# BIOB480/BIOE548 notes 9/10/2024

**Introduction**

- Check on how homework went
- Quiz #1 Thursday: In class, closed book. Bring a pen or pencil, scrap paper (if you want), a calculator. Topics covered: why genetics is relevant to conservation, types of genetic mnarkers / ways to study genetic variation, ways to quantify genetic variation, Hardy-Weinberg Proportions, Linkage Disequilibrium. Be able to convert genotype counts to genotype frequencies, genotype frequencies to allele frequencies, etc. HW1 will be good practice.
- HW2 will be posted after class. Because we have a quiz Thursday, we may not have time to discuss questions, so please come to office hours or shoot me an email if you need clarifications or help. It will primarily cover today's lecture material, which I will augment with slides and notes on D2L.
- LD Simulator introduction (see `05_slides.pdf`)

**Quantitative Genetics**

The majority of this class focuses on theory and data relative to one or two loci. In some cases (such as plumage polymorphisms in birds), a single locus is responsible for all phenotypic variation present in a population. However, many traits we are interested in are *quantitative*, i.e. vary continuously, not categorically. (Human height is perhaps the most obvious example.) To study quantitative traits, we will need some introduction to the quantitative genetics. Perhaps the most important concept in the field is that of heritability.

We define heritability as the proportion of total phenotypic variance ($P_V$) that is attributable to genetic variation, meaning variation that parents can pass on to offspring. We denote it $h^2 = \frac{V_A}{V_P}$—importantly, the "exponent" is not actually an exponent, but simply a convention of the field. Heritability is important because phenotypic variation also includes environmental influences:

$$\text{Phenotype} = \text{Genotype} + \text{Environment}$$

What is environmental influence? Height, for example, has a clear genetic basis. But it is also determined by nutrition during childhood—a non-genetic contribution of the environment a particular genotype finds itself in (and the resources available to it).

An important concept for estimating heritability is the definition of variance, or spread of data around the mean, which we borrow from statistics:

$$V_P = \frac{\sum_{i=1}^{n}(P_i - \bar{P})^2}{n-1}$$

where $P_i$ is an individual's phenotypic value, $\bar{P}$ is the mean phenotypic value for the sample, and $n$ is the sample size.

The standard deviation of a phenotype (also a measure of the spread around the mean) is the square root of its variance:

$$\sigma_P = \sqrt{V_P}$$

The covariance between offspring & parents is the sum of the products of the difference between individual values and the population (meaning all parents or all offspring) mean:

$$COV_{PO} = \frac{\sum_{i=1}^{n}(P_i - \bar{P})(O_i - \bar{O})}{n-1}$$

Building off this, the correlation between trait values for parents and offspring is:

$$r_{PO} = \frac{COV_{PO}}{\sqrt{(V_P * V_O)}}$$

where $V_P$ is parental trait variance and $V_O$ is offspring trait variance.

Heritability ($h^2$) can be directly estimated as the slope of a regression of offspring on parent trait values, which is simply the covariance of parent and offspring trait values over total phenotypic variance ($\frac{COV_{PO}}{V_P}$).

To make these concepts more concrete, consider the following data:

| Parent Height (cm) | Child Height (cm) |
|---|---|
| 160 | 163 |
| 170 | 169 |
| 164 | 162 |
| 180 | 171 |
| 161 | 173 |

We first calculate $V_P$ for the parents using a mean ($\bar{P}$) of (160+170+164+180+161)/5=167:

$$V_P = \frac{\sum_{i=1}^{n}(P_i - \bar{P})^2}{n-1} = \frac{(160-167)^2 + (170-167)^2 + (164-167)^2 + (180-167)^2 + (161-167)^2}{5-1} = 68 \text{ cm}$$

This gives us a standard deviation ($\sigma_{po}$) of $\sqrt{68} = 8.24$.

Following the same procedure, we calculate variance in offspring phenotypes, which requires mean offspring height ($\bar{O}$ = (163+169+162+171+173)/5=167.6): :

$$V_O = \frac{\sum_{i=1}^{n}(O_i - \bar{O})^2}{n-1} = \frac{(163-167.6)^2 + (169-167.6)^2 + (162-167.6)^2 + (171-167.6)^2 + (173-167.6)^2}{5-1} = 23.8 \text{ cm}$$

Next, we calculate the covariance between parent and offspring phenotypes:

$$COV_{PO} = \frac{\sum_{i=1}^{n}(P_i - \bar{P})(O_i - \bar{O})}{n-1}$$
$$= \frac{(160-167)(163-167.6) + ... + (161-167)(173-167.6)}{5-1} = 16.25 \text{ cm}$$

(Here "..." simply indicates the other values of $P_i$ and $O_i$ that don't fit on the page.)

With $COV_{PO}$ we can calculate $r_{PO}$:

$$r_{PO} = \frac{COV_{PO}}{\sqrt{(V_P * V_O)}} = \frac{16.25}{\sqrt{(68 * 23.8)}} = 0.403934$$

. . . and heritability:

$$h^2 = \frac{COV_{PO}}{V_P} = \frac{16.25}{68} = 0.2389706$$

This is exactly the same as the slope of a linear regression of offspring on parent height values:

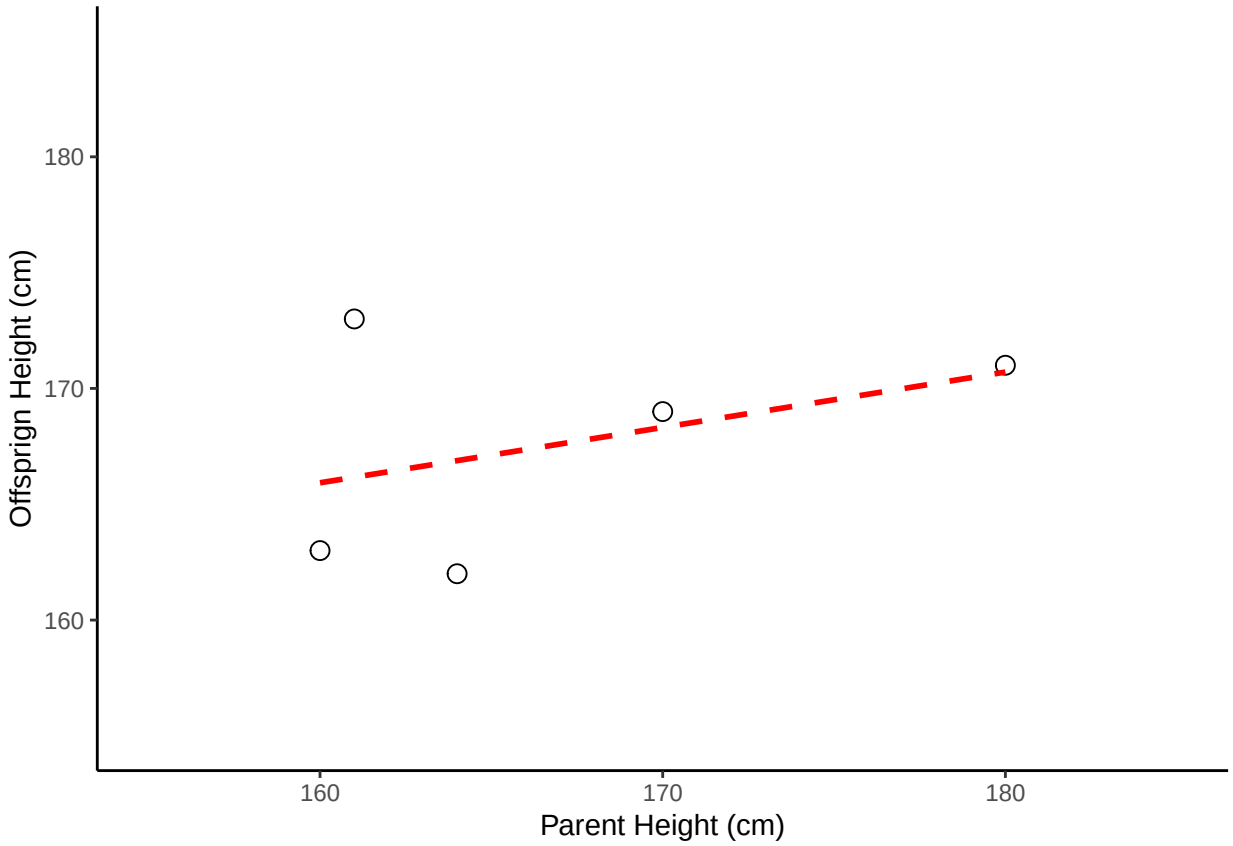
```
library(tidyverse)
p_i <- c(160, 170, 164, 180, 161)
o_i <- c(163, 169, 162, 171, 173)
df <- cbind(p_i, o_i) %>% as.data.frame()
model <- lm(o_i ~ p_i)
model$coefficients[2]
```

```
##       p_i
## 0.2389706
```

(Beyond quantitative genetics, the slope of *any* regression can be calculated as Cov(x, y)/Var(x)).

Though not particularly impressive with so few data, the relationship is obvious when plotted:

```
ggplot(df, aes(x=p_i, y=o_i)) +
  theme_classic() +
  geom_point(pch=21, size=3) +
  xlim(155, 185) +
  ylim(155, 185) +
  geom_smooth(method='lm', se = FALSE, linetype="dashed", color="red") +
  xlab("Parent Height (cm)") +
  ylab("Offsprign Height (cm)")
```




We can now also define total phenotypic variance (which we will also call $V_P$, sorry) as:

$$V_P = V_G + V_E + 2COV_{GE}$$

where $V_G$ is phenotypic genetic variance, or the proportion of phenotypic variance that is rooted in hertiable genetic variation; $V_E$ is phenotypic environmental variance, and $2COV_{GE}$ is the covarinnce between genetics and the environment, which is negligible when individuals are under te same environemntal condtitions.

We can further parition $V_G$ into effects from **additive**, **dominant**, or **partially dominant** loci:

$$V_G = V_A + V_D + V_{PD}$$

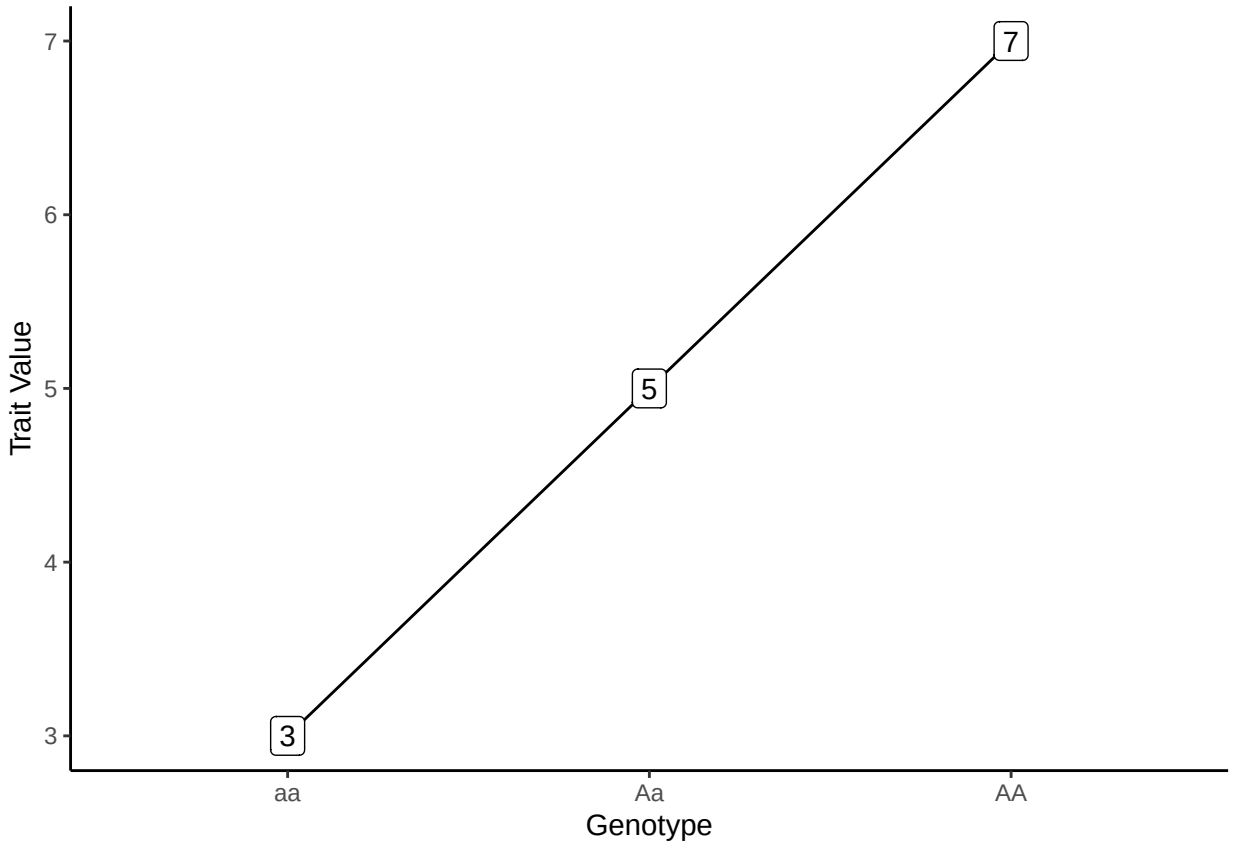
To determine which locus exhibits which mode of inheritance, we look at the relationship between genotypes and quantitative trait values.

First, we assign genotypes different values, which we represent algebraically with the letters $a$ and $d$:

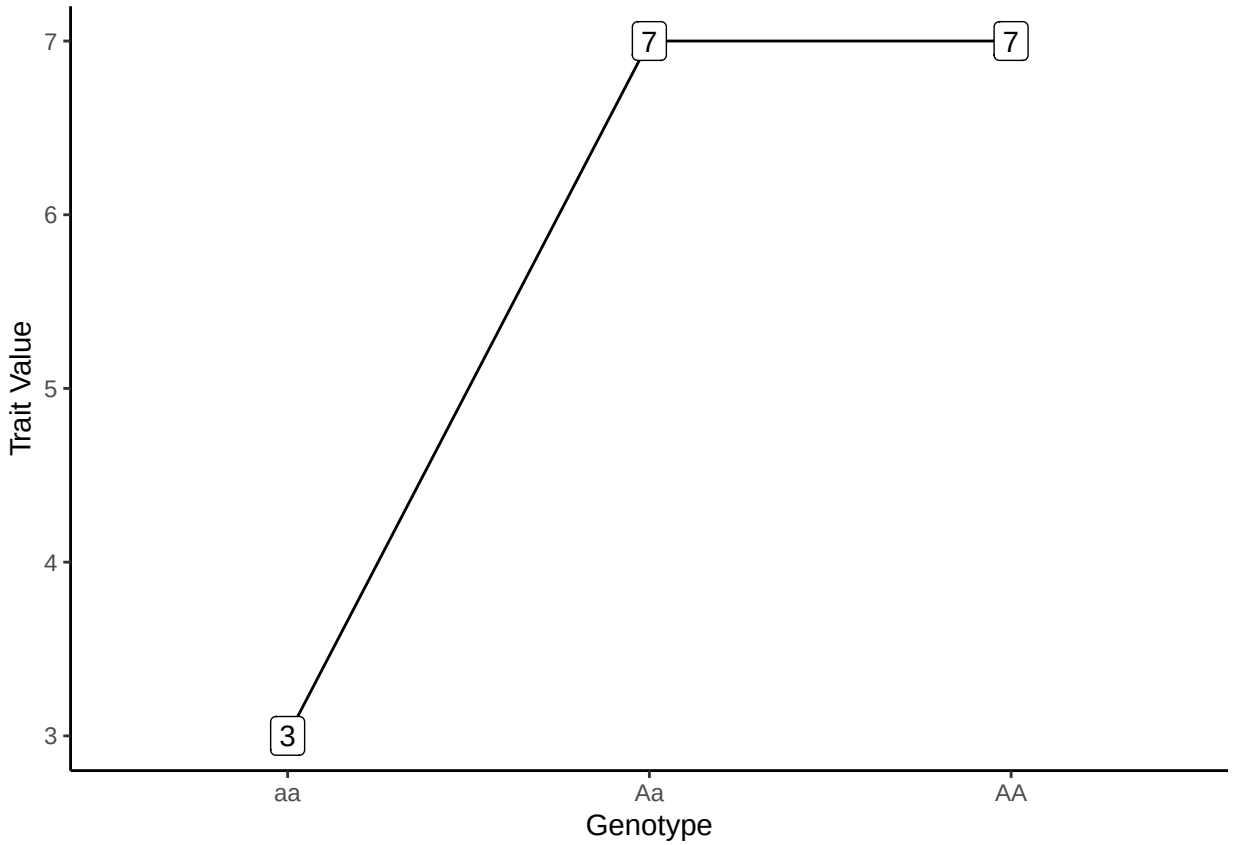
genotypes: $AA$, $Aa$, $aa$
genotypic values: $+a$, $d$, $-a$

In other words, $+a$ is the deviation of the trait value for $AA$ away from the mean of the two homozygotes, $d$ is the deviation of the trait value for the heterozygote away from the mean of the two homozygotes, and $-a$ is deviation of the trait value for $aa$ away from the mean of the two homozygotes. (You can thus think of the "mean" trait value of the two homozygotes as 0, as $(+a + -a)/2 = 0$) Homozygotes differ in genotypic value by $2a$, and hetozgotes differ from the mean of the two heterozygotes (again, 0) by $d$.

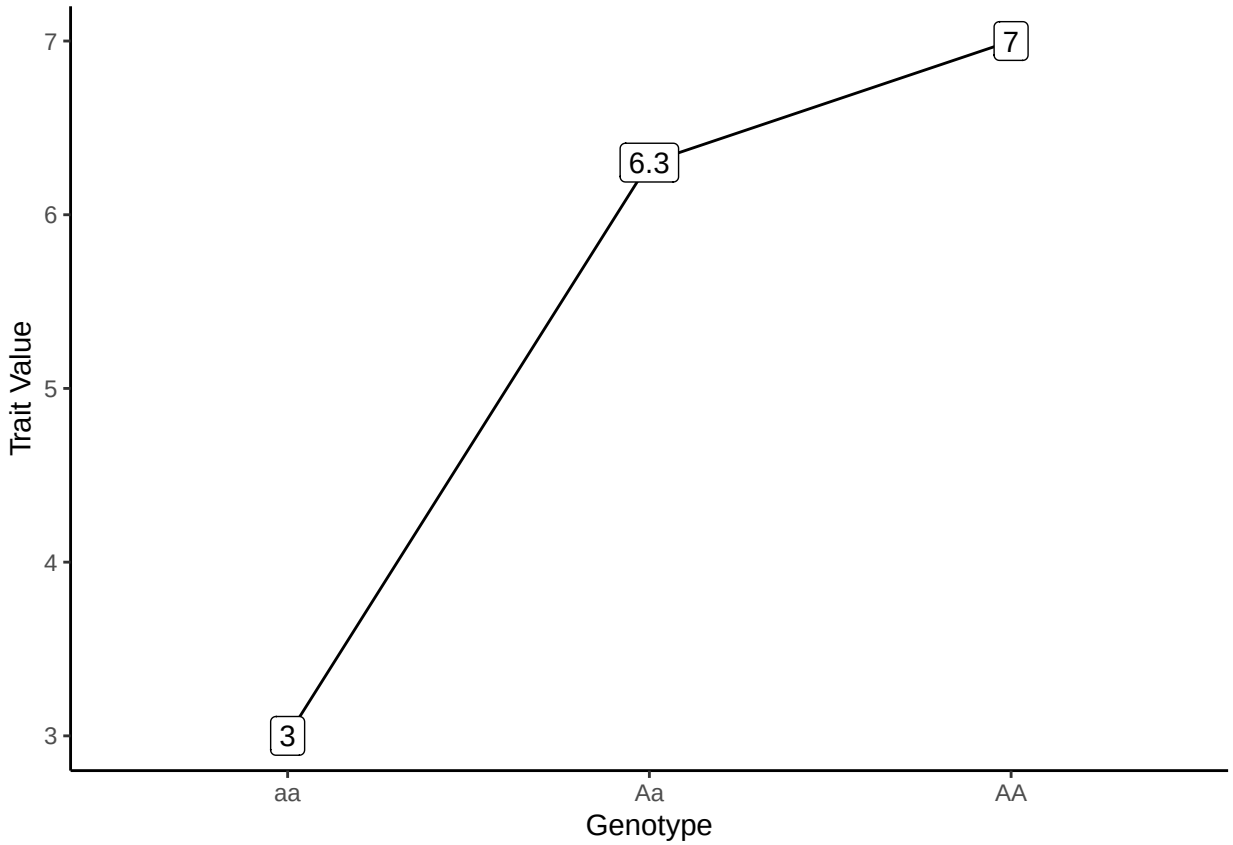
Different relationships between genotypes and genotypic values result from different modes of inheritence. In **additive genetic variance**, each alelle contributes equally to the value of a phenotype, and the heterozygote's trait values are the average of the two homozygotes ($+a = 2; -a = 2; d = 0$).




In contast, under **dominant genetic variance**, one copy of an allele is sufficient to attain the maximum value of a phenotype ($d = +a = 2$)




With **partially dominant genetic variance** one copy of an allele is not sufficient to attain the maximum value of a phenotype, but the genotypic value of the heterozygote is greater than the average value of the two homozygotes ($+a = 2; -a = 2; d = 1.3$)




As a shortcut, you can find $a$ by dividing the difference between the trait values of the two homozygotes by 2:

$$a = \frac{\text{(AA value - aa value)}}{2} = \frac{(7-3)}{2} = 2$$

You can find $d$ by first finding the midpoint (arithmetic mean) of the two homozygote trait values, and then subtracting that from the heterozygote trait value:

$$\text{midpoint} = \frac{\text{(AA value + aa value)}}{2} = \frac{(7+3)}{2} = 5$$
$$d = 6.3 - 5 = 1.3$$

Dan Bolnick has another app that helps connect this material to Mendelian single locus genetics: https://bolnicklab.shinyapps.io/MultilocusQuantGen/