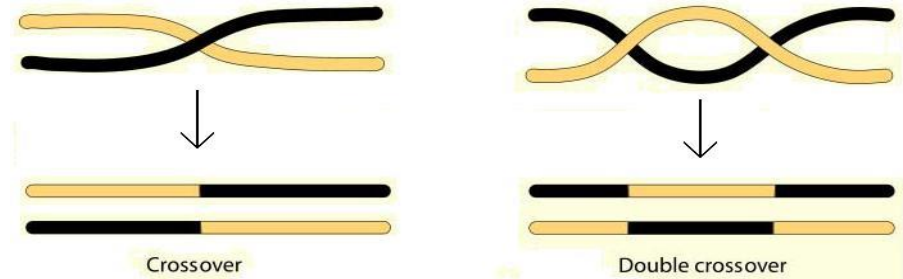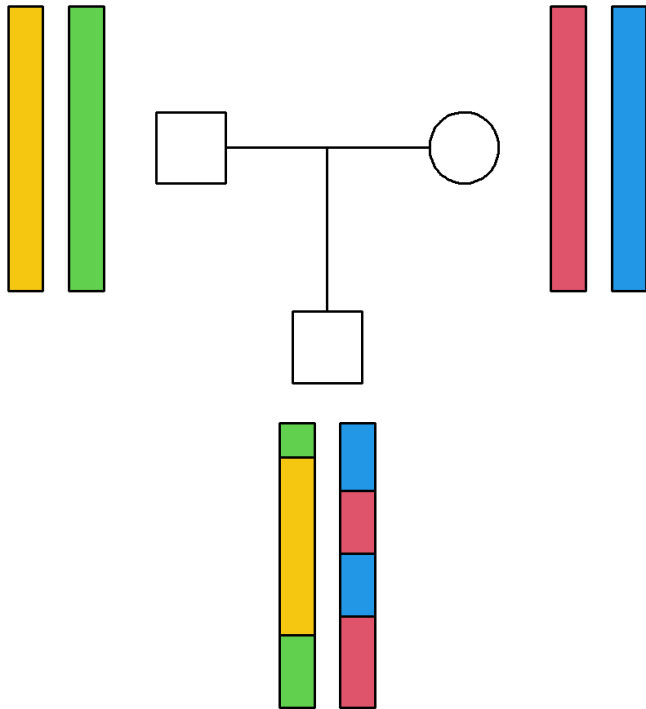
Lecture 5: Realised relatedness
or
Why are some siblings more alike than others?
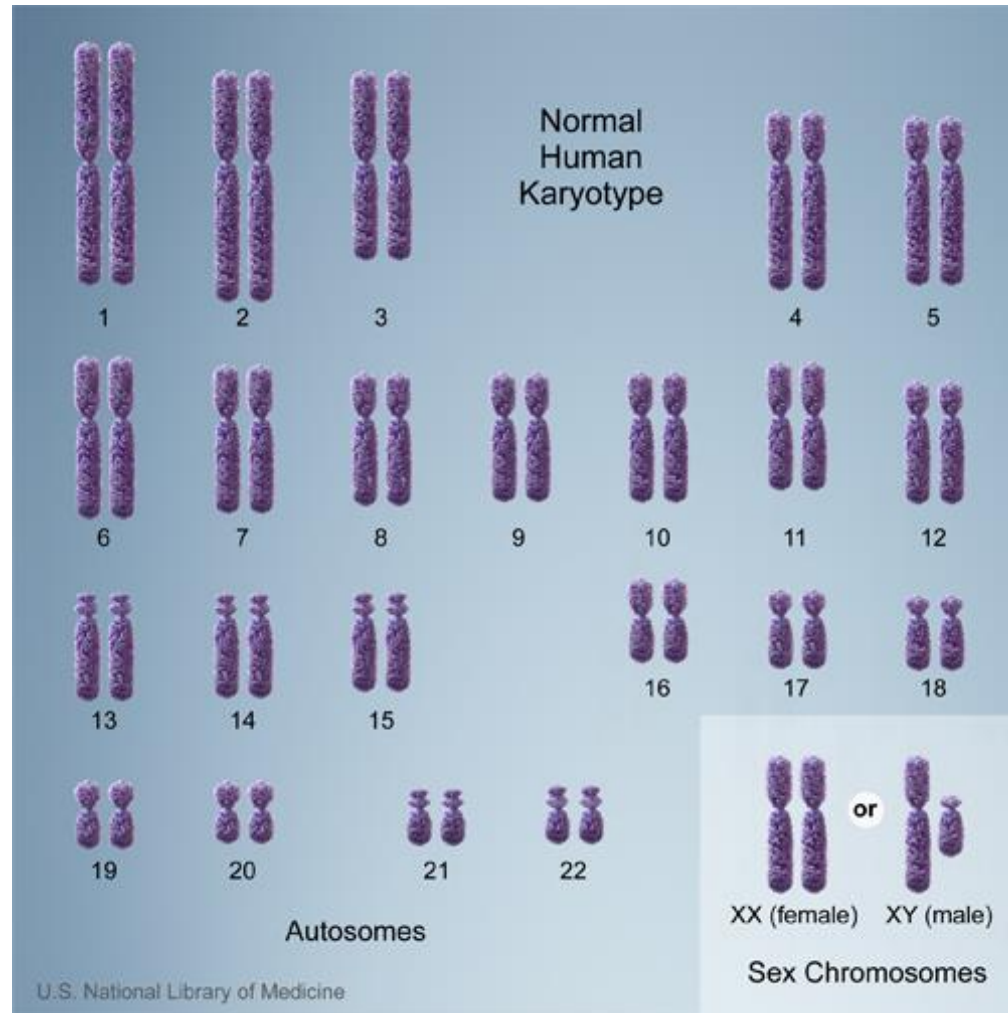
Magnus Dehli Vigeland

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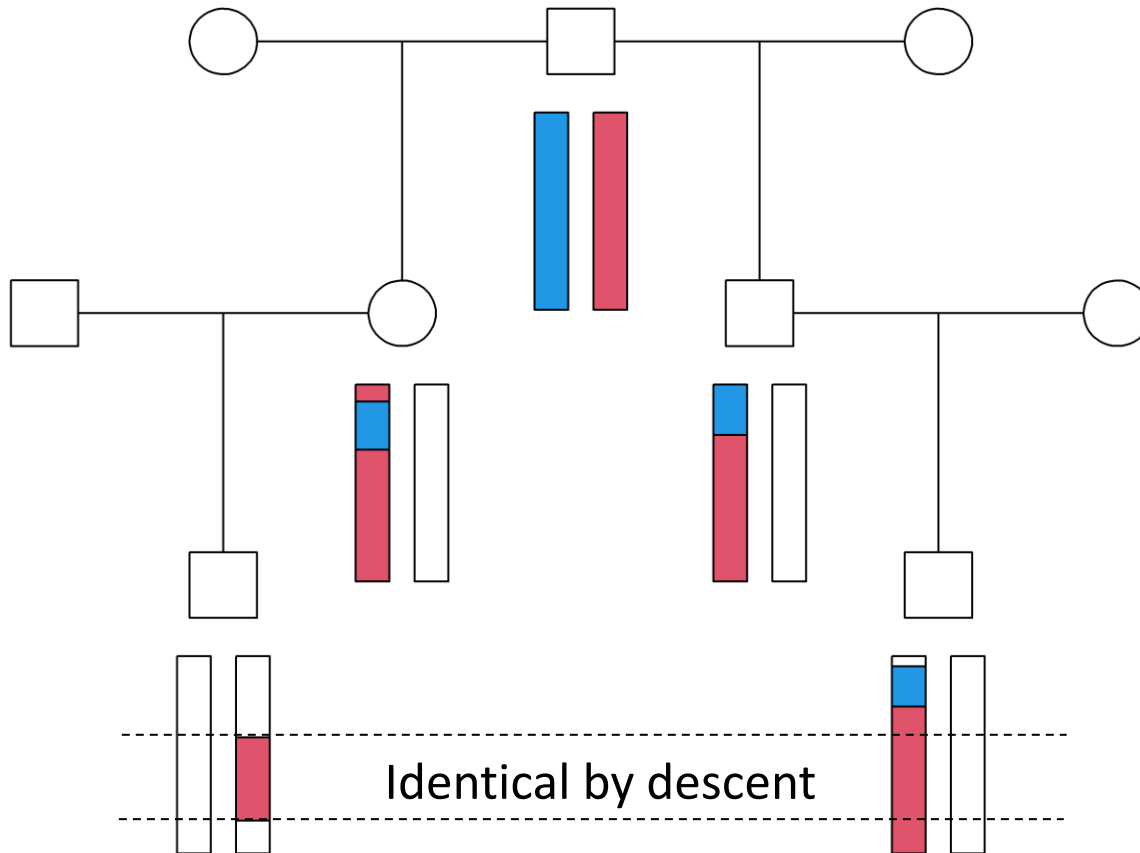**Kinship and pedigree analysis: Methods and applications**

Meiotic recombination

Crossover
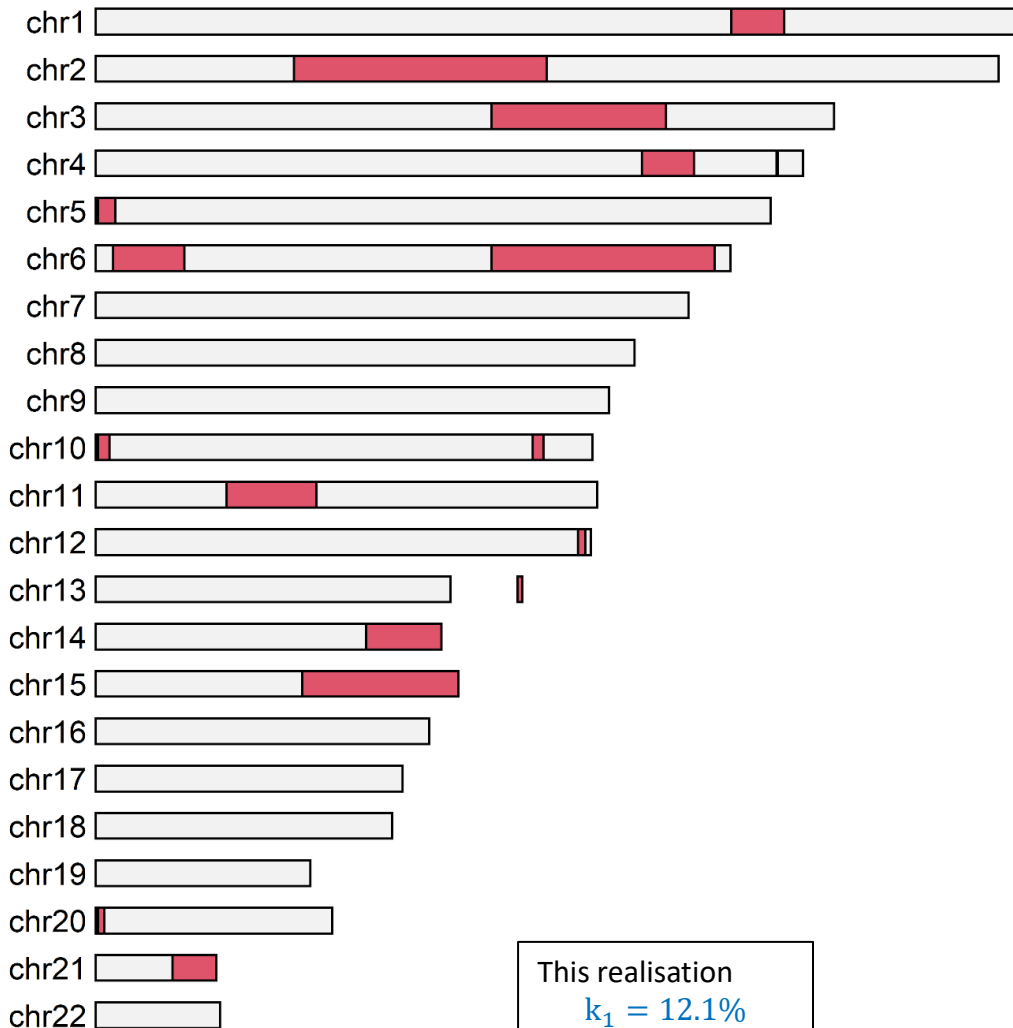
Double crossover

- **Genetic distance** between two loci:
  = *average # crossovers per meiosis*

- Units:
  - 1 Morgan (M) = 1 crossover per meiosis
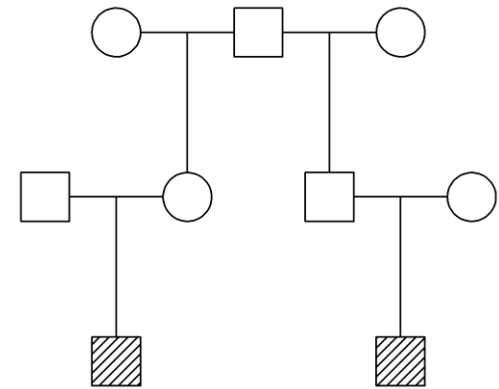 - 1 centiMorgan (cM) = 0.01 M

- The human genome: Ca 30 Morgan

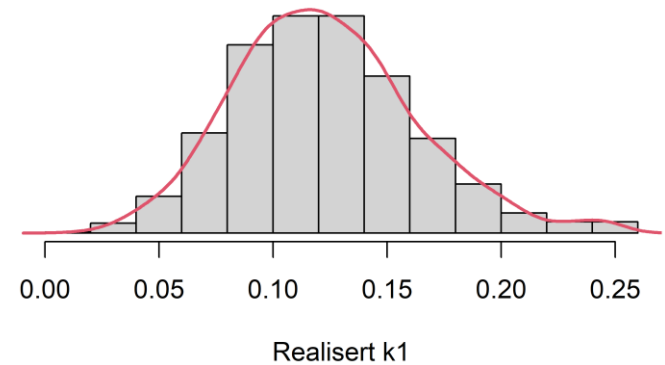# Rule of thumb: One crossover per chromosome arm

Identical by descent

chr1, chr2, chr3, chr4, chr5, chr6, chr7, chr8, chr9, chr10, chr11, chr12, chr13, chr14, chr15, chr16, chr17, chr18, chr19, chr20, chr21, chr22
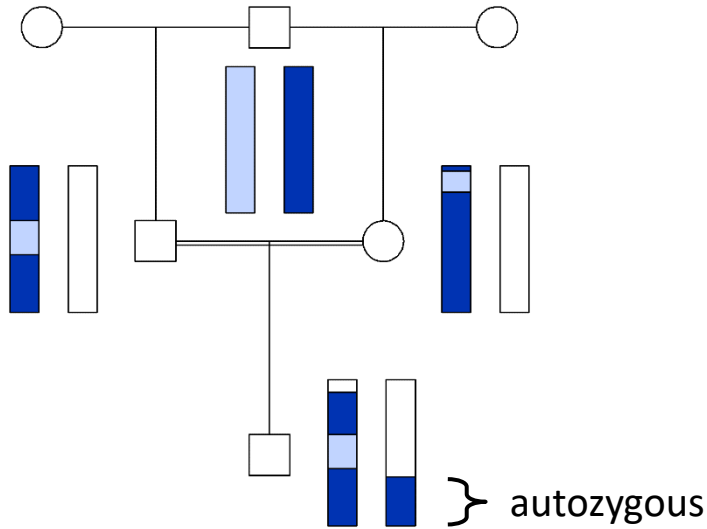
This realisation
$k_1 = 12.1\%$

Half first cousins, expected sharing:

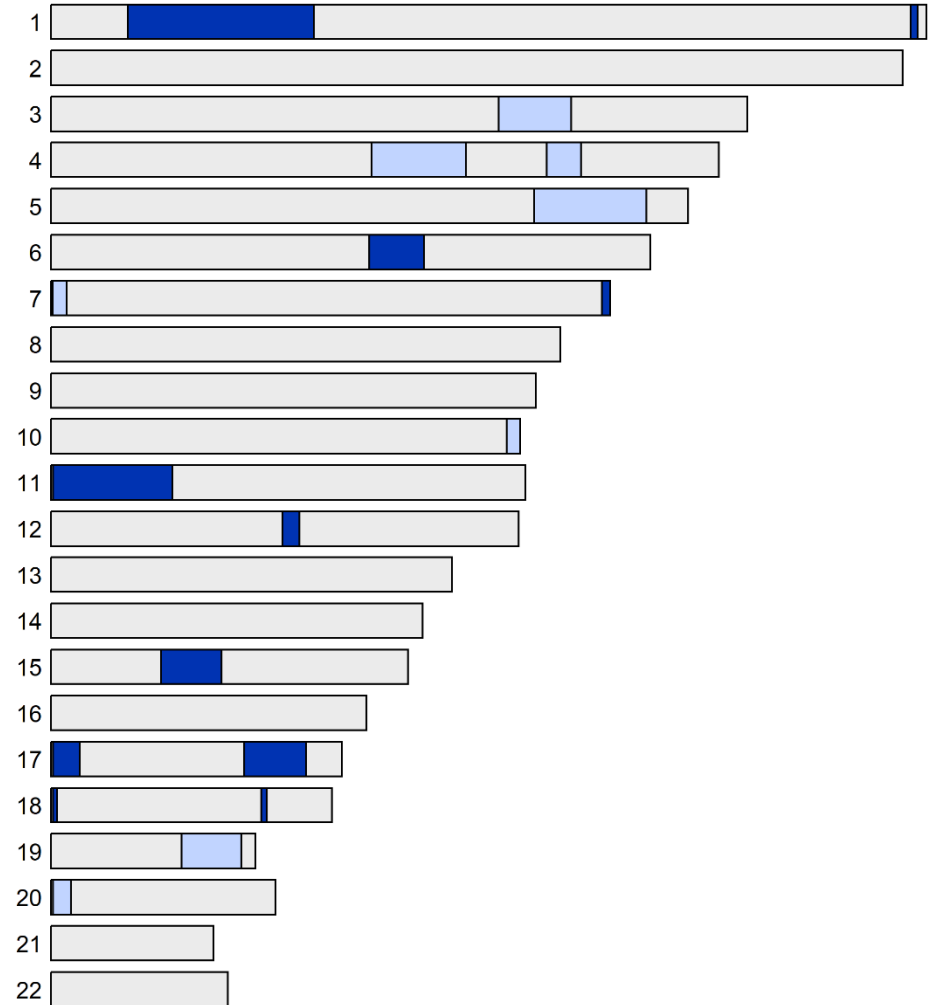$$\kappa_1 = 2 \cdot \left(\tfrac{1}{2}\right)^4 = \frac{1}{8} = 12.5\%$$

Realisert k1

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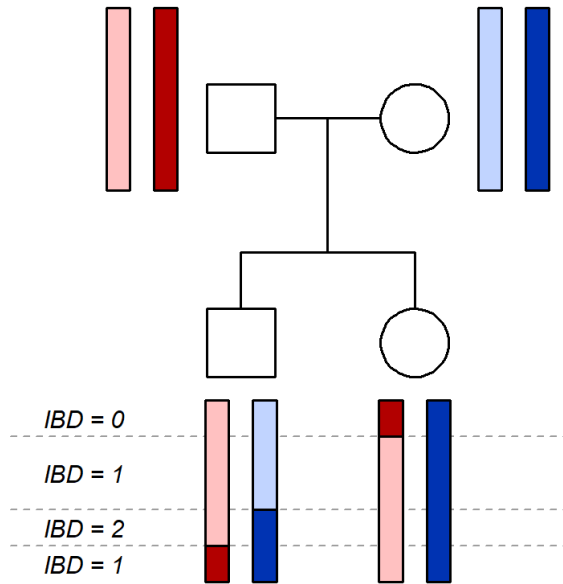
Realised inbreeding

Autozygous segments

autozygous

f_R = autozygous fraction of genome

500 sims

Expected value:
$f = 1/8$
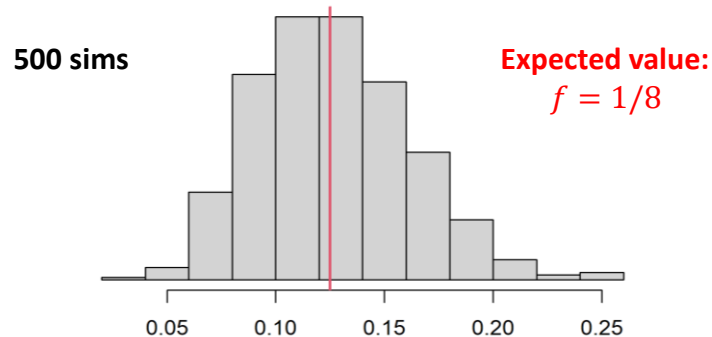
Realised IBD coefficients

Realised IBD coefficients:
Proportions of genome with IBD = 0, 1, 2

IBD = 0

IBD = 1

IBD = 2

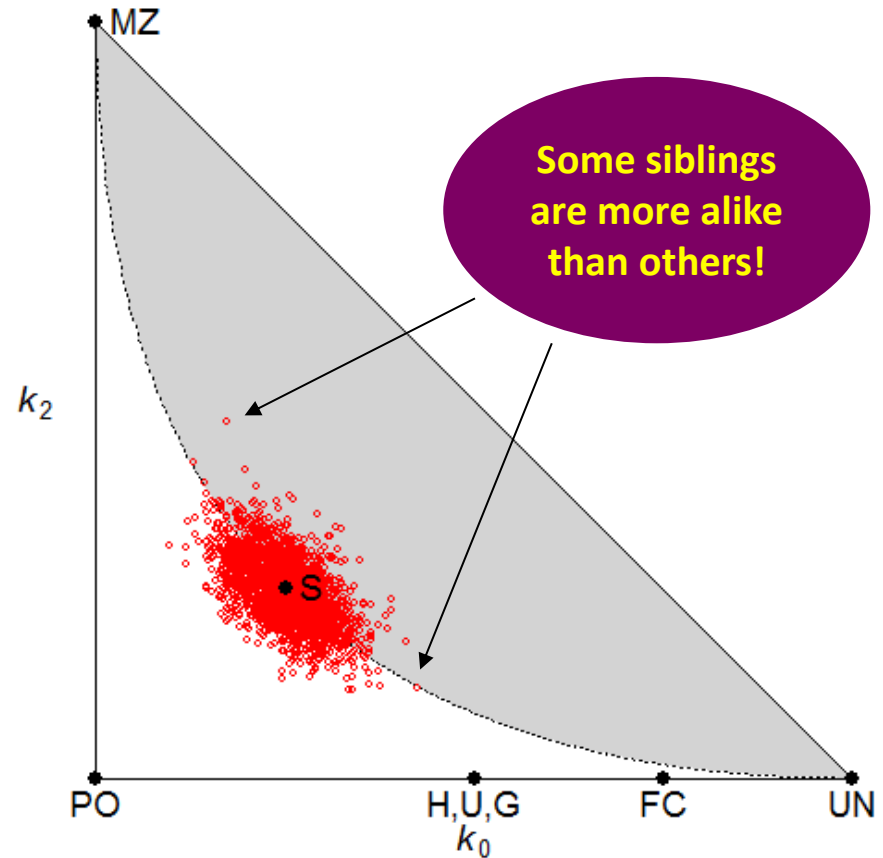IBD = 1
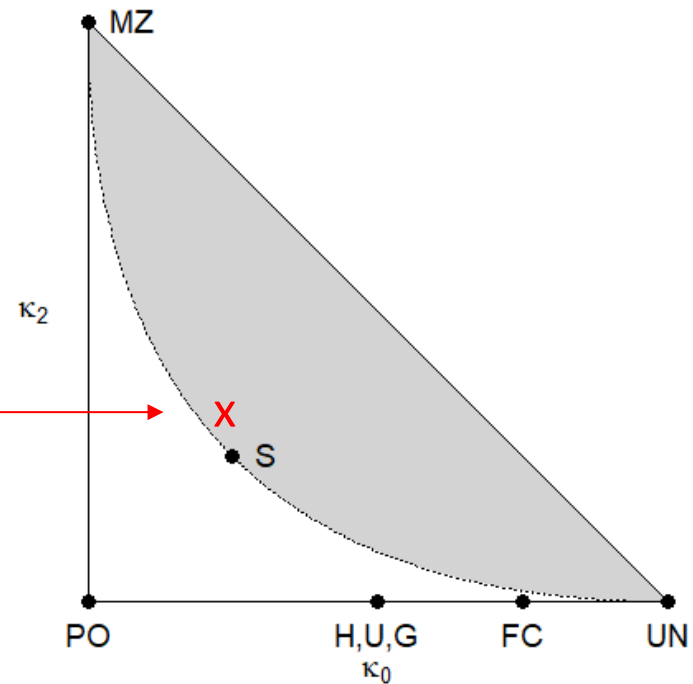
Variation in realised IBD coefficients
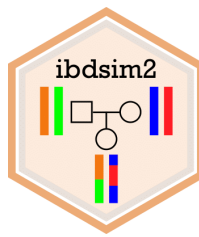
1000 simulations
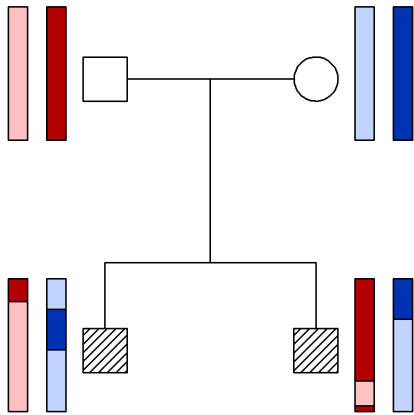

```
> library(pedsuite)
> library(ibdsim2)

> x = nuclearPed(2)
> s = ibdsim(x, N = 1000)
> k = realisedKappa(s, ids = 3:4)

> showInTriangle(k)
```
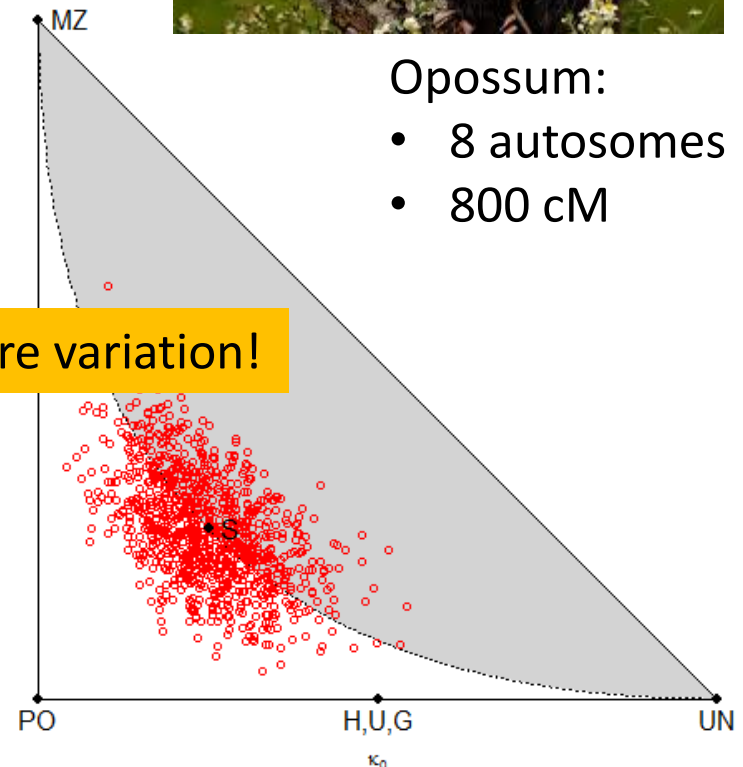
Some siblings are more alike than others!
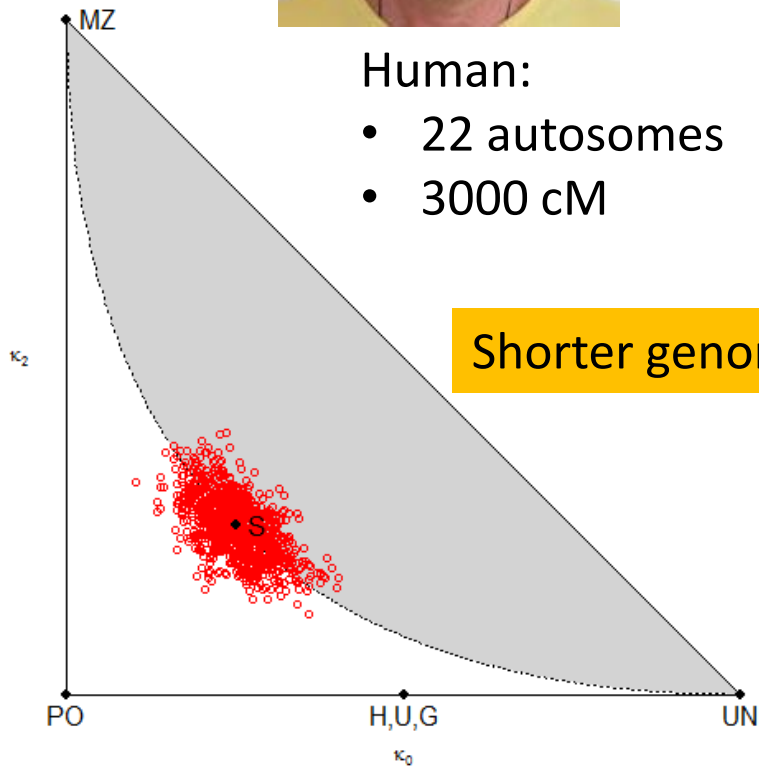
Variation depends on the genome

Human:
- 22 autosomes
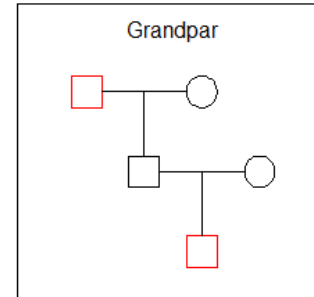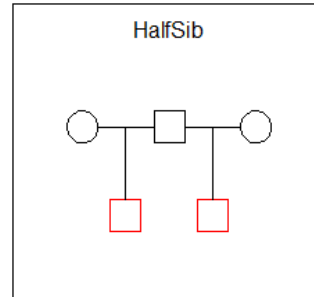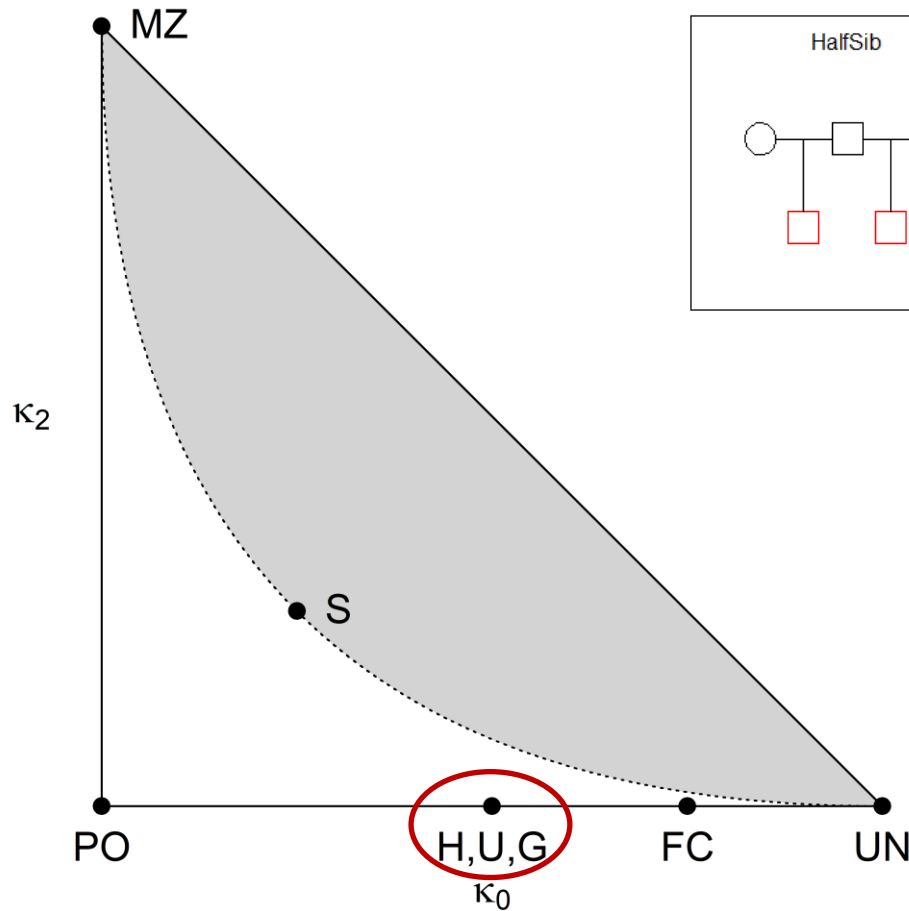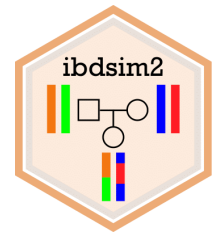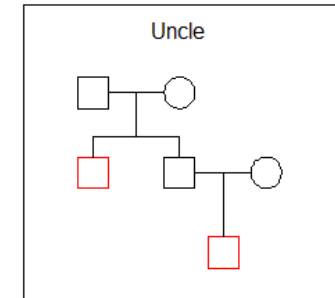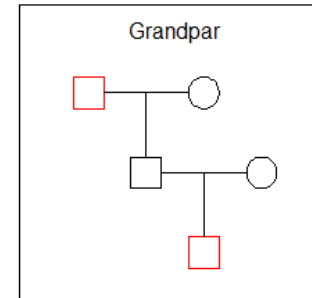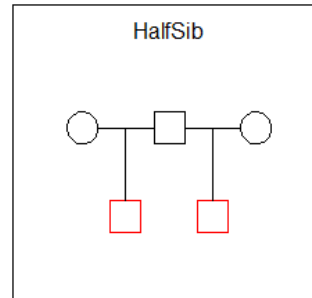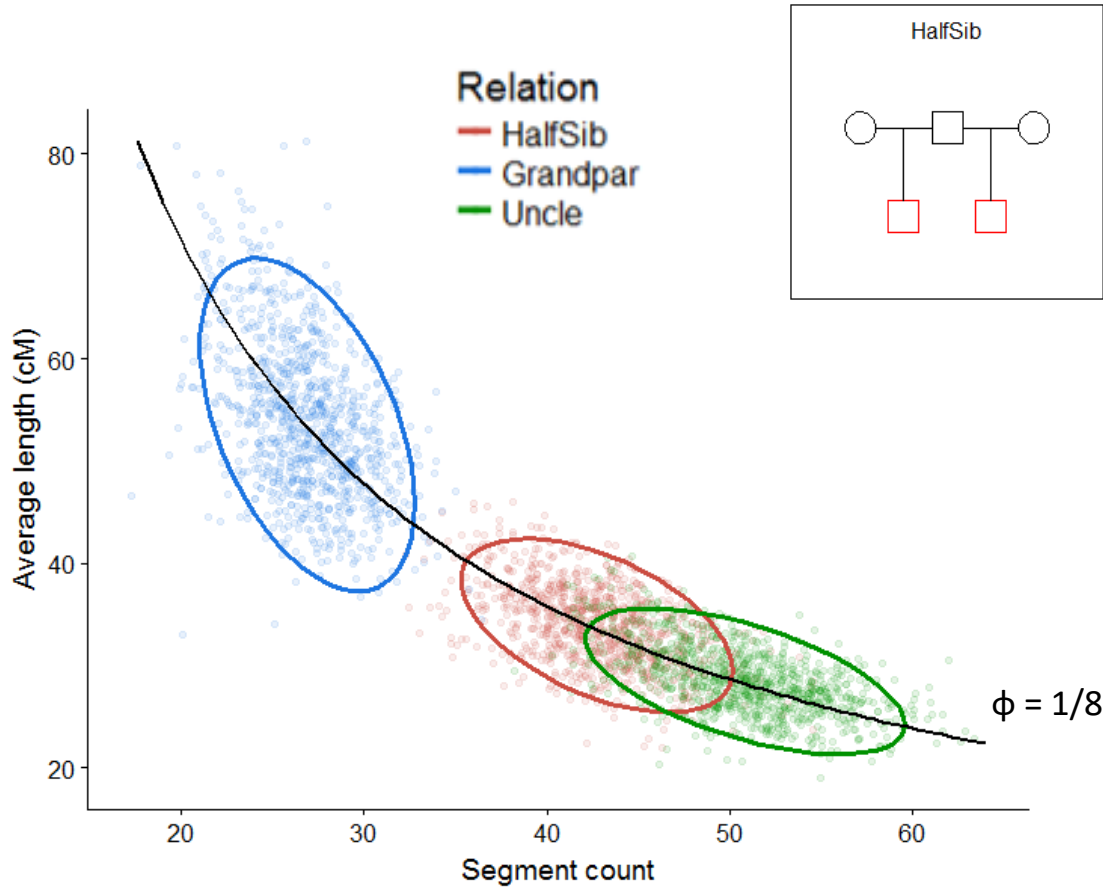- 3000 cM

Opossum:
- 8 autosomes
- 800 cM

Shorter genome = more variation!

Indistinguishable relationships?

$$\kappa_0 = 0.5$$
$$\kappa_1 = 0.5$$
$$\kappa_2 = 0$$
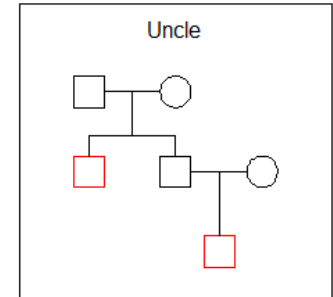
Simulated IBD distributions
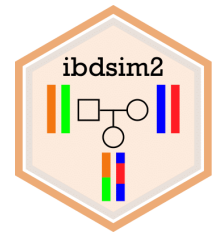
In theory distinguishable with linked markers!

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Let's not forget – Prince Harry and Meghan Markle are actually (very) distant) cousins

Richard Hartley-Parkinson for Metro.co.uk Monday 27 Nov 2017 11:35 am

18.8k

FASHION

CULTURE

FASHION | BEAUTY | GIFT GU

Ou, Awkward…Meghan Markle and Prince Harry are Apparently Related

By Meghan McKenna   Date November 2, 2017

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res | Most read | Wires | Disc

STJERNEPAR: Meghan Markle og prins Harry viser endelig kjærligheten sin offentlig, etter å ha holdt forholdet svært privat i lang tid. Nå kommer det frem at paret, som er fra to forskjellige kontinenter, faktisk er i slekt. Foto: NTB scanpix

Prins Harry er i slekt med kjæresten

SE OG HØR

SPIELE | NEWSLETTER | VIDEO | GEWINNSPIELE | FORUM | F-MAG | ACADEMY | SHOPPING | ABC

Aktuell | Mode | Beauty | Rezepte | Gesund | Liebe | Familie | Leben | Horo

Brigitte → Aktuell → Stars und TV → Meghan Markle und Prinz Harry sind "verwandt"

Stammbaum erforscht: Prinz Harry und Meghan Markle sind Cousins!

1.1K
shares

View o

niversitetssykehus

(Picture: Mail Online)

Ralph BOWES
(1480–1516)
of Streatlam, Co Durham
High Sheriff

14 15

GRANDCHILDREN

Sir George BOWES
Loyal to Queen Elizabeth I
during the rising of the North, 1596

Bridget BOWES
Married John Hussey
of Dorking

13 13

GRANDSON

Captain Christopher HUSSEY
(1598/9–1686)
A founder of Nantucket, Massachusetts

11

GREAT-GRANDSON

Sir William BOWES MP
(1657–1707)
During reign of Charles II
Royalist

10

Huldah HUSSEY
(1643–1740)
Married Lieutenant John SMITH

10

Sir George BOWES MP

9 9

Ma

8

Married J   art

P(any IBD) ≈ 0

FOUR

Claude George
(1854–19   )
14th Earl of Strathm

4   Lee MERRILL   5

George David MERRILL
(1861–1924)

3

Lady Elizabeth BOWES LYON
(1900–2001)
HM Queen Elizabeth
The Queen Mother

4

Gertrude May MERRILL
(1887–1938)
Married Frederick George SANDERS

3

HM The Queen
(1926–   )

2

Doris SANDERS
(1921–   )
Married Gordon Arnold Markle

2

Lady Diana Spencer
(1961–1997)

HRH Prince of Wales
(1948–   )

Thomas Wayne Markle
(1944–   )

Doria L. Ragland
(1956–   )

1   1

PRINCE HARRY

(RACHEL) MEGHAN MARKLE

15th cousins

13th cousins once removed

The probability of zero IBD

N'th cousins	P(zero IBD)
first	0.0 %
second	0.0 %
third	1.5 %
fourth	28 %
fifth	67 %
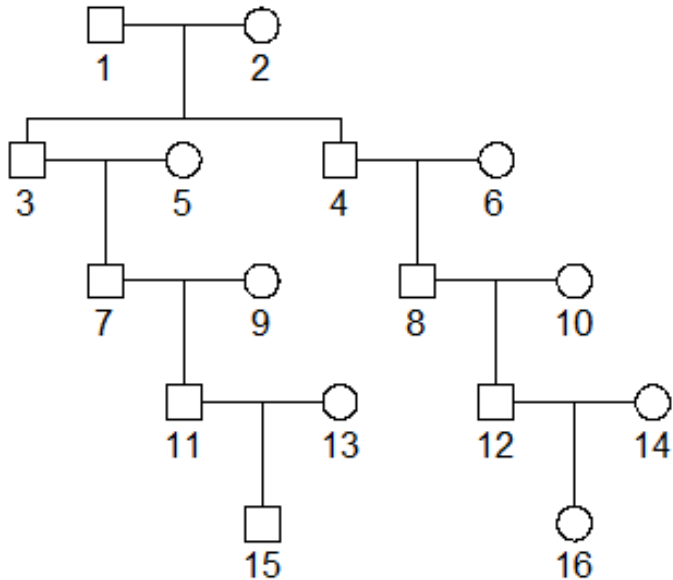
Third cousins

Expected fraction with IBD = 1:

$$k_1 = \frac{1}{64}$$

Two individuals can have a common ancestor without being genetically related

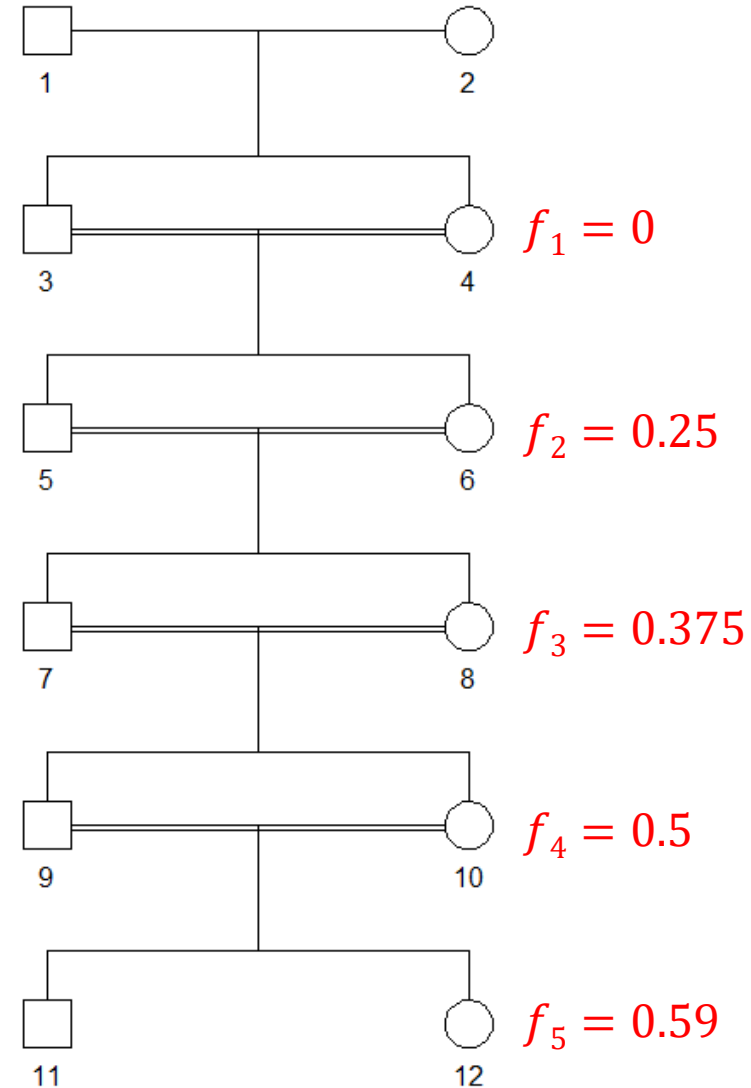# Distant cousins share either nothing or quite a bit
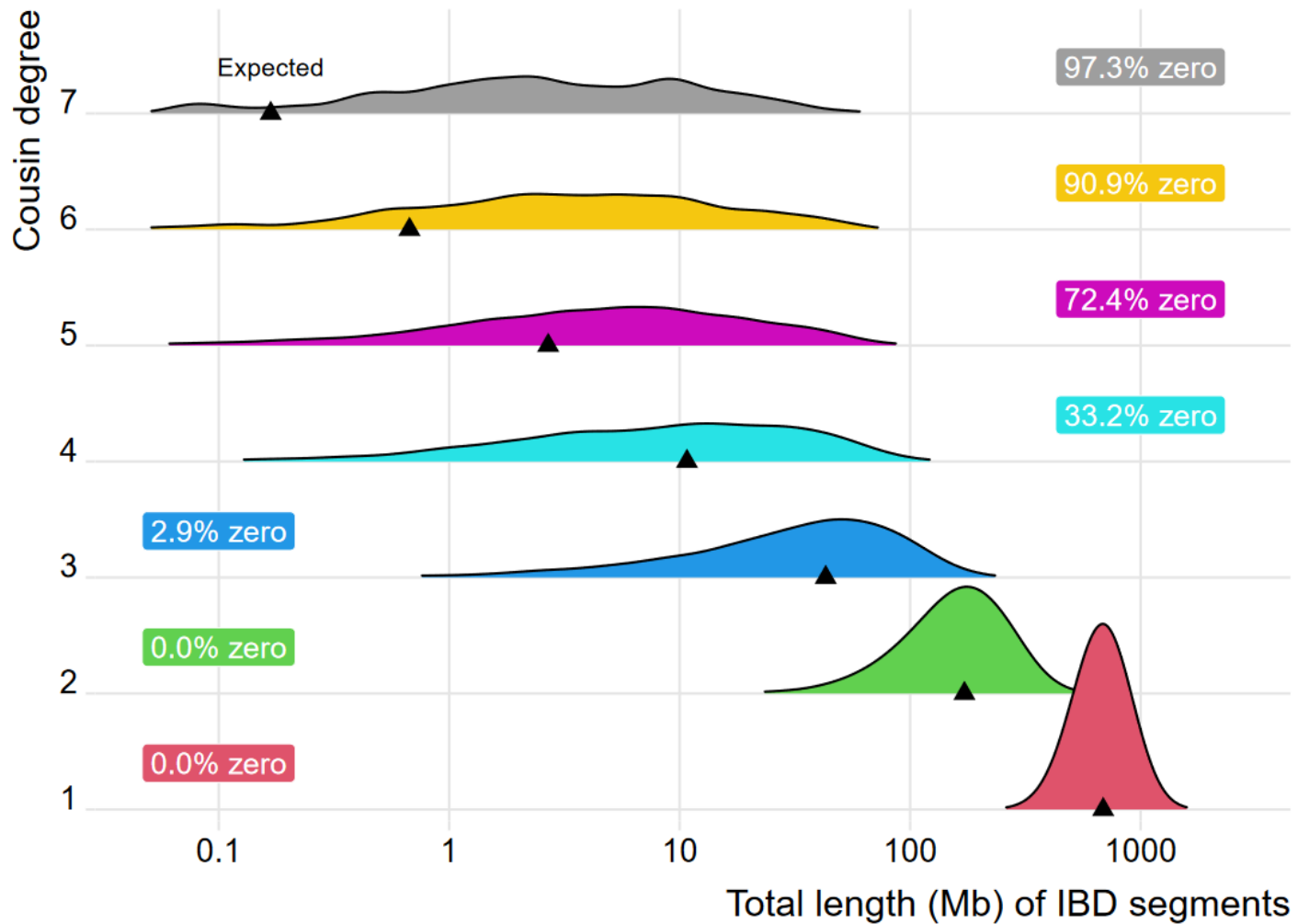
Reversely:
# Is 100 % inbreeding possible?

- Continuous full-sib mating

- Easy to show:
  - inbreeding coefficient $f \rightarrow 1$

- In finite pedigree:
  - pedigree-based f will *never* reach 1

But: After ~30 generations, the **realised inbreeding** typically reaches 1

$f_1 = 0$

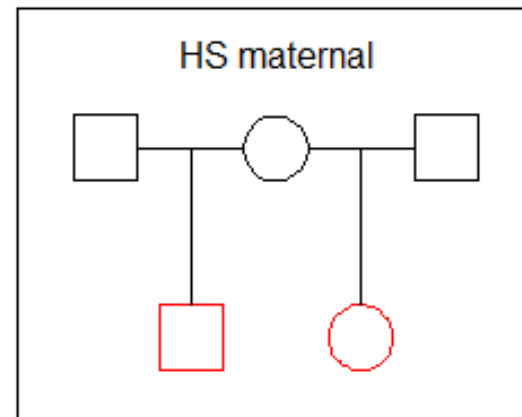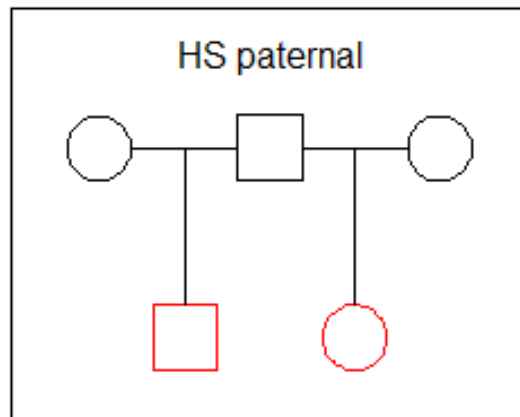$f_2 = 0.25$

$f_3 = 0.375$

$f_4 = 0.5$

$f_5 = 0.59$

The importance of sex

- Rule of thumb:

$$1 \text{ cM} \approx 1 \text{ Mb}$$

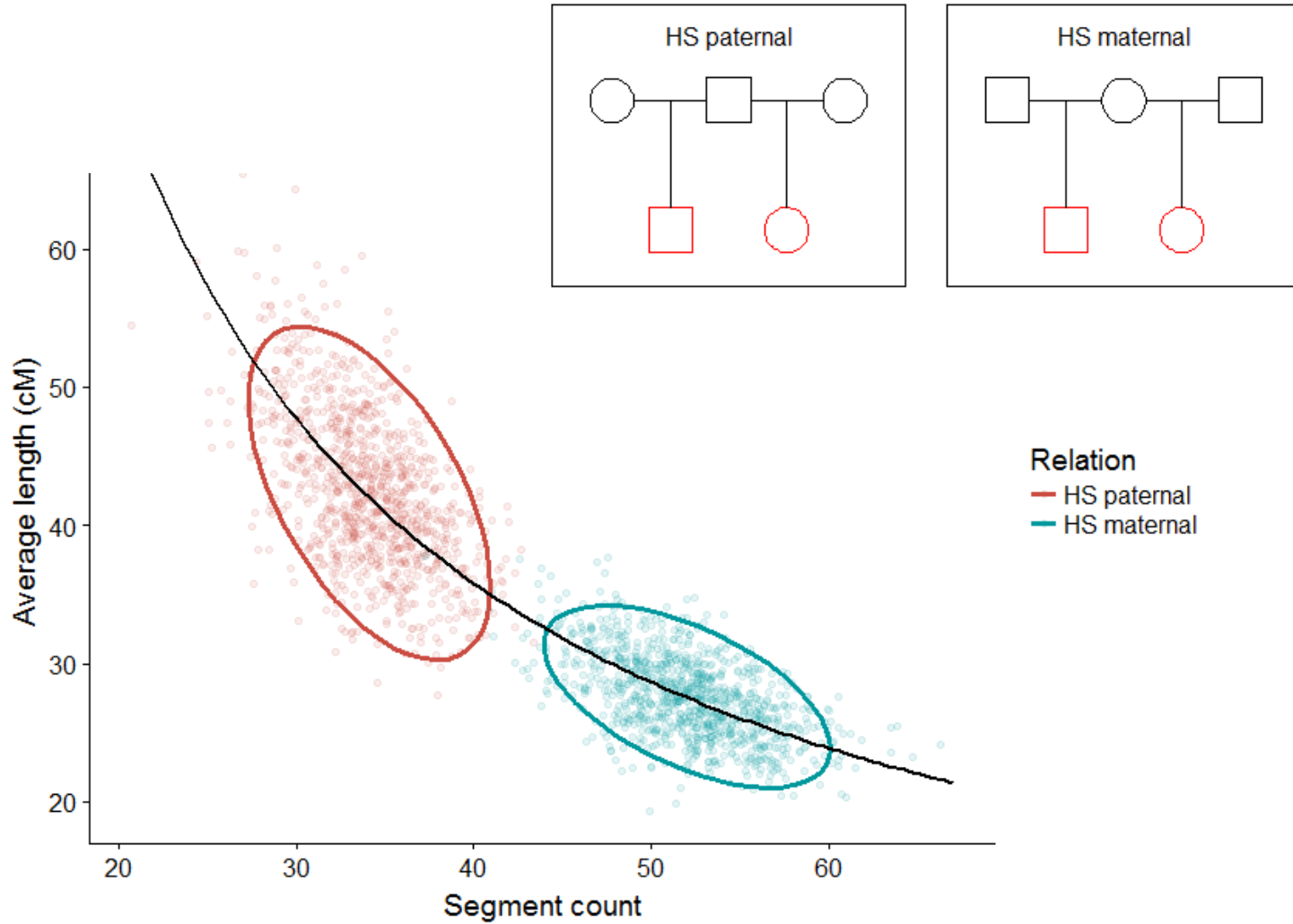- But: crossover rates vary
  – across the genome
  – males vs. females

Genetic map of chromosome 1
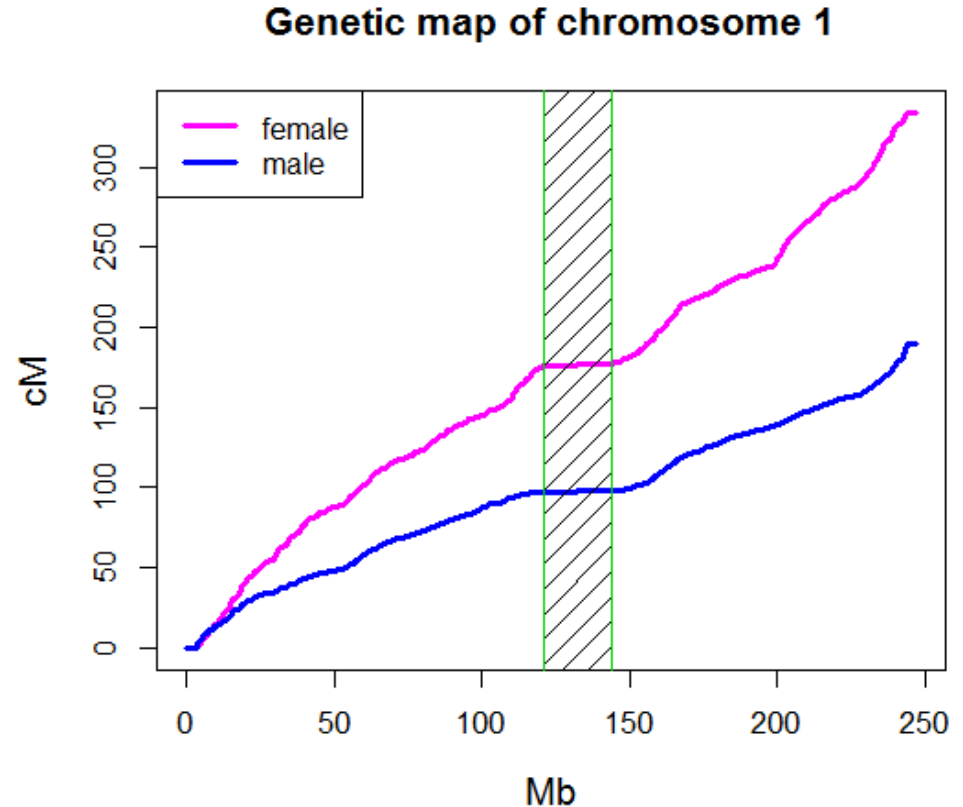
Females have a much longer genome!

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Can we separate these??

Yes!

Napoleon Bonaparte (1769 - 1821)

Jane Austen (1775 - 1817)

10 gen.
paternal line

10 gen.
maternal line

you

you
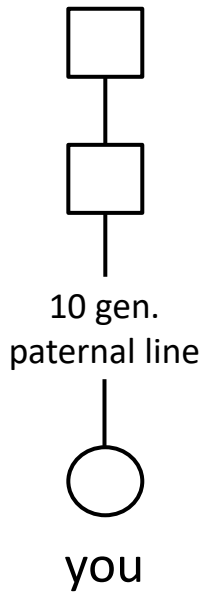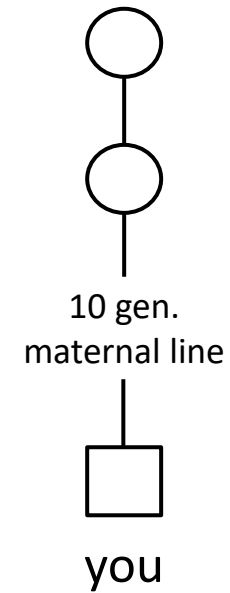
Exercise!

Summary of genetic relatedness

- Pedigree-based measures:
  - the kinship/inbreeding coefficient φ
  - the kappa coefficients $\kappa = (\kappa_0,\ \kappa_1,\ \kappa_2)$

- Each coefficient is
  - the probability of observing a certain IBD pattern in a random locus
  - the expected proportion of the genome in this state

- Realised relatedness:
  - IBD segments determined by meiotic recombination
  - females recombine more than males
  - may separate relationships with equal kappa's
  - 0% and 100% realised identity is possible!

So...what does it mean to be related?

- Pedigree based definition: $\varphi > 0$

    potentially having alleles IBD

- Genomic definition (**realised** relatedness):

    actually having alleles IBD