Quantitative Genetics (1)

LECTURE 5: HERITABILITY

2022

Background

<u>Quantifying VG</u>

-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)

<u>Causal agents of phenotypes</u>

-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:

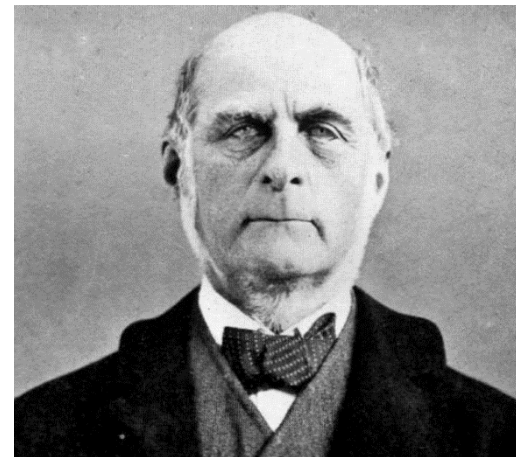
- A quantitative trait = a trait whose phenotypic expression is determined by many individual genes (i.e. variation at many individual loci) (polygenic)

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

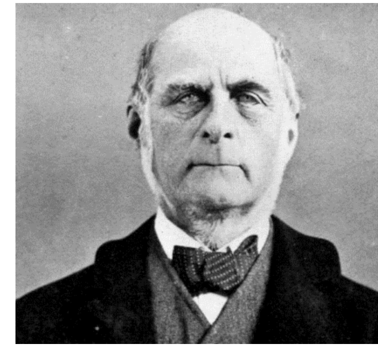
Francis Galton: ‘the apostle of quantification’



- 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)

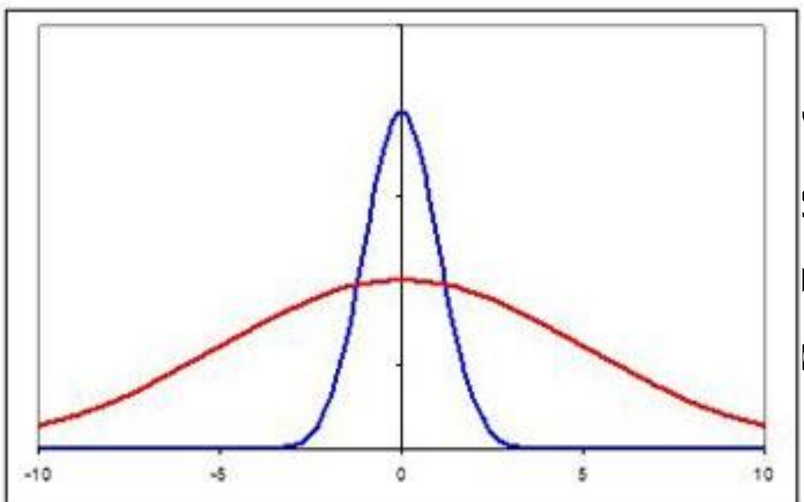
History of Quantitative Genetics

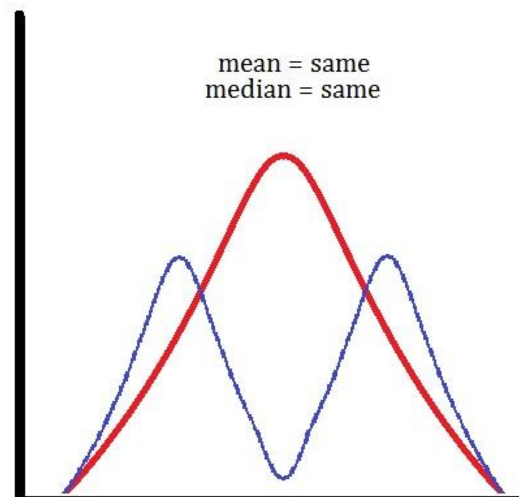


Francis Galton

Interested in *trait variation* rather than trait means

"It is difficult to understand why statisticians commonly limit their



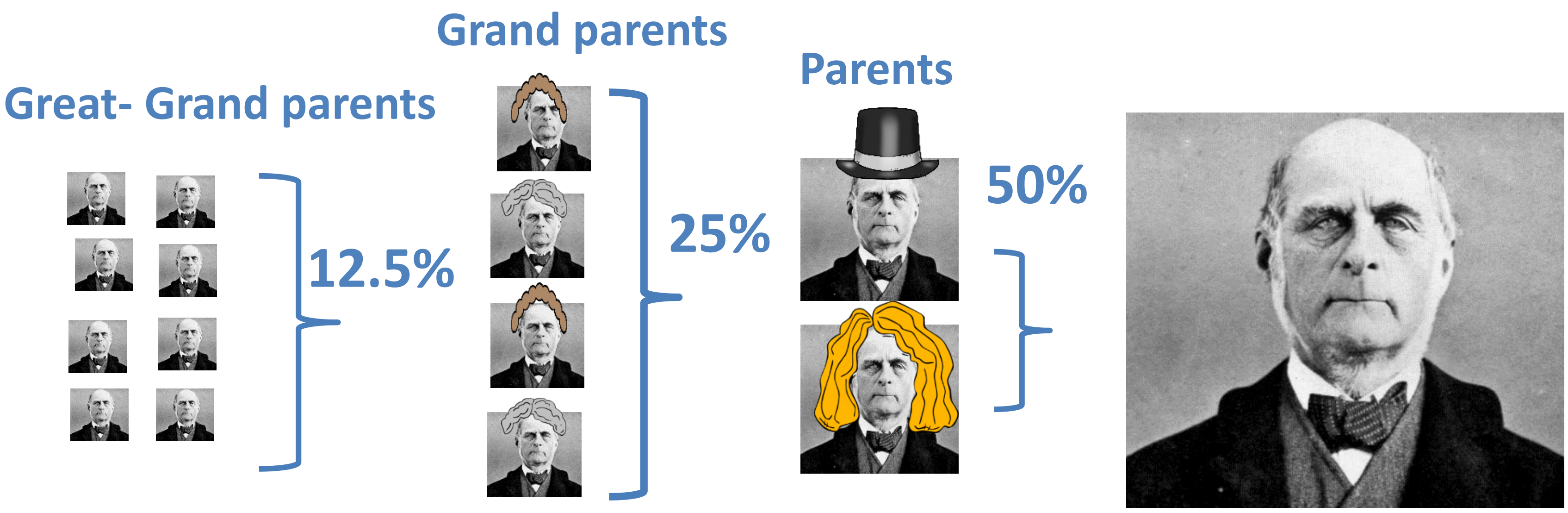


History of Quantitative Genetics

Francis Galton

Different theory of inheritance:

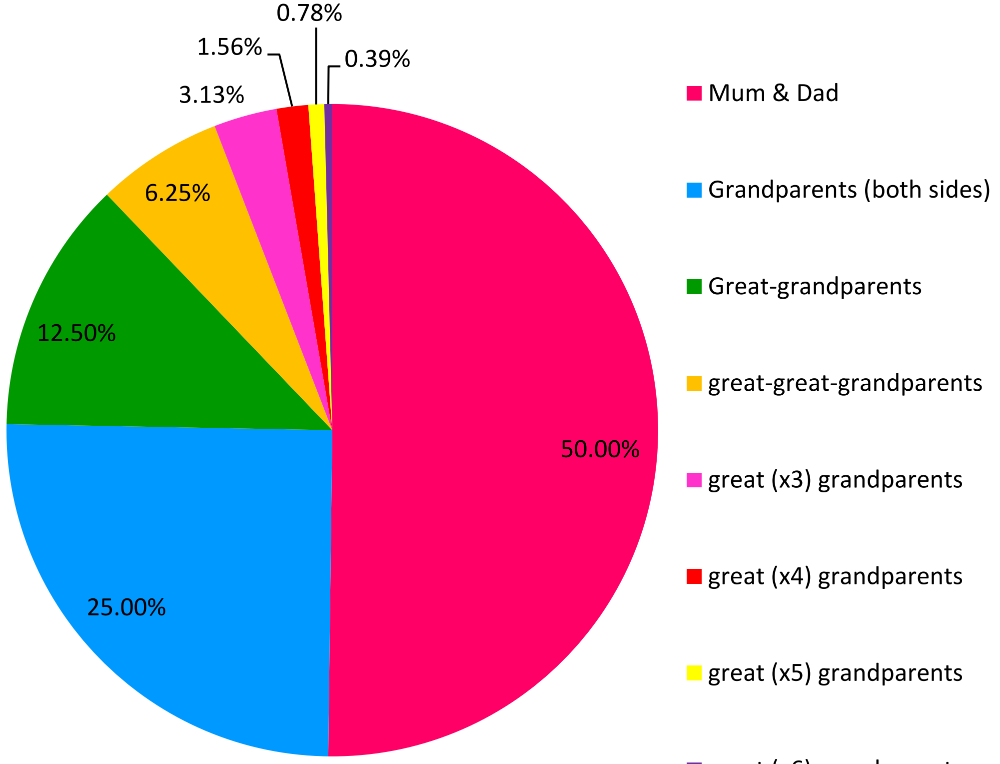
The parents of an individual together contribute on an average 50 percent of the total inherited characters, the 4 grandparents together 25 percent, the 3rd generation of ancestors together 12.5 percent, etc.

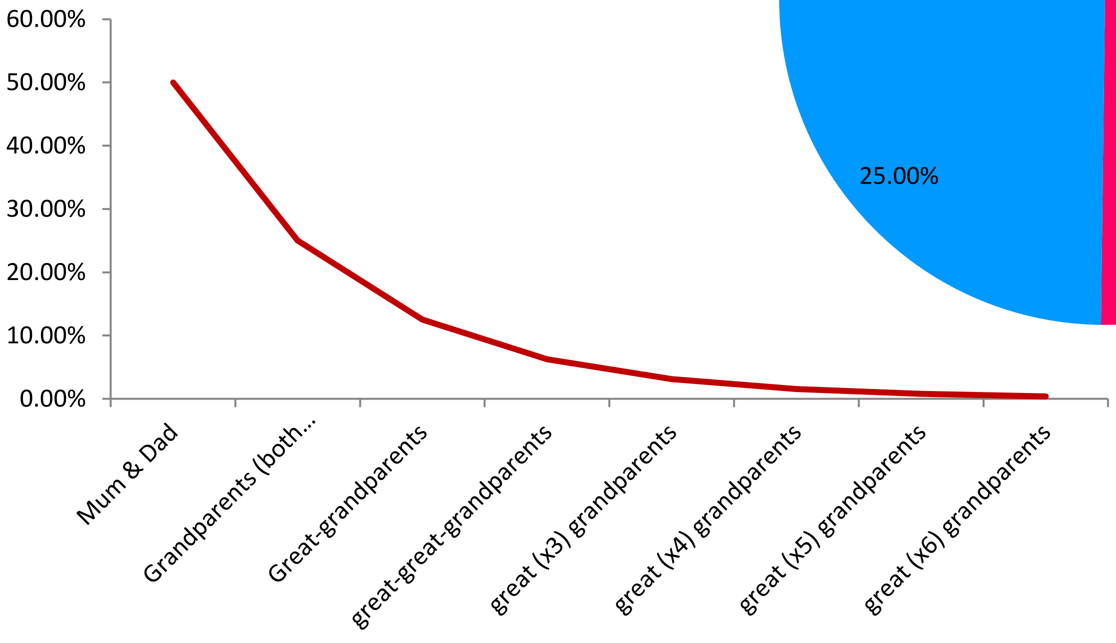


History of Quantitative Genetics

Francis Galton

Different theory of inheritance:





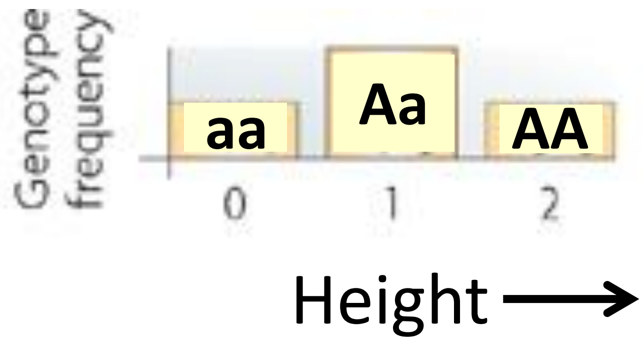
History: Galton vs. Mendel

Traits inherited in a Mendelian fashion. Phenotypes discrete characteristics

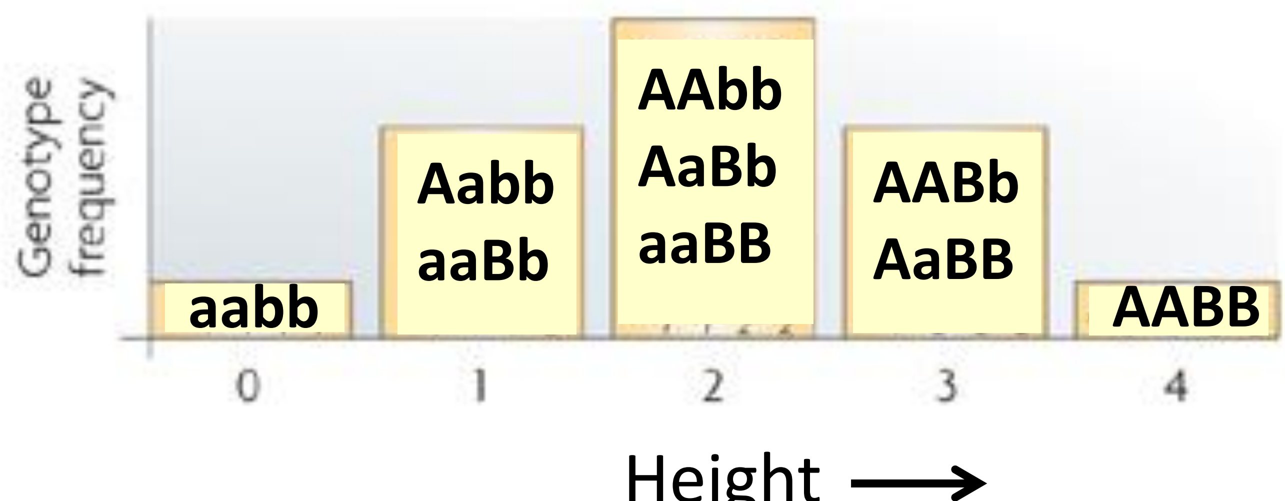
Traits inherited as complex averages of ancestral phenotypes. Continuously varying phenotypes

Quantitative traits and Mendelian laws

a One locus (A):



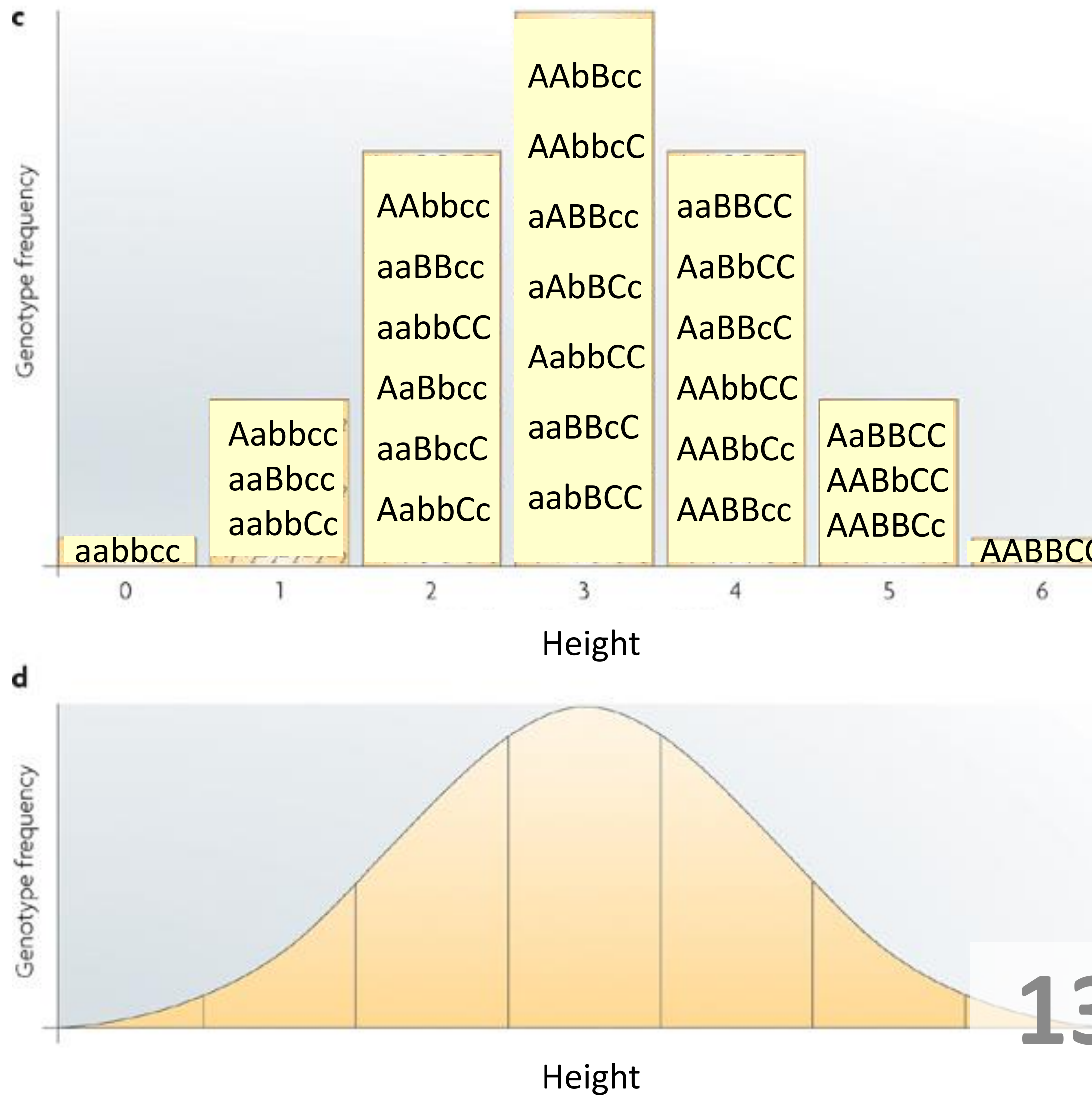
b Two Loci (A & B):



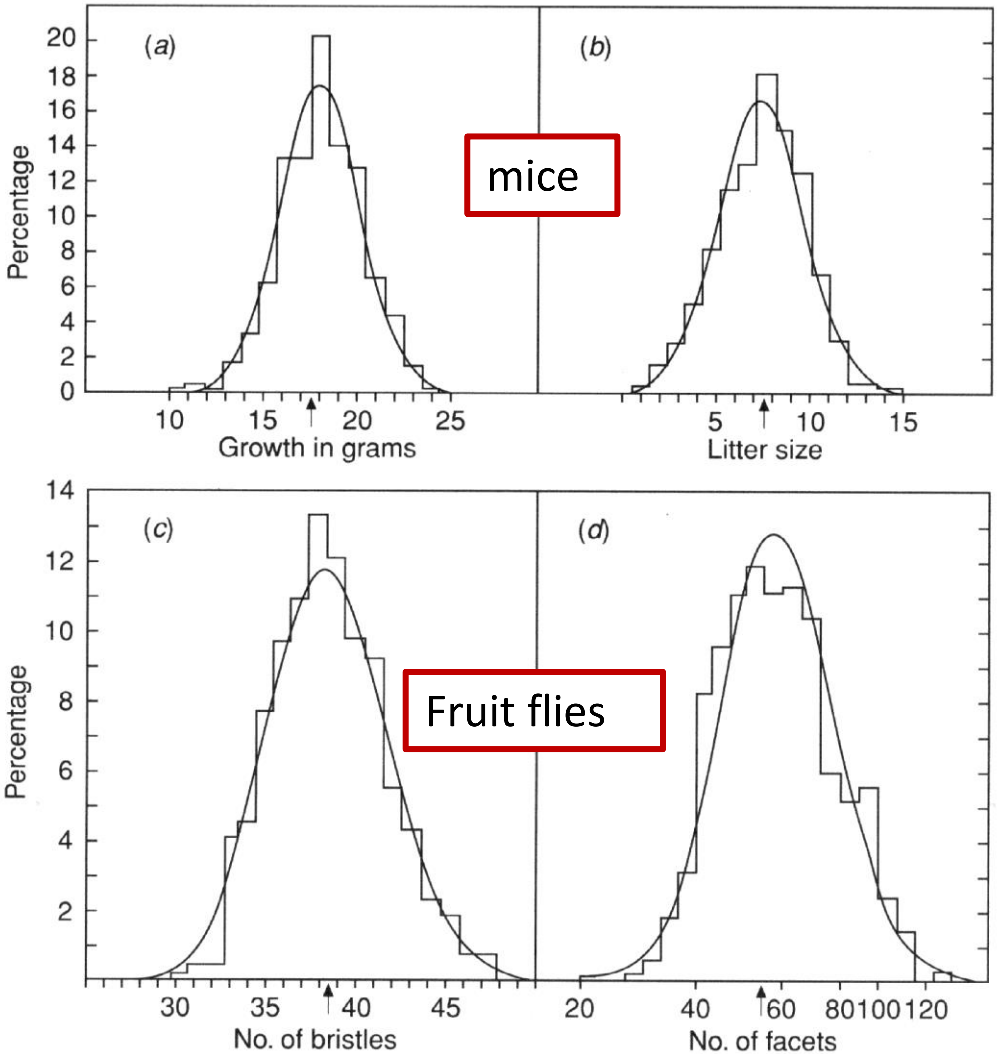
Quantitative traits and Mendelian laws

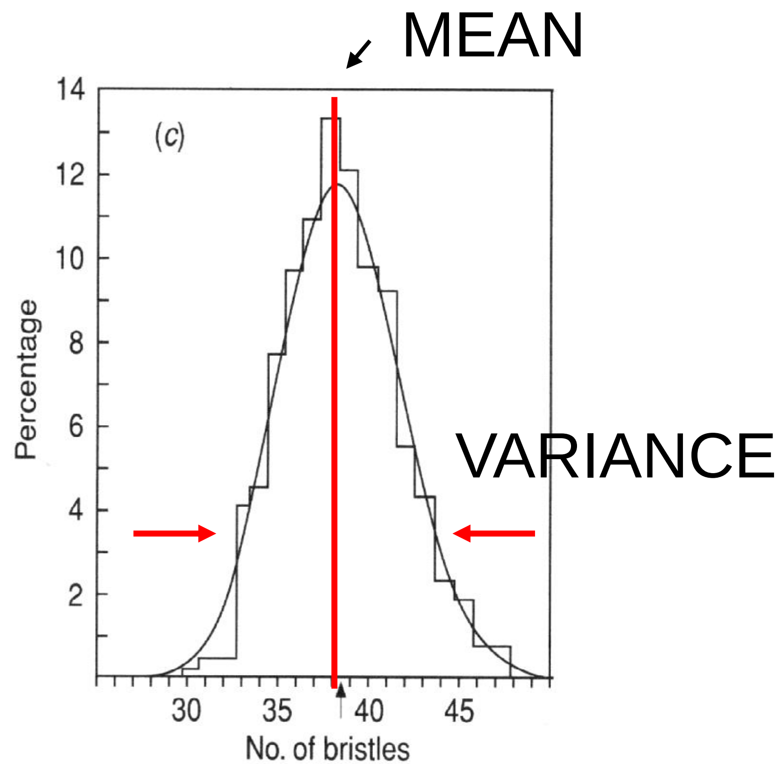
Three
Loci
(A, B & C):

Many
loci:



Normal Distribution of Phenotypes





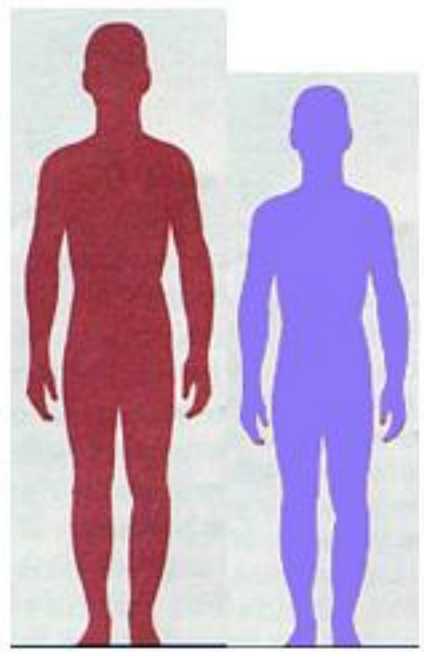
In: ***Introduction to Quantitative Genetics*** **Falconer & Mackay 1996**

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



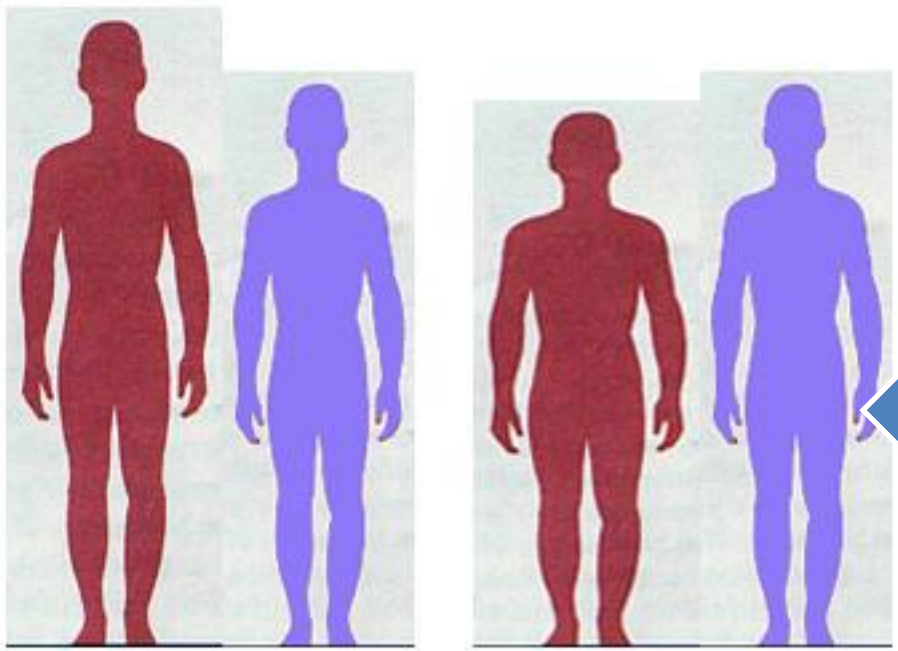
1. Normal development

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:

Difference due to different genes



1. Normal development

2. Red guy smoked!

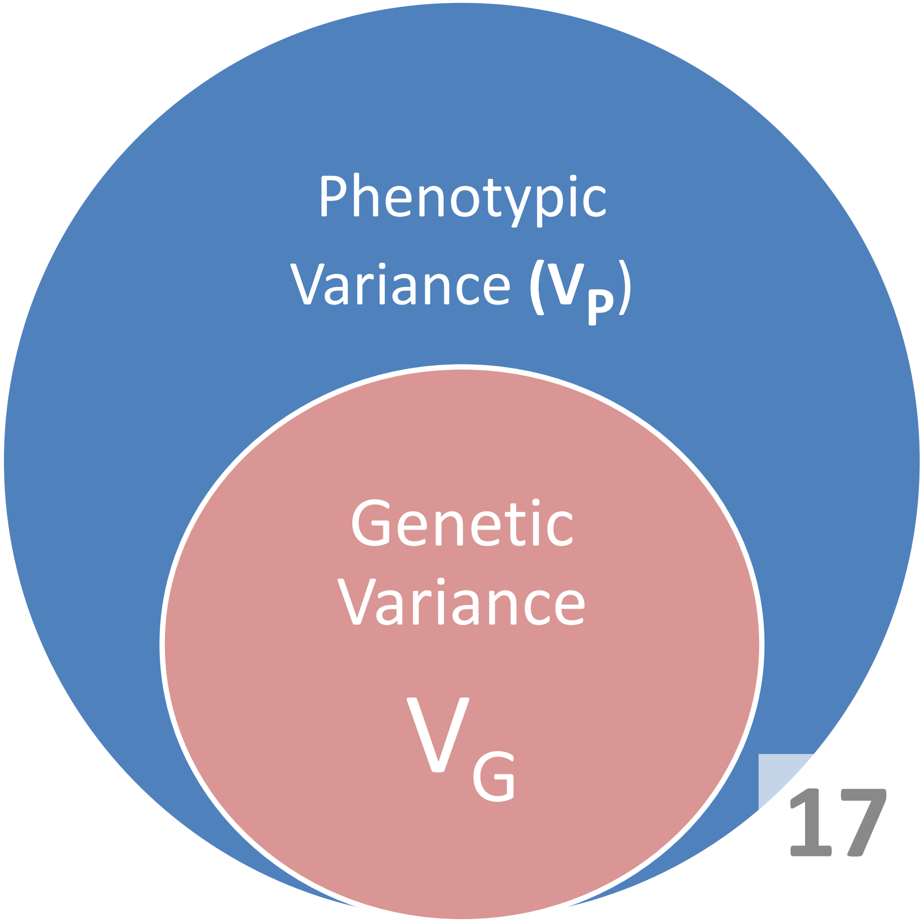
Difference due to genes & env.

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

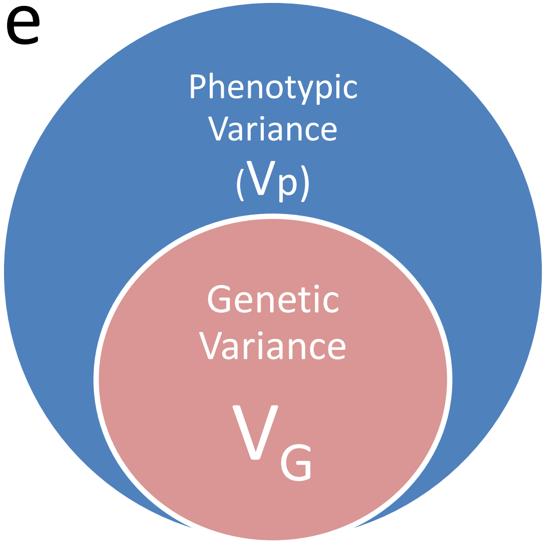
- This is called '**genetic variance**'



Heritability (H^2)

What Does it Measure?

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



Assuming additivity:

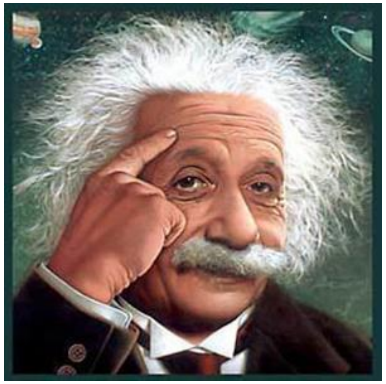
VP = VG + VE

H^2 = VG/VP

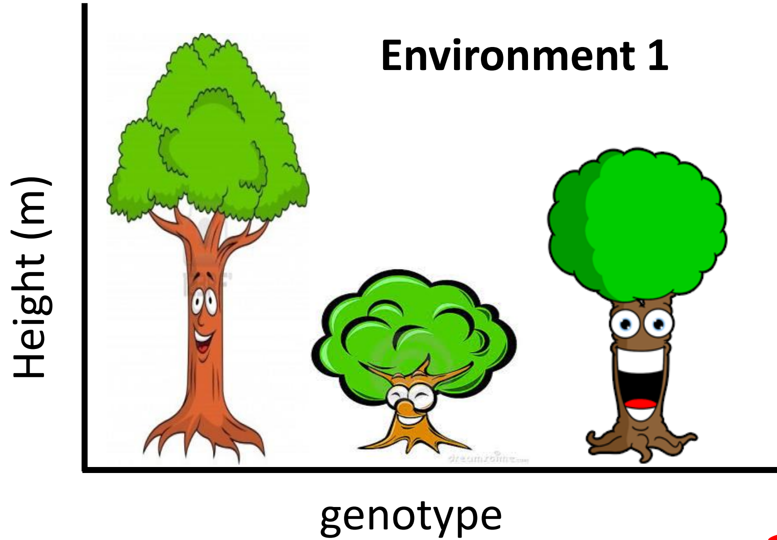
Proportion of Genetic variance to phenotypic variance

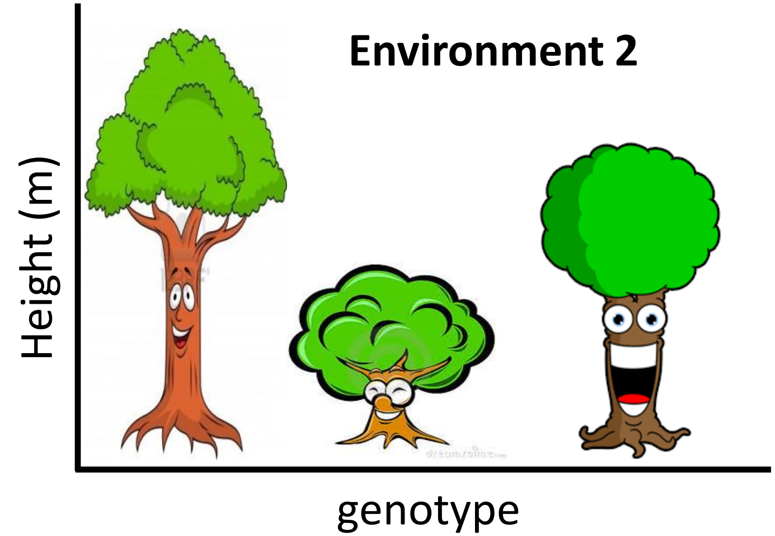
Heritability and Causation

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

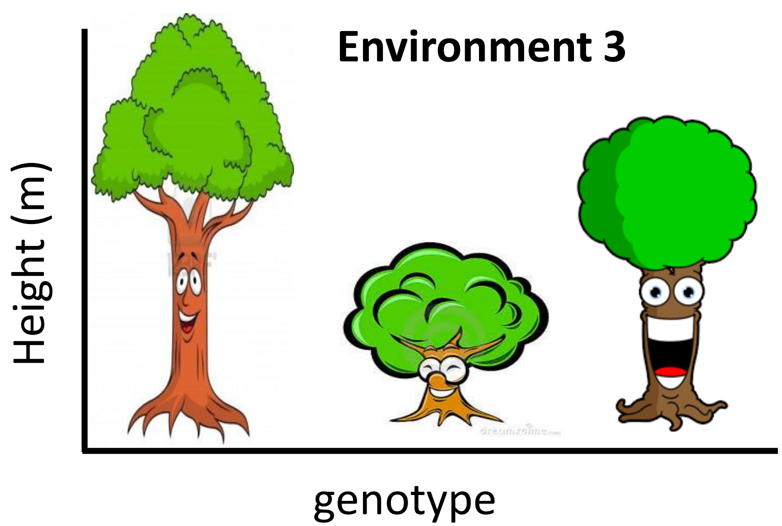


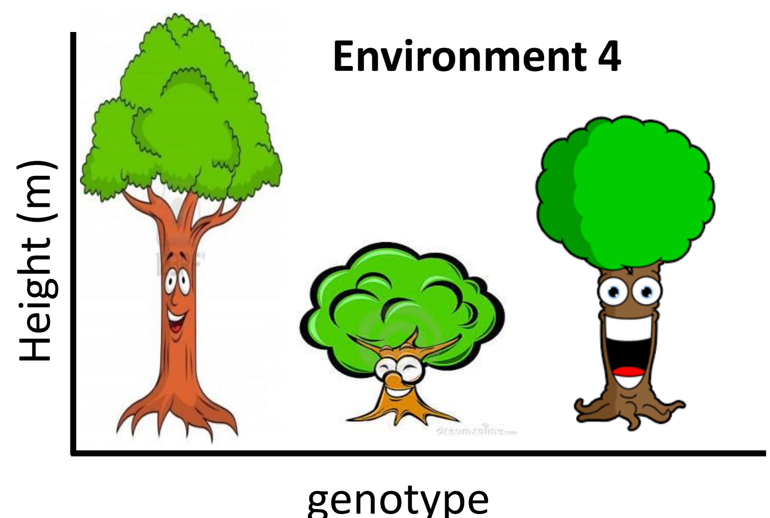
- *Specific types* of causal claims





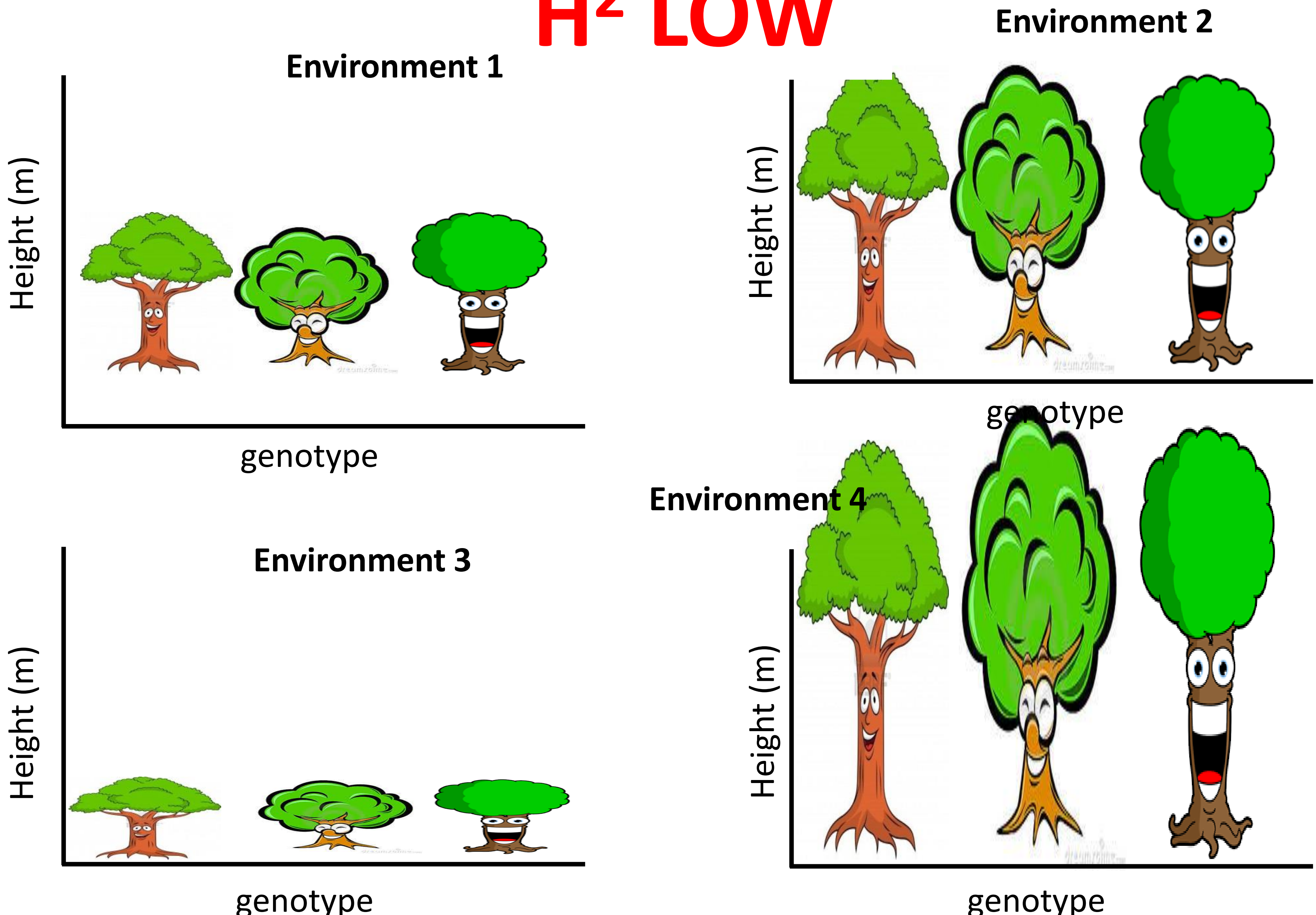
H^2 HIGH



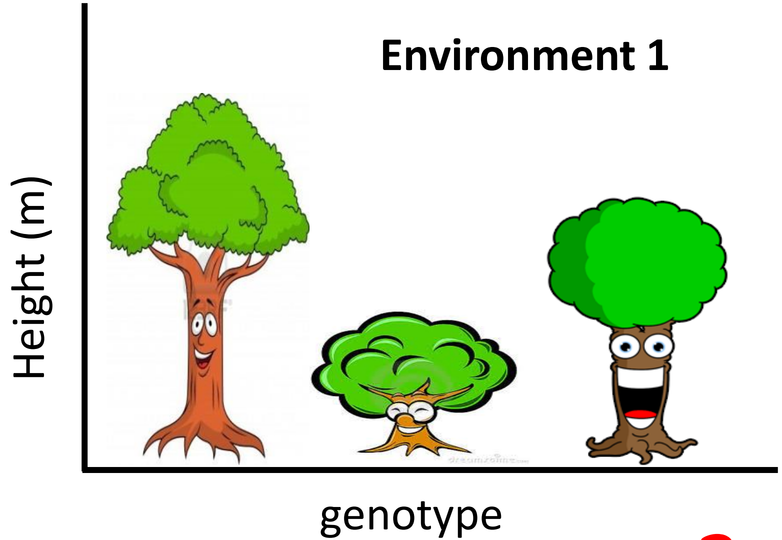


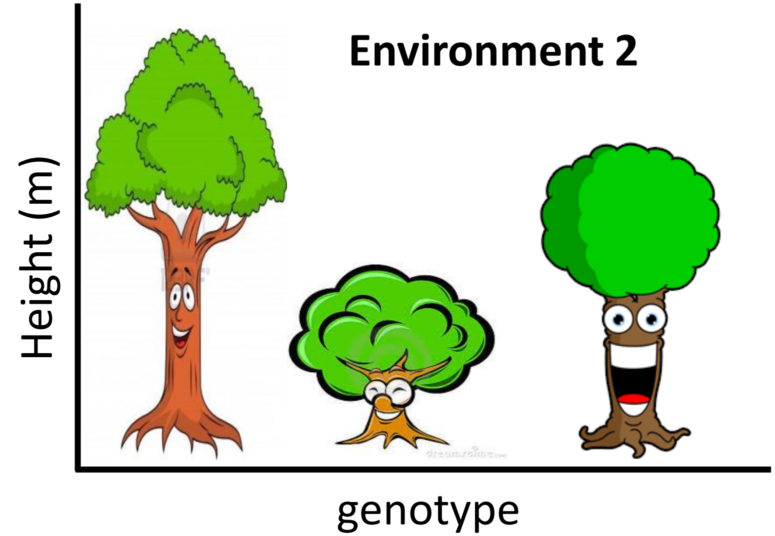
Environmental or Genetic?

H^2 LOW



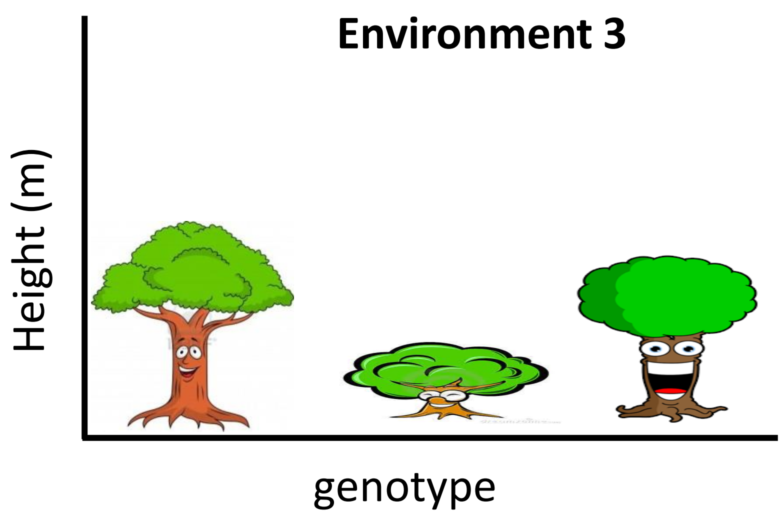
Environmental or Genetic?

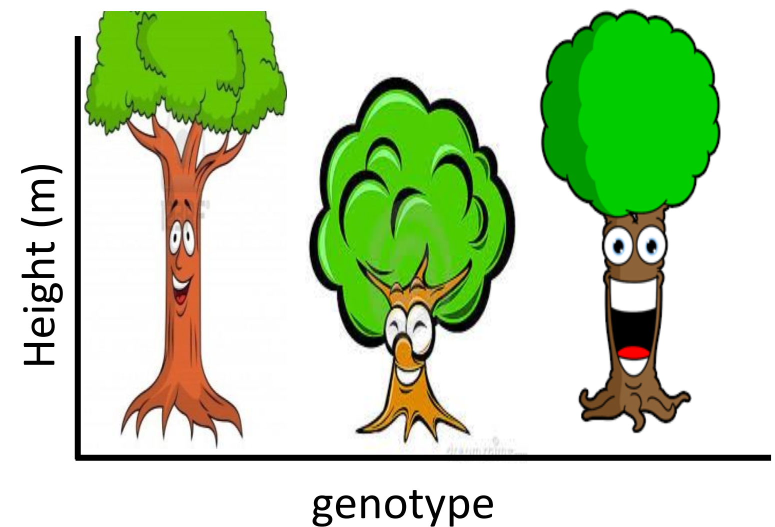




H^2 INTERMEDIATE

Environment 4





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.

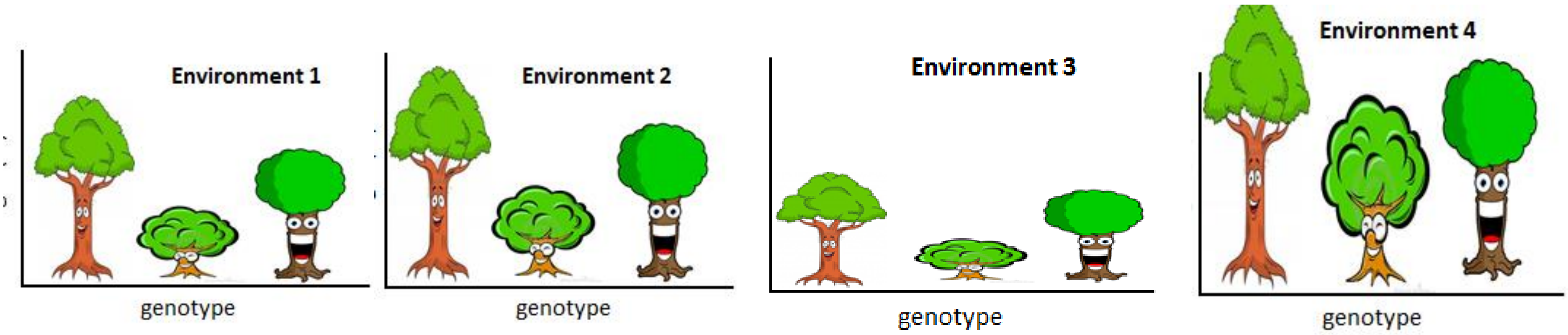
H^2 = VG / VP

VP = VG +VE

VG?

VE?

Where do the values come from?



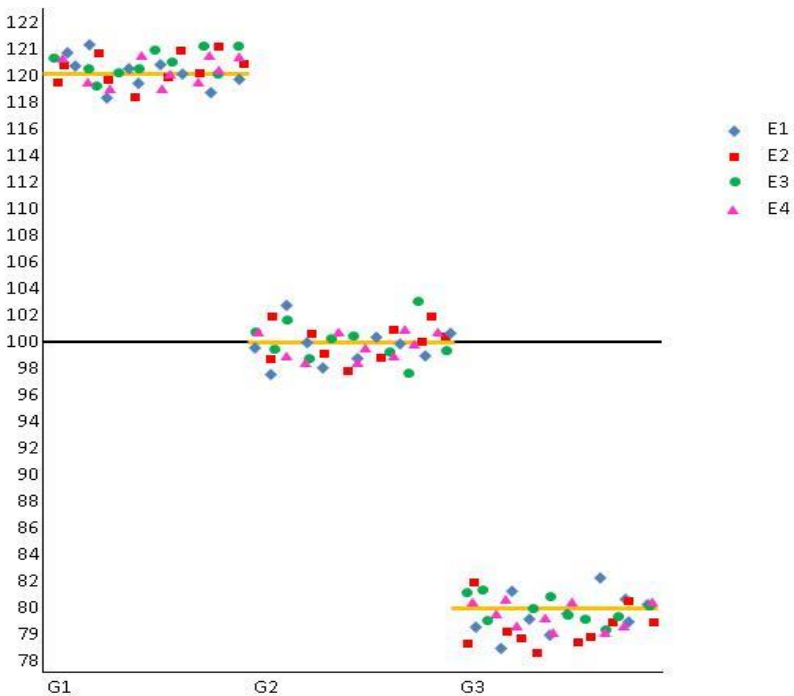
	E1 (75)	E2 (75)	E3 (75)	E4 (75)
G1 (100)				
G2 (100)				
G3 (100)				

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)	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
Environment Means	μ_{E1} =100	μ_{E2} = 100	μ_{E3} = 98.33	μ_{E4}= 101.67	$\ddot{X}$ = 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

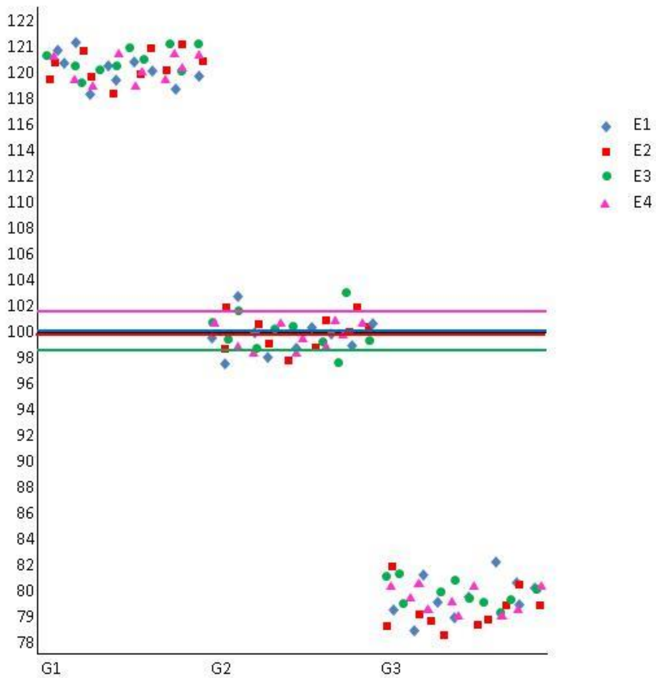


$$VG = \frac{(\mu_{G1} - \ddot{X})^2 + (\mu_{G2} - \ddot{X})^2 + (\mu_{G3} - \ddot{X})^2}{n_G}$$

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

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



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

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

VE = 1.38

Getting the heritability estimate

The phenotypic variance is assumed to be additive

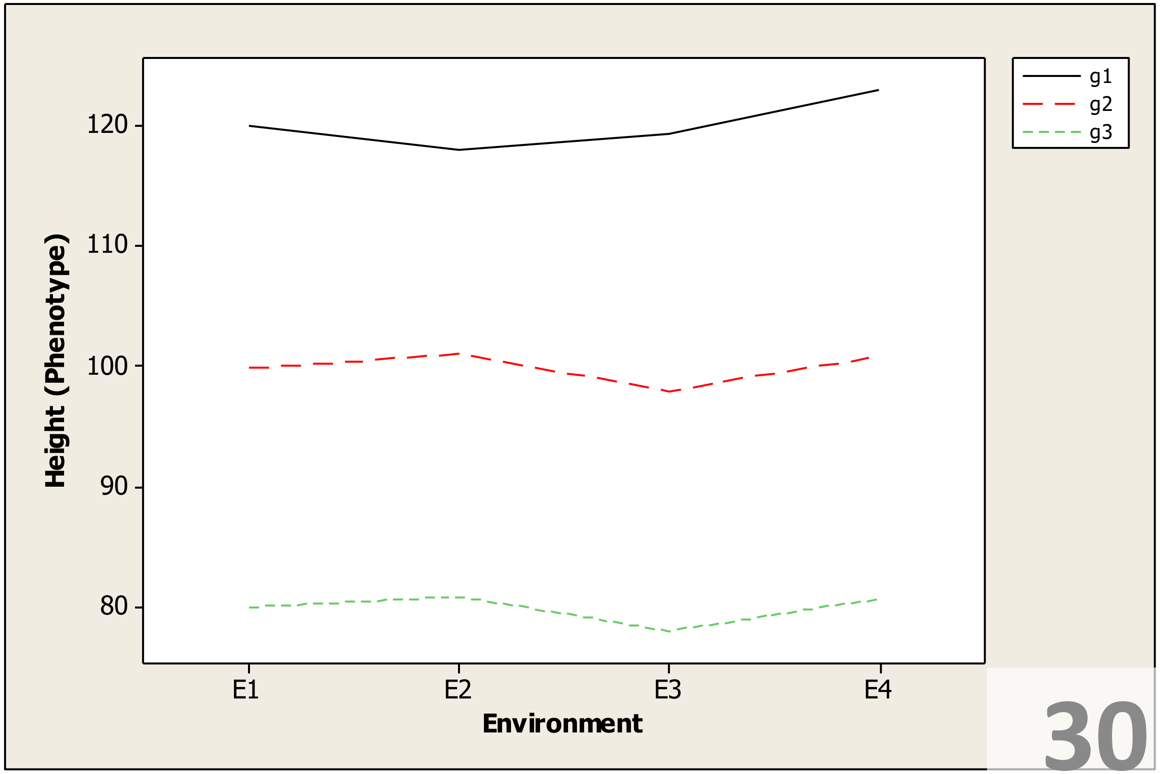
VP = VG + VE

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

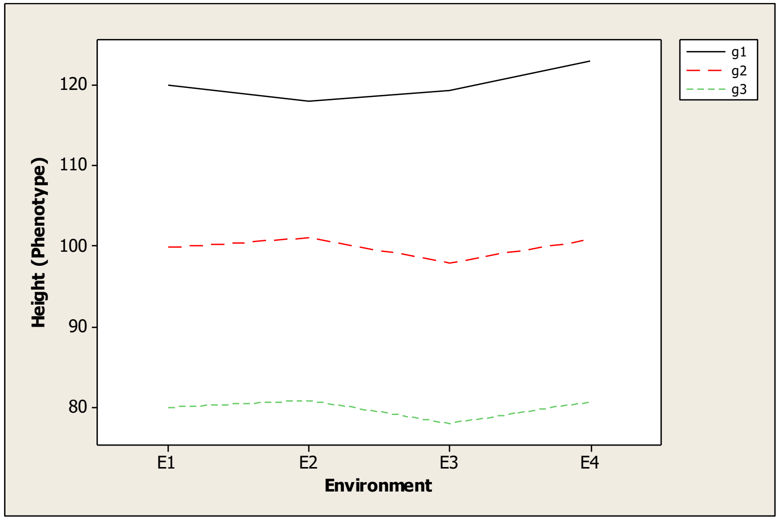
H^2 = VG / VP   or   VG / (VE + VG)

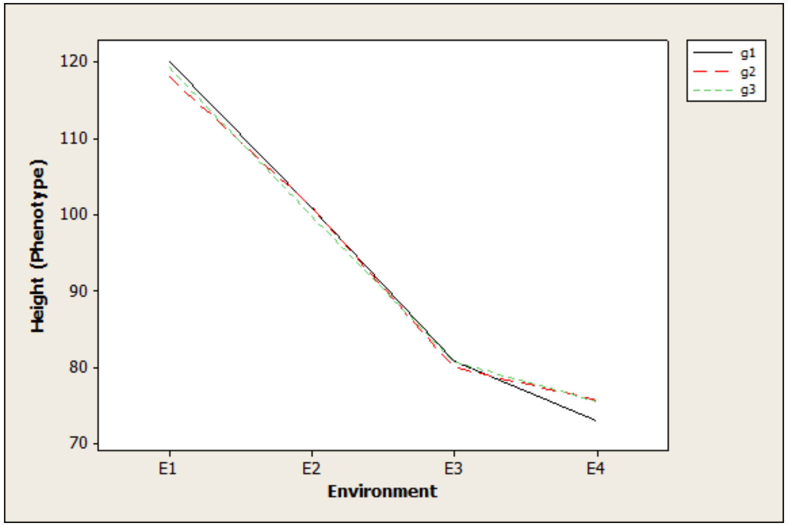
Usually a high heritability estimate accurately reflects an example in which differences in genotype are the major cause of differences in phenotype

VG = 266.67
VE = 1.38
VP = 268.05
<u>Genetic var (H^2)</u>
= VG / VP
= 266.67/268.05
= 0.9948
<u>Environmental var</u>
= VE / VP
=1.38/268.05
=0.0052

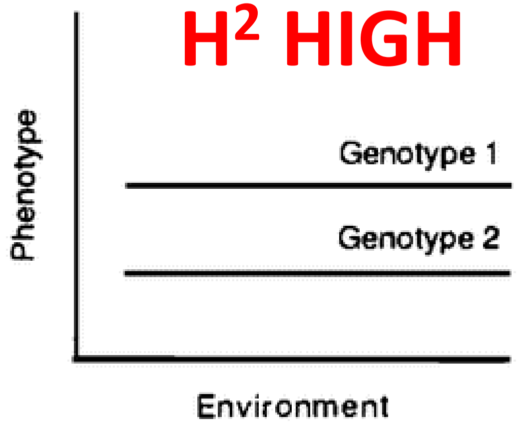


Norm of Reaction



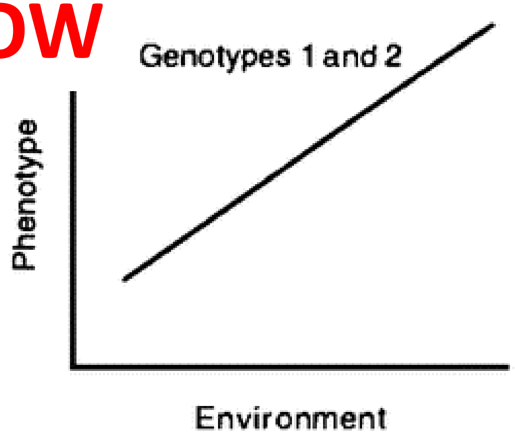


H^2 HIGH



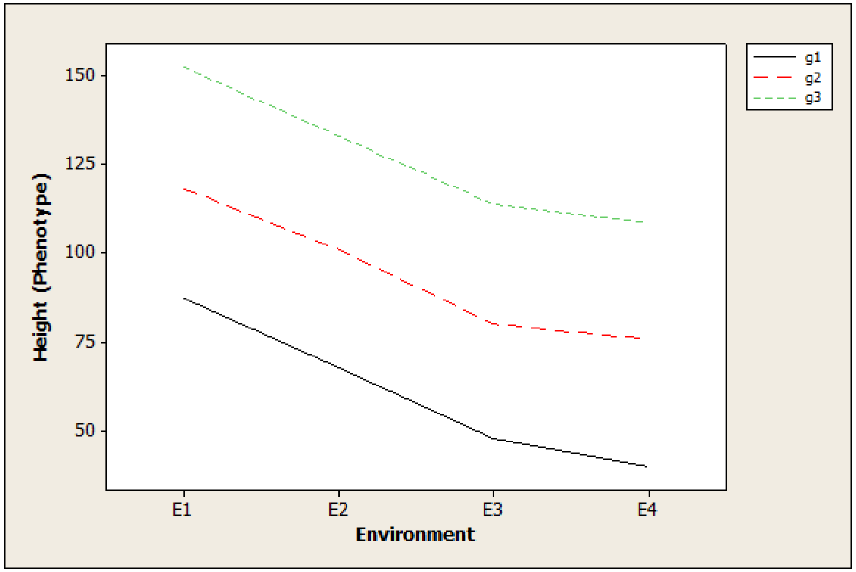
a) Biological determinism

H^2 LOW

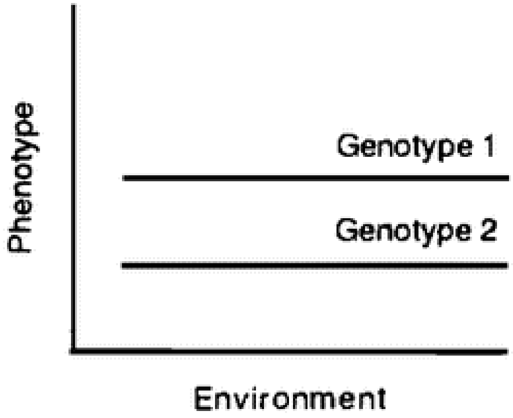


b) Social determinism

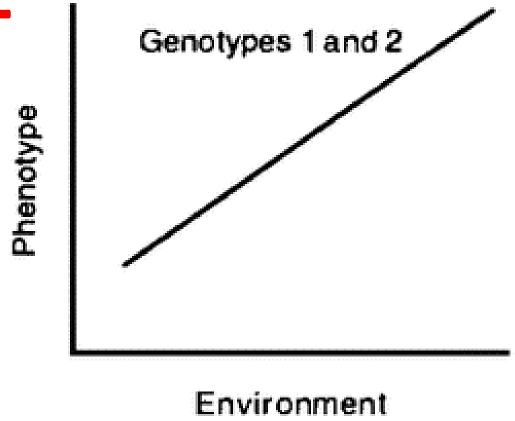
Norm of Reaction



H^2 INTERMEDIATE

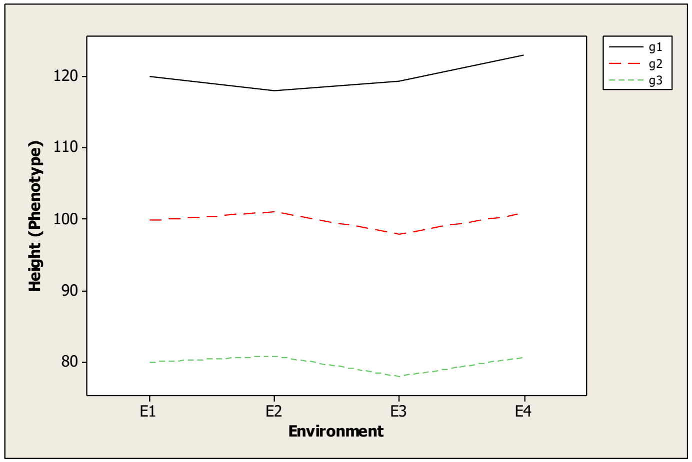


a) Biological determinism

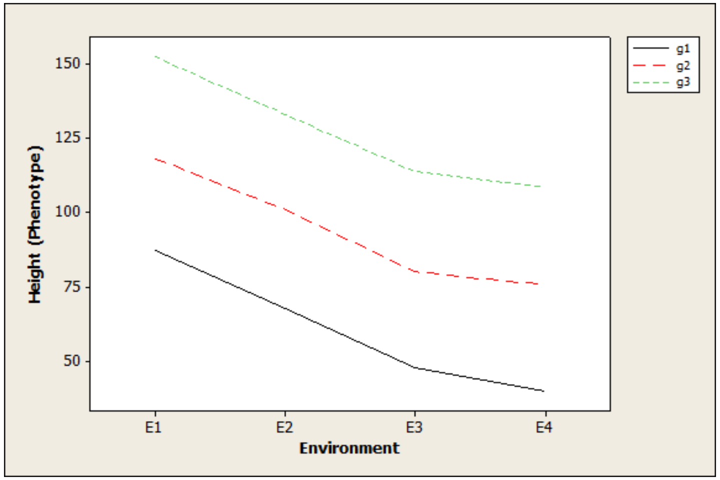


b) Social determinism

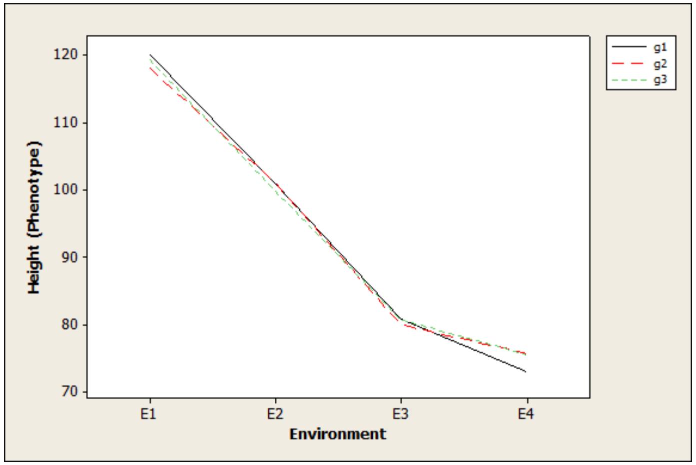
Norm of Reaction - GxE (Interaction)



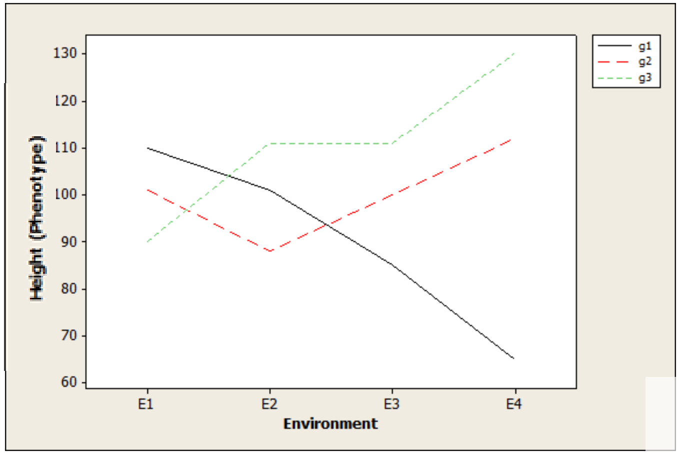
H^2 HIGH



H^2 INTERMEDIATE

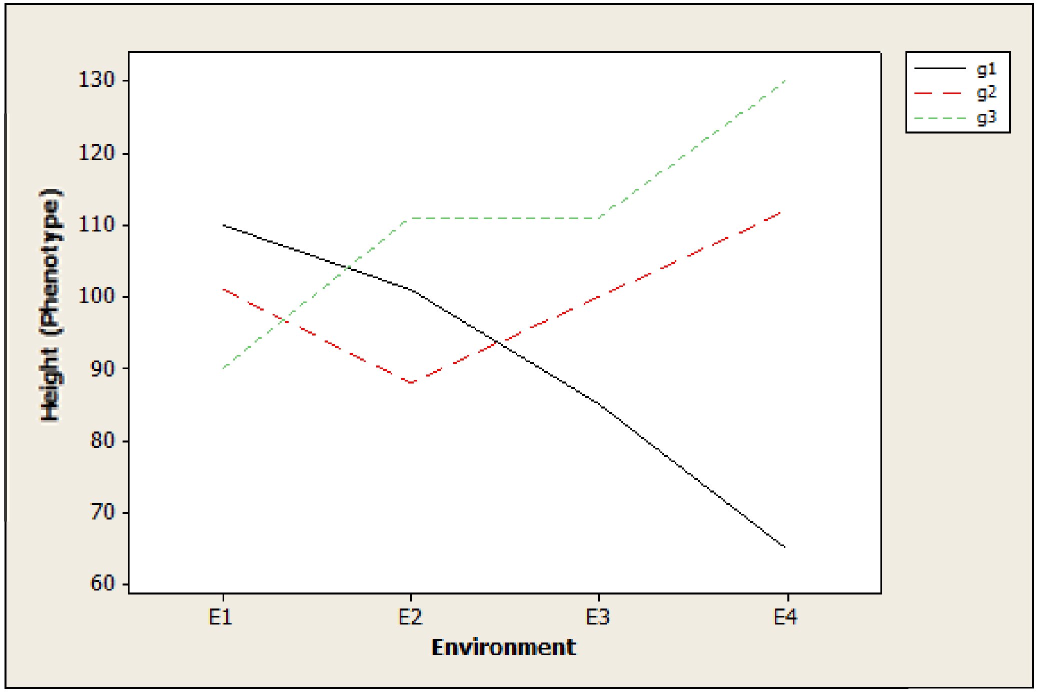


H^2 LOW



H^2 ??

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	$\ddot{X}$ = 100

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

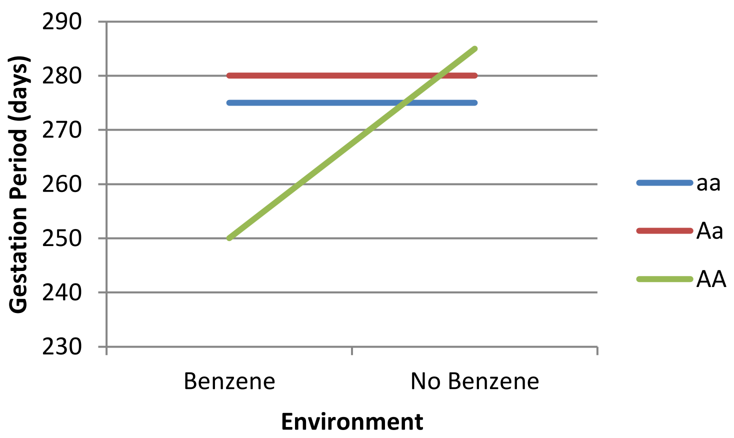
VG = 266.67

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

VE = 8.8089

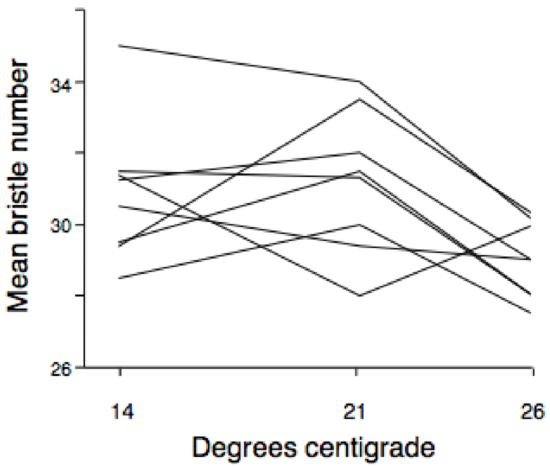
GxE (Gene-Environment Interaction)

- 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)



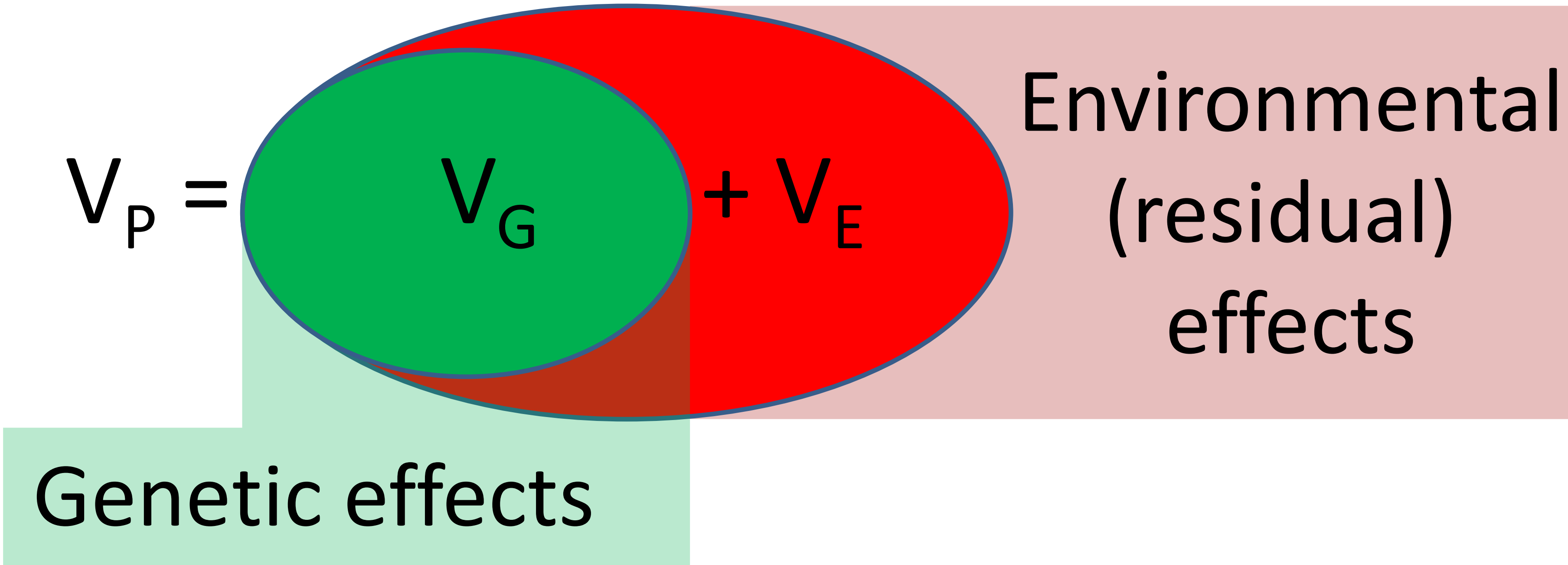
GxE (Gene-Environment Interaction)

- 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

<u>Non-Additive</u>

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

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

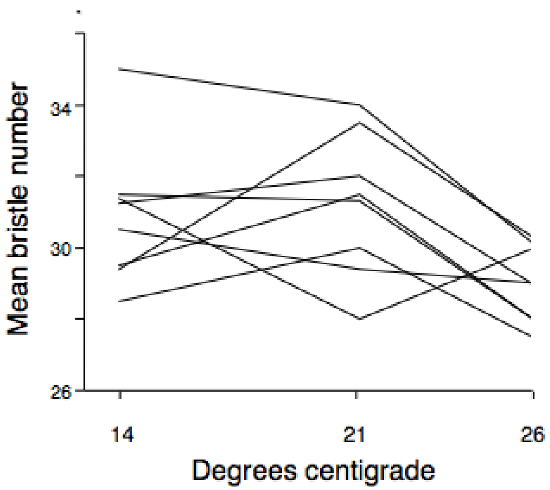
Araschnia levania *Precis octavia*

“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_{GxE}

  H^2 = VG / VP