

# Lecture 5

## Inbreeding and Crossbreeding

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Introduction to Quantitative Genetics  
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## Inbreeding

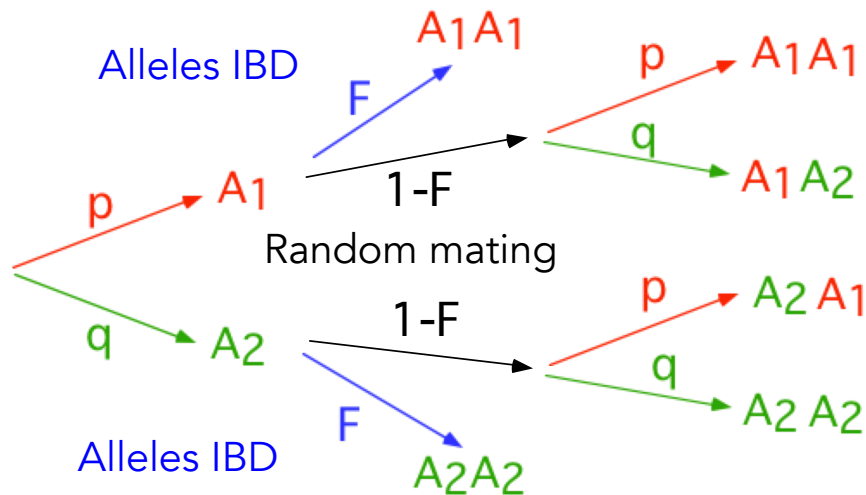
- Inbreeding = mating of related individuals
- Often results in a change in the mean of a trait
- Inbreeding is intentionally practiced to:
  - create genetic uniformity of laboratory stocks
  - produce stocks for crossing (animal and plant breeding)
- Inbreeding is unintentionally generated:
  - by keeping small populations (such as is found at zoos)
  - during selection

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# Genotype frequencies under inbreeding

- The inbreeding coefficient,  $F$
- $F = \text{Prob}(\text{the two alleles within an individual are IBD})$  -- identical by descent
- Hence, with probability  $F$  both alleles in an individual are identical, and hence a homozygote
- With probability  $1-F$ , the alleles are combined at random

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Genotype	Alleles IBD	Alleles not IBD	frequency
$A_1A_1$	$Fp$	$(1-F)p^2$	$p^2 + Fpq$
$A_2A_1$	0	$(1-F)2pq$	$(1-F)2pq$
$A_2A_2$	$Fq$	$(1-F)q^2$	$q^2 + Fpq$

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# Changes in the mean under inbreeding

Genotypes	$A_1A_1$	$A_1A_2$	$A_2A_2$
	0	a+d	2a

$$\text{freq}(A_1) = p, \quad \text{freq}(A_2) = q$$

Using the genotypic frequencies under inbreeding, the population mean  $\mu_F$  under a level of inbreeding  $F$  is related to the mean  $\mu_0$  under random mating by

$$\mu_F = \mu_0 - 2Fpqd$$

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**For  $k$  loci, the change in mean is**

$$\mu_F = \mu_0 - 2F \sum_{i=1}^k p_i q_i d_i = \mu_0 - BF$$

**Here  $B$  is the reduction in mean under complete inbreeding ( $F=1$ ), where**  $B = 2 \sum p_i q_i d_i$

- There will be a change of mean value if dominance is present ( $d \neq 0$ )
- For a single locus, if  $d > 0$ , inbreeding will decrease the mean value of the trait. If  $d < 0$ , inbreeding will increase the mean
- For multiple loci, a decrease (**inbreeding depression**) requires **directional dominance** --- dominance effects  $d_i$  tending to be positive.
- The magnitude of the change of mean on inbreeding depends on gene frequency, and is greatest when  $p = q = 0.5$

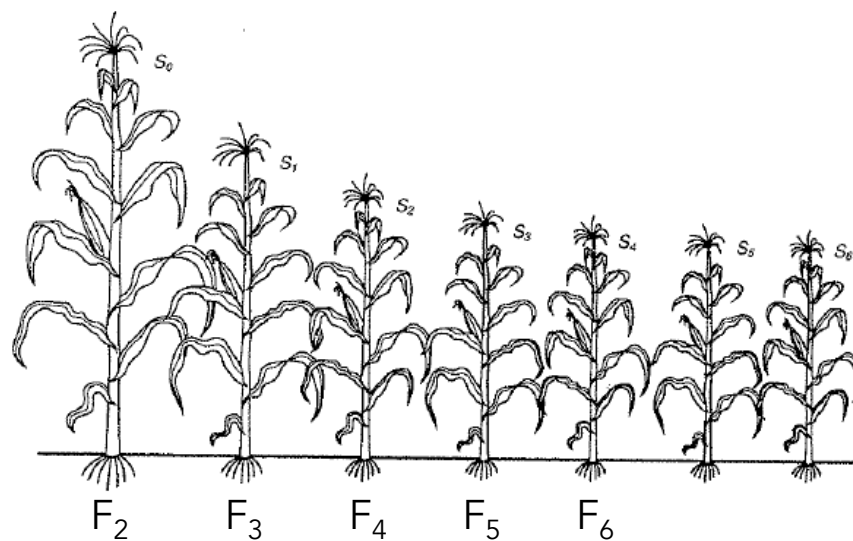
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# Inbreeding Depression and Fitness traits



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## Inbreeding depression



Example for maize height

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## Fitness traits and inbreeding depression

- Often seen that inbreeding depression is strongest on fitness-relative traits such as yield, height, etc.
- Traits less associated with fitness often show less inbreeding depression
- Selection on fitness-related traits may generate directional dominance

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## Why do traits associated with fitness show inbreeding depression?

- Two competing hypotheses:
  - **Overdominance Hypothesis**: Genetic variance for fitness is caused by loci at which heterozygotes are more fit than both homozygotes. Inbreeding decreases the frequency of heterozygotes, increases the frequency of homozygotes, so fitness is reduced.
  - **Dominance Hypothesis**: Genetic variance for fitness is caused by rare deleterious alleles that are recessive or partly recessive; such alleles persist in populations because of recurrent mutation. Most copies of deleterious alleles in the base population are in heterozygotes. Inbreeding increases the frequency of homozygotes for deleterious alleles, so fitness is reduced.

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# Inbred depression in largely selfing lineages

- Inbreeding depression is common in outcrossing species
- However, generally fairly uncommon in species with a high rate of selfing
- One idea is that the constant selfing have purged many of the deleterious alleles thought to cause inbreeding depression
- However, lack of inbreeding depression also means a lack of heterosis (a point returned to shortly)
  - Counterexample is Rice: Lots of heterosis but little inbreeding depression

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## Evolution of the Selfing Rate

- **Automatic selection** (the cost of **outcrossing**)
  - An allele that increases the selfing rate has a 50% advantage
  - Pollen discounting
- Selection for **reproductive assurance**
  - When population density is low, or pollinators rare, failure to outcross may occur
  - **Baker's law**: Colonizing species generally have the ability to self.

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What stops all plants from being selfers?

Inbreeding depression. If fitness of selfed-produced offspring is less than 50% of that from outcrossed-produced

$$w(\eta) = \eta \bar{w}_1 + \frac{1}{2} (1 - \eta) \bar{w}_0 + \frac{1}{2} (1 - \eta) \bar{w}_0$$

$$\frac{\partial w(\eta)}{\partial \eta} = \bar{w}_1 - \frac{\bar{w}_0}{2}$$

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## Lande and Schemske (1985)

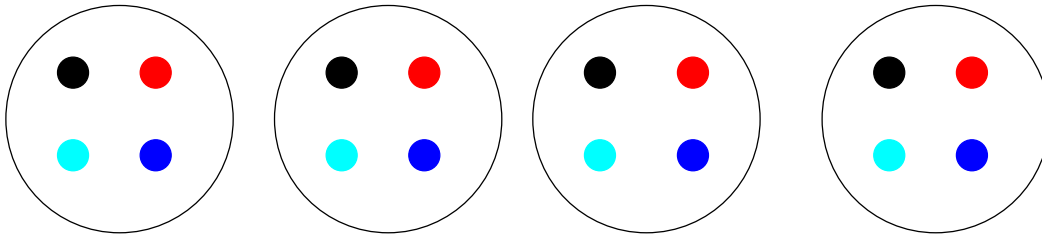
- As selfing rate increases, inbreeding load can decrease
  - If inbreeding largely due to recessive or partially recessive deleterious alleles, the mutation-selection equilibrium frequency decreases in selfers
  - As inbreeding load decreases, alleles that increase outcrossing rate are not favored
  - Hence, once largely selfing, very hard to revert

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# Variance Changes Under Inbreeding

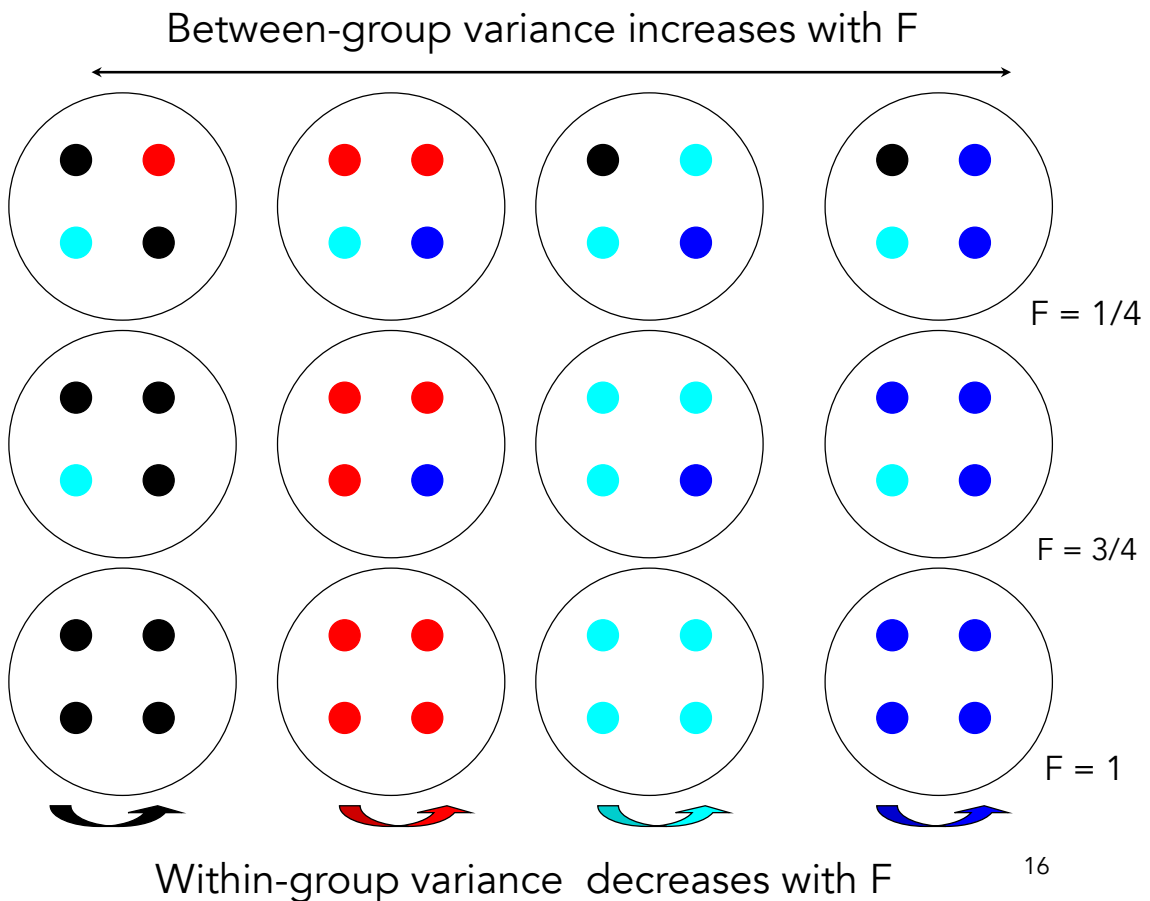
Inbreeding **reduces variation within each population**

Inbreeding **increases the variation between populations**  
(i.e., variation in the means of the populations)



$$F = 0$$

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# Implications for traits

- A series of inbred lines from an  $F_2$  population are expected to show
  - **more within-line uniformity** (variance about the mean within a line)
    - Less within-family genetic variation for selection
  - **more between-line divergence** (variation in the mean value between lines)
    - More between-family genetic variation for selection

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## Variance Changes Under Inbreeding

	General	$F = 1$	$F = 0$
Between lines	$2FV_A$	$2V_A$	0
Within Lines	$(1-F)V_A$	0	$V_A$
Total	$(1+F)V_A$	$2V_A$	$V_A$

The above results assume ONLY additive variance i.e., no dominance/epistasis. When nonadditive variance present, results very complex (see WL Chpt 11).

# Line Crosses: Heterosis

When inbred lines are crossed, the progeny show an increase in mean for characters that previously suffered a reduction from inbreeding.

This increase in the mean over the average value of the parents is called **hybrid vigor** or **heterosis**

$$H_{F_1} = \mu_{F_1} - \frac{\mu_{P_1} + \mu_{P_2}}{2}$$

A cross is said to show heterosis if  $H > 0$ , so that the  $F_1$  mean is larger than the average of both parents.

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## Expected levels of heterosis

If  $p_i$  denotes the frequency of  $Q_i$  in line 1, let  $p_i + \delta p_i$  denote the frequency of  $Q_i$  in line 2.

The expected amount of heterosis becomes

$$H_{F_1} = \sum_{i=1}^n (\delta p_i)^2 d_i$$

- **Heterosis depends on dominance:**  $d = 0$  = no inbreeding depression and no Heterosis. As with inbreeding depression, directional dominance is required for heterosis.
- **H is proportional to the square of the difference in allele frequencies between populations** H is greatest when alleles are fixed in one population and lost in the other (so that  $|\delta p_i| = 1$ ).  $H = 0$  if  $\delta p = 0$ .
- **H is specific to each particular cross.** H must be determined empirically, since we do not know the relevant loci nor their gene frequencies.

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# Heterosis declines in the F<sub>2</sub>

In the F<sub>1</sub>, all offspring are heterozygotes. In the F<sub>2</sub>, random mating has occurred, reducing the frequency of heterozygotes.

As a result, there is a reduction of the amount of heterosis in the F<sub>2</sub> relative to the F<sub>1</sub>,

$$H_{F_2} = \mu_{F_2} - \frac{\mu_{P_1} + \mu_{P_2}}{2} = \frac{(\delta p)^2 d}{2} = \frac{H_{F_1}}{2}$$

Since random mating occurs in the F<sub>2</sub> and subsequent generations, the **level of heterosis stays at the F<sub>2</sub> level.**

## Agricultural importance of heterosis

Crosses often show **high-parent heterosis**, wherein the F<sub>1</sub> not only beats the average of the two parents (**mid-parent heterosis**), it exceeds the best parent.

Crop	% planted as hybrids	% yield advantage	Annual added yield: %	Annual added yield: tons	Annual land savings
Maize	65	15	10	55 x 10 <sup>6</sup>	13 x 10 <sup>6</sup> ha
Sorghum	48	40	19	13 x 10 <sup>6</sup>	9 x 10 <sup>6</sup> ha
Sunflower	60	50	30	7 x 10 <sup>6</sup>	6 x 10 <sup>6</sup> ha
Rice	12	30	4	15 x 10 <sup>6</sup>	6 x 10 <sup>6</sup> ha

# Hybrid Corn in the US

Shull (1908) suggested objective of corn breeders should be to find and maintain the best parental lines for crosses

Initial problem: early inbred lines had low seed set

Solution (Jones 1918): use a hybrid line as the seed parent, as it should show heterosis for seed set

1930's - 1960's: most corn produced by double crosses

Since 1970's most from single crosses

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# A Cautionary Tale

1970-1971 the great Southern Corn Leaf Blight almost destroyed the whole US corn crop

Much larger (in terms of food energy) than the great potato blight of the 1840's

Cause: Corn can self-fertilize, so to make hybrids either have to manually detassel the pollen structures or use genetic tricks that cause male sterility.

Almost 85% of US corn in 1970 had Texas cytoplasm Tcms, a mtDNA encoded male sterility gene

Tcms turned out to be hyper-sensitive to the fungus *Helminthosporium maydis*. Resulted in over a billion dollars of crop loss

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# Crossing Schemes to Reduce the Loss of Heterosis: Synthetics

Take  $n$  lines and construct an  $F_1$  population by making all pairwise crosses

Allow random mating from the  $F_2$  on to produce a synthetic population

$$F_2 = F_1 - \frac{F_1 - \bar{P}}{n} \quad H/n$$

$$H_{F_2} = H_{F_1} \left( 1 - \frac{1}{n} \right) \quad \text{Only } 1/n \text{ of heterosis lost vs. } 1/2$$

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## Synthetics

- Major trade-off
  - As more lines are added, the  $F_2$  loss of heterosis declines
  - However, as more lines are added, the mean of the  $F_1$  also declines, as less elite lines are used
  - Bottom line: For some value of  $n$ ,  $F_1 - H/n$  reaches a maximum value and then starts to decline with  $n$

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# Types of crosses

- The  $F_1$  from a cross of lines A x B (typically inbreds) is called a **single cross**
- A **three-way cross** (also called a **modified single cross**) refers to the offspring of an A individual crossed to the  $F_1$  offspring of B x C.
  - Denoted A x (B x C)
- A **double** (or **four-way**) **cross** is (A x B) x (C x D), the offspring from crossing an A x B  $F_1$  with a C x D  $F_1$ .

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## Predicting cross performance

- While single cross (offspring of A x B) hard to predict, three- and four-way crosses can be predicted if we know the means for single crosses involving these parents
- The three-way cross mean is the average mean of the two single crosses:
  - $\text{mean}(A \times \{B \times C\}) = [\text{mean}(A \times B) + \text{mean}(A \times C)]/2$
- The mean of a double (or four-way) cross is the average of all the single crosses,
  - $\text{mean}(\{A \times B\} \times \{C \times D\}) = [\text{mean}(A \times C) + \text{mean}(A \times D) + \text{mean}(B \times C) + \text{mean}(B \times D)]/4$

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# Individual vs. Maternal Heterosis

- **Individual heterosis**
  - enhanced performance in a hybrid individual
- **Maternal heterosis**
  - enhanced maternal performance (such as increased litter size and higher survival rates of offspring)
  - Use of **crossbred dams**
  - Maternal heterosis is often comparable, and can be greater than, individual heterosis

## Individual vs. Maternal Heterosis in Sheep traits

Trait	Individual H	Maternal H	total
Birth weight	3.2%	5.1%	8.3%
Weaning weight	5.0%	6.3%	11.3%
Birth-weaning survival	9.8%	2.7%	12.5%
Lambs reared per ewe	15.2%	14.7%	29.9%
Total weight lambs/ewe	17.8%	18.0%	35.8%
Prolificacy	2.5%	3.2%	5.7%

# Estimating the Amount of Heterosis in Maternal Effects

Contributions to mean value of line A

$$z_A = z + g_A^I + g_A^M + g_A^{M^0}$$

Individual genetic effect (BV)
Maternal genetic effect (BV)
Grandmaternal genetic effect (BV)

Consider the offspring of an A sire and a B dam

$$z_{AB} = z + \frac{g_A^I + g_B^I}{2} + g_B^M + g_B^{M^0} + h_{AB}^I$$

Individual genetic value is the average of both parental lines
Contribution from (individual) heterosis

Maternal and grandmaternal effects from the B mothers



$$Z_{AB} = Z + \frac{g_A^I + g_B^I}{2} + g_B^M + g_B^{M^0} + h_{AB}^I$$

Now consider the offspring of an B sire and a A dam

$$Z_{BA} = Z + \frac{g_A^I + g_B^I}{2} + g_A^M + g_A^{M^0} + h_{AB}^I$$

Maternal and grandmaternal  
genetic effects for B line

Difference between the two line means estimates  
difference in maternal + grandmaternal effects  
in A vs. B

Hence, an estimate of individual heterotic effects is

$$\frac{Z_{AB} + Z_{BA}}{2} - \frac{Z_{AA} + Z_{BB}}{2} = h_{AB}^I$$

The mean of offspring from a sire in line C crossed to a dam from a A X B cross (B = granddam, AB = dam)

$$z_{C AB} = \frac{2g_C^I + g_A^I + g_B^I}{4} + \frac{h_{CA}^I + h_{CB}^I}{2} + \frac{g_A^M + g_B^M}{2} + h_{AB}^M + g_B^{M^0} + \frac{r_{ab}^I}{2}$$

Average individual genetic value (average of the line BV's) points to  $\frac{2g_C^I + g_A^I + g_B^I}{4}$

Genetic maternal effect (average of maternal BV for both lines) points to  $\frac{g_A^M + g_B^M}{2}$

Grandmaternal genetic effect points to  $g_B^{M^0}$

New individual heterosis of C x AB cross points to  $\frac{h_{CA}^I + h_{CB}^I}{2}$

Maternal genetic heterotic effect points to  $h_{AB}^M$

"Recombinational loss" --- decay of the F<sub>1</sub> heterosis in the F<sub>2</sub> points to  $\frac{r_{ab}^I}{2}$

One estimate (confounded) of maternal heterosis

$$z_{C AB} = \frac{z_{CA} + z_{CB}}{2} = h_{AB}^M + \frac{r_{ab}^I}{2}$$