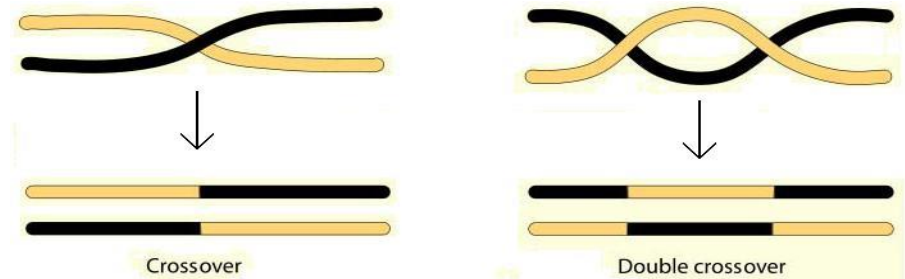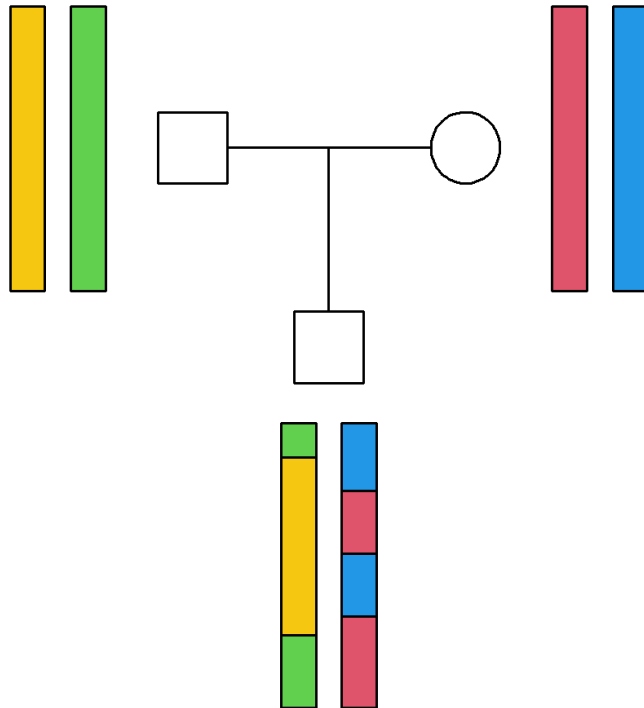# Relatedness part 2:
Realised relatedness

or

Why are some siblings more alike than others?

Magnus Dehli Vigeland

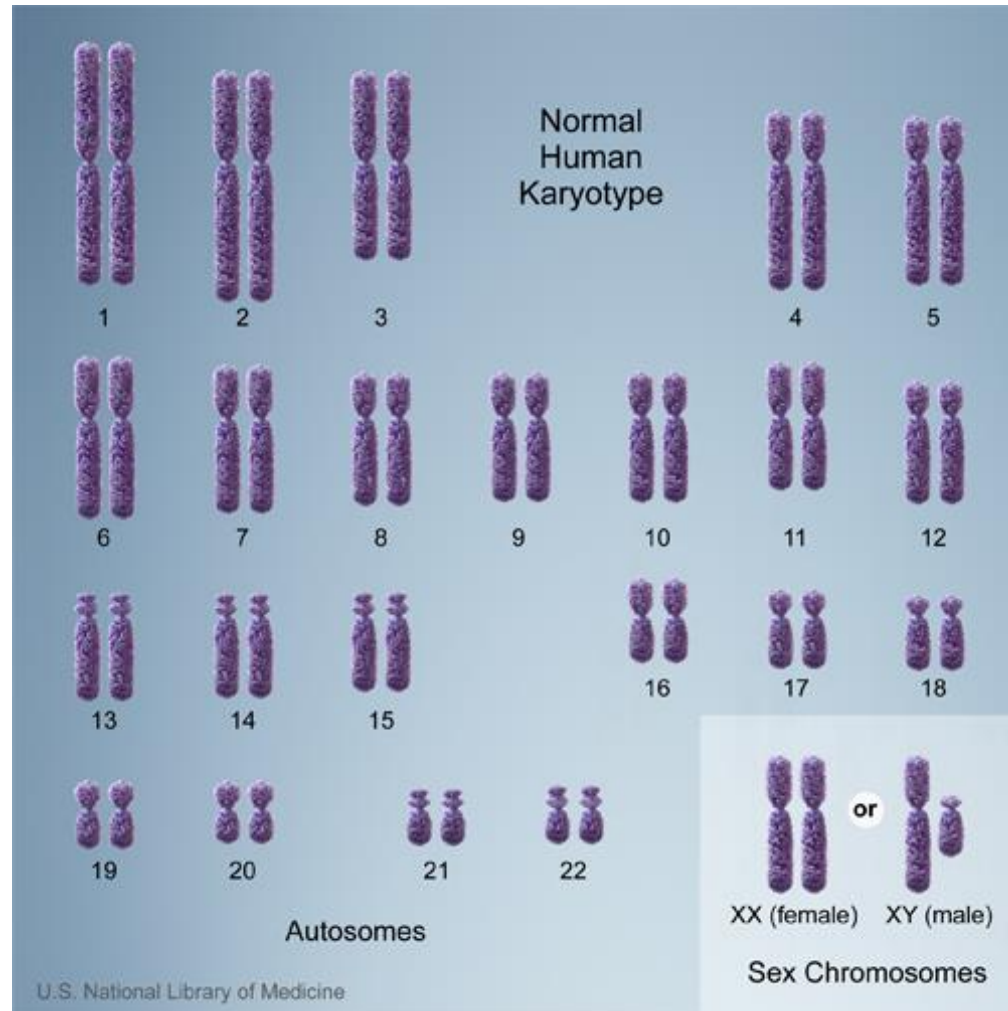**Statistical methods in genetic relatedness and pedigree analysis**

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

Meiotic recombination

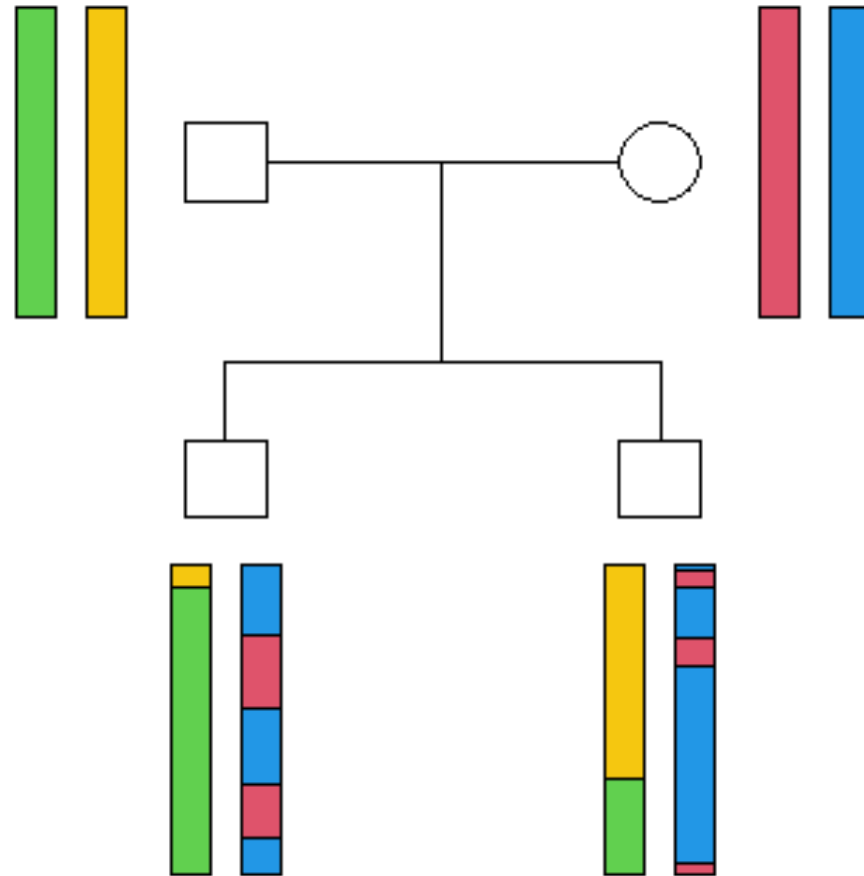Crossover

Double crossover

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

- Units:
  - 1 Morgan (M) = 1 crossover per meiosis
  - 1 centiMorgan (cM) = 0.01 M
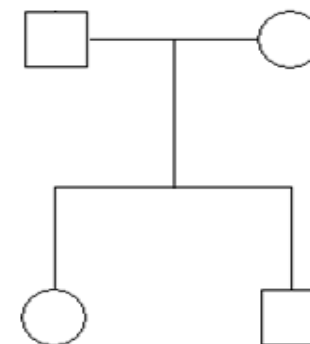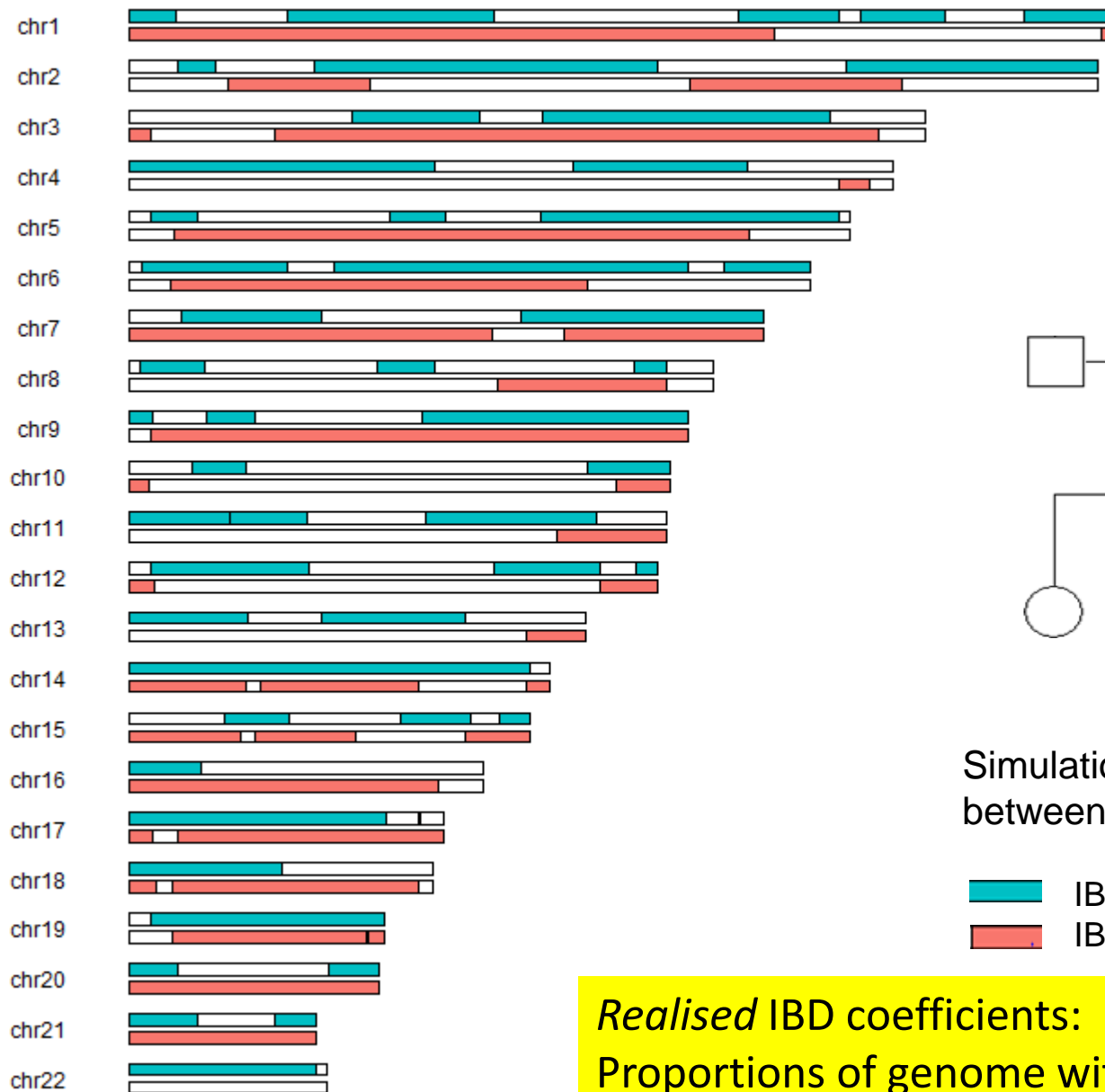
- The human genome: Ca 30 Morgan

Rule of thumb: One crossover per chromosome arm

Normal Human Karyotype

Autosomes

XX (female)   or   XY (male)

Sex Chromosomes

U.S. National Library of Medicine

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

Oslo universitetssykehus

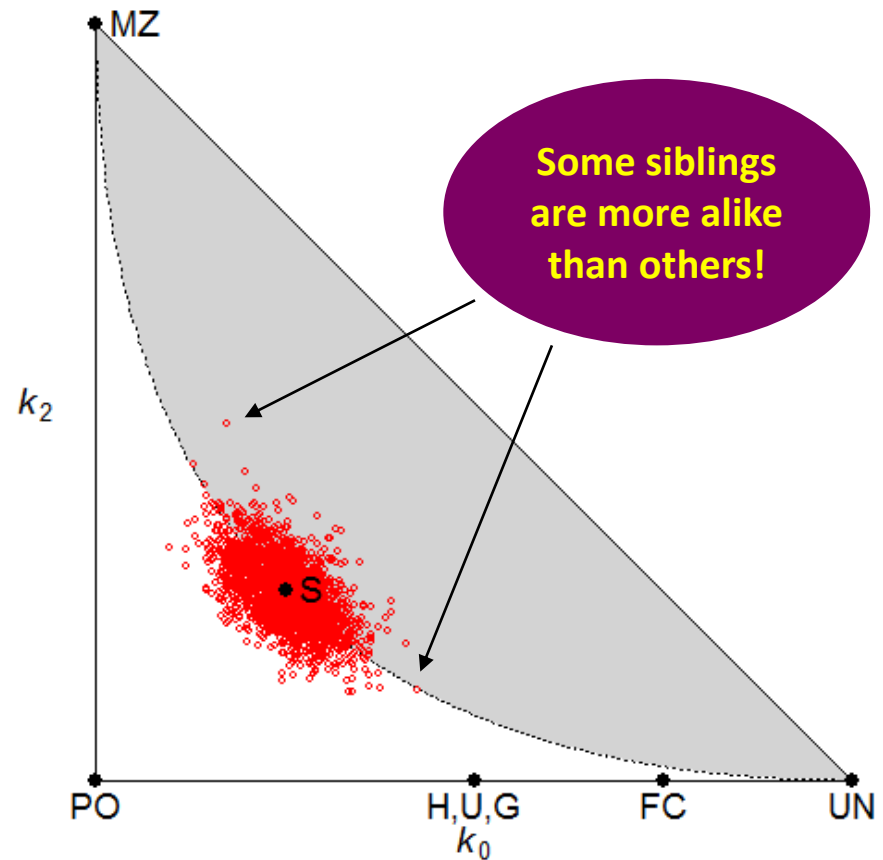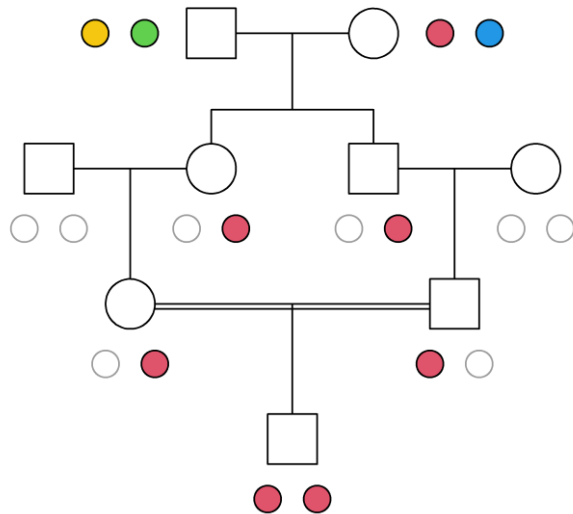# Variation in realised IBD coefficients

1000 simulations
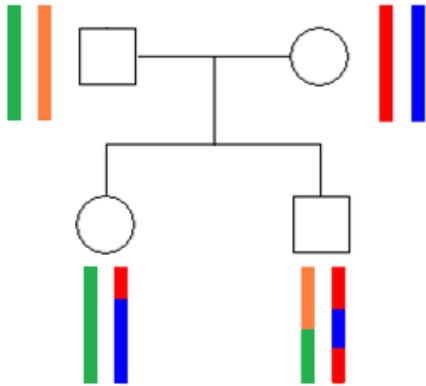

```
>  library(ibdsim2)


>  x = nuclearPed(2)

>  s = ibdsim(x, N = 1000)

>  k = realisedKappa(s, ids = 3:4)


>  ribd::showInTriangle(k)
```

Some siblings are more alike than others!
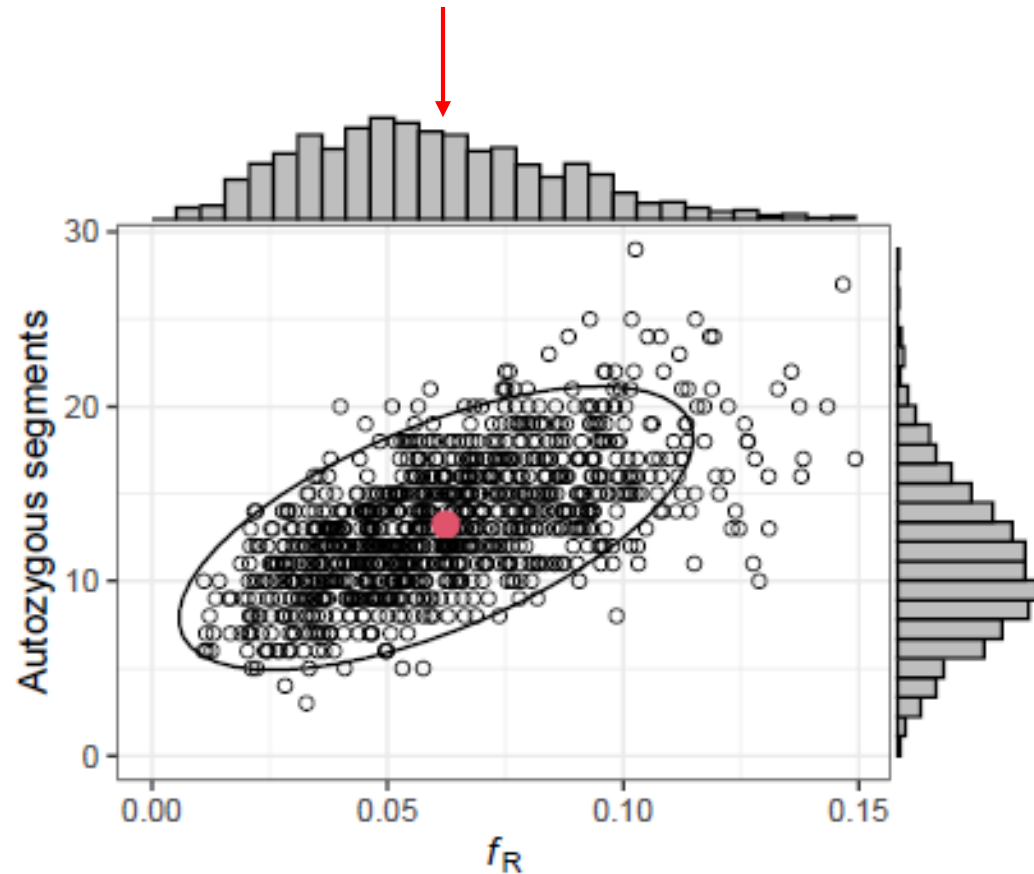
Variation in realised inbreeding

f = 0.0625

1000 simulations
- R-package: **ibdsim2**
- Decode recombination map
- All 22 human autosomes

Expected: f = 0.0625

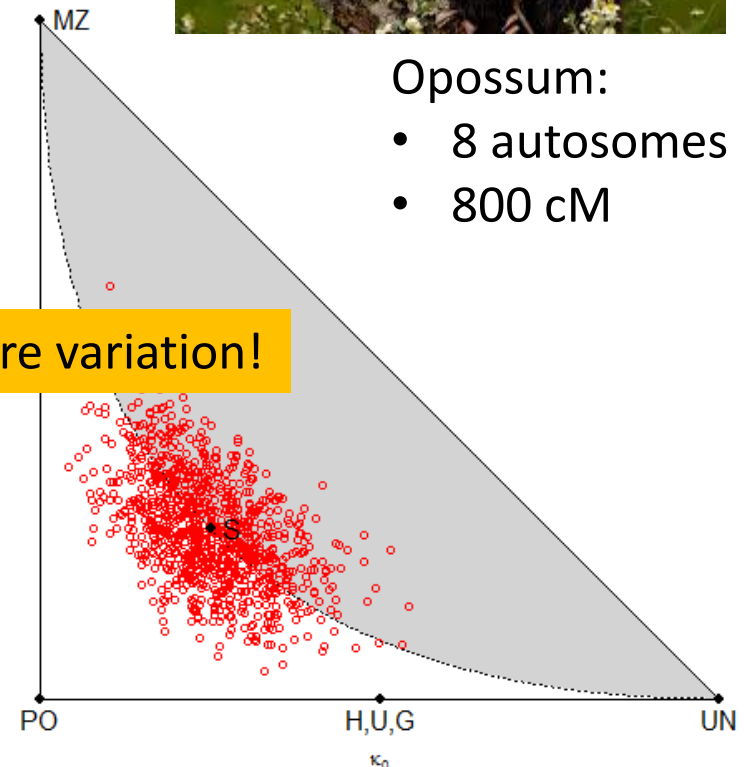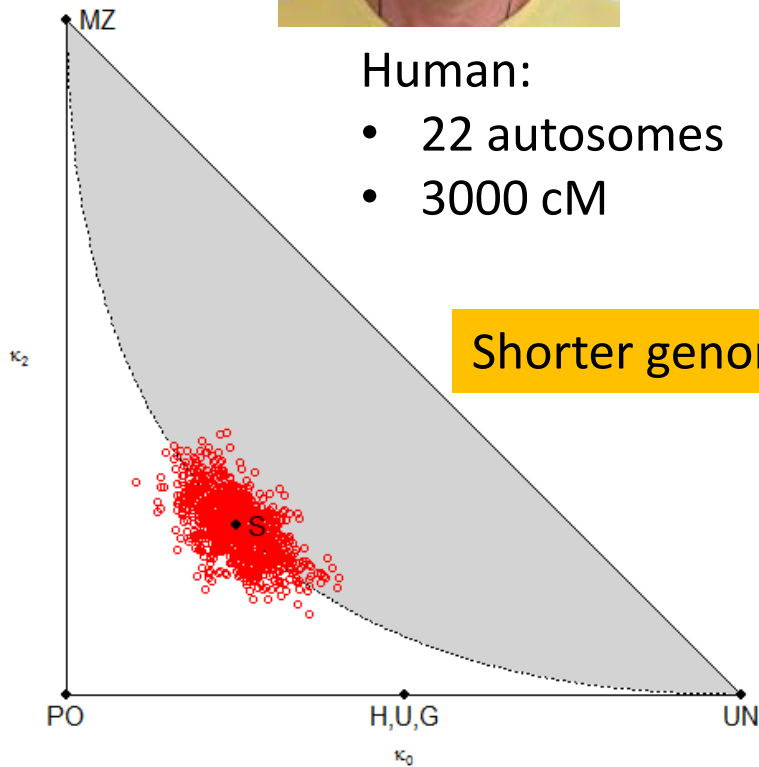# Variation depends on the genome
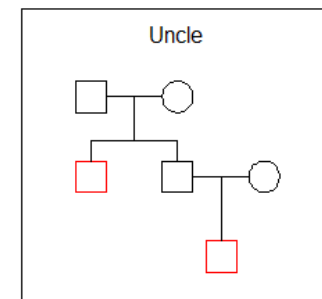

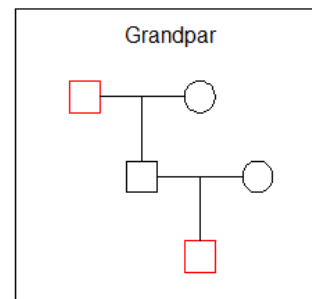Human:
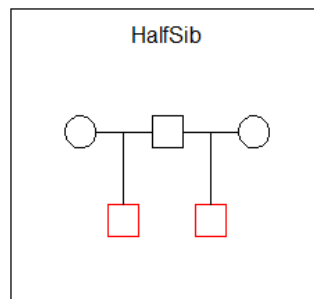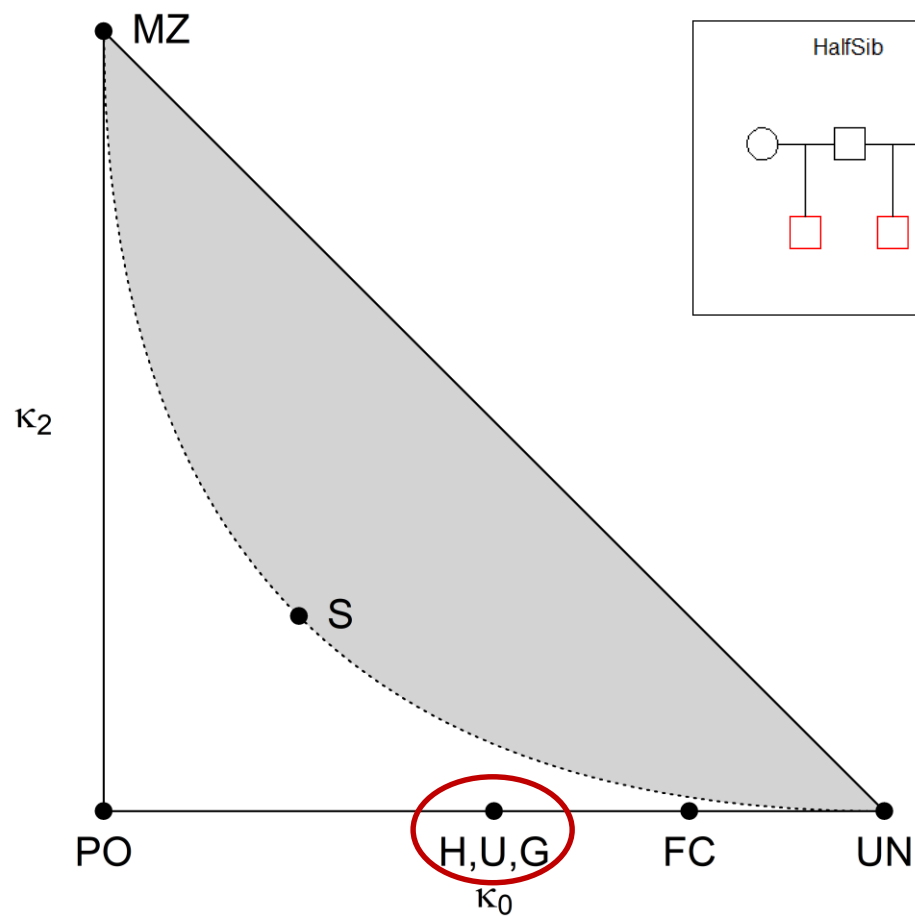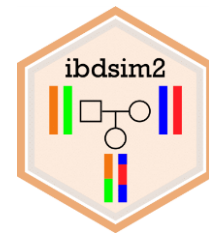- 22 autosomes
- 3000 cM

Opossum:
- 8 autosomes
- 800 cM

Shorter genome = more variation!

Indistinguishable relationships?

$$\kappa_0 = 0.5$$
$$\kappa_1 = 0.5$$
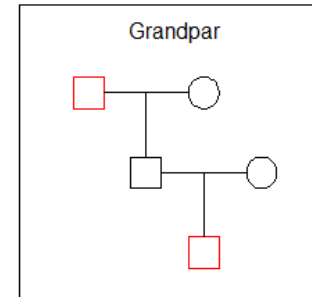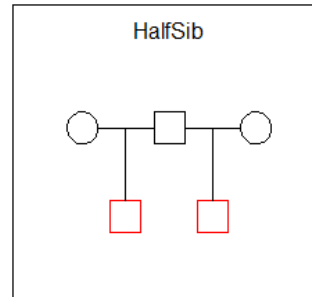$$\kappa_2 = 0$$

Simulated IBD distributions
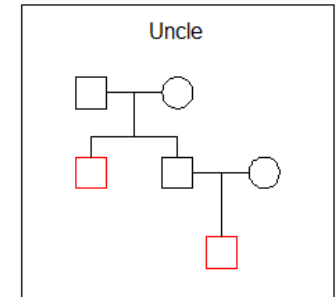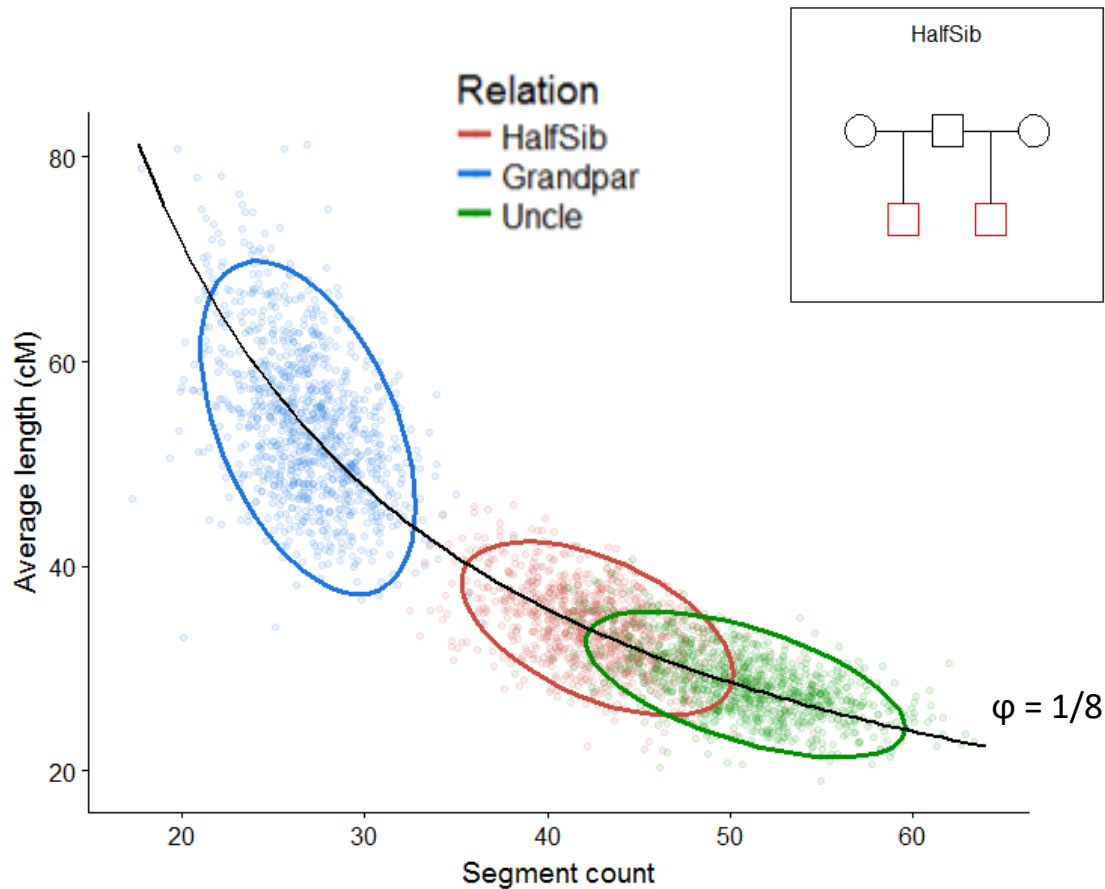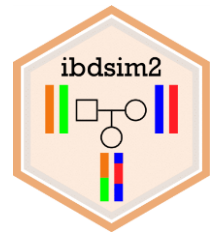
Conclusion
In theory often distinguishable!
In practice quite hard.

The probability of zero IBD

N'th cousins	P(zero IBD)
first	0.0 %
second	0.0 %
third	1.5 %
fourth	28 %
fifth	67 %
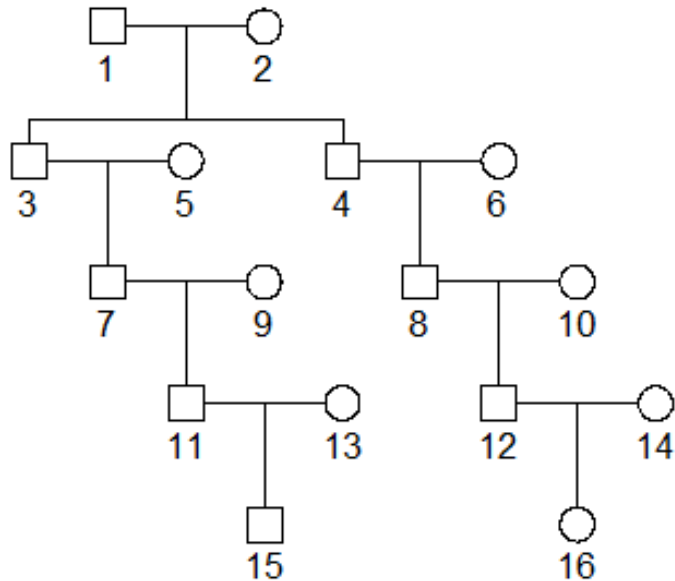
Third cousins: Expected fraction of the genome with IBD = 1:

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

Two individuals can have a common ancestor without being genetically related

Distant cousins share either nothing or quite a bit
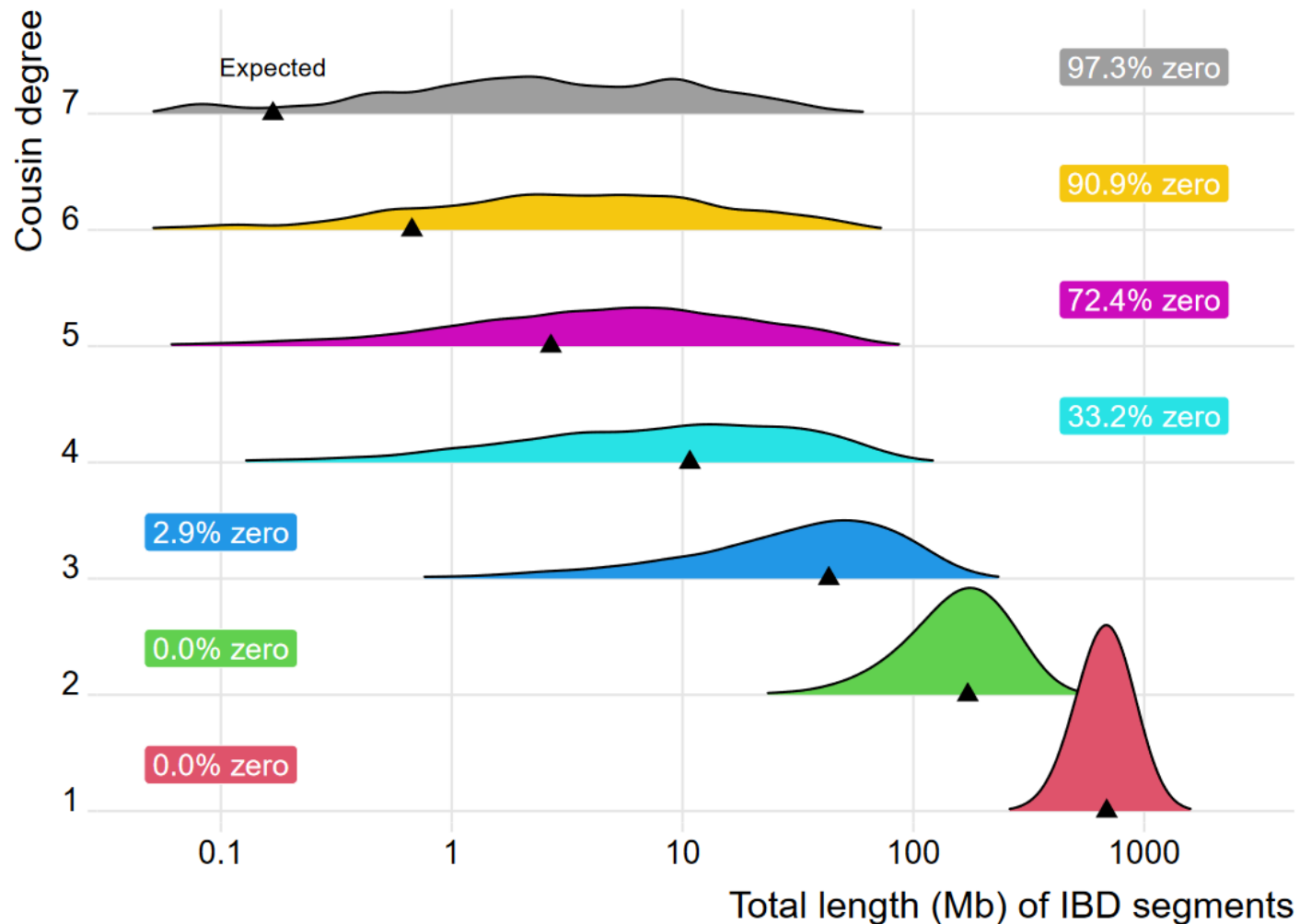
Relatedness: Summary

- 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 $\not\Rightarrow$ 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*