Pedigree and Relatedness

SPA DRP

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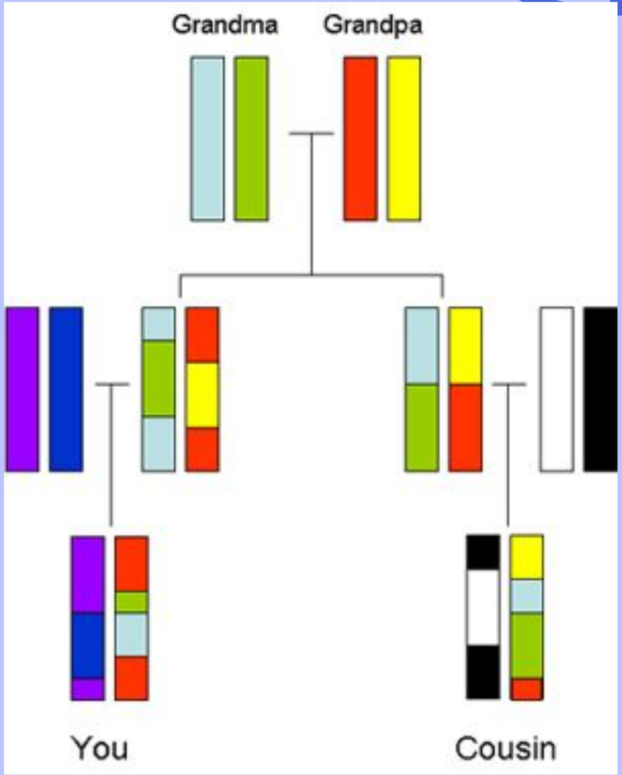
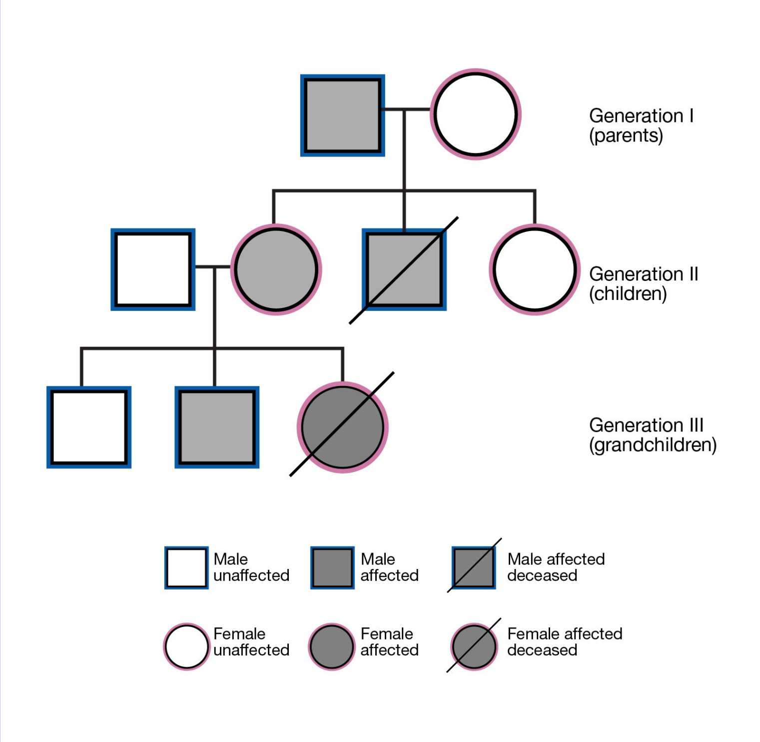
Meiosis

- Meiosis is a special type of cell division of germs cells in sexually-reproducing organisms that is used to produce gametes.
- DNA is passed down in blocks, forming a mosaic pattern with a tree like structure.



Pedigree (family tree)

- Recorded descent of an ancestral line.
- How individuals are related to each other.
- Special type of graph (nodes connected by edges)



Path Counting Formula

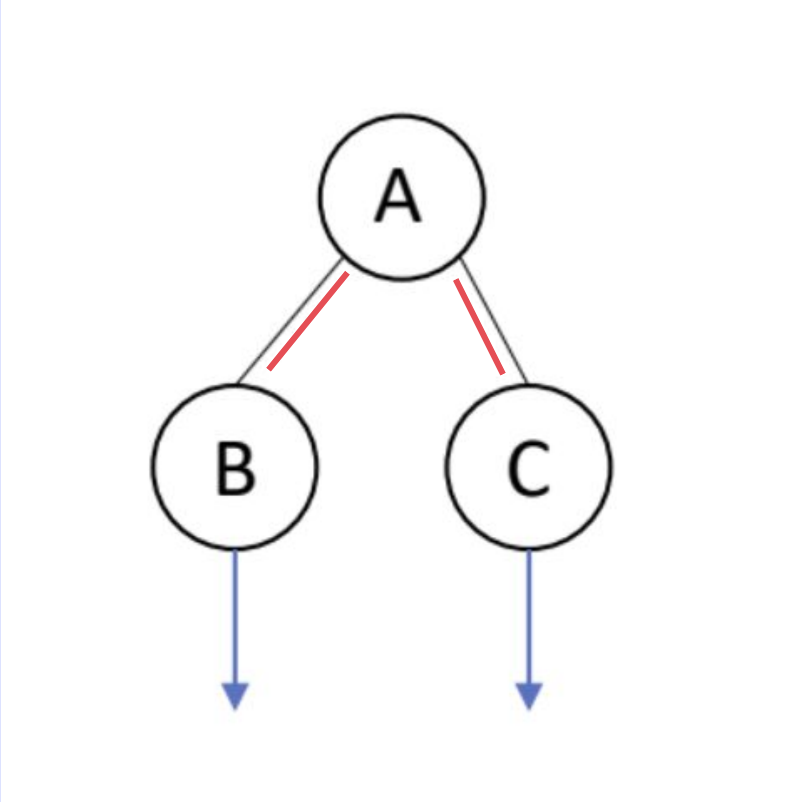
$$\psi(B,C) = \sum_{A} \sum_{P(A)} (1 + f_A)(\tfrac{1}{2})^{n(P(A))+1}$$

- $\sum_{A}$ - summation over all common ancestors
- $\sum_{P(A)}$ - summation over paths through ancestor A
- f_A - inbreeding coefficient
- n() - edges in path

Half-Siblings

- $\sum_{A} = 1$
- $\sum_{P(A)} = 1$
- $f_A = 0$
- $n = 2$

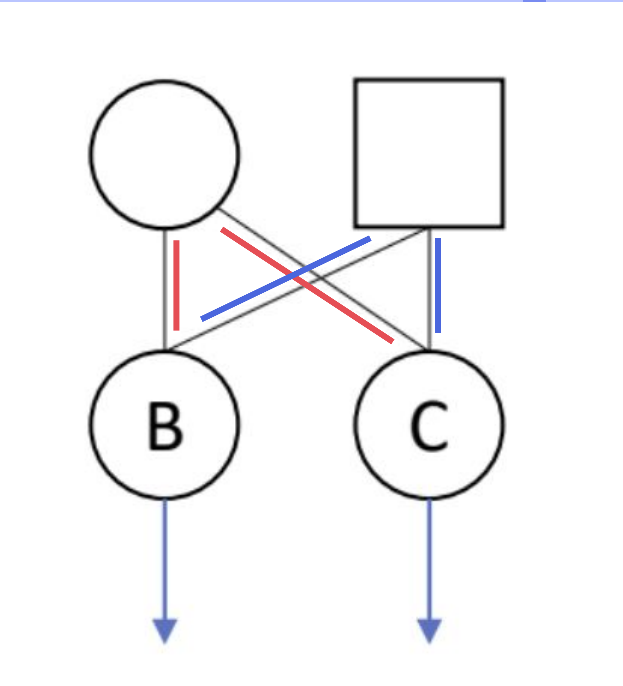
$$\Psi = (\tfrac{1}{2})^{2+1} = \tfrac{1}{8}$$



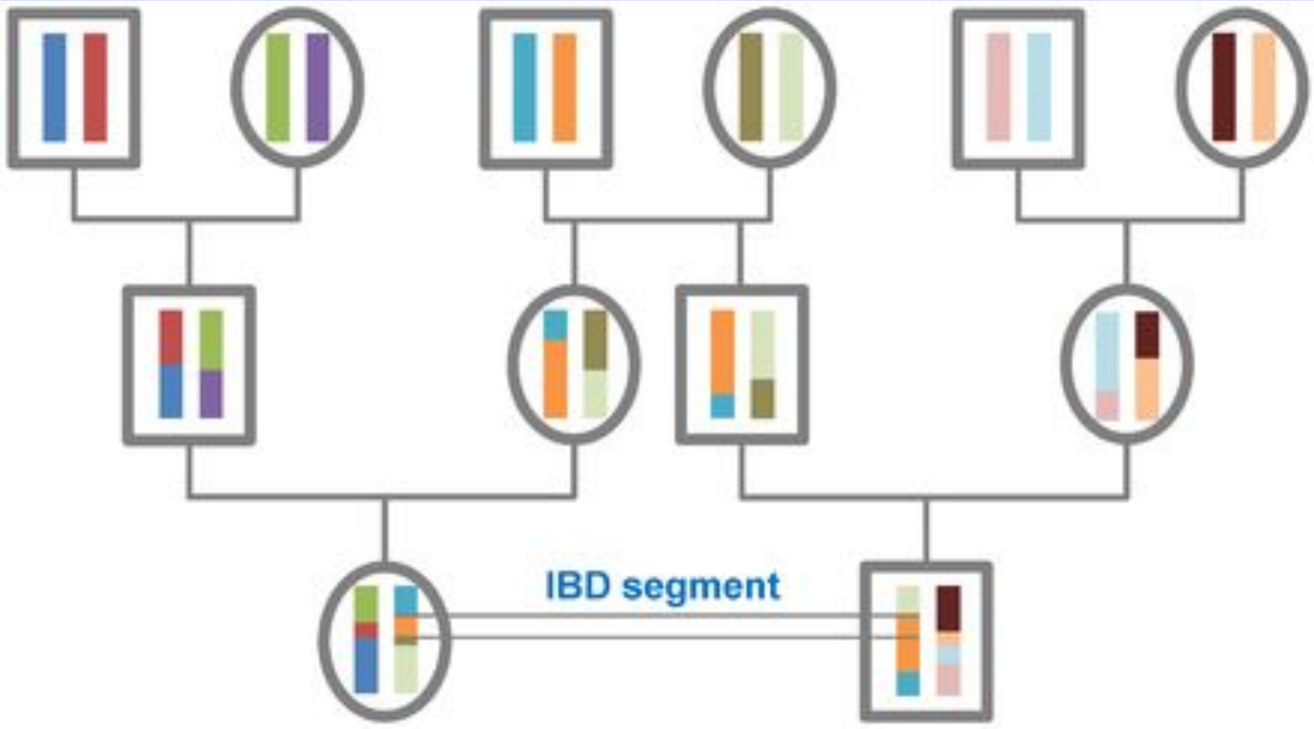
Full-Siblings

- $\sum_{A} = 2$
- $\sum_{P(A)} = 1$
- $f_A = 0$
- $n = 2$

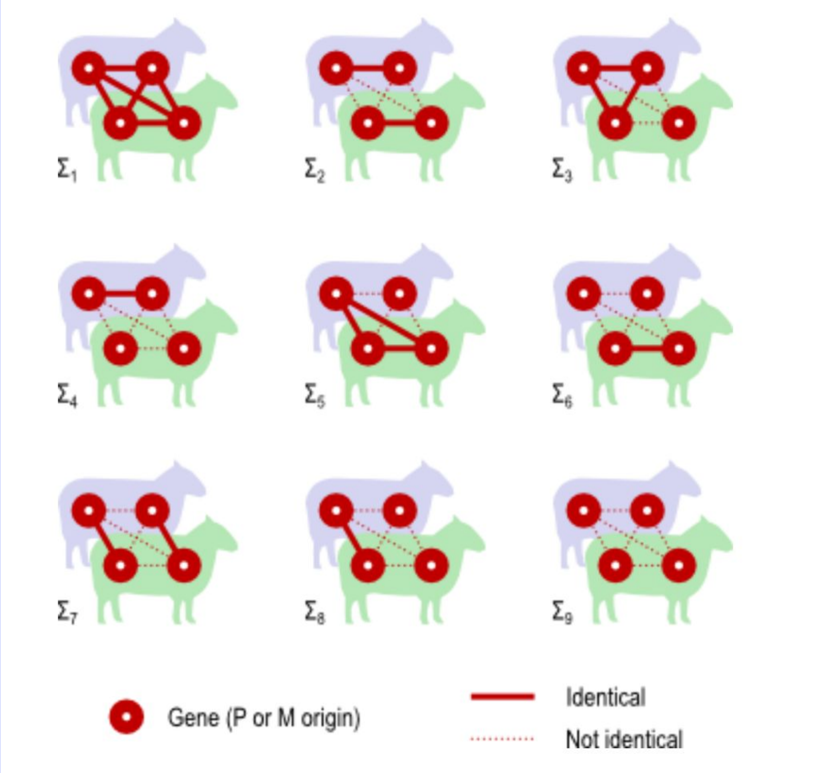
$$\Psi = 2(½)^{2+1} = ¼$$



Identity by Descent



Identity by Descent (States)



Identity by Descent (States)

RELATIONSHIP	Δ_1	Δ_2	Δ_3	Δ_4	Δ_5	Δ_6	Δ_7	Δ_8	Δ_9	ϕ_{ij}
Self	0	0	0	0	0	0	1	0	0	$\frac{1}{2}$
Parent-offspring	0	0	0	0	0	0	0	1	0	$\frac{1}{4}$
Half sibs	0	0	0	0	0	0	0	$\frac{1}{2}$	$\frac{1}{2}$	$\frac{1}{8}$
Full sibs/dizygotic twins	0	0	0	0	0	0	$\frac{1}{4}$	$\frac{1}{2}$	$\frac{1}{4}$	$\frac{1}{4}$
Monozygotic twins	0	0	0	0	0	0	1	0	0	$\frac{1}{2}$
First cousins	0	0	0	0	0	0	0	$\frac{1}{4}$	$\frac{3}{4}$	$\frac{1}{16}$
Double first cousins	0	0	0	0	0	0	$\frac{1}{16}$	$\frac{6}{16}$	$\frac{9}{16}$	$\frac{1}{8}$
Second cousins	0	0	0	0	0	0	0	$\frac{1}{16}$	$\frac{15}{16}$	$\frac{1}{64}$
Uncle-nephew	0	0	0	0	0	0	0	$\frac{1}{2}$	$\frac{1}{2}$	$\frac{1}{8}$
Offspring of sib-matings	$\frac{1}{16}$	$\frac{1}{32}$	$\frac{1}{8}$	$\frac{1}{32}$	$\frac{1}{8}$	$\frac{1}{32}$	$\frac{7}{32}$	$\frac{5}{16}$	$\frac{1}{16}$	$\frac{3}{8}$

Conditional probability

$$P(A|B,C) = \frac{P(A,B|C)}{P(B|C)}$$

Let A, B, C be events that occur with some probability.

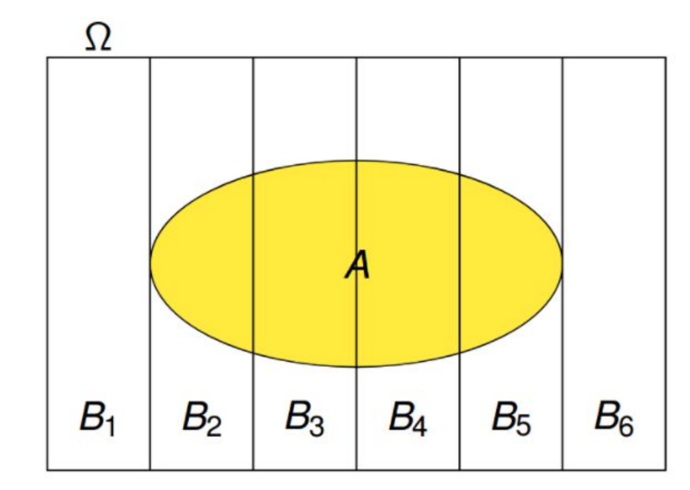
- A,B = some genotype configurations
- C = family tree

Law of total probability

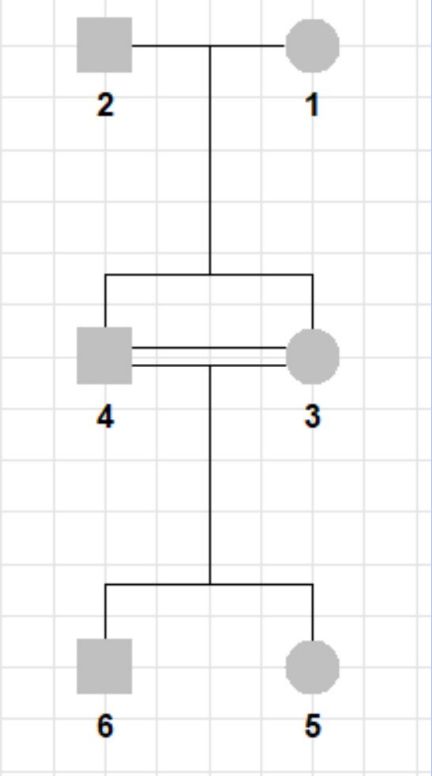
$$P(D) = \sum_i P(D, E_i) = \sum_i P(D|E_i)P(E_i)$$

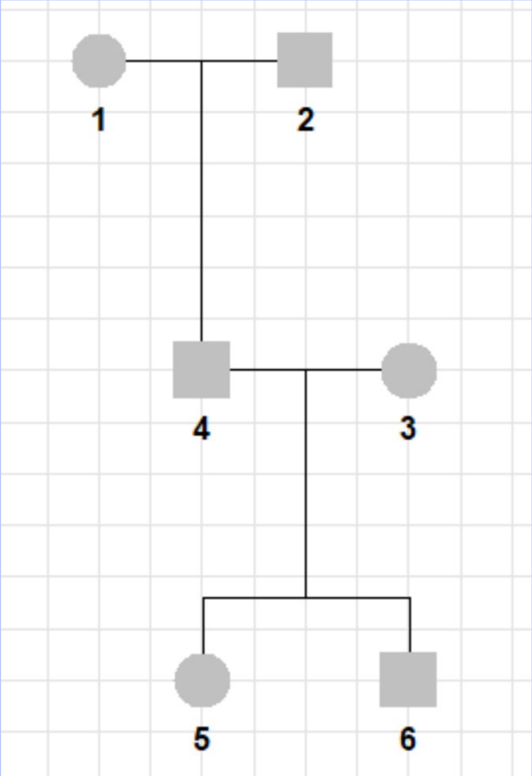
Let D, E_i be events that occur with some probability.

- D = {A, B | C}
- E_i = different ibd state configurations



Pedigree w/ and w/o sib-mating





Genotypes conditional on relatives

$$P(G_6 = aa | G_5 = aa, T) = \frac{P(G_6 = aa, G_5 = aa | T)}{P(G_5 = aa | T)} = \frac{P(G_6 = aa, G_5 = aa | T)}{p^2(1-f) + pf}$$

- G_5, G_6 are genotypes of nodes 5, 6.
- T is some tree relating nodes 5 and 6.
- Use total law of probability to get numerator, denominator
- Inbreeding coefficient f depends on 5's parents
- Numerator depends on type of relationship, the Delta values!

Genotype Probability of 6 (w/ inbreeding)

$$P(aa|aa,5) = \frac{P(aa|\ aa,5)}{P(aa|T)} = \frac{P(aa|\ aa,5)}{p^2(1-f_A) + pf_A} =$$

$$\frac{p^4 \cdot \Delta_9 + p^3(\Delta_4 + \Delta_6 + \Delta_8) + p^2(\Delta_2 + \Delta_7 + \Delta_3 + \Delta_5) + p \cdot \Delta_1}{p^2(1-f) + pf}$$

P(aa|aa, 5) = 44.5% (Yikes!)

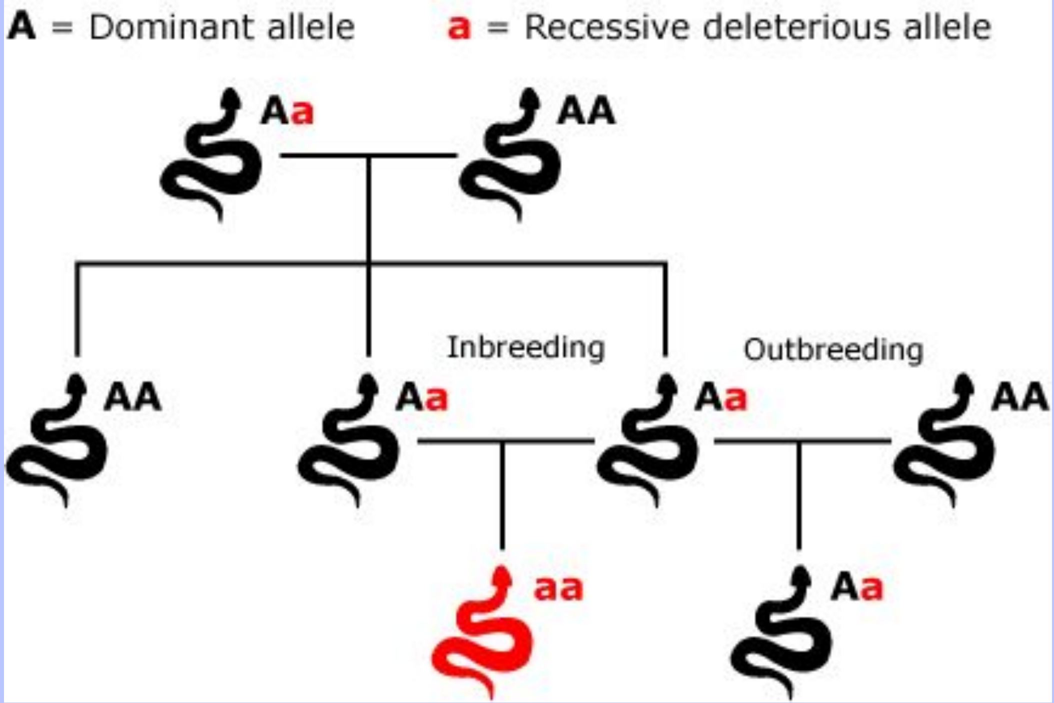
Genotype Probability of 6 (w/o inbreeding)

$$P(aa|aa, 5) = \frac{P(aa|\ aa, 5)}{P(aa|T)} = \frac{P(aa|\ aa, 5)}{p^2(1-f_A) + pf_A} = \frac{P(aa|\ aa, 5)}{p^2} =$$

$$\frac{p^4 \cdot \Delta_9 + p^3 \cdot \Delta_8 + p^2 \cdot \Delta_7}{p^2}$$

$P(aa|aa, 5) = 36.0\%$

Upshot: inbreeding increases the chances of homozygous recessive genotypes



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