

Inbreeding

Alan R. Rogers

March 23, 2020

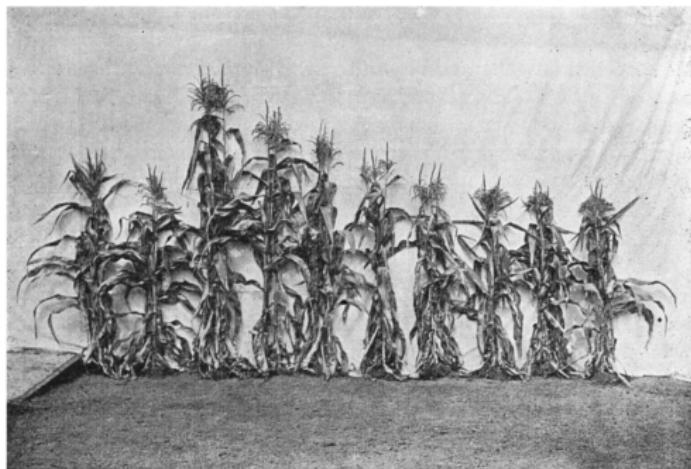
Inbreeding depression in corn



(JONES 1924)

- ▶ Two plants on left are from inbred homozygous strains.
- ▶ Next: the F_1 offspring of these strains
- ▶ Then offspring (F_2) of two F_1 s.
- ▶ Then F_3
- ▶ And so on.

Inbreeding depression in corn

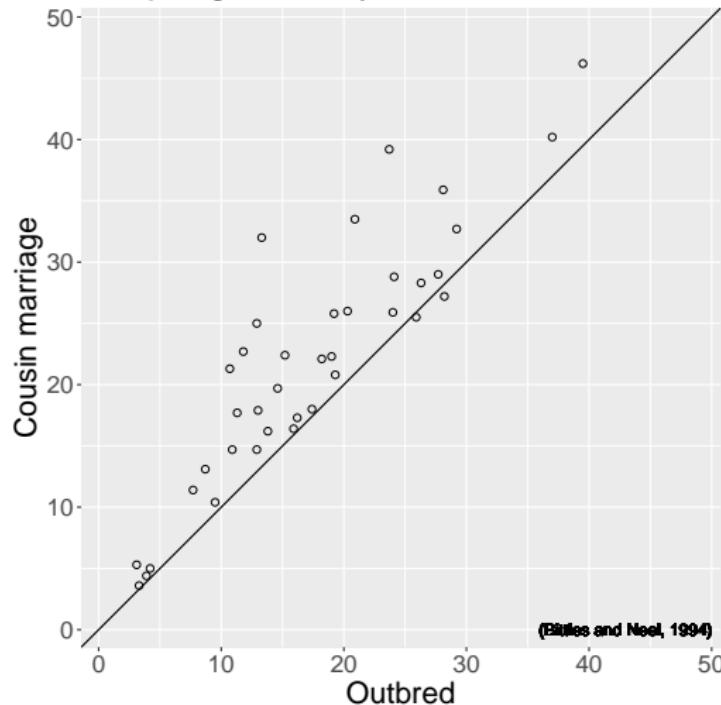


(JONES 1924)

- ▶ Two plants on left are from inbred homozygous strains.
- ▶ Next: the F_1 offspring of these strains
- ▶ Then offspring (F_2) of two F_1 s.
- ▶ Then F_3
- ▶ And so on.

Inbreeding depression in humans

Offspring mortality: inbred versus outbred



Offspring of cousin marriages are less likely to survive.

(BITTLES AND NEEL 1994)

Genotype frequencies without random mating

Genotype	Frequency
A_1A_1	$p^2 + pqF$
A_1A_2	$2pq(1 - F)$
A_2A_2	$q^2 + pqF$

Describes any bi-allelic locus.

$F = 0$ under random mating.

Reduces to Hardy-Weinberg.

$F > 0$ under inbreeding. Gives excess of homozygotes.

F is the *coefficient of inbreeding*.

Example

Assume $p = 1/2$

Genotype	Frequency	
	$F = 0$	$F = 0.1$
A_1A_1	0.25	0.275
A_1A_2	0.50	0.450
A_2A_2	0.25	0.275

Inbred population has more homozygotes.

Suffers if either

- ▶ Heterozygotes tend to have high fitness
- ▶ deleterious alleles tend to be recessive.

Outline of theory

Inbreeding increases F , which increases homozygosity, which decreases fitness.

Outline of theory

Inbreeding increases F , which increases homozygosity, which decreases fitness.

Outline of theory

Inbreeding increases F , which increases homozygosity, which decreases fitness.

Decay of heterozygosity under selfing

Gen.	A_1A_1	A_1A_2	A_2A_2
0		N	
		\vdots	
		$\frac{1}{2}$	
		\vdots	
1	$\frac{1}{4}N$	$\frac{1}{2}N$	$\frac{1}{4}N$
	\vdots	\vdots	\vdots
	$\frac{1}{4}$	$\frac{1}{2}$	$\frac{1}{4}$
	\vdots	\vdots	\vdots
2	$\frac{3}{8}N$	$\frac{1}{4}N$	$\frac{3}{8}N$

Decay of heterozygosity under selfing

Half of heterozygosity is lost each generation.

What about cousin mating, or mating between sibs?

It is *extremely* difficult to work this out, using the method we just used.

Between 1903 and 1915, no one could get it right.

Pearl (1913): Only for brother-sister matings does inbreeding reduce heterozygosity. [Wrong!]

Solution: build theory looking backwards in time, not forwards.

What about cousin mating, or mating between sibs?

It is *extremely* difficult to work this out, using the method we just used.

Between 1903 and 1915, no one could get it right.

Pearl (1913): Only for brother-sister matings does inbreeding reduce heterozygosity. [Wrong!]

Solution: build theory looking backwards in time, not forwards.

What about cousin mating, or mating between sibs?

It is *extremely* difficult to work this out, using the method we just used.

Between 1903 and 1915, no one could get it right.

Pearl (1913): Only for brother-sister matings does inbreeding reduce heterozygosity. [Wrong!]

Solution: build theory looking backwards in time, not forwards.

Kinds of gene identity

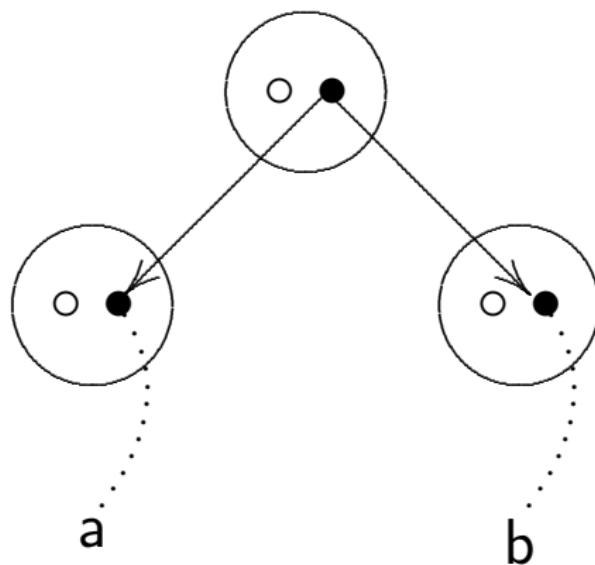
There are two senses in which a pair of gene copies may be “identical:”

identity in state : copies of same allele

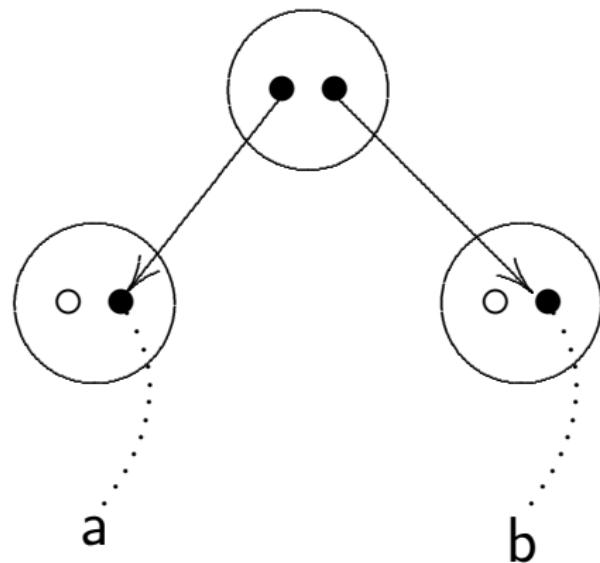
identity by descent : copies of same gene copy in an ancestor

Abbreviation: IBD = Identity by Descent

Gametes *a* and *b* are identical by descent



Identical in state, not by descent

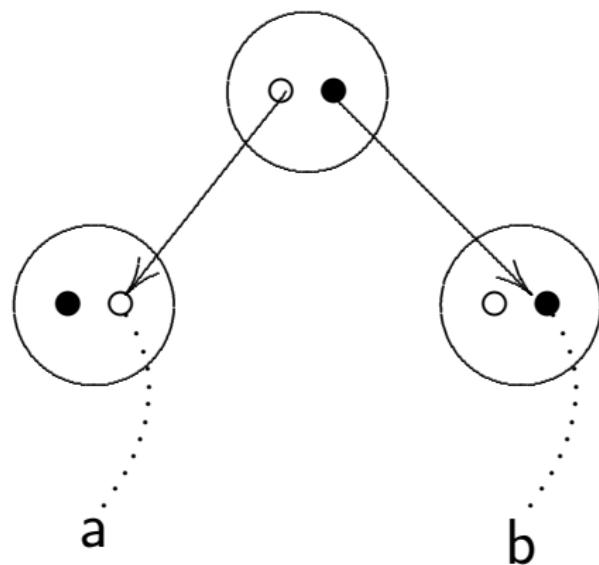


May be IBD relative to an earlier generation.

Not IBD relative to the pedigree shown here.

IBD is always relative to a particular generation.

Identical neither in state nor by descent



Uniting gametes

Consider the two gametes that unite to form an individual.

- ▶ F , is the probability that they are IBD
- ▶ What is the probability that they both carry A_1 ?

Event	Probability
IBD from A_1 -bearing ancestor	Fp
Descend from two random ancestors who both carry A_1	$(1 - F)p^2$

$$\begin{aligned}P_{11} &= Fp + (1 - F)p^2 \\&= p^2 + pqF\end{aligned}$$

Uniting gametes

Consider the two gametes that unite to form an individual.

- ▶ F , is the probability that they are IBD
- ▶ What is the probability that they both carry A_1 ?

Event	Probability
IBD from A_1 -bearing ancestor	Fp
Descend from two random ancestors who both carry A_1	$(1 - F)p^2$

$$\begin{aligned}P_{11} &= Fp + (1 - F)p^2 \\&= p^2 + pqF\end{aligned}$$

Uniting gametes

Consider the two gametes that unite to form an individual.

- ▶ F , is the probability that they are IBD
- ▶ What is the probability that they both carry A_1 ?

Event	Probability
IBD from A_1 -bearing ancestor	Fp
Descend from two random ancestors who both carry A_1	$(1 - F)p^2$

$$\begin{aligned} P_{11} &= Fp + (1 - F)p^2 \\ &= p^2 + pqF \end{aligned}$$

Uniting gametes

Consider the two gametes that unite to form an individual.

- ▶ F , is the probability that they are IBD
- ▶ What is the probability that they both carry A_1 ?

Event	Probability
IBD from A_1 -bearing ancestor	Fp
Descend from two random ancestors who both carry A_1	$(1 - F)p^2$

$$\begin{aligned}P_{11} &= Fp + (1 - F)p^2 \\&= p^2 + pqF\end{aligned}$$

All three genotypes

Genotype	Frequency
A_1A_1	$p^2 + pqF$
A_1A_2	$2pq(1 - F)$
A_2A_2	$q^2 + pqF$

Same formulas as before.

F is no longer arbitrary.

F is probability that uniting gametes are IBD.