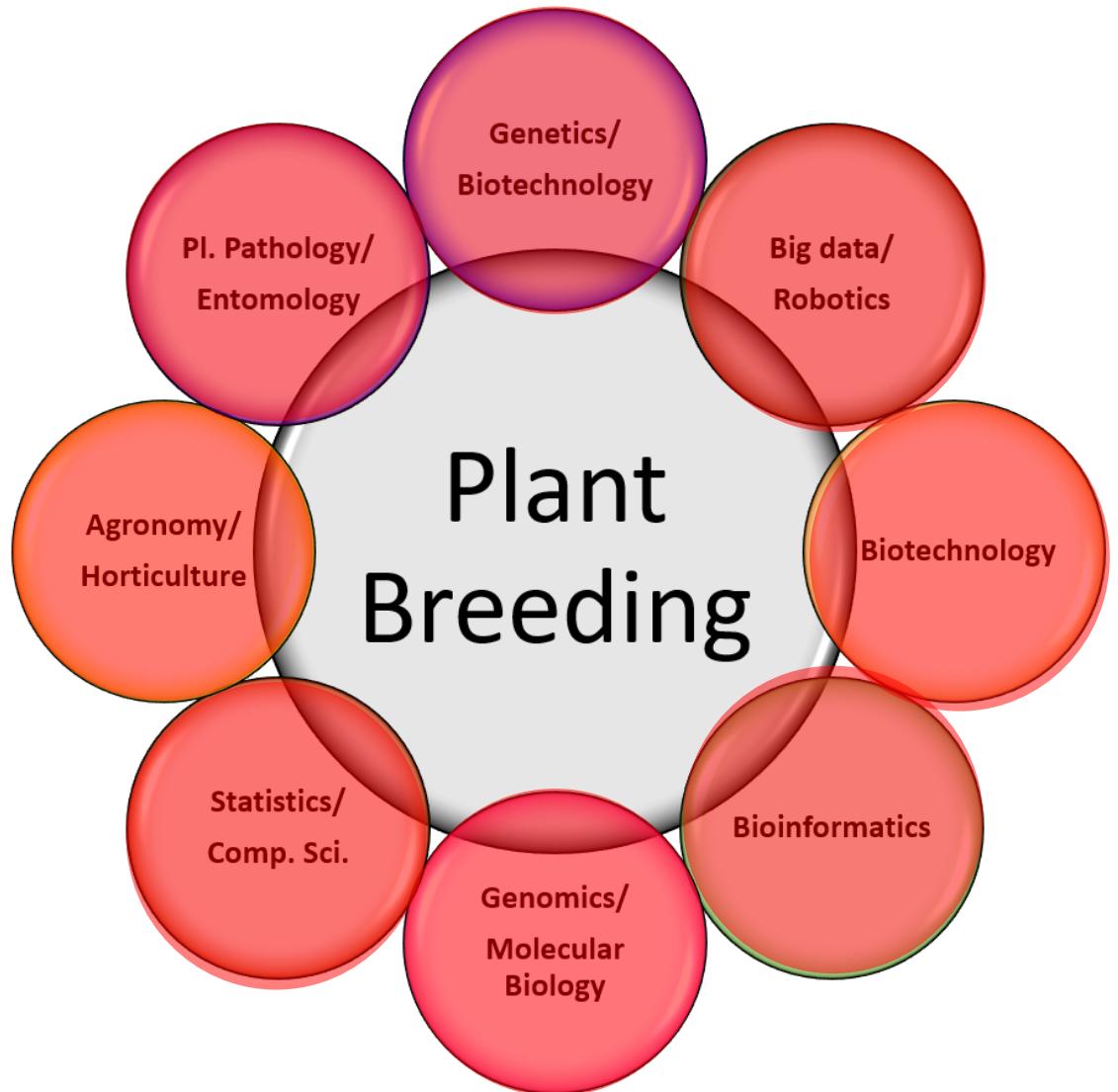
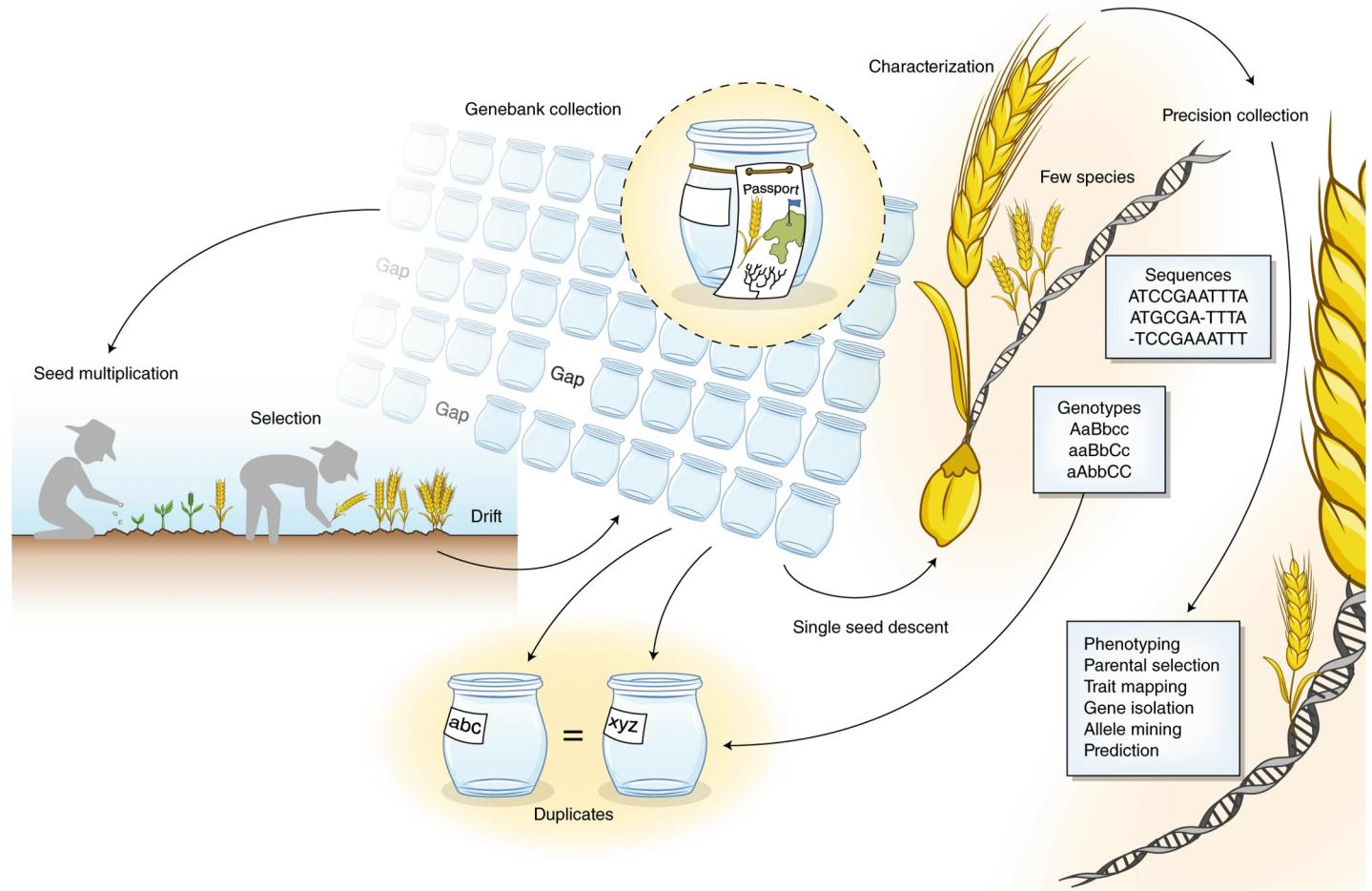


Quantitative Genetics



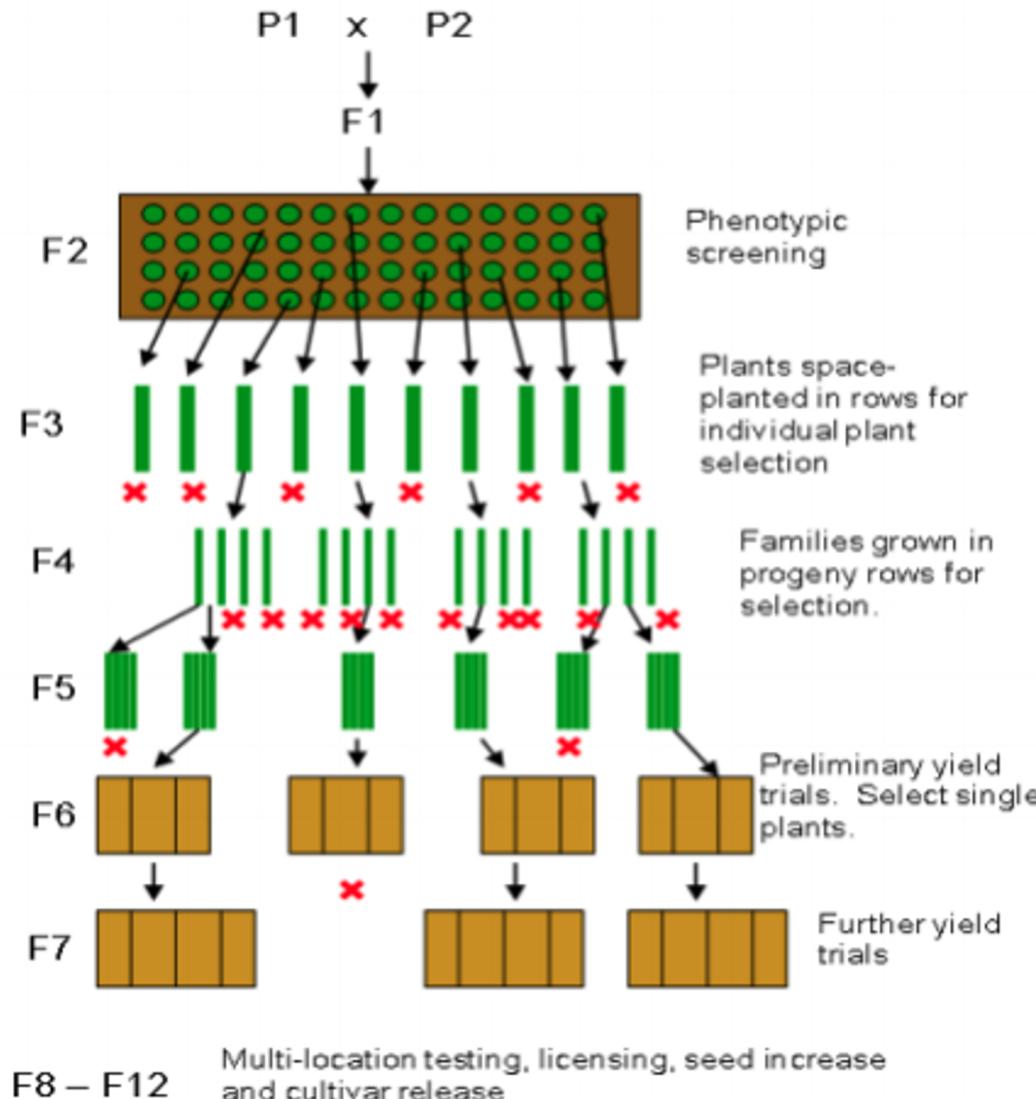
Where are we and where do we want to go?

- Conventional breeding
- Marker Assisted Selection
- Genomic Selection

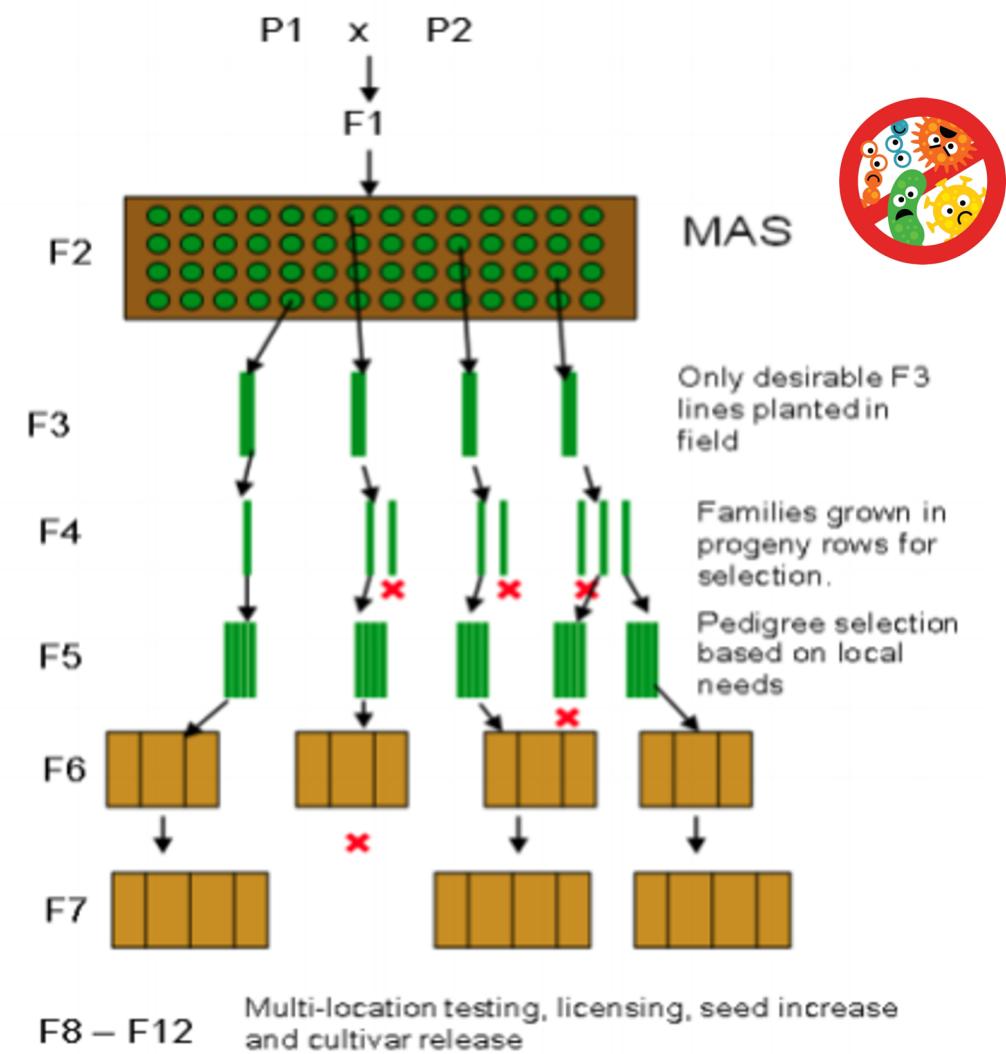


Mascher et al 2019

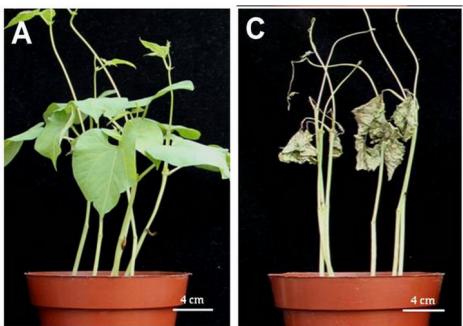
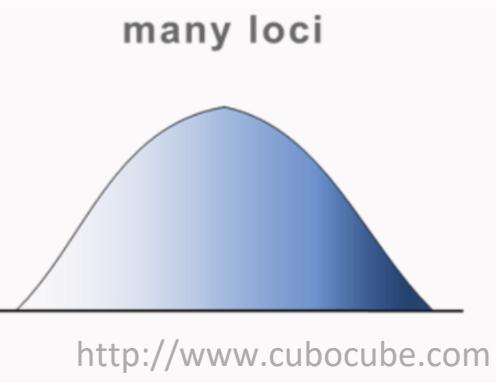
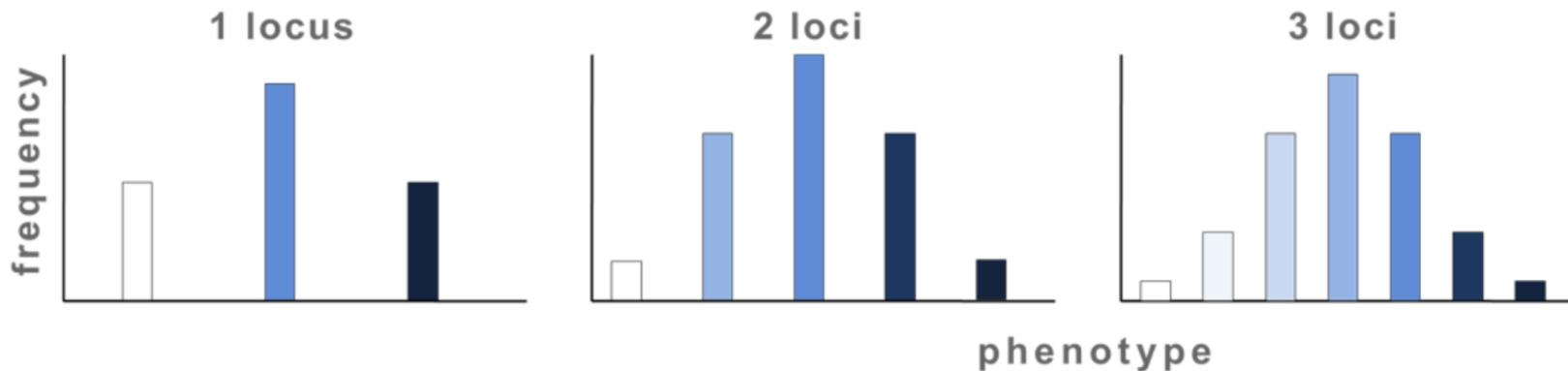
Conventional Plant Breeding



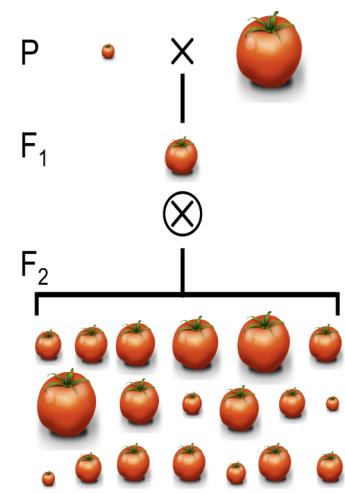
Marker Assisted Selection



What are quantitative traits?

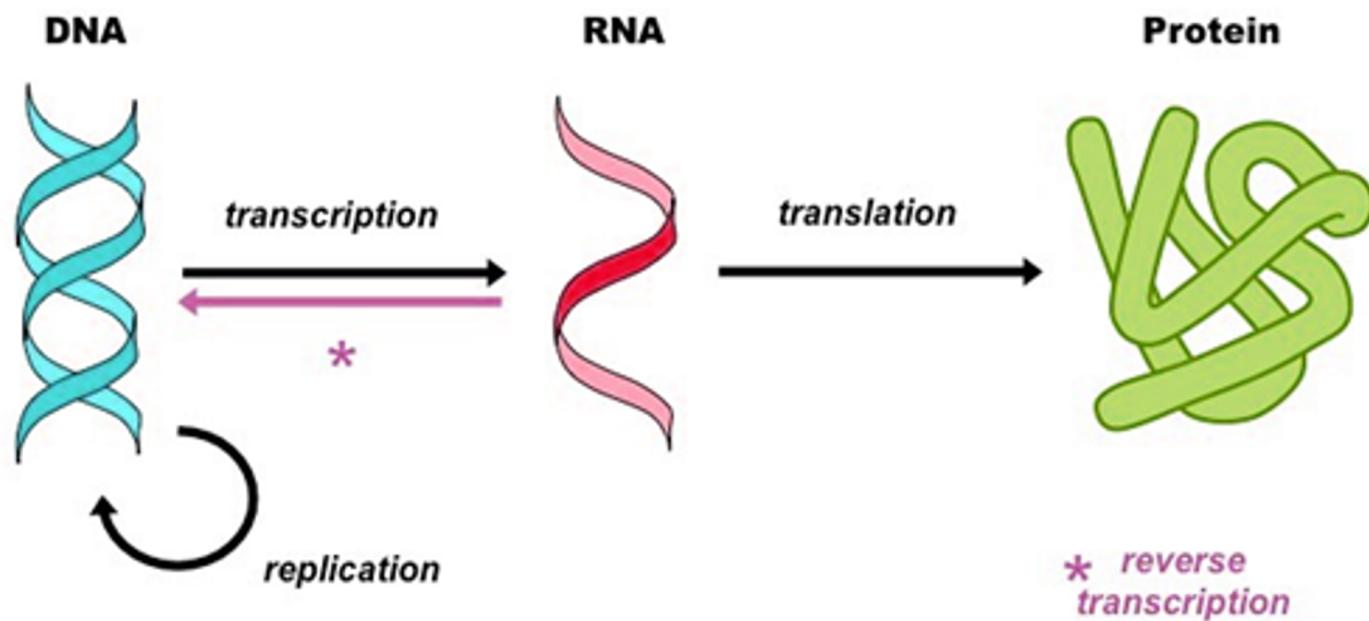


Chen et al 2017



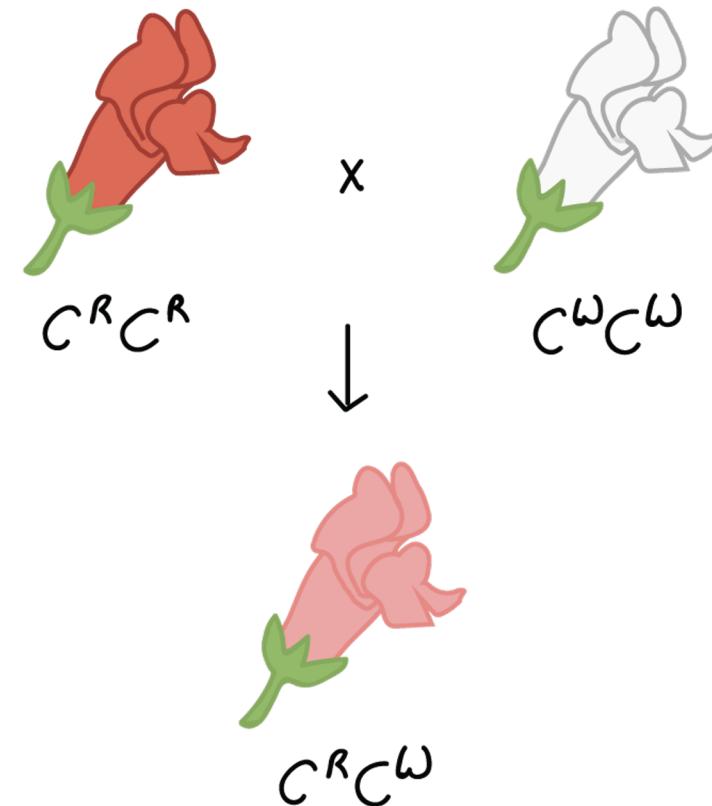
Important concepts

CENTRAL DOGMA



Alleles

- An allele is one of **two or more versions** of a gene.
- If two alleles are the same, the individual is homozygous for that gene.
- If the alleles are different, the individual is heterozygous.
- The use of the allele also refers to variation among non-coding DNA sequences.

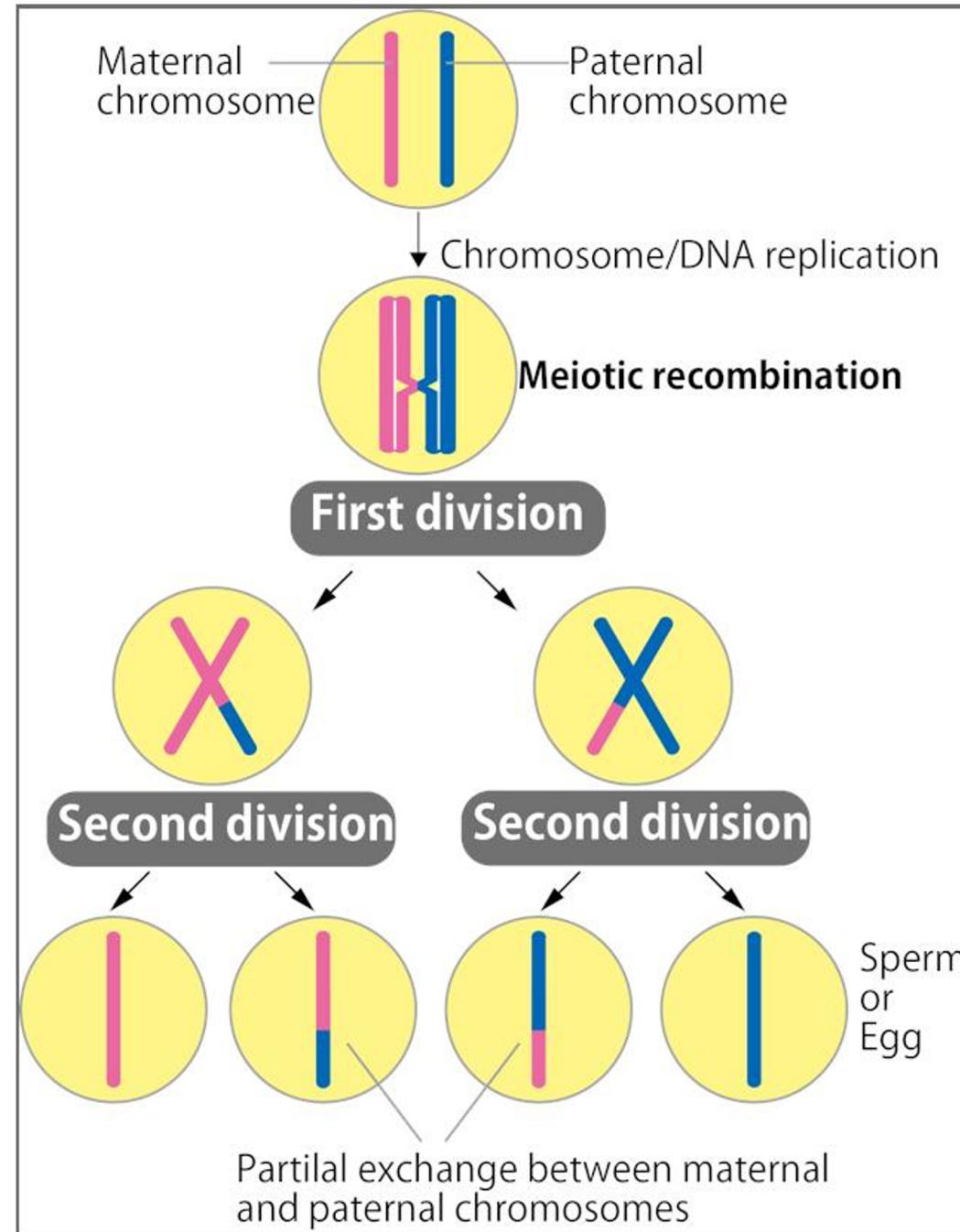


Meiosis

During meiosis, diploid cells undergo DNA replication, followed by two rounds of cell division in germ cells, producing four haploid sex cells.

Meiosis maintains genetic continuity from generation to generation and gives rise to genetic variation in gametes through:

- Crossing over of homologous chromosomes.
- Unique combinations of maternal/paternal chromosomes.



Population genetics

Allele Frequencies

- Consider a locus with two possible alleles (**A** and **a**)

$$A = p, a = q$$

- We can estimate the **frequency** of AA genotype by dividing the number of AA individuals by total number of individuals in the population.

$$AA + Aa + aa = 1$$

- Allele Frequencies:

$$p = f(AA) + \frac{1}{2} f(Aa) = \text{frequency of } A$$

$$p + q = 1$$

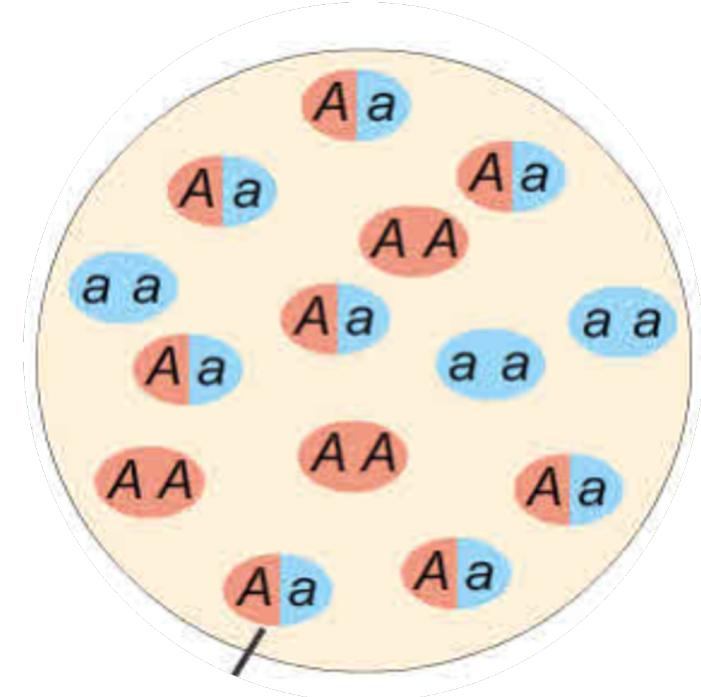
$$q = f(aa) + \frac{1}{2} f(Aa) = 1 - p \text{ frequency of } a$$

Hardy-Weinberg Equilibrium

HWE law, states that allele and genotype frequencies in a population will remain constant from generation to generation in the absence of other evolutionary influences.

Meiosis:

- Aa produces gametes A and a (in equal frequency)
- The homozygous AA only produce one gamete: A
- Likewise aa only produce one gamete: a

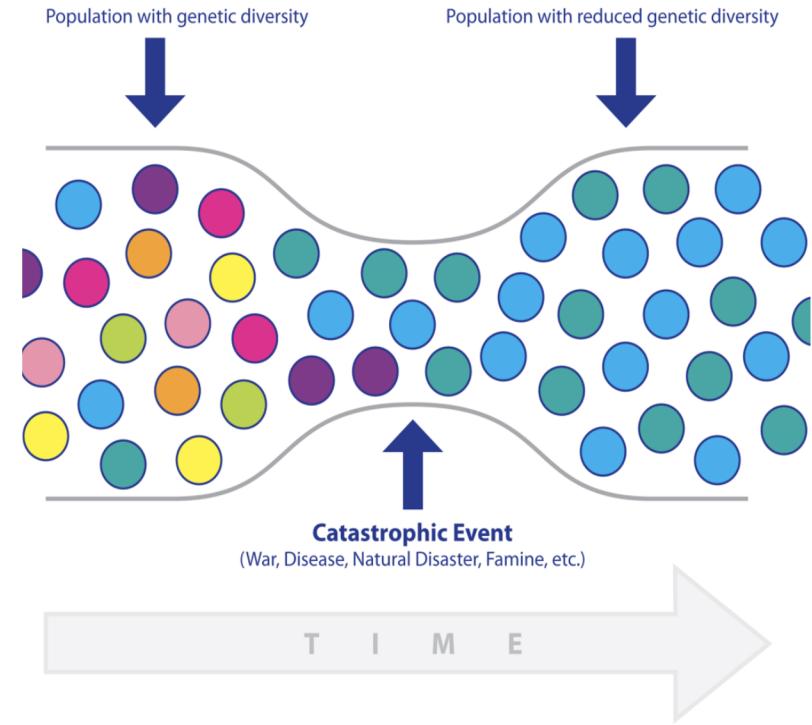


Hardy-Weinberg assumptions

- Random mating
- Genotypes have same viability
- Population must not be divided into subpopulations
- Apply only to large populations
- No migration
- No mutation
- No selection
- No drift

If any of these assumptions is not true, the population could depart from HWE.

These departures in most cases manifest as an excess of homozygosity relative to HWE.



<https://co.pinterest.com/>

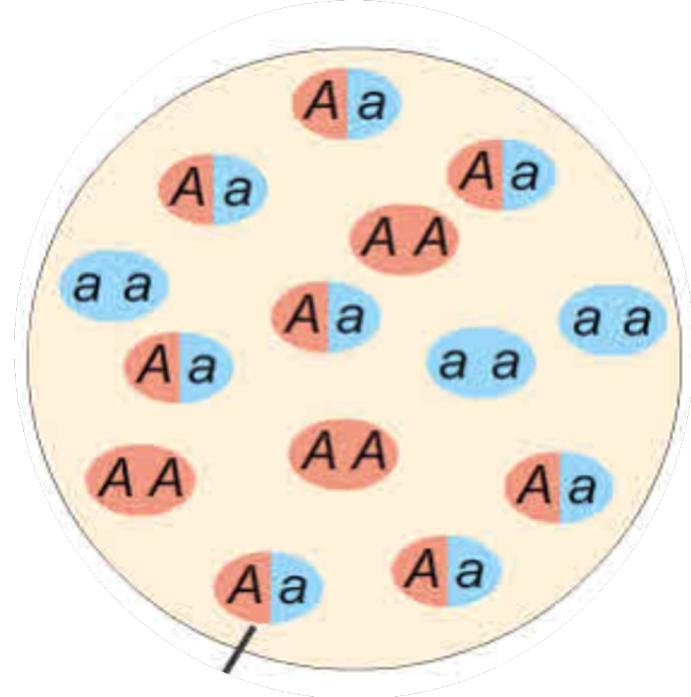
Hardy-Weinberg Equilibrium

Random sampling of gametes (random sampling of parents + **no mutation**)

$$p(A)=p \quad p(a) = q = (1-p)$$

Expected genotype frequencies (**random mating**)

$$\text{AA} = p^2 , \quad \text{aa} = q^2 , \quad \text{Aa} = 2pq$$



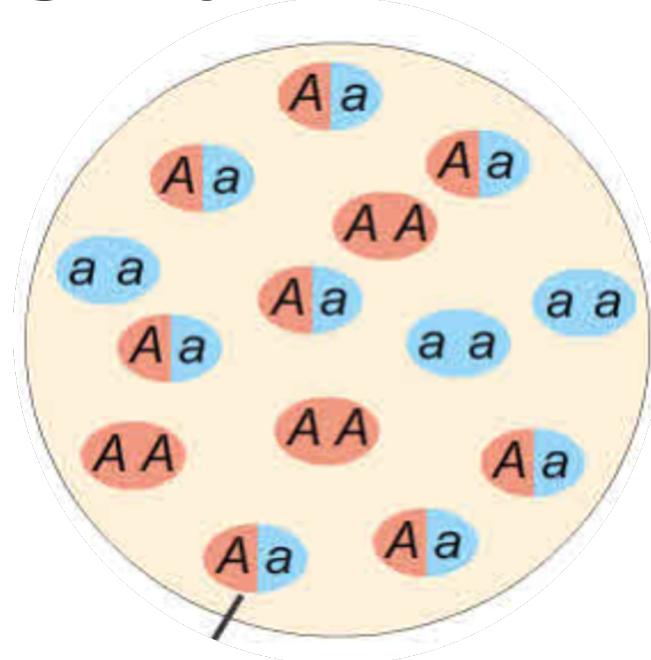
Hardy-Weinberg Equilibrium

$$N = 14$$

$$AA = 3$$

$$Aa = 8$$

$$aa = 3$$



$$p(A)=p \quad p(a) = q = (1-p)$$

$$p = f(AA) + \frac{1}{2} f(Aa) = \text{frequency of } A \qquad q = (1-p)$$

$$p = (3/14) + \frac{1}{2} (8/14) = 0.5 \qquad q = 1 - 0.5 = 0.5$$

Hardy-Weinberg Equilibrium

$N = 14$, AA = 3 , Aa = 8, aa = 3

$$p = 0.5$$

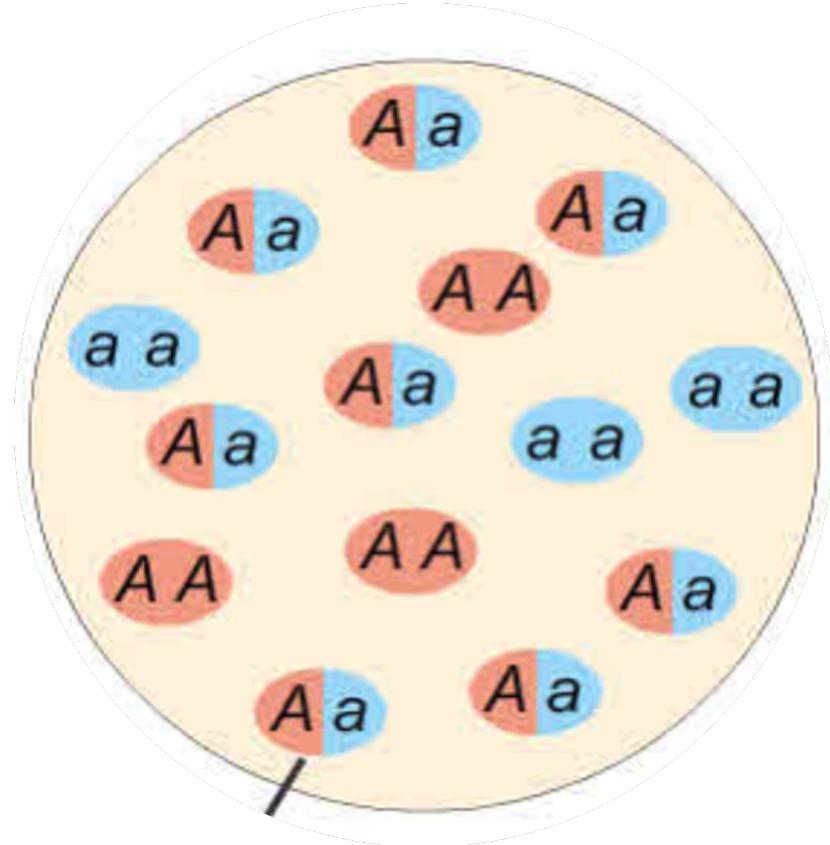
$$q = 0.5$$

Expected genotype frequencies :

$$p(AA) = p^2, p(Aa) = 2pq, p(aa) = q^2$$

$$p^2 + 2pq + q^2$$

$$0.5^2 + 2(0.5 \cdot 0.5) + 0.5^2 = 0.25, 0.5, 0.25$$

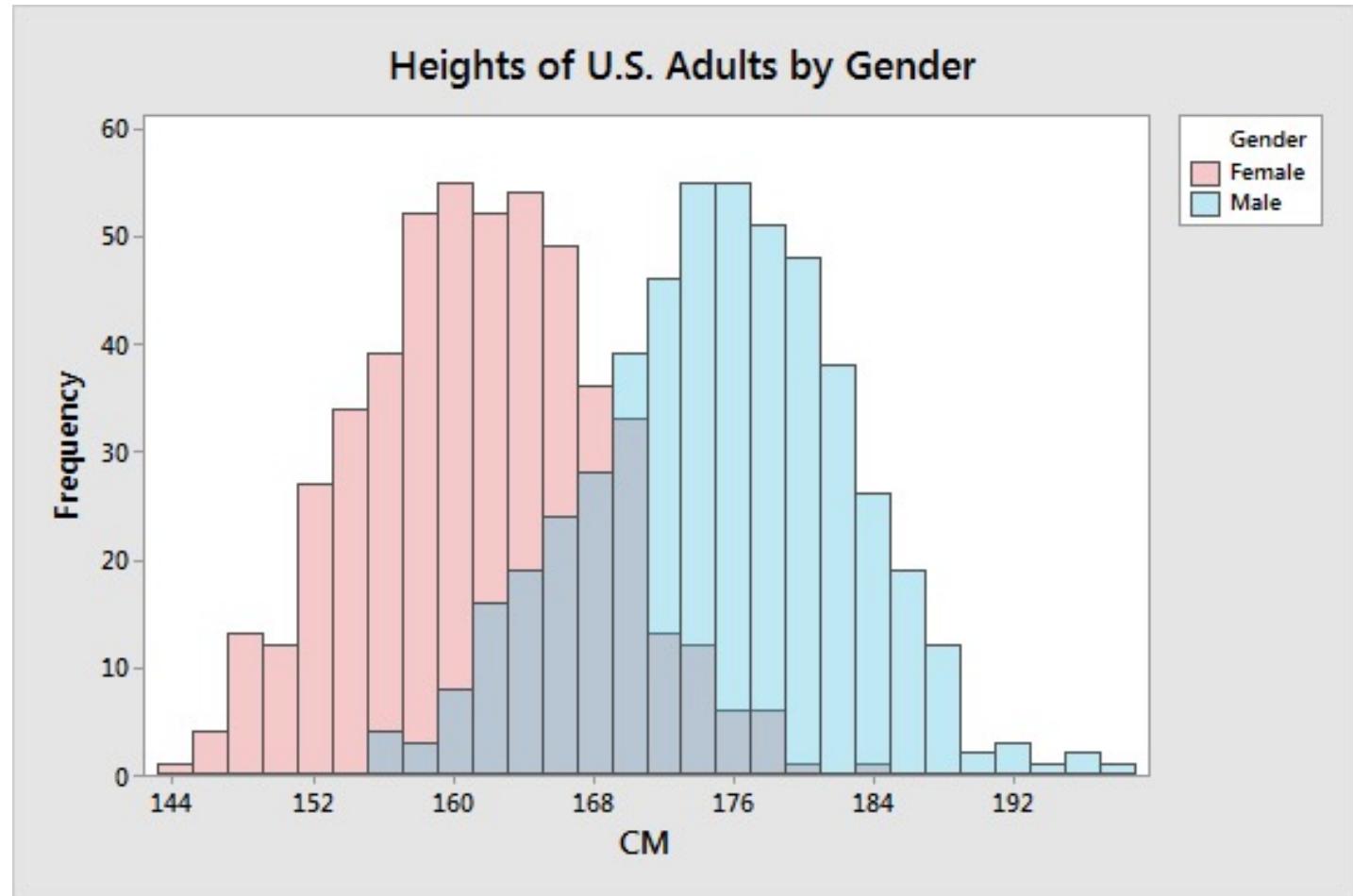


Review

- Central dogma
- Meiosis
- Allele frequencies
- genotype frequencies
- HWE

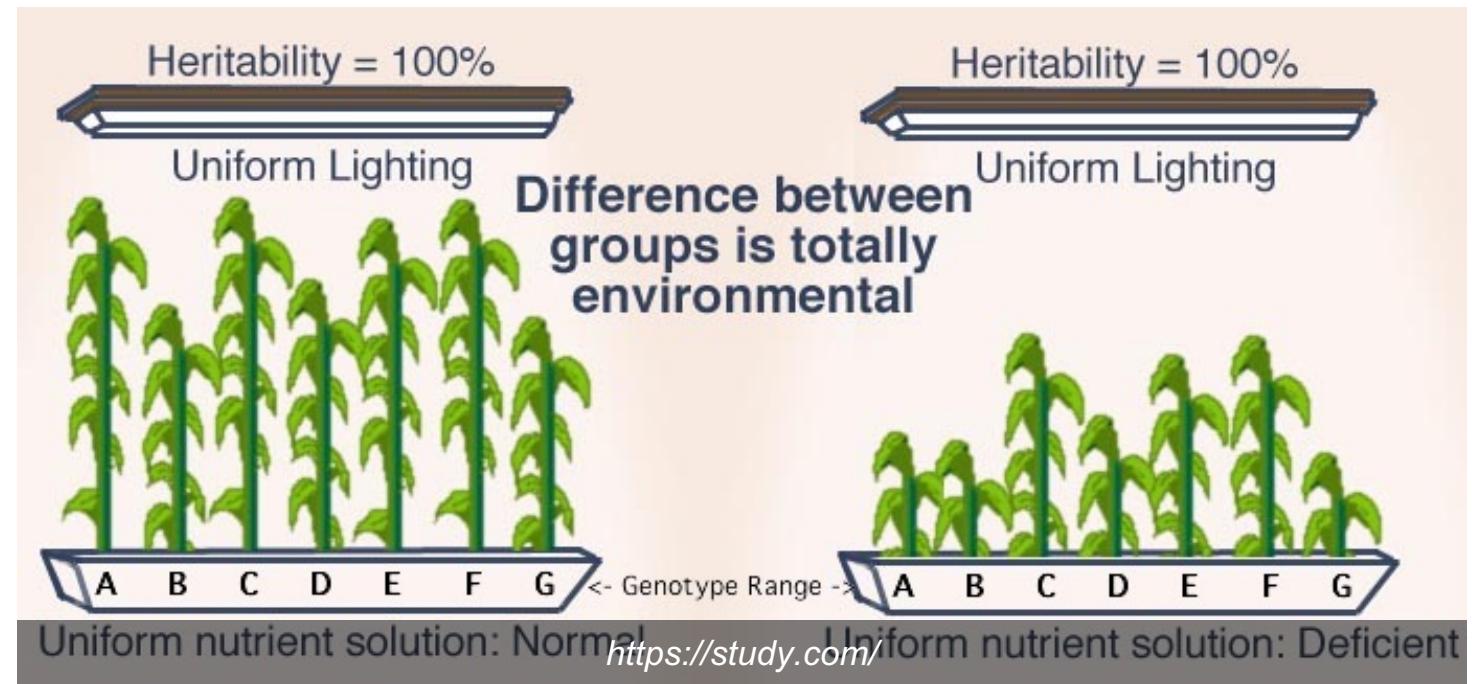


Quantitative Genetics



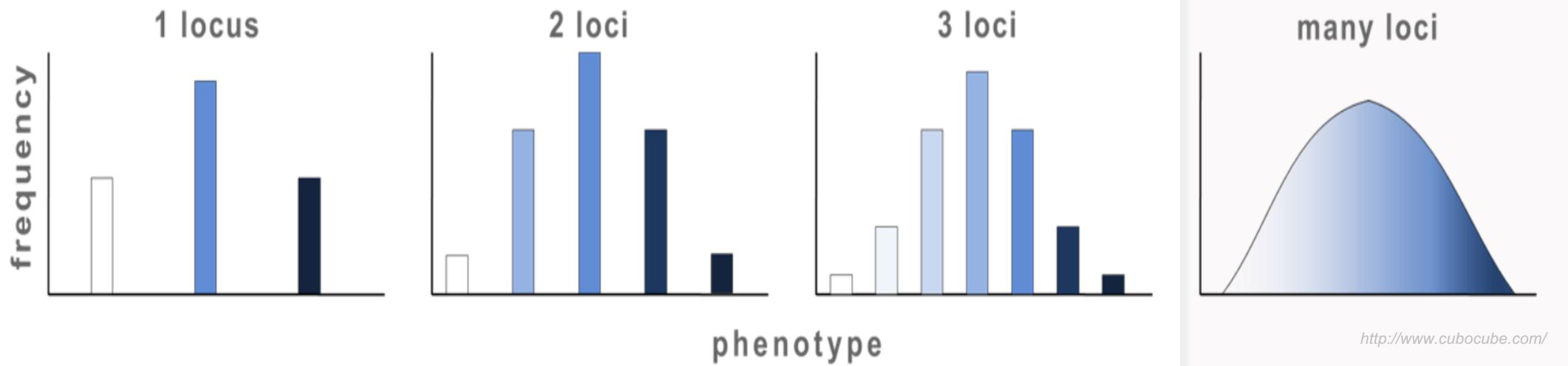
The inheritance of complex traits

- Quantitative variation:
Mean, variance, standard deviation
- Genetic model
- Genetic and environmental variances



Quantitative variation

Traits that show a continuous range of variation and don't behave in simple Mendelian fashion are known as quantitative or complex traits



Quantitative genetics!

Basic statistical concepts

Mean

$$\bar{X} = \frac{1}{n} \sum_{i=1}^n X_i$$

$$\bar{X} = \frac{X_1 + X_2 + X_3 \dots X_n}{n}$$

Where

\bar{X} = mean

X_1 = first value

X_2 = second value

X_3 = third value

X_n = last value

n = number of samples

Basic statistical concepts

Mean

$$\bar{X} = \sum_{i=1}^k f_i X_i$$

Where
 \bar{X} = mean
k = classes
f = frequency

$$\bar{X} = (X_1 * f_1) + (X_2 * f_2) + (X_3 * f_3)$$

Height (cm)	Count	Frequency x Height
156	1	1.56
157	2	3.14
158	1	1.58
...
184	2	3.68
sum	100	170

Griffiths et al 2012

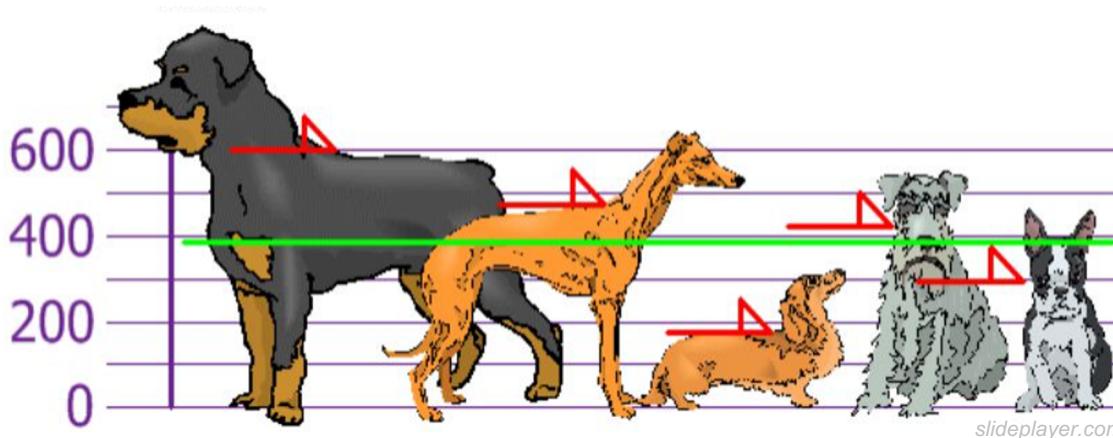
$$\bar{X} = (0.01 \times 156) + (0.02 \times 157) + \dots + (0.02 \times 184) = 170$$

Basic statistical concepts

Variance:

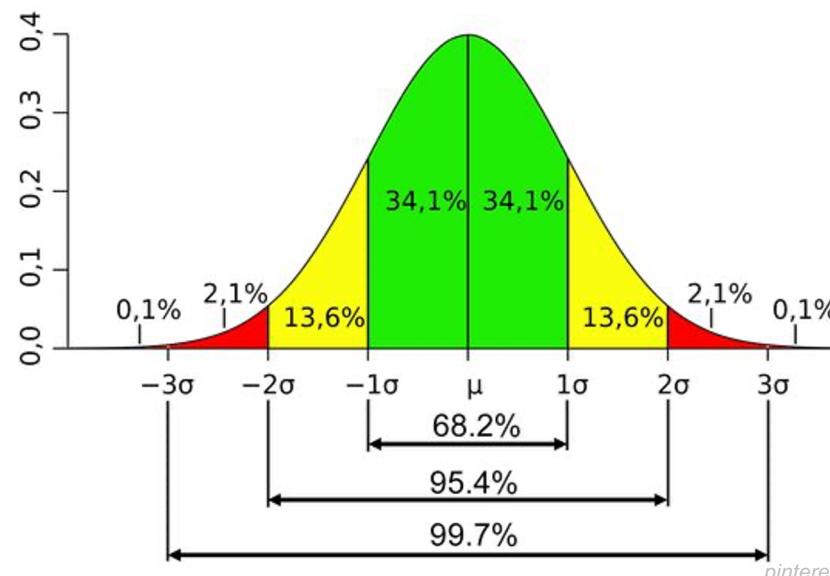
Measure of dispersion around the mean.

$$s^2 = \frac{1}{n-1} \sum_i (X_i - \bar{X})^2$$



Standard deviation:

$$\begin{aligned}s &= \sqrt{\frac{1}{n} \sum_i (X_i - \bar{X})^2} \\ &= \sqrt{s^2}\end{aligned}$$



Basic statistical concepts

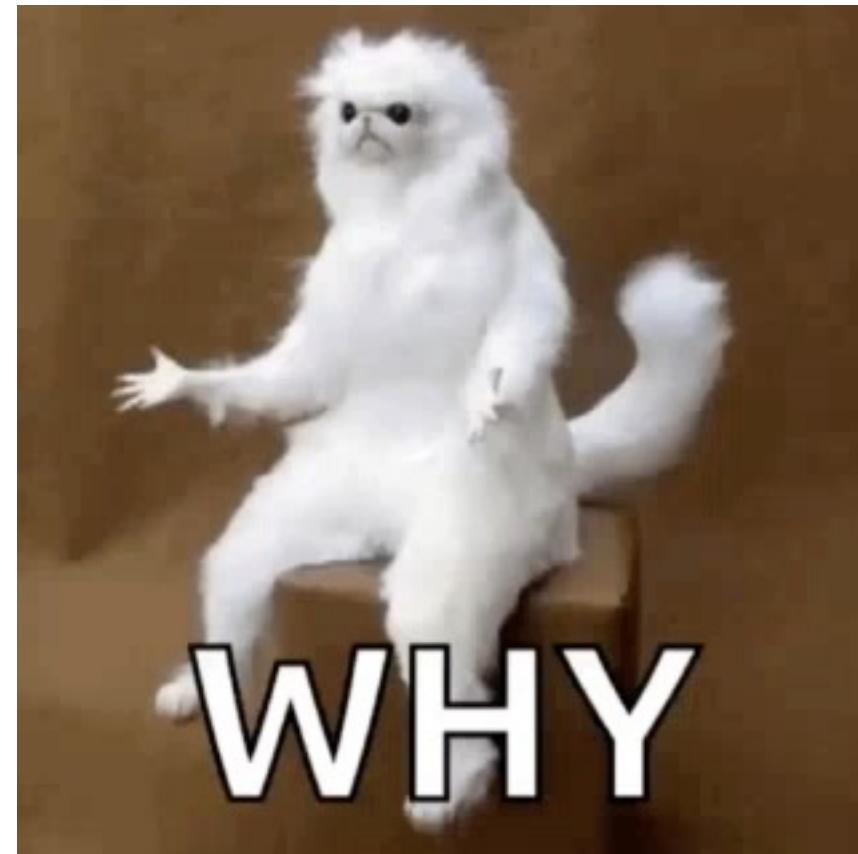
Variance:

Measure of dispersion around the mean.

$$s^2 = \frac{1}{n-1} \sum_i (X_i - \bar{X})^2$$

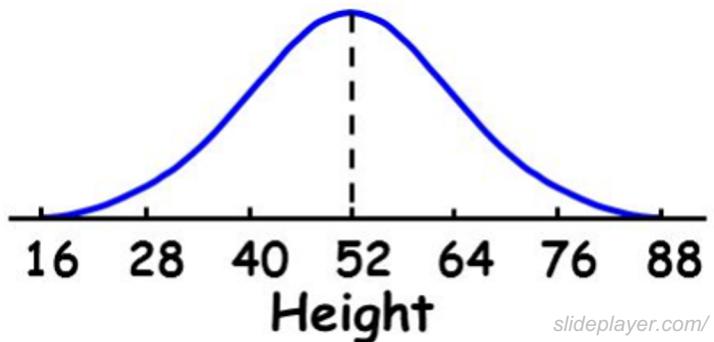
Standard deviation:

$$\begin{aligned}s &= \sqrt{\frac{1}{n} \sum_i (X_i - \bar{X})^2} \\ &= \sqrt{s^2}\end{aligned}$$

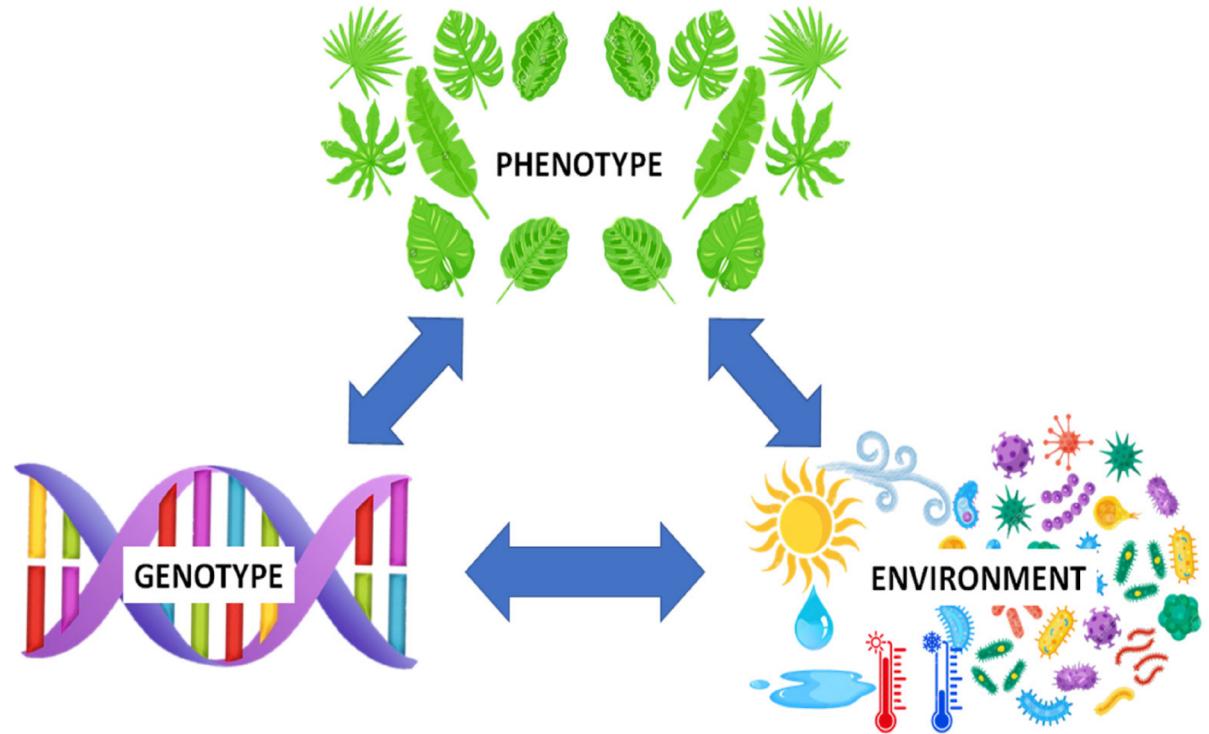


Simple genetic model

- $X = \bar{X} + g + e$



slideplayer.com/



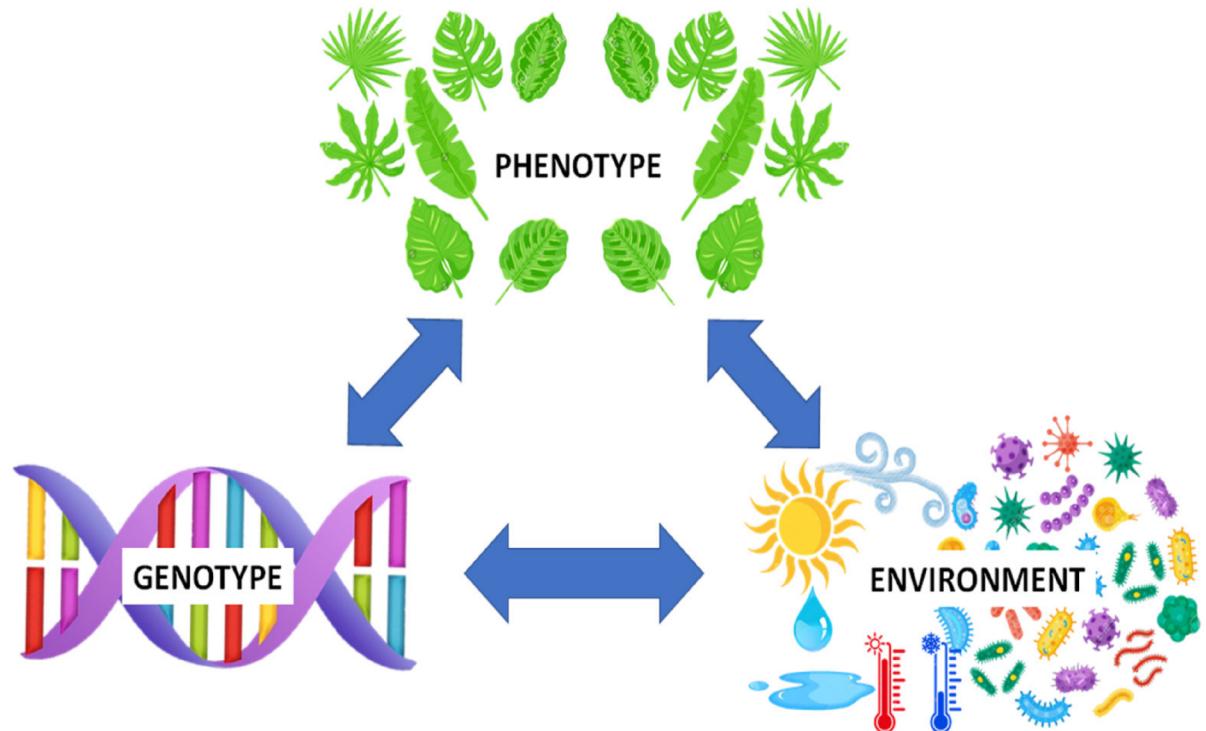
Djande et al 2020

Simple genetic model

$$X = \bar{X} + g + e$$

- $x = g + e$

x is the individual's phenotypic deviation.



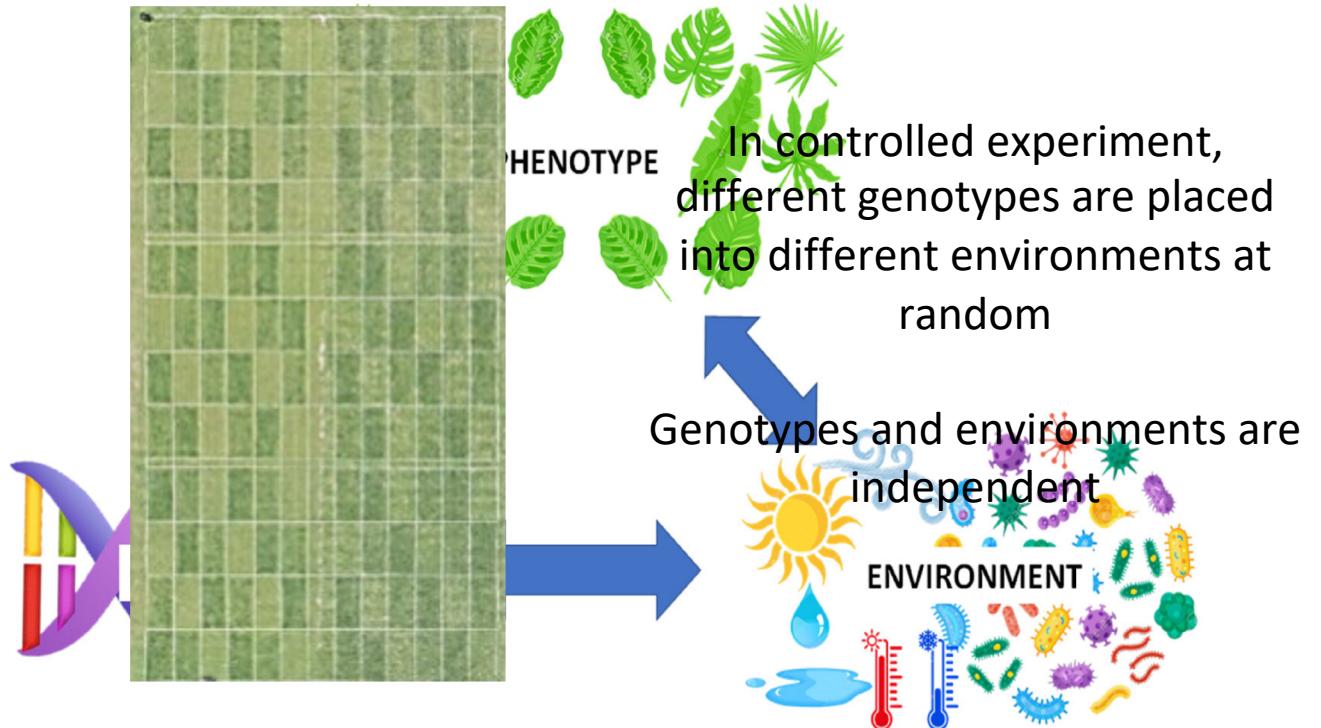
Djande et al 2020

Genetic and environmental variances

$$x = g + e$$

$$V_x = Vg + Ve + 2\text{cov}_{ge}$$

$$V_x = Vg + Ve$$



Djande et al 2020

Review

- $\bar{X} = \sum_{i=1}^k f_i X_i$
- $s^2 = \frac{1}{n-1} \sum_i (X_i - \bar{X})^2$
- $s = \sqrt{s^2}$
- $x = g + e$
- $V_x = Vg + Ve + 2\text{cov}_{ge}$



Heritability

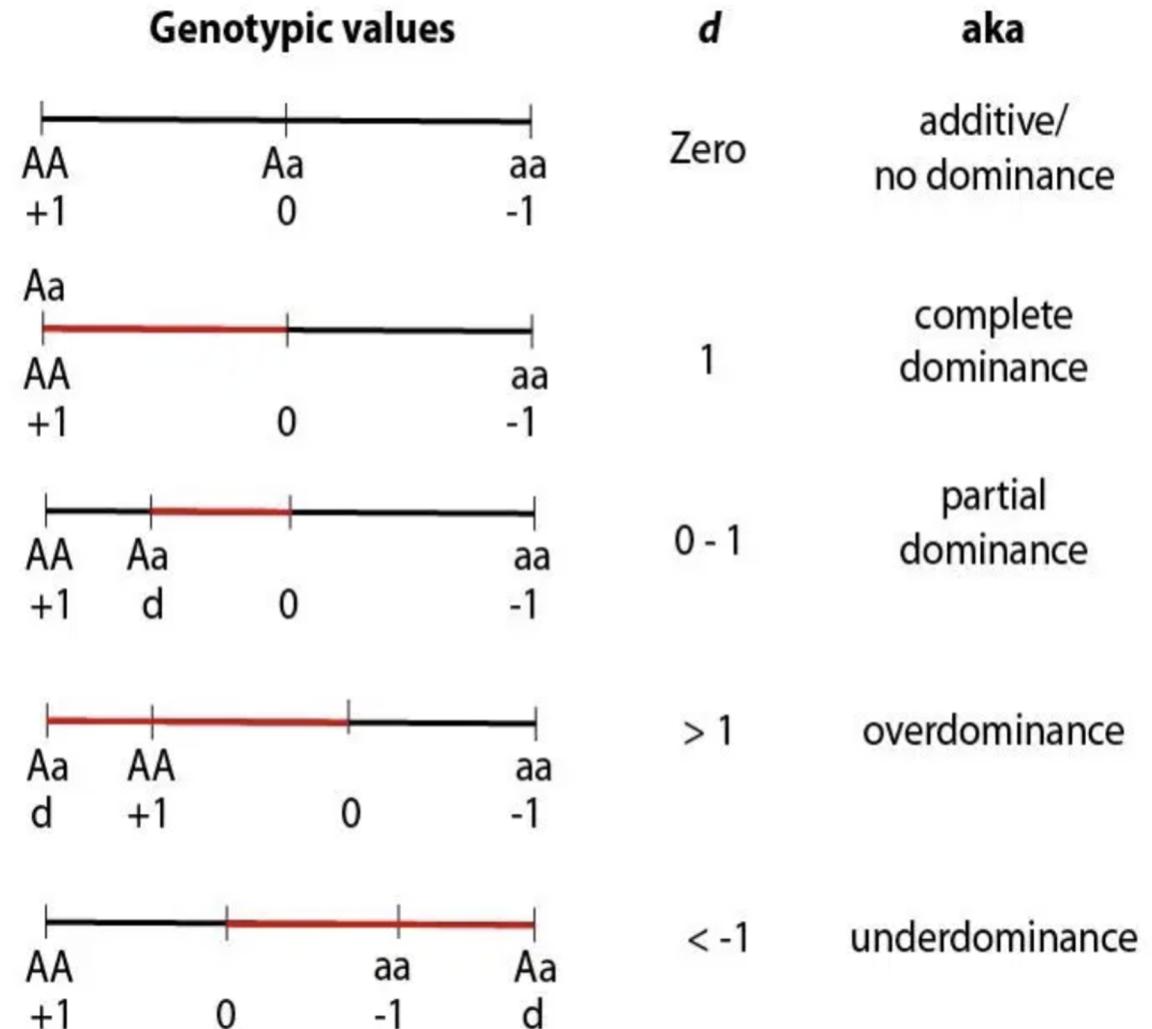
The degree of variation in a phenotypic trait in a population that is due to genetic variation between individuals in that population.

$$V_x = Vg + Ve$$

Broad-sense heritability (H^2)

$$H^2 = \frac{Vg}{Vx}$$

$$V_g = V_A + V_D + V_I$$



Heritability

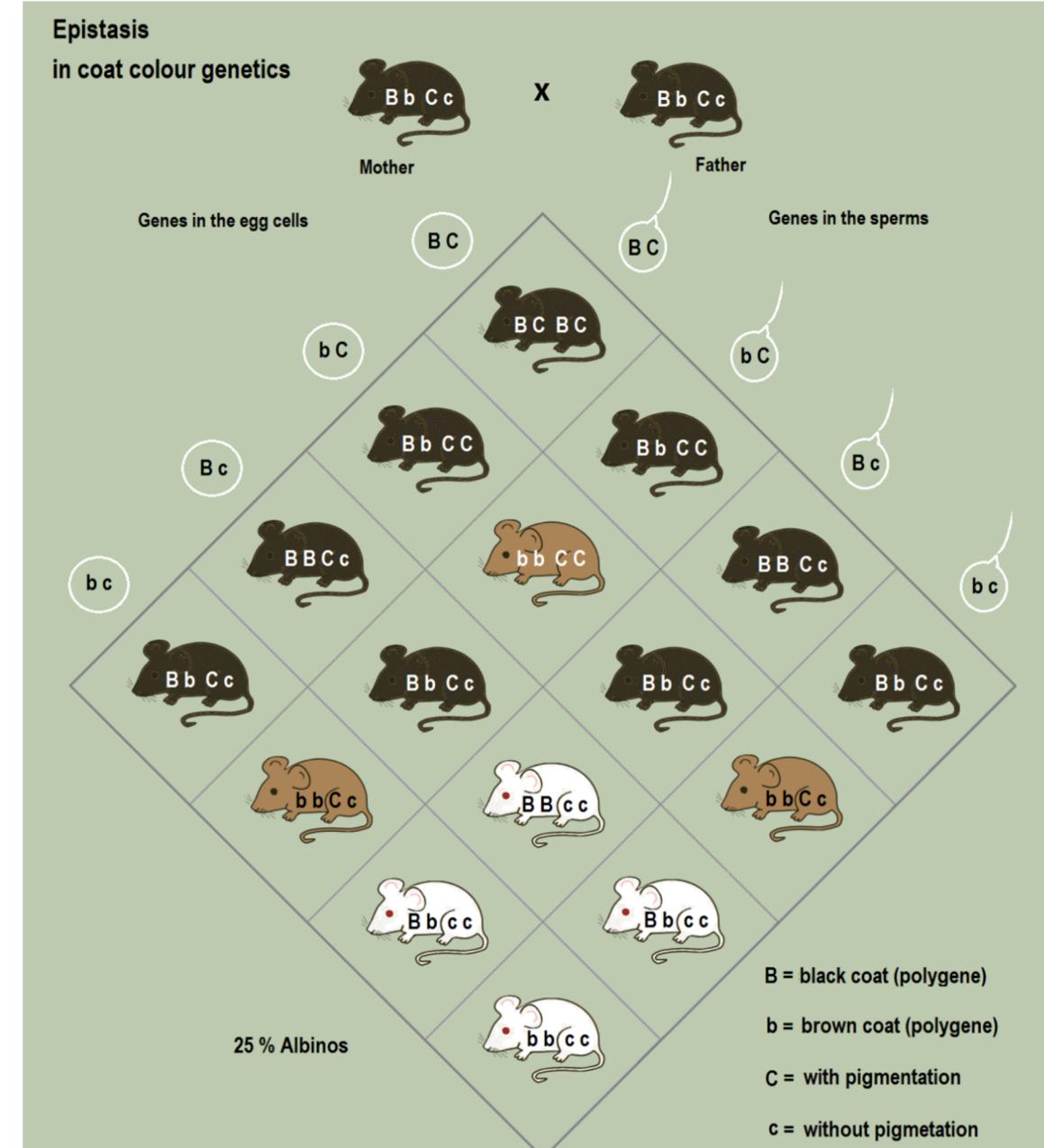
The degree of variation in a phenotypic trait in a population that is due to genetic variation between individuals in that population.

$$V_x = Vg + Ve$$

Broad-sense heritability (H^2)

$$H^2 = \frac{Vg}{Vx}$$

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Heritability

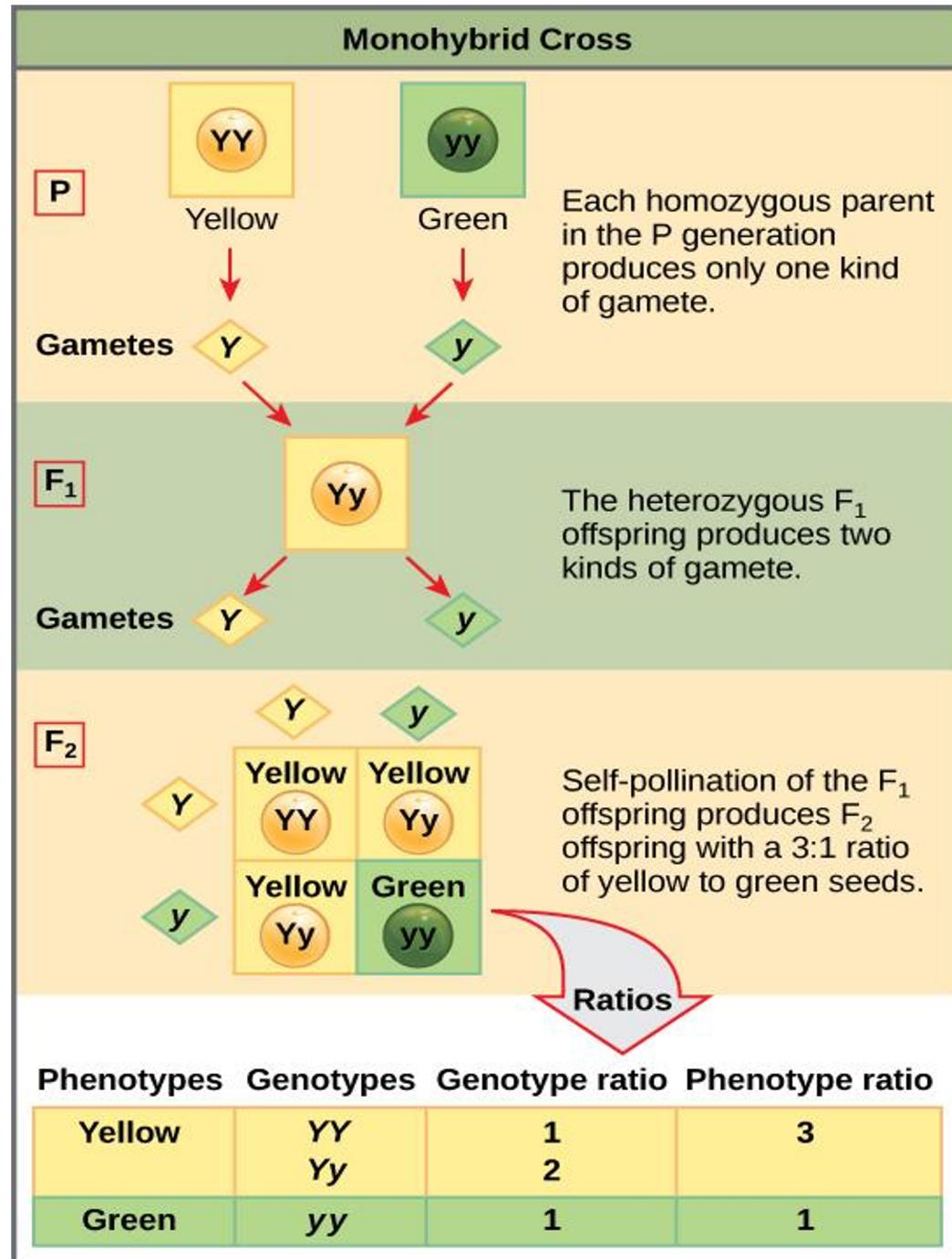
Broad-sense heritability (H^2)

$$H^2 = \frac{V_g}{V_x}$$

$$V_g = V_a + V_d + V_i$$

H^2 is not transmissible to the next generation in a predictive way!

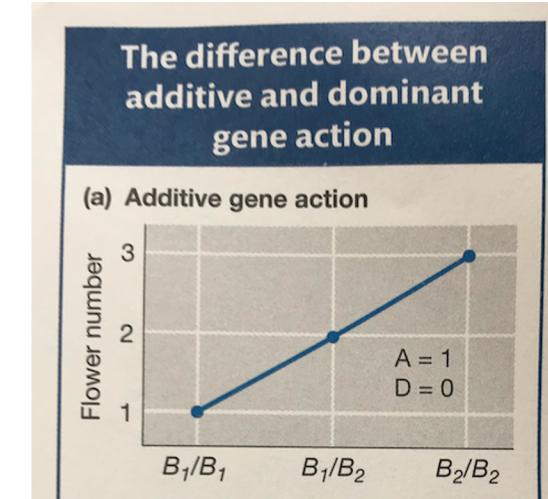
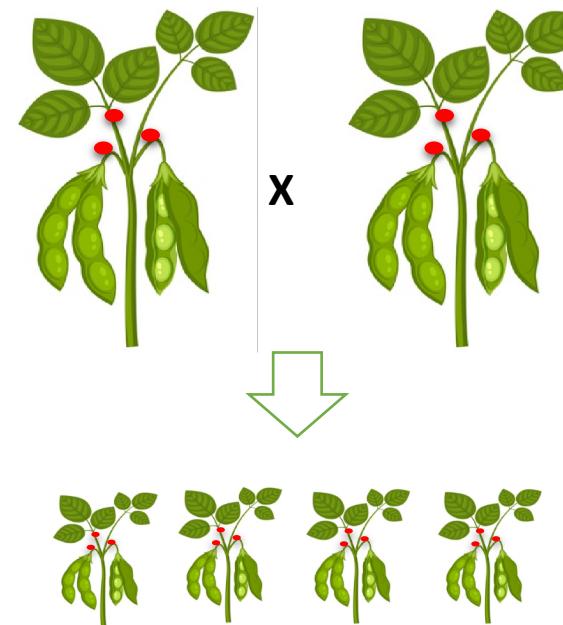
Parents transmit their genes **but not** their genotypes!



Heritability

Narrow-sense heritability (h^2)

$$h^2 = \frac{Va}{Vx} = \frac{Va}{Va+Vd+Vi+Ve}$$



h^2 is transmissible to the next generation in a predictive way!

Griffiths et al 2012

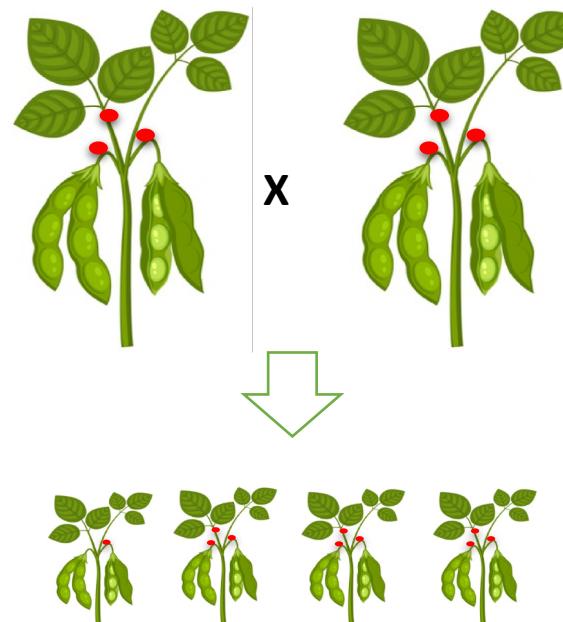
Genotype	Frequency	Trait value (no. of flowers)	Contribution to the mean (frequency × value)
B ₁ /B ₁	0.25	1	0.25
B ₁ /B ₂	0.50	2	1.0
B ₂ /B ₂	0.25	3	0.75
Mean = 2.0			

Heritability

Narrow-sense heritability (h^2)

$$h^2 = \frac{Va}{Vx} = \frac{Va}{Va+Vd+Vi+Ve}$$

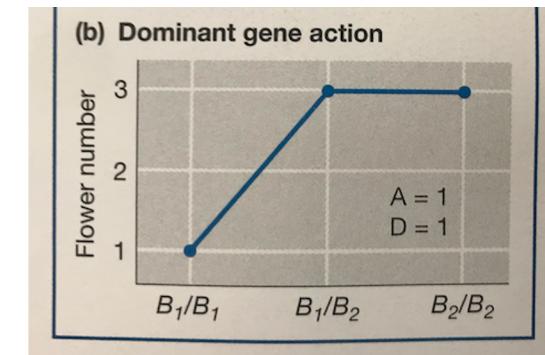
parents = 3



Offspring < 3 (2.78)

The phenotype is not fully heritable!

The difference between additive and dominant gene action



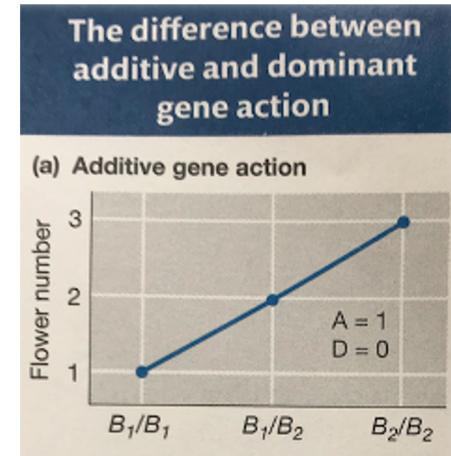
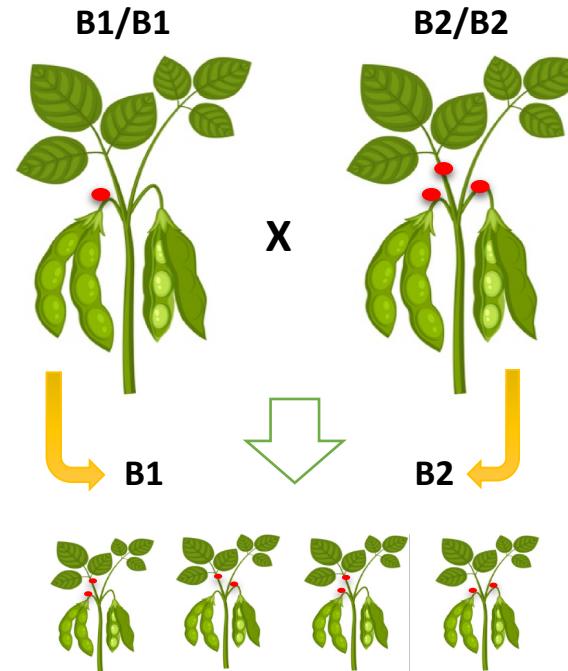
Griffiths et al 2012

Genotype	Frequency	Phenotype	Contribution to the mean (frequency × value)
B_1/B_1	0.25	1	0.25
B_1/B_2	0.50	3	1.5
B_2/B_2	0.25	3	0.75
Mean = 2.5			

Heritability

Narrow-sense heritability (h^2)

$$\beta_{O \sim Mp} = \frac{Cov(u_{ih}, u_i)}{Var(y_i)} = \frac{\sigma_a^2}{\sigma_p^2} = h^2$$



Genotype	Frequency	Trait value (no. of flowers)	Contribution to the mean (frequency × value)
B_1/B_1	0.25	1	0.25
B_1/B_2	0.50	2	1.0
B_2/B_2	0.25	3	0.75
Mean = 2.0			

Review

- $V_g = V_a + V_d + V_i$
- $H^2 = \frac{Vg}{Vx}$
- $h^2 = \frac{Va}{Vx}$

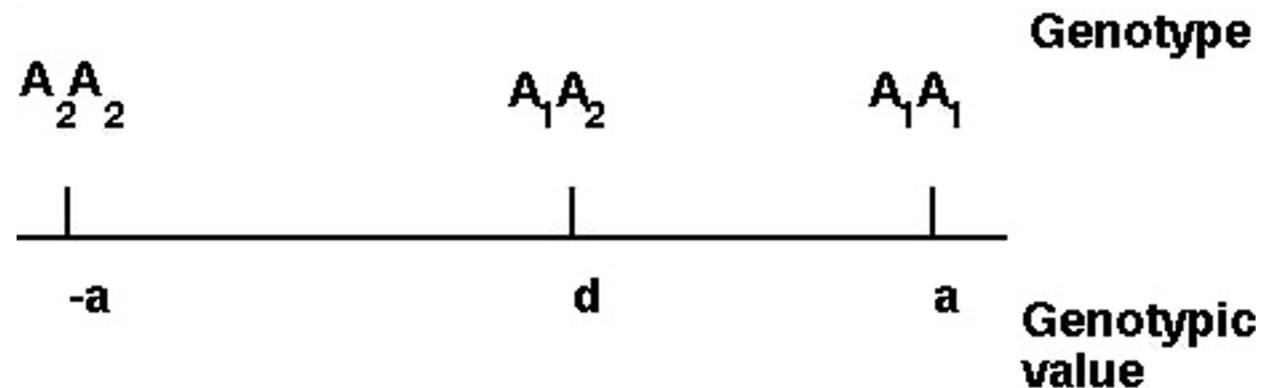


Values and means
in a single locus

Values and means in a single locus

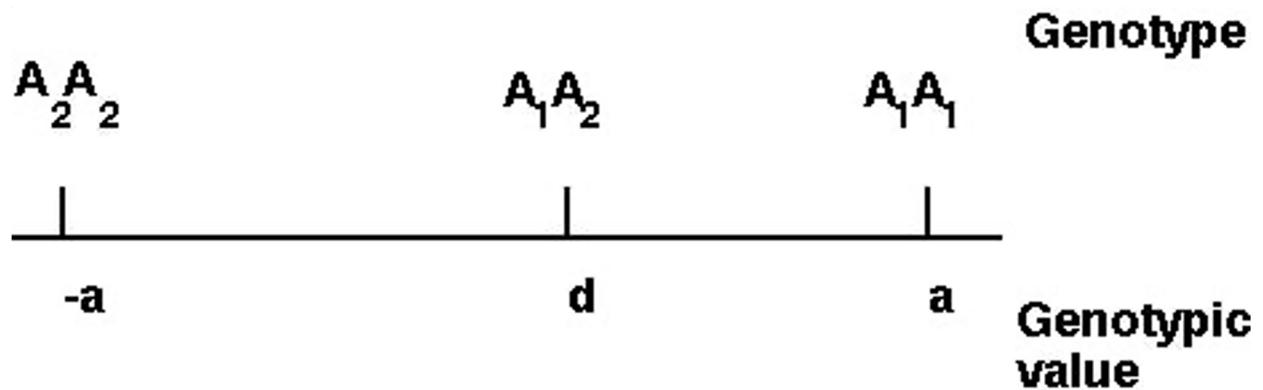
- Genetic values
- Population mean
- Average allele effect
- Average allele substitution effect

$$\bar{X} = \sum_{i=1}^k f_i X_i$$

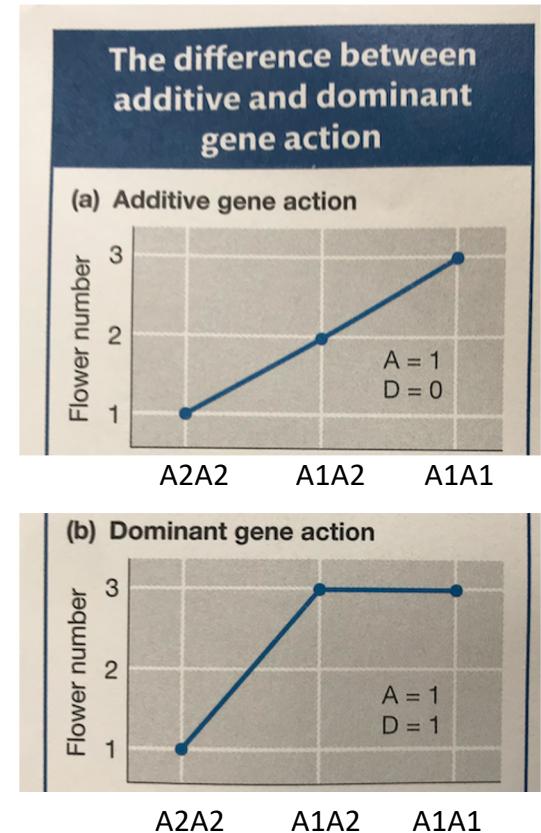
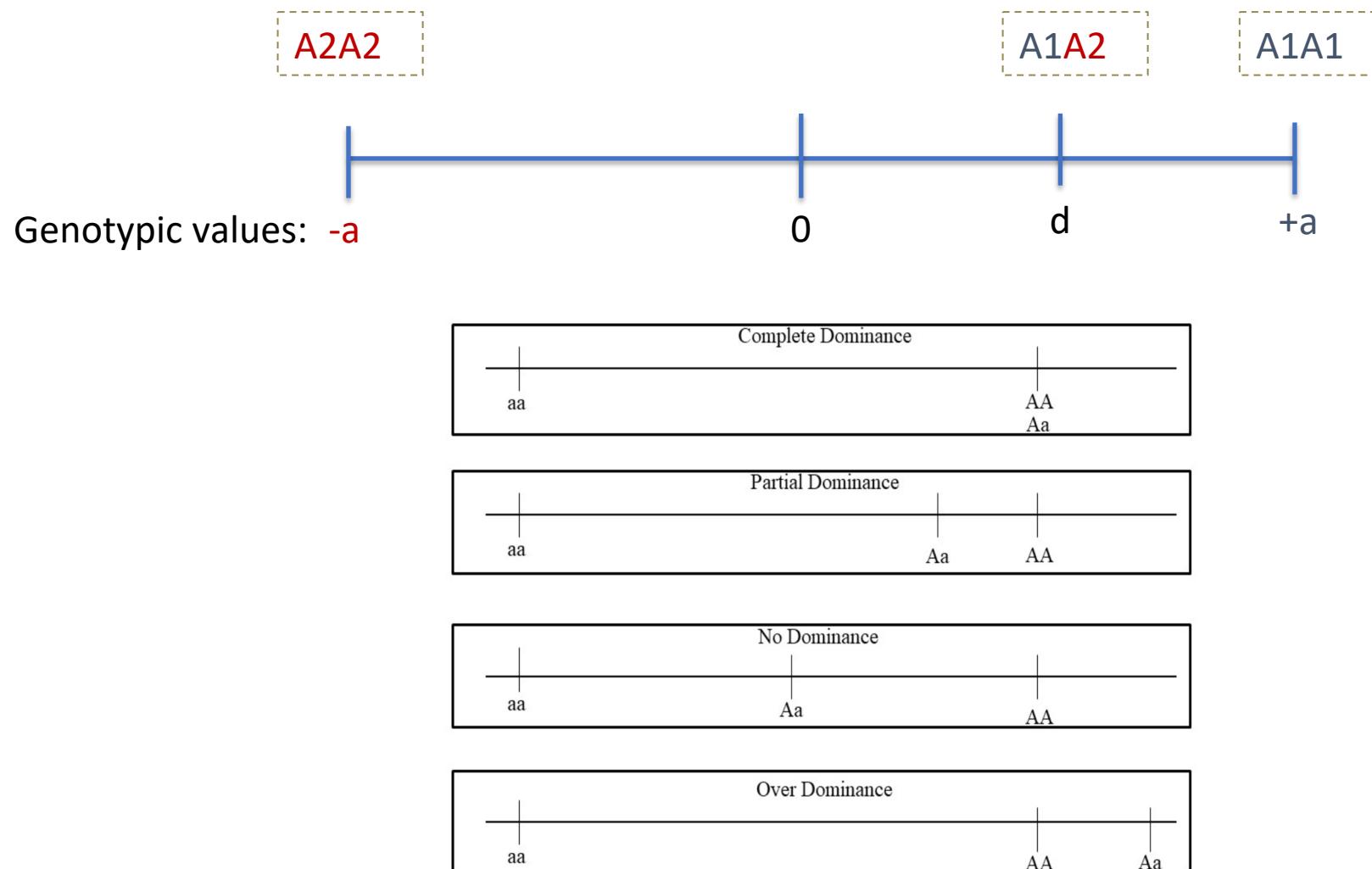


Values and means in a single locus

- Genetic values
- Population mean
- Average allele effect
- Average allele substitution effect



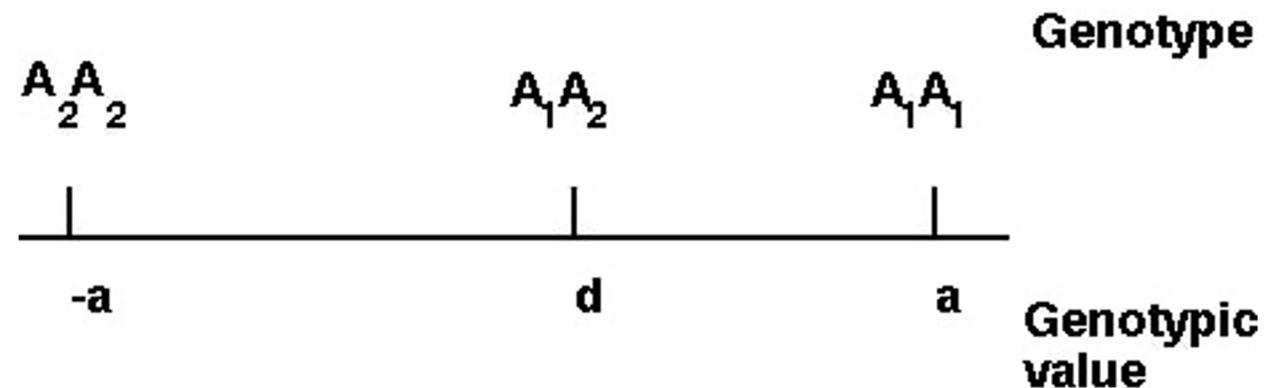
Genetic values



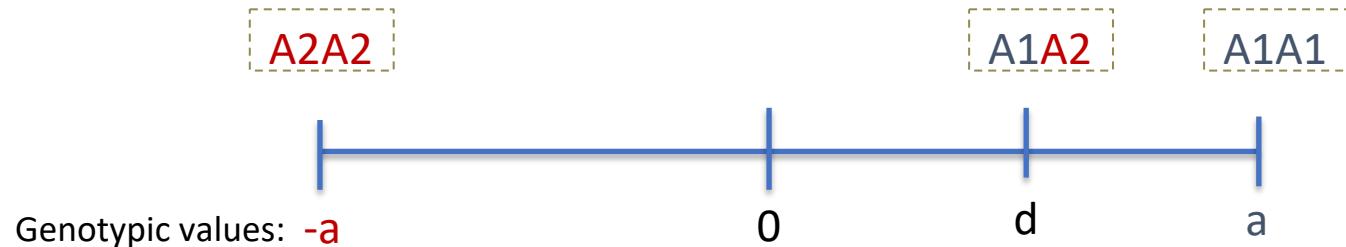
Griffiths et al 2012

Values and means in a single locus

- Genetic values
- Population mean
- Average allele effect
- Average allele substitution effect



Population mean



Genotype	Freq	Value	Freq × Value
A1A1	p^2	a	p^2a
A1A2	$2pq$	d	$2pqd$
A2A2	q^2	-a	$-q^2a$
Sum	1		$a(p-q)+2pqd$

$$\bar{X} = \sum_{i=1}^k f_i X_i$$

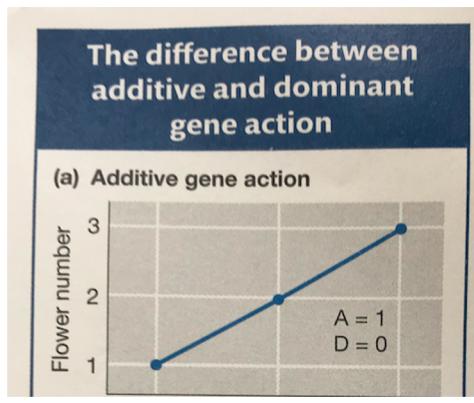
$$E[u] = a(p - q) + 2pqd$$

$$E[u] = a(p - q)$$

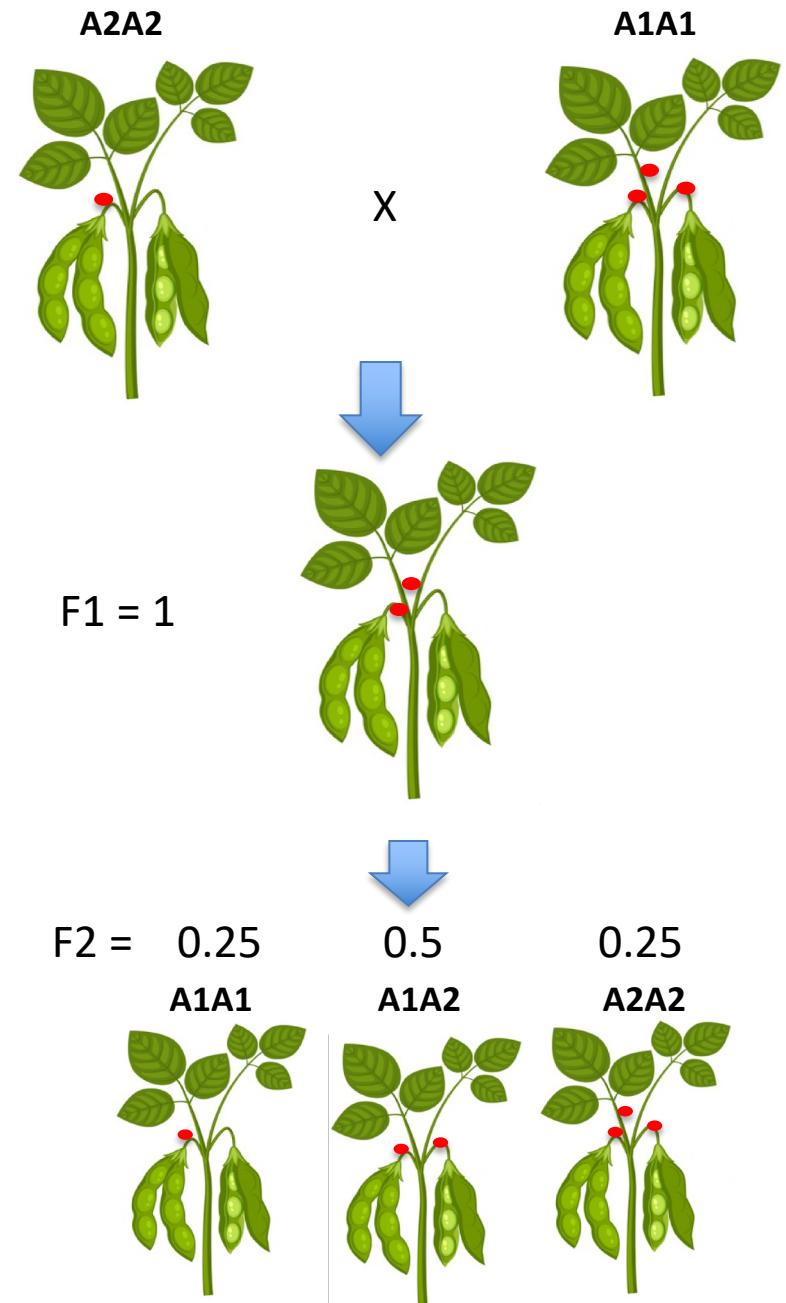
Population mean

$$u = \sum_{i=1}^k f_i X_i$$

Genotype	Freq	Value	Freq × Value
A1A1	p^2	a	p^2a
A1A2	$2pq$	d	$2pqd$
A2A2	q^2	-a	$-q^2a$
Sum	1		$a(p-q)+2pqd$



Griffiths et al 2012

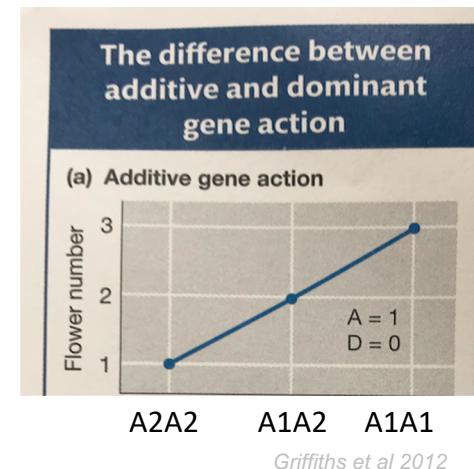
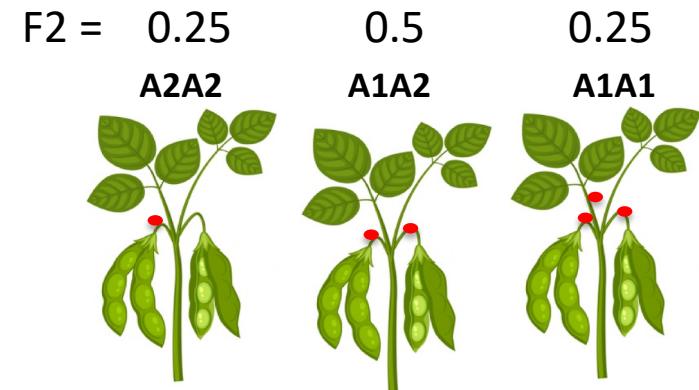
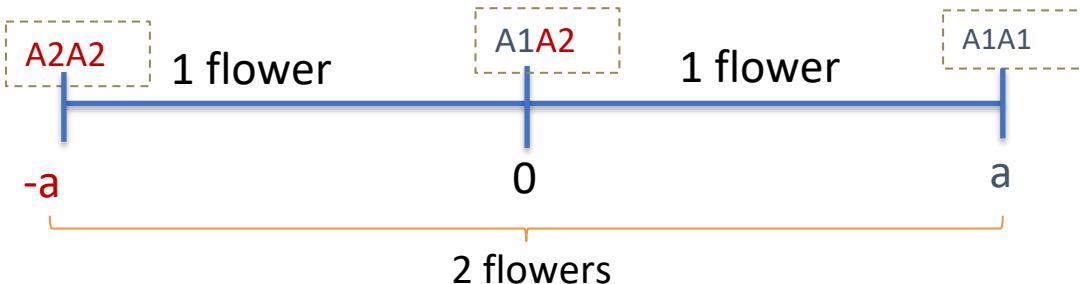


Population mean

Genotype	Freq	Value	Freq × Value
A1A1	p^2	a	p^2a
A1A2	$2pq$	d	$2pqd$
A2A2	q^2	-a	$-q^2a$
Sum	1		$a(p-q)+2pqd$

$$p = \sqrt{0.25} = 0.5$$

$$q = 1 - p = 0.5$$



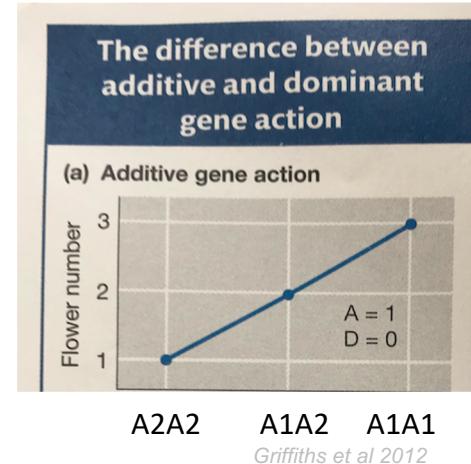
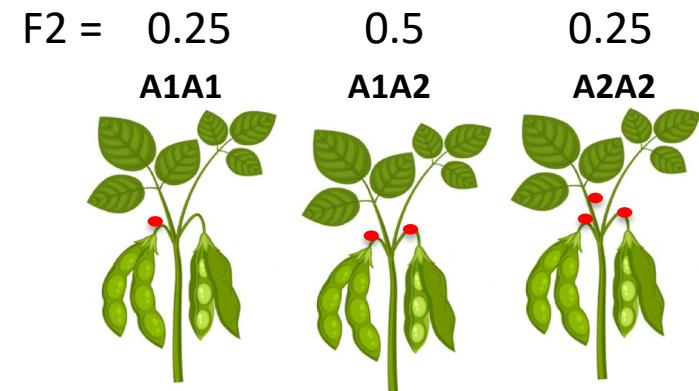
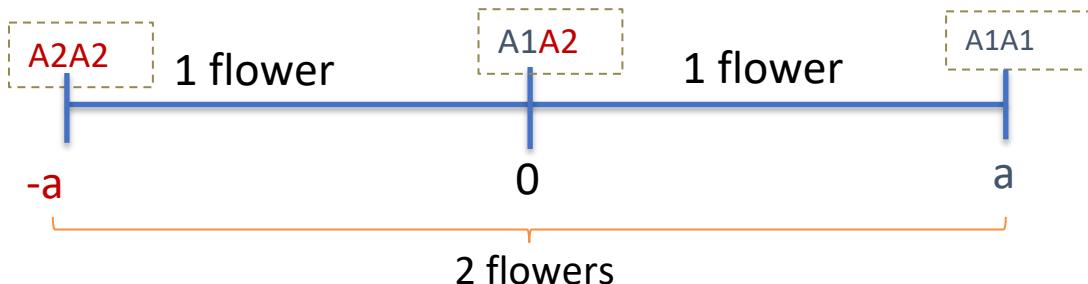
Population mean

Genotype	Freq	Value	Freq × Value
A1A1	0.5^2	1	$0.25*1$
A1A2	$2*0.5*0.5$	0	$2*0.5*0.5*0$
A2A2	0.5^2	-1	$-0.25*-1$
Sum	1		$1(0.5-0.5)+2*0.5*0.5*0$

$$a(p-q) + 2pqd = 0$$

$$p = \sqrt{0.25} = 0.5$$

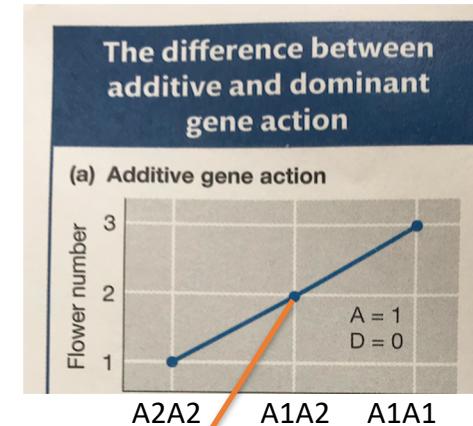
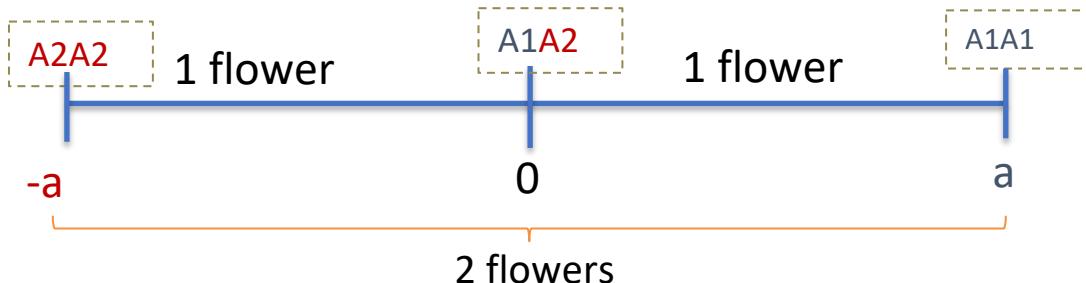
$$q = 1 - p = 0.5$$



Population mean

Genotype	Freq	Value	Freq × Value
A1A1	0.5 ²	1	0.25*1
A1A2	2*0.5*0.5	0	2*0.5*0.5*0
A2A2	0.5 ²	-1	-0.25*1
Sum	1		1(0.5-0.5)+2*0.5*0.5*0

$$a(p-q) + 2pqd = 0$$



This value of mean is measured from the mid-homozygote point, which is 2 flowers

Frequency	Trait value (no. of flowers)	Contribution to the mean (frequency × value)
A2A2	0.25	1
A1A2	0.50	2
A1A1	0.25	3
Mean = 2.0		

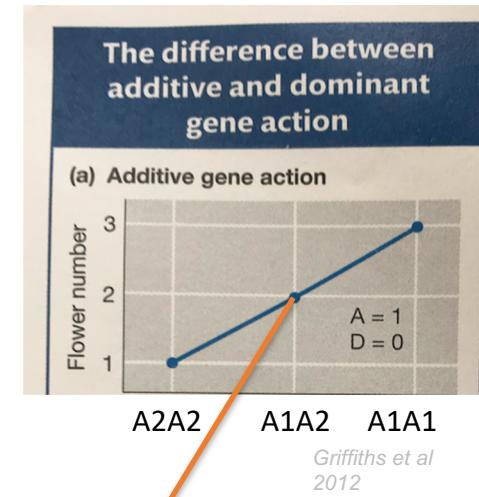
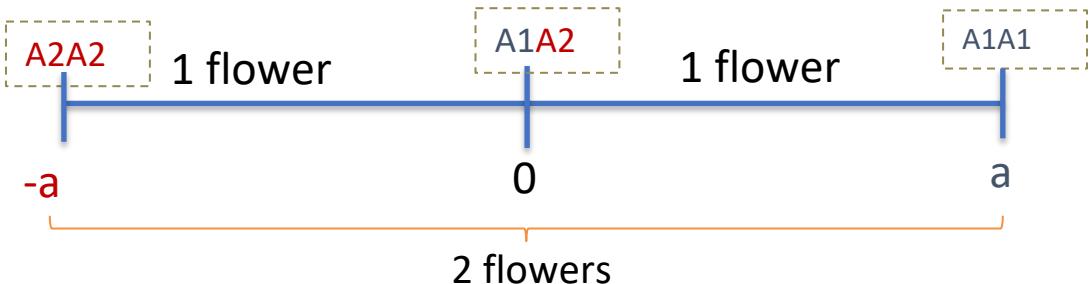
Population mean

Genotype	Freq	Value	Freq × Value
A1A1	0.9 ²	1	0.81*1
A1A2	2*0.9*0.1	0	0.18*0
A2A2	0.1 ²	-1	-0.01*1
Sum	1		1(0.8)+2*0.09*0

$$a(p-q) + 2pqd = 0.8$$

$$p = 0.9$$

$$q = 0.1$$



$$2 + 0.8 = 2.8 \text{ flowers}$$

Population mean

Genotype	Freq	Value	Freq × Value
A1A1	p^2	a	p^2a
A1A2	$2pq$	d	$2pqd$
A2A2	q^2	-a	$-q^2a$
Sum	1		$a(p-q)+2pqd$

$$E[u] = a(p - q) + 2pqd$$

Single locus

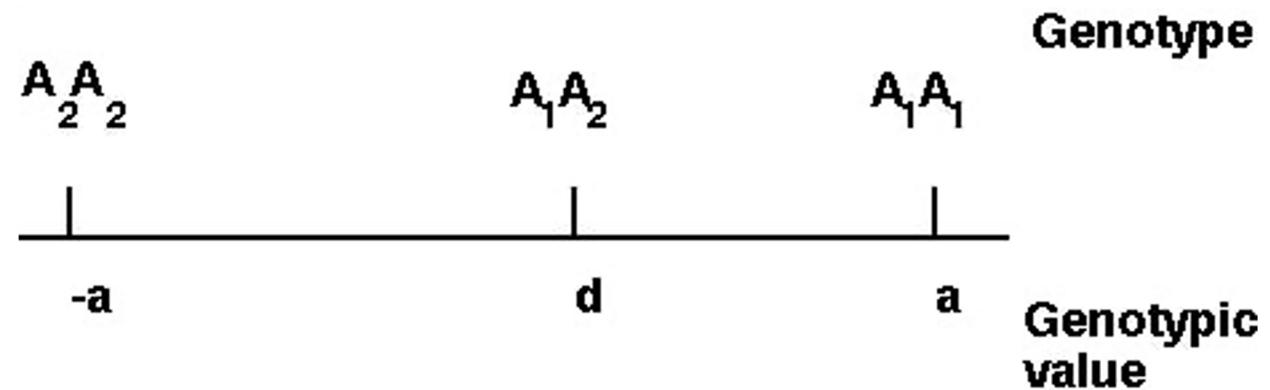
The population mean resulting from joint effects of several loci is the sum of the contributions of each of separate loci

$$E[u] = \sum a(p - q) + 2 \sum dpq$$

Several loci

Values and means in a single locus

- Genetic values
- Population mean
- Average allele effect
- Average allele substitution effect



Average allele effect

Deviation from the population mean of individuals which received an allele (A_1 or A_2) from one parent when the other allele come at random from the population

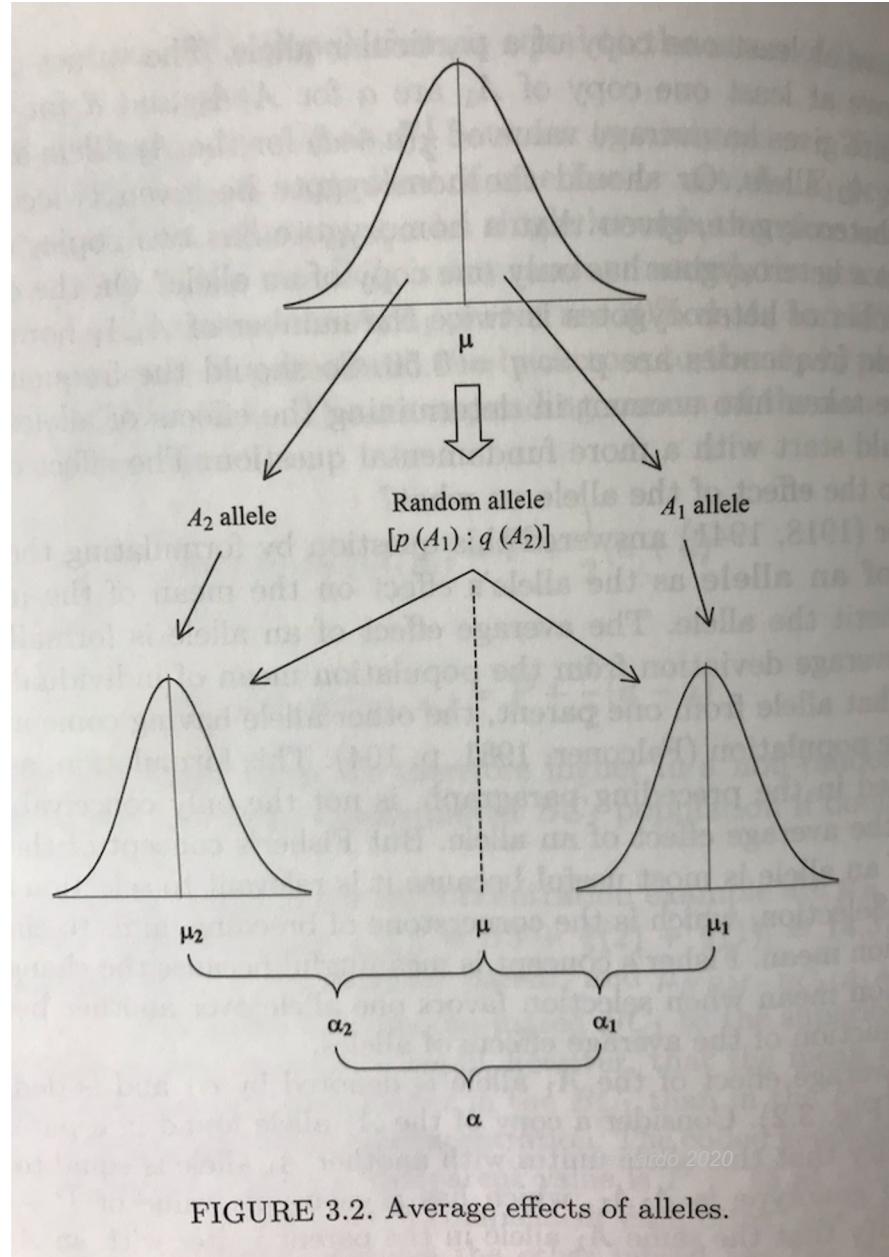
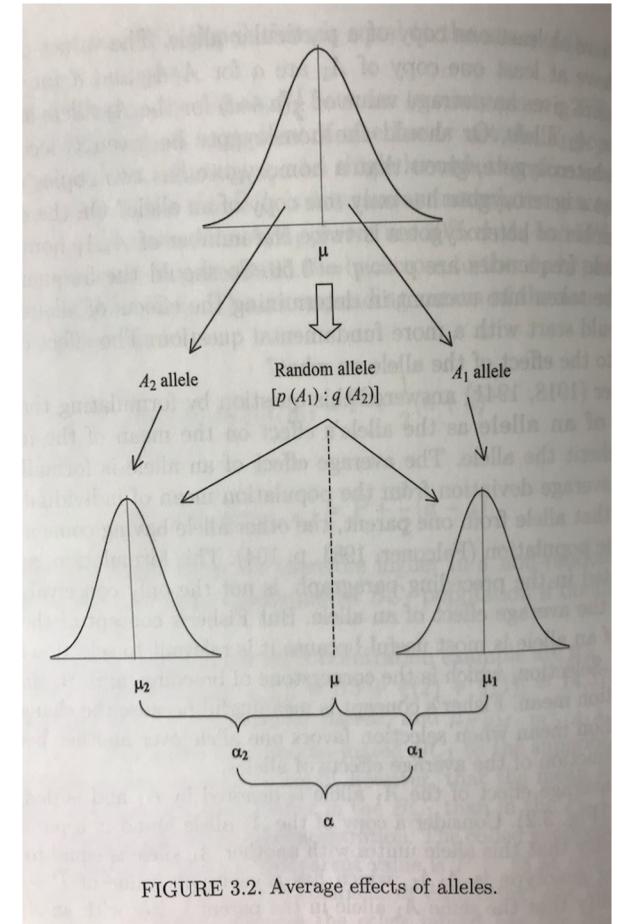


FIGURE 3.2. Average effects of alleles.

Average allele effect

Type of gamete	Values and frequencies of genotypes produced			Mean value of genotypes	Population mean to be deducted	Average effect of gene
	A_1A_1	A_1A_2	A_2A_2			$a(p-q) + 2pqd$
	a	d	$-a$			
A_1	p	q		$pa + qd$	$-(a(p-q) + 2dpq)$	$q[a+d(q-p)]$
A_2		p	q	$-qa + pd$	$-(a(p-q) + 2dpq)$	$-p[a+d(q-p)]$

Falconer & Mackay 1996

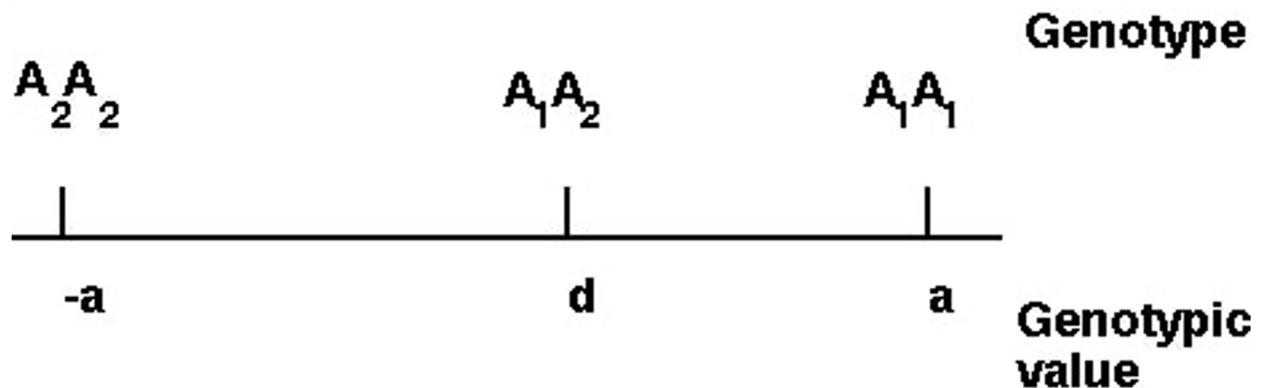


Average effects of the alleles: $\alpha_1 = q[a + d(q - p)]$ $\alpha_2 = -p[a + d(q - p)]$

Average effects of the gene substitution: $\alpha = \alpha_1 - \alpha_2 = a + d(q - p)$

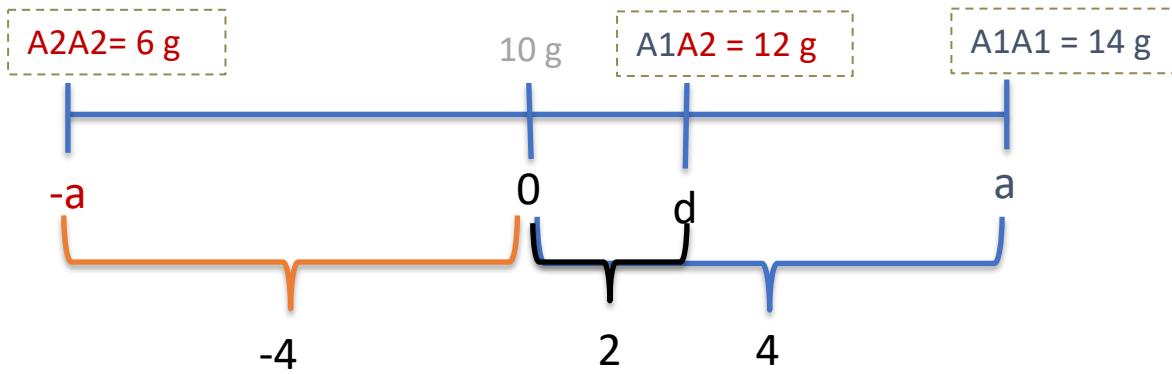
Values and means in a single locus

- Genetic values
- Population mean
- Average allele effect
- Average allele substitution effect



Average effects of gene substitution

$$\begin{aligned}\alpha &= \alpha_1 - \alpha_2 \\ &= a + d(q - p)\end{aligned}$$



$$\alpha = a + d(q - p)$$

Population s	p	q
Pop 1	0.9	0.1
Pop 2	0.6	0.4

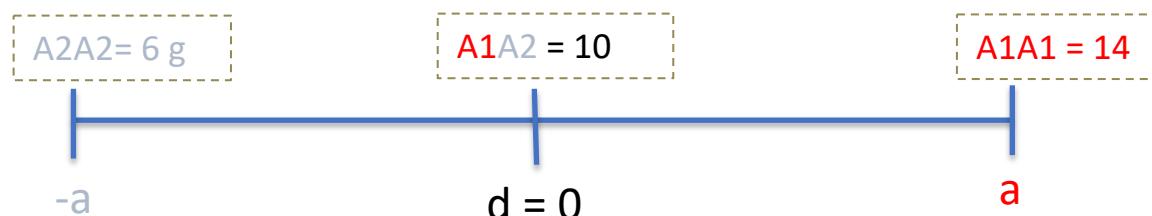
$$\alpha = 4 + 2(0.1 - 0.9) = 2.4$$

$$\alpha = 4 + 2(0.4 - 0.6) = 3.6$$

Average effects of gene substitution

Type of gamete	Values and frequencies of genotypes produced			Mean value of genotypes	Population mean to be deducted	Average effect of gene
	A1A1	A1A2	A2A2			
	a	d	-a			
A1	p	q		pa + qd	-[a(p-q) + 2dpq]	q[a+d(q-p)]
A2		p	q	-qa + pd	-[a(p-q) + 2dpq]	-p[a+d(q-p)]

Falconer & Mackay 1996



Populations	p	q
Pop 1	0.5	0.5

$$\alpha = 4 + 0 (0.5 - 0.5) = 4$$

$$\alpha = a + d(q - p)$$

$$\alpha_1 = q[a + d(q - p)] = q\alpha$$

$$\alpha_2 = -p[a + d(q - p)] = -p\alpha$$

$$\alpha_1 = 0.5 * 4 = 2$$

$$\alpha_2 = -0.5 * 4 = -2$$

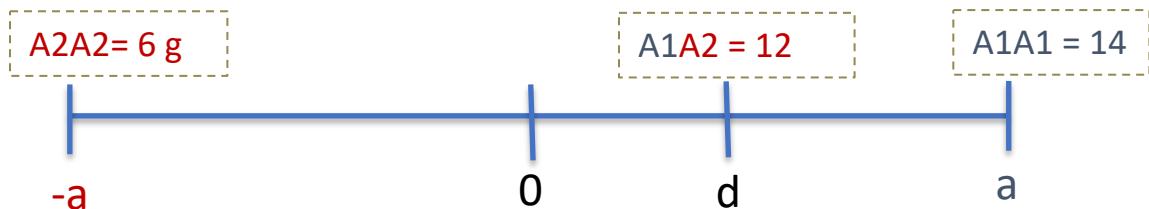
$$\alpha = \alpha_1 - \alpha_2 = 2 - (-2) = 4$$

Average effects of gene substitution

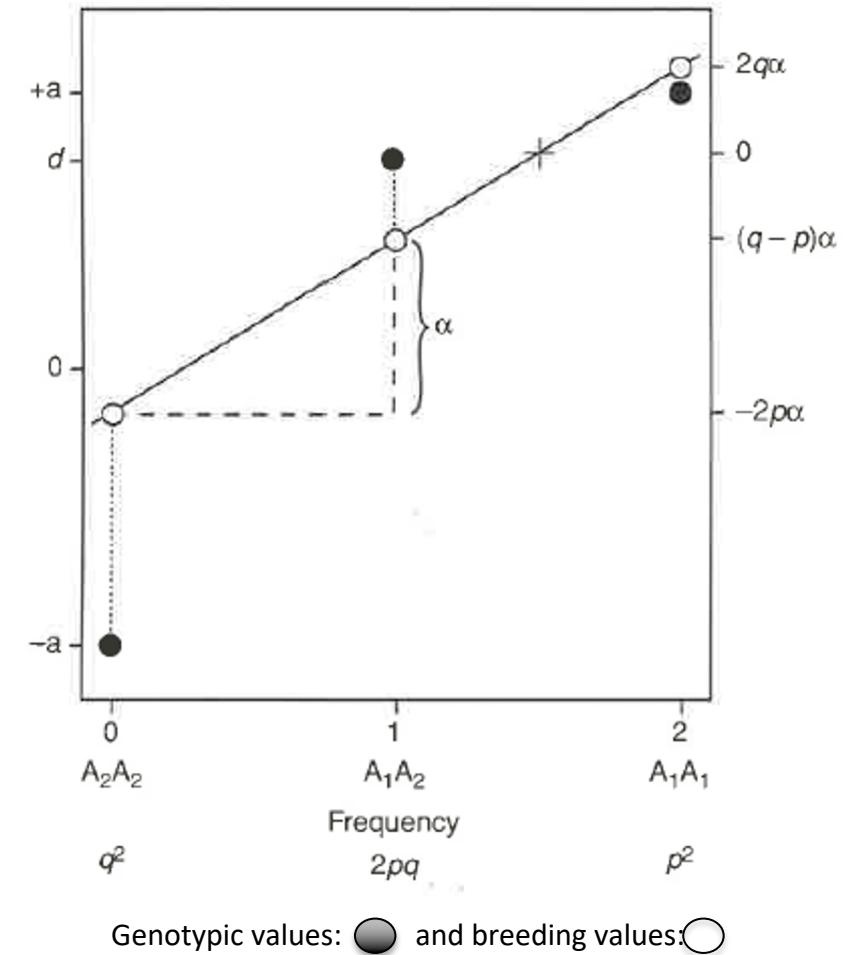
$$\alpha = a + d(q - p)$$

One half of the difference between the two homozygous

Deviation due to dominance



Breeding value
$2\alpha_1 = 2q\alpha$
$\alpha_1 + \alpha_2 = (q - p)\alpha$
$2\alpha_2 = -2p\alpha$



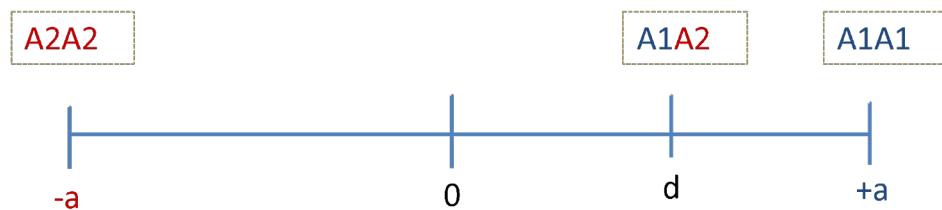
Review:

Average effects of alleles:

$$\alpha_1 = q[a + d(q - p)]$$

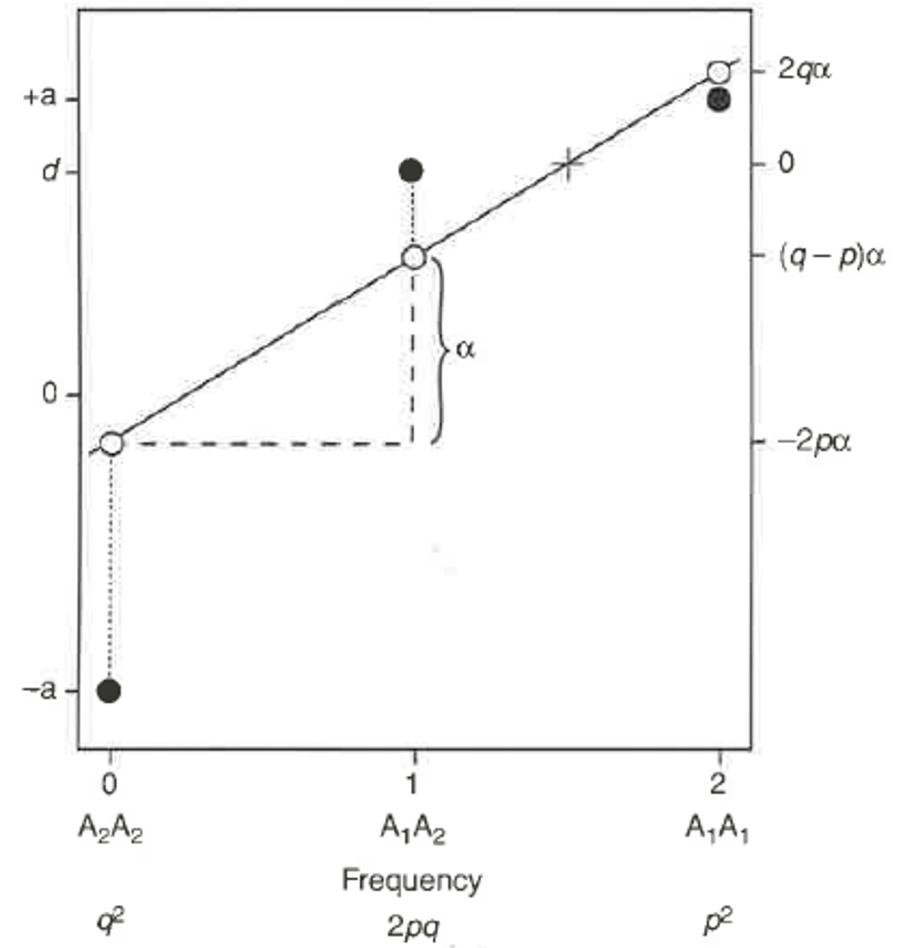
$$\alpha_2 = -p[a + d(q - p)]$$

Genotypic values:



Average effects of the gene substitution:

$$\alpha = \alpha_1 - \alpha_2 = a + d(q - p)$$



Genotypic values: and breeding values:

Super review!!!



1

- Central dogma
- Meiosis
- Allele frequencies
- genotype frequencies
- HWE

2

$$\bar{X} = \sum_{i=1}^{\kappa} f_i X_i$$

$$s^2 = \frac{1}{n-1} \sum_i (X_i - \bar{X})^2$$

$$x = g + e$$

$$V_x = Vg + Ve + 2\text{cov}_{ge}$$

3

$$V_g = V_a + V_d + V_i$$

$$H^2 = \frac{Vg}{Vx}$$

$$h^2 = \frac{Va}{Vx}$$

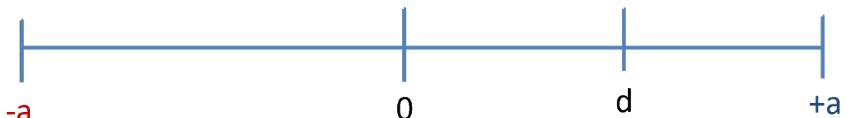
4

Genotypic values

A2A2

A1A2

A1A1



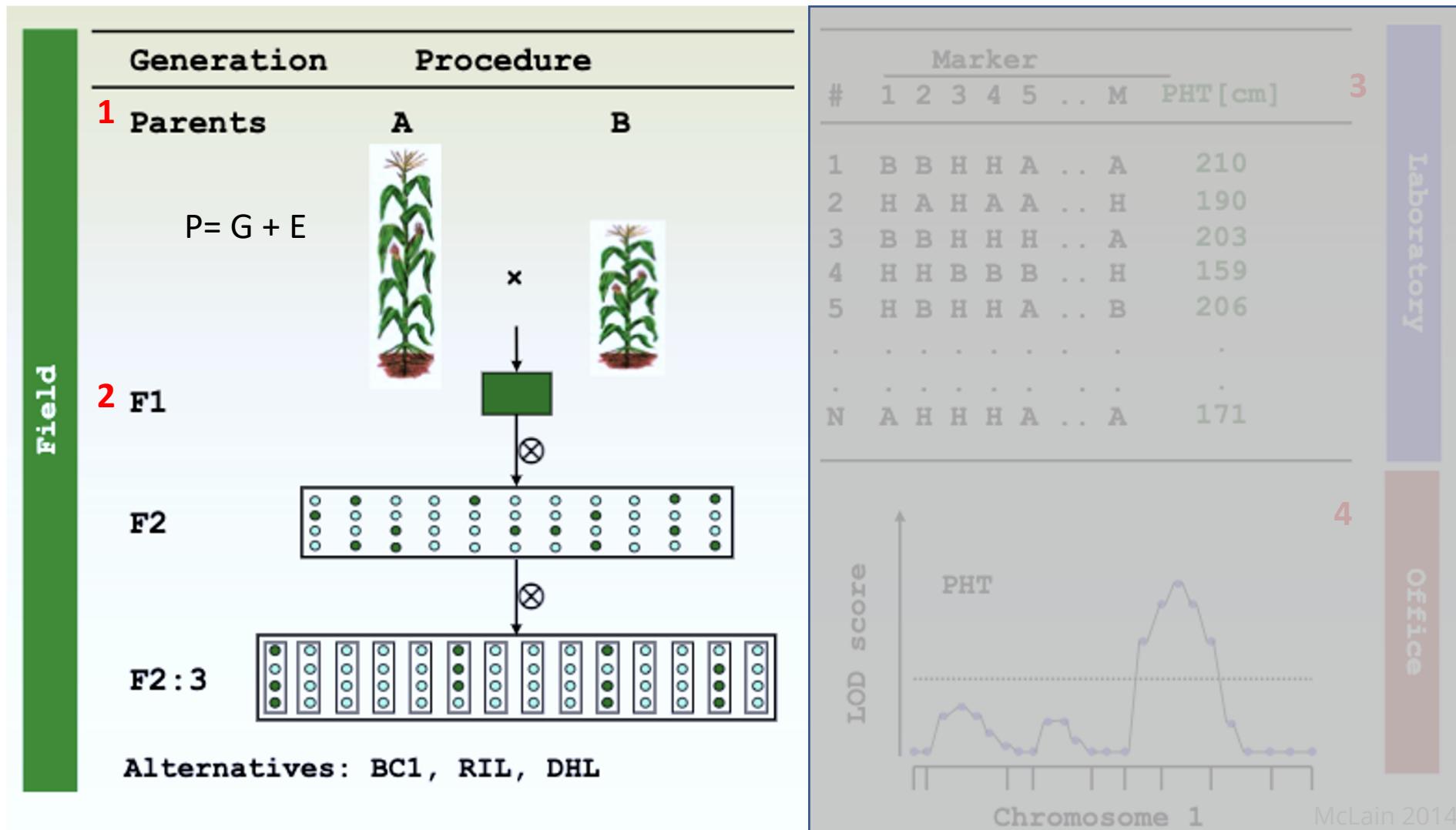
Average effects of the gene substitution:

$$\alpha = \alpha_1 - \alpha_2 = a + d(q - p)$$



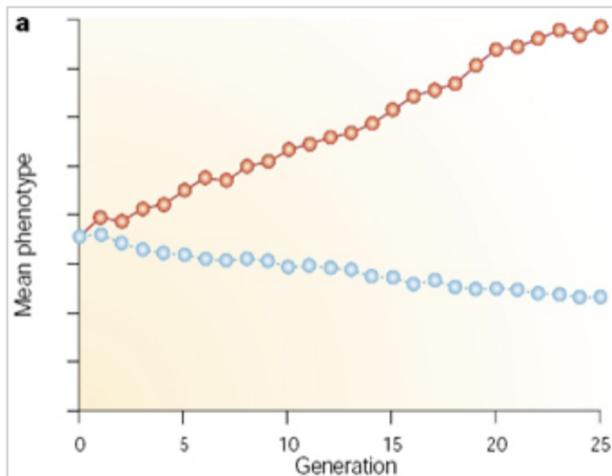
Quantitative Trait Loci (QTL)

Quantitative trait loci

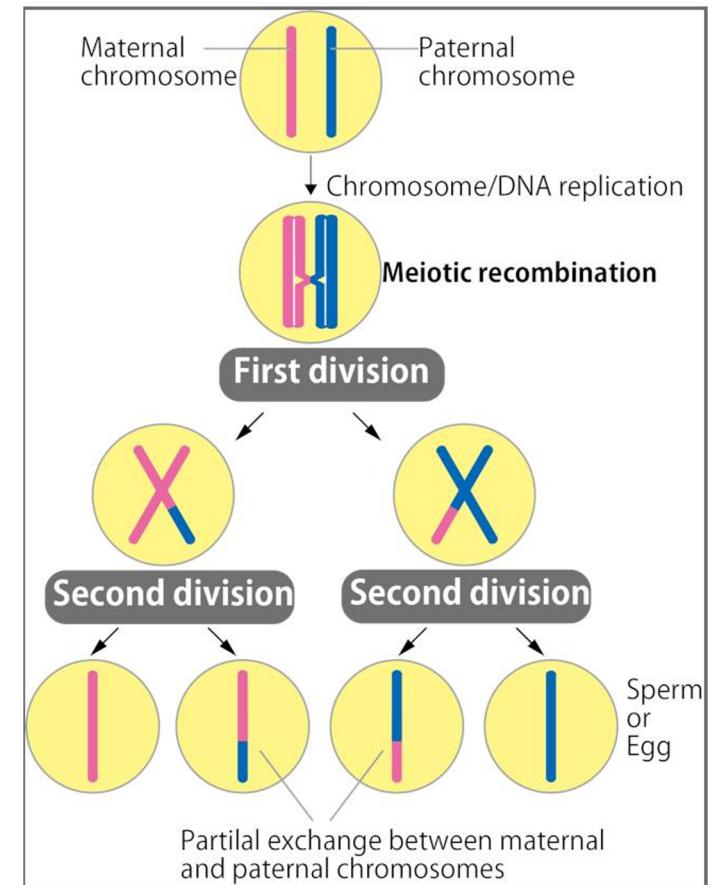
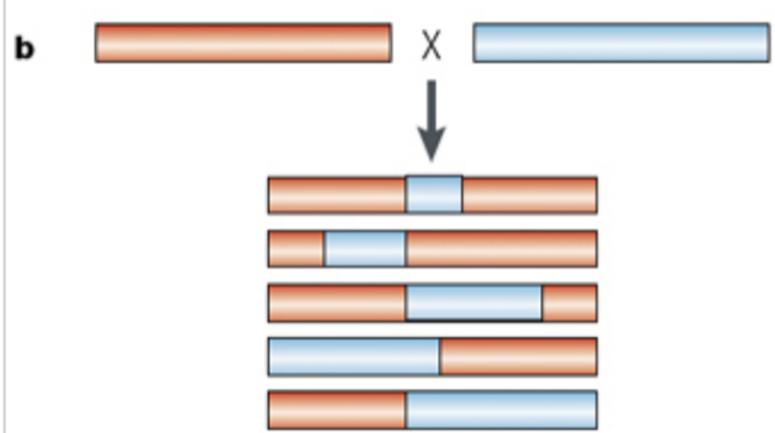


1 – 2. Parents and Population

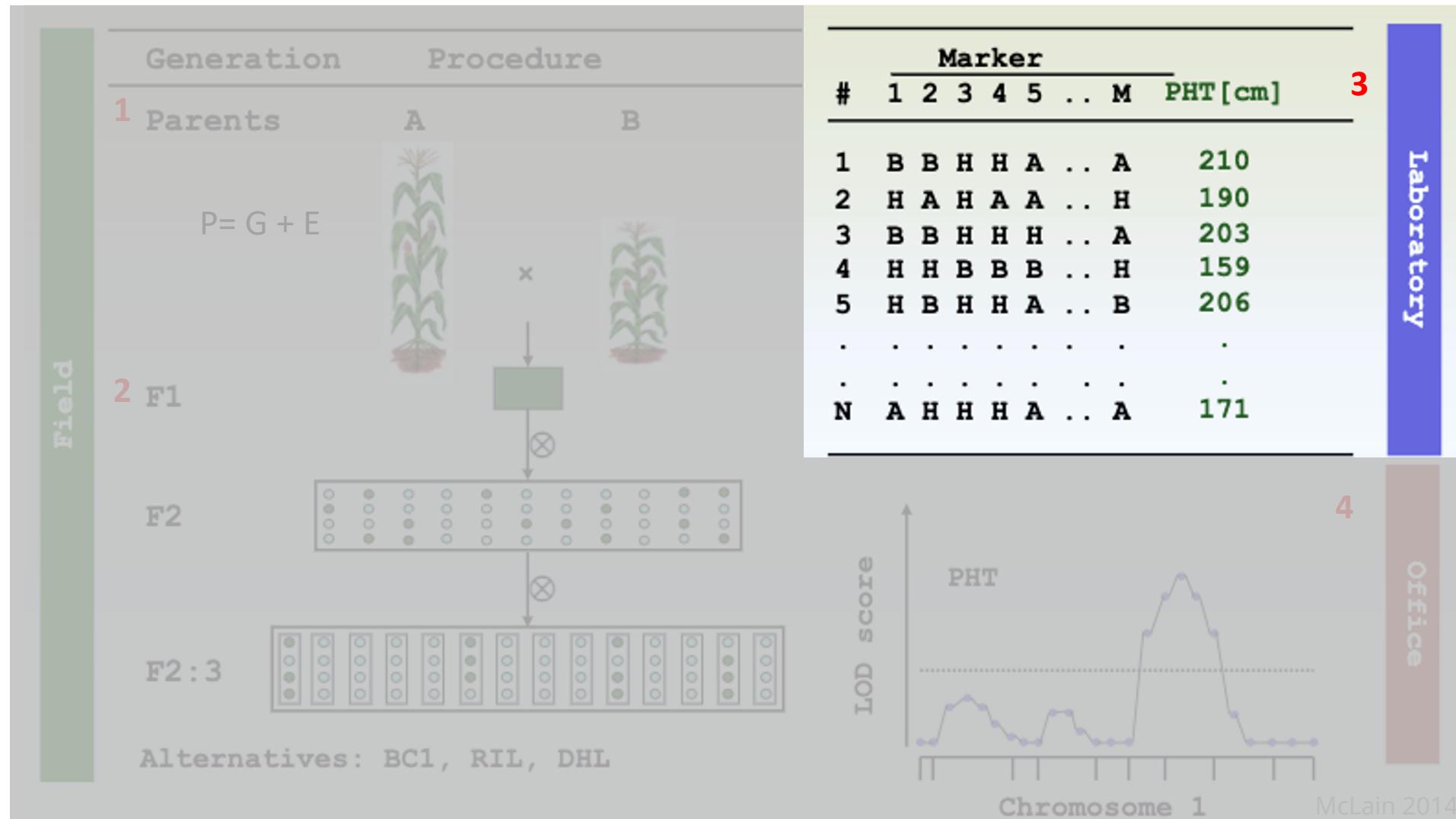
Select parents



bi-parental populations

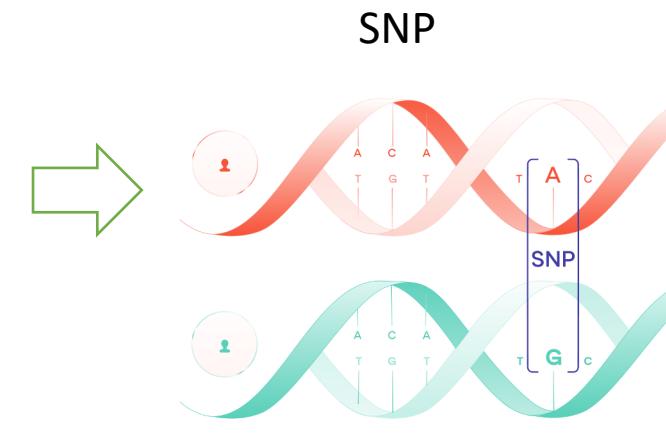
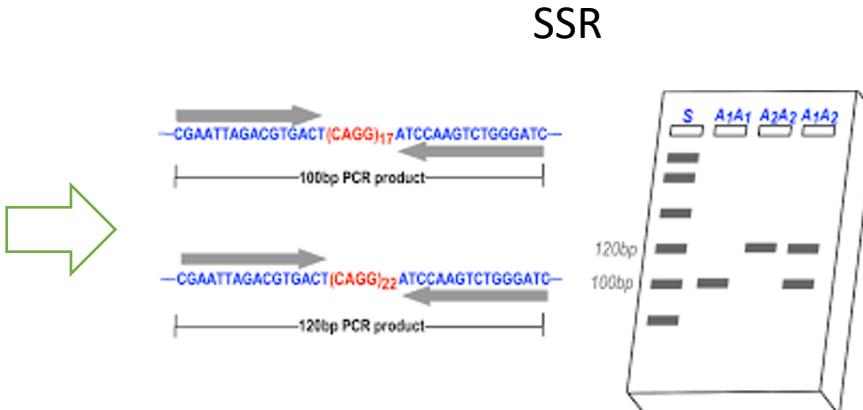
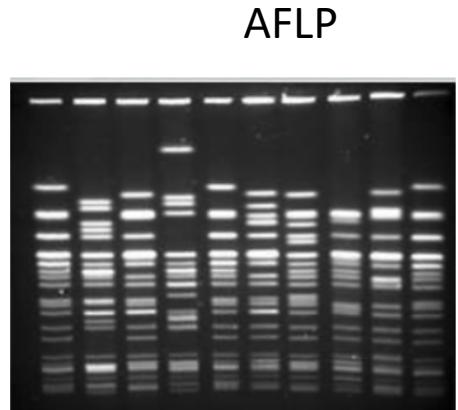
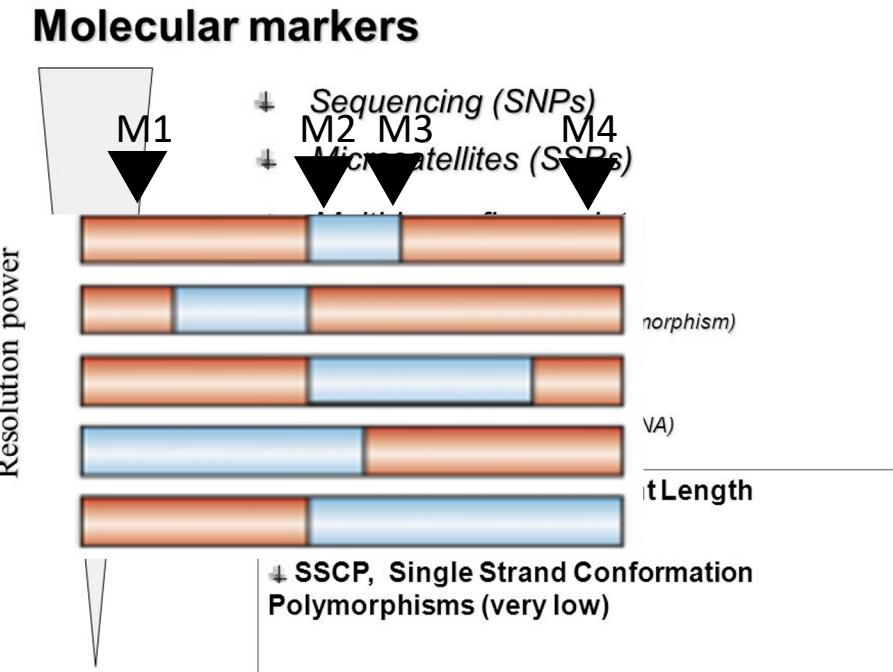


Quantitative trait loci



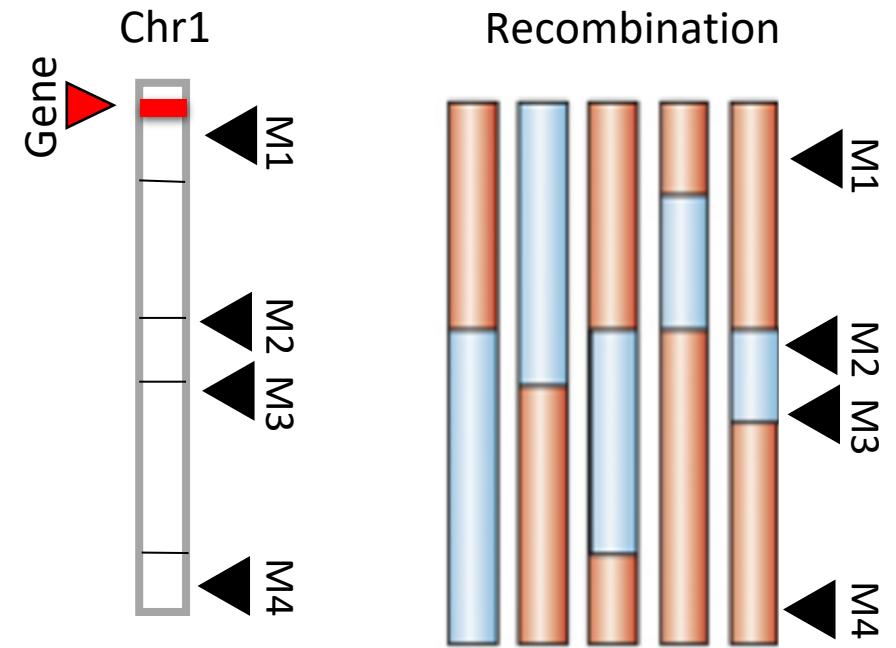
3. Markers and linkage maps

- In genetics, a **molecular marker** is a fragment of DNA that is associated with a certain location within the genome.

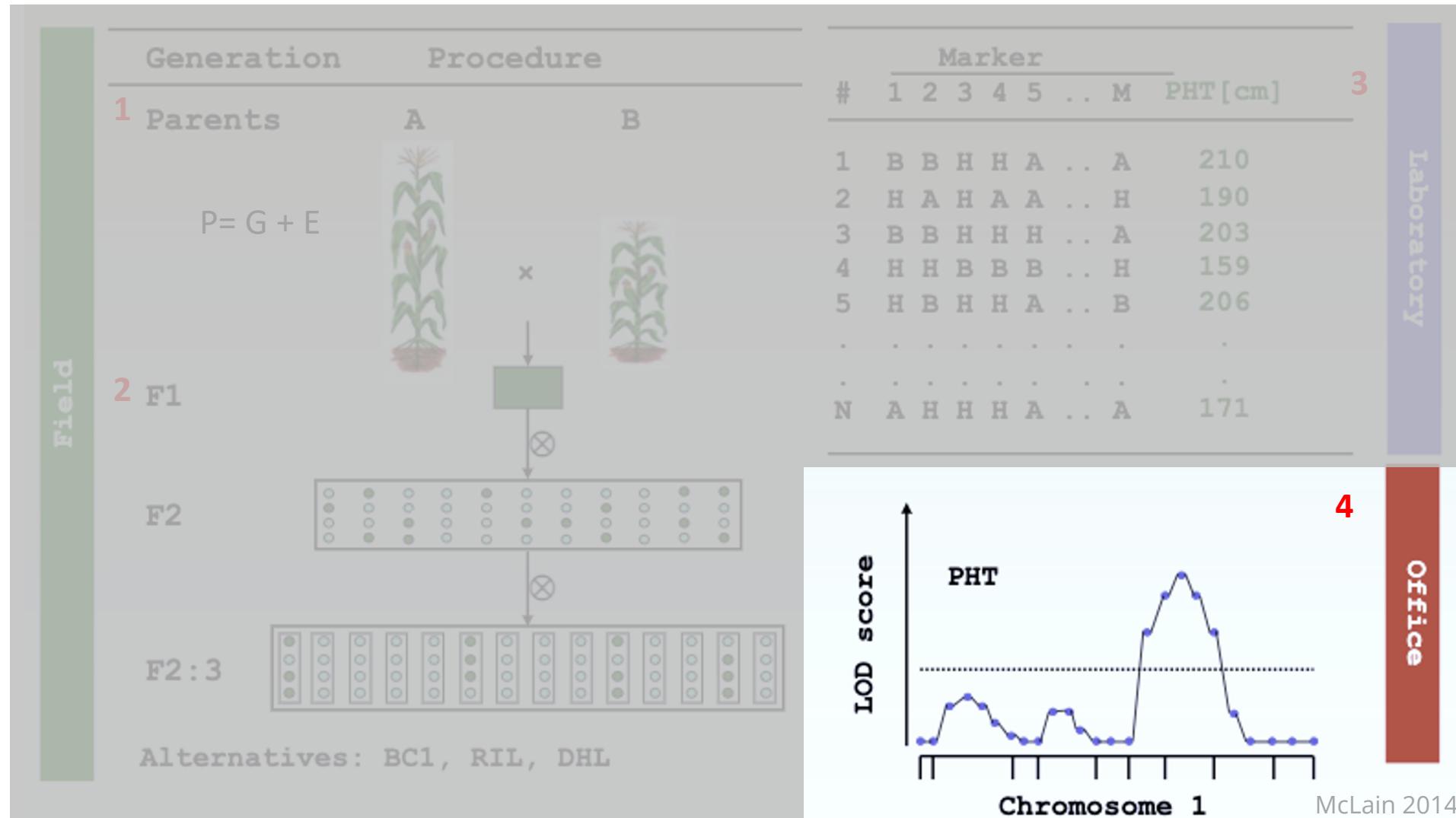


3. Markers and linkage maps

- Linkage maps indicate the position and relative genetic distances between markers along chromosomes.
- QTL mapping is based on the principle that genes and markers segregate via chromosome recombination during meiosis.



Quantitative trait loci



4. QTL detection

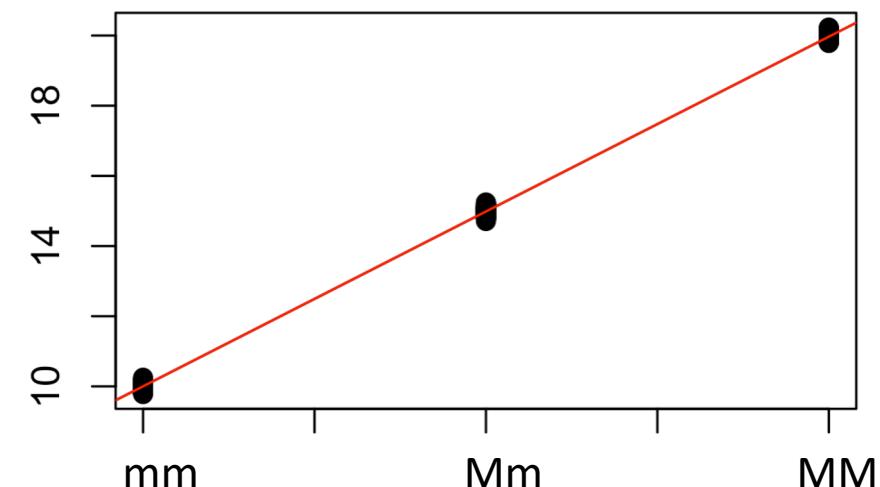
The statistical methods used for single-marker analysis include t-tests, analysis of variance (ANOVA) and linear regression.

$$t = \frac{\overline{MM} - \overline{mm}}{\sqrt{\frac{\hat{V}(MM)}{N} + \frac{\hat{V}(mm)}{N}}}$$

T-test: compare the mean of 2 groups. To compare 3 or more groups, one must use an ANOVA.

$$y_i = b_0 + b_1 x + e$$

Estimated (or predicted) y value
Estimate of the regression intercept
Estimate of the regression slope
Independent variable
Error term



4. QTL detection

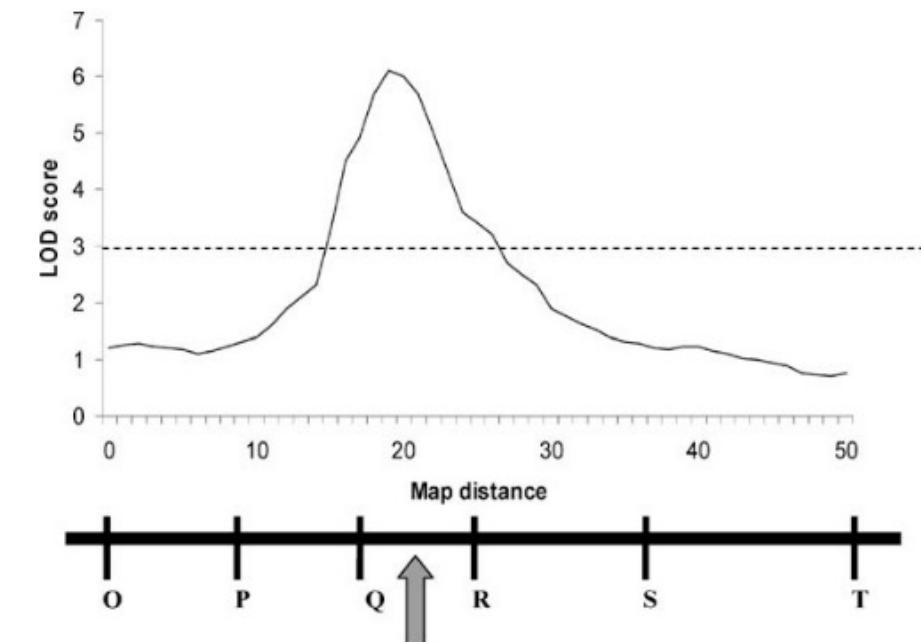
Interval mapping

- **Simple Interval Mapping (SIM)**

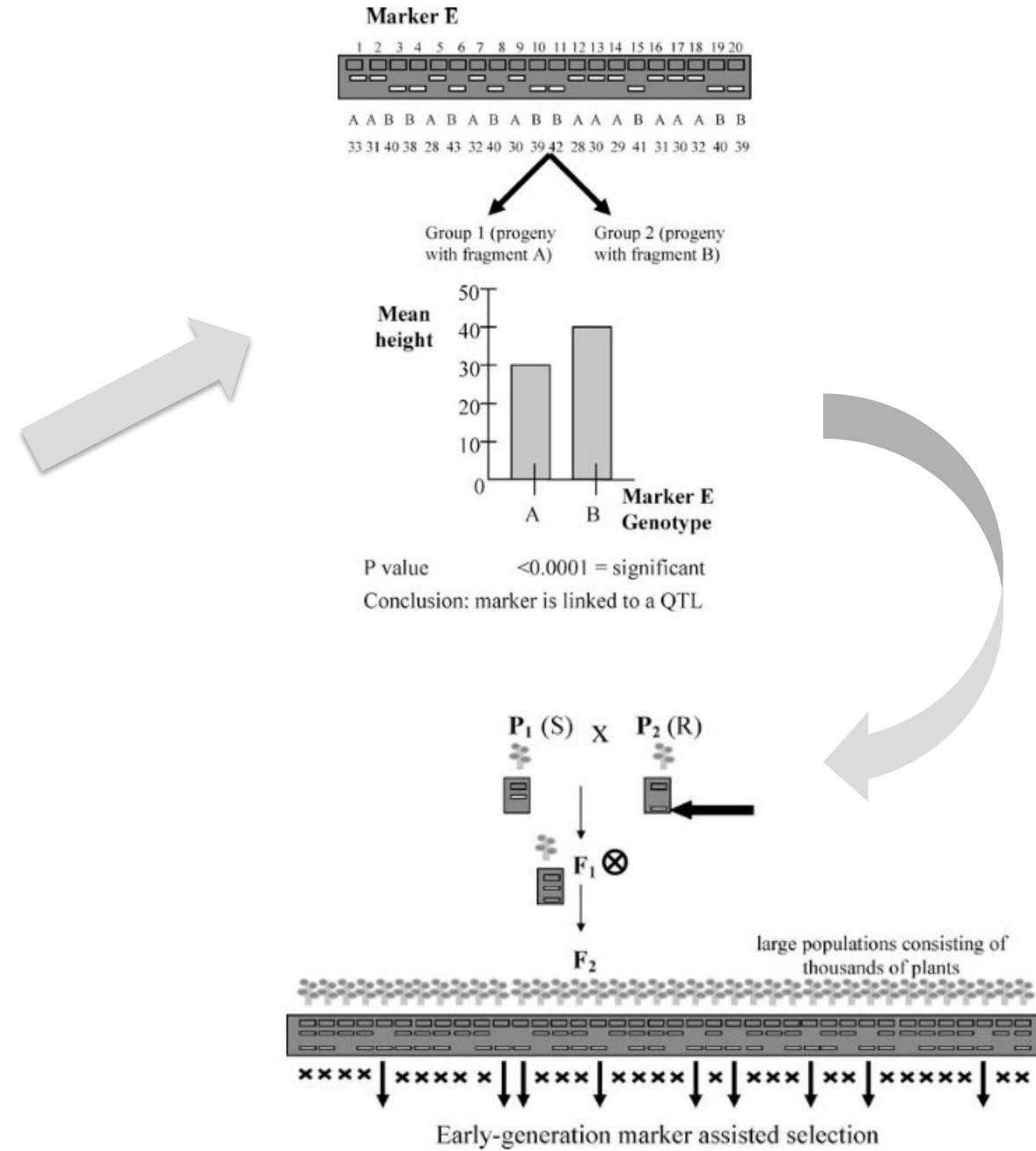
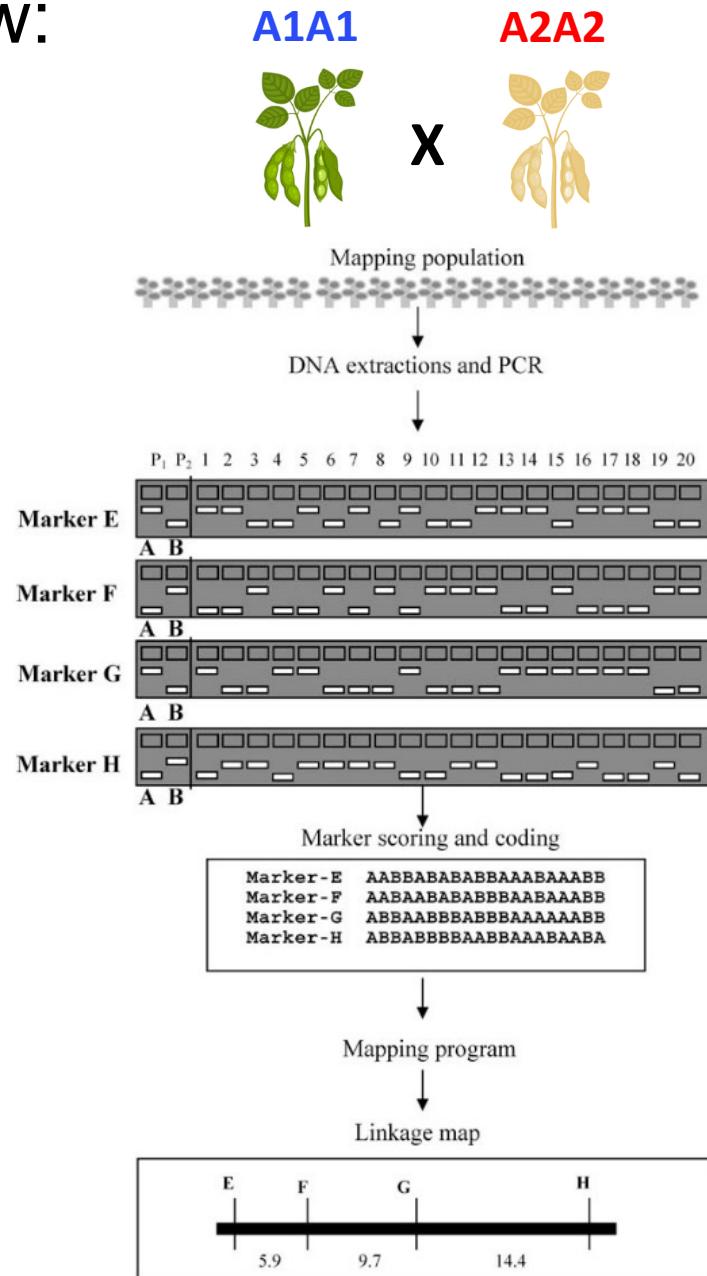
SIM uses adjacent markers to estimate a QTL location.

- **Composite Interval Mapping (CIM)**

CIM uses interval mapping and includes genetic markers in the statistical model in addition to an adjacent pair of linked markers for interval mapping.



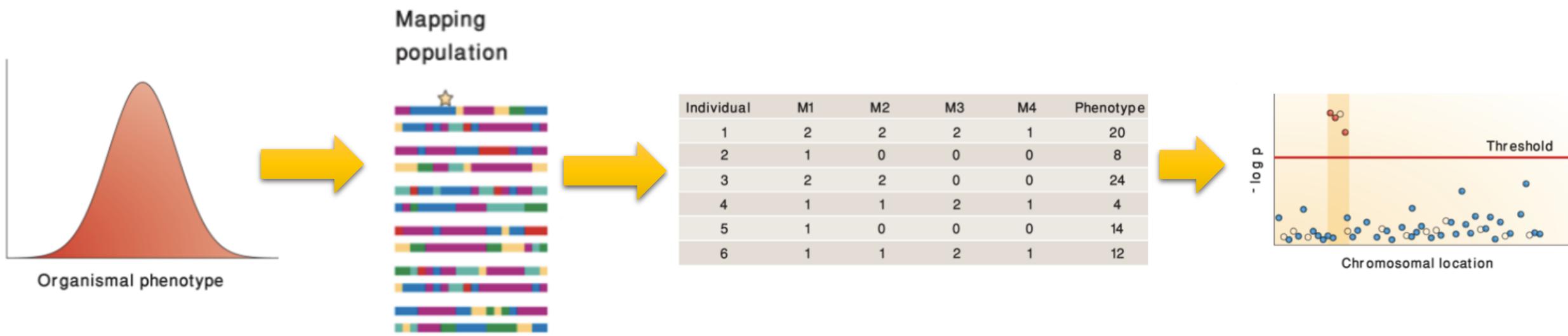
Review:



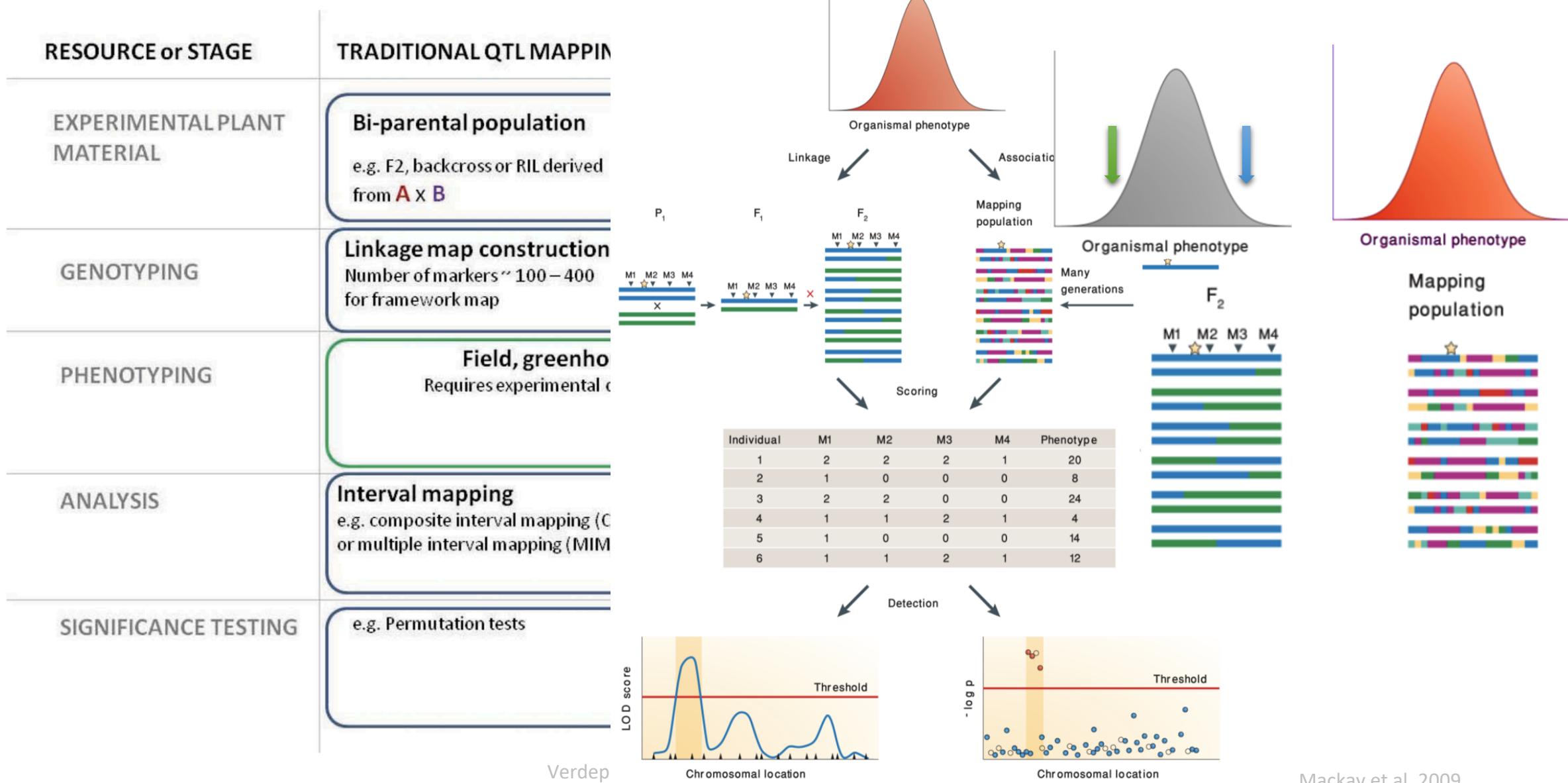
Association mapping

Association mapping

- Association analysis uses historical recombination events over many generations within a short interval surrounding a trait locus
- Association analysis is advantageous for the identification of relatively small genomic regions, in which only few genes may reside.



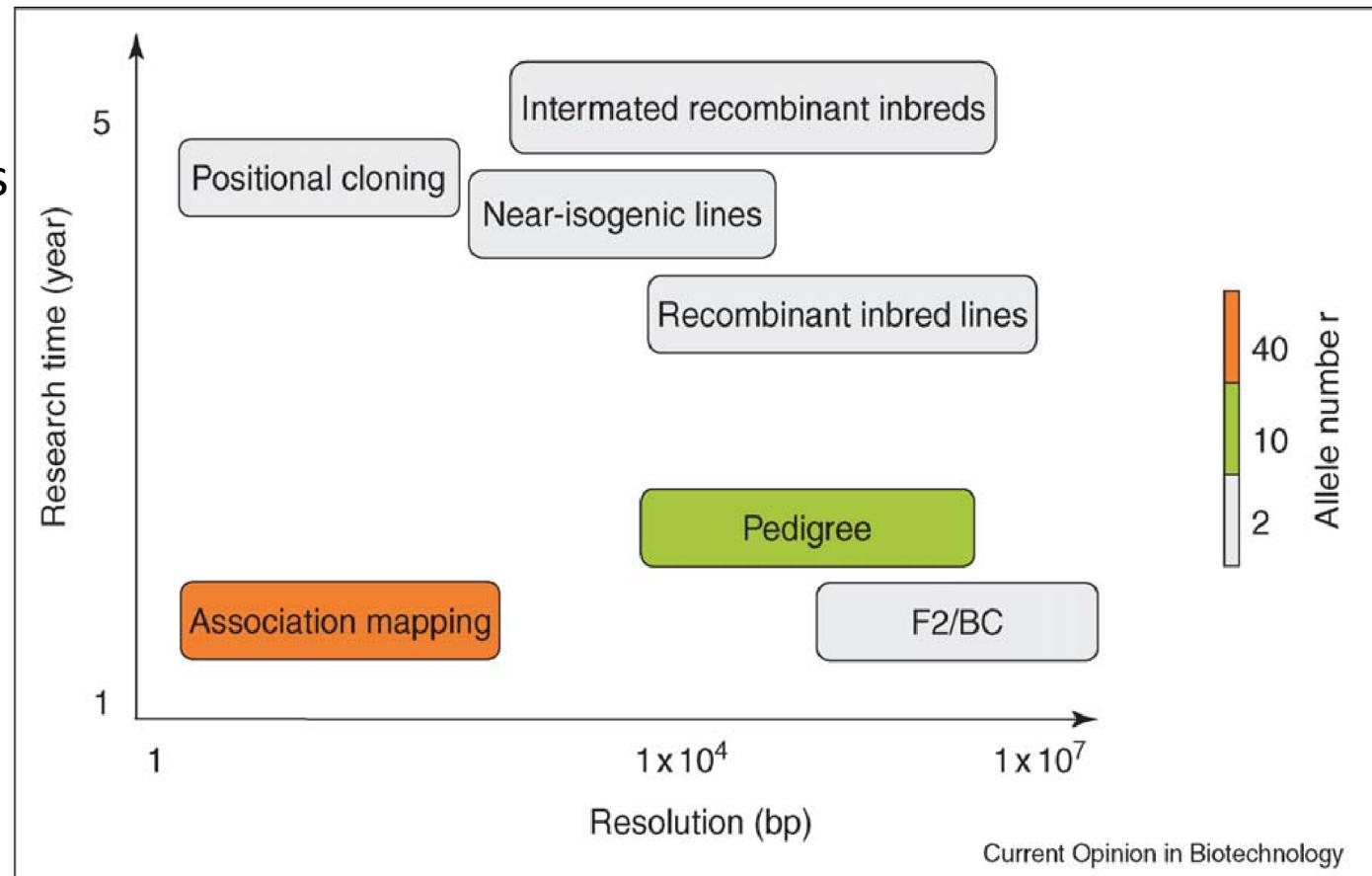
Mapping population vs Association mapping



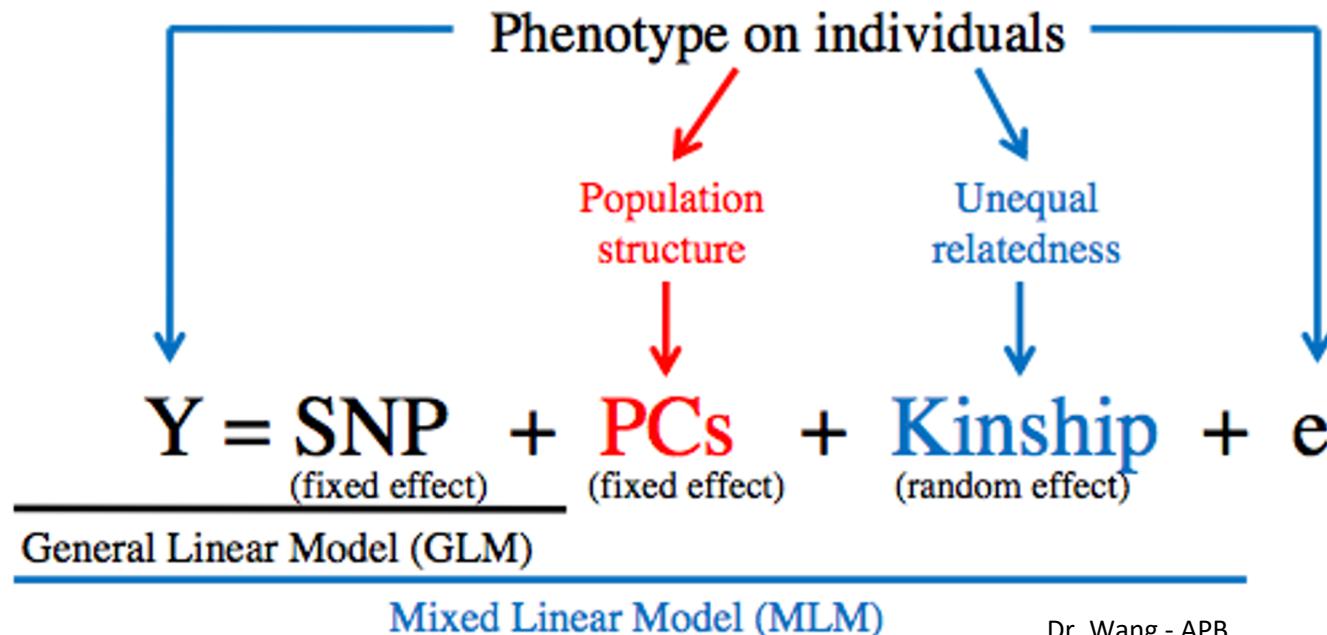
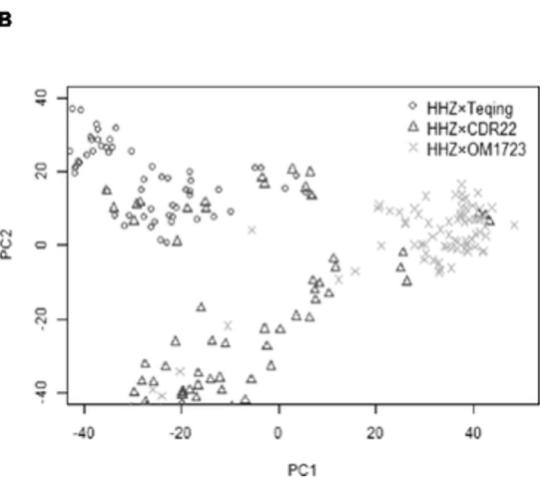
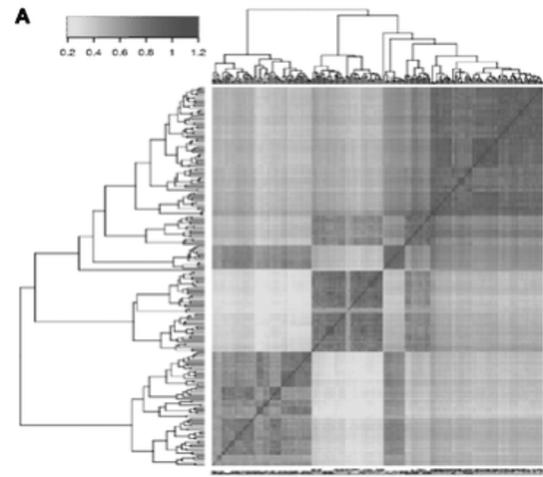
Mapping population vs Association mapping

Association mapping offers three advantages over linkage analysis:

- Higher mapping resolution
- Greater allele number
- Less research time in establishing an association

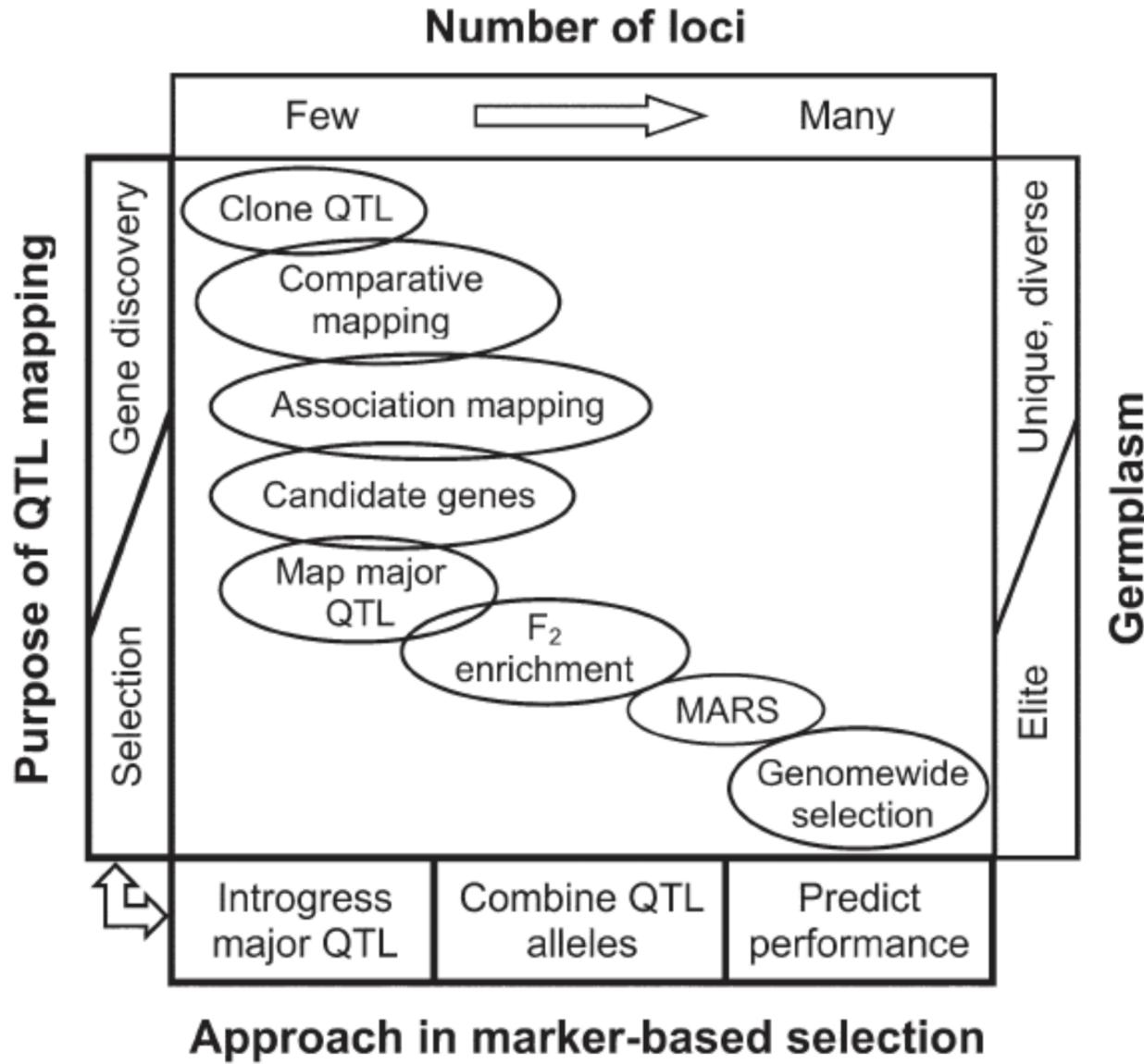


Statistical approaches

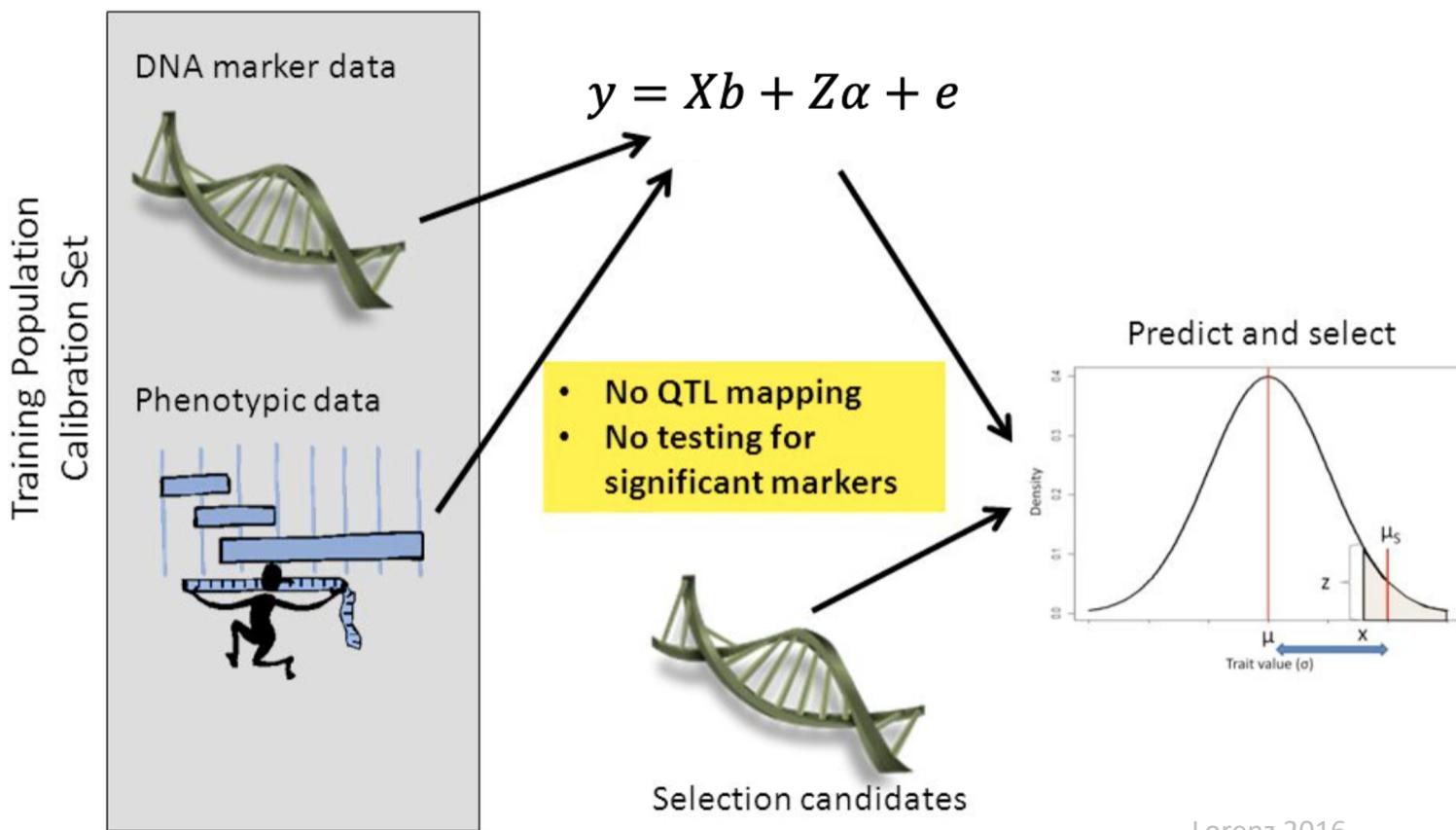


Dr. Wang - APB

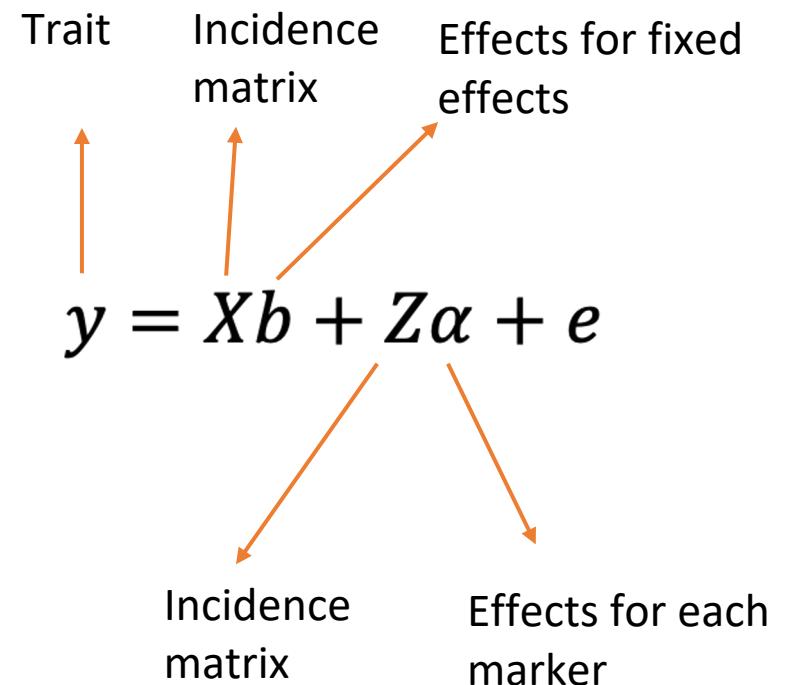
Genomic selection



Genomic selection



Lorenz 2016

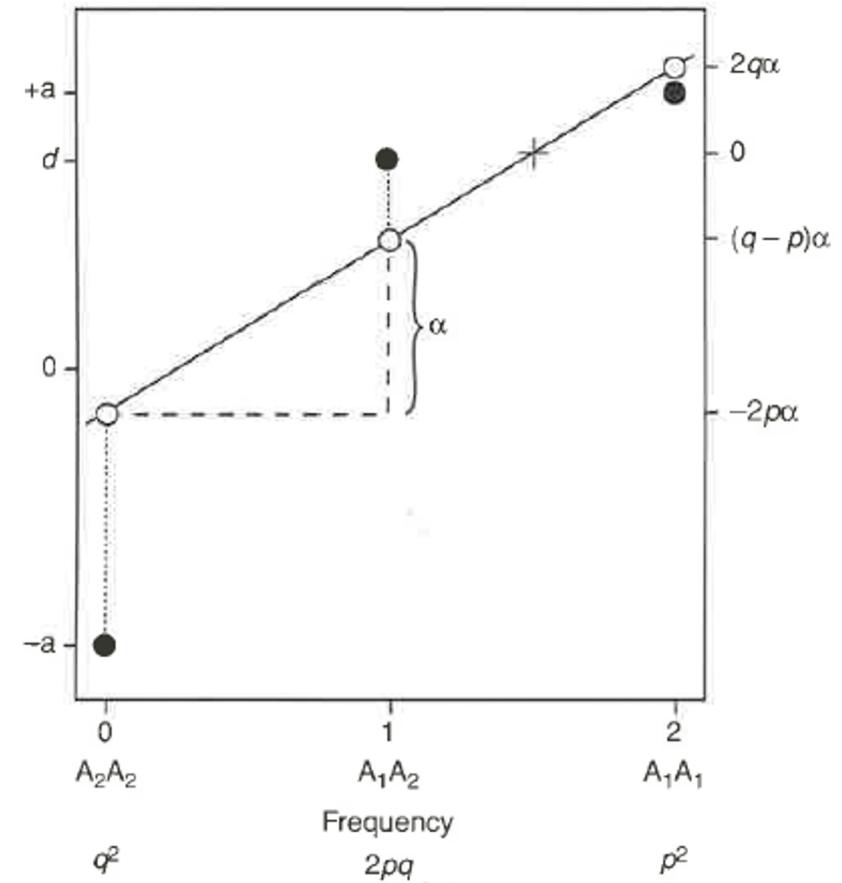


Genomic selection

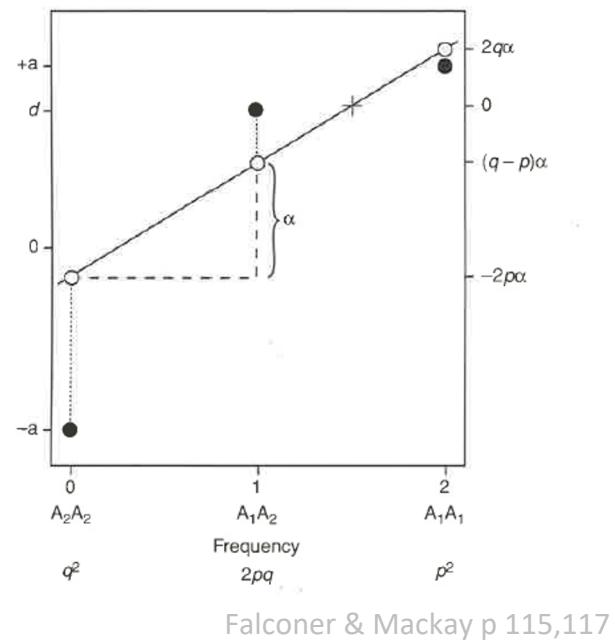
GS uses all molecular markers to predict genomic estimated breeding values (**GEBV**).

Genotype	Breeding value
A1A1	$2\alpha_1 = 2q\alpha$
A1A2	$\alpha_1 + \alpha_2 = (q - p)\alpha$
A2A2	$2\alpha_2 = -2p\alpha$

$$GEBV = \sum_i^p Z_i \alpha_i$$



Genomic selection



Average effects of the alleles

$$\alpha_1 = q[a + d(q - p)] \quad \alpha_2 = -p[a + d(q - p)]$$

Average effects of gene substitution

$$\alpha = \alpha_1 - \alpha_2 = a + d(q - p)$$

$$GEBV = \sum_i^p Z_i \alpha_i$$

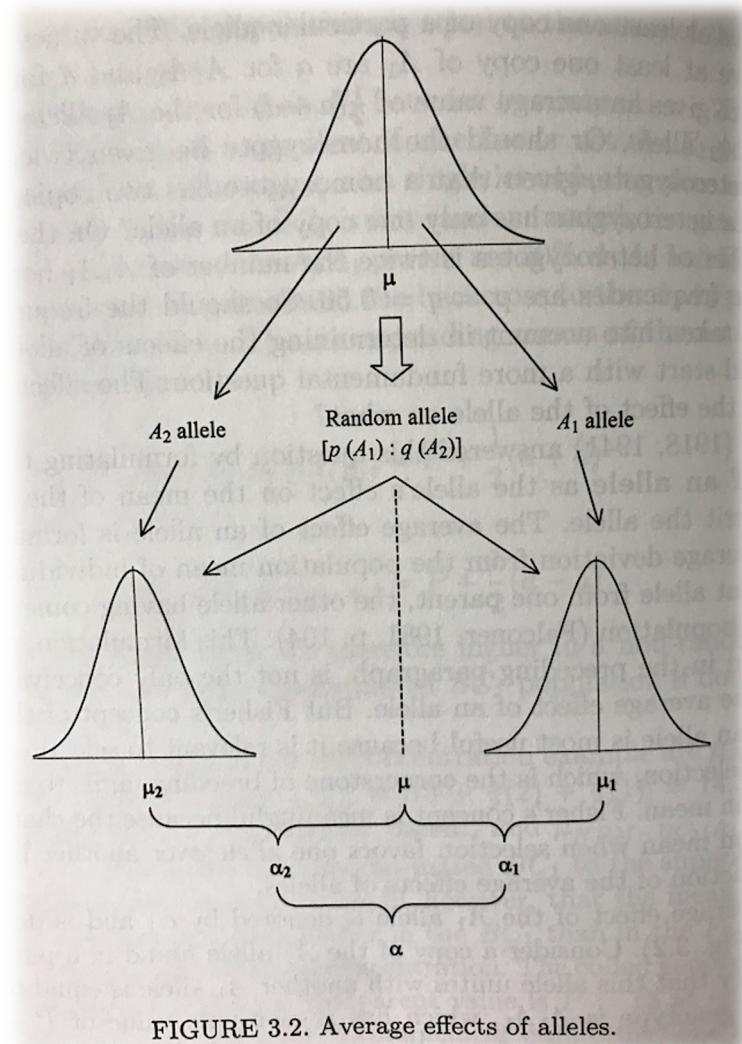
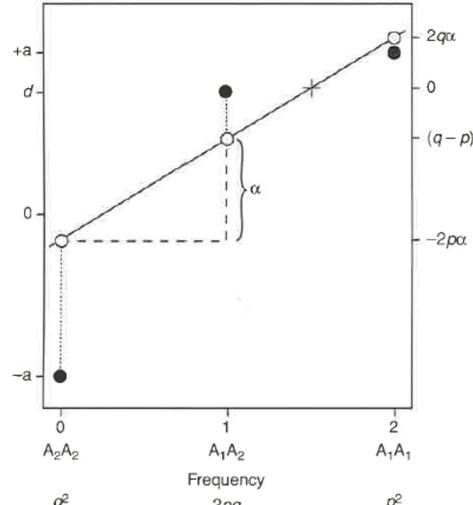


FIGURE 3.2. Average effects of alleles.

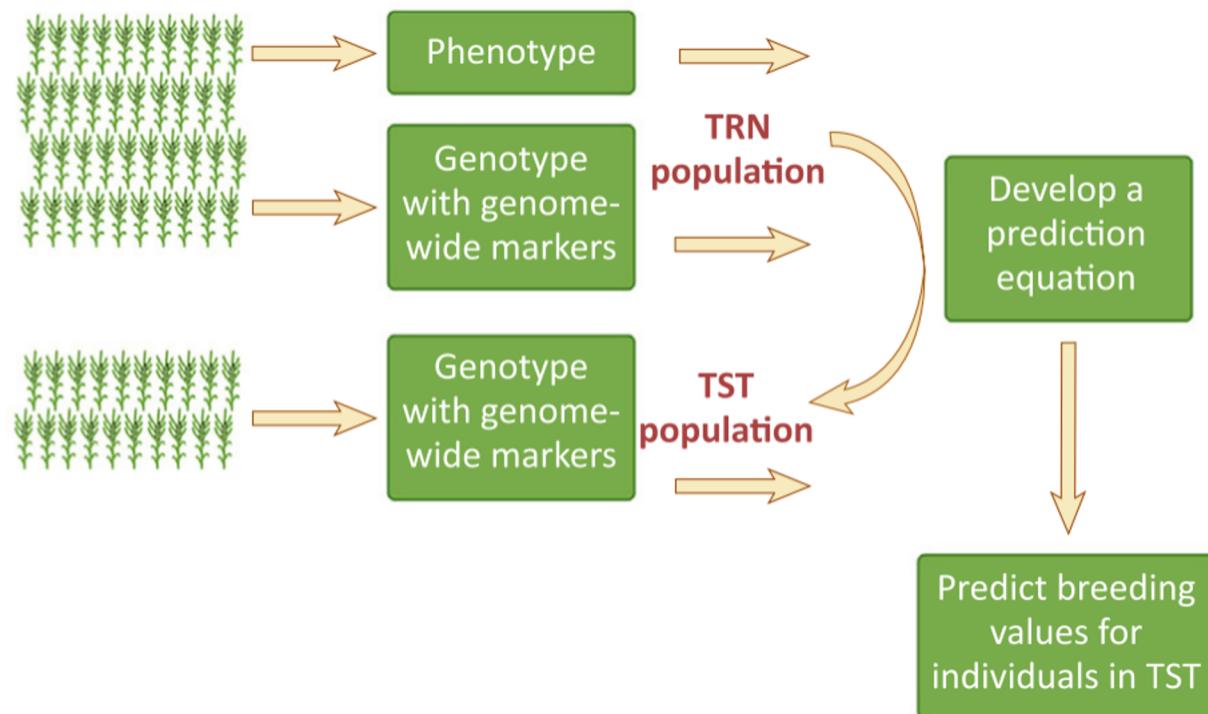
Bernardo 2020

Genomic selection

- GS uses all molecular markers to predict genomic estimated breeding values (**GEBV**).
- GS combines molecular and phenotypic data in a training population to obtain the GEBV of individuals in a testing population that have been genotyped but not phenotyped.



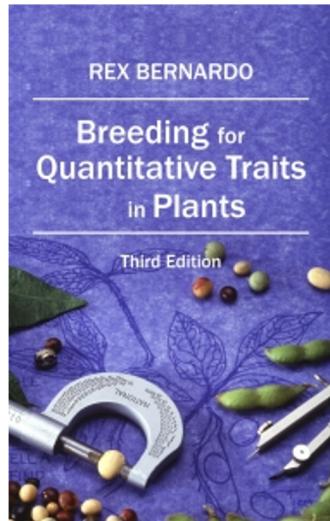
$$GEBV = \sum_i^p Z_i \alpha_i$$



Genomic selection

- Are interested in go deeper in GS basic model?

$$GEBV = \sum_i^p Z_i \alpha_i$$



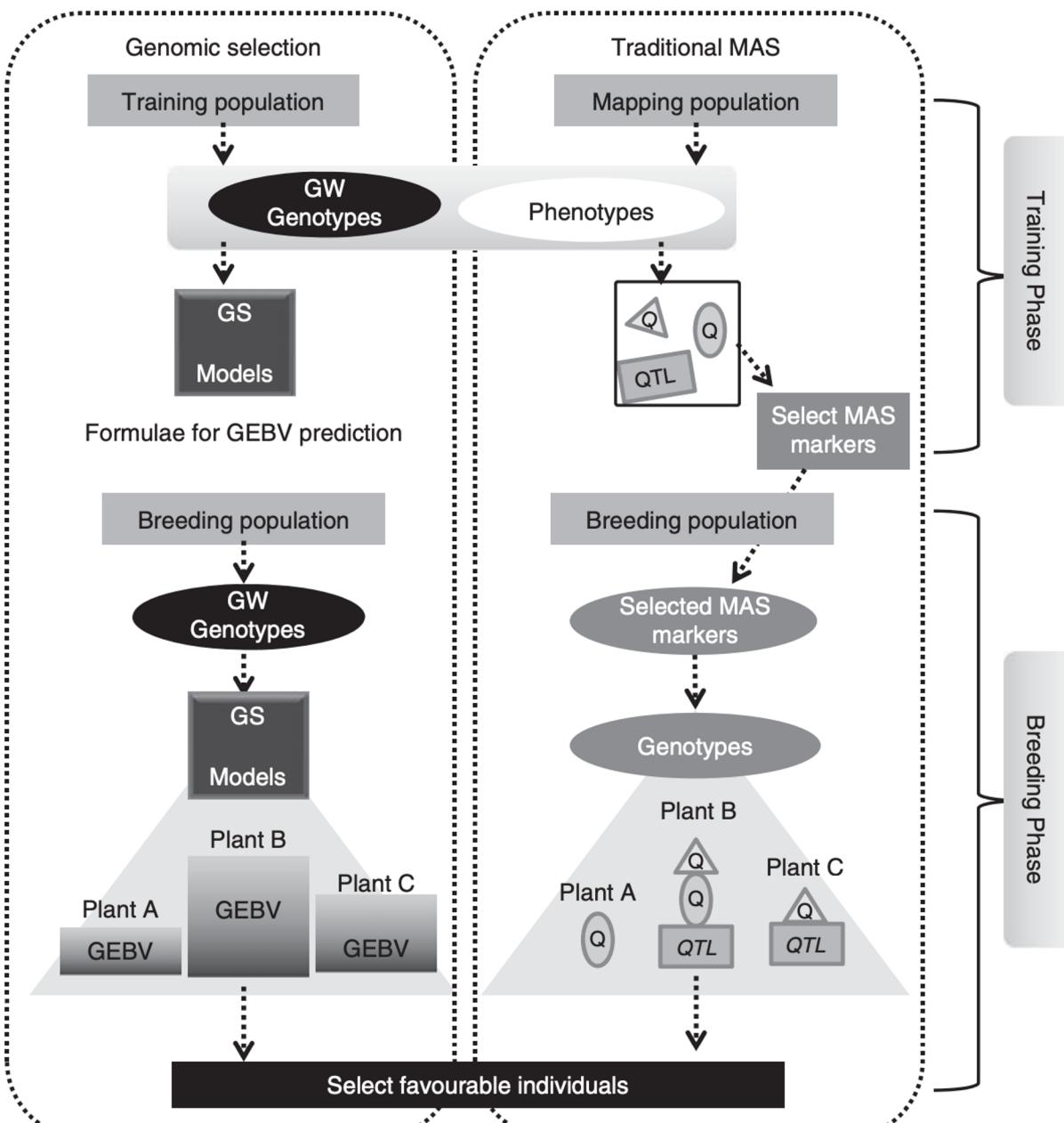
University of Minnesota



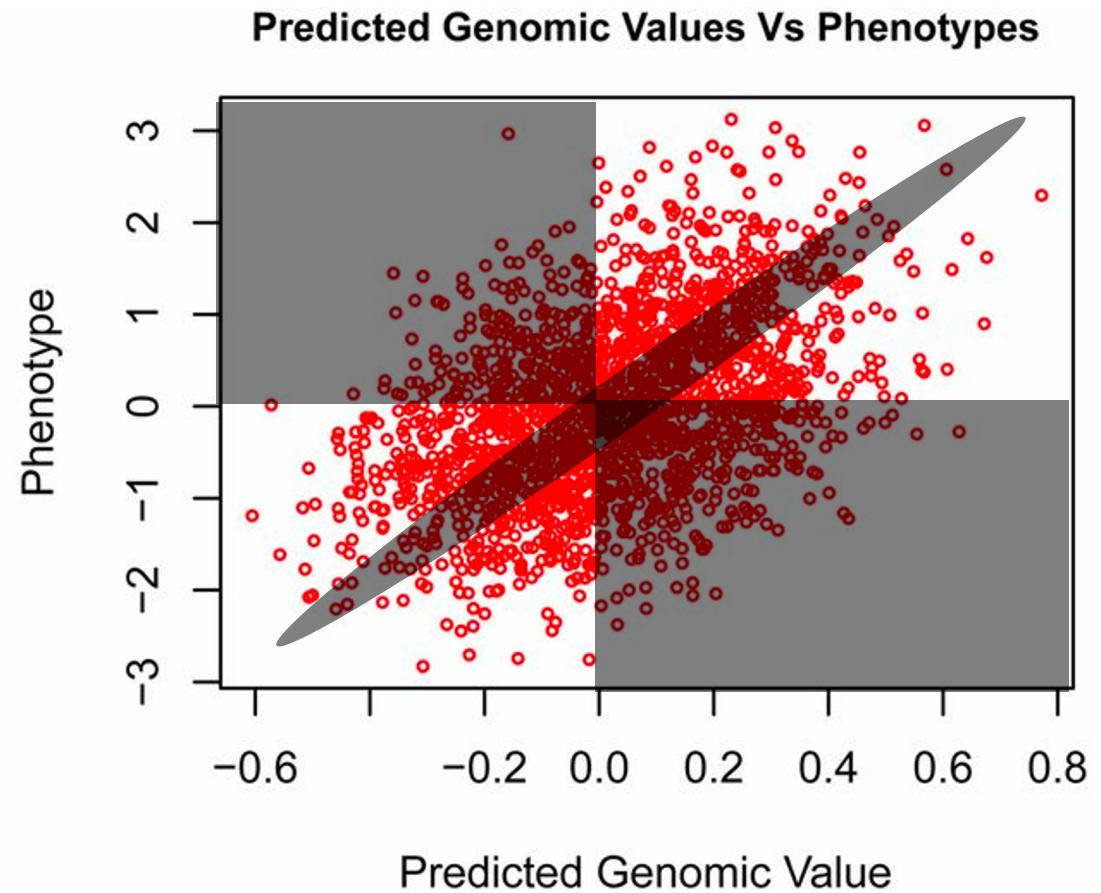
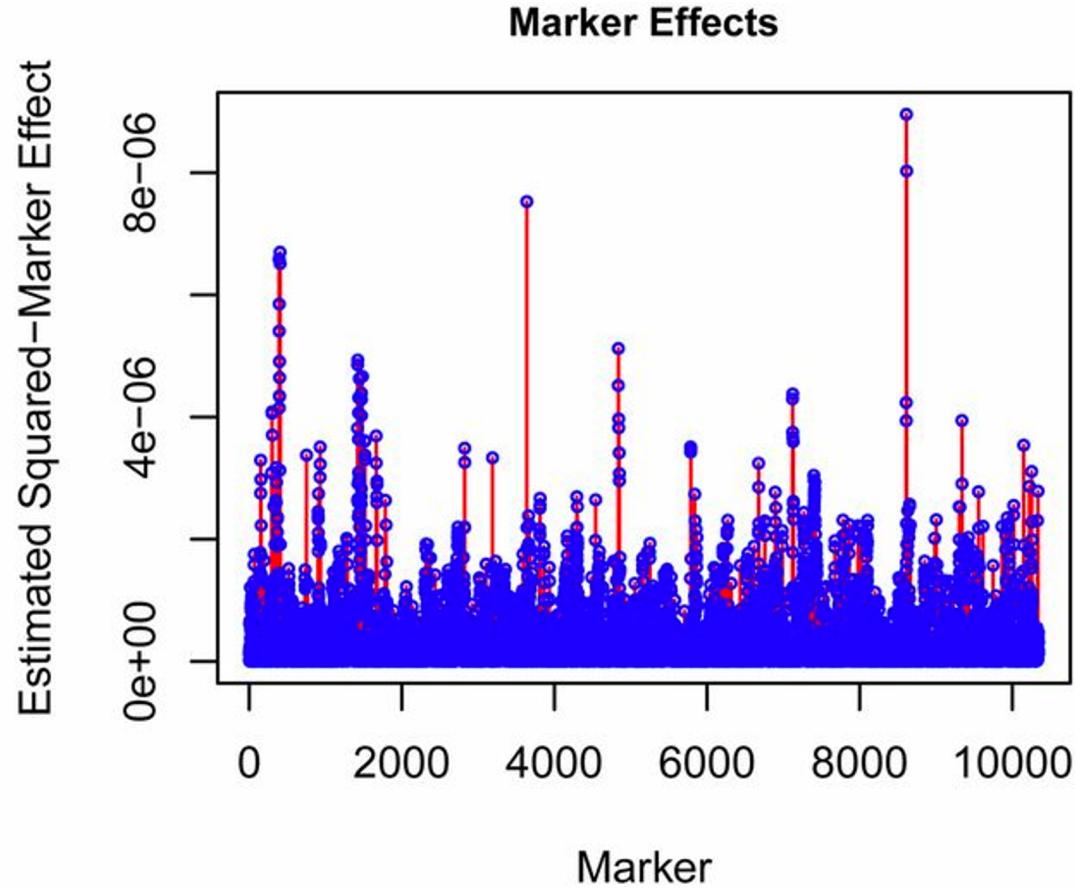
<https://www.youtube.com/watch?v=O7KYISOZhZo&t=1939s>

MAS vs GS

Schemes of GS and traditional MAS for the selection of quantitative traits (right).



Framework for GS



GS is not the solution of all our problems

...but it is helpful

- Reduce breeding cycle
- Increase selection intensity
- Increase genetic variance
- Reduce costs

$$\Delta G_{\text{year}} = \frac{i r_{\text{AI}} \sigma_A}{L}$$

i = Selection intensity

r_{AI} = Accuracy

σ_A = Genetic standard deviation

L = Generation interval