

COMPLEX TRAITS AND QUANTITATIVE GENETICS

#4

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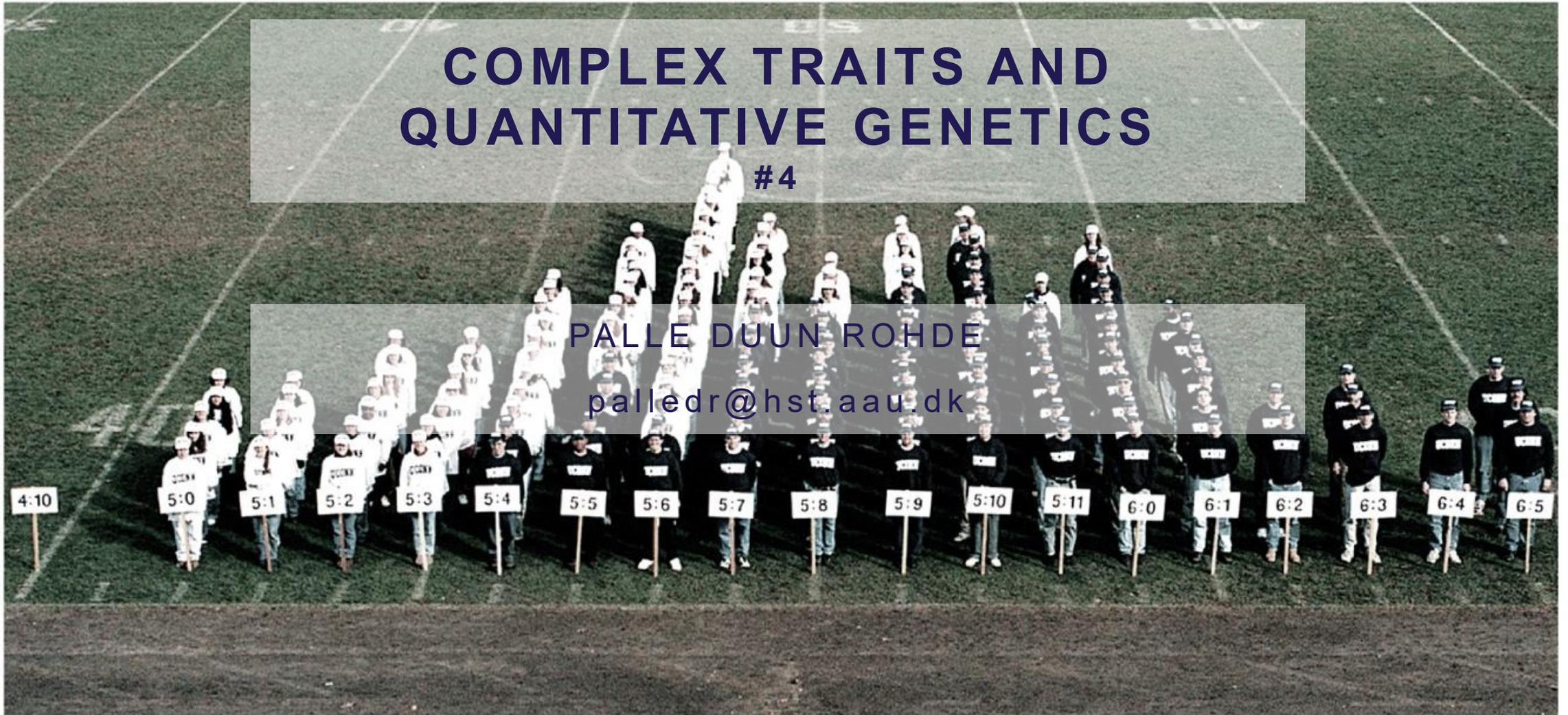
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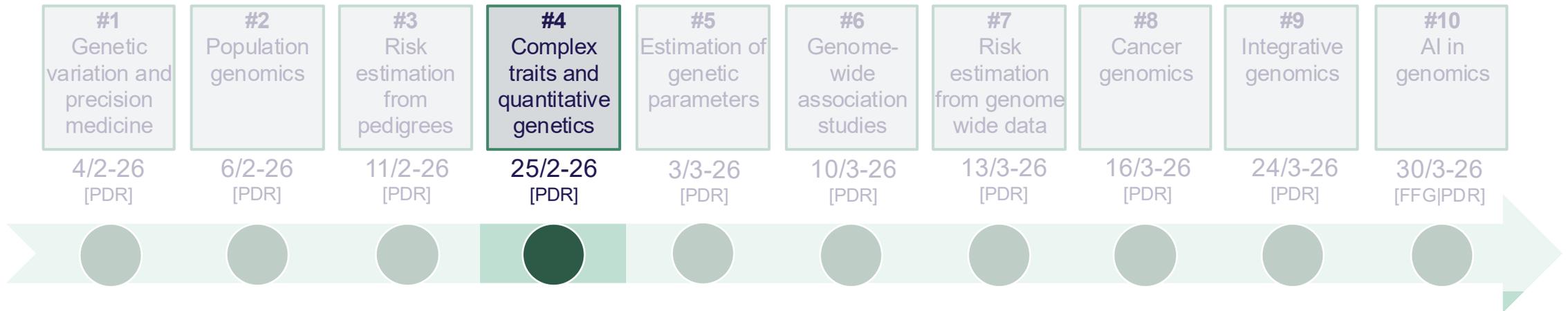
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LETS GET STARTED



LINKAGE AND GENETIC TESTING

Today we will talk about

- ▶ Molecular tools for diagnosis;
 - › direct vs indirect test
- ▶ Complex traits and multifactorial diseases
- ▶ Quantitative genetics

**Moved from
session 3**

AGENDA

- 08:15 – 09:00** **Lecture 1** [*Recap + indirect testing*]
- 09:00 – 09:45** Break + **Exercises A**
- 09:45 – 10:10** **Lecture 2** [*Multifactorial traits*]
- 10:10 – 10:20** **Exercises B**
- 10:20 – 11:00** Break + **Group work**
- 11:00 – 11:30** **Lecture 3** [*Quantitative genetic theory*]
- 11:30 – 11:55** **Exercises C**
- 11:55 – 12:00** **Evaluation at Moodle**

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TOPICS THAT NEED CLARIFICATION

- ▶ Bayes theorem
- ▶ Linkage
- ▶ Gene mapping

BAYES EXAMPLE

$$P(A|B) = \frac{P(B|A)P(A)}{P(B)}$$

$$P(\text{Fire}|\text{Alarm}) = \frac{P(\text{Alarm}|\text{Fire})P(\text{Fire})}{P(\text{Alarm})}$$

- ▶ 1% of houses are on fire
- ▶ Alarm detects fire 95% of the time
- ▶ Alarm falsely rings 5% of the time
- ▶ **If the alarm rings, what is the probability there is actually a fire?**

$$P(\text{Alarm}|\text{Fire}) = 0.95$$

$$P(\text{Fire}) = 0.01$$

$$P(\text{Alarm}|\text{NO Fire}) = 0.05$$

$$P(\text{NO Fire}) = 0.99$$

→

$$P(\text{Alarm}) = 0.95 * 0.01 + 0.05 * 0.99$$

$$P(\text{Fire}) = 0.01 \text{ (prior)}$$

$$P(\text{Alarm}|\text{Fire}) = 0.95 \text{ (likelihood)}$$

$$P(\text{Alarm}) = P(\text{Alarm and Fire}) + P(\text{Alarm and NO fire})$$

-->

$$P(\text{Alarm and Fire})$$

$$= P(\text{Alarm}|\text{Fire}) * P(\text{Fire})$$

$$P(\text{Alarm and NO Fire})$$

$$= P(\text{Alarm}|\text{NO Fire}) * P(\text{NO Fire})$$

$$P(\text{Fire}|\text{Alarm}) = \frac{0.95 * 0.01}{0.95 * 0.01 + 0.05 * 0.99} = 0.16$$

BAYES EXAMPLE

$$P(A|B) = \frac{P(B|A)P(A)}{P(B)}$$

- Disease prevalence = 1 in 10,000
- Carrier frequency \approx 1 in 50
- Test sensitivity = 99%
- False positive rate = 1%
- **If a person tests positive, what is the probability they are actually affected?**

$$P(\text{Positive}|\text{Disease}) = 0.99$$

$$P(\text{Disease}) = 0.0001$$

$$P(\text{Positive}|\text{NO Disease}) = 0.01$$

$$P(\text{NO Disease}) = 0.9999$$

→

$$P(\text{Positive}) = 0.99 * 0.0001 + 0.01 * 0.9999$$

$$\begin{aligned} &P(\text{Disease}|\text{Positive}) \\ &= \frac{P(\text{Positive}|\text{Disease})P(\text{Disease})}{P(\text{Positive})} \end{aligned}$$

$$P(\text{Disease}) = 0.0001 \text{ (prior)}$$

$$P(\text{Positive}|\text{Disease}) = 0.99 \text{ (likelihood)}$$

$$P(\text{Positive}) = P(\text{Positive and Disease}) + P(\text{Positive and NO disease})$$

-->

$$P(\text{Positive and Disease})$$

$$= P(\text{Positive}|\text{Disease}) * P(\text{Disease})$$

$$P(\text{Positive and NO Disease})$$

$$= P(\text{Positive}|\text{NO Disease}) * P(\text{NO Disease})$$

$$P(\text{Disease}|\text{Positive})$$

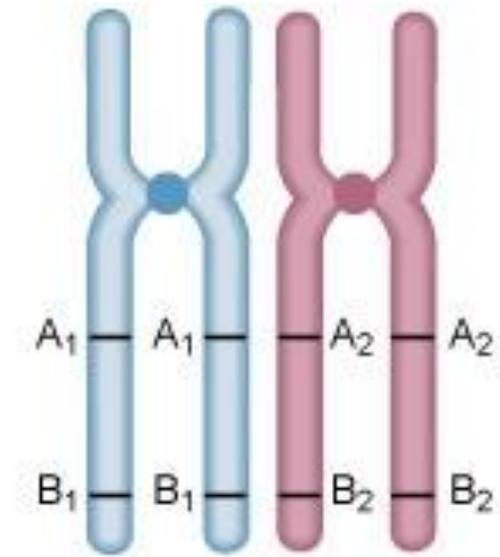
$$= \frac{0.99 * 0.0001}{0.99 * 0.0001 + 0.01 * 0.9999} = 0.009$$

LINKAGE

Mendel's 2. postulate: *Alleles in different loci segregate independently during meiosis*

When two loci are linked (are physically close) the alleles segregate together more often than by chance

We can measure the distance between two loci with **genetic distance** (cM): probability of recombination (R) during meiosis $[(\text{number of R chromosomes} / \text{total chromosomes}) \times 100]$



CROSSTOVERS

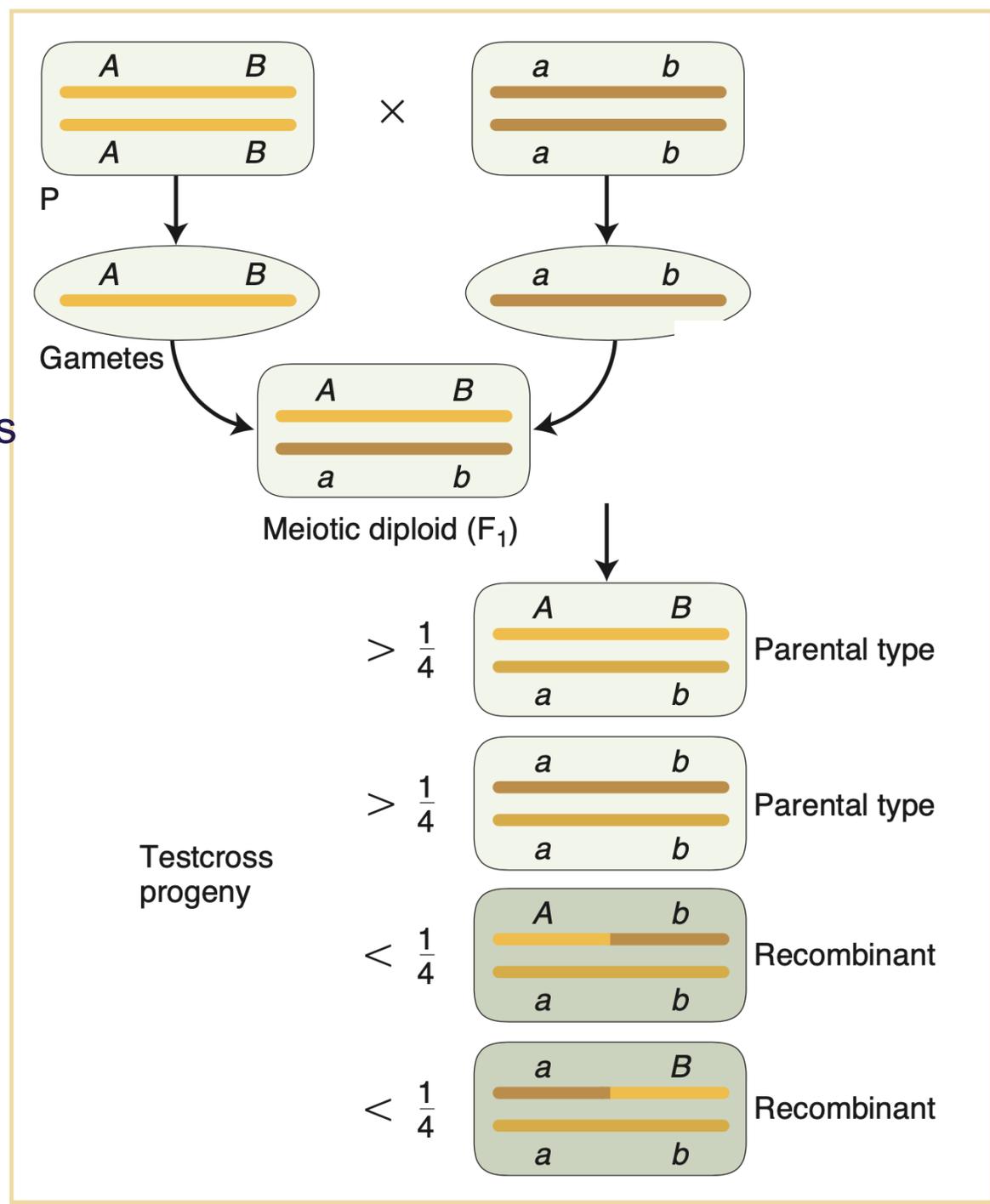
BETWEEN NON-SISTER CHROMATIDS

	Meiotic chromosomes	Meiotic products	
Meioses with no crossover between the genes			Parental Parental Parental Parental
Meioses with a crossover between the genes			Parental Recombinant Recombinant Parental

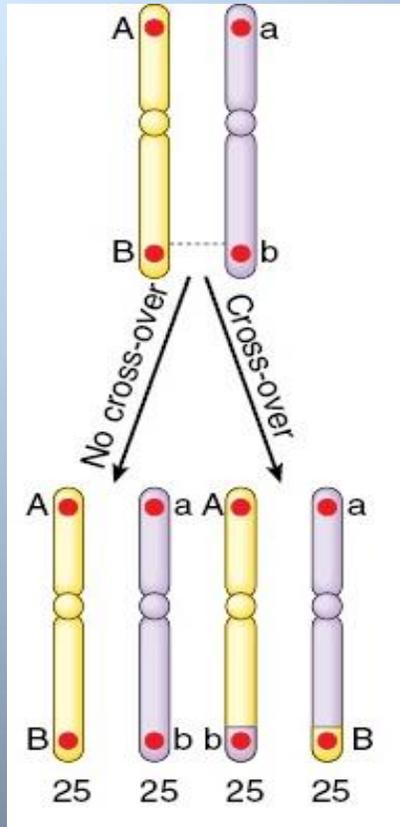
LINKAGE RECOMBINATION

Maximum 50% of the gametes can be recombinants

If 50% of the gametes are recombinants then there will be two parental and two recombinant gametes.



Why is the maximum genetic distance between two loci 50cM?



Genetic distance = [(number of R chromosomes / total chromosomes) x 100] = 50 / 100 * 100 = 50 cM

If there is 10 cM between locus A and locus B – what are the expected gamete frequencies from an individual with the following haplotype AB|ab ?



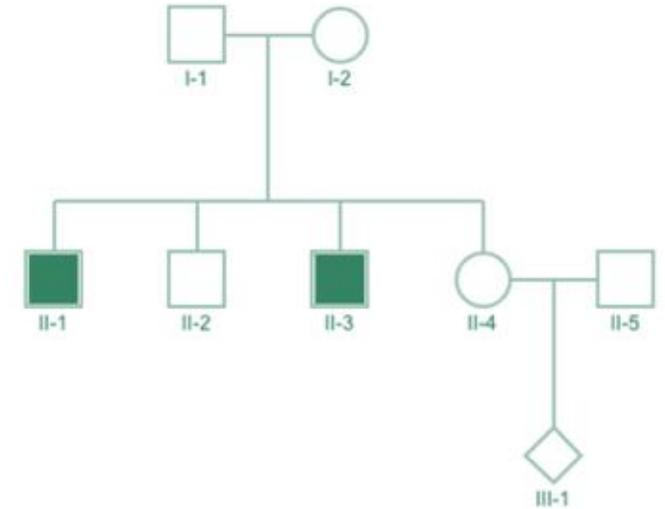
GENETIC TESTING

Direct test

- ❖ When the pathogenic variant is known
 - Track the mutation in a pedigree and design a molecular test

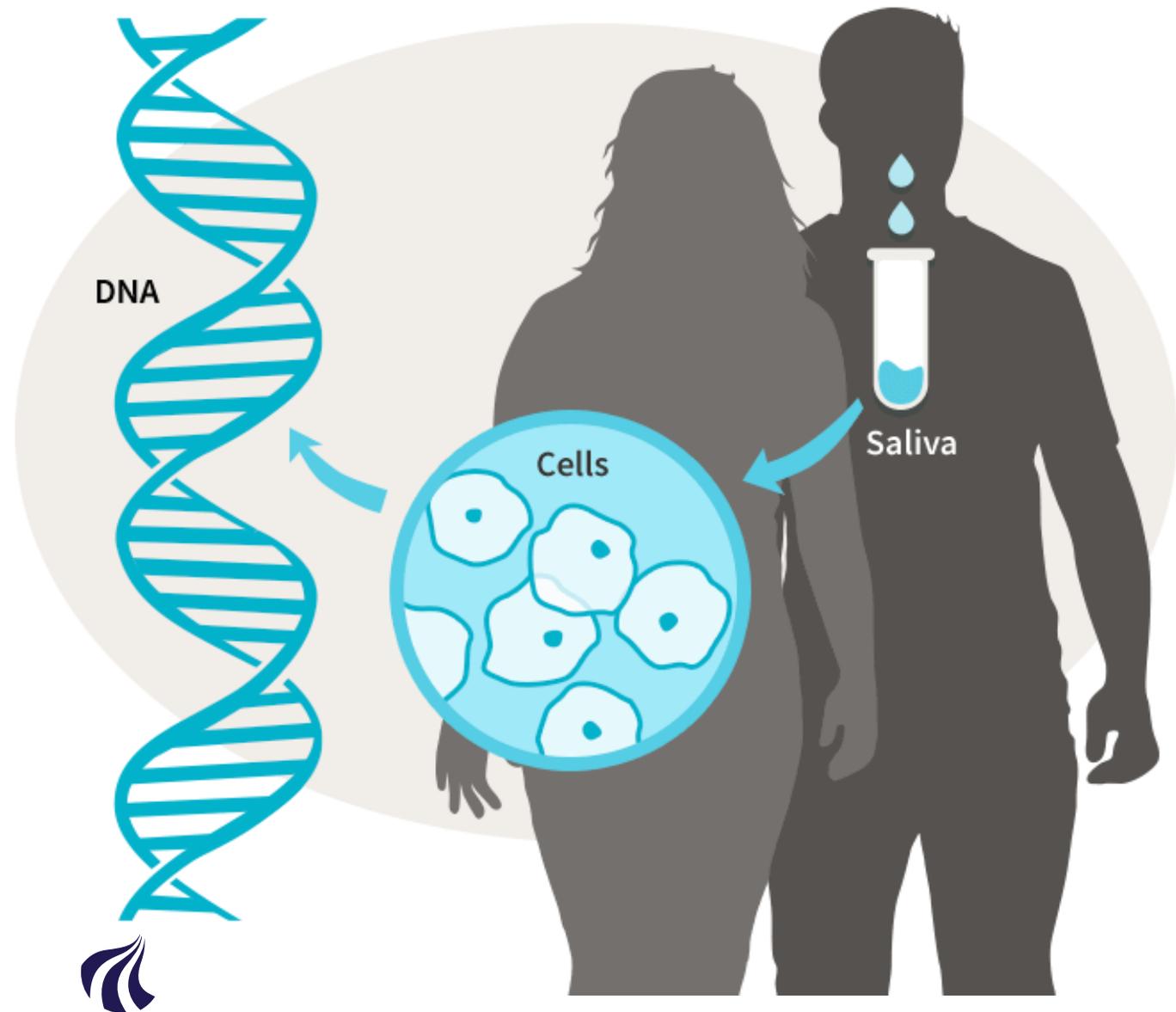
Indirect test

- ❖ When the pathogenic variant is unknown
 - Recurrence risk from family history
 - Recurrence risk from linkage
 - NGS



GENETIC TESTS

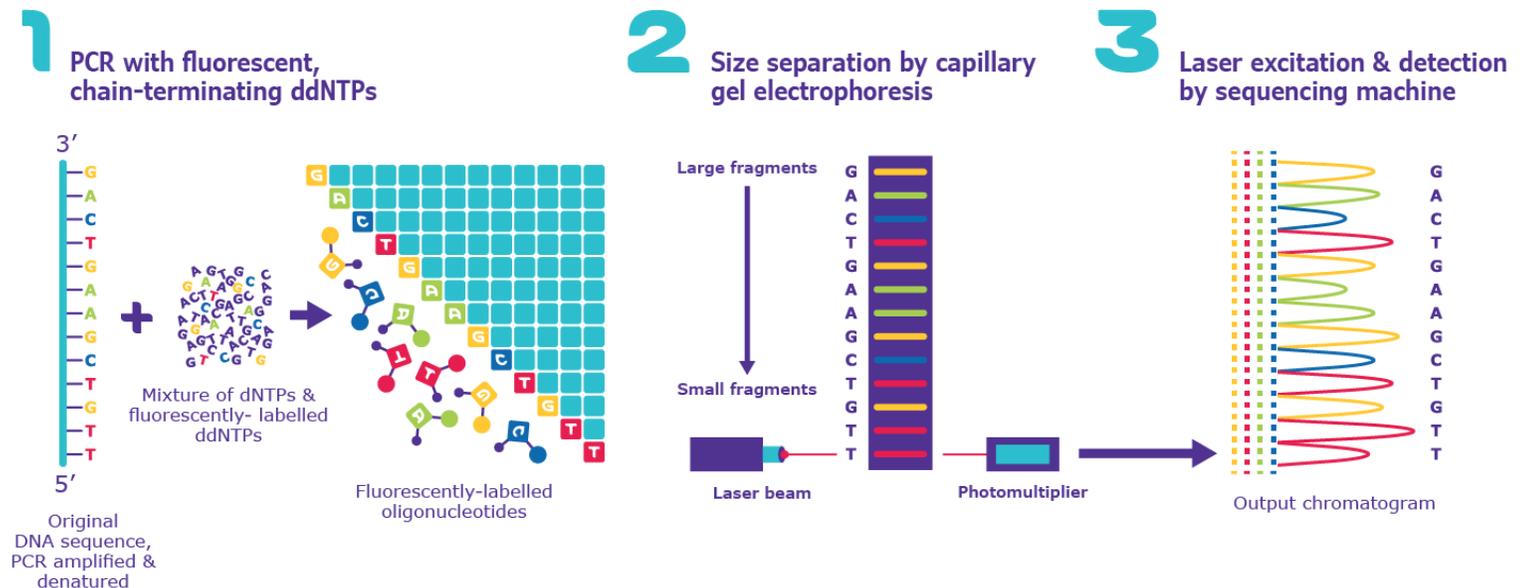
- ❖ **Direct diagnosis** – *known pathogenic variant*
- ❖ **Indirect diagnosis** – *unknown pathogenic variant*
- ❖ Clinical application of Next-generation sequencing (NGS)



DIRECT GENETIC DIAGNOSIS

KNOWN PATHOGENIC VARIANT

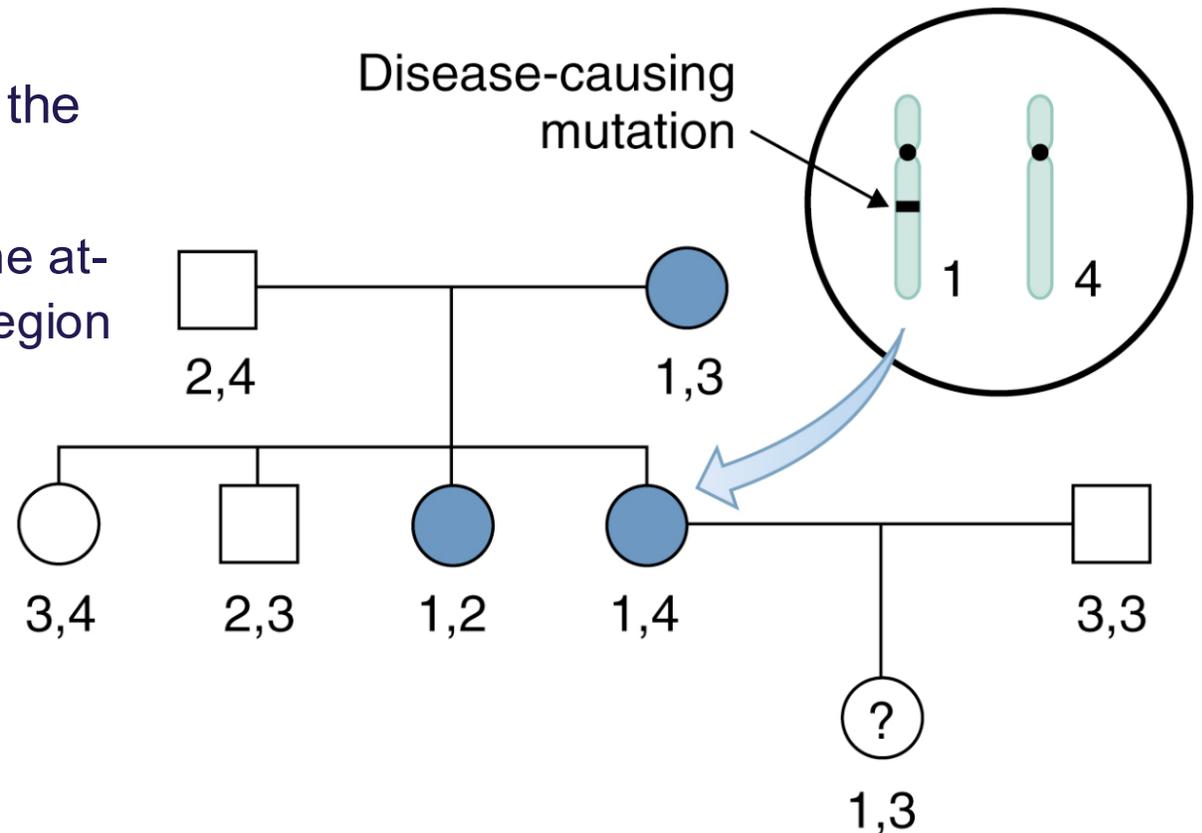
- ▶ We know the disease-causing mutation.
- ▶ Design a molecular assay that can target that specific mutation, e.g., Sanger sequencing



INDIRECT GENETIC DIAGNOSIS

UNKNOWN PATHOGENIC VARIANT

- ▶ We do not know the exact disease-causing mutation.
- ▶ Instead, we look at genetic **markers** close to the disease-causing mutation.
- ▶ *Advantage* – the marker tells us whether the at-risk person has inherited the chromosome region that contains a disease-causing mutation.



LINKAGE MAPPING

- Follow the genotype with the disease through the pedigree
 - Linkage phase (identify haplotypes)

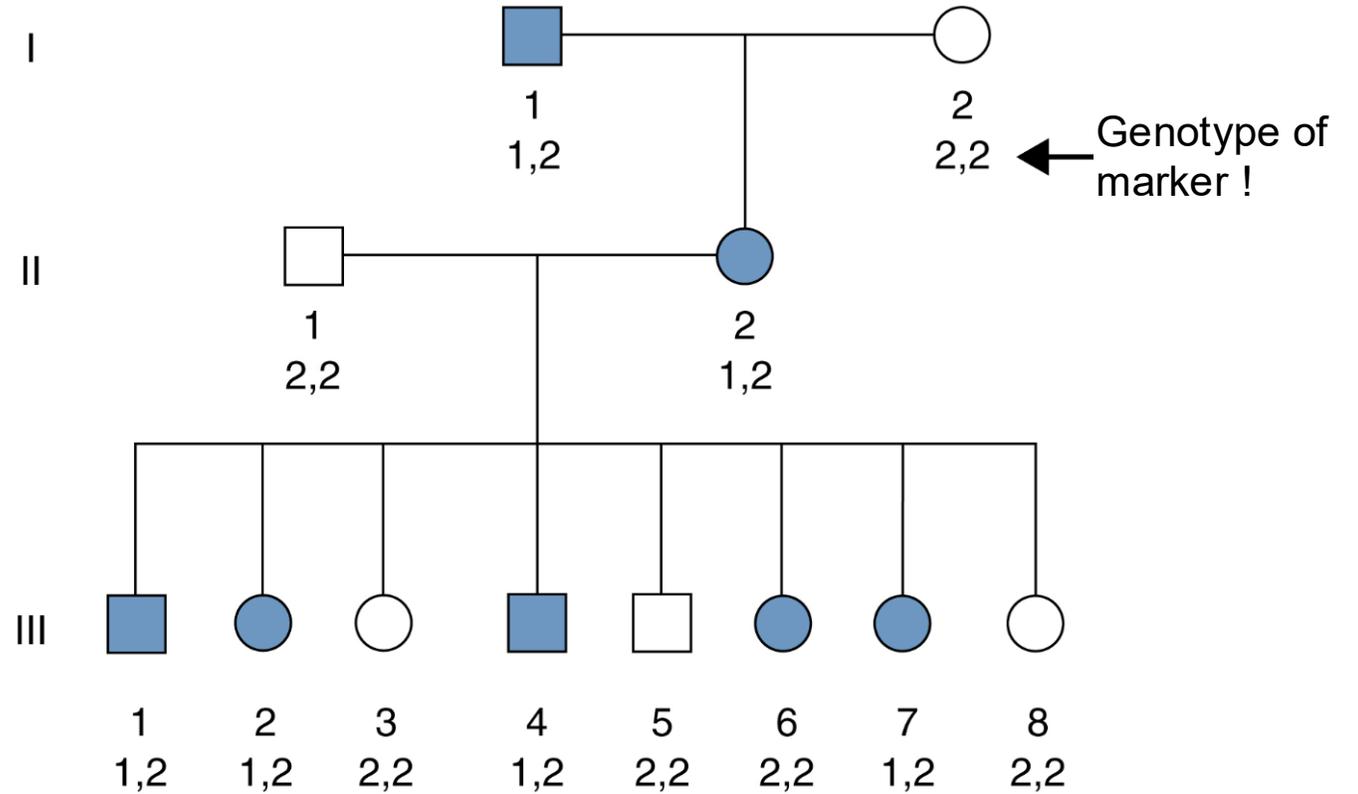
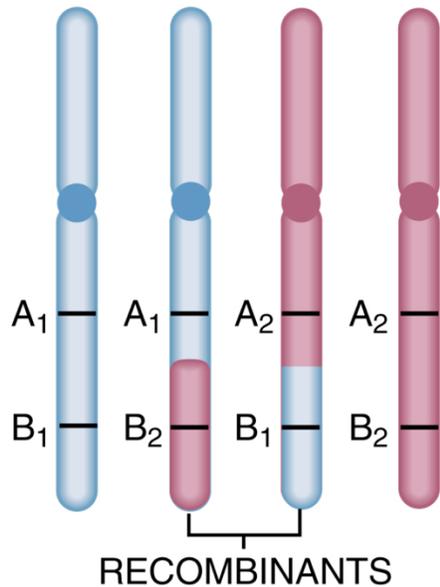


Fig. 8.4

LINKAGE MAPPING

- ▶ Is there something strange going on in the 3rd generation?

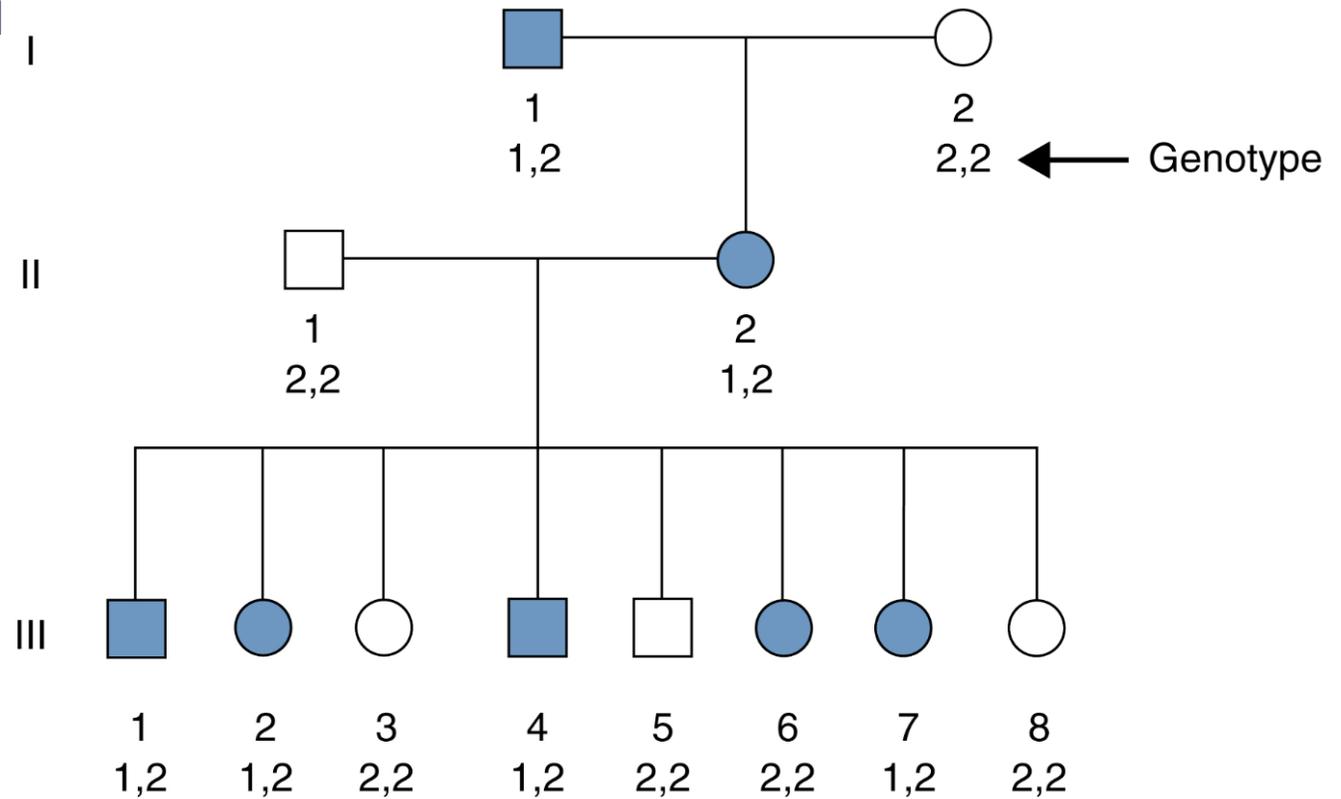
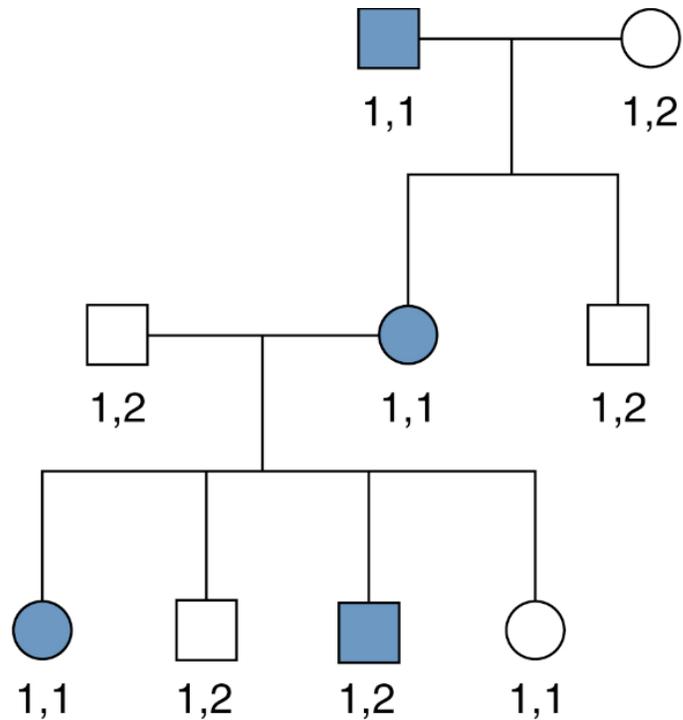


Fig. 8.4

(UN)INFORMATIVE MARKERS

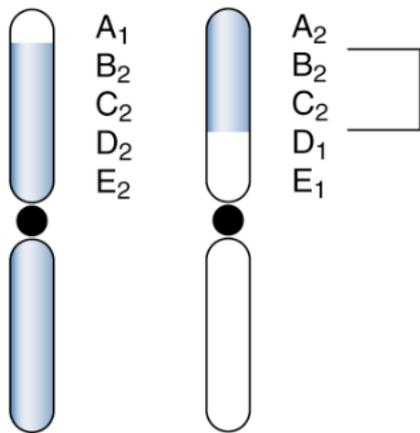


Which marker is linked with the disease?

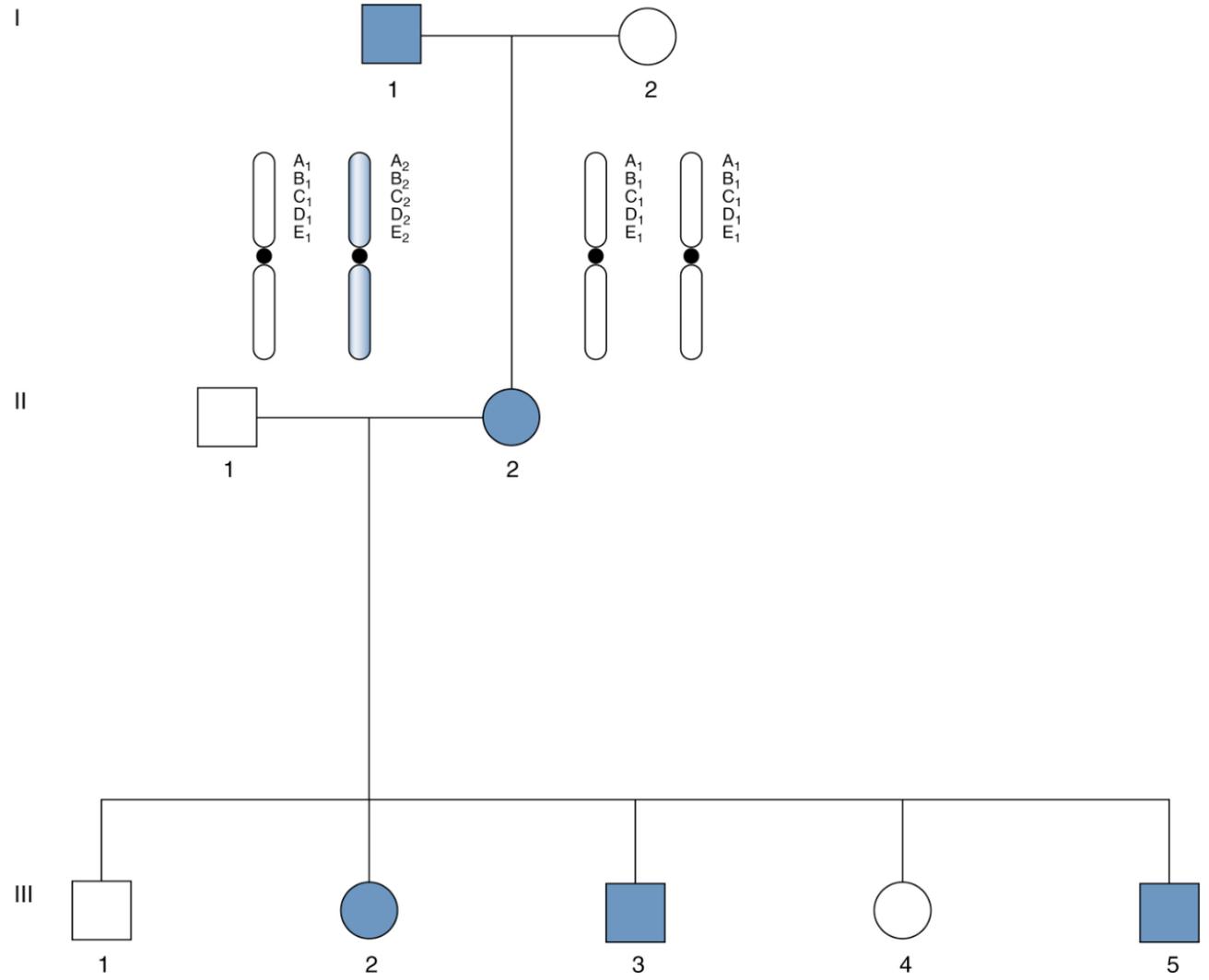
Much better to find a highly polymorphic variant!

MANY POLYMORPHIC MARKERS HELPS

Recombination events aids to pinpoint the disease-causing region



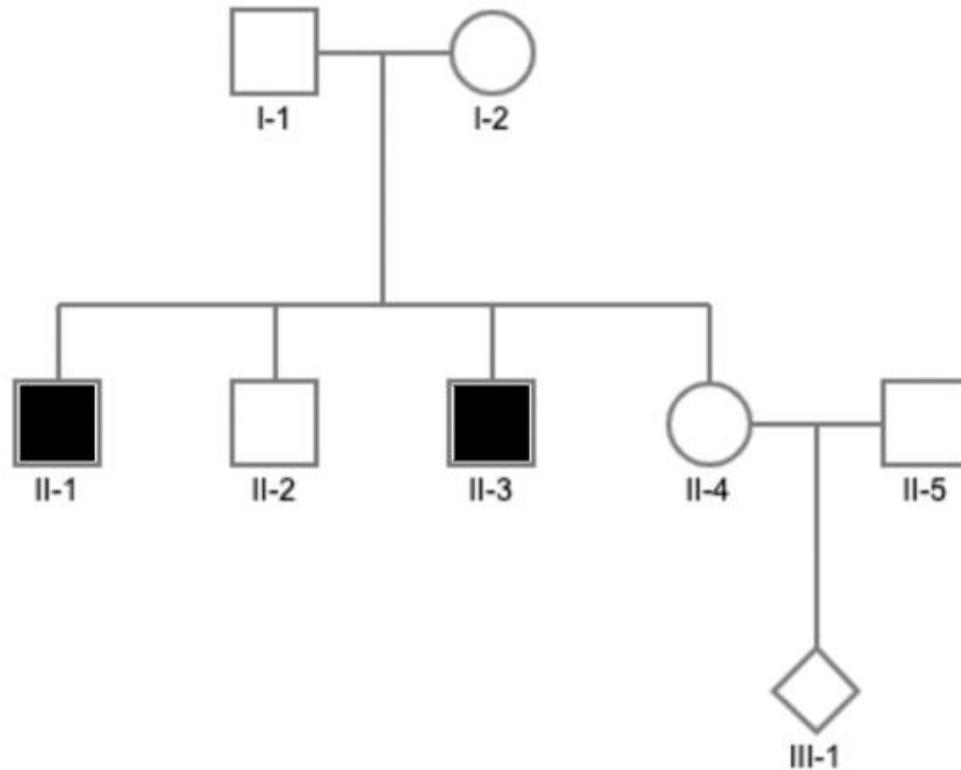
Recombinants localize the disease-causing gene to the region between markers A and D



FOLLOW THE DISEASE AND GENETIC MARKERS

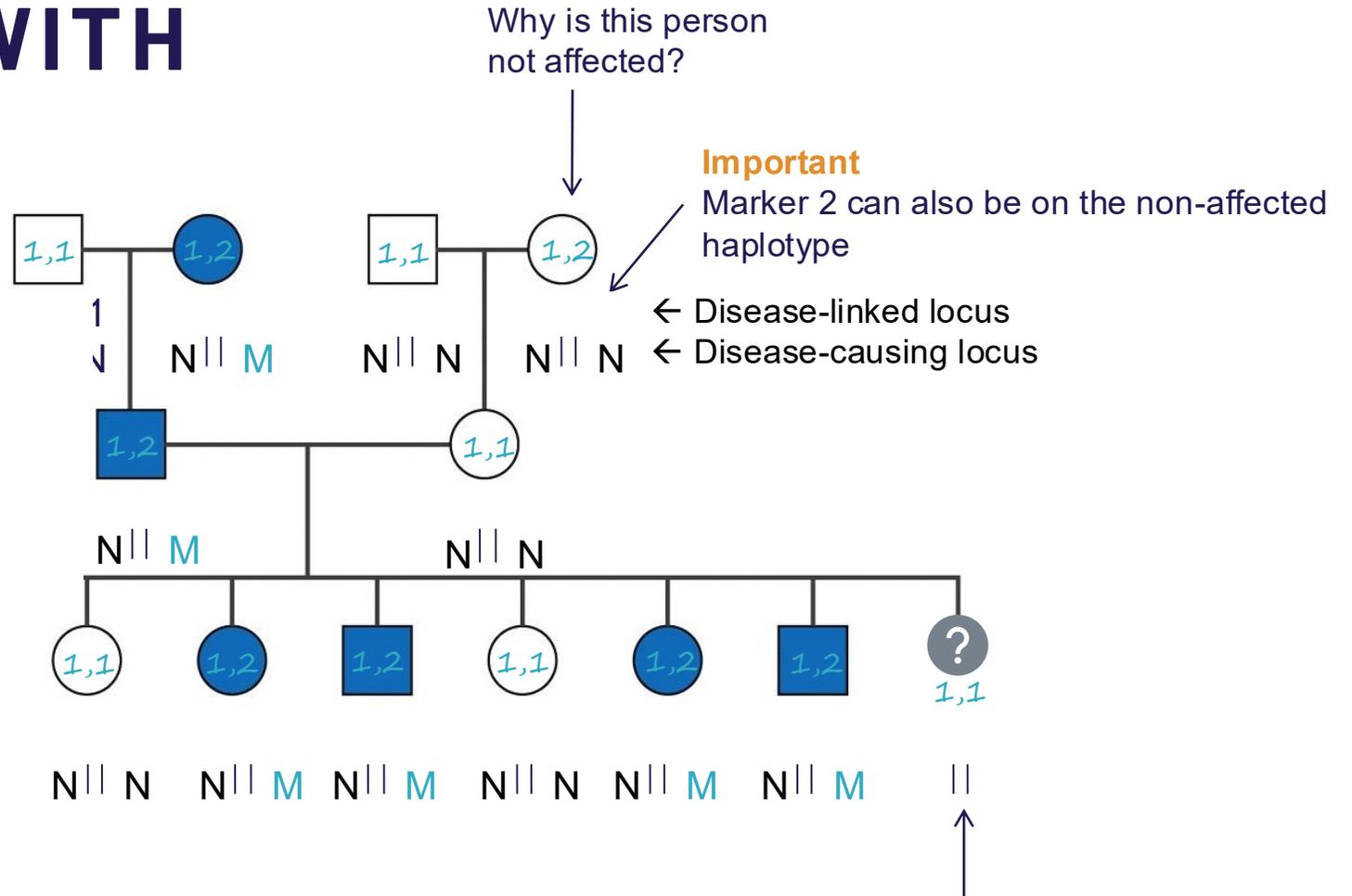
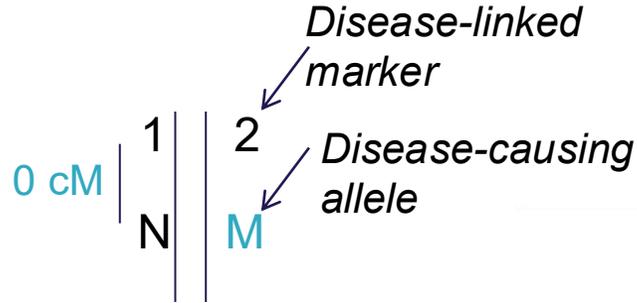
1) Based on the pedigree, what is the risk that III-1 will have the disease?

Assume X-linked



2) Based on the molecular data, what is the risk that III-1 will have the disease?

RISK OF CHILD WITH DISEASE?



Important

Marker 2 is the disease-linked allele in the disease-linked locus

Allele 2 is not pathogenic in itself

Allele 2 can also be on the non-affected haplotype

INDIRECT VS DIRECT DIAGNOSIS

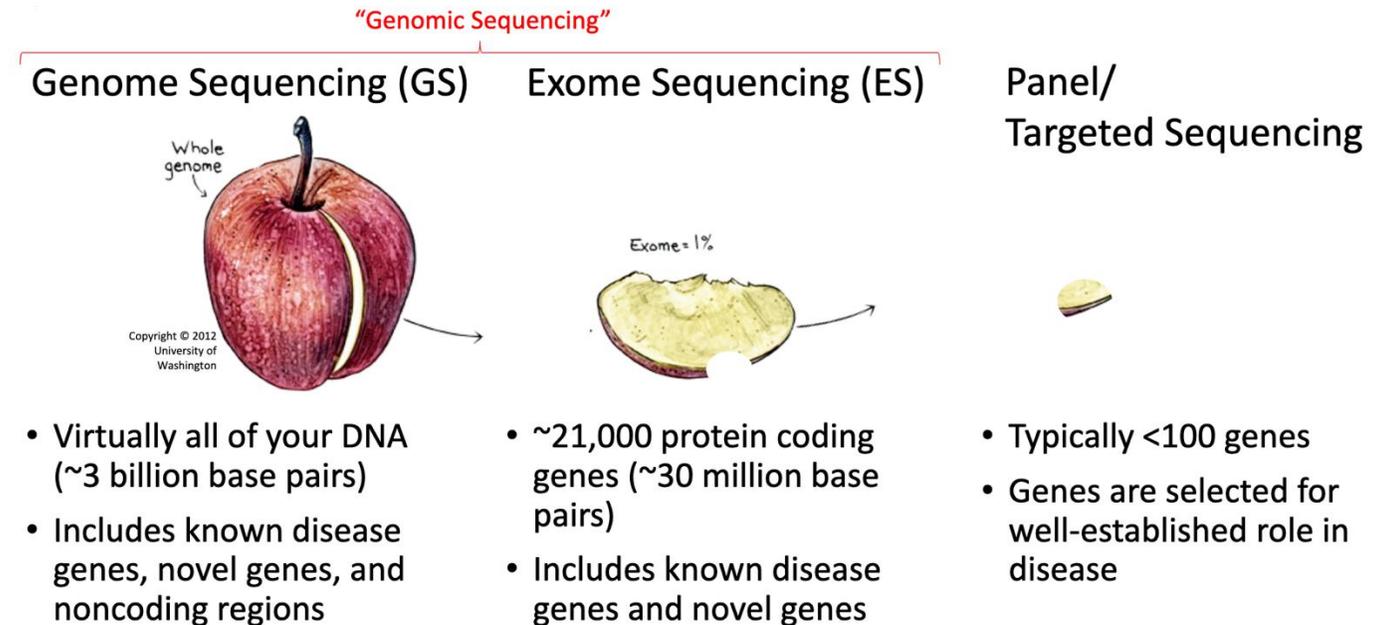
Because we know the mutation, family information is not needed, uninformative markers and recombination is not an issue

Attribute	Indirect Diagnosis	Direct Diagnosis
Family information needed	Yes	No
Errors possible because of recombination	Yes	No
Markers may be uninformative	Yes	No
Single test can uncover multiple mutations	Yes	Yes (by DNA sequencing)
Disease-causing mutation must be identified	No	Yes

- Markers should be informative
- Large families are needed to establish linkage phase
- Recombination events make it tricky – chose markers that are 0 cM to disease-causing locus

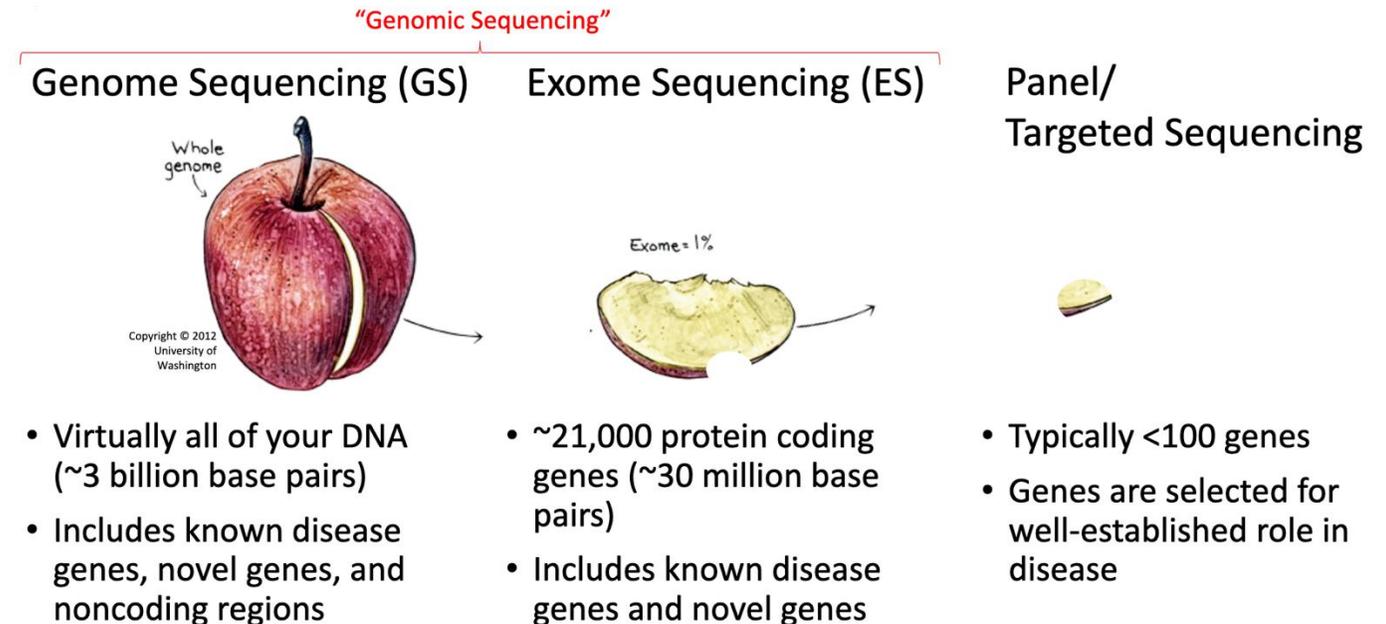
CLINICAL APPLICATION OF NEXT-GENERATION SEQUENCING (NGS)

- ▶ A general disadvantage is that often multiple different assays are needed – NGS solves this
 - ▶ e.g., in the case of genetic heterogeneity
- ▶ NGS can be used on disorders that have variable penetrance



CLINICAL APPLICATION OF NEXT-GENERATION SEQUENCING (NGS)

- ❖ In principle all variants detected
- ❖ Relatively low cost (3000 kr)
- ❖ Things that took 20 years can now be done in few days
- ❖ Produces lots of data
- ❖ Can be hard to find the real pathogenic variant, if not seen before
- ❖ Mutations, that we were not looking for (e.g., *BRCA1* mutation) – incidental finding



GENETIC TESTS

When the pathogenic variant is known

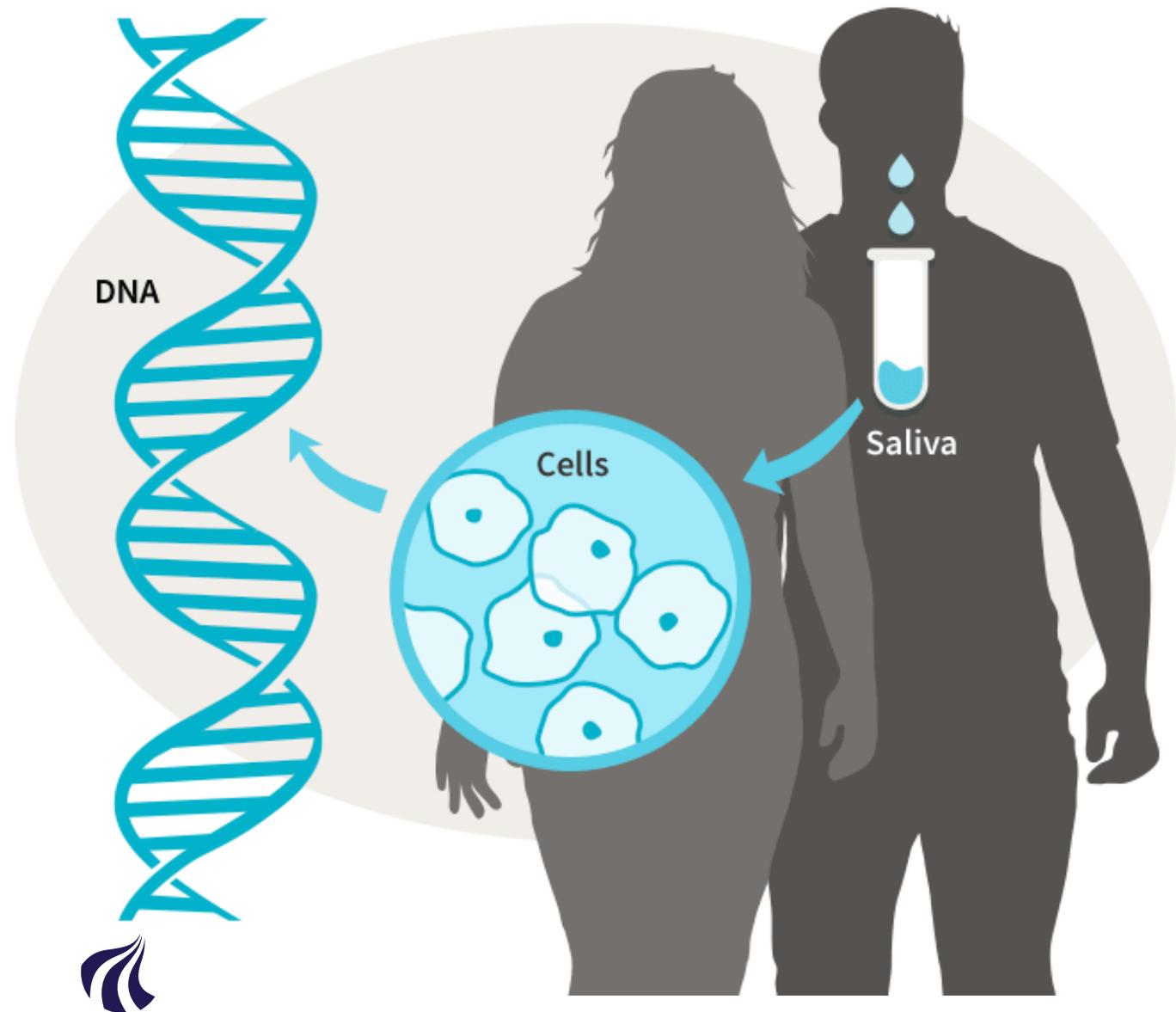
→ Risk from direct test

When the pathogenic variant is unknown

→ Risk from pedigree [inheritance pattern]

→ Risk from indirect test [genomic region]

→ Risk from NGS [filter, filter, filter...]



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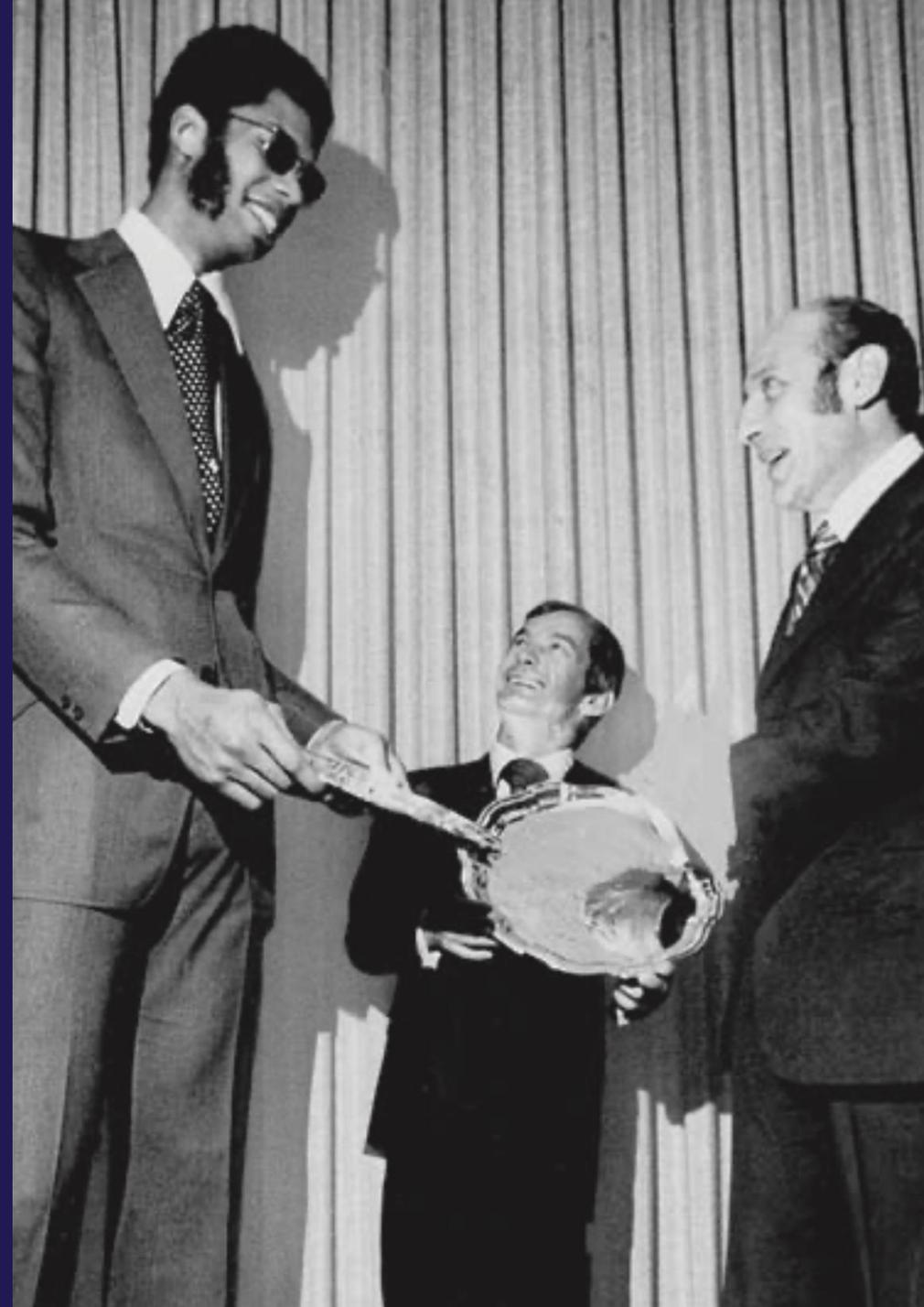


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MULTIFACTORIAL TRAITS

- ❖ Types of trait-inheritance
- ❖ Liability model
- ❖ Recurrence risk
- ❖ Environmental exposures modulate outcomes



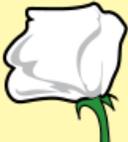
DIFFERENT MODE OF INHERITANCES

- ❖ Monogenic (single gene variant)
- ❖ Polygenic (many gene variants)
- ❖ Multifactorial (many gene variants plus environment exposures)



MENDELIAN (MONOGENIC) TRAITS

QUALITATIVE TRAITS

Seed		Flower	Pod		Stem	
Form	Cotyledons	Color	Form	Color	Place	Size
						
Grey & Round	Yellow	White	Full	Yellow	Axial pods, Flowers along	Long (6-7ft)
						
White & Wrinkled	Green	Violet	Constricted	Green	Terminal pods, Flowers top	Short \leq -1ft
1	2	3	4	5	6	7

QUANTITATIVE TRAITS

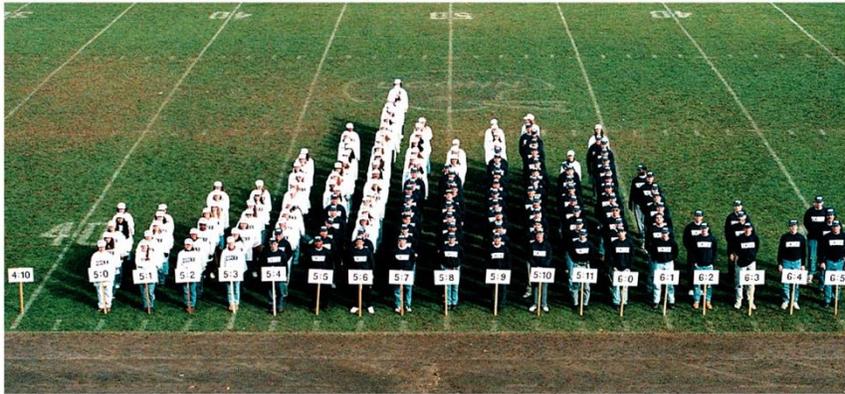


Many quantitative traits has **continuous variation**

QUANTITATIVE TRAITS

IN DIFFERENT SHAPES

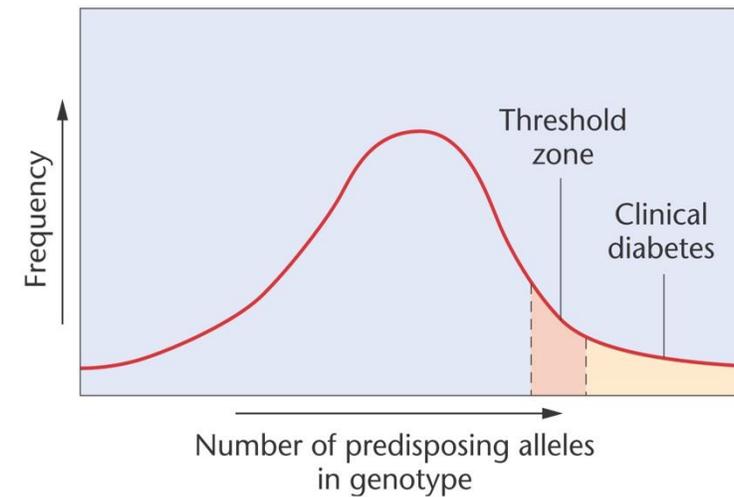
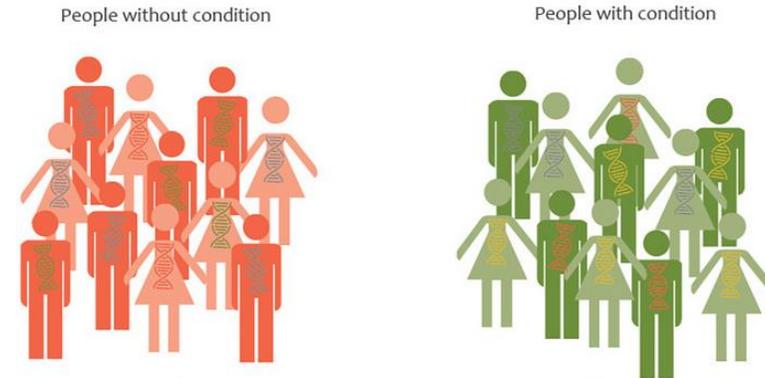
Continuous variation



Categorical variation



Threshold traits

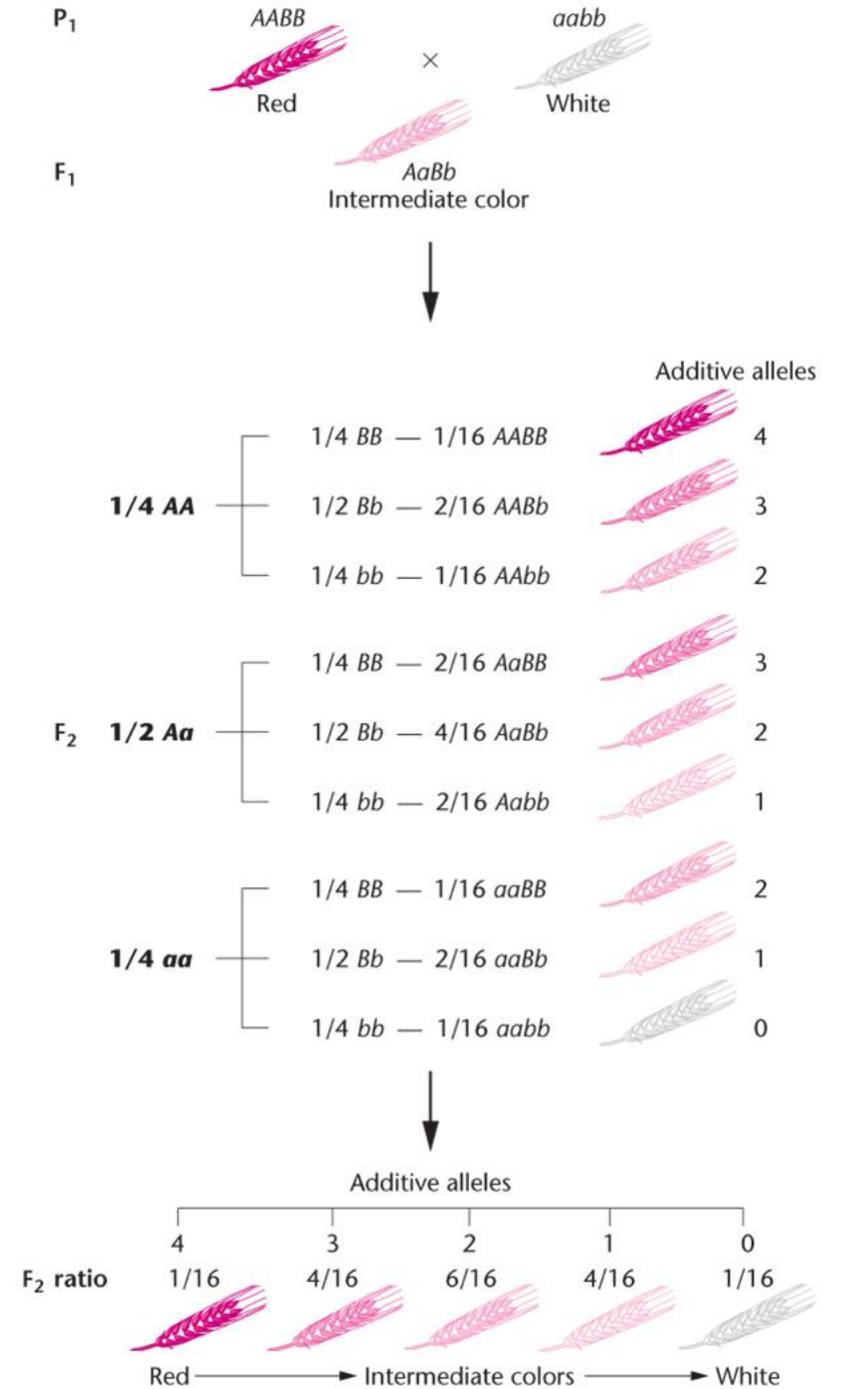


Why do quantitative traits
follow a normal distribution?



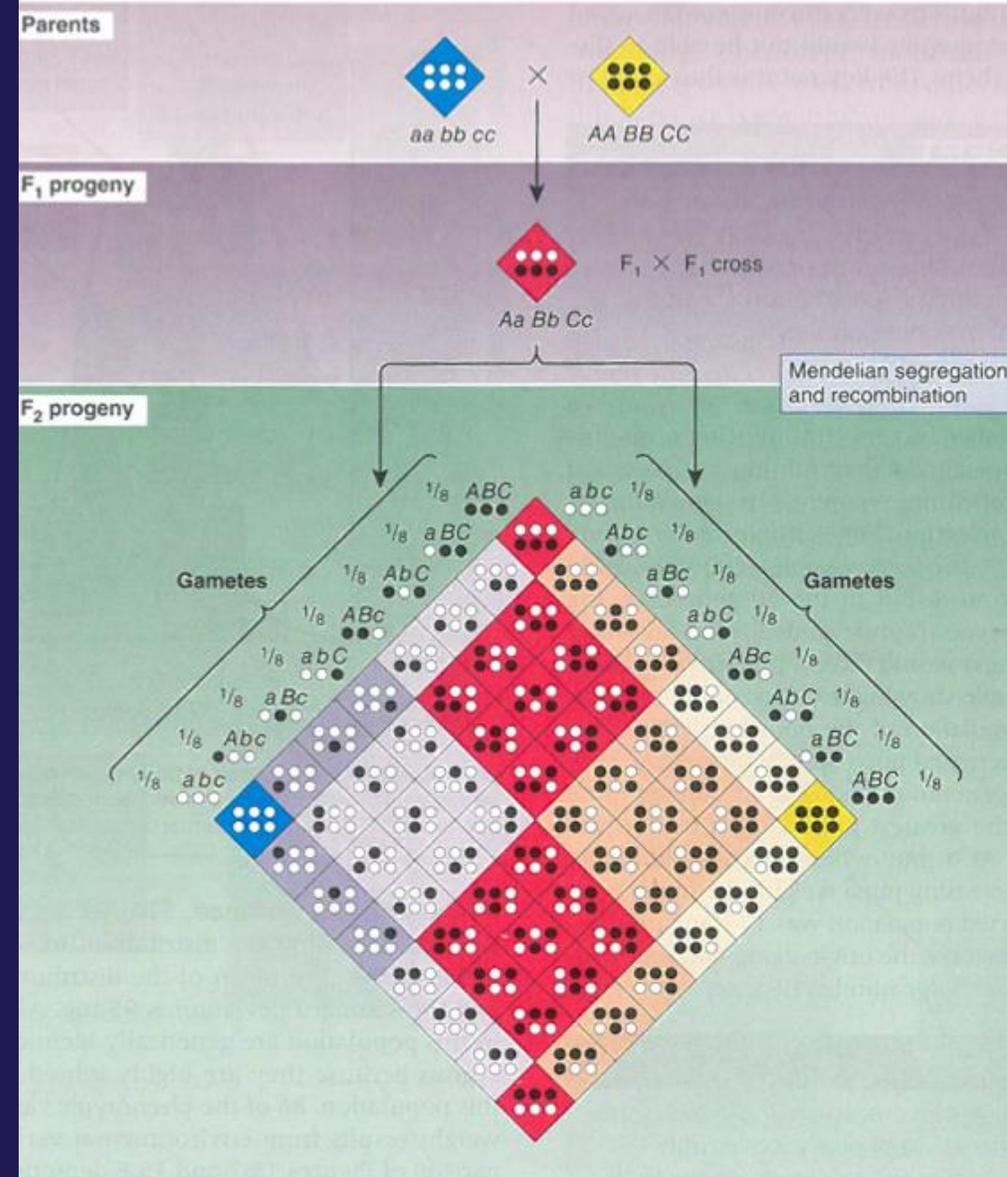
MULTIPLE GENE MODEL

The normal distribution of quantitative traits is caused by the joint action of *many gene varieties with additive genetic effects*.

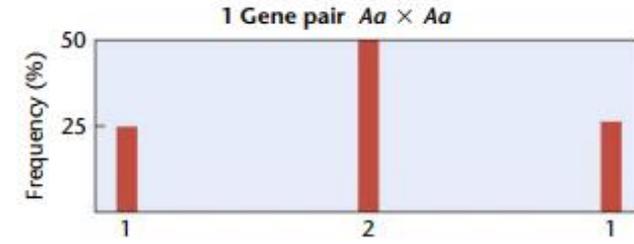
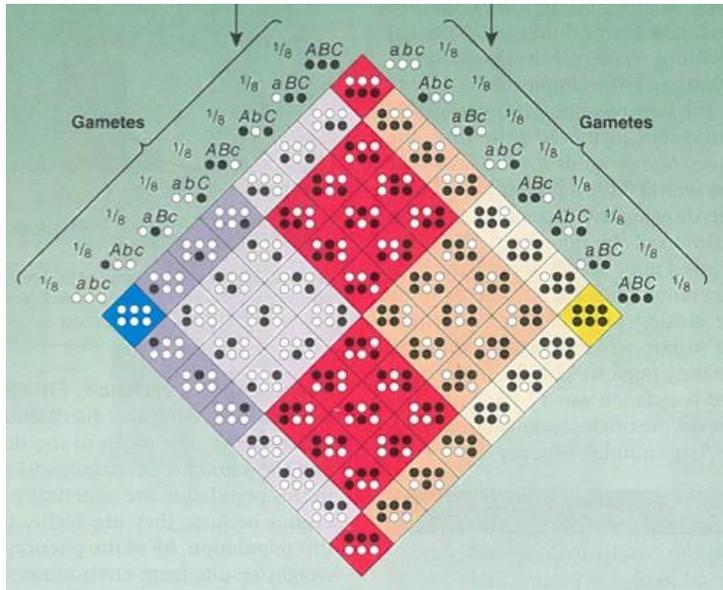
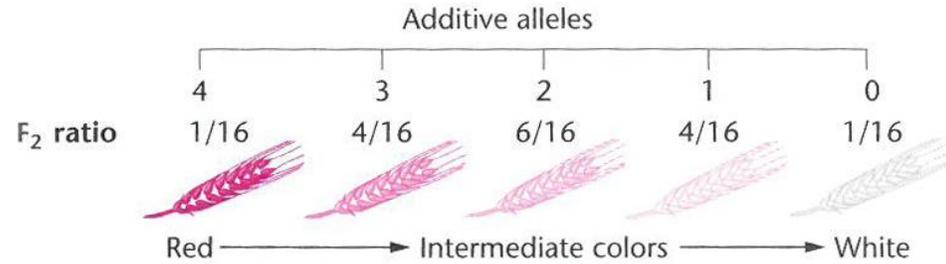


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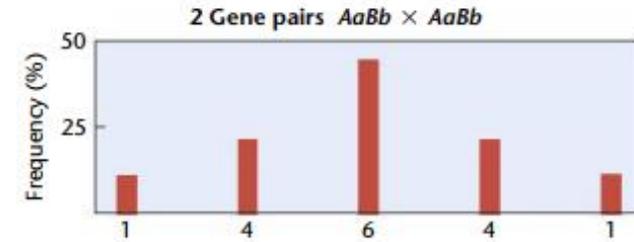
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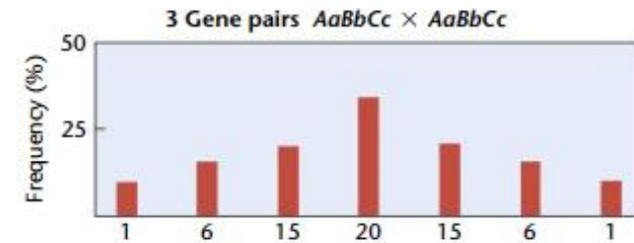
POLYGENIC TRAITS



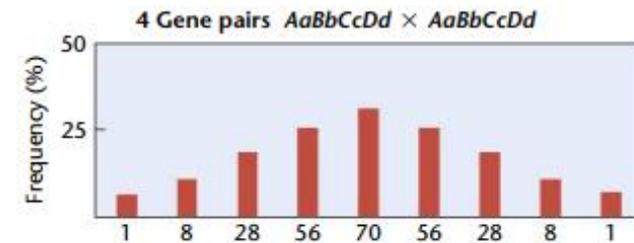
3 classes



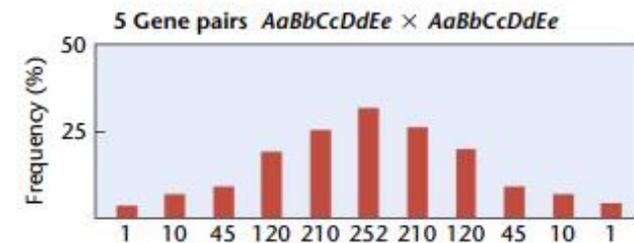
5 classes



7 classes



9 classes

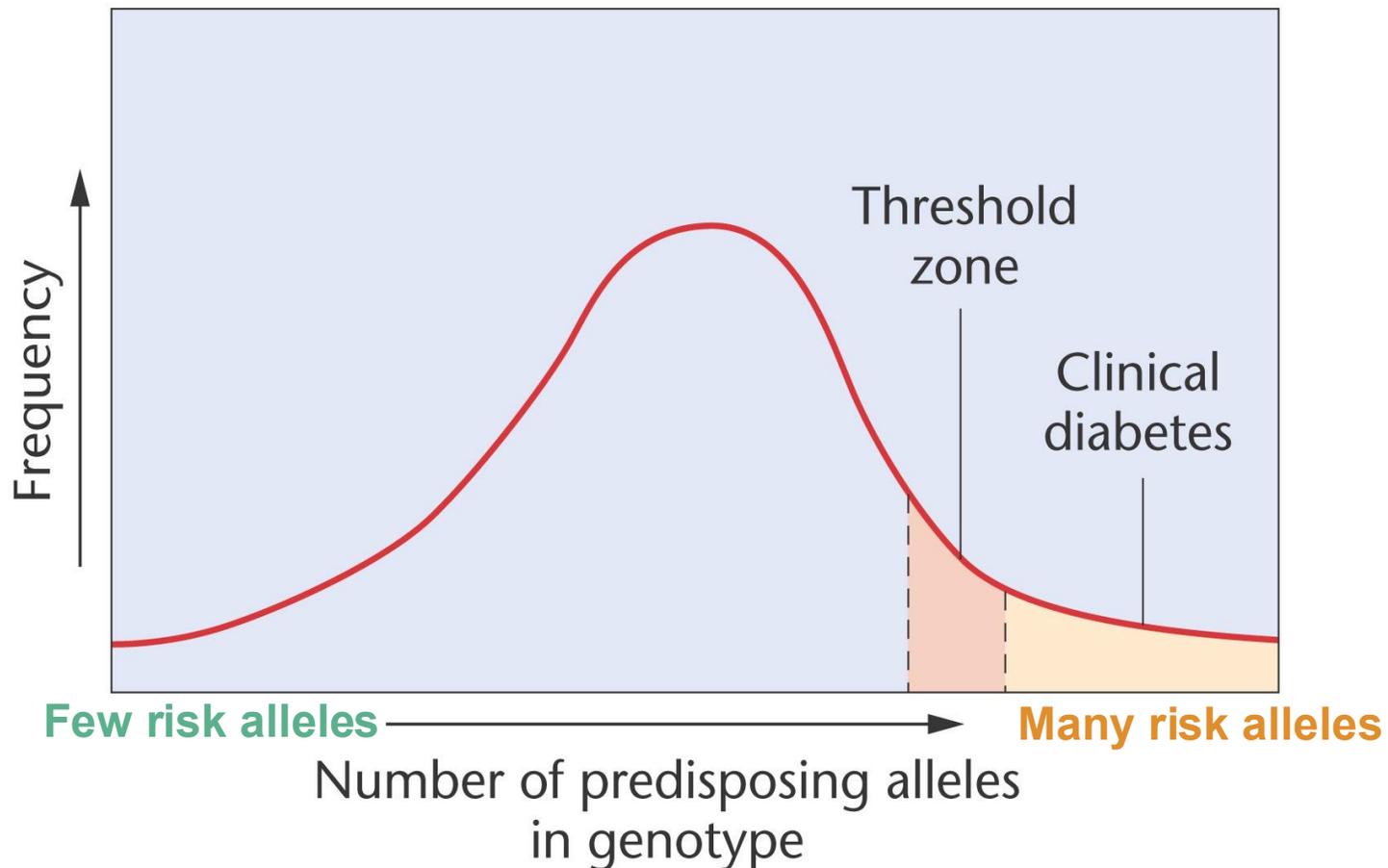


11 classes

How can dichotomous
traits (i.e., diseases)
have a polygenic
distribution?



LIABILITY (THRESHOLD) MODEL

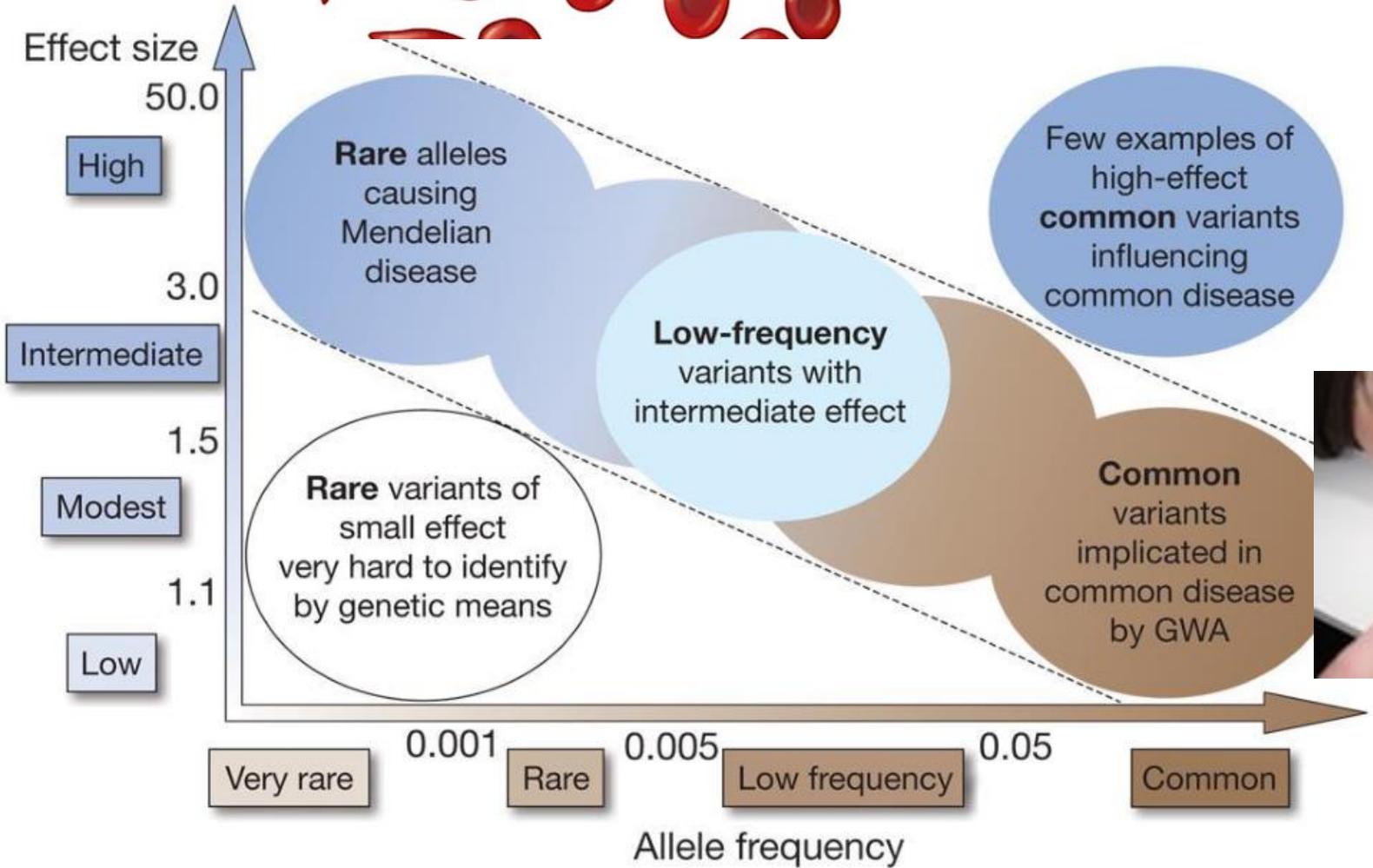
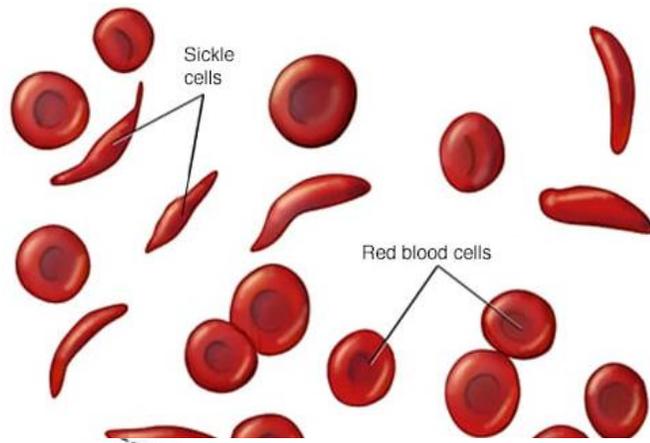


Liability model

Only individuals with a liability over a certain threshold will become affected

The **sum** of many genetic variants with **small effect/risk**.

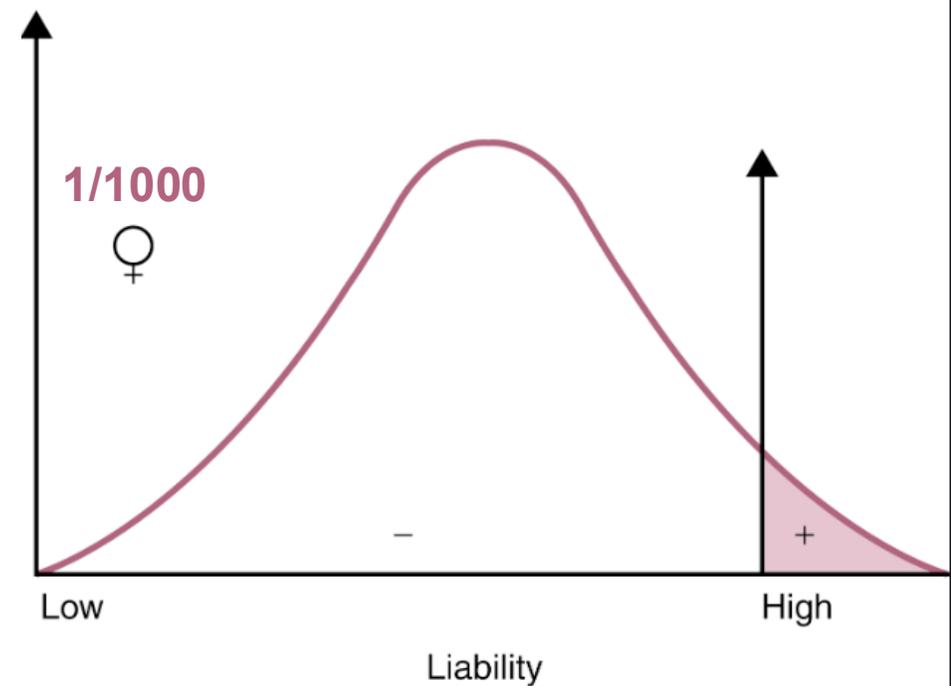
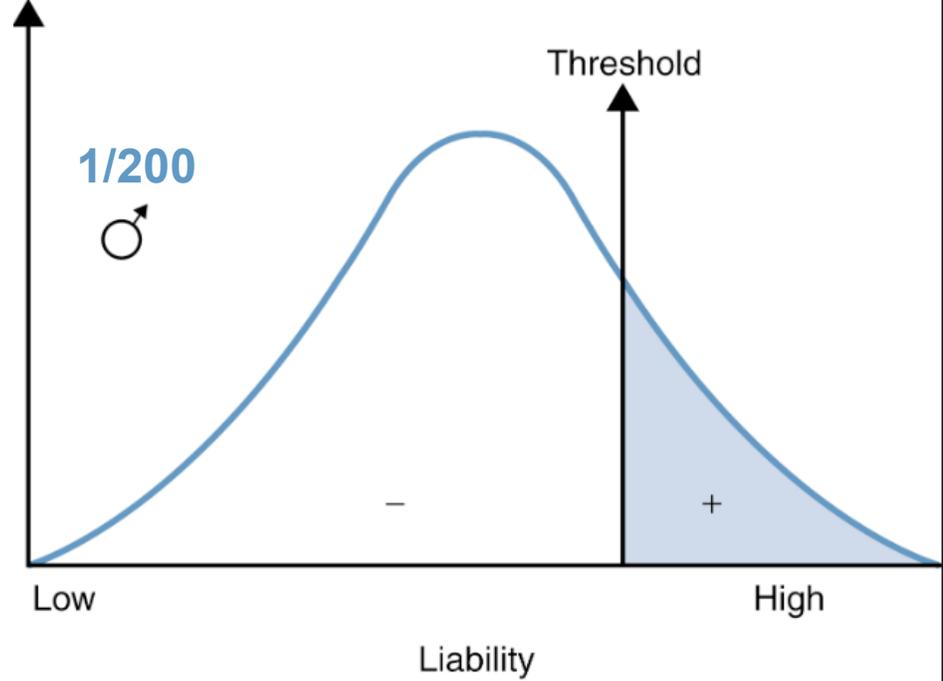
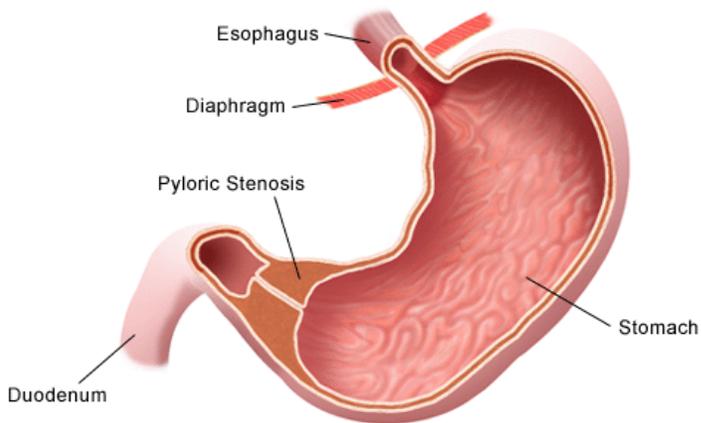
Each locus follow Mendelian inheritance pattern, although the trait does not



DIFFERENT THRESHOLD VALUES BETWEEN SEXES

Pylorus-stenose is a condition that is more frequent among boys than girls.

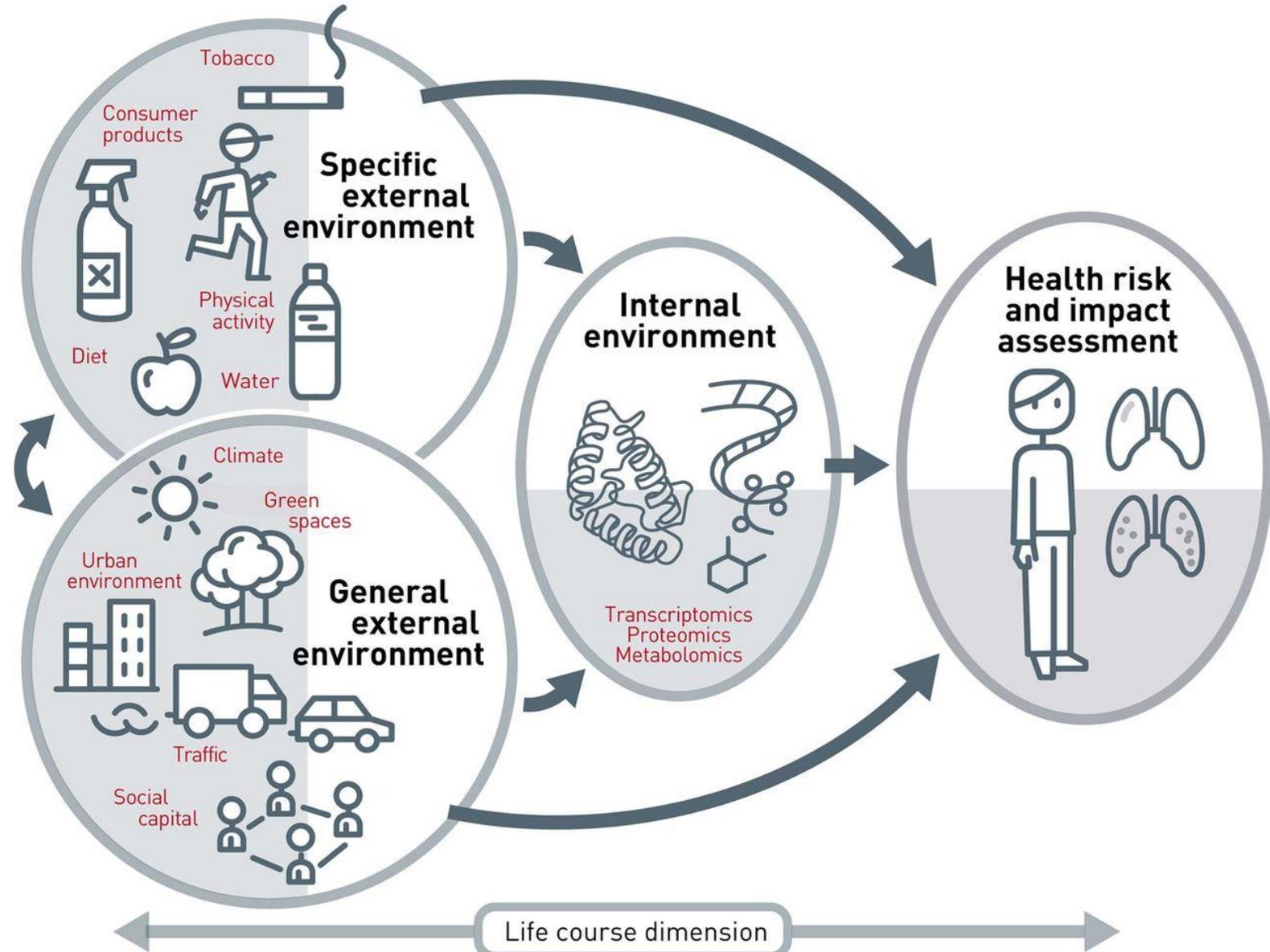
Boys have a lower genetic threshold value than girls → **do not need as many genetic risk variants to become affected** as girls need.



ENVIRONMENTAL EXPOSURE

Complex traits have a **genetic component** and an **environmental component**

The relative genetic contribution is called **heritability**.



INHERITANCE PATTERN OF MULTIFACTORIAL TRAITS

The exact inheritance pattern depends on

- ❖ The number of risk genes/alleles involved
- ❖ The effect size distribution of the genetic risk variants
- ❖ The interaction among genetic variants
- ❖ The interaction with environmental exposures

→ The **genetic architecture of the complex trait**
[Session 6 on GWAS]

RECURRENCE RISK

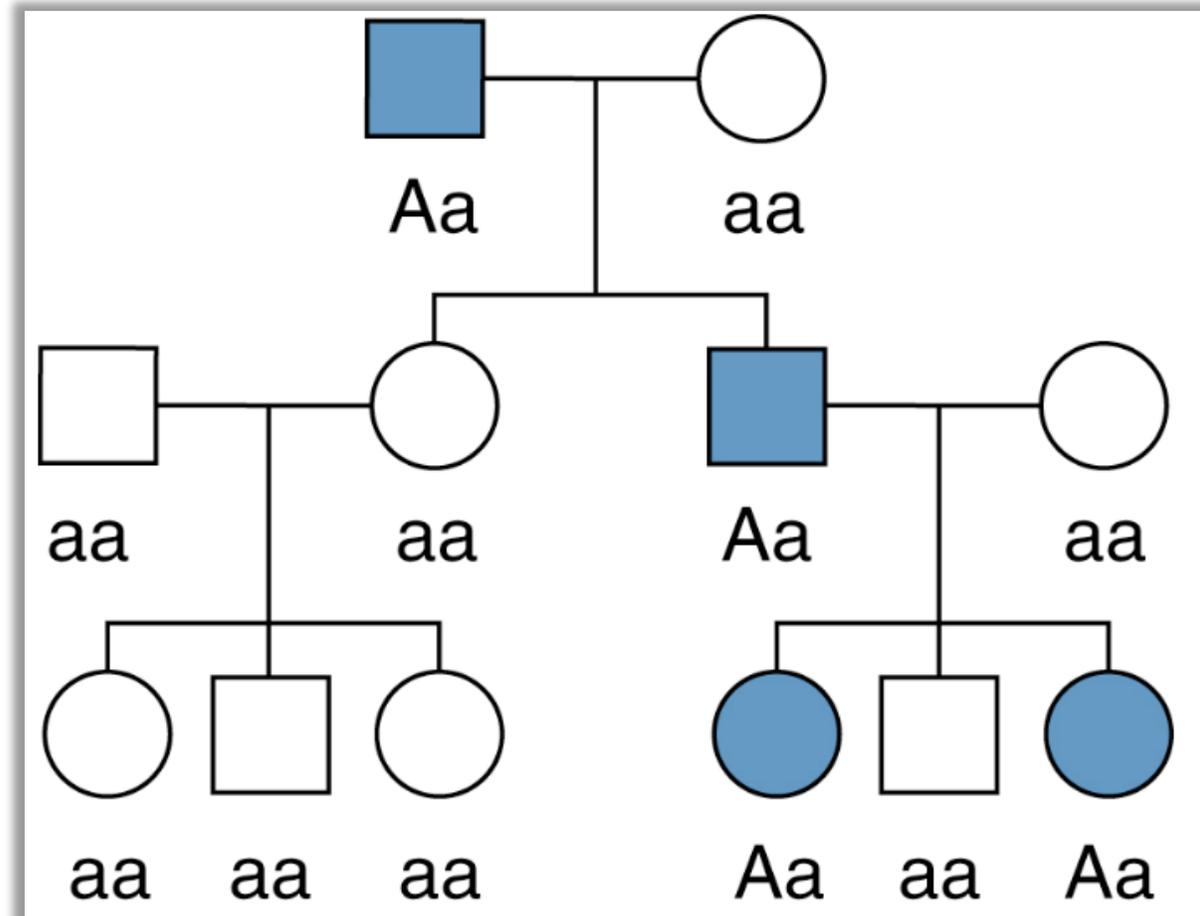
MONOGENIC TRAITS

The probability that a future children will be affected.

What is the recurrence risk that II.3 and II.4 gets a fourth child that is affected?

→ 1/2

Independent on the population.



RECURRENCE RISK

MULTIFACTORIAL TRAITS

The probability that a future children will be affected.

Much harder to determine because

- ❖ Risk genes are unknown
- ❖ Environmental factors unknown

Empirical estimates (collect families with one affect proband)

→ *The empirical recurrence risk estimates become population specific*

DIFFERENTIAL RECURRENCE RISK

1. **Higher recurrence risk when proband is a girl**
 → *Affected girls have higher genetic burden on average compared to affected boys (more risk alleles segregate in the family).*
2. **Higher risk for brothers**
 → *Boys have lower genetic threshold value*
3. **Same trend in Belfast and London**
 → *there are different environmental factors in the two cities*

TABLE 12-1

Recurrence Risks (%) for Pyloric Stenosis, Subdivided by Gender of Affected Proband and Relatives*

Relatives	Male Proband		Female Proband	
	London	Belfast	London	Belfast
Brothers	3.8	9.6	9.2	12.5
Sisters	2.7	3.0	3.8	3.8

*Note that the risks differ somewhat between the two populations.
 (Adapted from Carter CO: Genetics of common single malformations. Br Med Bull 1976;32:21-26.)

How to distinguish a multifactorial disease from a monogenic disease with low penetrance and variable expressivity?



Imagine a disease which have a recurrence risk of 5% for siblings.

This risk could be a result of two different scenarios

- ❖ Multifactorial inheritance
- ❖ An autosomal dominant gene with 10% penetrance

How can we test which one is the correct one?



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This risk could be a result of two different scenarios

- ❖ An autosomal dominant gene with 10% penetrance
- ❖ Multifactorial inheritance



Four criteria supportive for it to be a multifactorial disease

If we observe larger recurrence risk in families with more affected individuals → **multifactorial**

If we observe larger recurrence risk in families with more severely affected proband → **multifactorial**

If we observe a different threshold values for boys and girls, and we see higher risk in families where affected individual are the “rare” gender → **multifactorial**

If we observe that the recurrence rate decrease faster with increasing genealogical distance → **multifactorial**



***Why is the recurrence risk
population specific?***

*Because it is “measured” in different
populations with*

- 1) different environmental exposures,*
- 2) difference in allele frequencies*



MULTIFACTORIAL TRAITS

- ❖ Types of trait-inheritance
- ❖ Liability model
- ❖ Recurrence risk
- ❖ Environmental exposures modulate outcomes



AGENDA

- 08:15 – 09:00** Lecture 1 [*Recap + indirect testing*]
- 09:00 – 09:45** Break + Exercises A
- 09:45 – 10:10** Lecture 2 [*Multifactorial traits*]
- 10:10 – 10:20** Exercises B
- 10:20 – 11:00** Break + Group work
- 11:00 – 11:30** Lecture 3 [*Quantitative genetic theory*]
- 11:30 – 11:55** Exercises C
- 11:55 – 12:00** Evaluation at Moodle



GROUP WORK

Understanding a Complex Disease

Wrap-up (2 min):

Explain why this disease is *multifactorial* using today's models.

- 1) Form groups of 3
- 2) Choose one complex trait
- 3) Discuss using today's concepts

i. Liability model

- What determines whether someone crosses the disease threshold?
- Would men and women have the same threshold?

ii. Genes

- Why is this disease not Mendelian?
- What does it mean that many variants may contribute?

iii. Environment

- Which exposures could increase liability?
- Would they act independently or interact with genetics? Genes

iv. Family patterns

- Would you expect the disease to cluster in families?
- Why does that not imply single-gene inheritance?

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QUANTITATIVE GENETICS

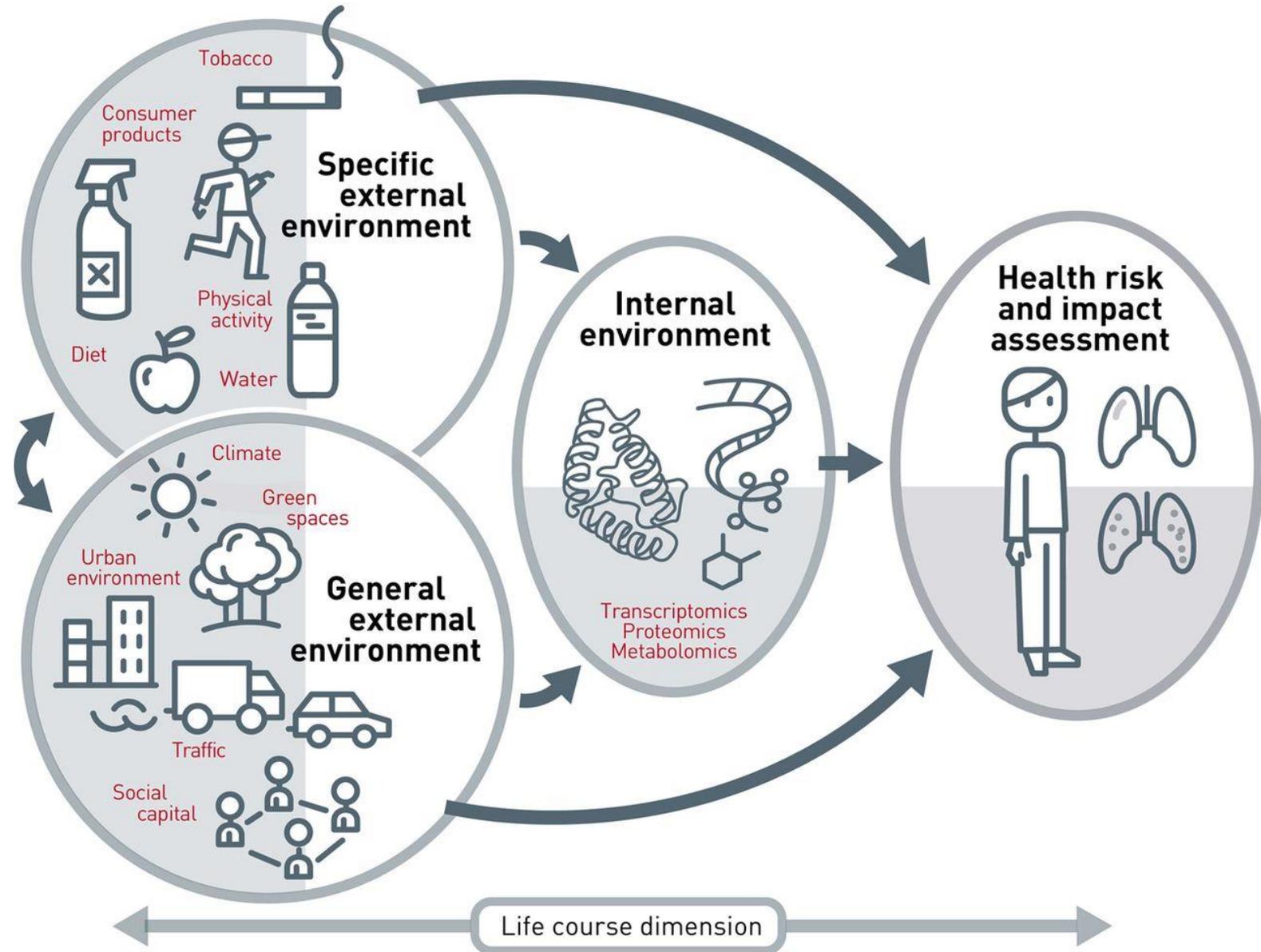
- ▶ Unidentified genotypes but measured trait variability.
- ▶ Phenotypic vs Genotypic values
- ▶ Gene action
- ▶ Heritability



Complex traits have a **genetic component** and an **environmental component**

The relative genetic contribution is called **heritability**.

How do we separate the genetic and environmental contribution?



THE PHENOTYPIC VALUE

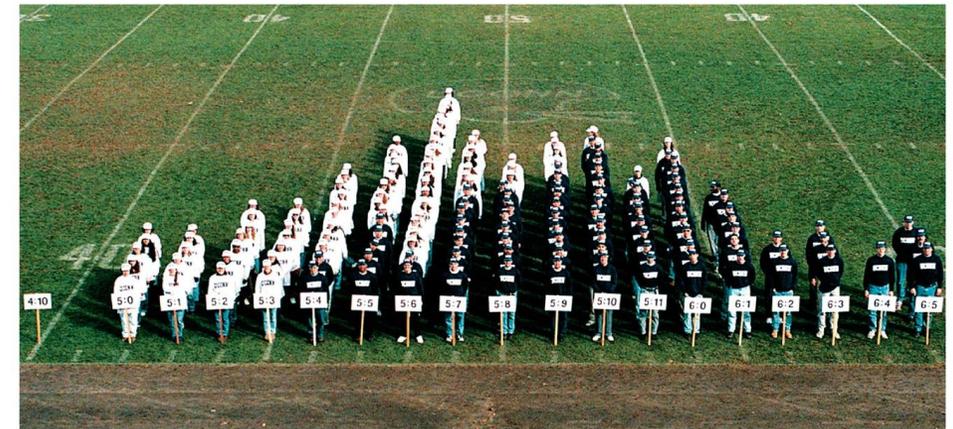
The phenotypic value can be partitioned in different components:

$$P = G + E$$

Phenotypic value \swarrow P
Genotypic value \swarrow G
Environmental deviation \swarrow E

The value that we observe when we measure a trait, is the **phenotypic value for that individual**.

Every individual has a phenotypic value.



ENVIRONMENTAL DEVIATION

$$P = G + E$$

External effects that modulates the phenotypic value.

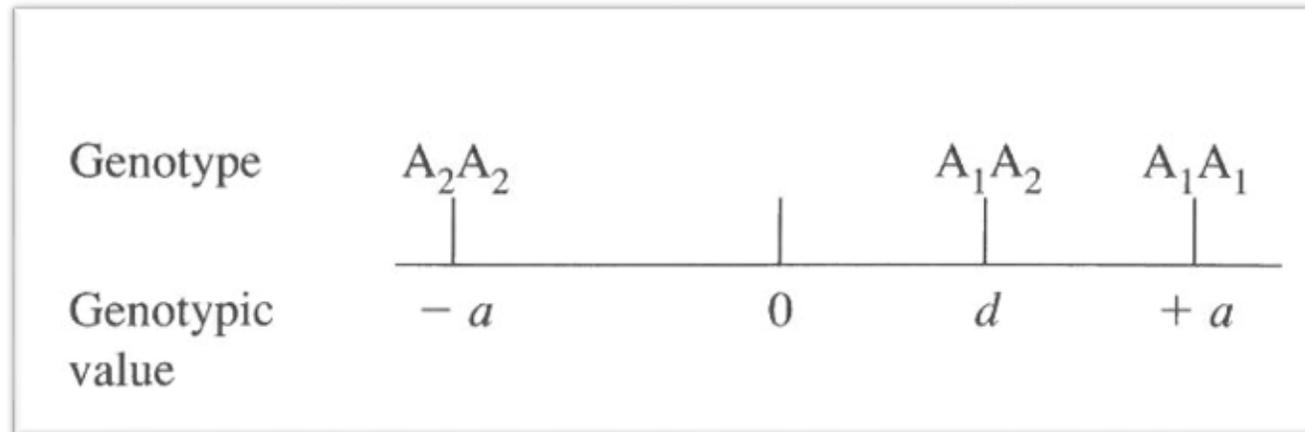
... or things that we cannot explain



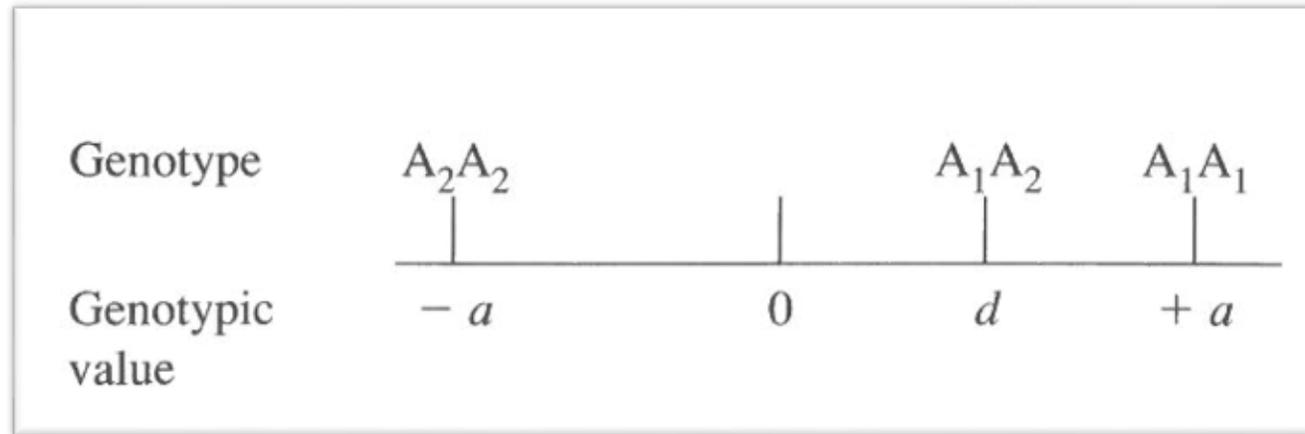
THE GENOTYPIC VALUE

$$P = G + E$$

If we consider one locus with two alleles; A_1 and A_2 , and we assume additivity, then we can assign genotypic values to each genotype:



THE GENOTYPIC VALUE



If the genotypic value of A_1A_2 is zero (pure additiv)

$$d = 0$$

If, A_1 is dominant over A_2 :

$$d > 0$$

If, A_2 is dominant over A_1 :

$$d < 0$$

Complete dominance

$$d = a \text{ | } -a$$

Partial dominance of A_1

$$0 < d < a$$

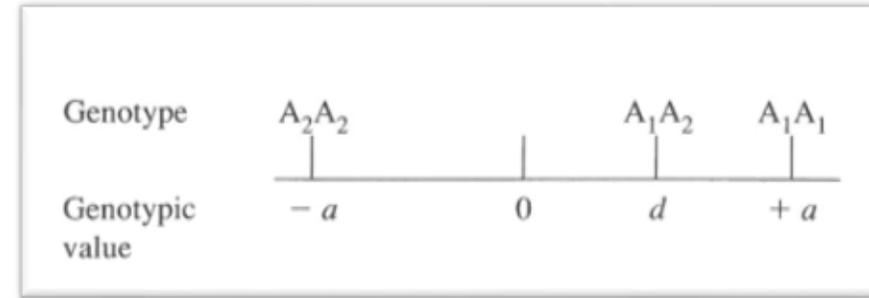
If A_1A_2 is greater than homozygote (overdominance)

$$d > a$$

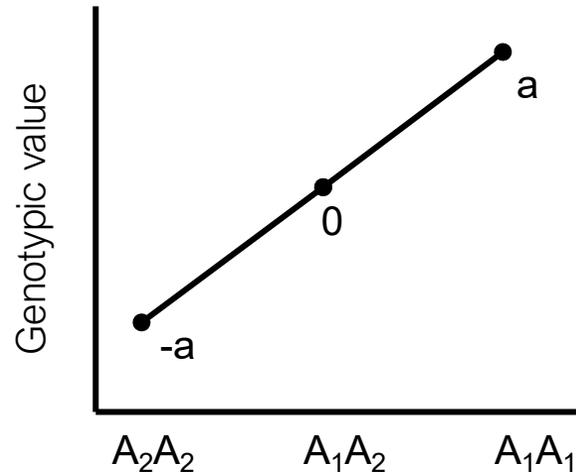
If A_1A_2 is lesser than homozygote (underdominance)

$$d < -a$$

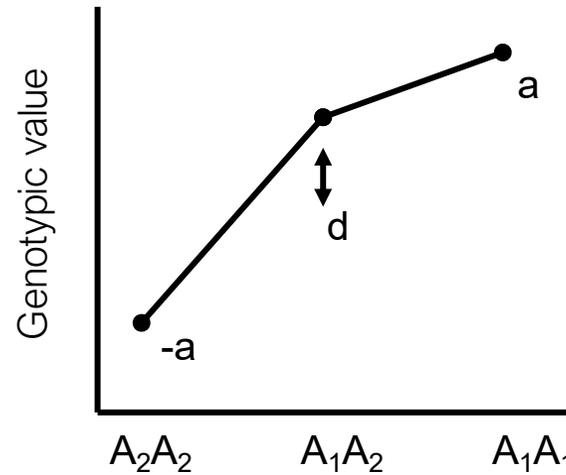
THE GENOTYPIC VALUE



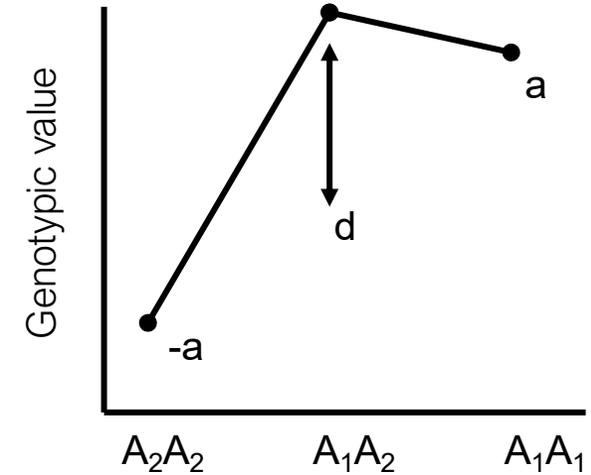
Additive gene effect



Partial dominance



Overdominance



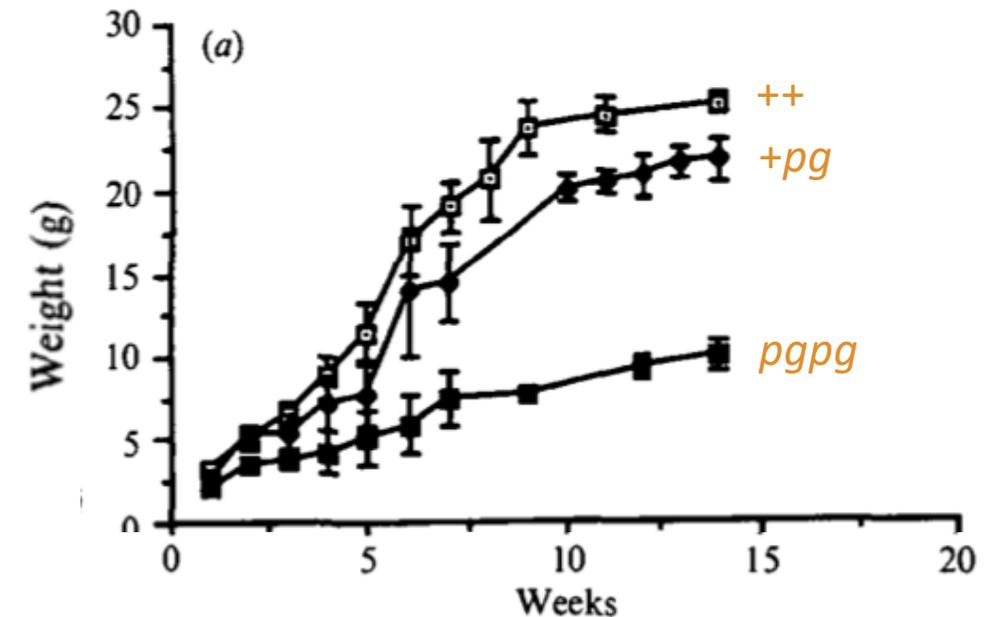
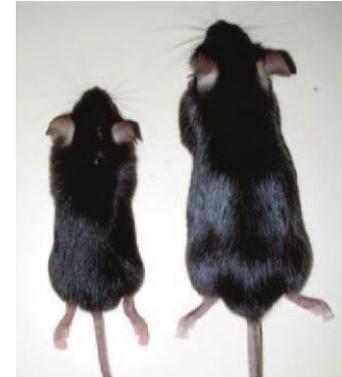
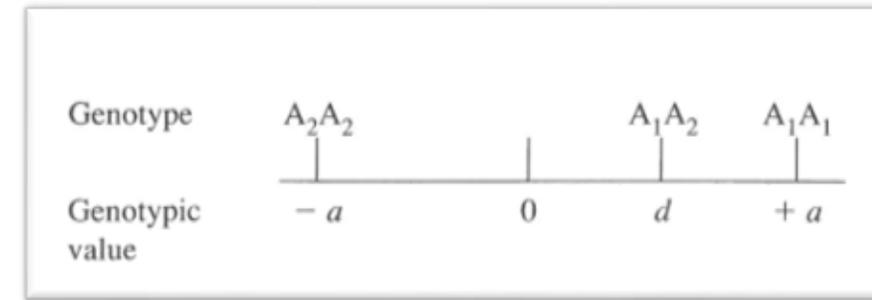
ESTIMATE G

$$P = G + E$$

In mice, the gene *pygmy* (*pg*) is strongly correlated with body size.

Genotype	++	+ pg	pg pg
Weight (g)	25	22	10

Is the effect of *pg* additive?



Benson and Chada 1994, Genet Res Camb

ESTIMATE G

$$P = G + E$$

Genotype	++	+ pg	pg pg
Weight (g)	25	22	10

m is the mean of the homozygotes:

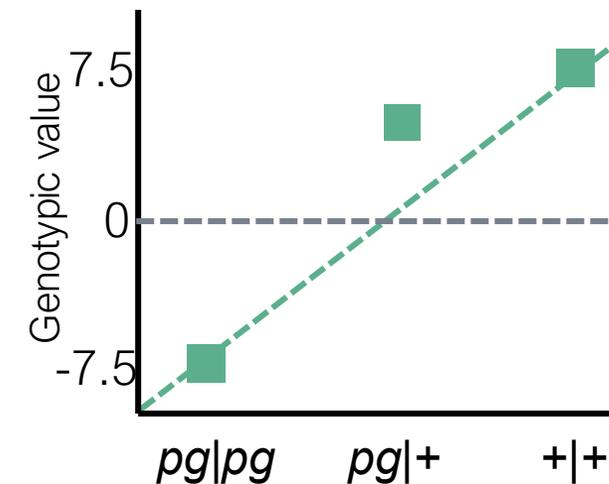
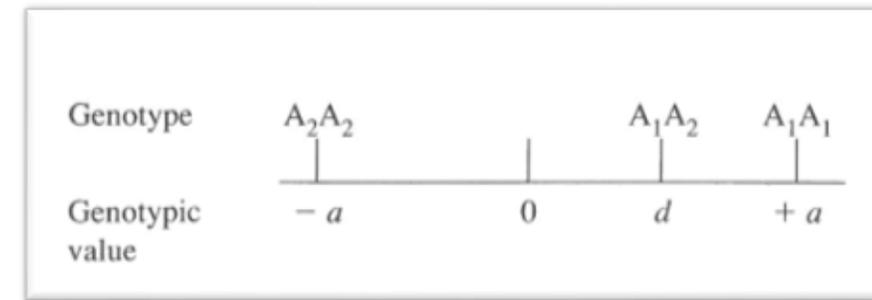
$$m = (25+10)/2 = 17.5$$

a is the difference between homozygote and m

$$a = 25 - 17.5 = 7.5$$

d is the difference between heterozygote and m

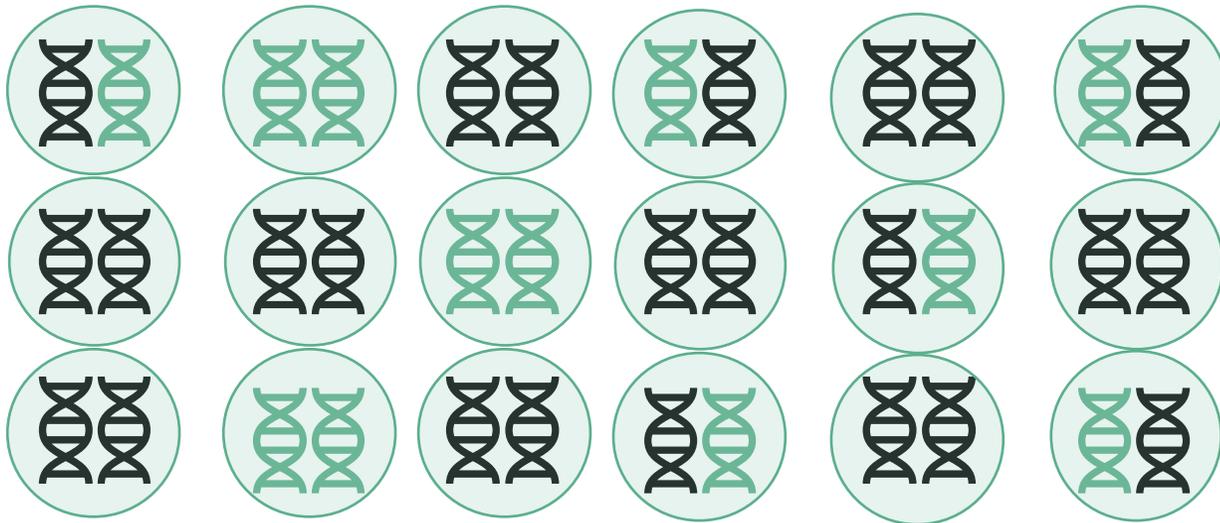
$$d = 22 - 17.5 = 4.5$$



pg does act additive, but with partial dominance

ALLELE FREQUENCY

Allele frequency is the proportion of the one allele out of all alleles in the population



	12	$12/36=0.33$	<i>q</i>
	24	$24/36=0.66$	<i>p</i>
	<hr/>	36	

ALLELE FREQUENCY

CHANGE THE POPULATION MEAN

Allele frequency has an influence on the trait population mean

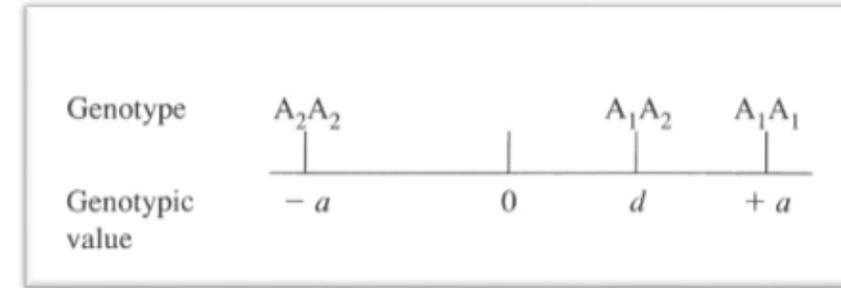
<i>Genotype</i>	<i>Frequency</i>	<i>Value</i>	<i>Freq. × Val.</i>
A_1A_1	p^2	$+a$	p^2a
A_1A_2	$2pq$	d	$2pqd$
A_2A_2	q^2	$-a$	$-q^2a$
		Sum =	$a(p - q) + 2dpq$

Population mean (expressed as the deviation from the mid-homozygote value m):

$$M = a(p - q) + 2dpq$$

M is expressed as the deviation from the mid-homozygote value

POPULATION MEAN



$$M = a(p - q) + 2dpq$$

$$m = 17.5 \quad a = 7.5 \quad d = 4.5$$

If $p = 0.9$ and $q = 0.1$

$$M = 7.5(0.9 - 0.1) + 2 * 4.5 * 0.9 * 0.1 = 6.81$$

Population mean is then,

$$m + M = 17.5 + 6.81 = 24.31$$

If $p = 0.6$ and $q = 0.4$

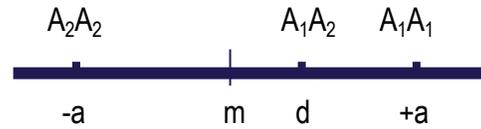
$$M = 7.5(0.6 - 0.4) + 2 * 4.5 * 0.6 * 0.4 = 3.66$$

Population mean,

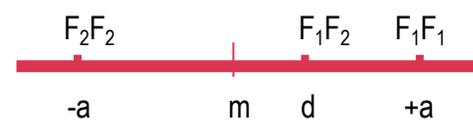
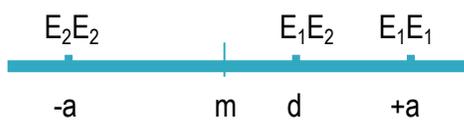
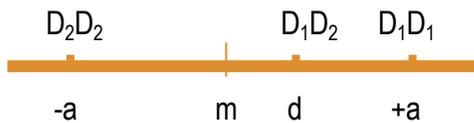
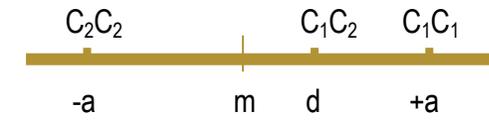
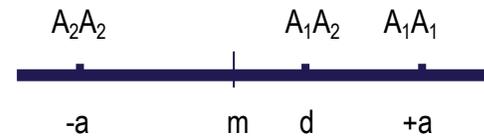
$$m + M = 17.5 + 3.66 = 21.16$$



FROM ONE LOCUS TO MANY LOCI



$$M = a(p - q) + 2dpq$$



$$M = \sum a(p - q) + 2 \sum dpq$$

AVERAGE EFFECT

- Because parents pass on their alleles and not their genotypes to the next generation, we need another metric than the genotypic value.
- The average effect (α) depends on the genotypic values and allele frequencies, $\alpha = a + d(q - p)$.

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

- The average effect of a particular allele is the mean deviation from the population mean of individuals which received that allele from one parent, the allele received from the other parent having from at random from the population

ADDITIVE GENETIC VALUE OR BREEDING VALUE

- The average effect is useful because parents pass on their alleles and not their genotypes to the progeny.
- Thus, it is the average effects of the parents' alleles that determine the mean genotype value of the progeny.

<i>Genotype</i>	<i>Breeding value</i>
A_1A_1	$2\alpha_1 = 2q\alpha$
A_1A_2	$\alpha_1 + \alpha_2 = (q - p)\alpha$
A_2A_2	$2\alpha_2 = -2p\alpha$

PHENOTYPIC VARIANCE

In quantitative genetics, our interests is to investigate how much of the observed variation that is due to genetic differences among individuals and how much is due to environmental variation.



VARIANCE NOT MEAN

$$P = G + E$$

$$V_P = V_G + V_E$$

Phenotypic
variance

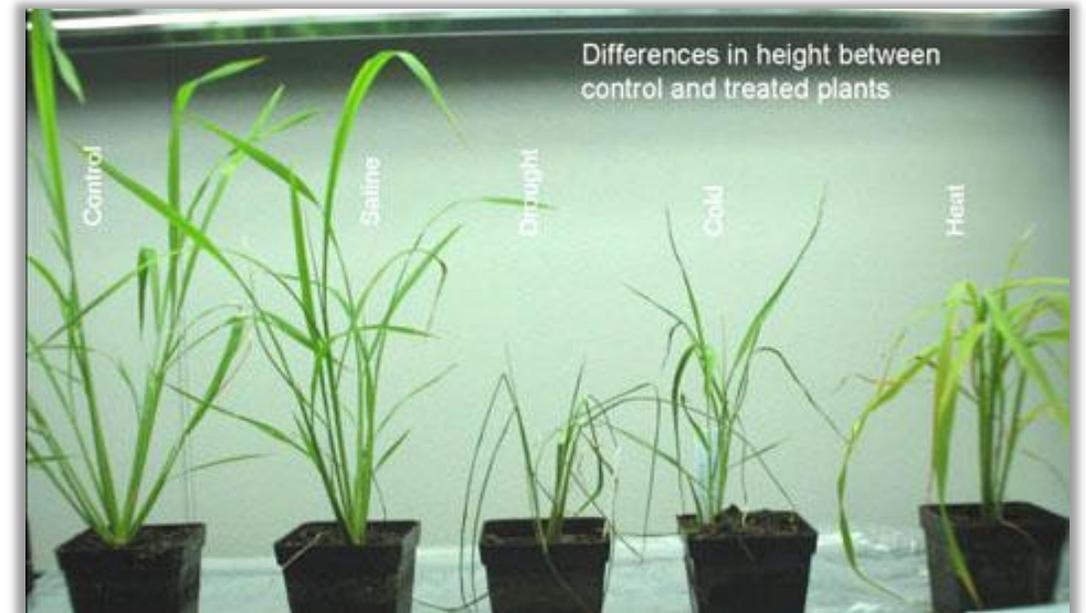
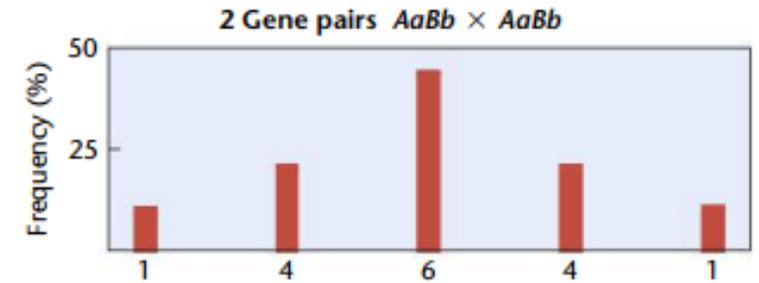
Genotypic
variance

Environmental
variance

ENVIRONMENTAL VARIATION

Individuals with the same genotype are subjected to slightly different micro-environment

→ this blurs the genotypic classes.



PARTITION OF PHENOTYPIC VARIANCE

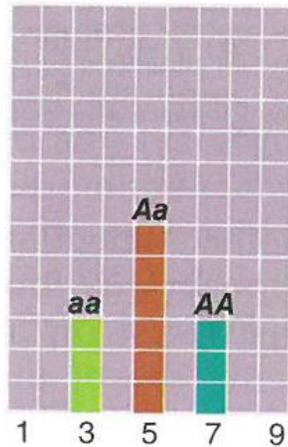
Genetic variance

Environmental variance

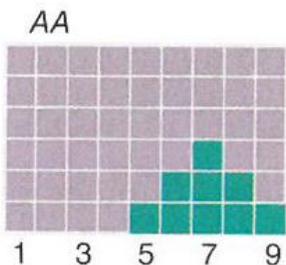
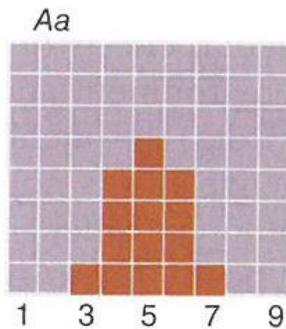
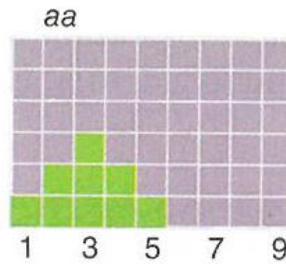
$$V_P = V_G + V_E$$

Phenotypic variance

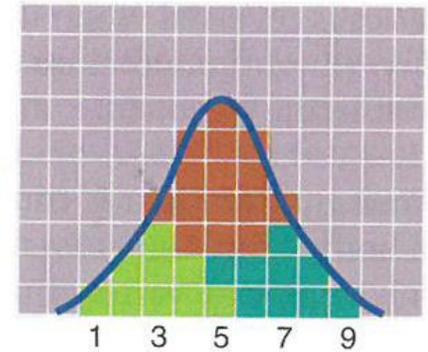
Genotypic variance
 $\sigma_g^2 = 2.0$



Environmental variance
 $\sigma_e^2 = 1.0$



Phenotypic variance
 $\sigma_p^2 = \sigma_g^2 + \sigma_e^2 = 3.0$



GENETIC AND ENVIRONMENTAL VARIANCE

Important...!

$$V_P = V_G + V_E$$

This partition only holds when V_G and V_E are independent:

$$\sigma^2(x + y) = \sigma^2(x) + \sigma^2(y) + 2Cov(x, y)$$

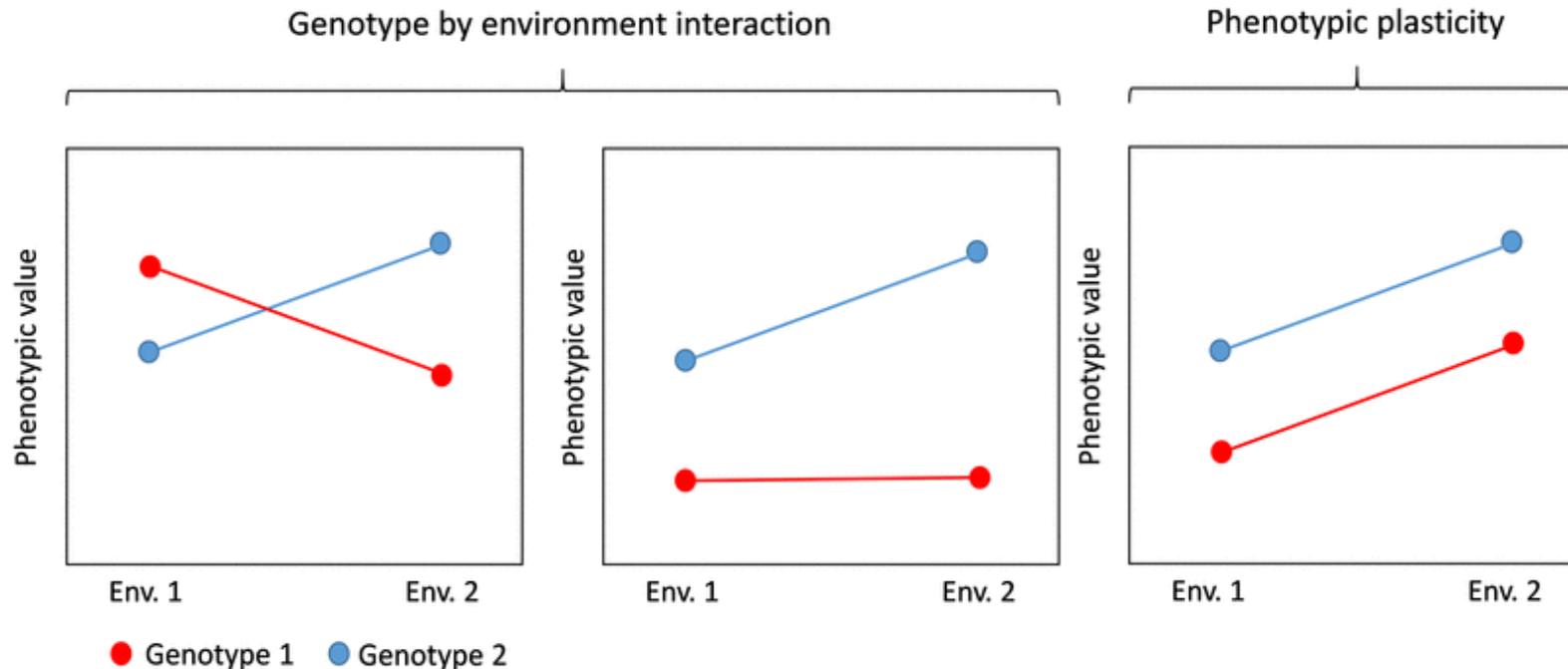
$$Cov(x, y) = 0$$

GENETIC AND ENVIRONMENTAL VARIANCE

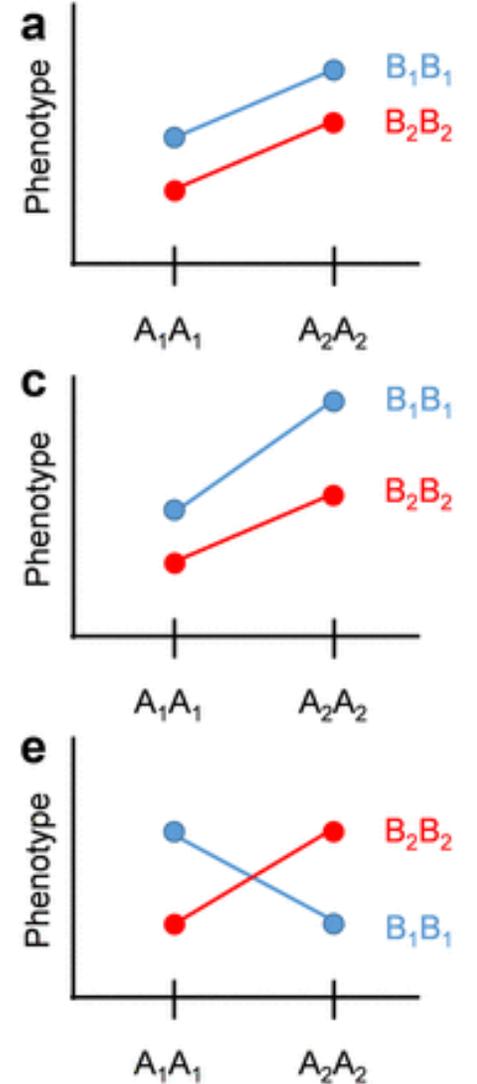
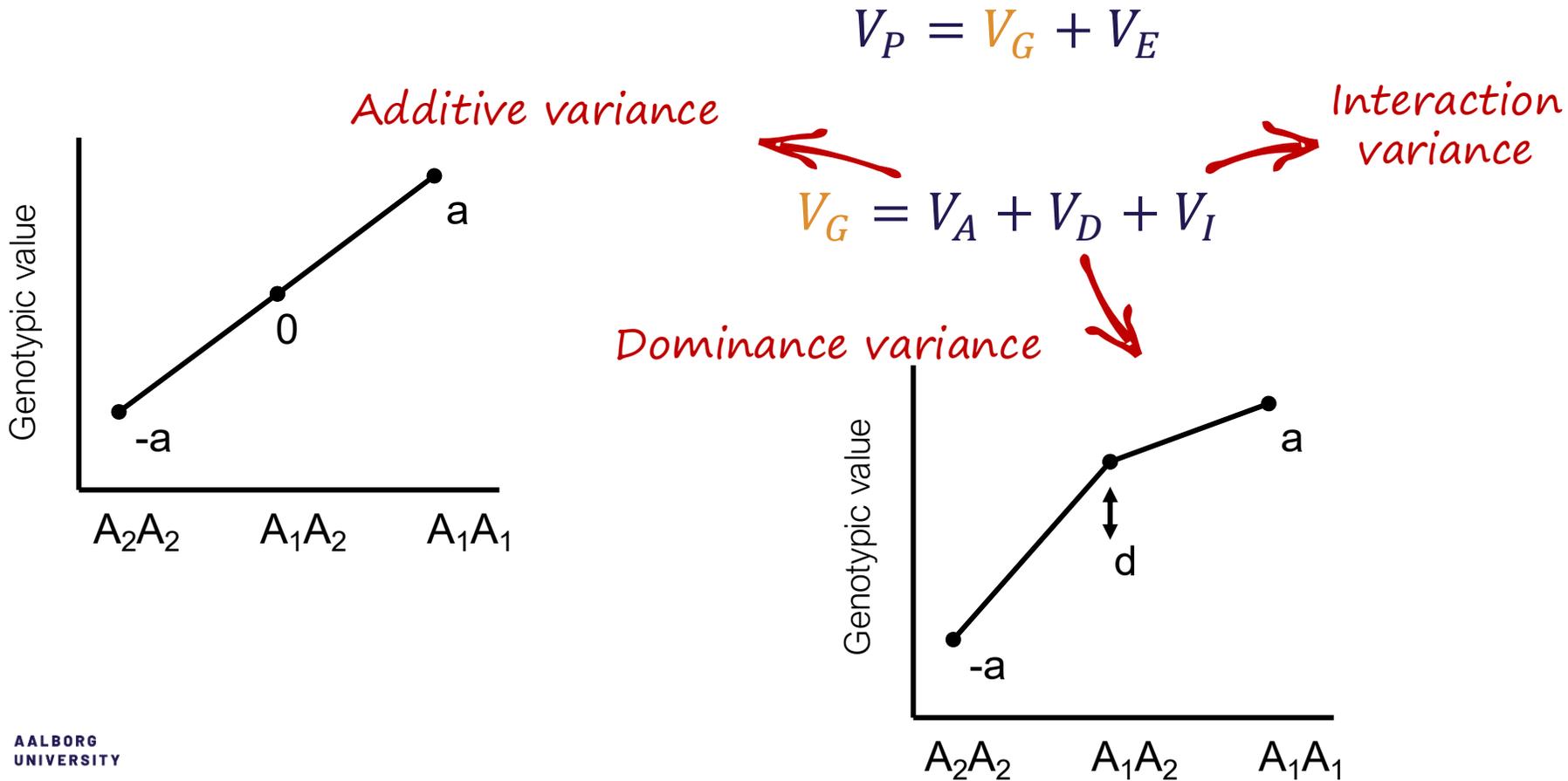
If, they are not independent:

Genotype-by-environment interaction

$$V_P = V_G + V_E + V_G \times V_E$$



PARTITION OF GENETIC VARIANCE



HERITABILITY

The concept **heritability** is an important concept as it describes the proportion of the *phenotypic variance that is due to genetic variation*.

HERITABILITY



CAUTION I



But... **the heritability** of a trait is specific for **an environment** and **a population**.

The heritability is **NOT A QUANTITY FOR THE IMPORTANCE** of the genotypes for the trait

HERITABILITY



CAUTION II



A heritability of 0.70 for human height do not mean that your height is due to 70% of genes.

A heritability of 0.70 means that in a specific population, 70% of the variation in height can be explained by genetic difference between individuals in the sample, from which is was estimated.

HERITABILITY



CAUTION !!!



Traits with low heritability can be under strong genetic control.

Traits that are evolutionary important have low heritability estimates (due to selection)

BROAD-SENSE HERITABILITY

Broad-sense heritability (H^2) describes the proportion of the phenotypic variance that is explained by genetic difference between individuals in the population.

$$V_P = V_G + V_E$$

$$H^2 = \frac{V_G}{V_P} = \frac{V_G}{V_G + V_E}$$

H^2 can take values between 0 and 1:

$H^2 = 0 \rightarrow$ all variation is due to environmental variation

$H^2 = 1 \rightarrow$ all variation is due to genetic variation

NARROW-SENSE HERITABILITY

$$V_P = V_G + V_E$$
$$V_P = V_A + V_D + V_I + V_E$$

Narrow-sense heritability (h^2) is the proportion of the phenotypic variance that is explained by additive genetic variance

$$h^2 = \frac{V_A}{V_P}$$

H^2 VS h^2

Broad-sense heritability (H^2)

is an estimate for the proportion of phenotypic variation that is due to genetic variation

Narrow-sense heritability (h^2)

Is an estimate of the proportion of phenotypic variation that is caused by additive genetic variation – the part of the genetic variation that is directly transmitted from generation to generation

Additive genetic variance: hereditary | one allele from mom, one from dad

Dominance variance: is established after gamete formation

Interaction variance: is established after gamete formation

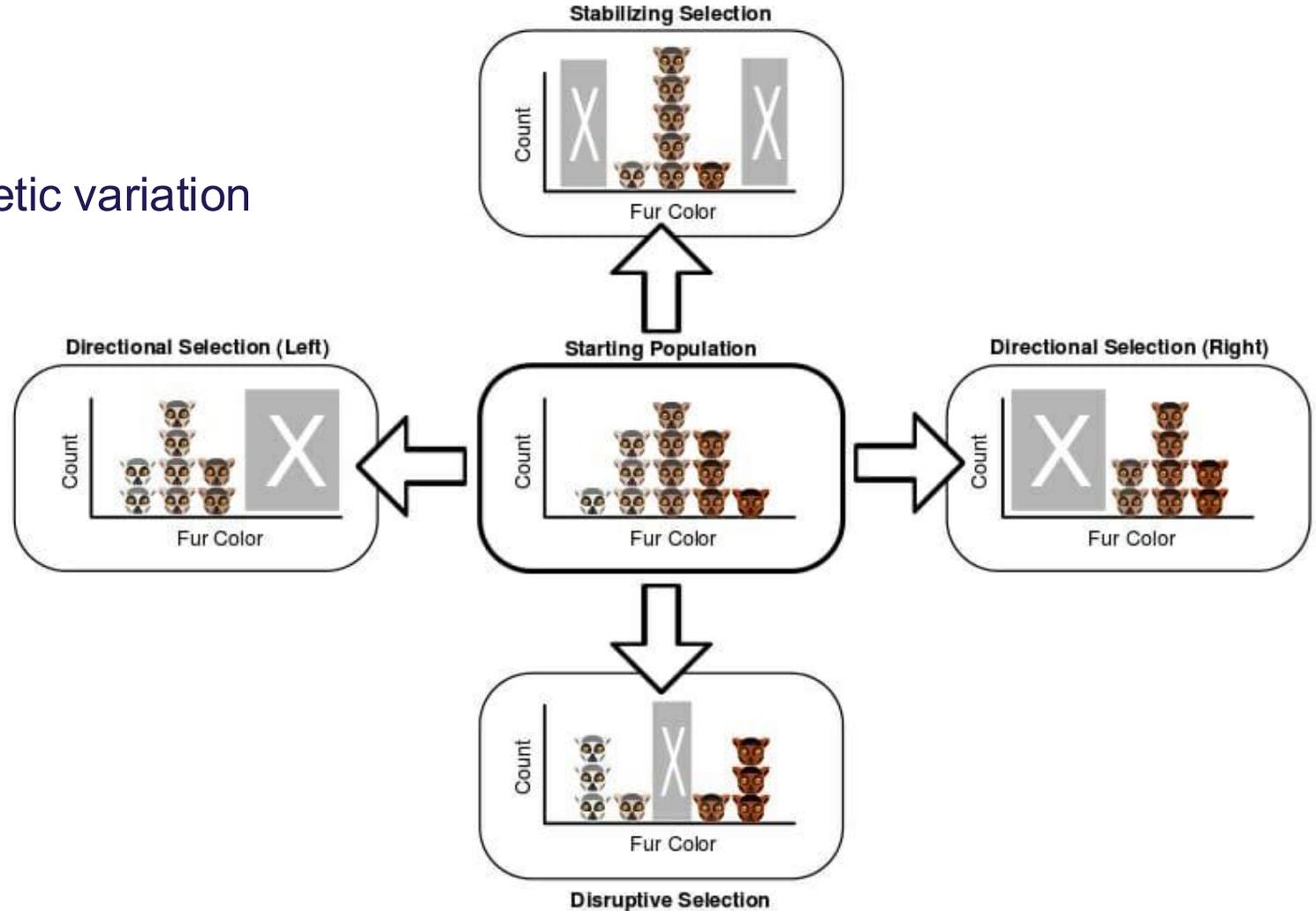
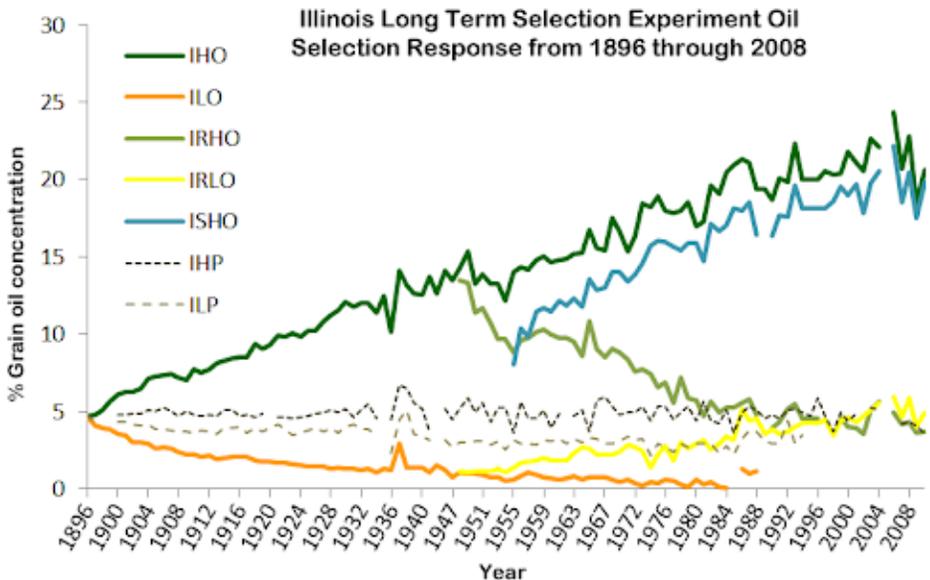
h^2 is always smaller than H^2

SELECTION AND GENETIC VARIATION

Selection reduces amount of genetic variation

$$V_P = V_G + V_E$$

→ reduce the heritability



HERITABILITY AND SELECTION

Traits closely linked to **fitness** (under strong directional selection) have **low heritability** estimates (because selection removed V_A).

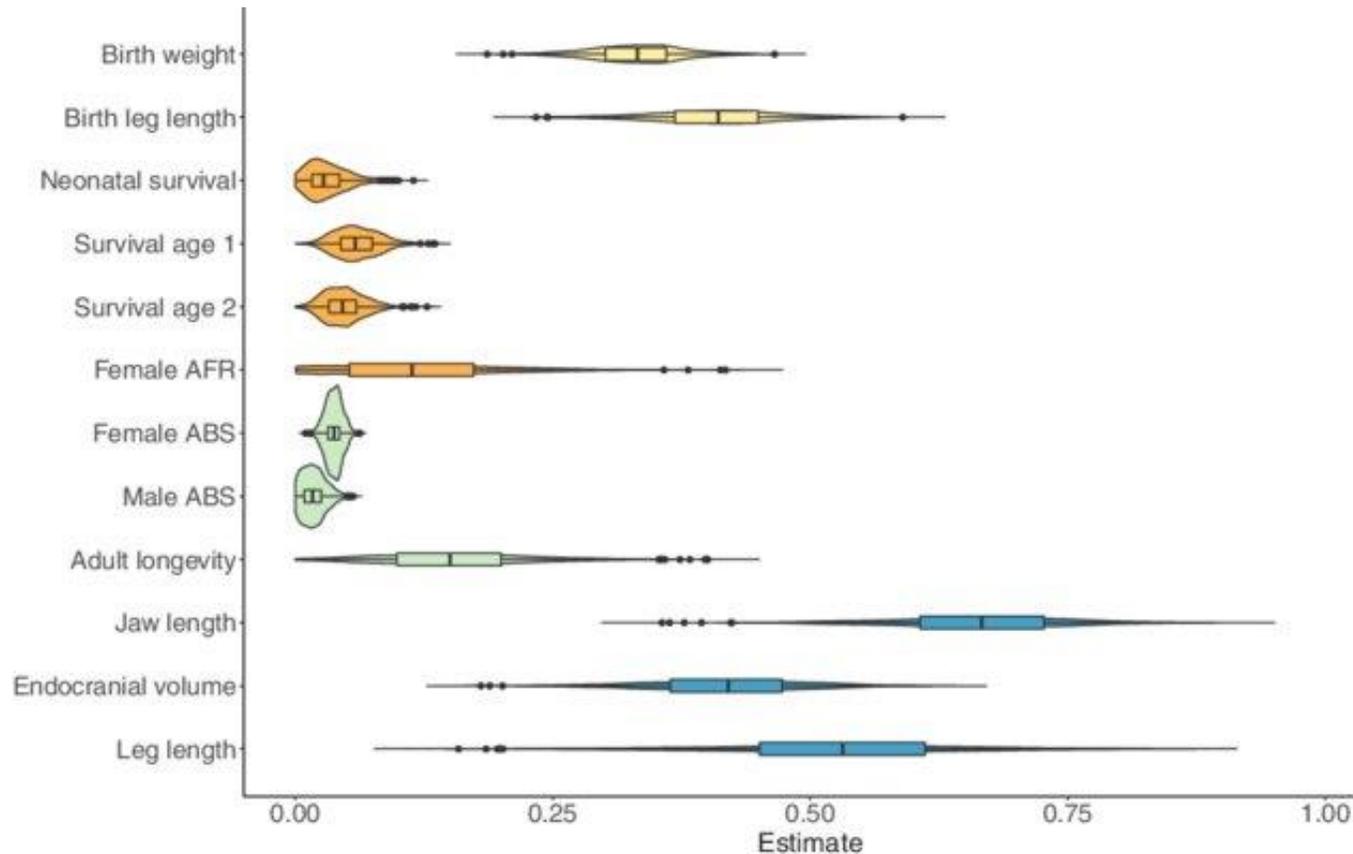


TABLE 24.4

ESTIMATES OF HERITABILITY FOR TRAITS IN DIFFERENT ORGANISMS

Trait	Heritability (h^2)
Mice	
Tail length	60%
Body weight	37
Litter size	15
Chickens	
Body weight	50
Egg production	20
Egg hatchability	15
Cattle	
Birth weight	45
Milk yield	44
Conception rate	3

QUANTITATIVE GENETICS

- ▶ Unidentified genotypes but measured trait variability.
- ▶ Phenotypic vs Genotypic values
- ▶ Gene action
- ▶ Heritability

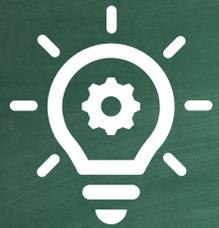


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REFLECT TOGETHER 2 AND 2



- What will you remember from today?
- What do you need to follow-up on?



E-evaluation	
What did you find difficult?	Improvements for next session?
<input type="text"/>	<input type="text"/>