Contribution of Genotype and Environment to Phenotypic variance Nature versus Nurture

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Contribution of Genes

- Why family members look like each other?
- They share common genes
- Why do we think traits are determined by genotype?
- Because there are similarities among relatives for that trait.
  - Since relatives have common genes and phenotype is similar in relatives, the traits are affected by genes.

Contribution of Genes

- Francis Galton studied human genetics
  - Lived in the same area as Mendel and Darwin
  - Created the statistical concept of correlation
  - He was a pioneer in eugenics, (improving genetic quality of the humans) and the phrase “nature versus nurture”
    - Nazi Germany racial hygiene
    - Eugenic wars in star trek

Contribution of Genes

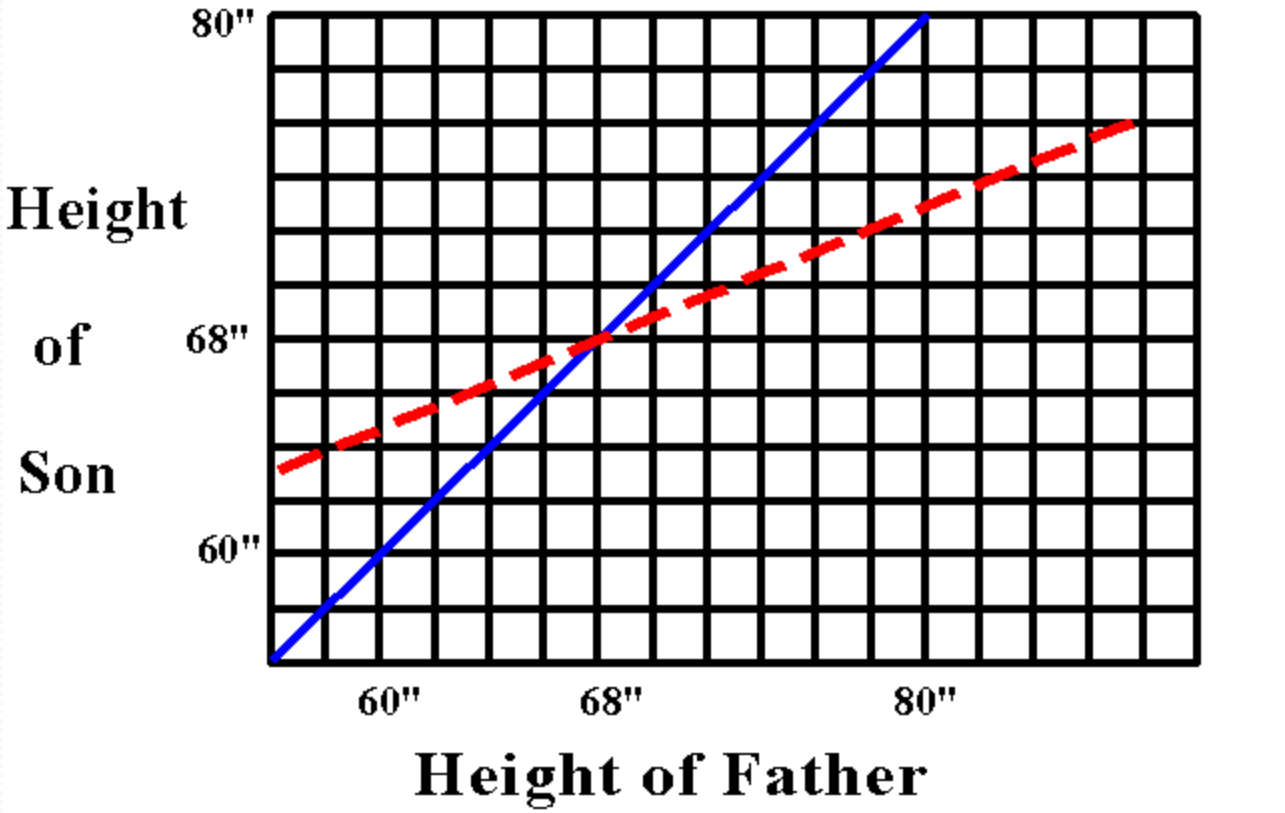
- Mendel studied discrete characters, green peas vs. yellow peas, tall vs. dwarf, etc.
- There was no overlap of phenotype in Mendel's studies.
- Characters fit into one of two classes.
- There was no blending in the heterozygotes.
- On the other hand, Galton studied the inheritance of continuous characters, height in humans, intelligence in humans, etc.

Contribution of Genes

- In 1906, visiting a livestock fair, Galton stumbled upon an intriguing contest.
- An ox was on display, and the villagers were invited to guess the animal's weight after it was slaughtered and dressed.
- 800 participated, but not one person hit the exact mark: 1,198 pounds.
- The mean of the guesses, at 1,197 pounds, was accurate.
- This is the same when estimating genotypic value.
- When there are many relatives in a group, some values are increased by the environment while some other values are decreased by the environment. Thus, the mean is closer to the actual genetic value.

Contribution of Genes

- He tried to quantify similarities of the relatives such as those between father and son.
  - Tall fathers did not have sons that are as tall, short fathers did not have sons as short, but they had values closer to the mean.
  - "Tallness" or "shortness" didn't breed true like they did in Mendel's pea experiments.
  - He called this the regression to mediocrity.



If the son's height were determined only by the father's height, the correlation should be that of the solid line. The dashed line is what is observed. Galton called this "regression to mediocrity."

Father and Son

- This is expected if there is no dominance.
- The son only gets half of his father's genes; the other half comes from his mother.
- Since the wives of tall men tend to represent the general population of women, they will not have, on the average, as many "tall" genes to pass on to their offspring as their husbands.
- Thus, the son will receive half of the father's "tall" genes, on average, and half of the mother's "tall" genes, on average, but his total genes for "tallness," on average, will be less than his father's.

Polygenic Inheritance

- For many years the argument raged between the "Mendelians" and the "Galtonians" as to which of the two paradigms was the correct one for human inheritance.
- There was no question that Mendelian inheritance was correct for some diseases, but these were rare, affecting only a small portion of the population.
- They were considered trivial by the Galtonians.

Polygenic Inheritance

- On the other hand, the inheritance of quantitative traits could not be used to predict outcomes, only average estimates measured in large population studies.
- Mendelians considered the study of quantitative traits to be trivial because they had no predictive value.
- R. A. Fisher resolved the dispute by showing that the inheritance of quantitative traits can be reduced to Mendelian inheritance at many loci.
  - Polygenic Inheritance, each gene follows Mendel's rules

Galton and r

- Galton coined a new term: correlation coefficient (r)
- Using this coefficient, he discovered that he can measure the strength of the relationship between two relatives.

Galton and r

- In a trait that is determined only by genotype, meaning there is not effect of the environment:
- Correlation coefficient between two individual is the same as coefficient of relationship.

Dermal ridge count: # ridges in fingerprint

- A study from England:

Relationship	Observed r	Expected r
Parent-offspring	0.48	0.50
Full sibs	0.50	0.50
Twins	0.95	1.00
Mom-Dad	0.05	0.00

The very small difference between the fine details of ridges, valleys, and swirls defining twins fingerprints are influenced by random stresses experienced in the womb. Different umbilical cord length changes the fingerprint.

- Observed and expected correlations are very close
- Is this because of genetics, or because the relatives share the same environment?
- Take a closer look at the last correlation
  - Though they share the same environment, r=0
- All these indicate that dermal ridge count is determined by genetics only. Nature vs. nurture here?

Relationship	Observed r	Expected r
Parent-offspring	0.48	0.50
Full sibs	0.50	0.50
Twins	0.95	1.00
Mom-Dad	0.05	0.00

- Using the correlation coefficient, it can be determined whether a continuous trait has an underlying genetic basis.
- The correlation coefficient can also provide a rough estimate of the contribution of the genotype and environment.

However, a better measure is used to quantify the contribution of genes and environment:

HERITABILITY

HERITABILITY

- To understand heritability, we first have to look at quantitative variation.
- What do we observe when we look at a trait?
- Phenotypic variation
- The basic information used in quantitative genetics is phenotypic variation (V_P)

- Phenotypic variation (V_P) is the result of genotype x environment interaction.
- Phenotypic variance occurs due to variance of the genes and variance of the environmental factors.
  - Just like P=G+E, phenotypic variance has a similar structure.

$$V_P = V_G + V_E$$

- Phenotypic variance is the sum of genetic variance and environmental variance.
- The variance related to environment is in the model because animals are exposed to different environmental conditions.

$$V_P = V_G + V_E$$

- This is just the beginning to start explaining simple and quantitative variation
  - We need to open up our model to take all variations into consideration.

$$V_P = V_G + V_E + COV_{G*E}$$

- Sometimes genotype and environment have covariation; they change in the same direction together.
  - Height and arm length in humans, measured in a tailor shop.
- Correlation is a standardized measure, while covariance is shown as data units.

$$V_P = V_G + V_E + cov_{G*E}$$

- Example:
- A farmer has dairy cows. This farmer keeps the higher producing cows on a higher plane of nutrition. What happens?
  - Rich is richer, poor is poorer
  - Genotype and environment moves in the same direction together, which is covariance.

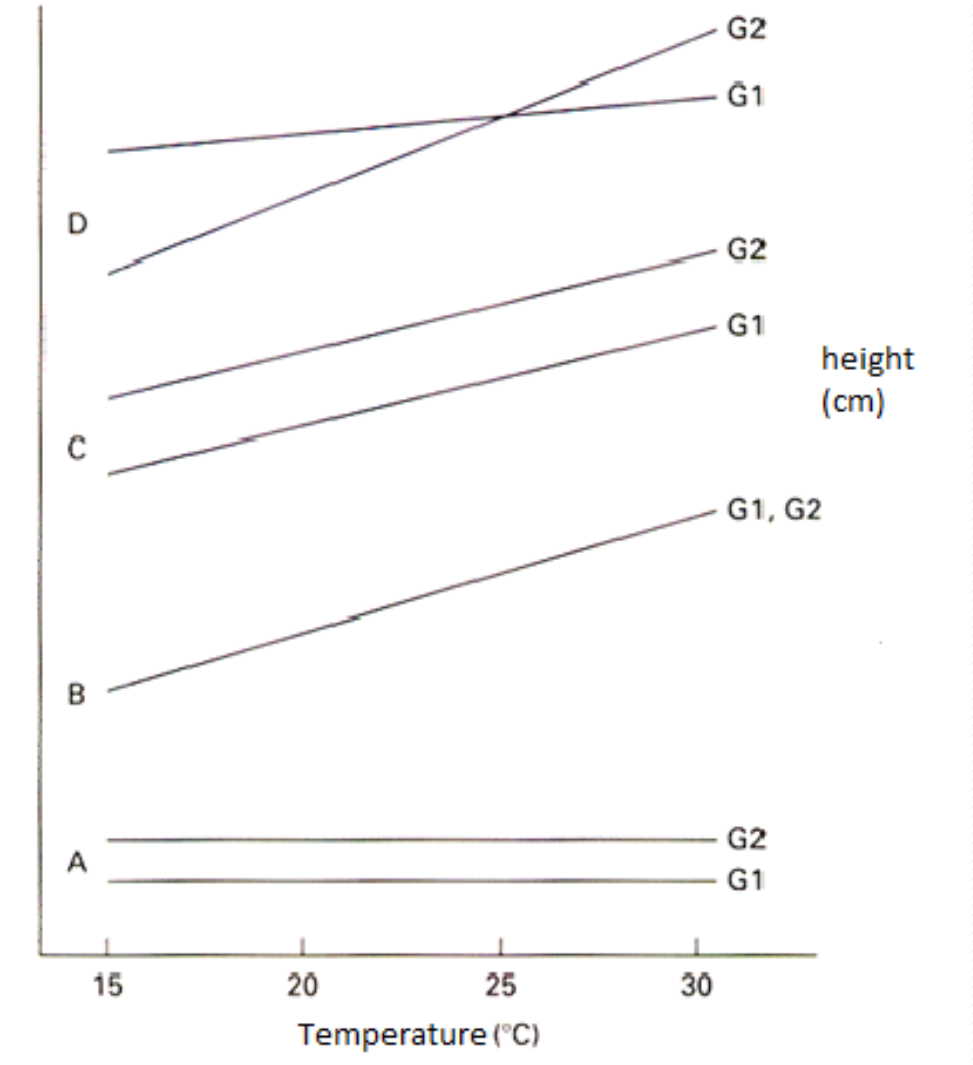
$$V_P = V_G + V_E + cov_{G*E}$$

- Superior genotypes are exposed to a better environment than inferior genotypes.
- Thus, you get more from the superior animals.
- Phenotypic variance increases because the rich is richer, poor is poorer and the difference increased.

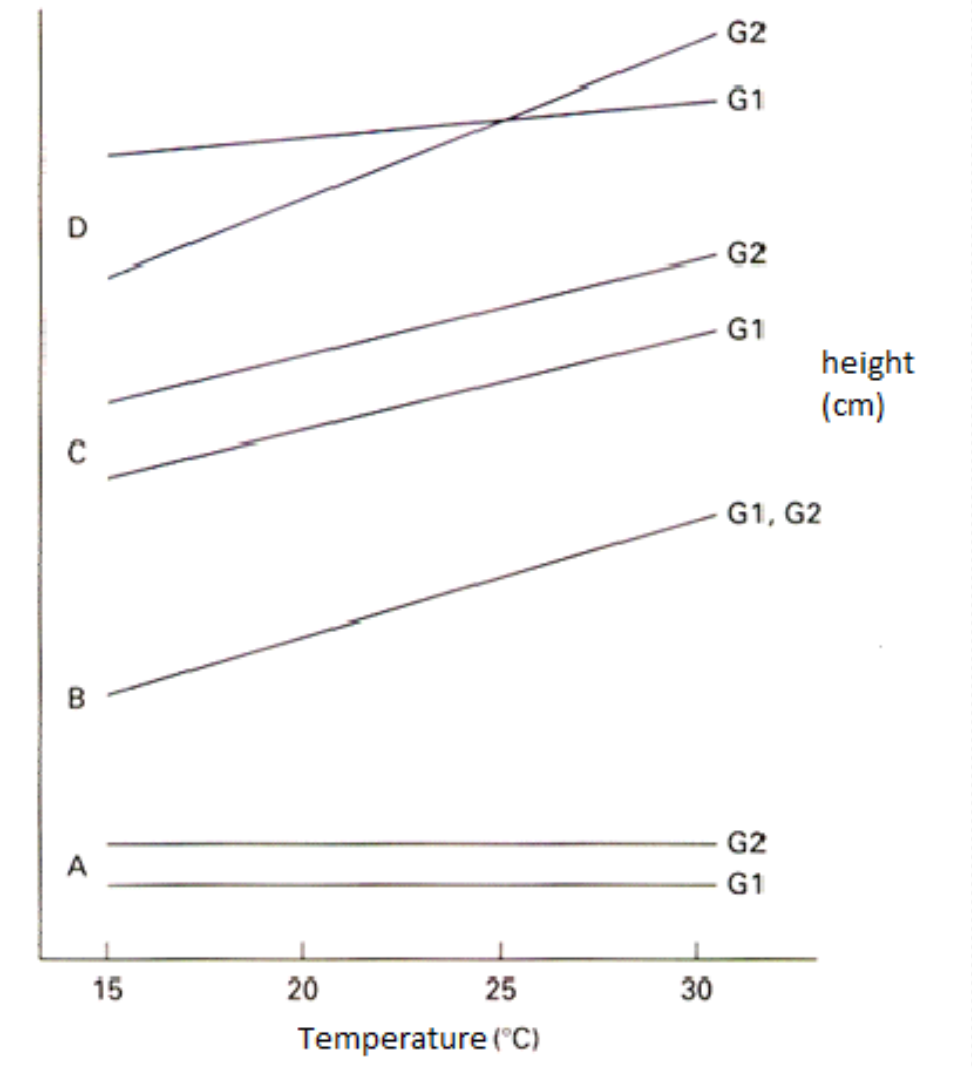
$$V_P = V_G + V_E + cov_{G*E}$$

- Genotype can interact with the environment in many ways possible.

Effects of different levels of temperature (environment) on height (phenotype)

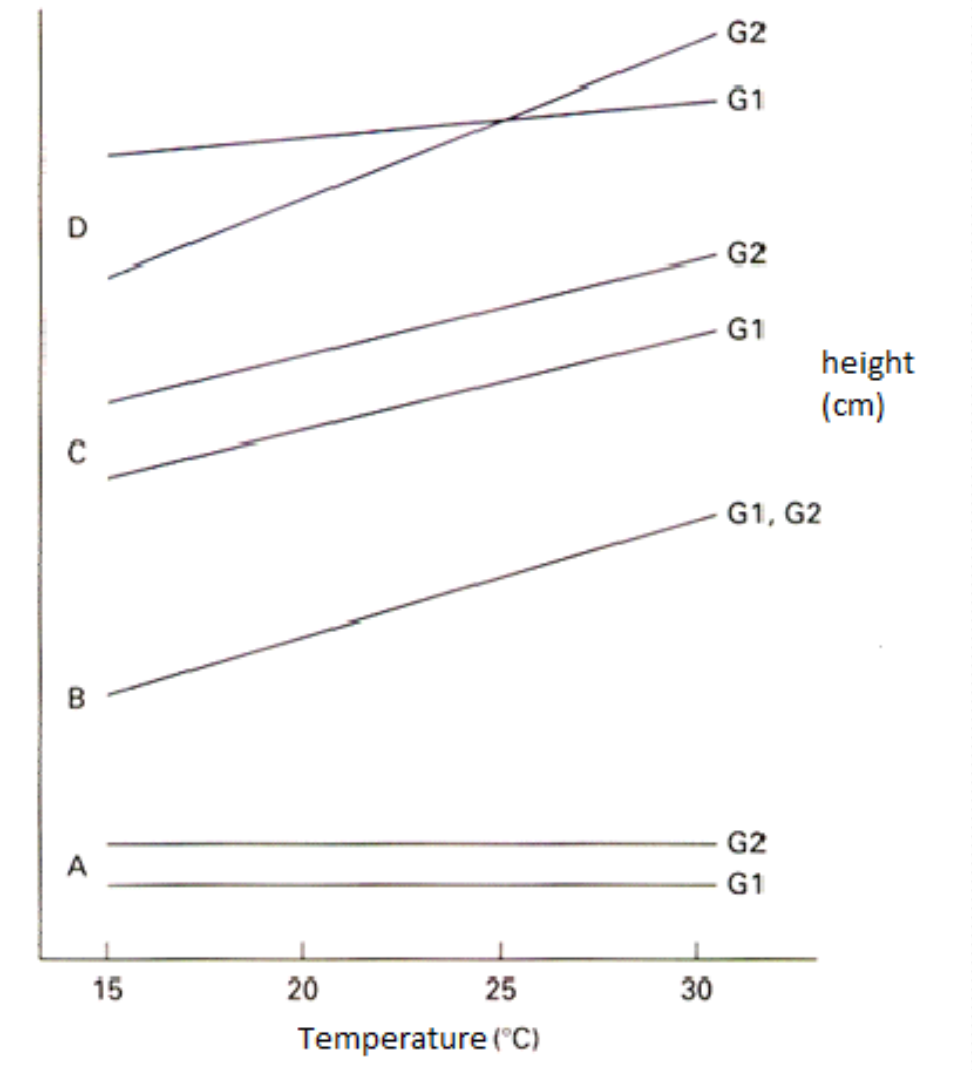


(A): Genotype G2 is always better than G1, differences do not change in different levels of temperature – All variation is genetic (eye color etc.)

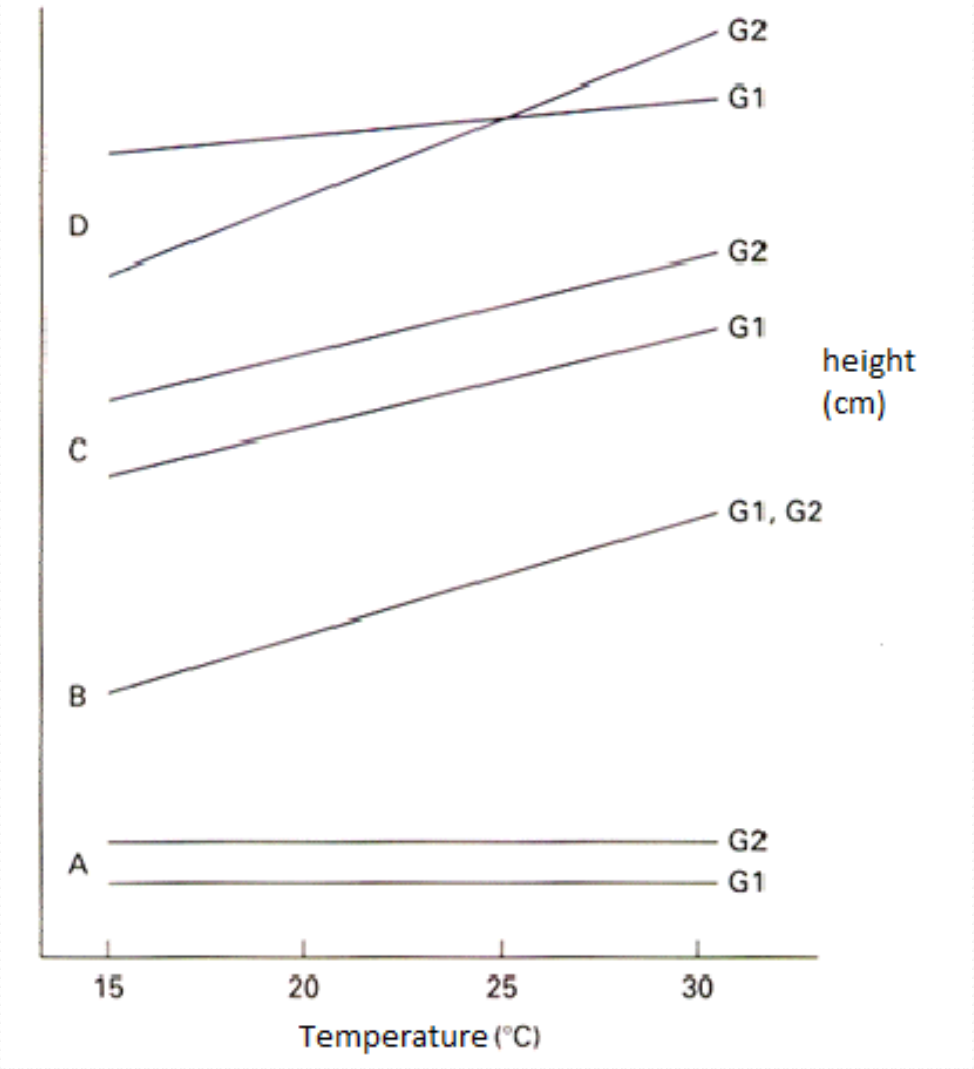


(B): All variation is because of environment, two genotypes are the same

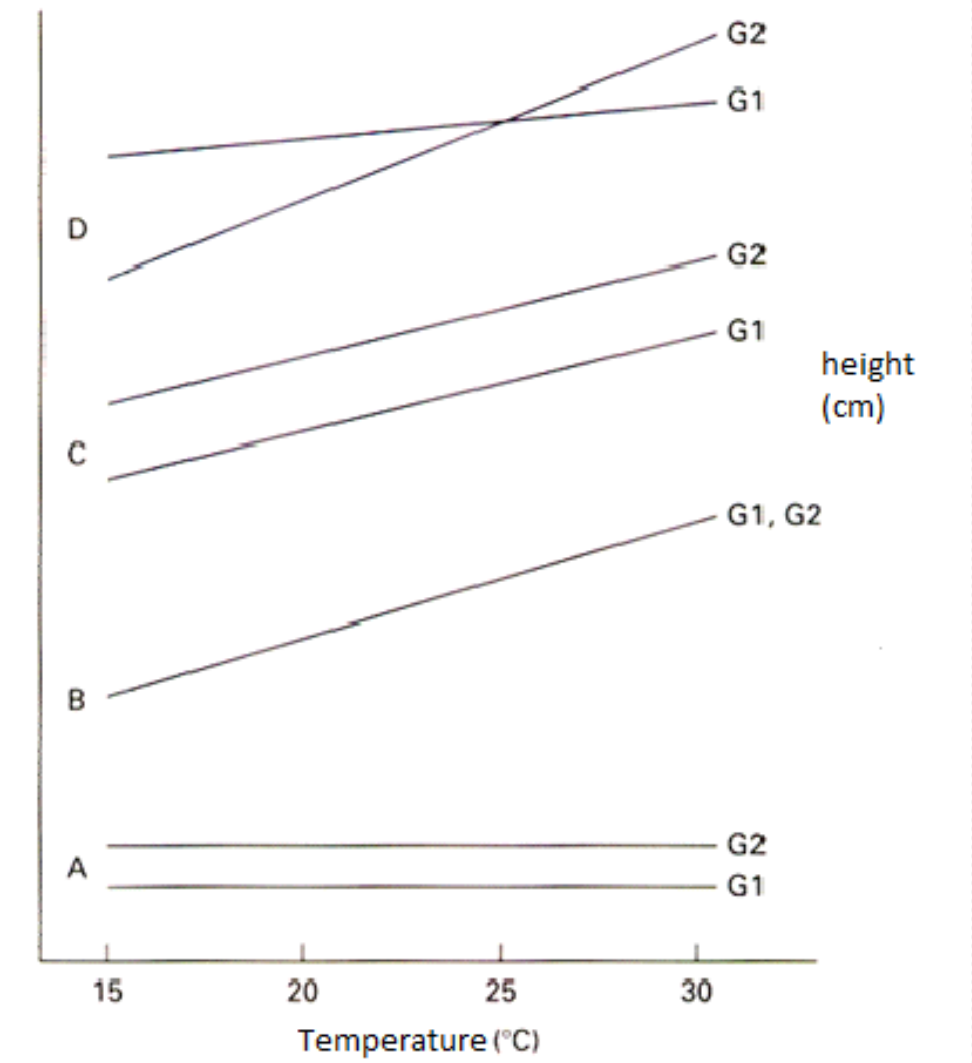
They are both on the same line, the only thing that changes them is temperature (environment)



(C): Levels of genotype and environment are additive. There is no interaction, fully parallel)



(D): G1 is better at lower temperatures, G2 is better at high temperatures. This is an example of genotype*environment interaction: due to chance?



$$V_P = V_G + V_E + cov_{GxE} + V_{GxE}$$

- To be able to take this interaction into consideration, we need to add a new piece to our equation.
- Genotype environment interaction causes parent and offspring to be different (if they are raised under different environments, they will be different phenotypically.

$V_P = V_G + V_E + cov_{GxE} + V_{GxE}$

- Environmental variance V_E can be opened up some more, can be explained using more parameters

$V_E = V_{Ep} + V_{Et} + V_{Em}$

- V_{Ep} = Permanent environment, environmental factors affecting performance permanently.
- INTER Individual variance: there may be differences among individuals. Because it is permanent, and not temporary, it does not change within individual, it stays the same for life.

- Examples:
- Effects of plane of nutrition as a newly born on mature weight
- In humans, effects of plane of nutrition up to age 3 to IQ in age 30
- Broken leg
- Chopped off udder tip

$V_E = V_{Ep} + V_{Et} + V_{Em}$

- V_{Et} = Environment factors affecting an individuals performance temporarily (temporary environment).
- INTRA Individual variance: differences are observed on the same individual:
- The phenotype is different when measured in different times.
- Example:
  - Effects of age on weight during growth
  - Effects of season on skin color

$$V_E = V_{Eg} + V_{Es} + V_{Em}$$

- V_{Em} = Maternal specific effects. It is especially important in mammals.
- Example:
  - Uterus situation, feeding, exposure to radiation etc.
  - Suckling situation
    - More milk-less milk,
    - More affection and love-less affection,
    - More nurture-less nurture

$$V_P = V_G + V_{Eg} + V_{Es} + V_{Em} + cov_{GxE} + V_{GxE}$$

- What was seemingly simple at the beginning turned into this complex equation.
- Now, we can see the variance due to environment more accurately.
- How about genetic variance?

Contribution of Genotype to variance

$$V_P = V_G + V_{Ep} + V_{Et} + V_{Em} + cov_{GxE} + V_{GxE}$$

V_G has to be opened up, because there is more than one source of genetic variation

$$V_P = V_G + V_{Ep} + V_{Et} + V_{Em} + cov_{GxE} + V_{GxE}$$

Sources of Genetic variance

- Some of the sources of variance in mammals occur due to differences in skin color in humans or percentage fat in milk in dairy cows.
- These types of variances are due to additive gene action.
- Additive genes are the first and foremost source of resemblance among relatives.

Sources of Genetic variance

- Variance due to these genes is called additive genetic variance (V_A).
- V_A is the variance produced by each and every allele and adds them all up.
- Thus, it is the sum of all independent gene effects.

Sources of Genetic variance

- V_A is the variance that can be used in selection. Why?
  - Only V_A is heritable, transmitted to the next generation.
  - For an individual: Breeding value

Sources of Genetic variance

- One can run selection using the variance of fat percentage in milk, increasing the fat percentage in the next generation.
- These animals are expected to provide more fatty milk in the next generation.

Sources of Genetic variance

- Additive gene effects are used in selection (same in natural selection).
- However, interactions between the alleles should be taken into consideration as well.
  - These interactions contribute to genetic variance and they are a piece of the whole.

Sources of Genetic variance

- Inter gene interactions cause dominance variance (V_D)
- Can you think of a population where you have genotypic variation, but there is no phenotypic variation?
- In the population, there are dominant homozygous individuals (AA) and dominant heterozygous individuals (Aa)

Sources of Genetic variance

- There are dominant homozygous individuals (AA) and dominant heterozygous individuals (Aa) in the population.
- In this case, there is genotypic variation, but there is no phenotypic variation.

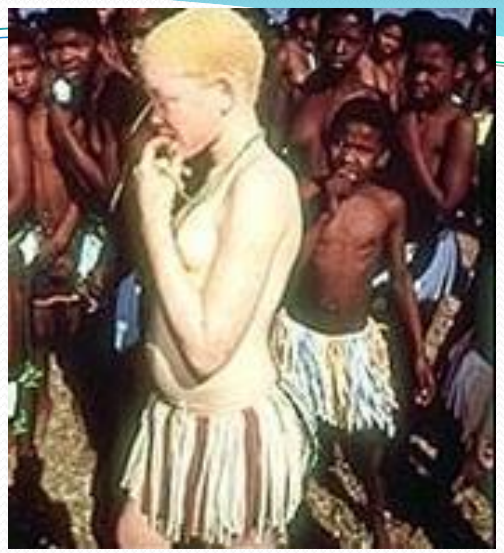
Sources of Genetic variance

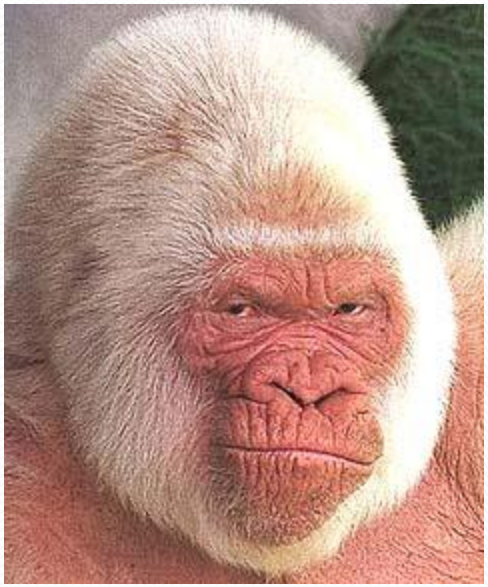
- There is also an interaction between non-allelic genes.
- Variance due to this interaction is called epistatic variance (V_I).
- Can you think of a situation where there are additive gene differences, but there are no phenotypic differences?

- AA bb cc and aa BB cc are different.
- If cc here is the albino gene, both are all albino because pigment producing pathway is intervened/disrupted.
- There are expected differences due to additive gene action, but the albino gene prevents any color.

Sources of Genetic variance

- Lets consider humans from different parts of the world.
- They all have different race, color, phenotype, and additive genes and dominance cause these changes.
- If they are all albino, they are all without color/white!
  - They have differences in their additive genes but epistatic effects of the albino gene masks everything and only colorlessness is observed.



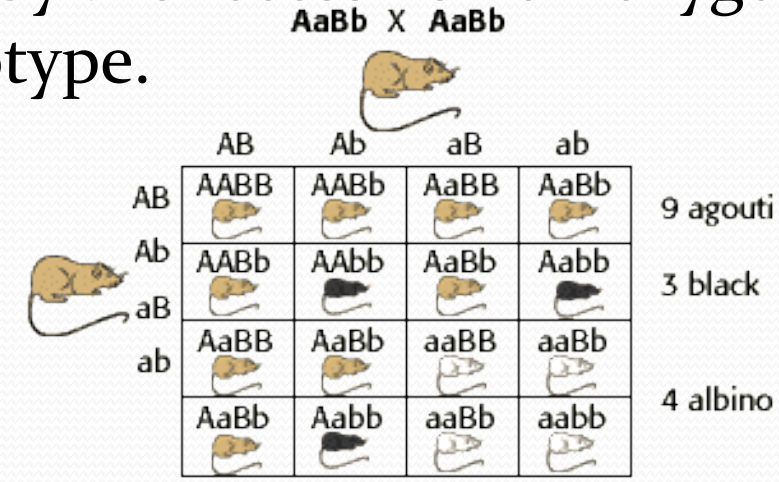


Two unlinked loci affecting mouse hair color.

- **AA** or **Aa** mice are agouti.
- Mice with genotype **aa** are albino because all pigment production is blocked, regardless of the phenotype at the second locus.
- At the second locus, the **B** allele (agouti coat) is dominant to the **b** allele (black coat).
- Cross two agouti mice of genotype AaBb

Punnet for the AaBb x AaBb cross

- There are only three different phenotypes for hair color, agouti, black and albino.
- The individual with genotype recessive for both traits, i.e. aabb, has the same albino phenotype as the aaBB and aaBb individuals due to epistasis.
- The albino phenotype masks any phenotype that might be caused by the recessive homozygous, recessive bb genotype.



Sources of Genetic variance

- When we put together all these sources of variation, we get this equation for genetic variation:

$$V_G = V_A + V_D + V_I$$

- When we add this to the phenotypic variance equation

Sources of Phenotypic variance

- $V_P = V_A + V_D + V_I + V_{Ep} + V_{Et} + V_{Em} + cov_{GxE} + V_{GxE}$

- This equation illustrates the sources of phenotypic variation
- Taking the Phenotypic variance into pieces like this helps us understand the sources of variation in a population.

Sources of Genetic variance

- $V_P = V_A + V_D + V_I + V_{Ep} + V_{Et} + V_{Em} + cov_{GxE} + V_{GxE}$

- These sources help us answer this question: how much of the phenotypic variance is due to genotypic variance and how much of it is due to environment?

This ratio of genetic variance versus environment is measured using heritability

Heritability

- Heritability is the ratio of phenotypic variance due to genotypic variance.

$$H^2 = V_G / V_P$$

- This is called broad sense heritability and it includes all genetic effects.
- It can change from zero to 1.
- If H=0 then this means that all variance observed is due to non-genetic factors.

Heritability

$\mathbf{H^2 = V_G / V_P}$

- Ranges from 0 to 1.
- H^2 =0 means all variance observed is due to non genetic factors.
- H^2 =1 means all variance observed is due to genetic factors.

Heritability

- The broad sense heritability H^2 is not used in selection.
- The true beneficial tool is something that measures only the variance due to additive gene action.
- Such a coefficient is useful because breeders who wants to run selection can estimate the variance that will be transmitted to next generation.

Heritability

- V_A helps us estimate phenotype of the progeny by looking at the parent's phenotype.

$$\mathbf{h^2 = V_A / V_P}$$

- h^2 = narrow sense heritability.

Heritability

$$h^2 = V_A / V_P$$

- Narrow sense heritability is the ratio of additive genetic variance to total phenotypic variance.
- The heritability used by geneticists is almost always narrow sense heritability and when it is stated that heritability is low, middle or high, narrow sense heritability is understood.

Heritability

- Heritability is normally calculated to measure how heritable a trait is, but there are common misconceptions.
- Heritability is the ratio of additive genetic variance to total phenotypic variance.
  - It does not show if a trait/characteristic is genetic.

Heritability

- All characteristics are determined by genes, so they are all “genetic”.
- If all individuals in a population had the same alleles for a trait, heritability would be zero because genetic variance would be zero.
  - The genes would be effective in phenotypes of clones, but their genetic variance would be zero ($h^2=0/n=0$).
  - If all animals have the same genetic capacity for milk fat (lets say 3 %), all variance would be due to environment.
  - All animals have the same # of heads. All animals in a species have the same # of legs.

Heritability

- When h^2 is low, the genetic variance may be low and the individuals are similar to each other in terms of their genotype, and majority of the differences we see in phenotype is due to environment.
  - This means that selecting animals based on phenotype will have low accuracy, because we mostly select them based on environmental differences.
- If the h^2 is high, this could be due to high genetic variance or low environmental variance, so selecting animals would be mostly based on their genetic differences and thus, the selection of parents is more accurate, and they pass their "good genes" on to the next generation.

Heritability

- When heritability is high, this could be due to low environmental variance as well as high genetic variance.
- If the environmental conditions are leveled up, and kept the same for all animals, then heritability increases.
- Therefore, heritability is valid only under one environmental condition, if the environment changes, then so the h^2.

Heritability

- Heritability is not a stable value, it changes with the sample's genetic and environmental variation.

Heritability, Example

- **2015 study:** Mosquitoes attracted to people based on genes; info may help control diseases like dengue, malaria.
- The twin study finds that there is a correlation in our attractiveness to mosquitoes by odor and our genetics, providing evidence that the likelihood of getting bitten is heritable.
  - **Citation:** Fernández-Grandon GM, Gezan SA, Armour JAL, Pickett JA, Logan JG (2015) Heritability of Attractiveness to Mosquitoes. PLoS ONE 10(4): e0122716.

Heritability, Example

- Female mosquitoes display preferences for certain individuals over others, which is determined by differences in volatile chemicals produced by the human body and detected by mosquitoes.
  - Most scents or odors are of Volatile organic compounds (VOCs).
  - Formaldehyde, which evaporates from paint, has a boiling point of only –19 °C.

Heritability of Attractiveness to Mosquitoes

- Body odor can be controlled genetically but the existence of a genetic basis for differential attraction to insects has never been formally demonstrated.
- This study investigated heritability of attractiveness to mosquitoes by evaluating the response of *Aedes aegypti* (=*Stegomyia aegypti*) mosquitoes to odours from the hands of identical and non-identical twins in a dual-choice assay.

Heritability of Attractiveness to Mosquitoes

- Volatiles from individuals in an identical twin pair showed a high correlation in attractiveness to mosquitoes, while non-identical twin pairs showed a significantly lower correlation.
- Overall, there was a strong narrow-sense heritability of 0.62 (SE 0.124) for relative attraction and 0.67 (0.354) for flight activity based on the average of ten measurements.
  - Odor cues associated with genetic similarity are thought to be controlled via the major histocompatibility complex (MHC) genes—often cited as being potentially involved in mate selection and inbreeding avoidance.

Heritability of Attractiveness to Mosquitoes

- The results demonstrate an underlying genetic component detectable by mosquitoes through olfaction.
- Understanding the genetic basis for attractiveness could create a more informed approach to repellent development.
- Individualized strategies for avoiding insect bites could be formulated if the genetic basis for variation between individuals were known.
  - Novel methods to enhance the production of natural repellents by human beings, thus creating a novel repellent technology that could minimize the need for topical application.

Female Aedes aegypti mosquito.

Fernández-Grandon GM, Gezan SA, Armour JAL, Pickett JA, Logan JG (2015) Heritability of Attractiveness to Mosquitoes. PLoS ONE 10(4): e0122716. doi:10.1371/journal.pone.0122716
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PLOS | ONE

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