



MACQUARIE
University

Quantitative Genetics (1)

LECTURE 5: HERITABILITY

2022



Background

Quantifying VG

- so far limited to single locus

H, A, ne, P,

- Looking at genetics from a phenotypic level

- Used to attribute causality to traits (nature vs. nurture)

Causal agents of phenotypes

- Alleles segregating at many loci

- Interactions among alleles (dominance and/or epistasis)

- Environmental effects

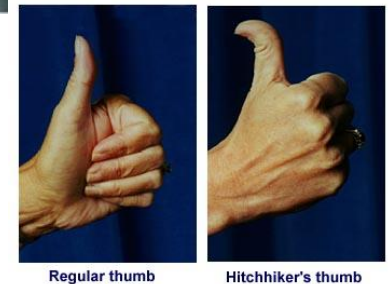
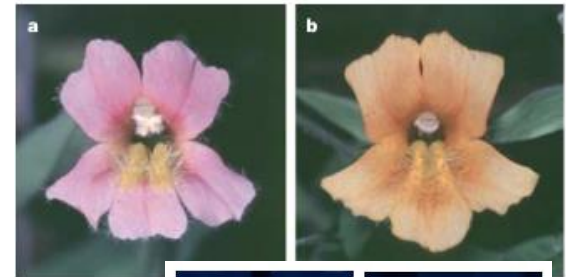
- Interactions & correlations between genetic and environmental effects

Lecture Outline

- Quantitative and Qualitative Traits
- History of Heritability
- Heritability (H^2) and Genetic Causes
- Relationship with Conservation Biology
- Worked Example for H^2 (ANOVA)
- GxE Interaction
- Phenotypic Plasticity

'Mendelian loci'

- Blood Type (A, B, O, AB)
- Flower colour (yellow, pink)
- Thumb shape
- Coat colour (black, orange –X linked)
- Goat beard (beard, no beard)
- Phenotypes take discrete values
- Predictable using Mendel's laws



22,480 known Mendelian traits in man
(as of 14 Aug 2014), OMIM:

<http://www.omim.org/>

3,057 known Mendelian traits in animals,
OMIA: <http://omia.angis.org.au/home/>

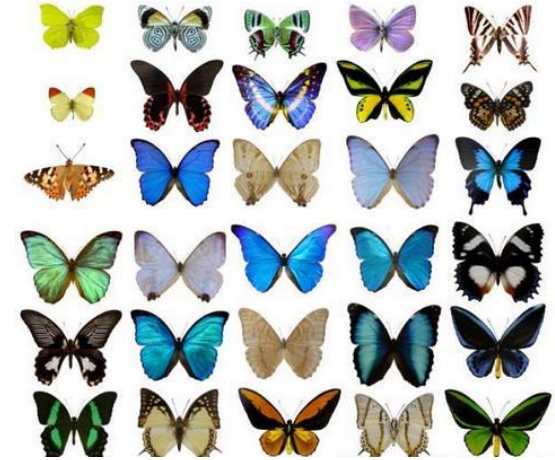
Quantitative genetics

- The genetic appraisal and analysis of '**complex**', '**continuous**', or '**quantitative**' traits, where:
- A quantitative trait = a trait whose phenotypic expression is determined by many individual genes (i.e. variation at many individual loci) (polygenic)



Examples of Quantitative Traits:

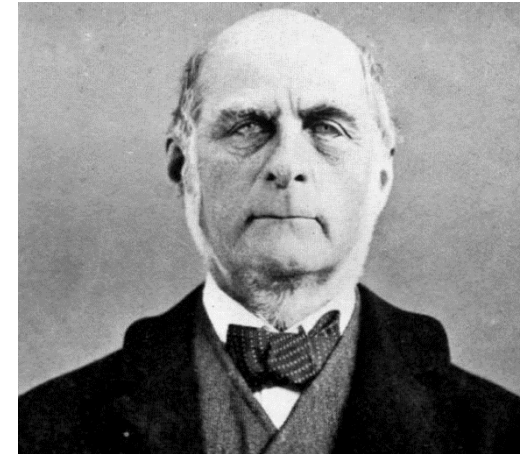
- Morphological traits:
 - Body size (height, weight)
 - Colouration (e.g. Bird plumage)
- Physiological traits
 - Enzyme activity
 - Blood pressure, cardiovascular performance
- Behavioural traits
 - Aggression, mate preferences, IQ etc.
- Life history traits
 - Developmental rates, age at maturity, etc.



History of Quantitative Genetics

Francis Galton: 'the apostle of quantification'

- the weather (1863)
- height (1889)
- finger print patterns (1888; 1892; 1893)
- beauty (1909)
- boredom (1909)
- criminal characteristics (1885)
- the effectiveness of prayers (1872)

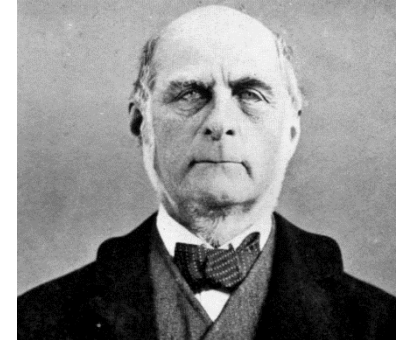


Introduced the terms 'nature' and 'nurture'
(*English Men of Science*, 1874)

History of Quantitative Genetics

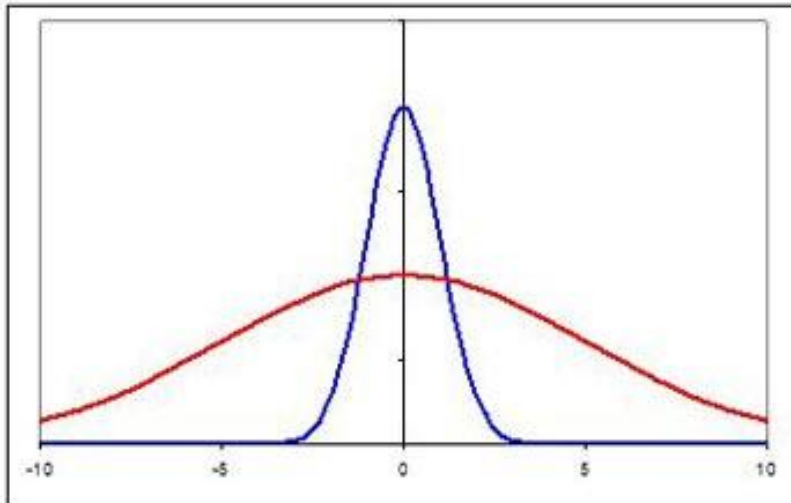
Francis Galton

Interested in *trait variation* rather than trait means

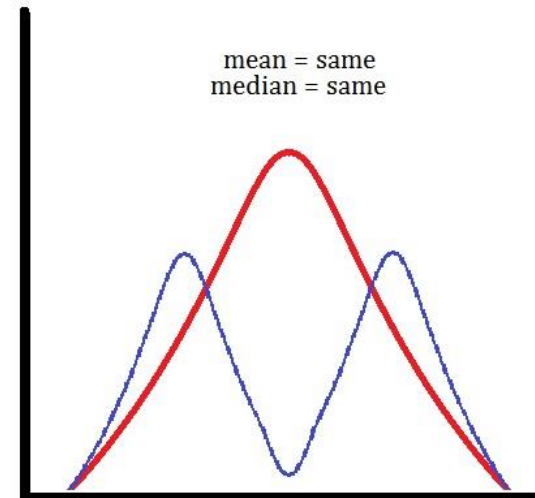


“It is difficult to understand why statisticians commonly limit their

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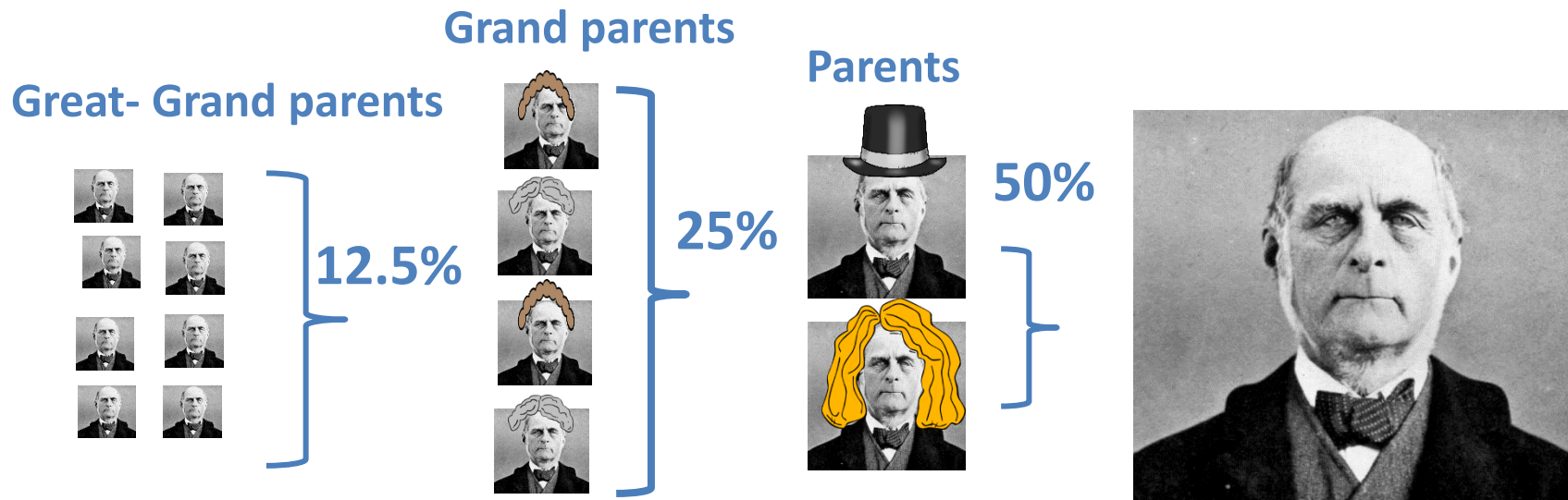
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History of Quantitative Genetics

Francis Galton

Different theory of inheritance:

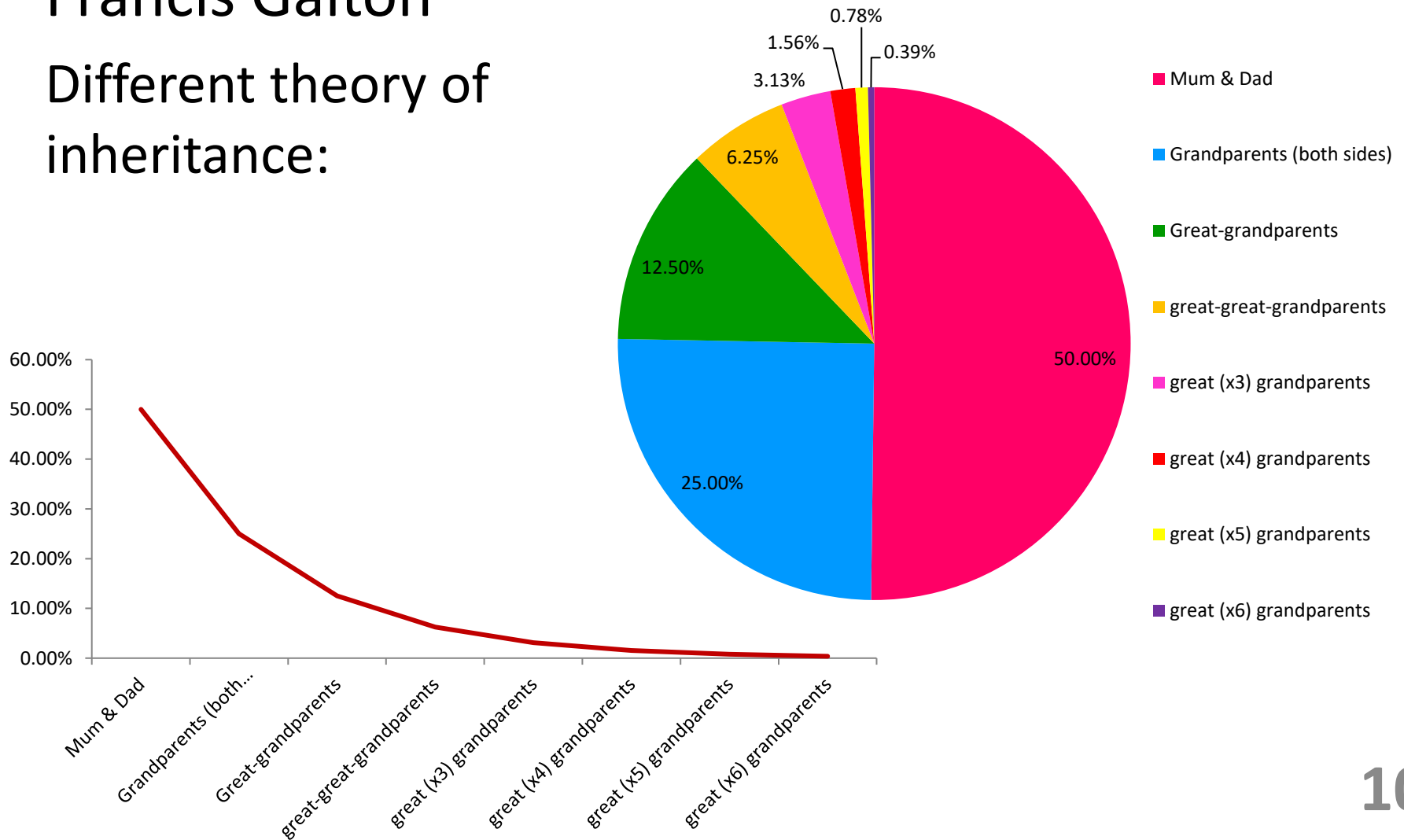
The parents of an individual together contribute on an average 50 percent of the total inherited characters, the 4 grandparents together 25 percent, the 3rd generation of ancestors together 12.5 percent, etc.



History of Quantitative Genetics

Francis Galton

Different theory of inheritance:

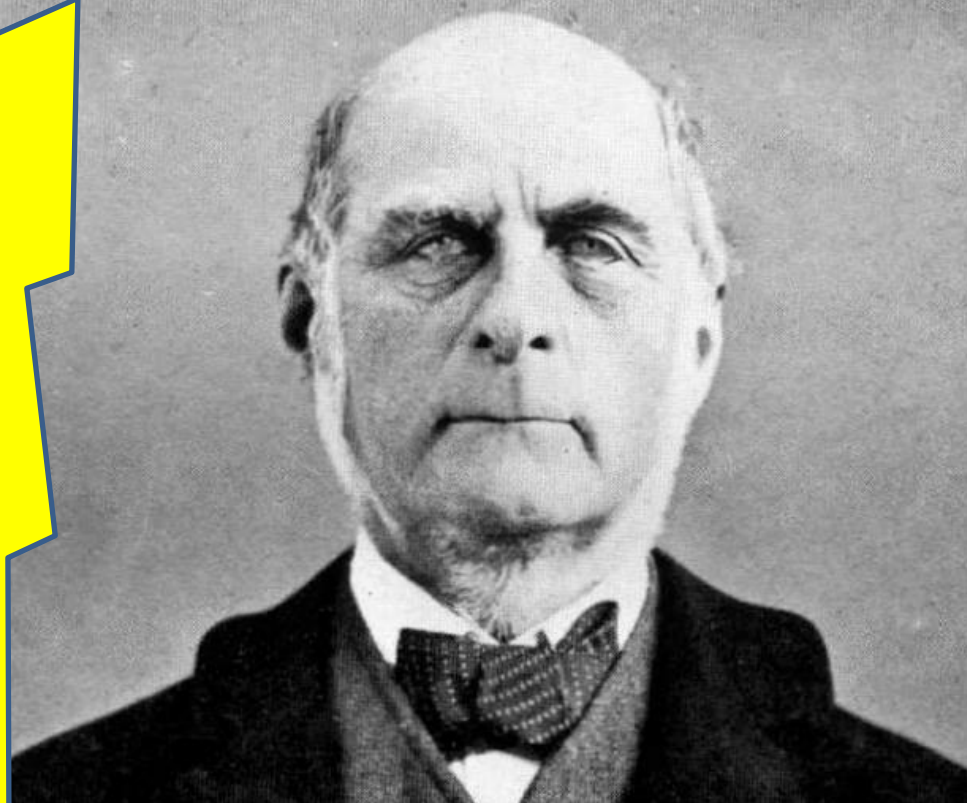


History: Galton vs. Mendel



MENDELIAN GENETICS

Traits inherited in a Mendelian fashion. Phenotypes discrete characteristics

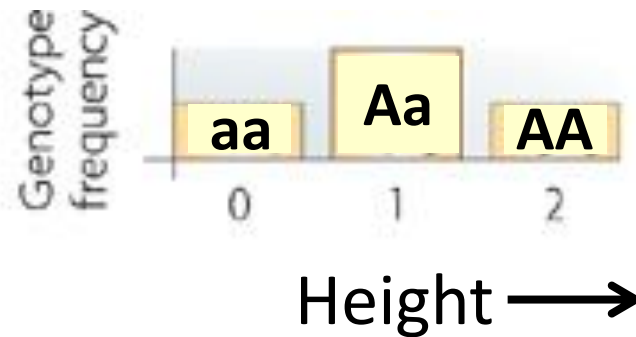


QUANTITATIVE GENETICS

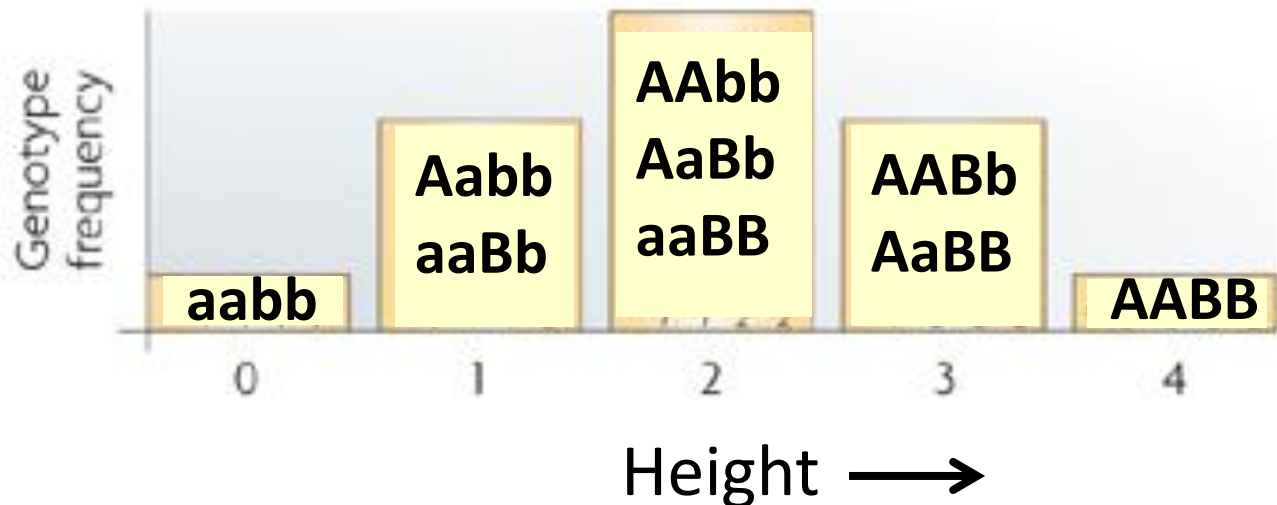
Traits inherited as complex averages of ancestral phenotypes. Continuously varying phenotypes

Quantitative traits and Mendelian laws

a One locus
(A):

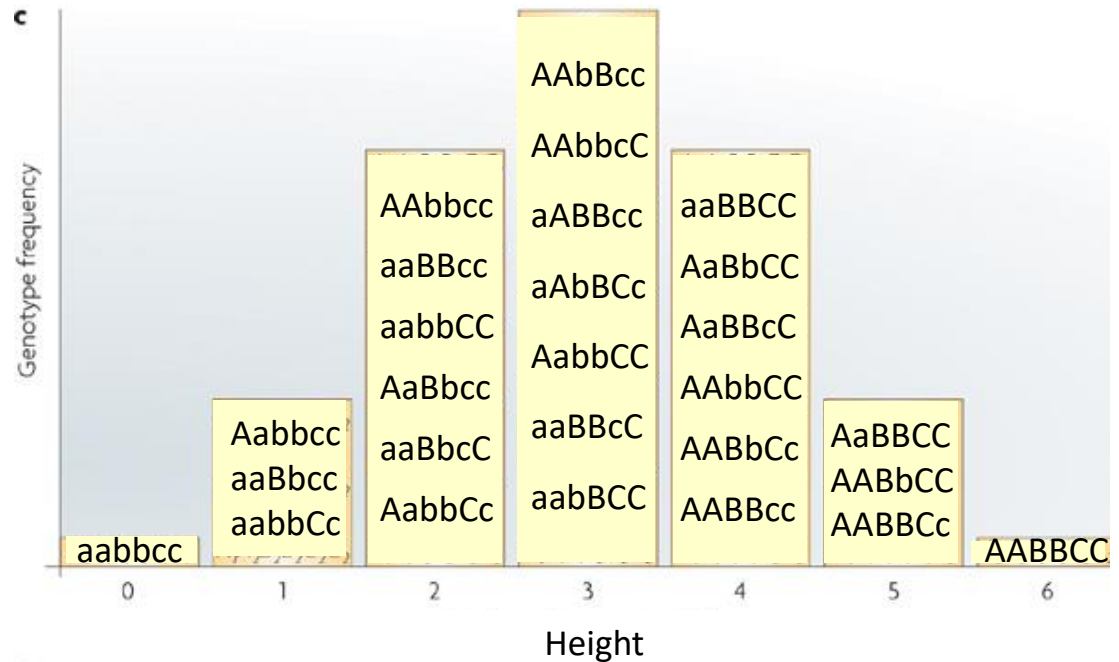


b Two
Loci
(A & B):

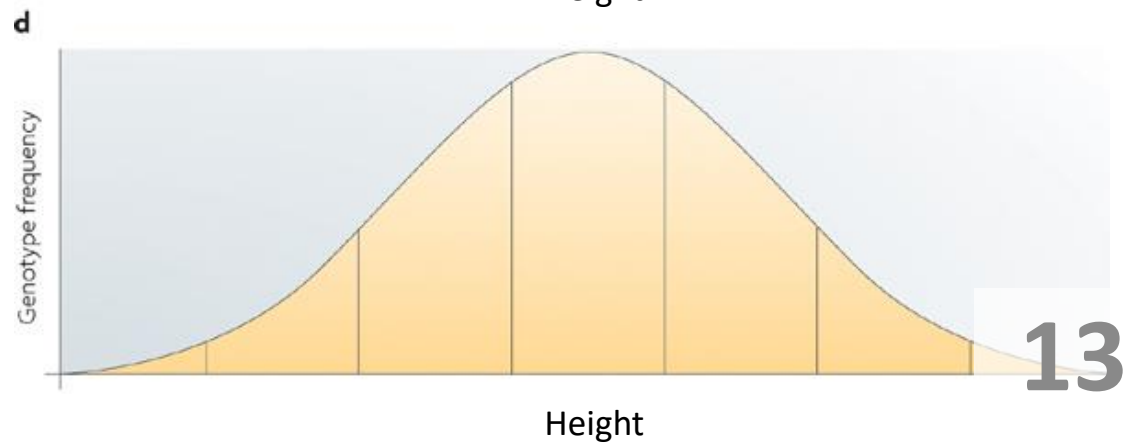


Quantitative traits and Mendelian laws

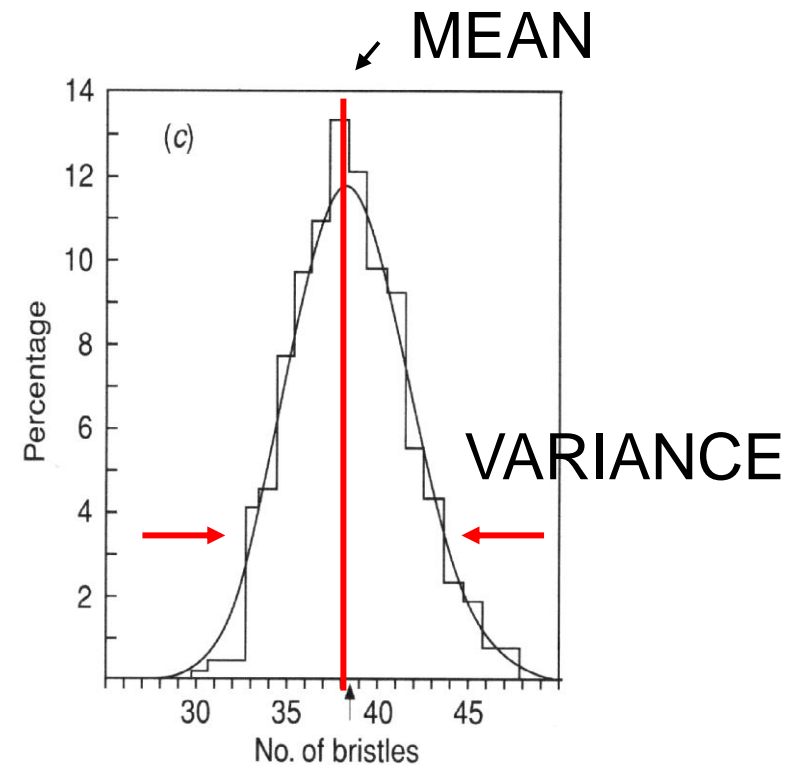
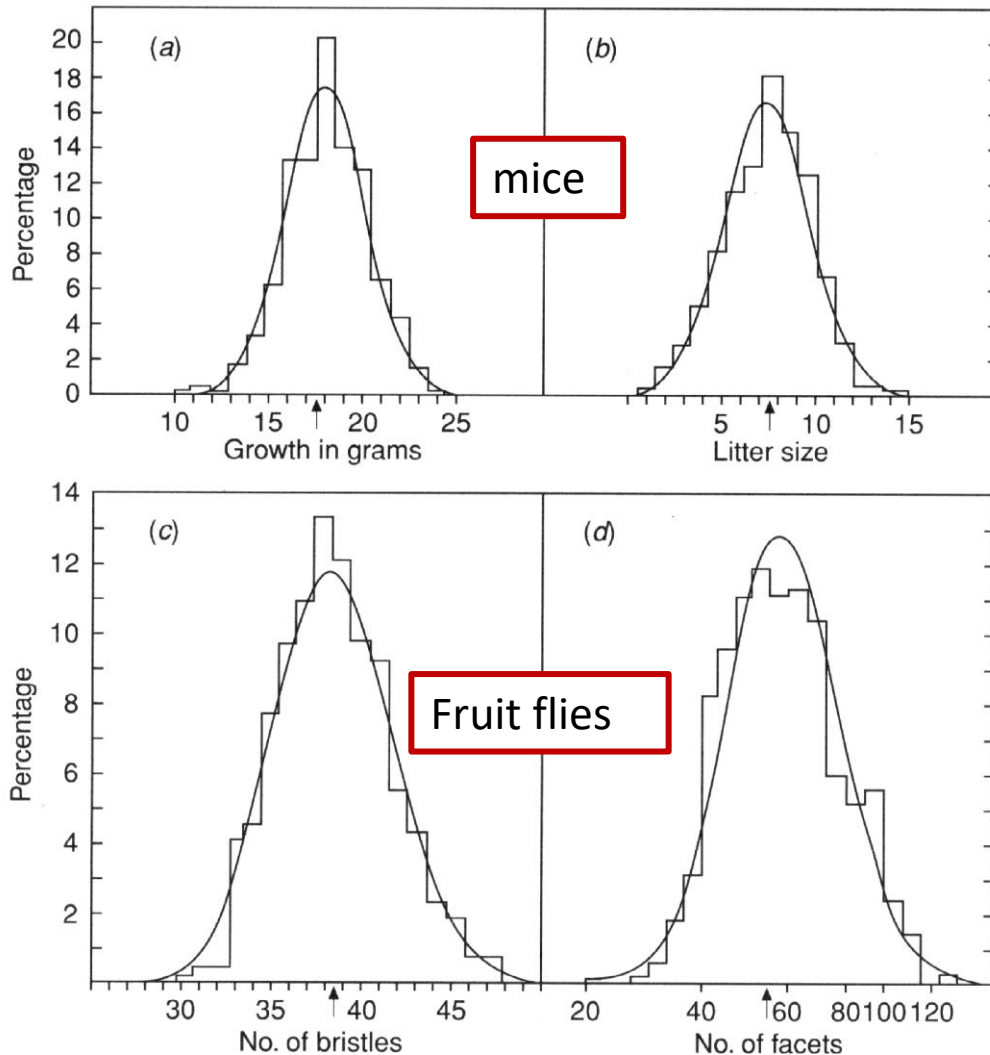
Three
Loci
(A, B & C):



Many
loci:



Normal Distribution of Phenotypes

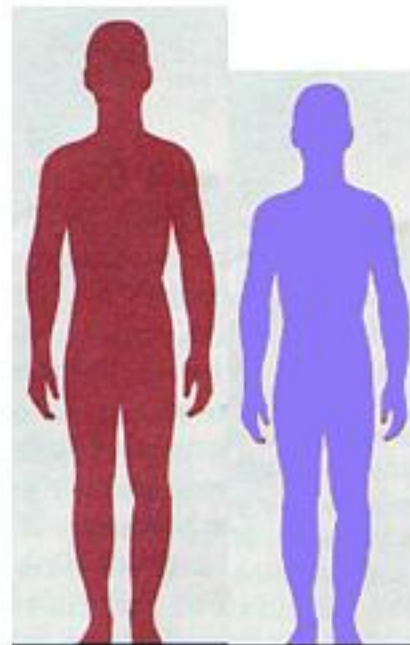


Nature versus Nurture?

- Two influences on the expression of quantitative traits:
 - (1) Genetic (effects of many genes)
 - (2) Environmental (effects of environment)

- E.g. height:

**Difference due
to different
genes**

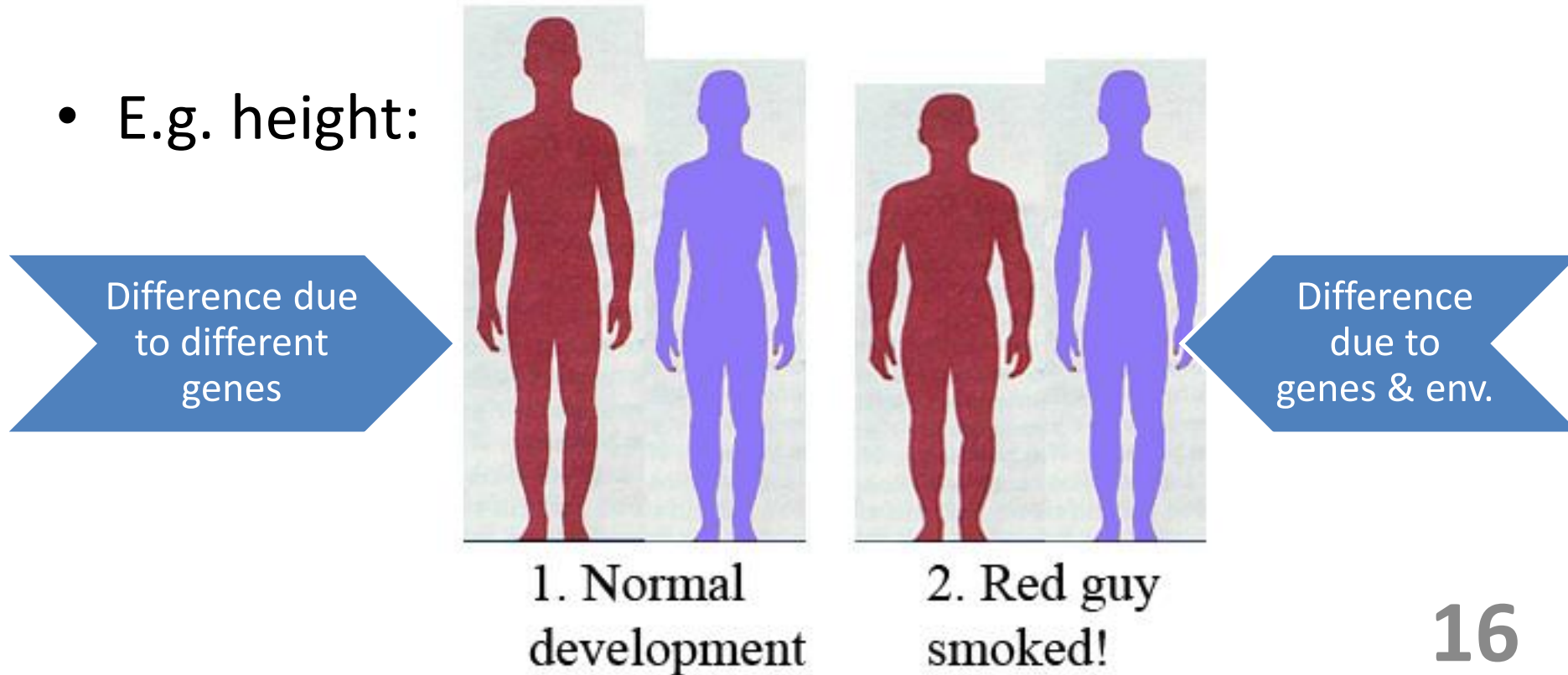


1. Normal
development

Nature versus Nurture?

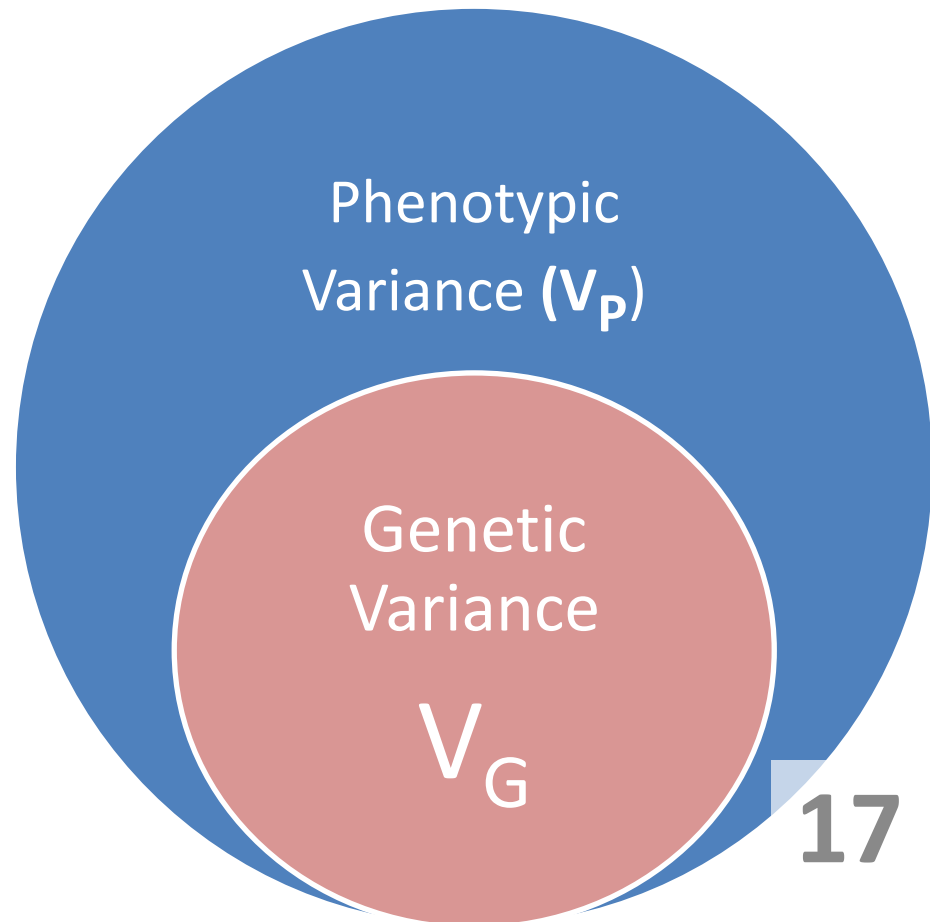
- Two influences on the expression of quantitative traits:
 - (1) Genetic (effects of many genes)
 - (2) Environmental (effects of environment)

- E.g. height:



Partitioning trait variation:

- Most traits influenced by both genes and environment (nature & nurture)
- If we represent all the **phenotypic variation** in the population as a solid circle, we can recognise the portion that is due to different genes
- This is called '**genetic variance**'



Heritability (H^2)

What Does it Measure?

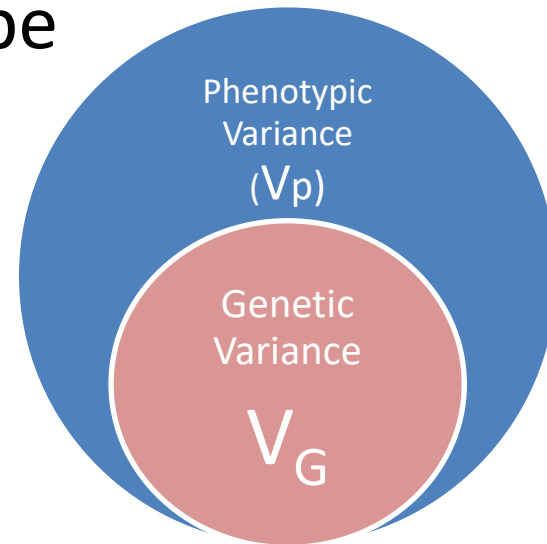
Measure of how much *variation* in a phenotype is caused by *variation* in genotype

Assuming additivity:

$$VP = VG + VE$$



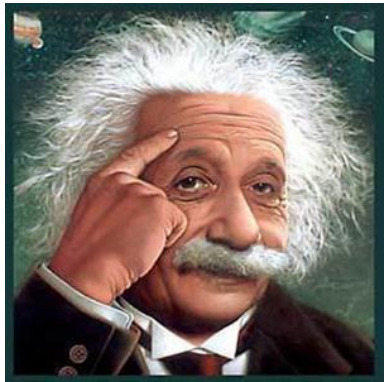
$$H^2 = VG/VP$$



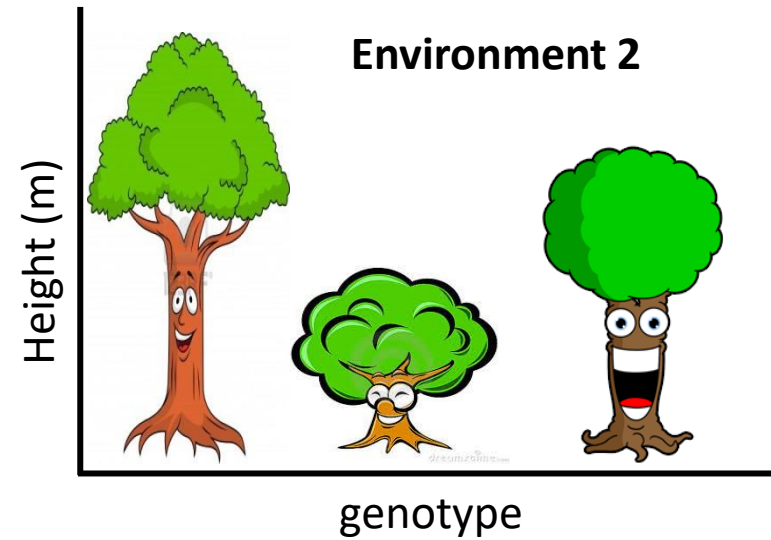
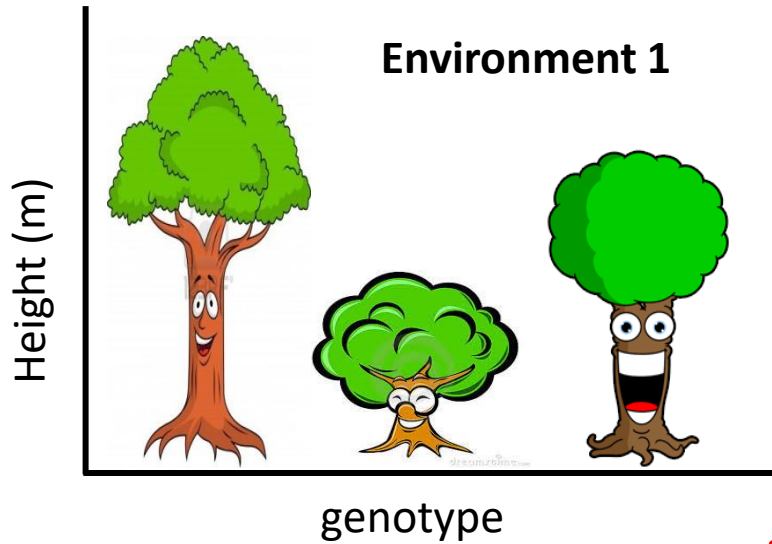
Proportion of Genetic variance to phenotypic variance

Heritability and Causation

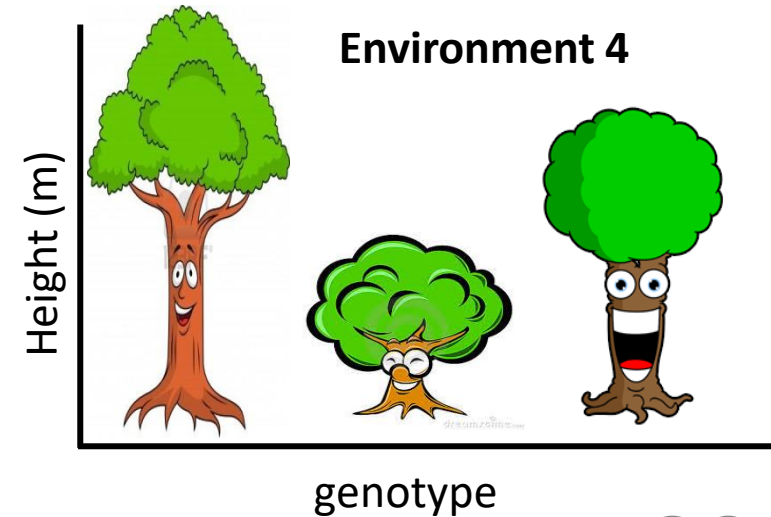
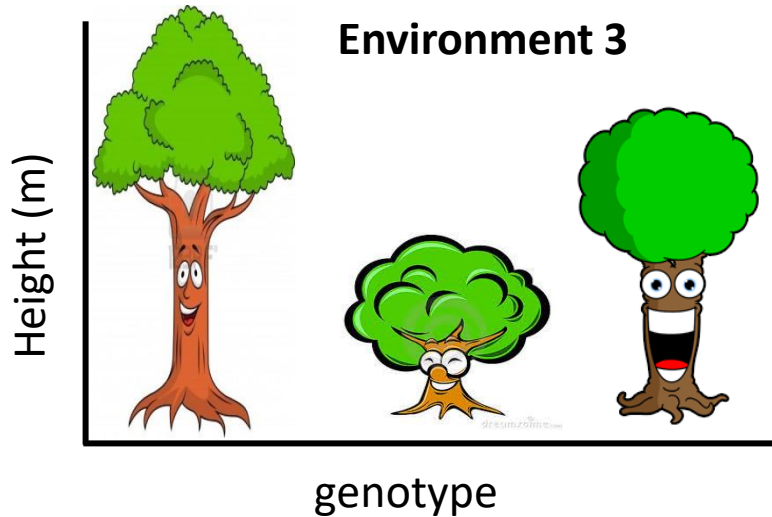
- Heritability can be used to make causal claims about the relative effects of genes (nature) and the environment (nurture)
- Which is more causally important?



- *Specific types* of causal claims



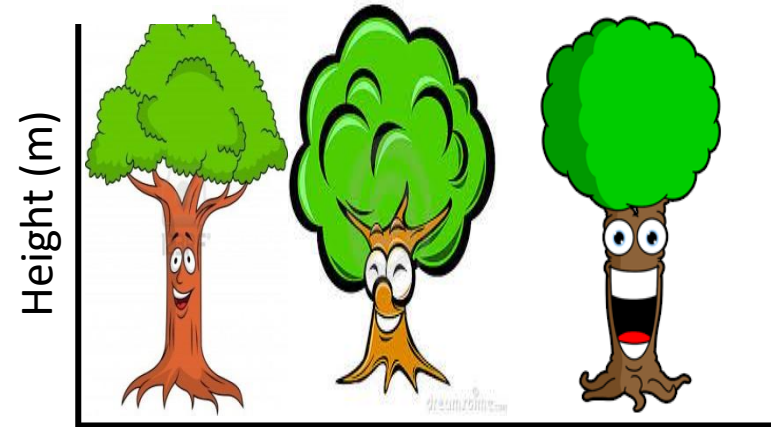
H² HIGH



Environmental or Genetic?

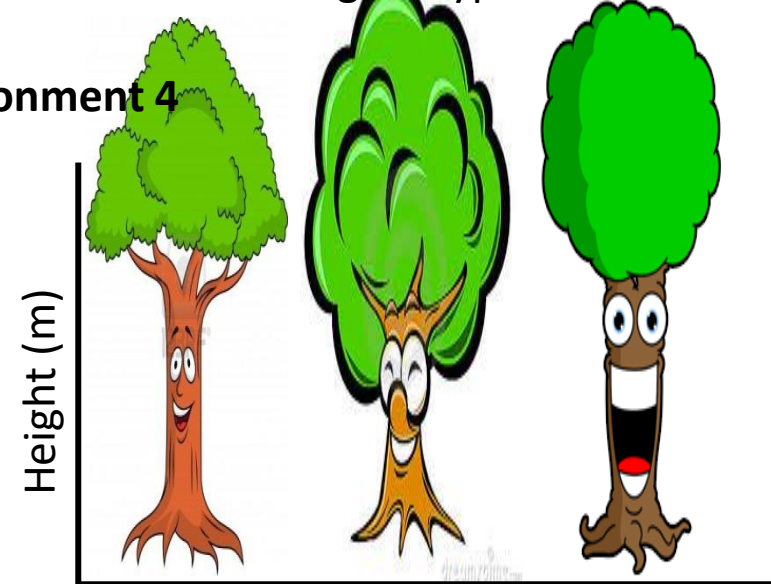
H² LOW

Environment 2



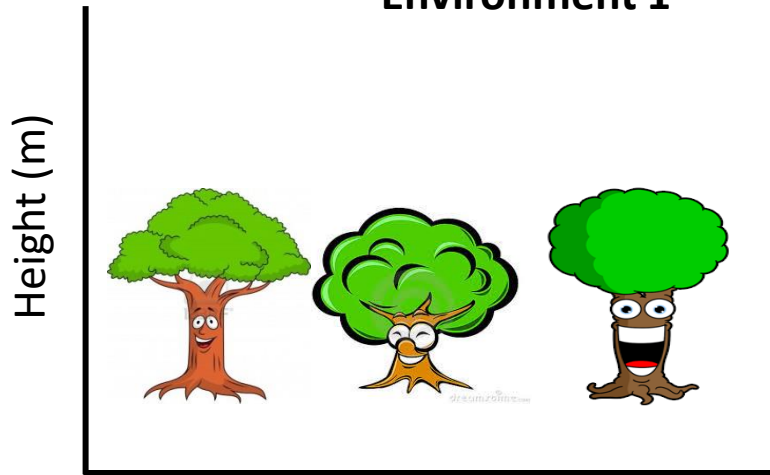
genotype

Environment 4



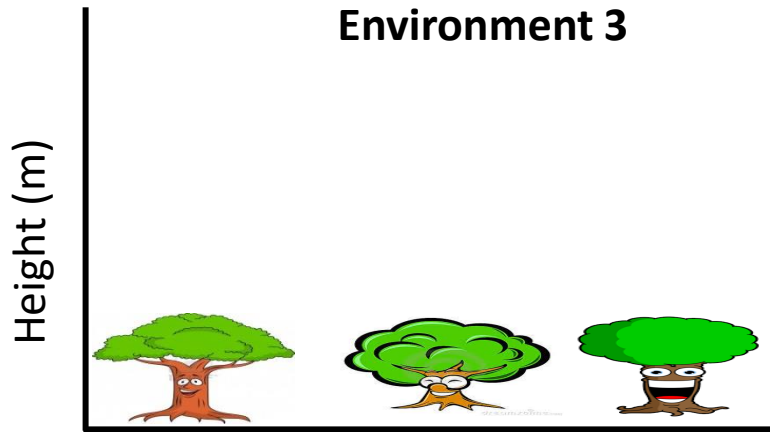
genotype

Environment 1



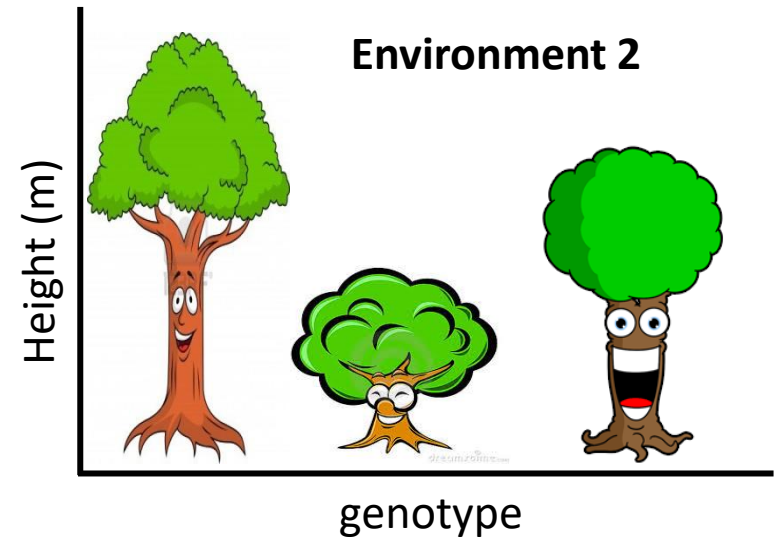
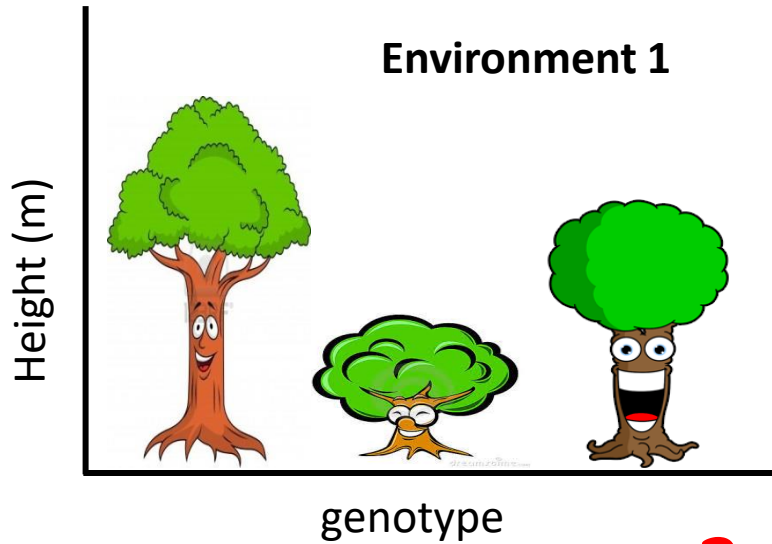
genotype

Environment 3

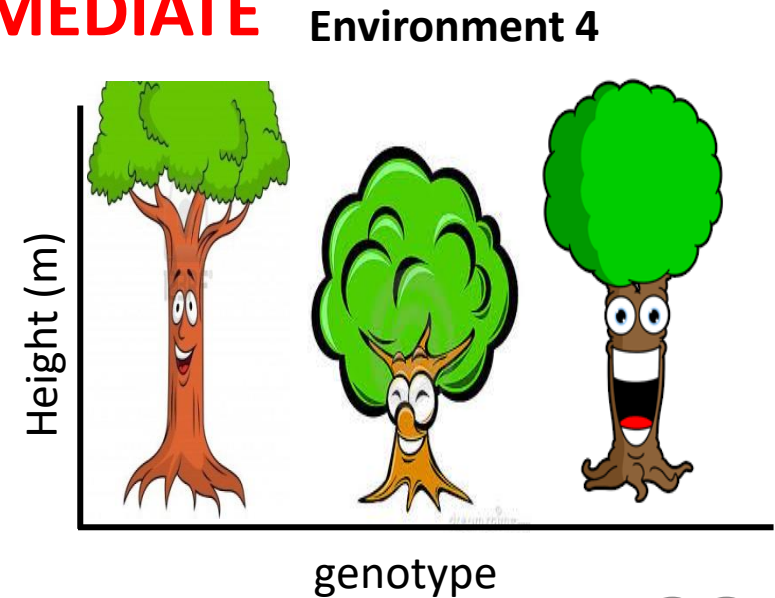
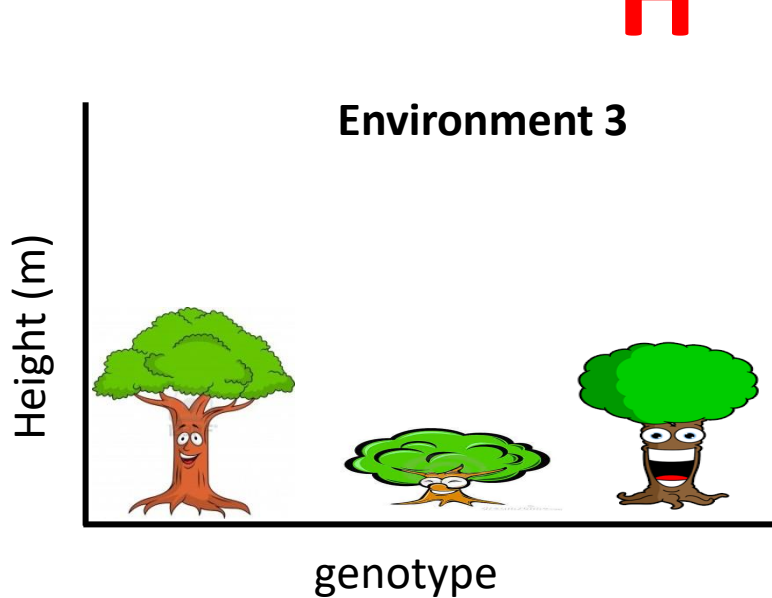


genotype

Environmental or Genetic?



H² INTERMEDIATE

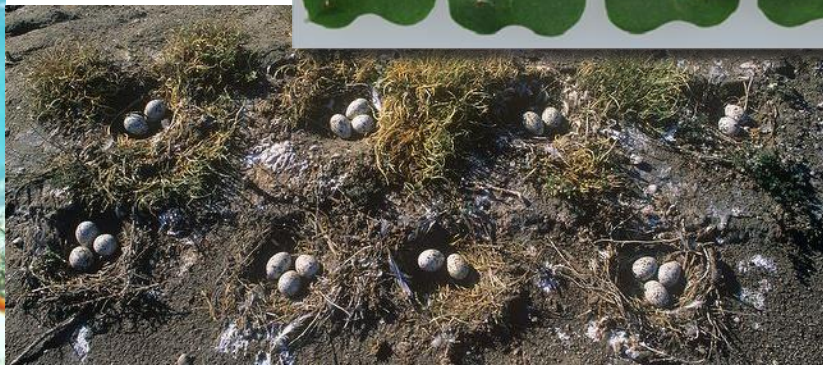


Environmental or Genetic?

How does this relate to Conservation Biology?

Knowledge of quantitative fitness traits

- Clutch size
- Resistance to disease / introduced organisms
- Resistance to climate change
- Lifetime fecundity
- Age of first litter
- Days to flowering



Where do the values come from?

Heritability of postchallenge survival, an indicator of disease resistance, was estimated to be 0.35 ± 0.09.

Silverstein, J. T., et al. (2009). Rainbow trout resistance to bacterial cold-water disease is moderately heritable and is not adversely correlated with growth. *Journal of animal science* 87(3), 860-867.

Broad-sense heritabilities ranged from 0.55 in the F2 population (Fargo, N.D.) to 0.95 in the F_{2,4} progenies at

León, A. J., Lee, M., & Andrade, F. H. (2001). Quantitative trait loci for growing degree days to flowering and photoperiod response in sunflower (*Helianthus annuus* L.). *Theoretical and Applied Genetics*, 102(4), 497-503.

and the heritability estimates (95 % confidence intervals) for boldness and aggressiveness were 0.76 (0.49, 0.90) and 0.36 (0.10, 0.72) respectively. Furthermore, there were

Ariyomo, T. O., Carter, M., & Watt, P. J. (2013). Heritability of Boldness and Aggressiveness in the Zebrafish. *Behavior genetics*, 43(2), 161-167.

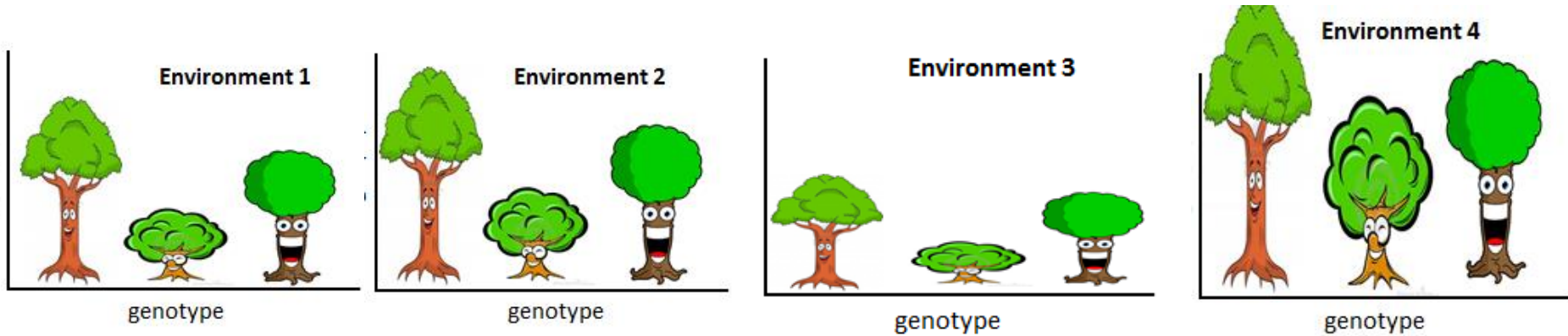
$$H^2 = VG / VP$$

$$VP = VG + VE$$

VG?

VE?

Where do the values come from?



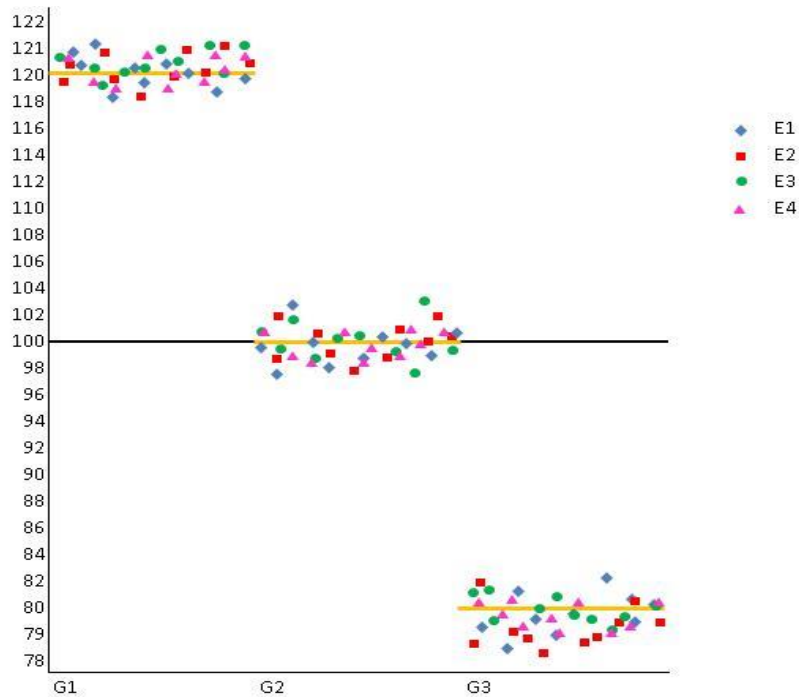
	E1 (75)	E2 (75)	E3 (75)	E4 (75)
G1 (100)				
G2 (100)				
G3 (100)				

The height of the trees are measured...

	E1 ($n_e = 75$)	E2 ($n_e = 75$)	E3 ($n_e = 75$)	E4 ($n_e = 75$)	Genotype Means
G1 ($n_g = 100$)	$\mu = 120$	$\mu = 118$	$\mu = 119$	$\mu = 123$	$\mu_{G1} = 120$
G2 ($n_g = 100$)	$\mu = 100$	$\mu = 101$	$\mu = 98$	$\mu = 101$	$\mu_{G2} = 100$
G3 ($n_g = 100$)	$\mu = 80$	$\mu = 81$	$\mu = 78$	$\mu = 81$	$\mu_{G3} = 80$
Environment Means	$\mu_{E1} = 100$	$\mu_{E2} = 100$	$\mu_{E3} = 98.33$	$\mu_{E4} = 101.67$	$\bar{X} = 100$

Trees with G1 genotype are significantly taller than G2, who in turn are taller than G3. Differences between environments are negligible.

	E1 (n _e =75)	E2 (n _e =75)	E3 (n _e =75)	E4 (n _e =75)	N=300
G1 (n _g =100)	μ= 120	μ= 118	μ= 119	μ= 123	μ _{G1} = 120
G2 (n _g =100)	μ= 100	μ= 101	μ= 98	μ= 101	μ _{G2} = 100
G3 (n _g =100)	μ= 80	μ= 81	μ= 78	μ= 81	μ _{G3} = 80
N=300	μ _{E1} =100	μ _{E2} = 100	μ _{E3} = 98.33	μ _{E4} = 101.67	$\ddot{X} = 100$

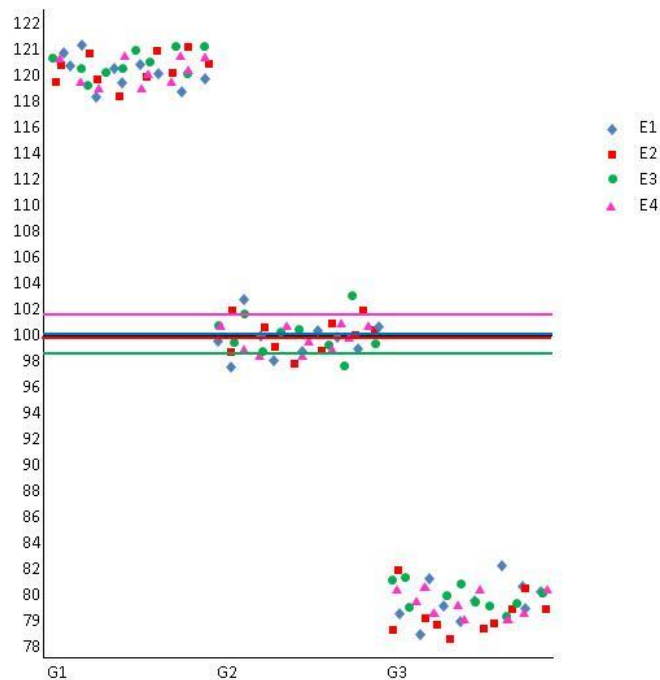


$$VG = \frac{(\mu_{G1} - \ddot{X})^2 + (\mu_{G2} - \ddot{X})^2 + (\mu_{G3} - \ddot{X})^2}{ng}$$

$$VG = \frac{(\underline{120} - \underline{100})^2 + (\underline{100} - \underline{100})^2 + (\underline{80} - \underline{100})^2}{3}$$

$$VG = 266.67$$

	E1 (n _e =75)	E2 (n _e =75)	E3 (n _e =75)	E4 (n _e =75)	N=300
G1 (n _g =100)	μ= 120	μ= 118	μ= 119	μ= 123	μ _{G1} = 120
G2 (n _g =100)	μ= 100	μ= 101	μ= 98	μ= 101	μ _{G2} = 100
G3 (n _g =100)	μ= 80	μ= 81	μ= 78	μ= 81	μ _{G2} = 80
N=300	μ _{E1} =100	μ _{E2} = 100	μ _{E3} = 98.33	μ _{E4} = 101.67	$\ddot{X} = 100$



$$VE = \frac{(\mu_{E1} - \ddot{X})^2 + (\mu_{E2} - \ddot{X})^2 + (\mu_{E3} - \ddot{X})^2 + (\mu_{E4} - \ddot{X})^2}{nE}$$

$$VE = \frac{(\underline{100} - \underline{100})^2 + (\underline{100} - \underline{100})^2 + (\underline{98.33} - \underline{100})^2 + (\underline{101.67} - \underline{100})^2}{4}$$

$$VE = 1.38$$

Getting the heritability estimate

The phenotypic variance is assumed to be additive

$$VP = VG + VE$$

Heritability (H^2) is the proportion of the genotypic variance from the total phenotypic variance

$$H^2 = VG / VP \quad \text{or} \quad VG / (VE + VG)$$

Usually a high heritability estimate accurately reflects an example in which differences in genotype are the major cause of differences in phenotype

$$VG = 266.67$$

$$VE = 1.38$$

$$VP = 268.05$$

Genetic var (H^2)

$$= VG / VP$$

$$= 266.67 / 268.05$$

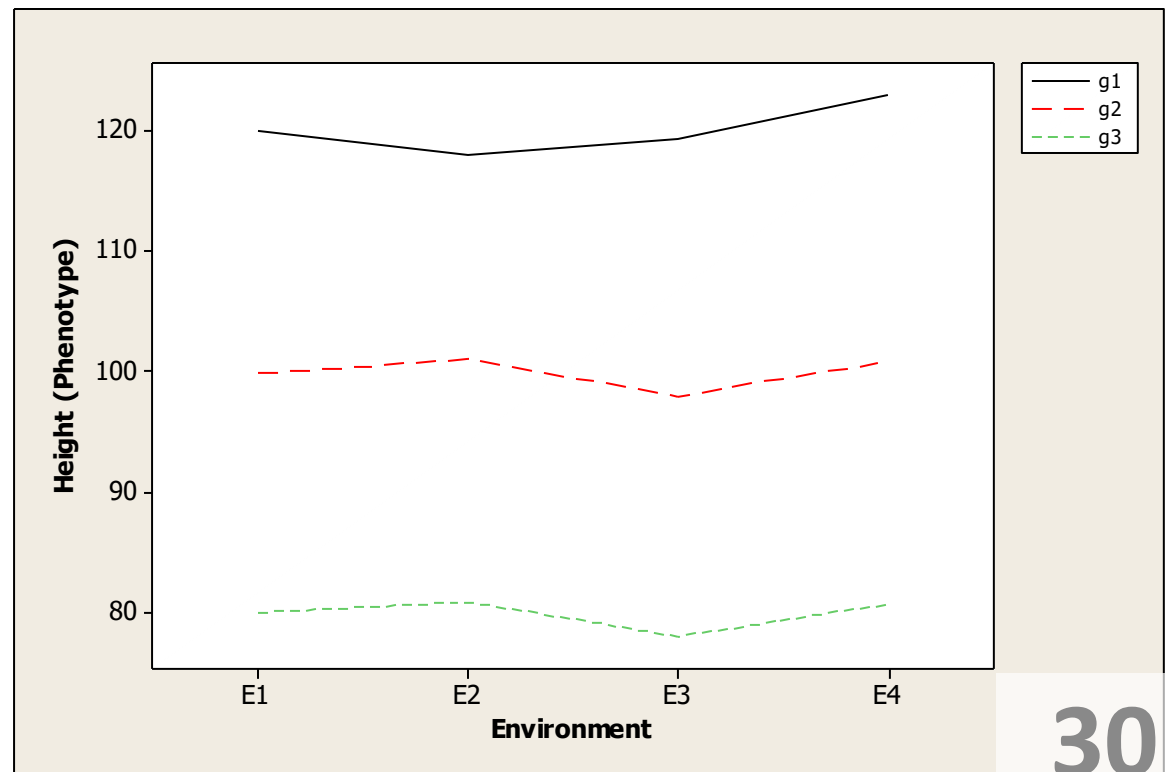
$$= 0.9948$$

Environmental var

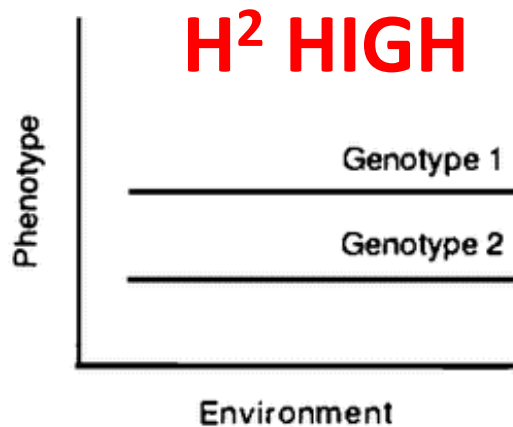
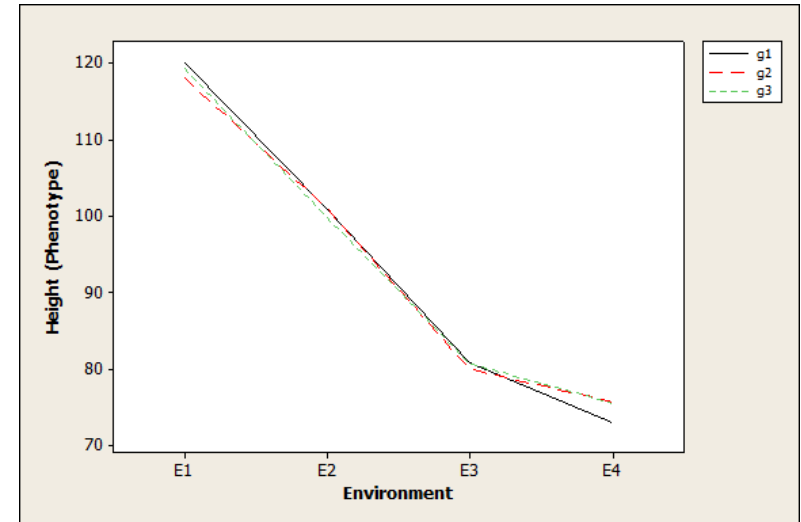
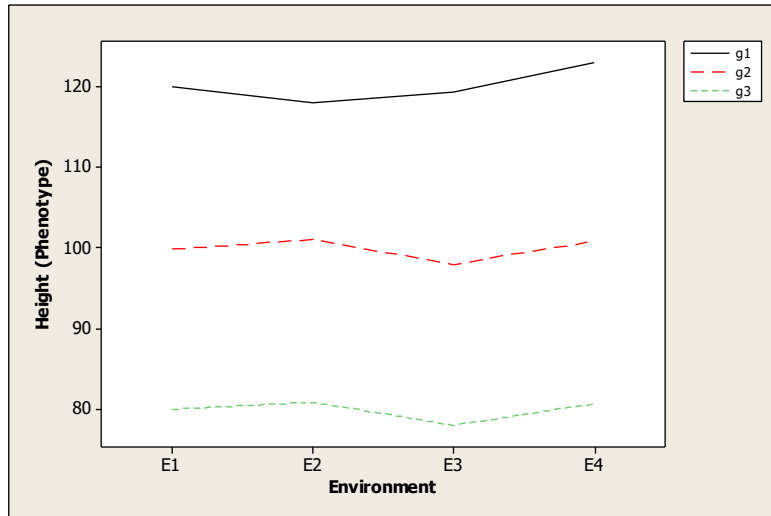
$$= VE / VP$$

$$= 1.38 / 268.05$$

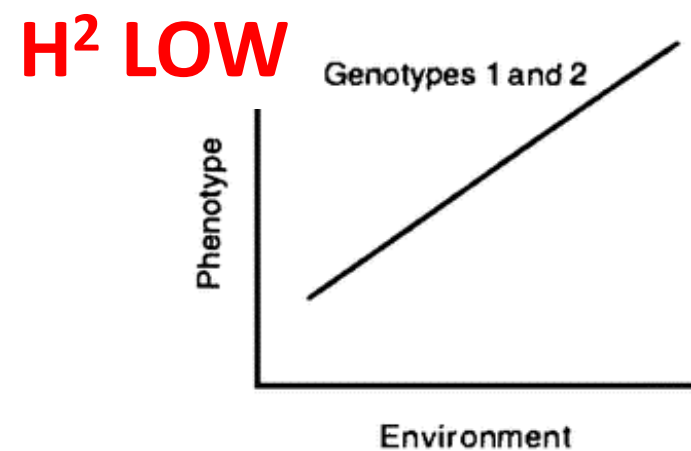
$$= 0.0052$$



Norm of Reaction

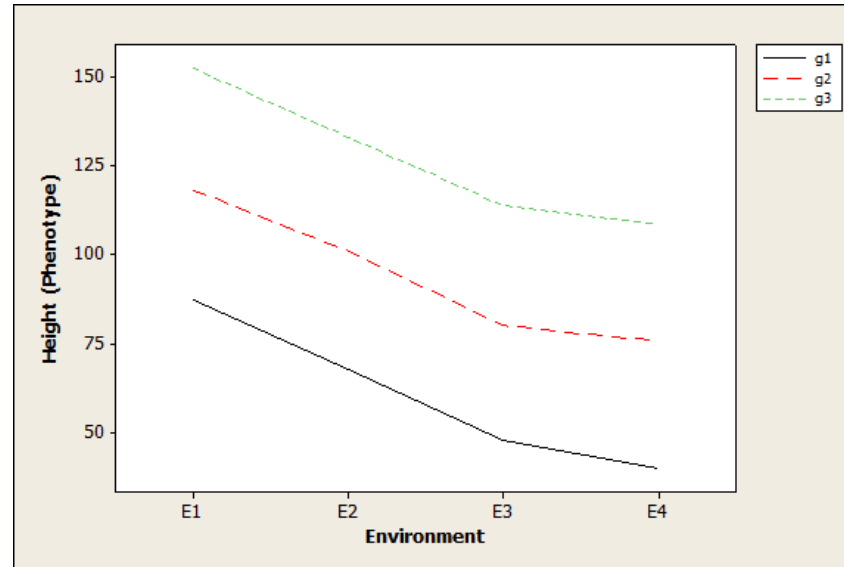


a) Biological determinism

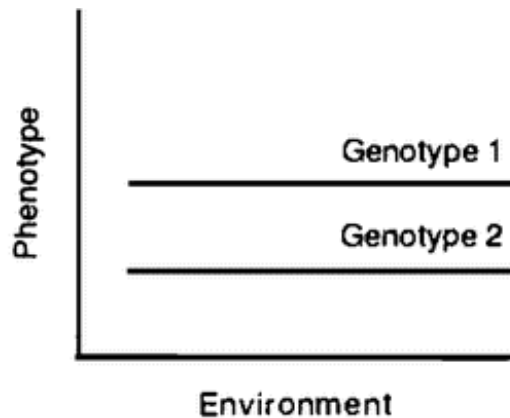


b) Social determinism

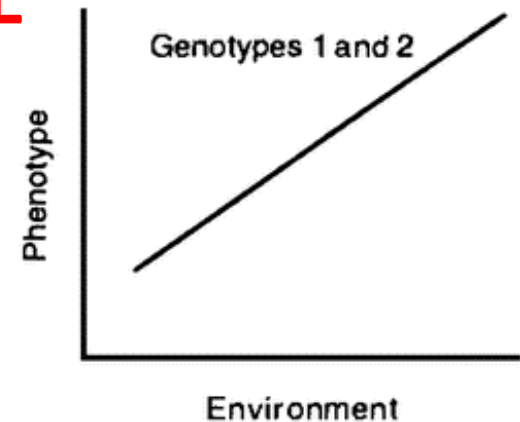
Norm of Reaction



H^2 INTERMEDIATE

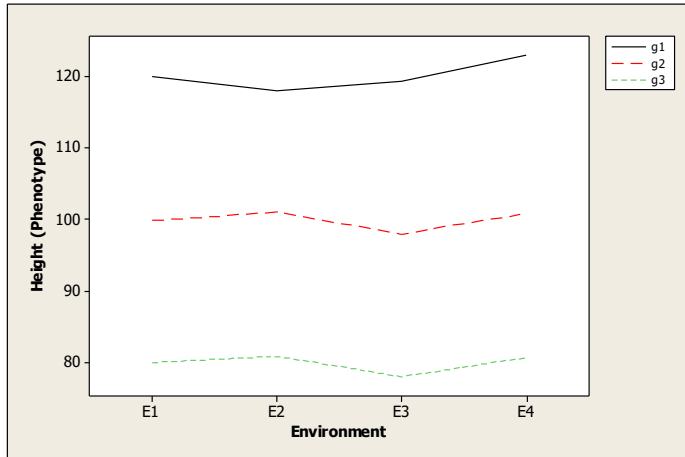


a) Biological determinism

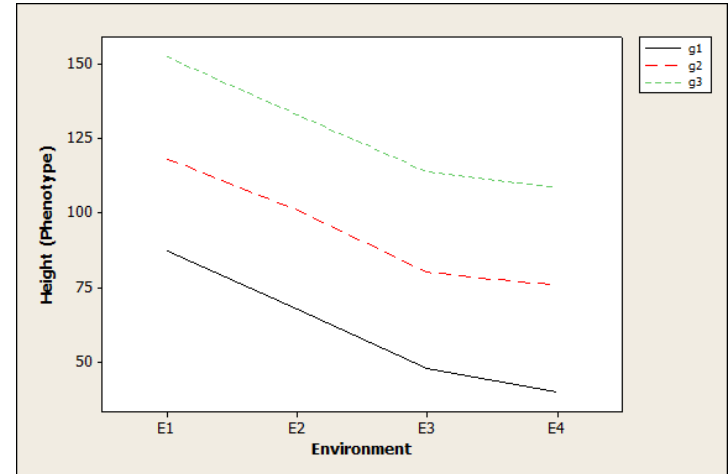


b) Social determinism

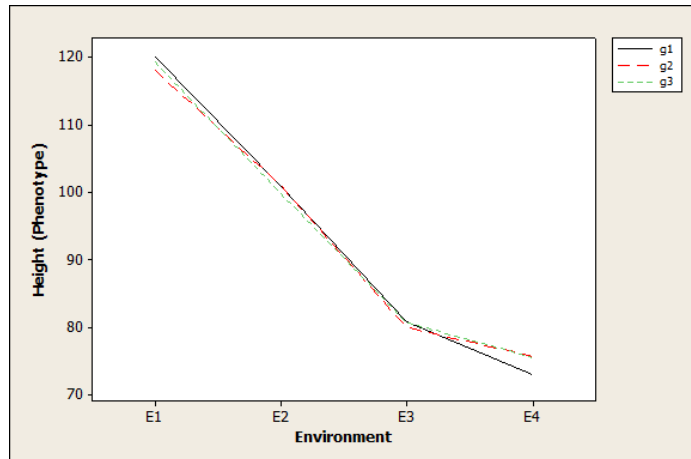
Norm of Reaction - GxE (Interaction)



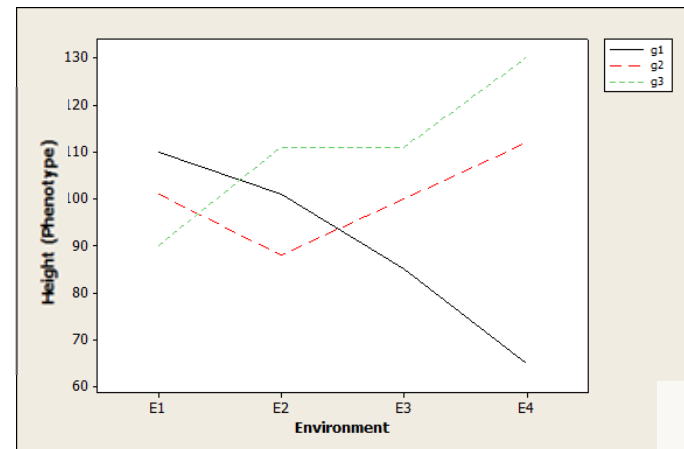
H² HIGH



H² INTERMEDIATE

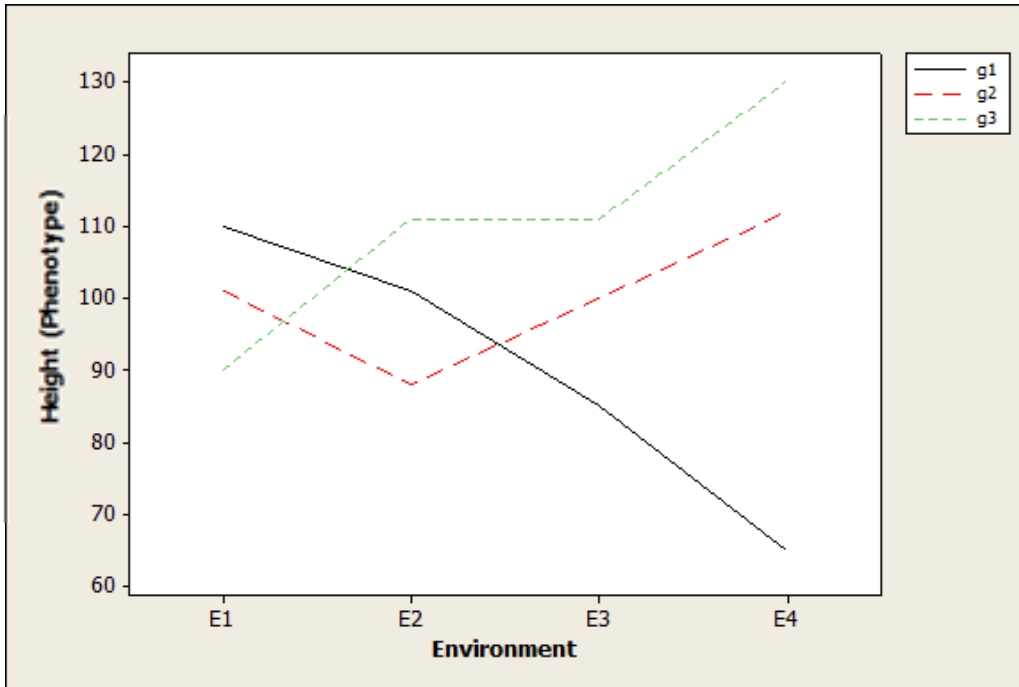


H² LOW



H² ??

$H^2 = 0.968$ (VERY HIGH!)



$$VG = 266.67$$

$$VE = 8.8089$$

$$VP = 275.4789$$

$$266.67/275.4789$$

$$H^2 = 0.968$$

	E1	E2	E3	E4	Means
G1	110	100	85	65	90
G2	100	88	100	112	100
G3	90	110	110	130	110
Means	100	99.33333	98.33333	102.3333	$\bar{X} = 100$

$$VG = \frac{(\mu_{G1} - \bar{X})^2 + (\mu_{G2} - \bar{X})^2 + (\mu_{G3} - \bar{X})^2}{n_G}$$

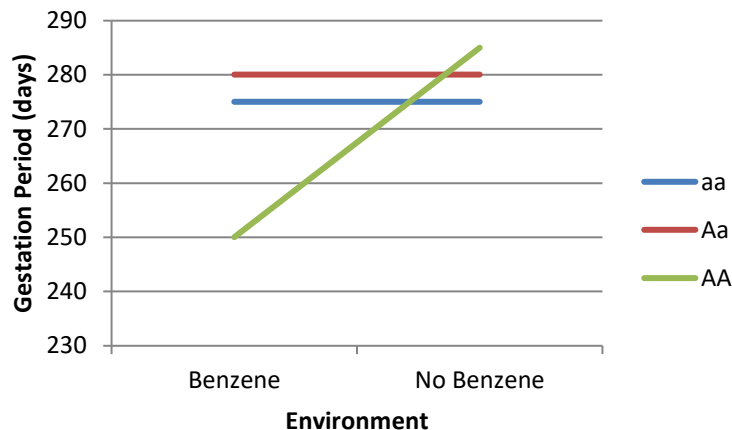
$$VG = 266.67$$

$$VE = \frac{(\mu_{E1} - \bar{X})^2 + (\mu_{E2} - \bar{X})^2 + (\mu_{E3} - \bar{X})^2 + (\mu_{E4} - \bar{X})^2}{n_E}$$

$$VE = 8.8089$$

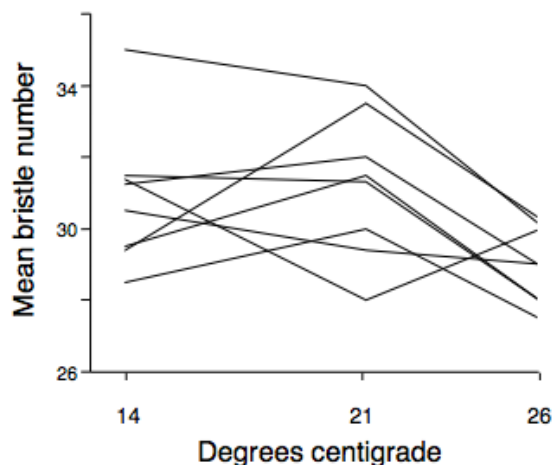
GxE (Gene-Environment Interaction)

- Trait expression varies over different environments – may not be directional
- Genome produces different phenotypes depending on developmental environment
- Example 1: benzene exposure is significantly associated with shorter gestation periods in pregnant women possessing the AA allele of *CYP1A1*, while there is no association for those with Aa or aa (Wang et al. 2000)




GxE (Gene-Environment Interaction)

- Trait expression varies over different environments – may not be directional
- Genome produces different phenotypes depending on developmental environment
- Example 2: Bristle number in drosophila is determined by genotypic differences, and temperature. How temperature affects bristle number depends on the flies genetic background (Gupta and Lewontin 1981)



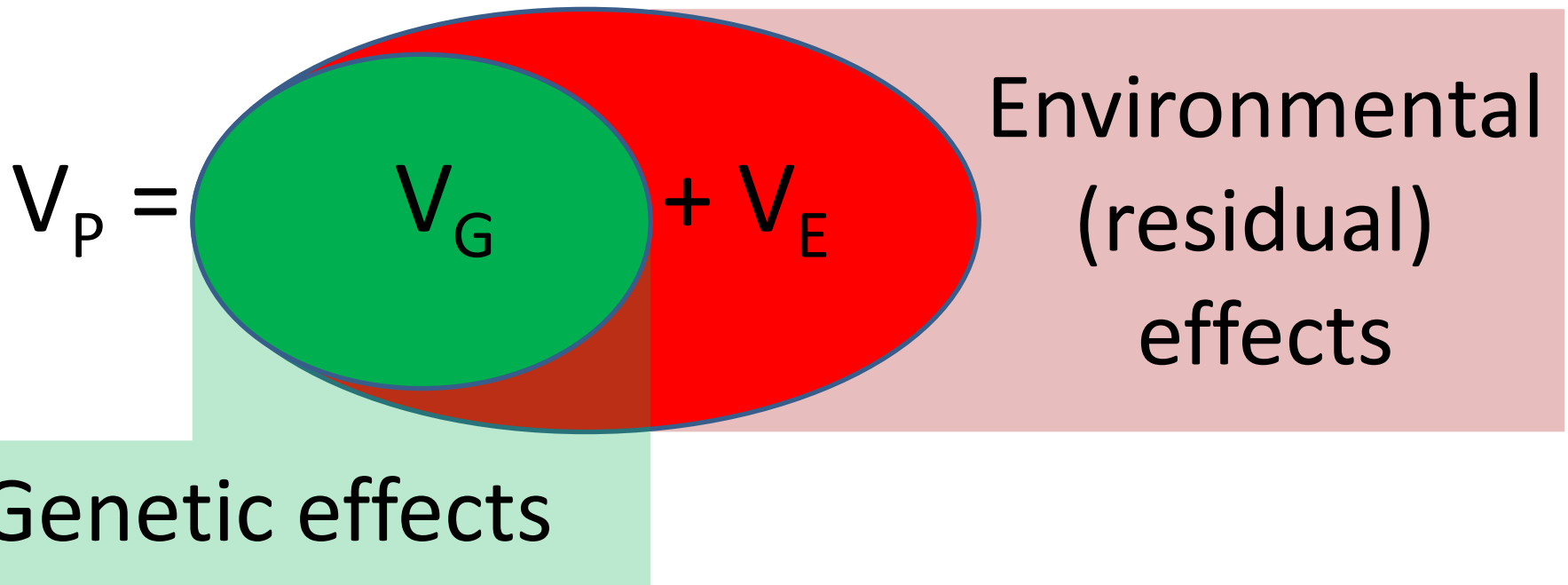
GxE (Gene-Environment Interaction)

- GxE doesn't always mean an high heritability
- Could also result in low H^2 if not accounted for 
- Demonstrates when interaction occurs and is unaccounted for – one cannot get a good understanding without looking at the NOR.
- GxE can lead to a heritability estimate that does not accurately reflect the contribution of environmental or genetic variation
- Can add GxE term into heritability model so it no longer skews results

Non-Additive

$$VP = VG + VE + \mathbf{V_{GxE}} + 2CovGE + Error$$

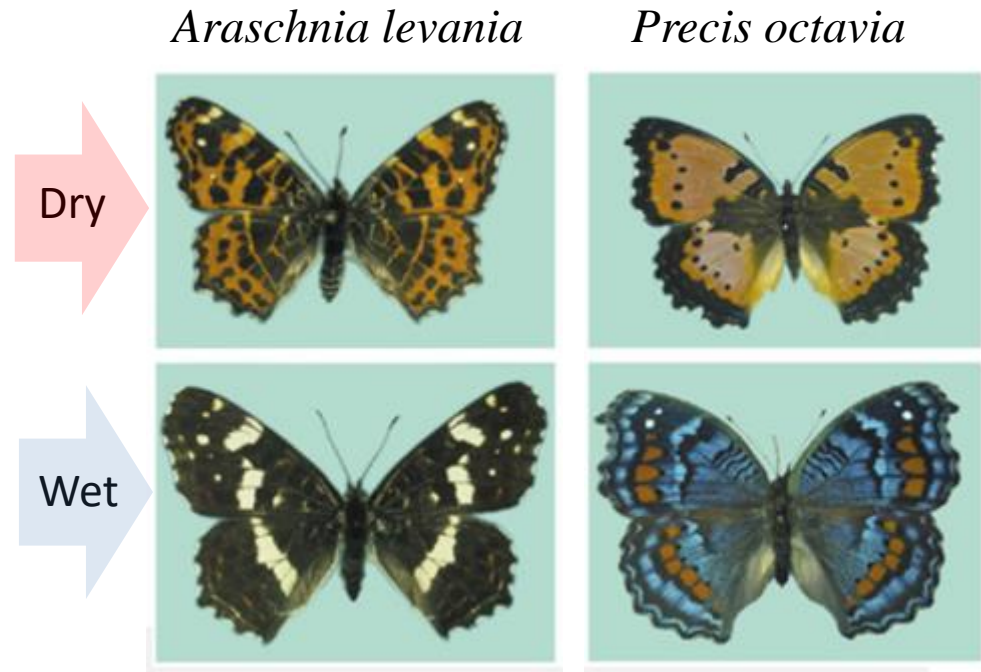
NATURE... versus ...NURTURE



....assuming that genetic and environmental effects are **additive**

Phenotypic plasticity

The ability of a single genome to produce different phenotypes depending upon the environment experienced during development



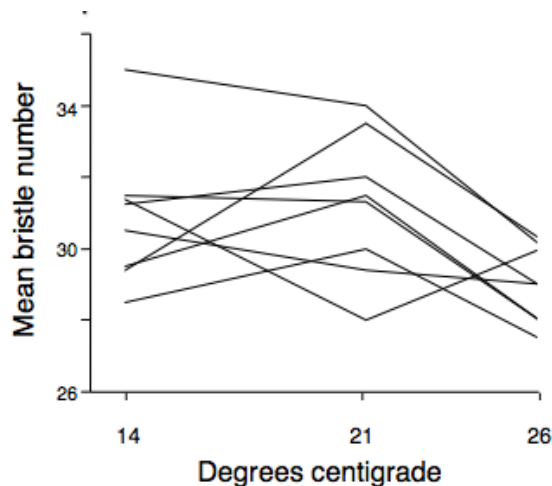
“Normal”

“Plague”

GxE (Gene-Environment Interaction)

GxE = A form of phenotypic plasticity

Single genotype produces multiple phenotypes, depending on environmental interaction.



Summary

- Quantitative traits are characterised by heritability estimates (H^2)
- Estimates partition the relative effects of environmental variation (VE) and genetic variation (VG) on differences in a phenotype (VP) *within a population*.

$$VP = VG + VE$$

$$H^2 = VG / VP$$

- Can estimate the influence of genes just by studying the phenotype (no molecular techniques needed)
- Conservation biologists are interested in the genetic basis of fitness traits
- Limitations to estimates: non-additivity (GxE interaction)

$$VP = VG + VE + V_{G \times E}$$

$$H^2 = VG / VP$$