

Relatedness part 2: Realised relatedness or

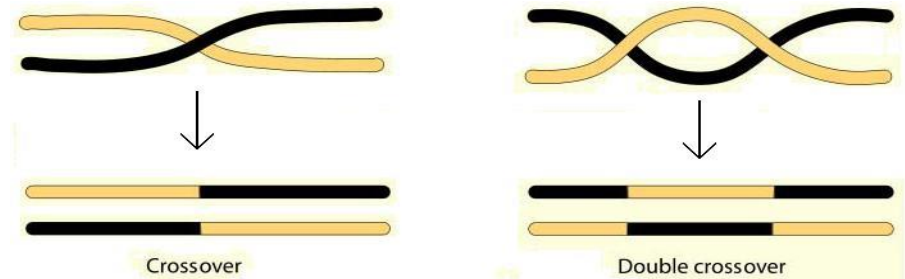
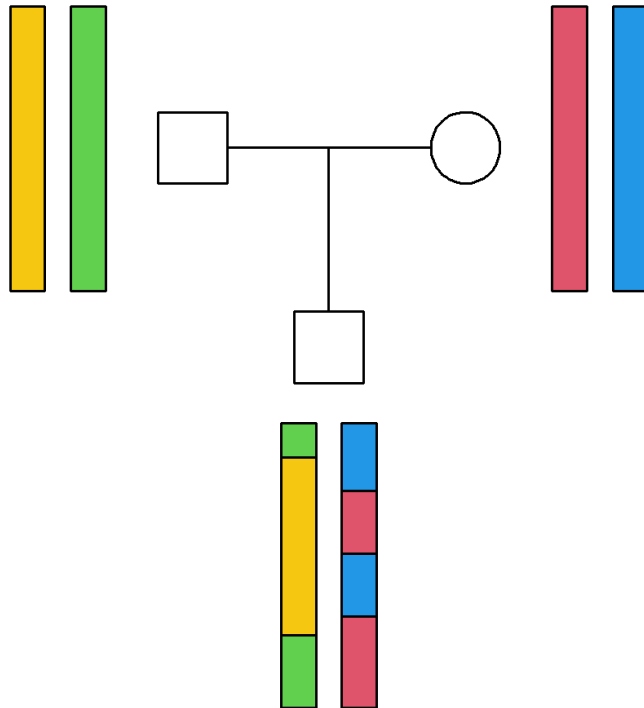
Why are some siblings more alike than others?

Magnus Dehli Vigeland

Statistical methods in genetic relatedness and pedigree analysis

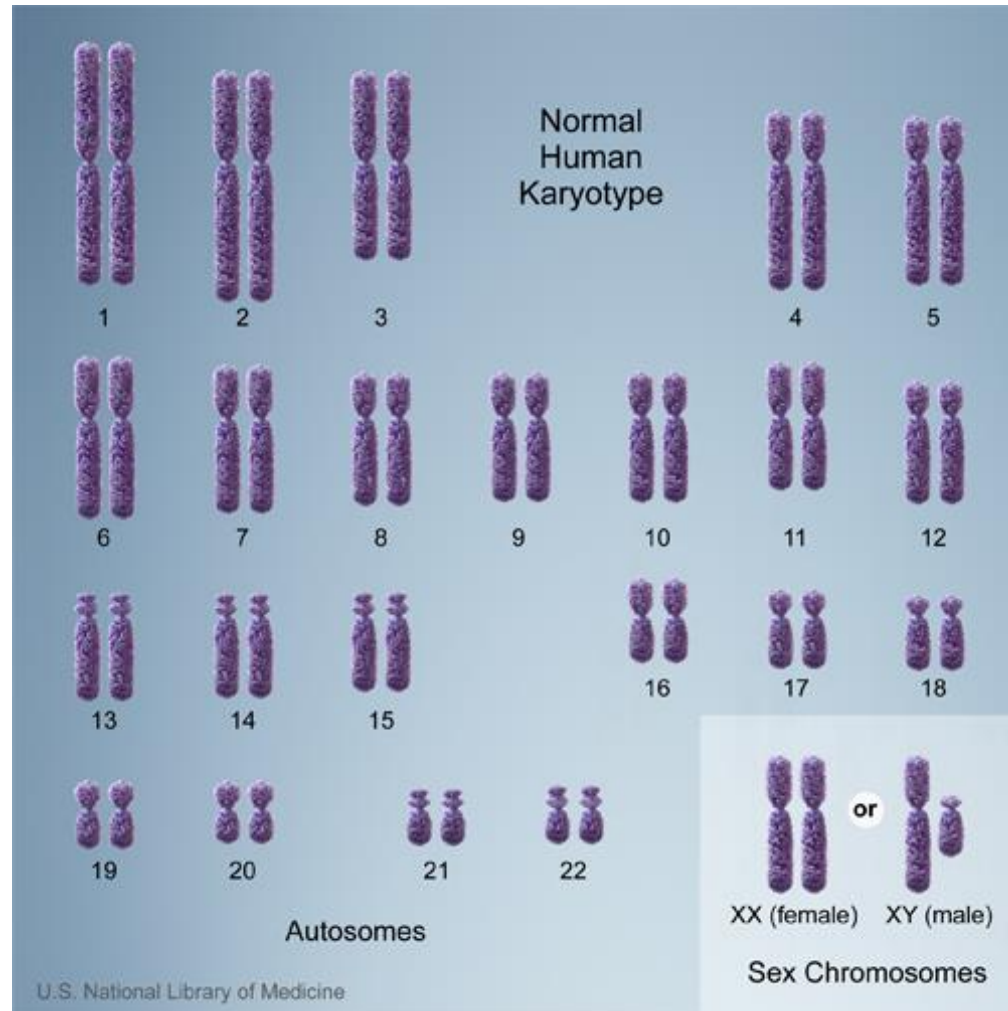
NORBIS course, 13th – 17th of June 2022, Oslo

Meiotic recombination

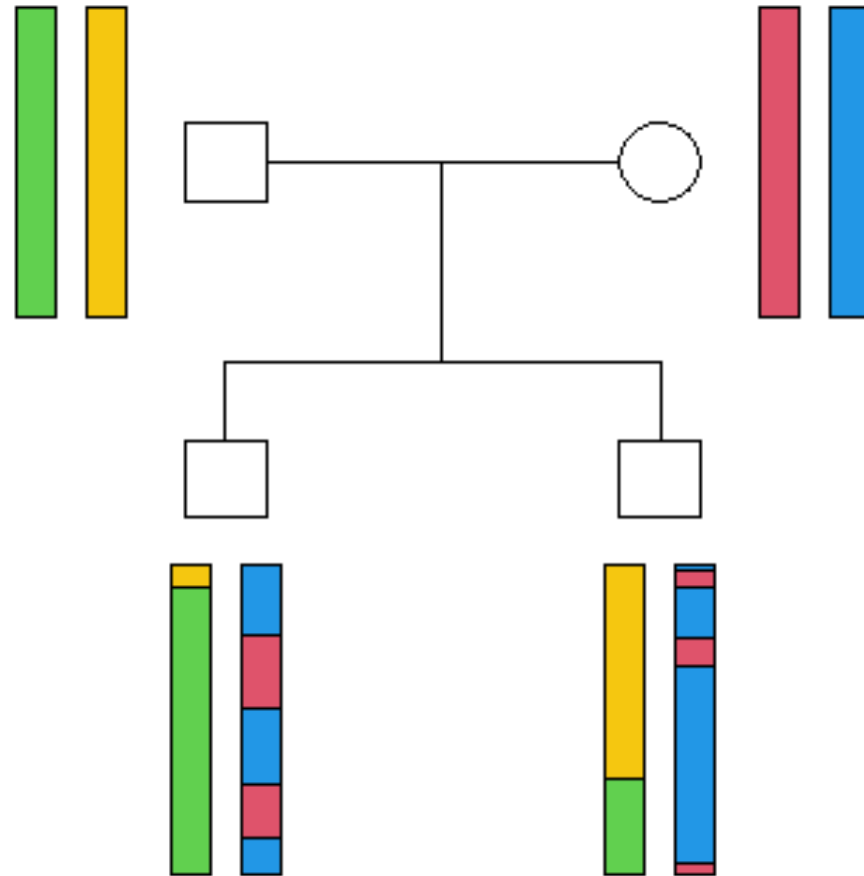


- **Genetic distance** between two loci:
= average # crossovers/ meiosis
- Units:
 - 1 Morgan (M) = 1 crossover per meiosis
 - 1 centiMorgan (cM) = 0.01 M
- The human genome: Ca 30 Morgan

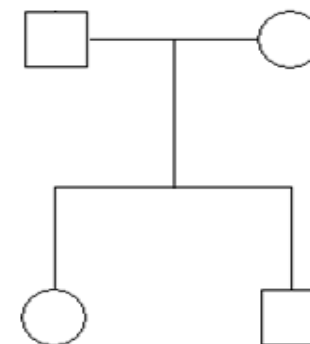
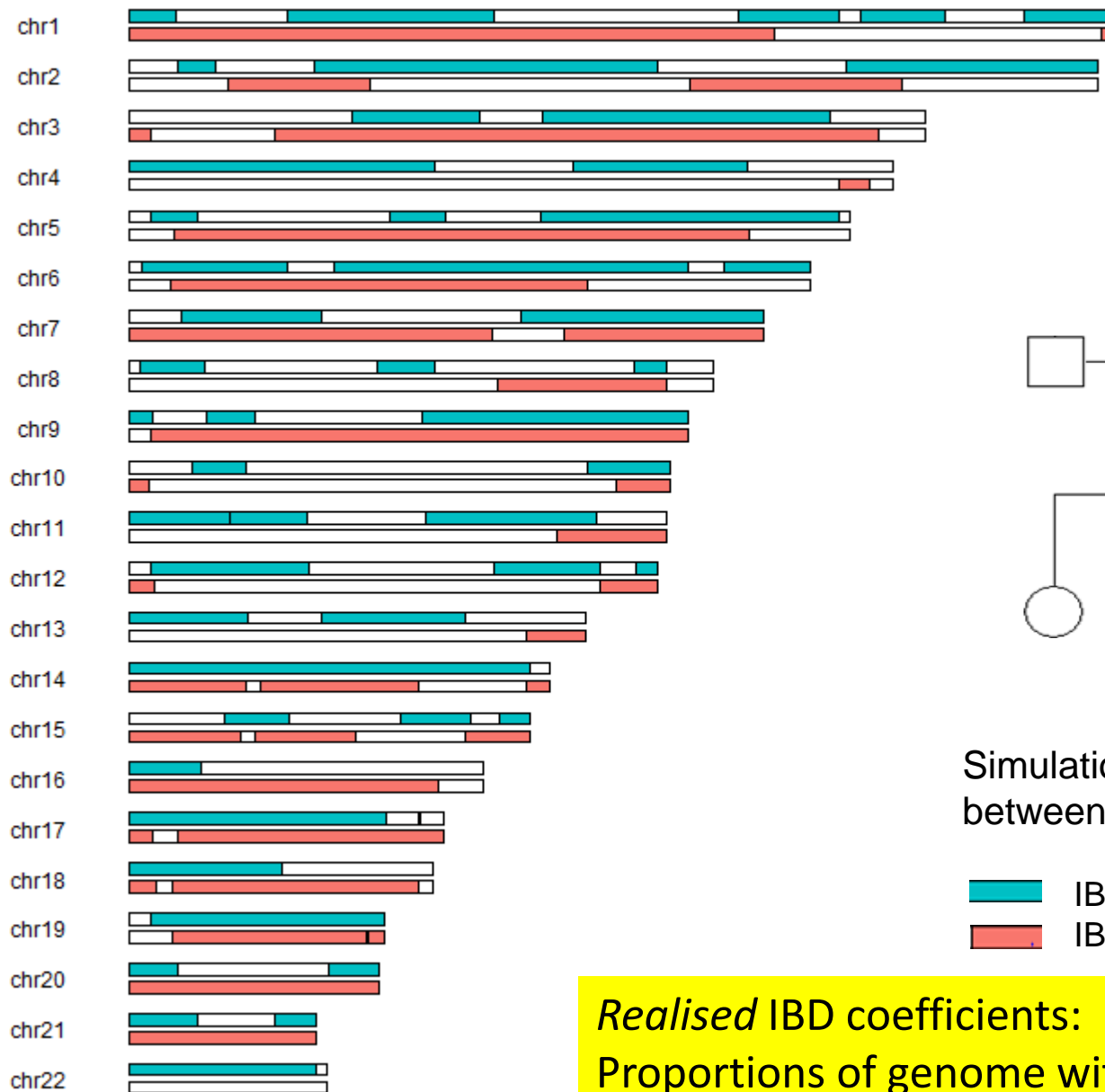
Rule of thumb: One crossover per chromosome arm



Realised sharing between siblings



IBD: Full siblings



Simulation of IBD sharing
between full siblings

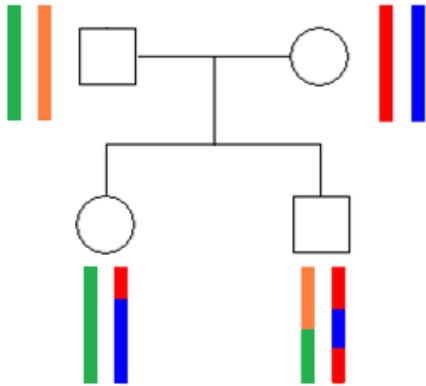
IBD from father
IBD from mother

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

Variation in realised IBD coefficients



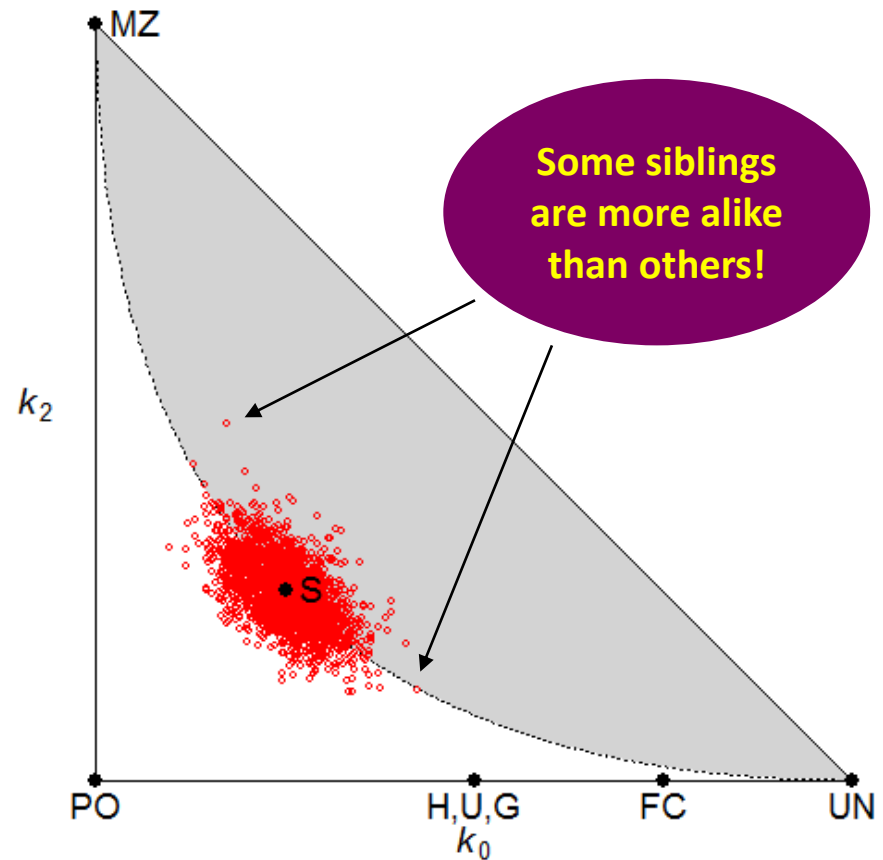
1000 simulations



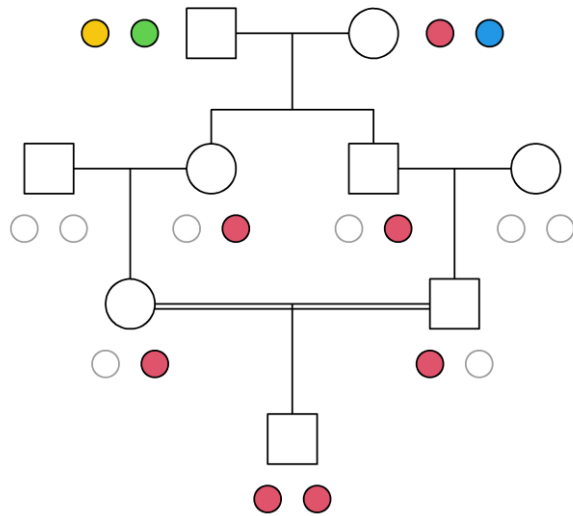
```
> library(ibdsim2)

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

> ribd::showInTriangle(k)
```



Variation in realised inbreeding

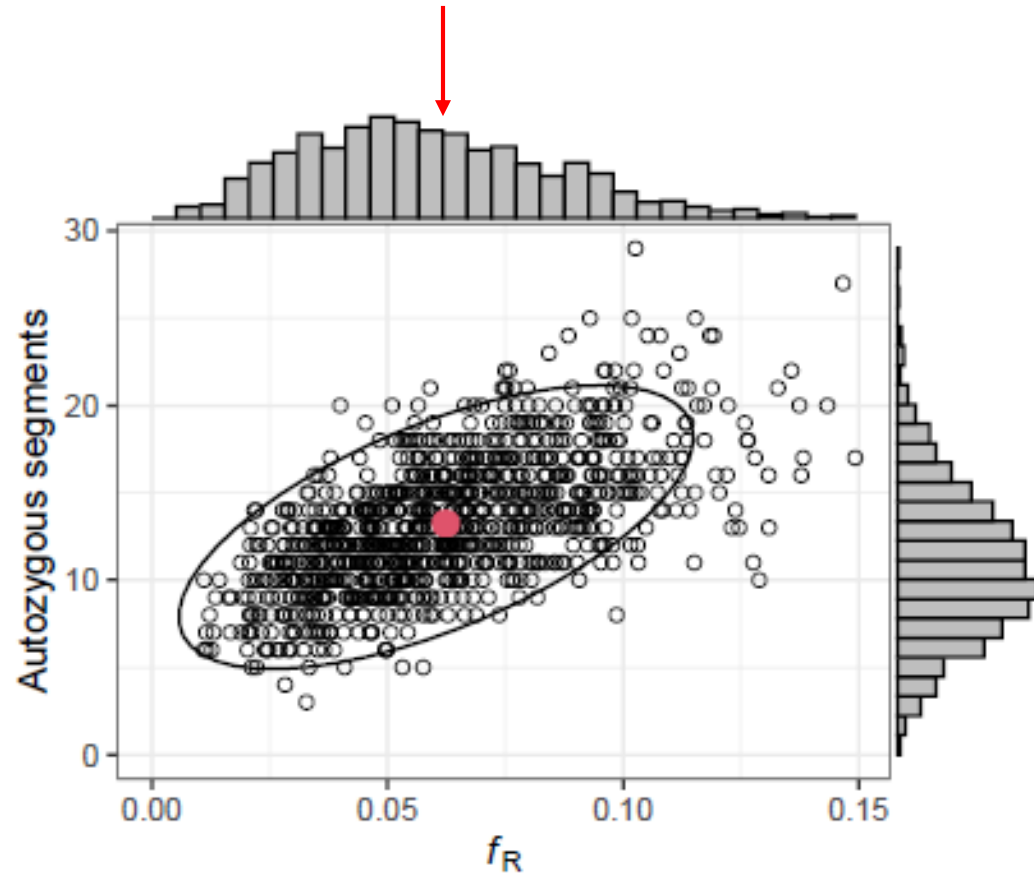


$$f = 0.0625$$

1000 simulations

- R-package: **ibdsim2**
- Decode recombination map
- All 22 human autosomes

Expected: $f = 0.0625$



Variation depends on the genome



Human:

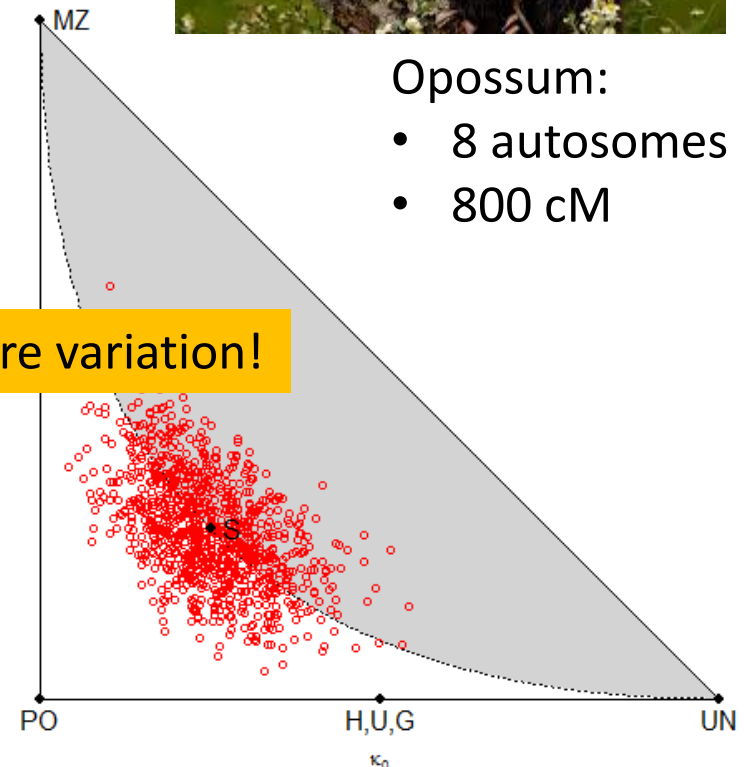
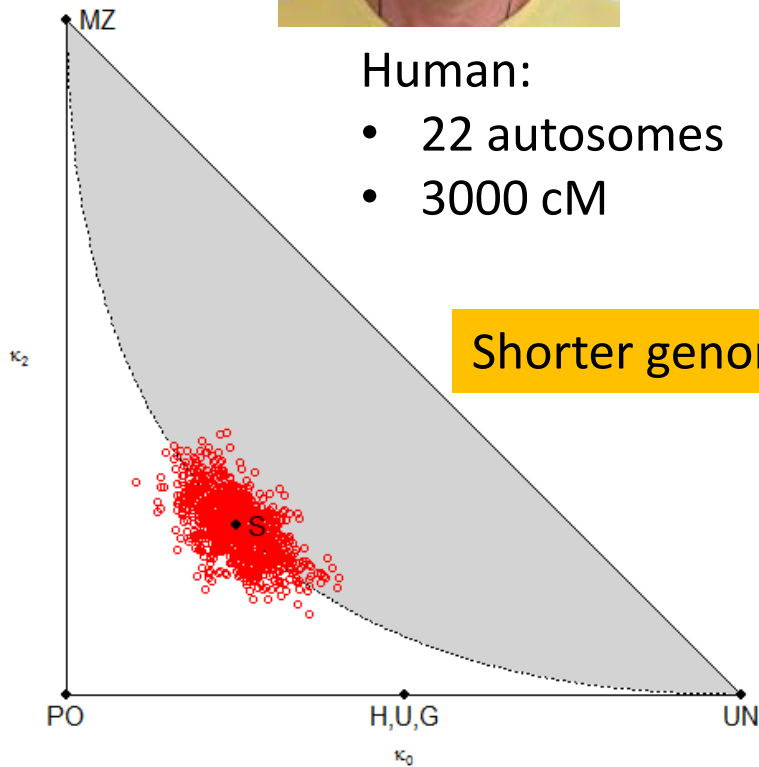
- 22 autosomes
- 3000 cM



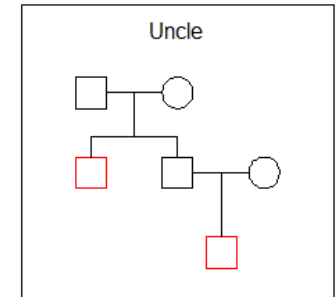
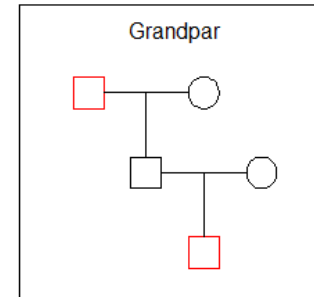
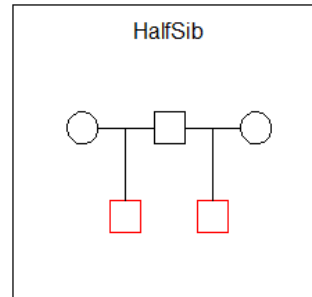
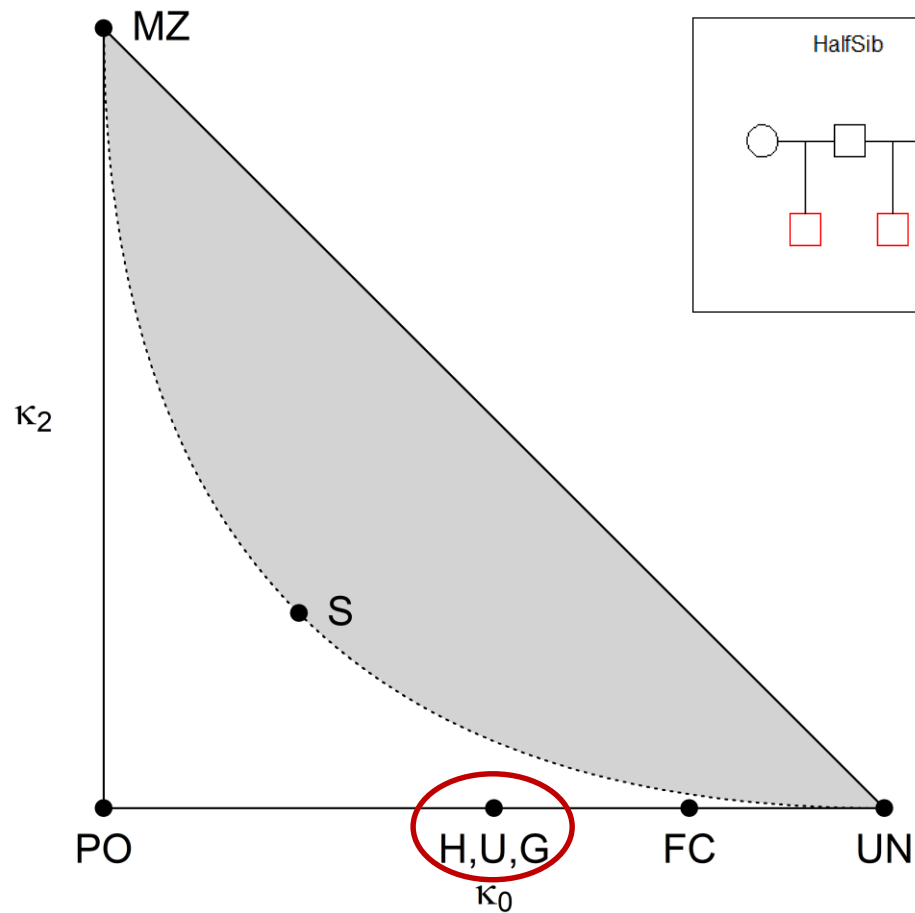
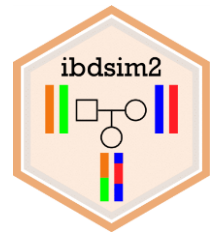
Opossum:

- 8 autosomes
- 800 cM

Shorter genome = more variation!



Indistinguishable relationships?

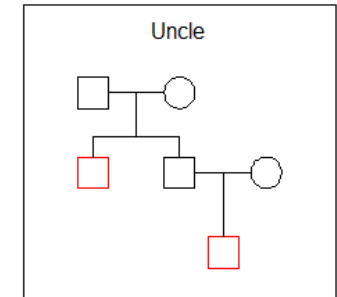
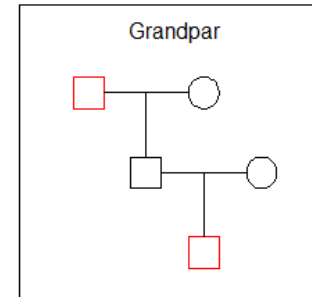
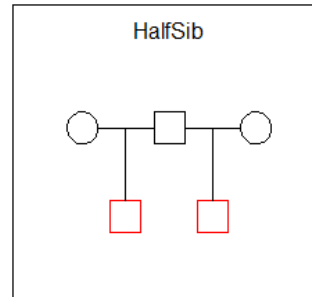
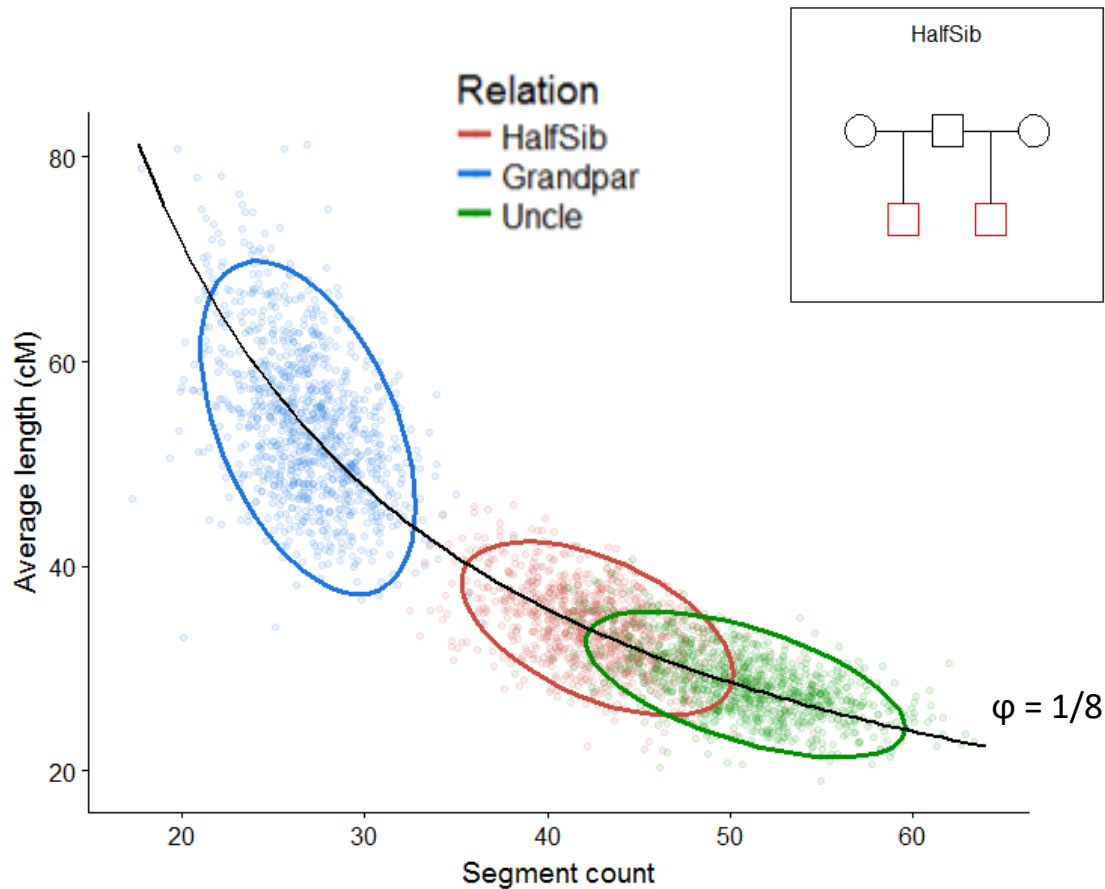
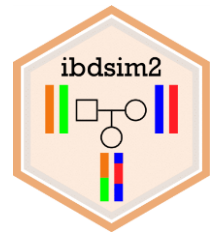


$$\kappa_0 = 0.5$$

$$\kappa_1 = 0.5$$

$$\kappa_2 = 0$$

Simulated IBD distributions



Conclusion

In theory often distinguishable!
In practice quite hard.

METRO

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UK WORLD WEIRD TECH

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

Brigitte

SPIELE NEWSLETTER VIDEO GEWINNSPIELE FORUM F-MAG ACADEMY SHOPPING ABC
Aktuell Mode Beauty Rezepte Gesund Liebe Familie Leben Horor

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

Stammbaum erforscht: Prinz Harry und Meghan Markle sind Cousins!

universitetssykehus



FASHION CULTURE

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

By Meghan McKenna Date November 2, 2017

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Cousins!



STJERNENR: Meghan Markle og prins Harry viser endelig kjærligheten sin offentlig, etter å ha holdt forholdet svært privat i lang tid. Nå kommer det fram 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

View c

1.1K shares

(Picture: Mail Online)

14

13

10

9

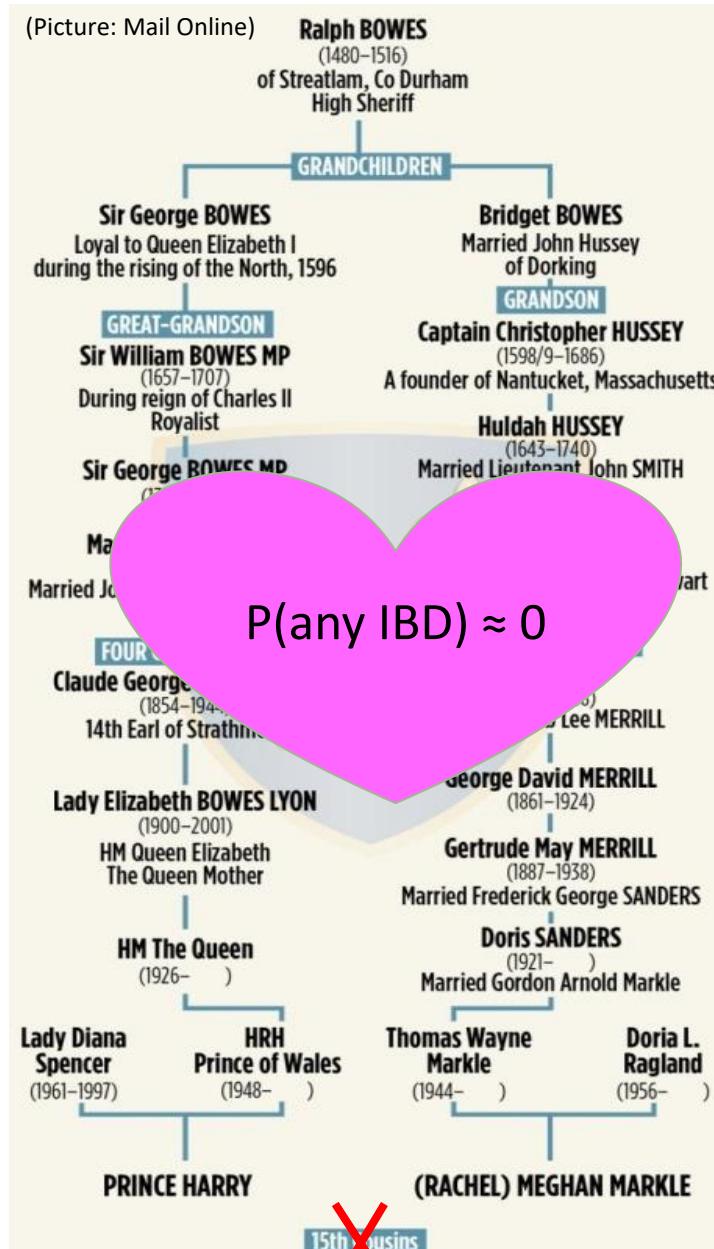
8

4

3

2

1



15

13

11

10

9

5

4

3

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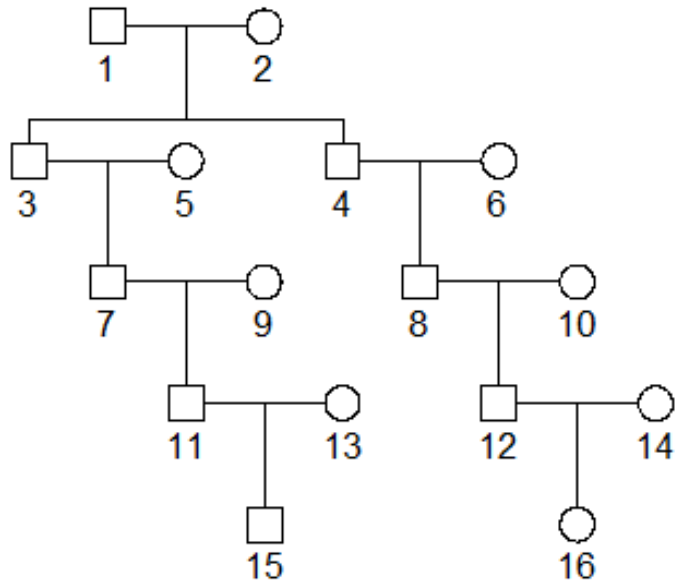
1

$P(\text{any IBD}) \approx 0$



13th cousins once removed

The probability of zero IBD



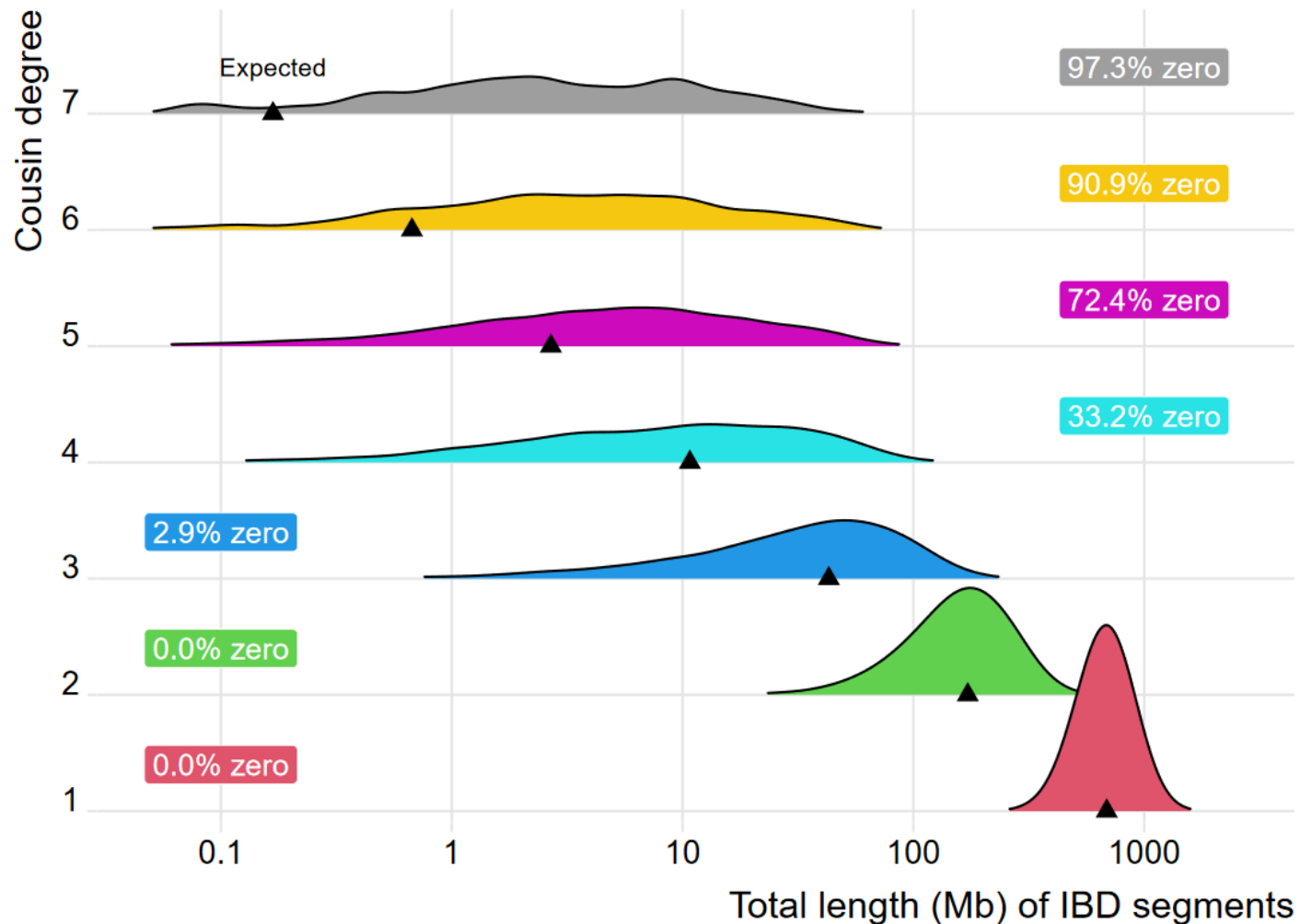
Third cousins: Expected fraction of the genome with IBD = 1:

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

N'th cousins	$P(\text{zero IBD})$
first	0.0 %
second	0.0 %
third	1.5 %
fourth	28 %
fifth	67 %

Two individuals can have a common ancestor without being genetically related

Distant cousins share either **nothing** or **quite a bit**

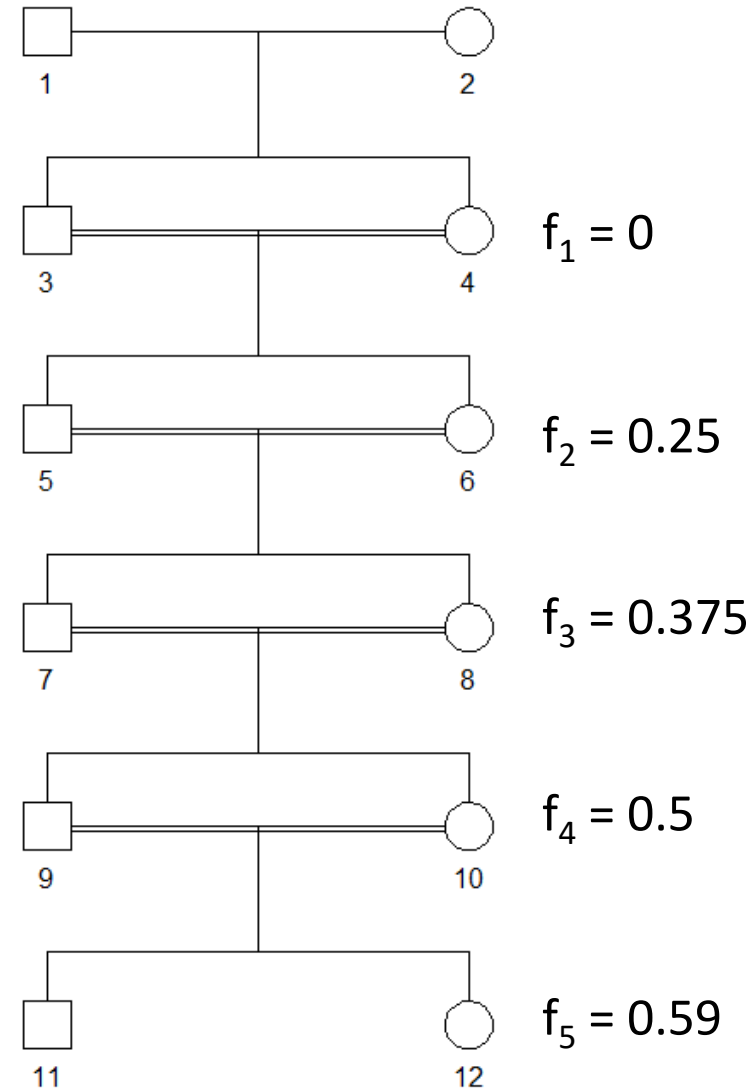


Reversely:

Is 100 % inbreeding possible?

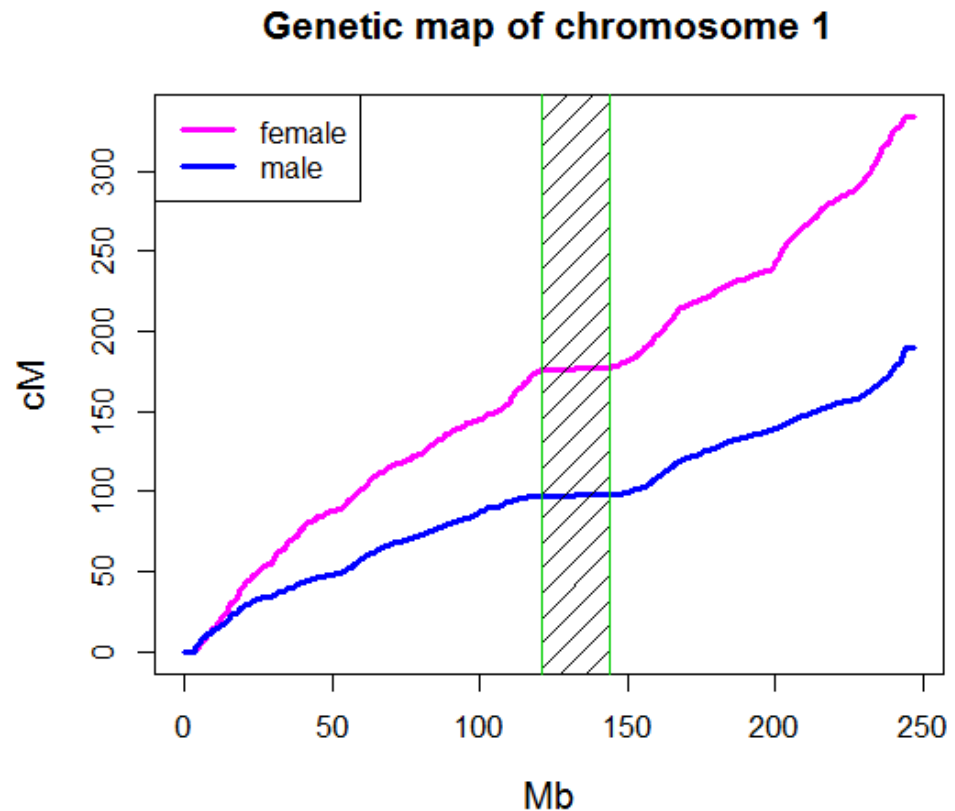
- Full sibs mating scheme
- Easy to show:
 - inbreeding coefficient $f \rightarrow 1$
- But *never* $f = 1$! (in a finite pedigree)

Realised inbreeding
After ~30 generations,
usually $f_{\text{real}} = 1$.



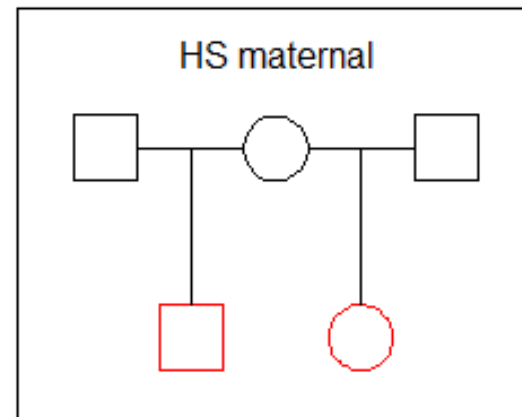
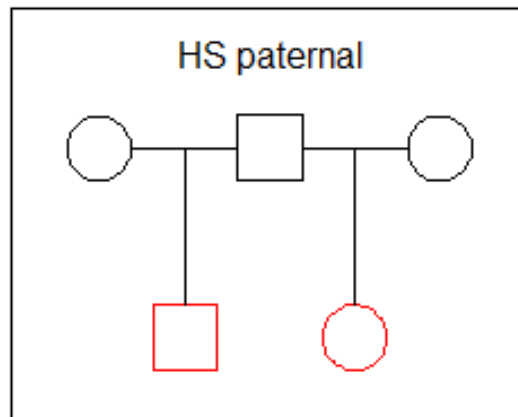
Map distance

- Rule of thumb:
 $1 \text{ cM} \approx 1 \text{ Mb}$
- But: crossover rates vary
 - across the genome
 - males vs. females

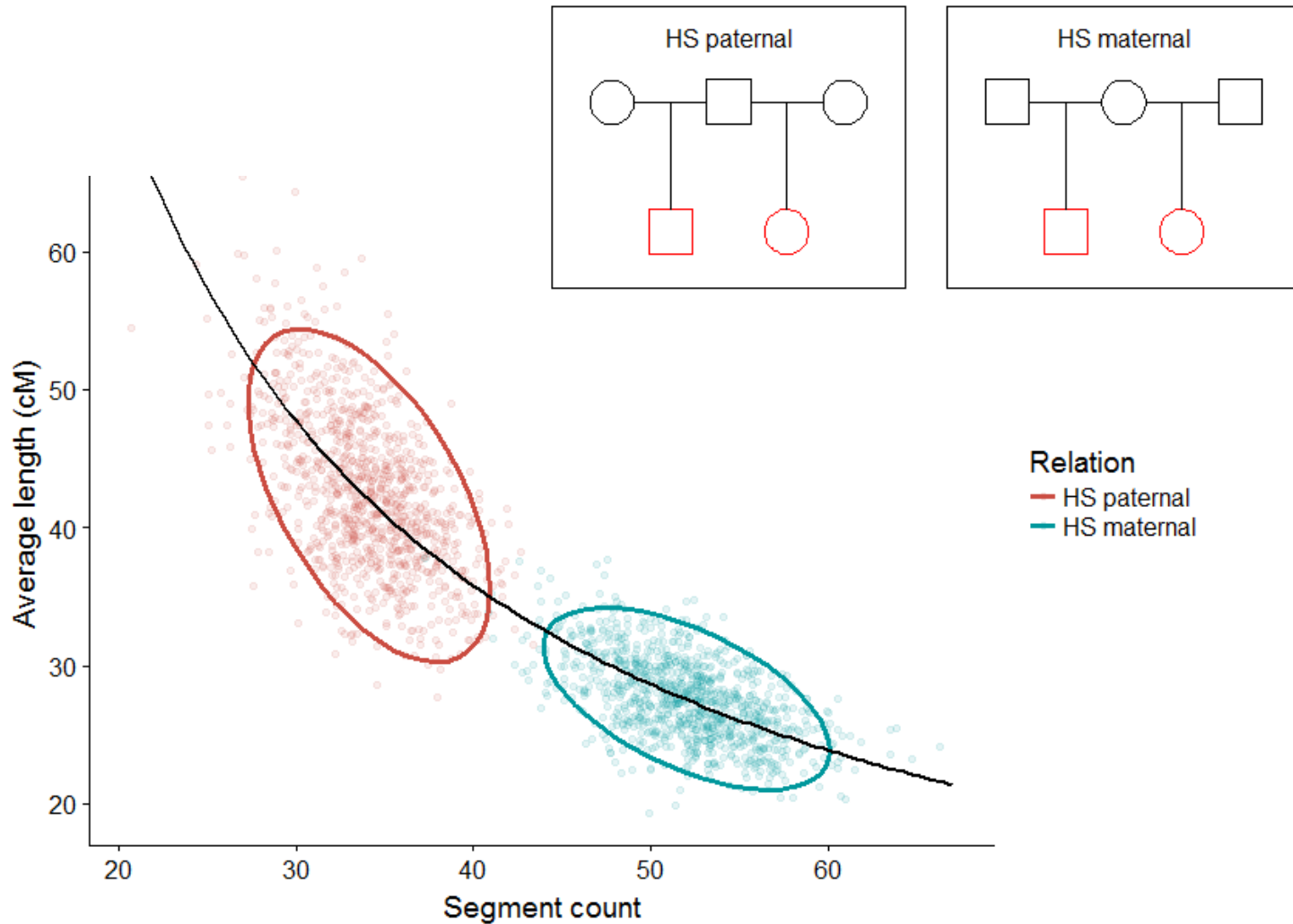


Females have a much longer genome!

Can we separate these??

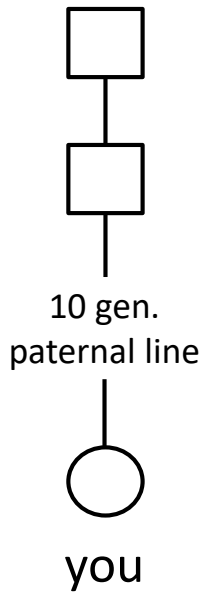


Yes!

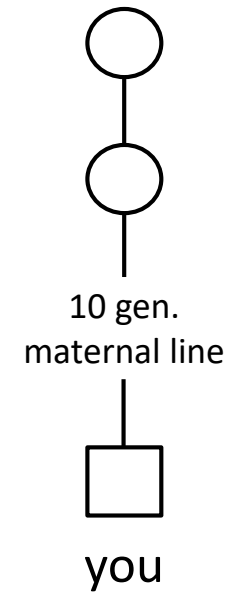




Napoleon Bonaparte (1769 - 1821)



Jane Austen (1775 - 1817)



Exercise!

Relatedness: Summary

- Measuring relatedness with increasing precision:
 - the kinship/inbreeding coefficient φ
 - the IBD 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
- IBD is not a pointwise phenomenon: Always in segments
 - determined by meiotic crossovers
 - consequence: Variation in the *realised* IBD!
- Family relation \nRightarrow genetic relation

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