COMPLEX TRAITS AND QUANTITATIVE GENETICS

#4

PALLE DUUN ROHDE

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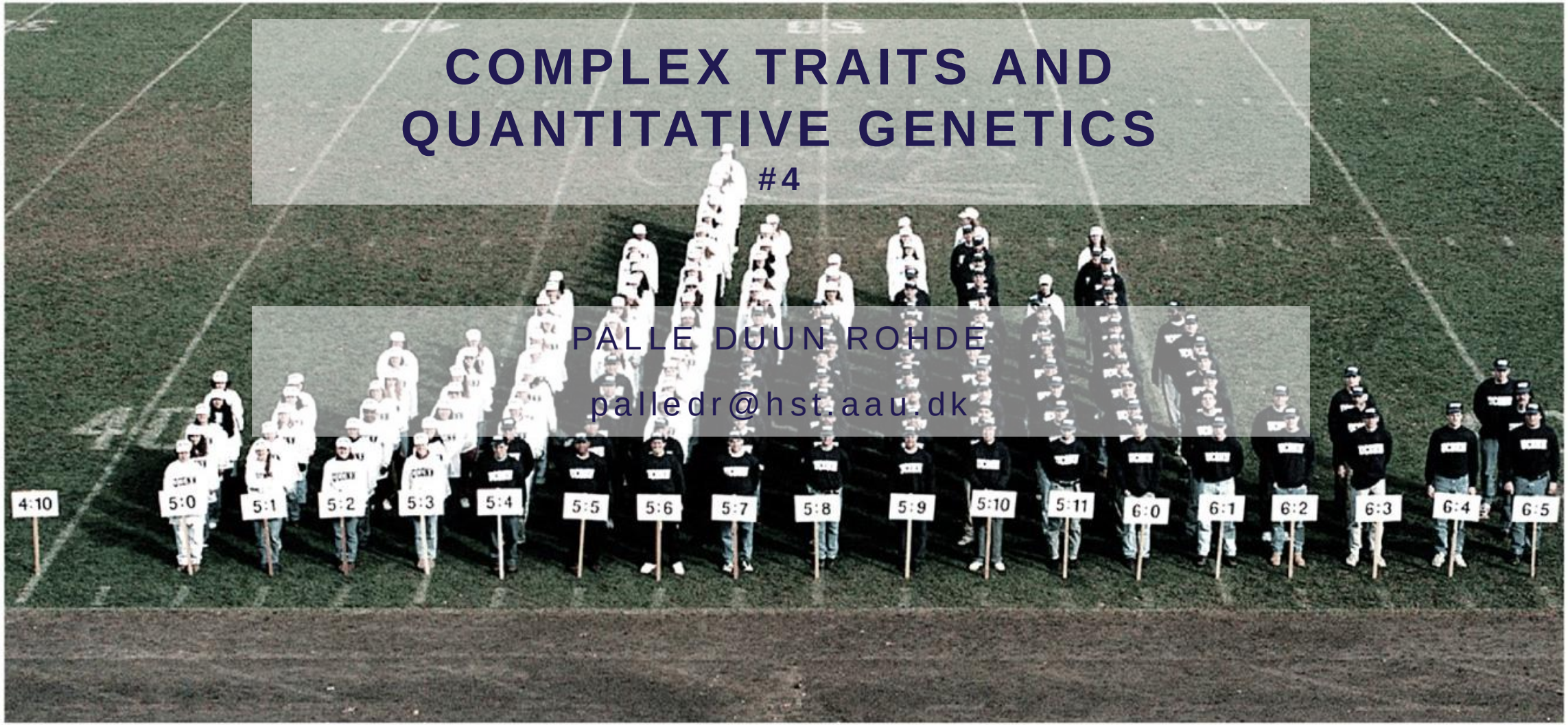

LETS GET STARTED

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 – 08:45	Lecture 1 [*Recap + indirect testing*]
08:45 – 09:15	Exercises A + Break
09:15 – 09:40	Lecture 2 [*Multifactorial traits*]
09:40 – 10:00	Exercises B
10:00 – 10:40	Break + Group work
10:40 – 11:15	Lecture 3 [*Quantitative genetic theory*]
11:15 – 11:50	Break + Exercises C
11:50 – 12:00	Evaluation at Moodle

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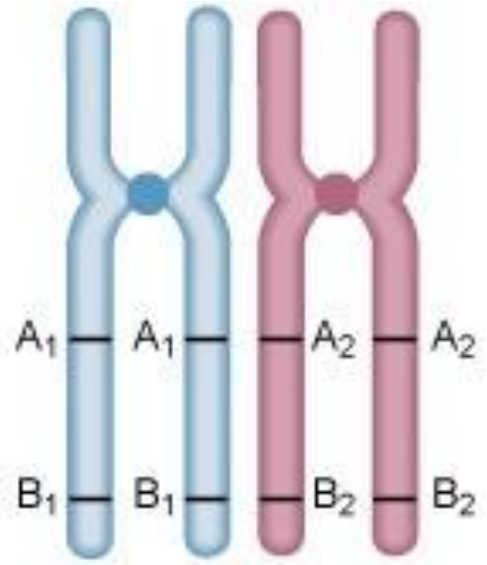
LINKAGE

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

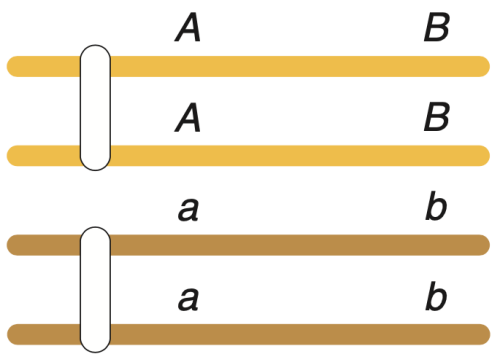
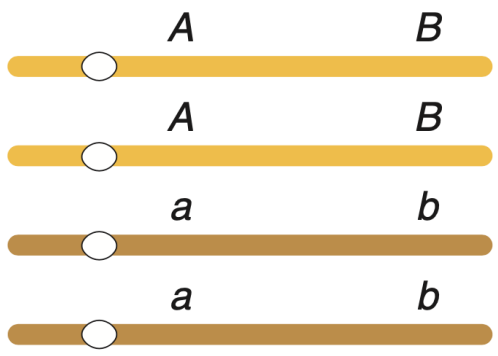
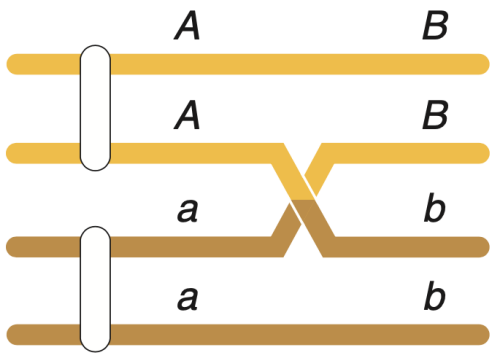
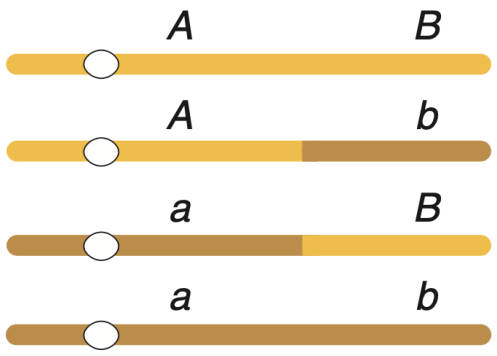


When two loci are linked (are physically close) the alleles segregate together more often than by chance

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

CROSSOVERS

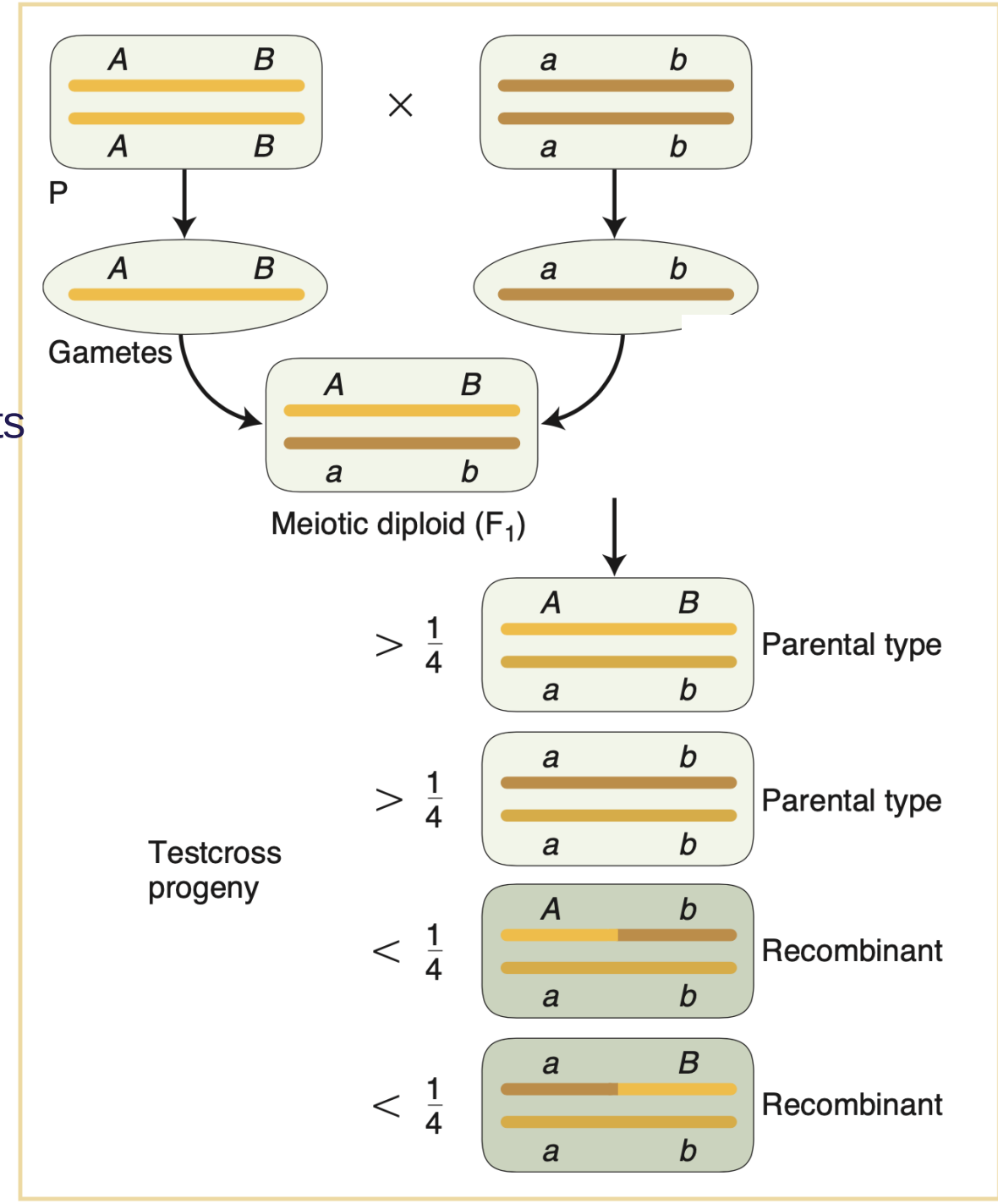
BETWEEN NON-SISTER CHROMATIDES

	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

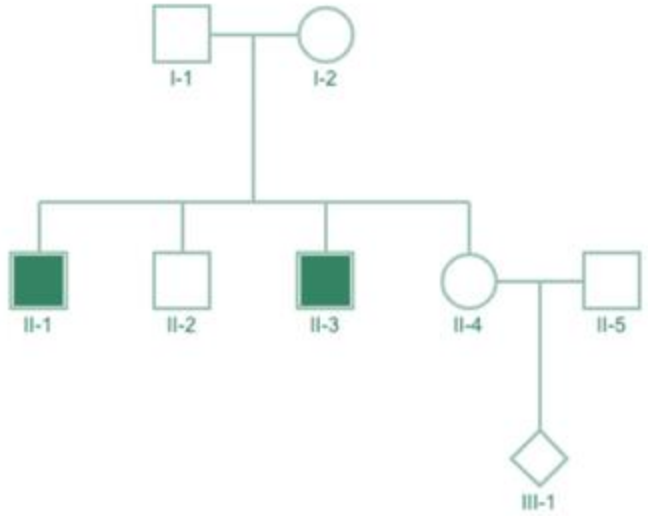
If 50% of the gametes are recombinants then there will be two parental and two recombinant gametes.



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

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

GENETIC TESTING



Direct test

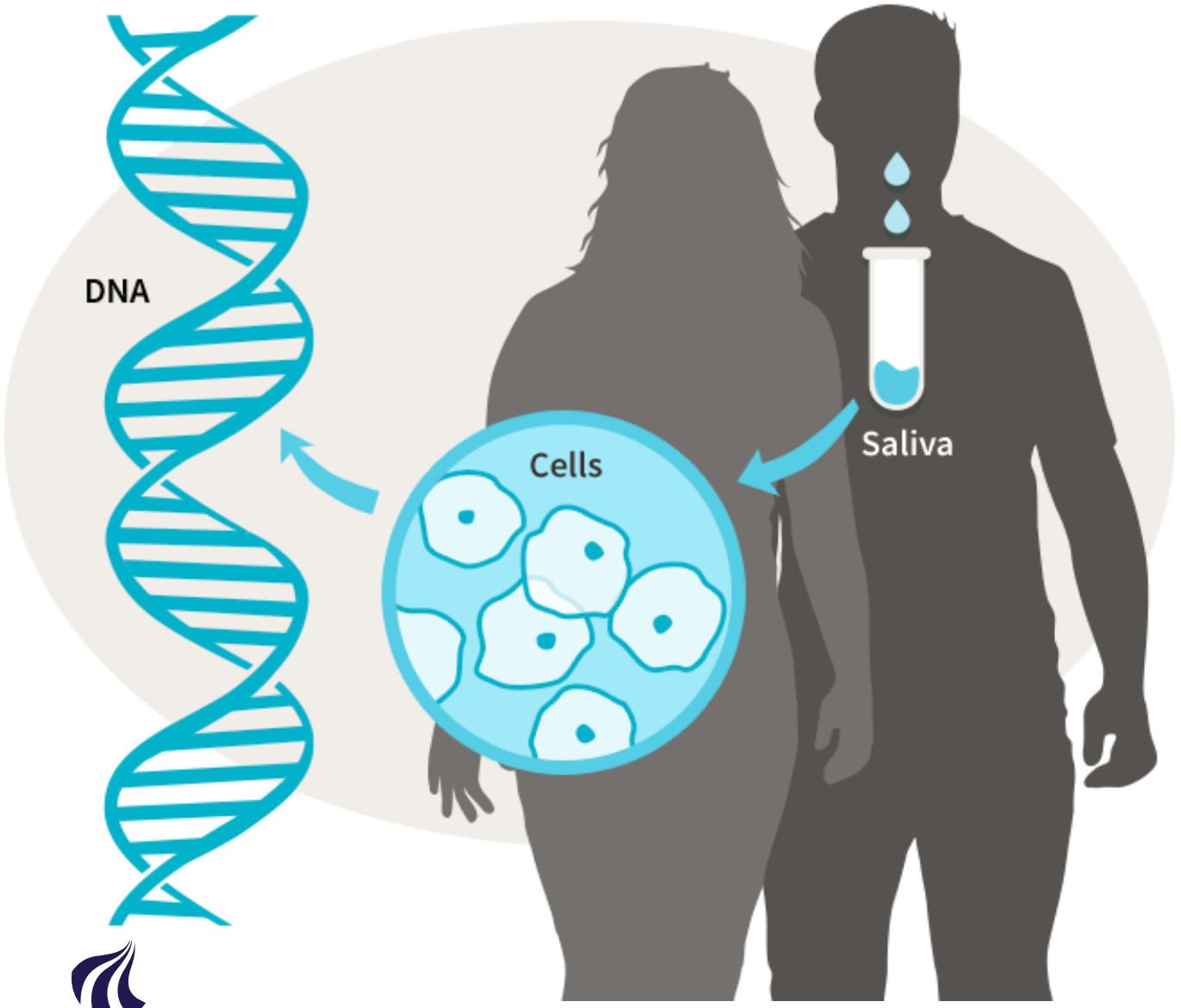
- When the pathogenic variant is known
  - Track the mutation in a pedigree and design a molecular test

Indirect test

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

GENETIC TESTS

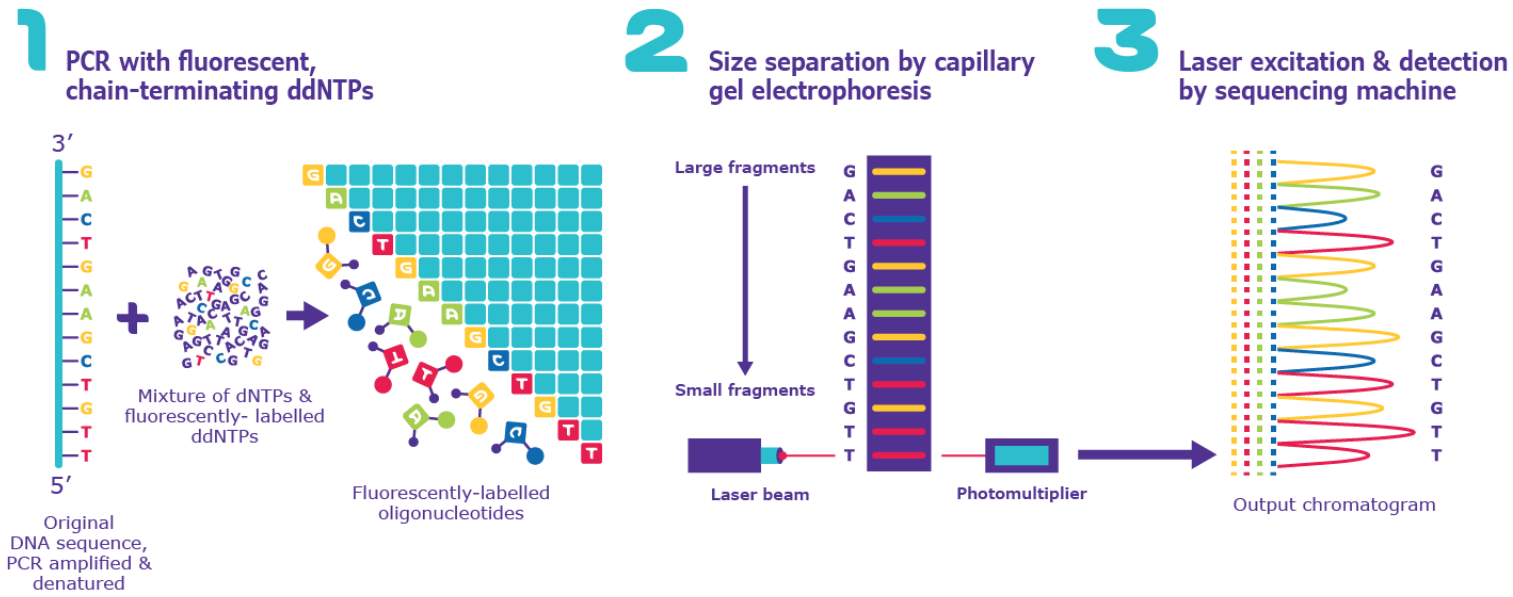
- **Direct diagnosis** – *known pathogenic variant*
- **Indirect diagnosis** – *unknown pathogenic variant*
- Clinical application of Next-generation sequencing (NGS)



DIRECT GENETIC DIAGNOSIS

KNOWN PATHOGENIC VARIANT

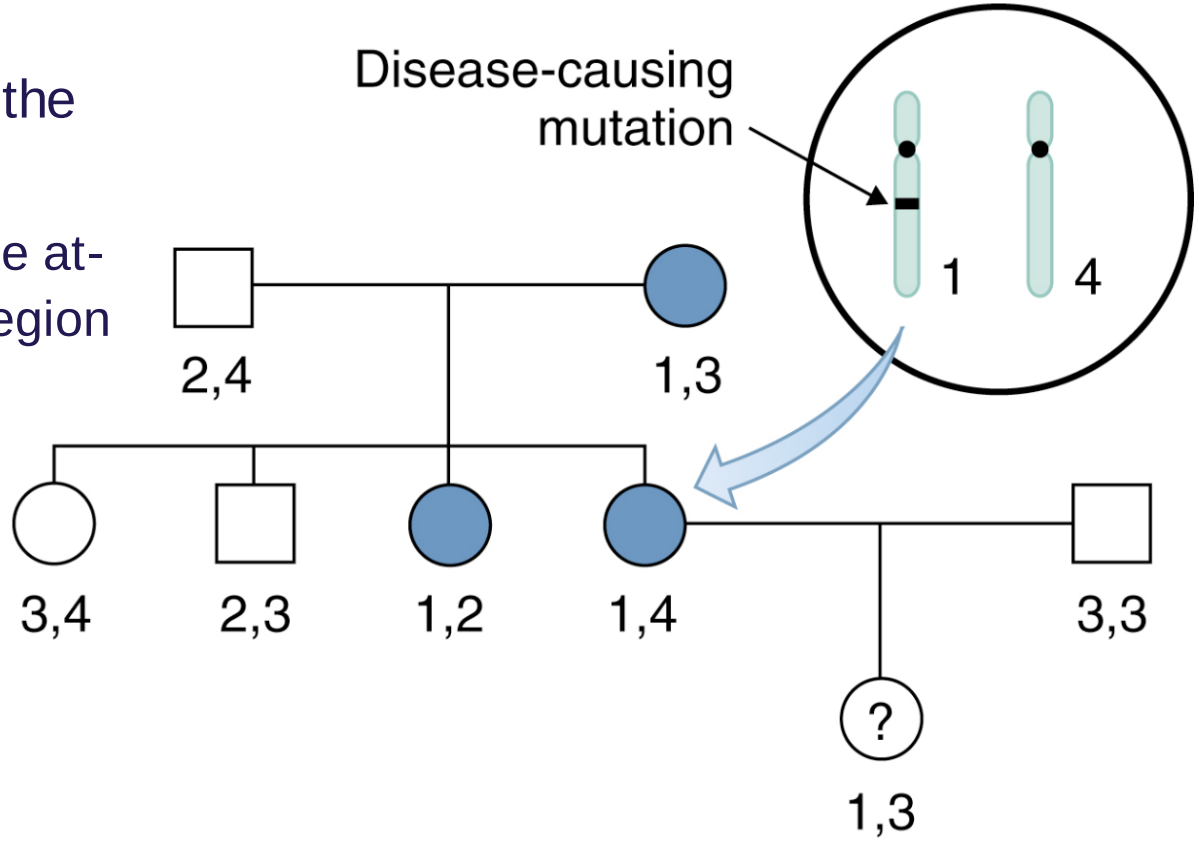
- We know the disease-causing mutation.
- Design a molecular assay that can target that specific mutation, e.g., Sanger sequencing



INDIRECT GENETIC DIAGNOSIS

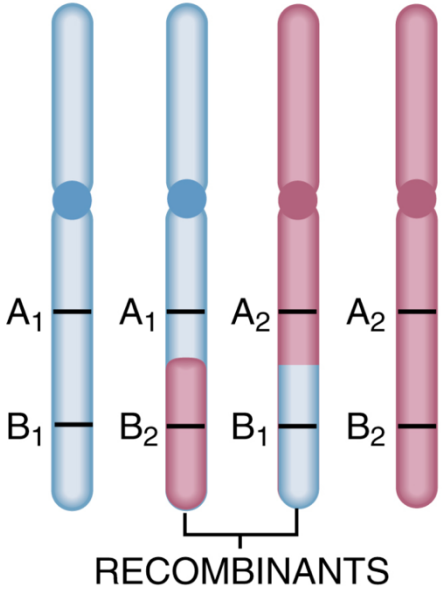
UNKNOWN PATHOGENIC VARIANT

- We do not know the exact disease-causing mutation.
- Instead, we look at genetic **markers** close to the disease-causing mutation.
  - *Advantange* – 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 thorugh the pedigree
  - Linkage phase (identify haplotypes)



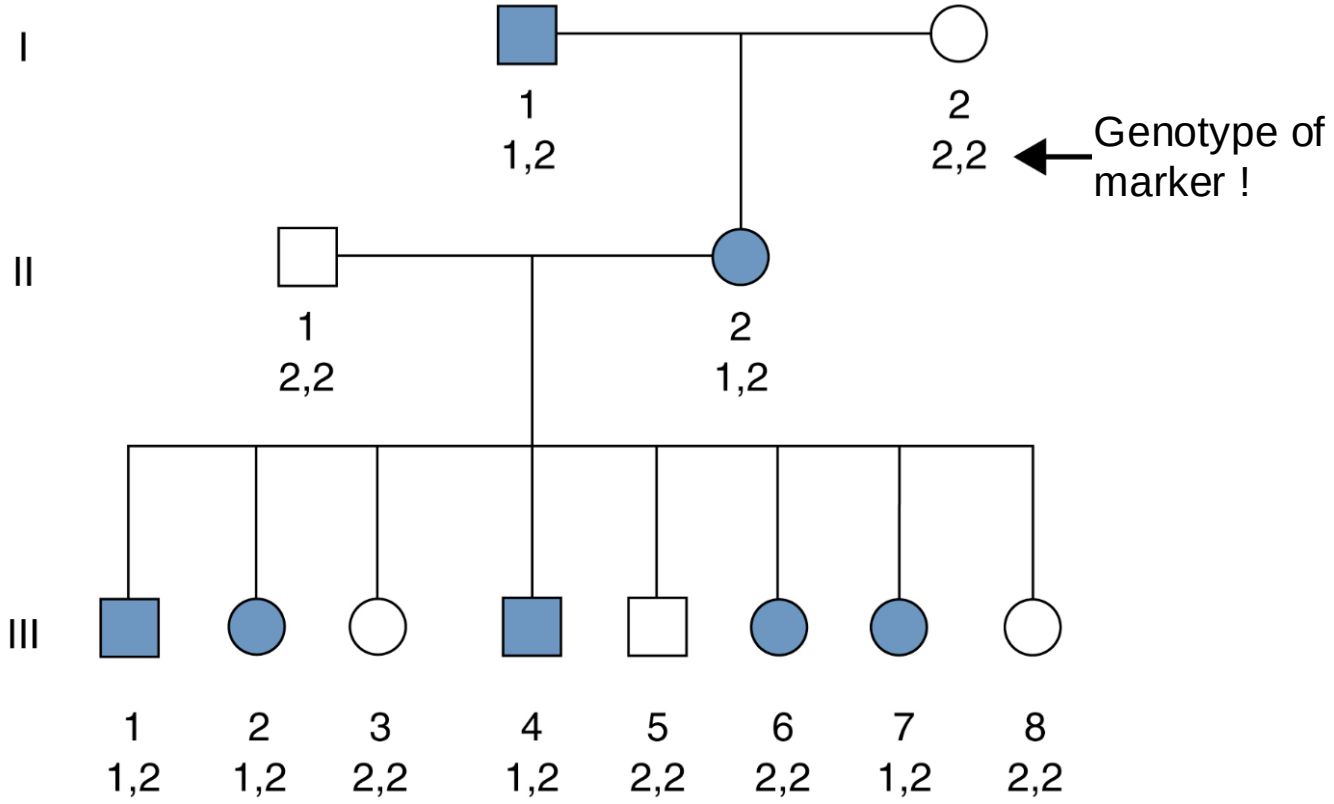


Fig. 8.4

LINKAGE MAPPING

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

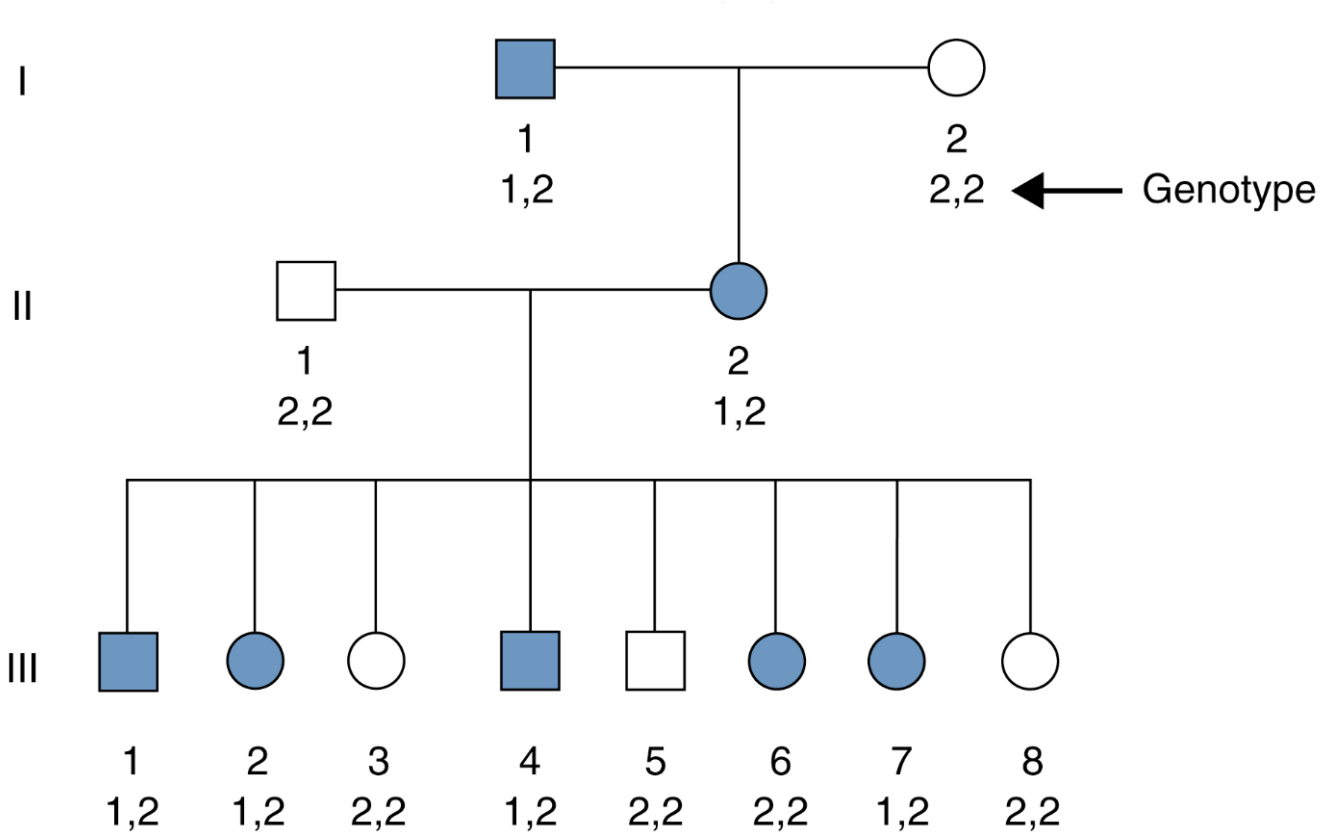
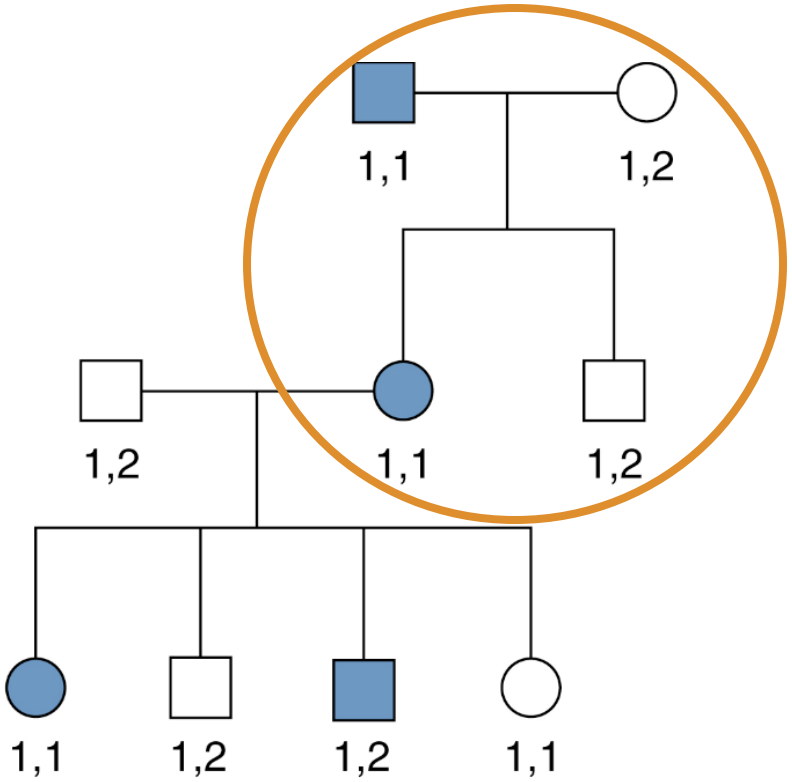
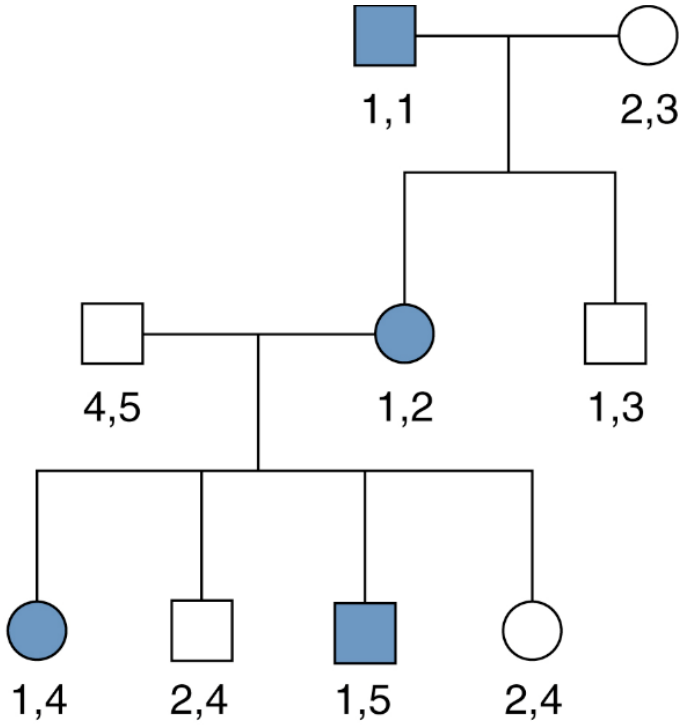


Fig. 8.4

(UN)INFORMATIVE MARKERS





Which marker is linked with the disease?

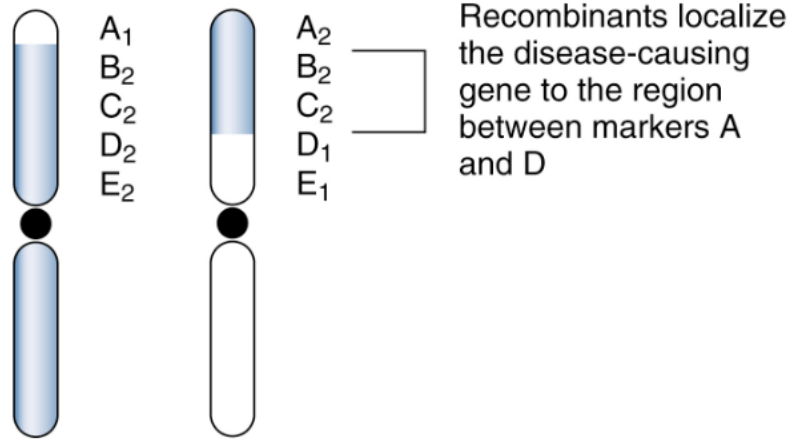
We cannot tell by certainty because we don't know the linkage phase

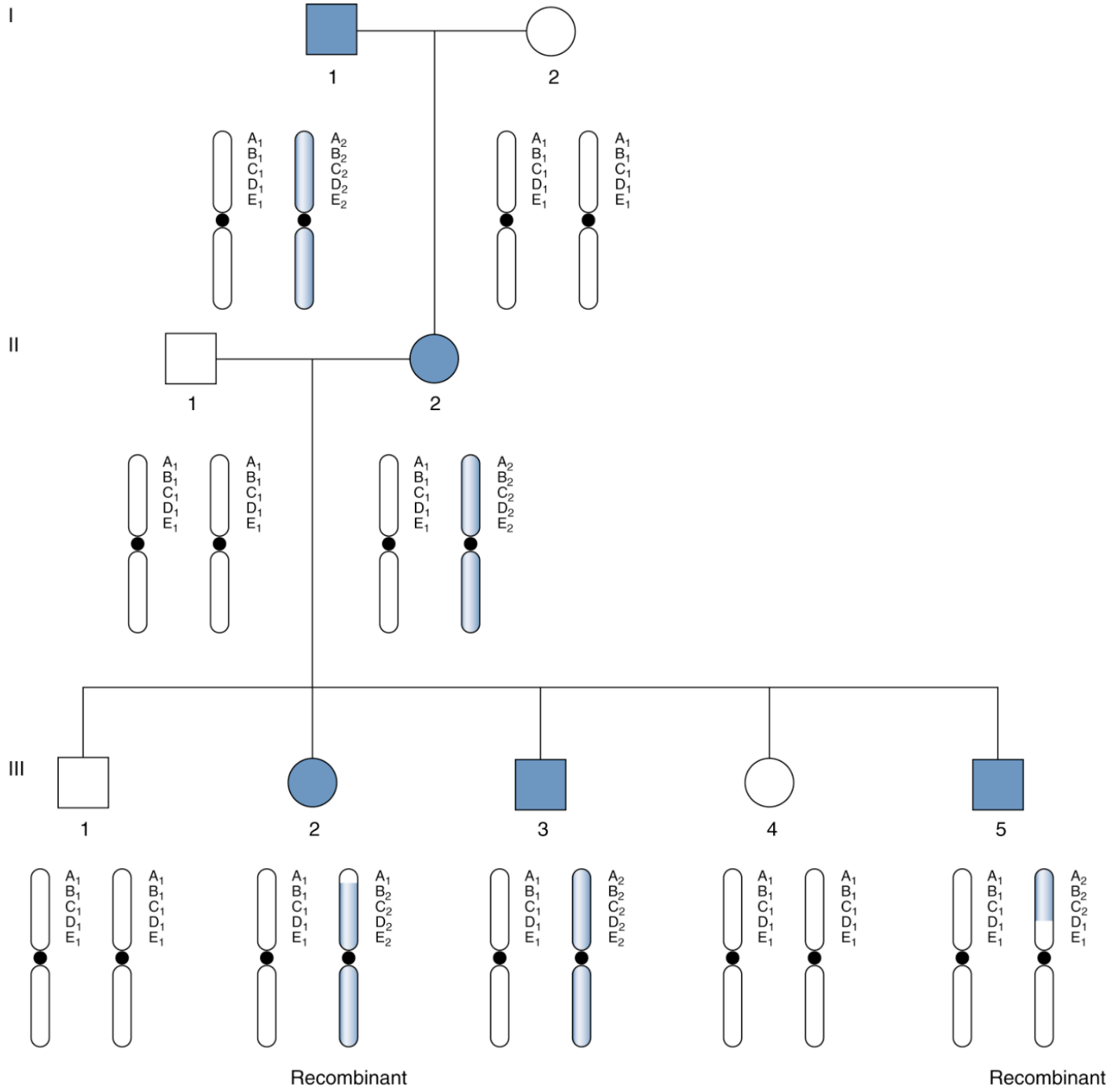
Much better to find a highly polymorphic variant!

Marker 1 is closely linked to the disease-causing variant

MANY POLYMORPHIC MAKRERS HELPS

Recombination events aids to pinpoint the disease-causing region

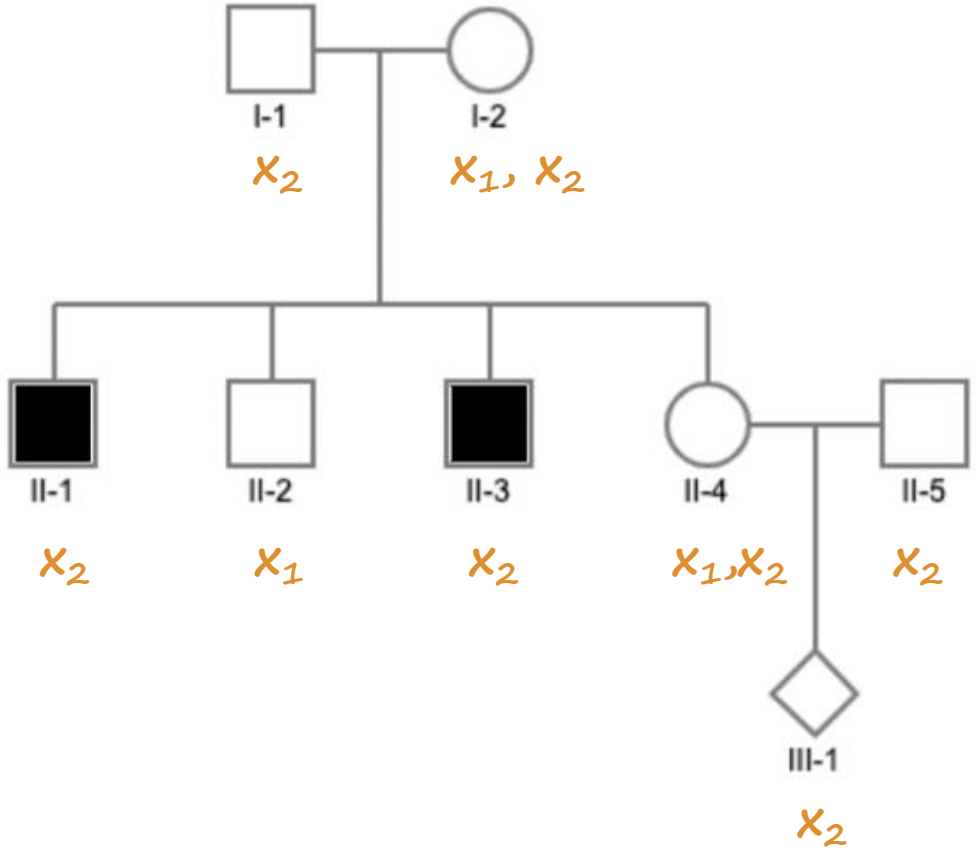




AALBORG UNIVERSITY

FOLLOW THE DISEASE AND GENETIC MARKERS

Assume X-linked



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

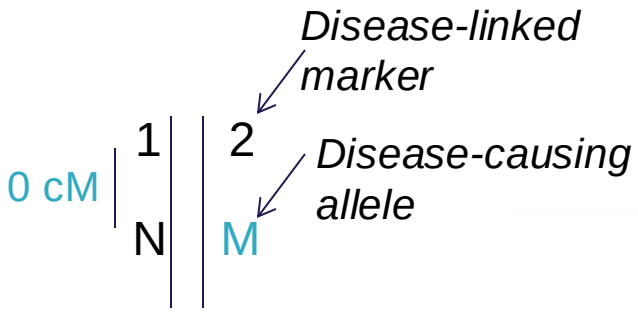
=p(II.4 XX´)*p(transmit to III.1)*p(male)
=1/2*1/2*1/2
=1/8

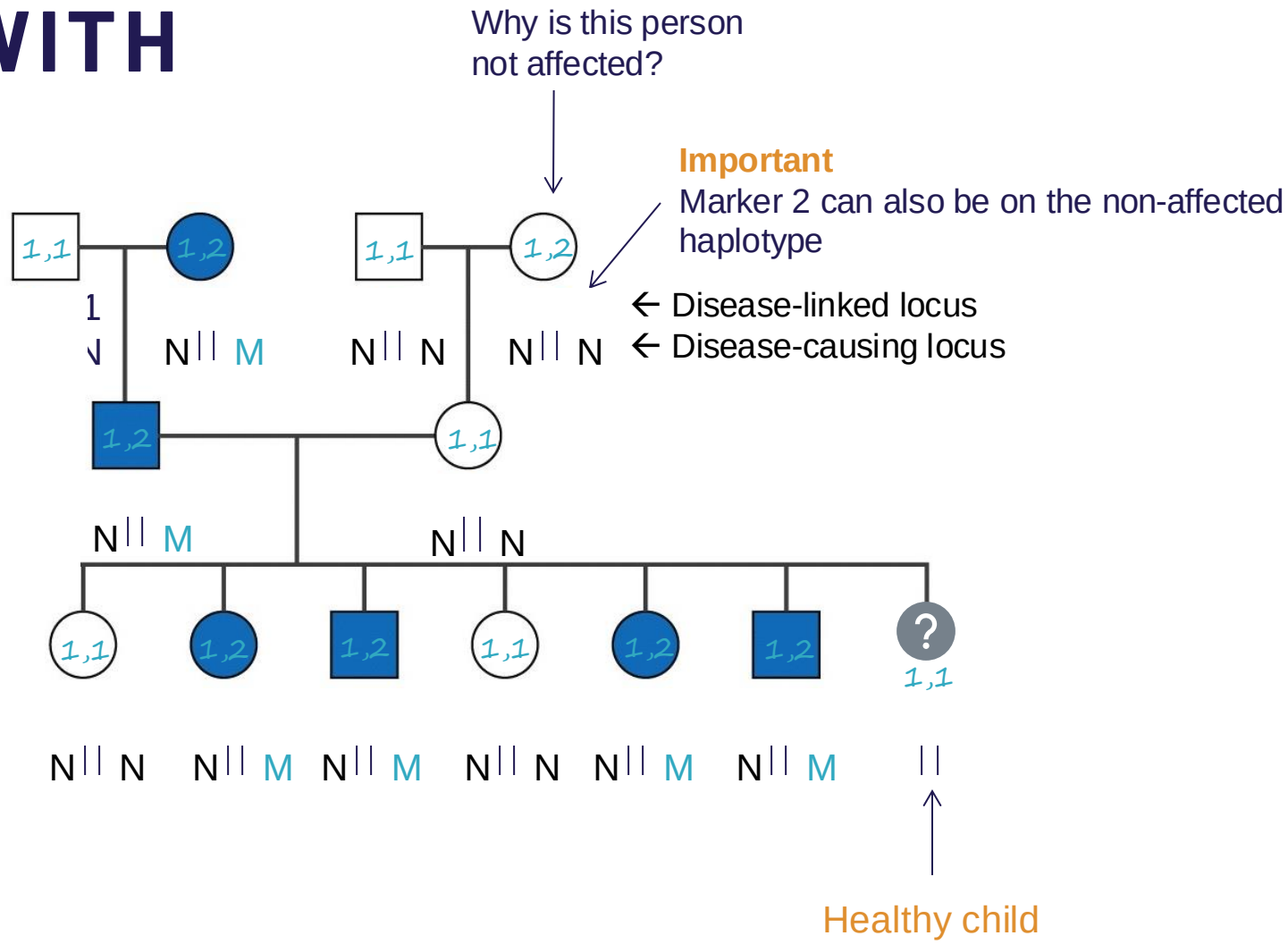
2) Based on the molecular data, what is the risk that III-1 will have the disease?

=0

Assume dominant inheritance, full penetrance

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

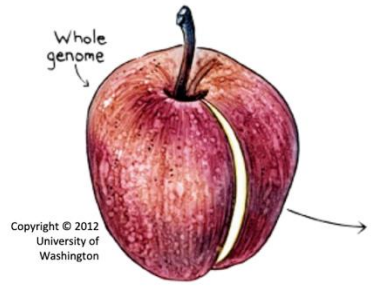
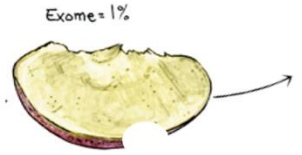
Attribute	Indirect Diagnosis	Direct Diagnosis
Family information needed	Yes	No
Errors possible because of recombination	Yes	No
Markers may be uninformative	Yes	No
Single test can uncover multiple mutations	Yes	Yes (by DNA sequencing)
Disease-causing mutation must be identified	No	Yes

- 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

"Genomic Sequencing"

Genome Sequencing (GS)	Exome Sequencing (ES)	Panel/ Targeted Sequencing
 Copyright © 2012 University of Washington		
• Virtually all of your DNA (~3 billion base pairs) • Includes known disease genes, novel genes, and noncoding regions	• ~21,000 protein coding genes (~30 million base pairs) • Includes known disease genes and novel genes	• Typically <100 genes • Genes are selected for well-established role in disease

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

"Genomic Sequencing"

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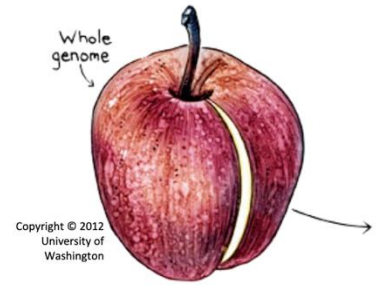	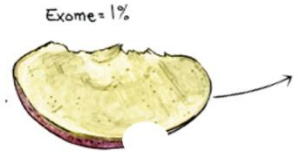	
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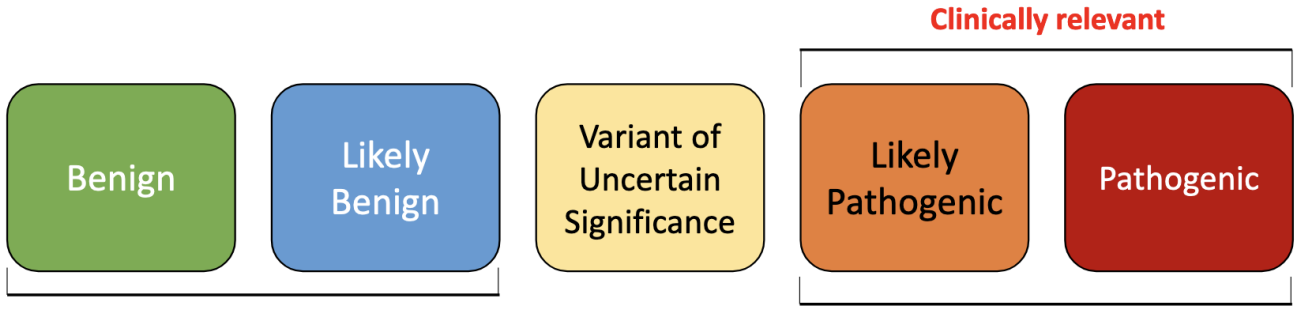
VARIANTS ON INTEREST?

- ACMG guidelines [American College of Medical Genetics and Genomics]
  - Put all variants into any of these categories by looking at the variants impact on the protein (missense, synonymous, nonsens)



- Population frequency > disease prevalence
- No impact on amino acid sequence
- Changes amino acid at a poorly conserved position
- Inheritance not supportive of a disease causing role

- Rare
- Severe protein impact
- Reported in other individuals with consistent phenotypes
- Segregates with disease in families
- De novo occurrences
- Functional studies supportive of an impact

GENETIC TESTS

When the pathogenic variant is known

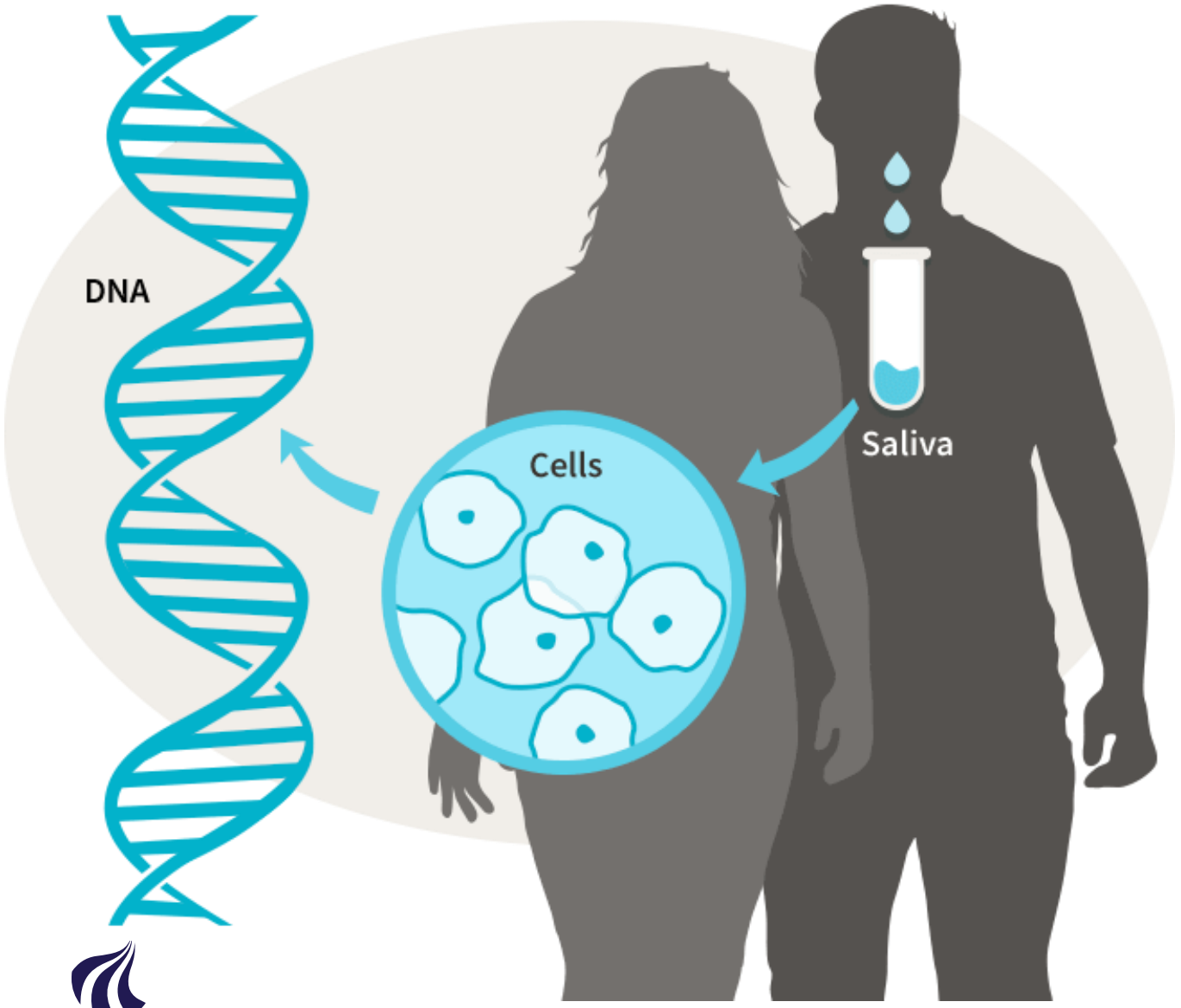
→ Risk from direct test

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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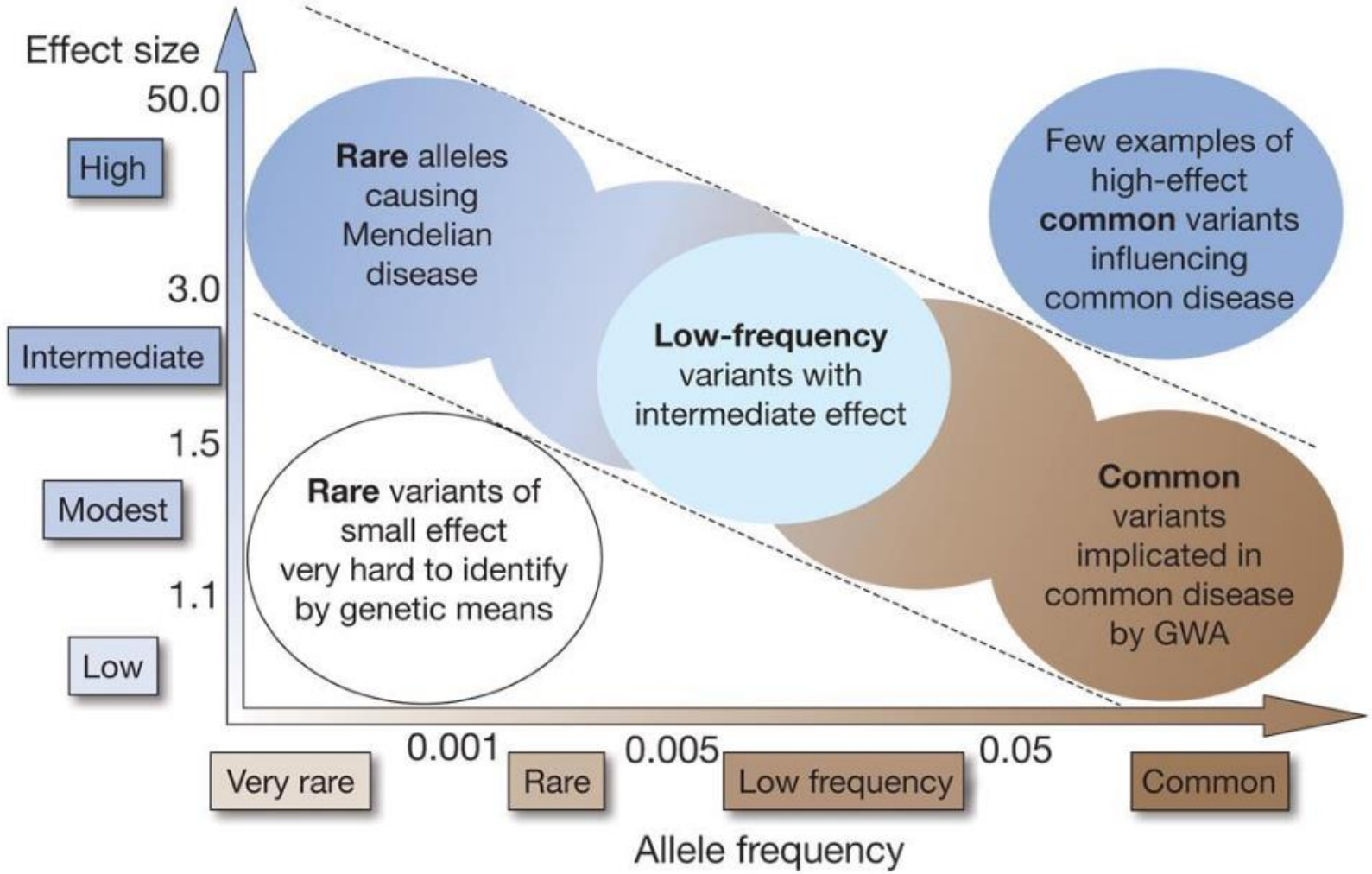
Effect size
50.0
High
3.0
Intermediate
1.5
Modest
1.1
Low
Rare alleles causing Mendelian disease
Few examples of high-effect common variants influencing common disease
Low-frequency variants with intermediate effect
Rare variants of small effect very hard to identify by genetic means
Common variants implicated in common disease by GWA
0.001
0.005
0.05
Very rare
Rare
Low frequency
Common
Allele frequency

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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 (½ -1ft)
1	2	3	4	5	6	7

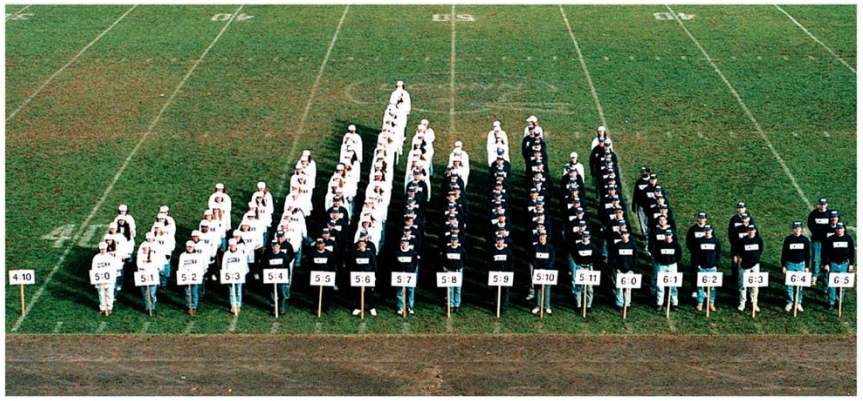
QUANTITATIVE TRAITS

Many quantitative traits has continous variation

QUANTITATIVE TRAITS

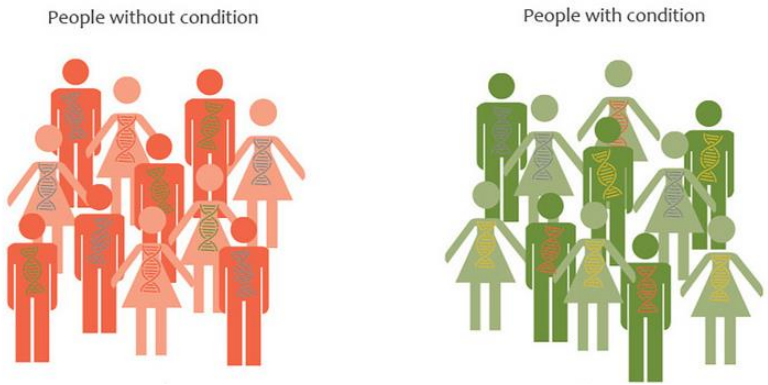
IN DIFFERENT SHAPES

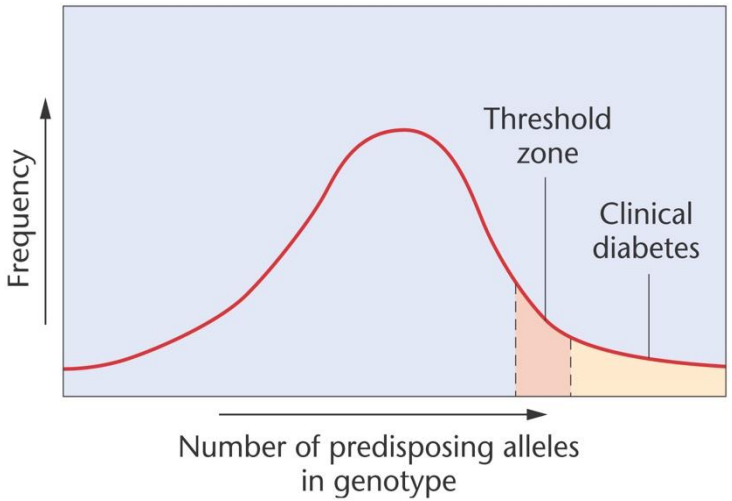
Continous variation



Categorical variation

Threshold traits



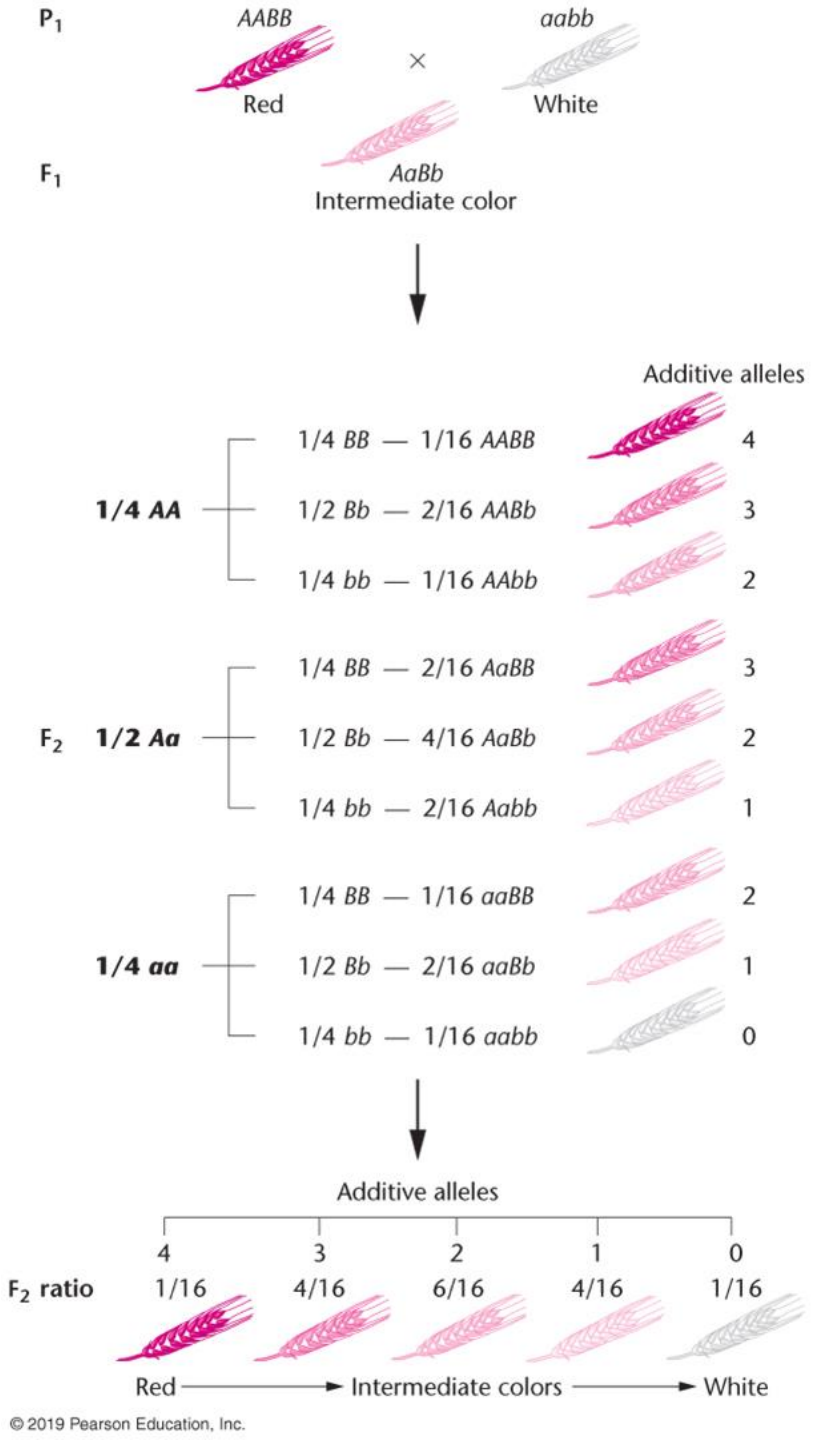


Why do quantitative traits

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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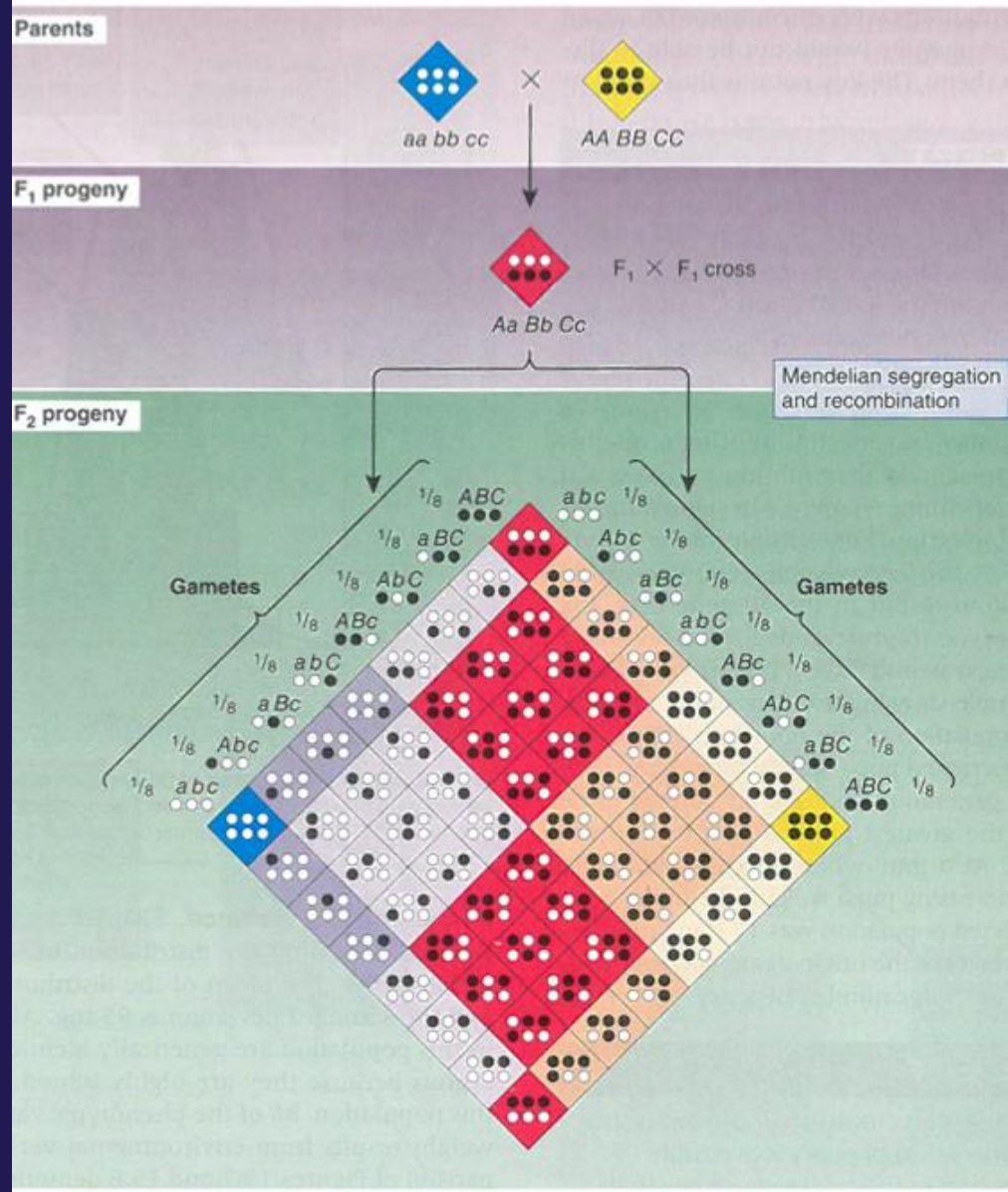
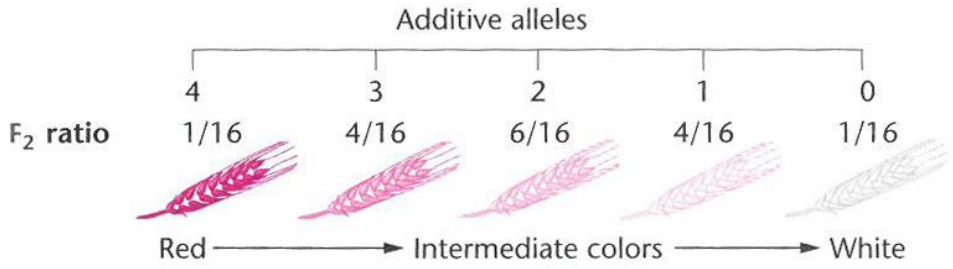
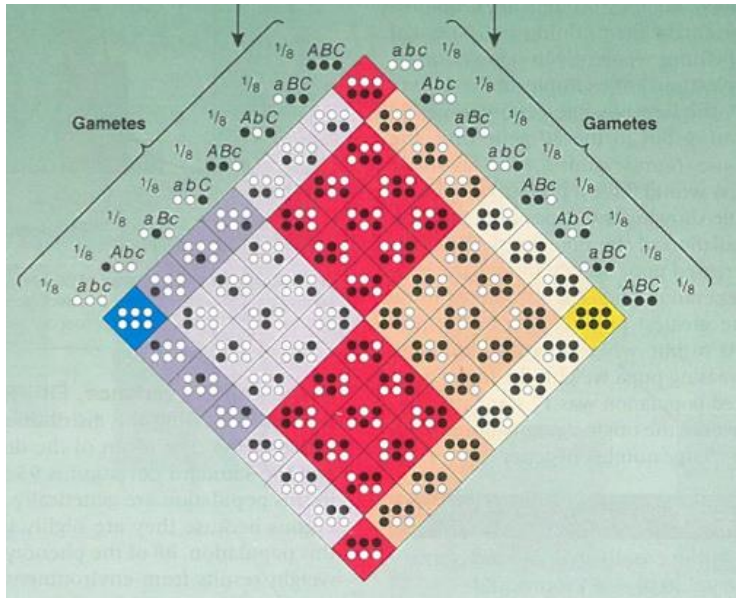
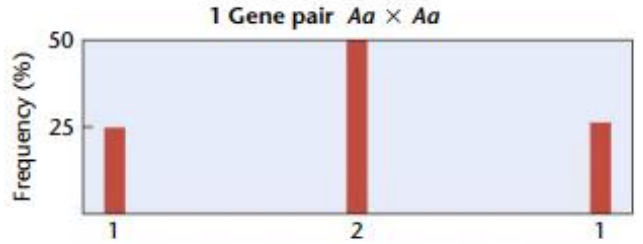


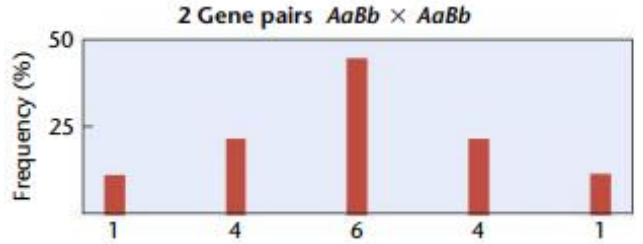
POLYGENIC TRAITS



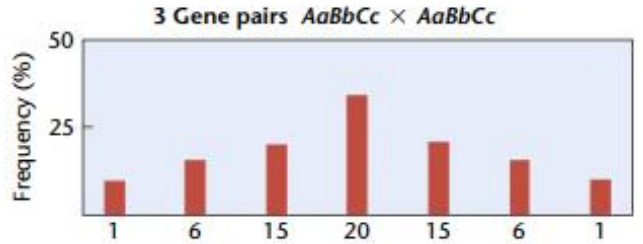




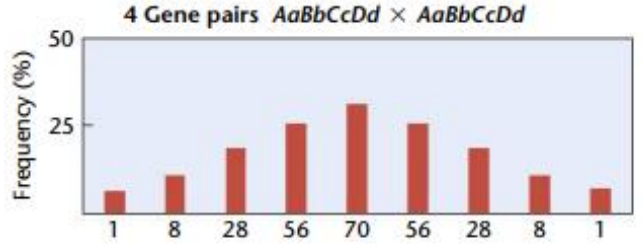
3 classes



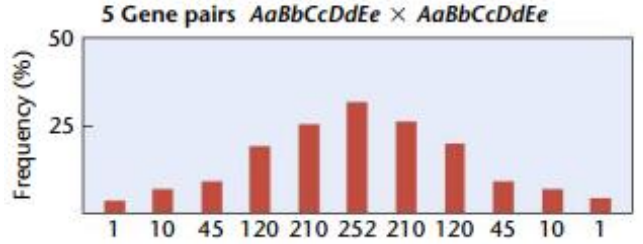
5 classes



7 classes



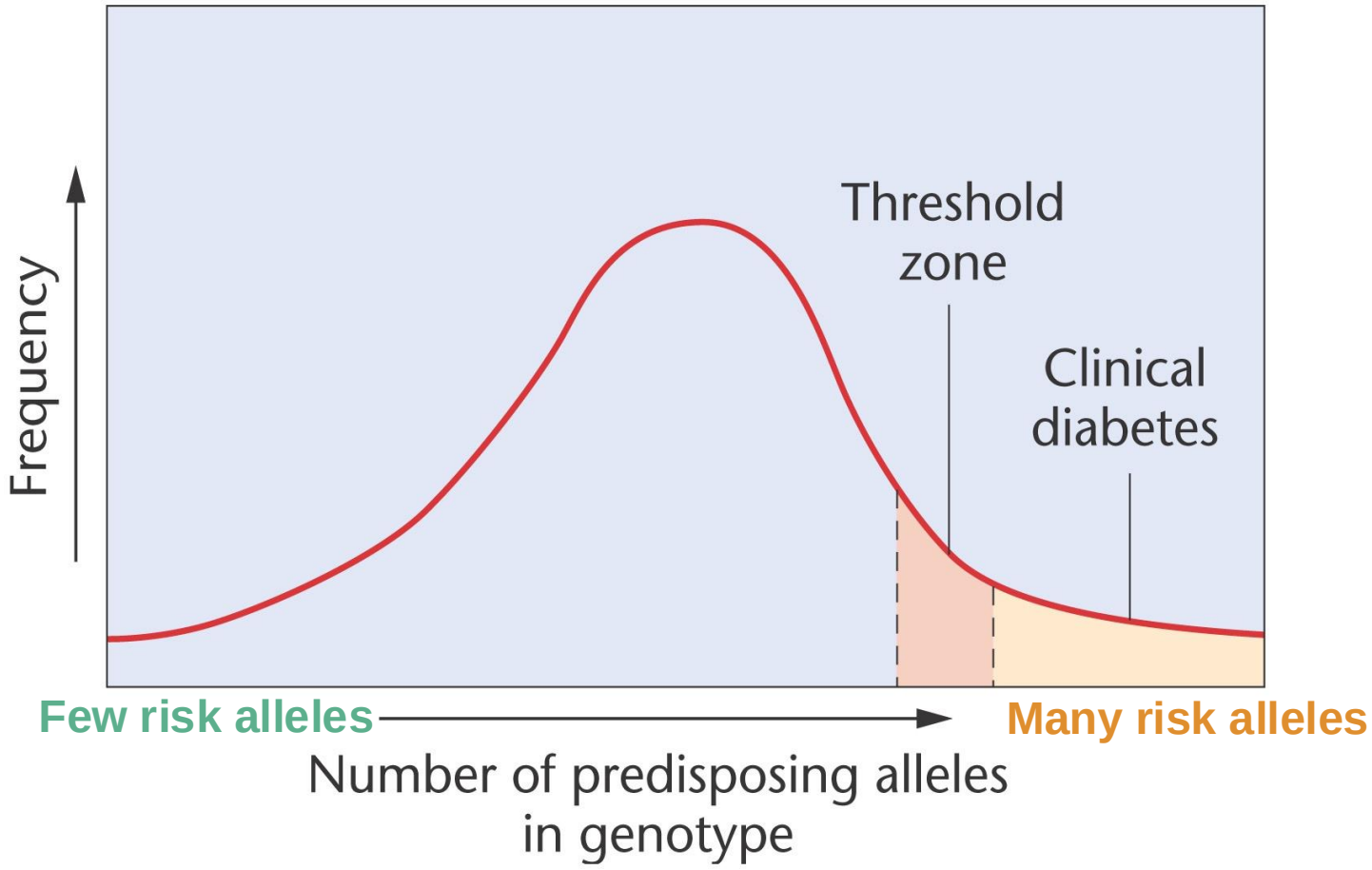
9 classes



11 classes

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

LIABILITY (THRESHOLD) MODEL

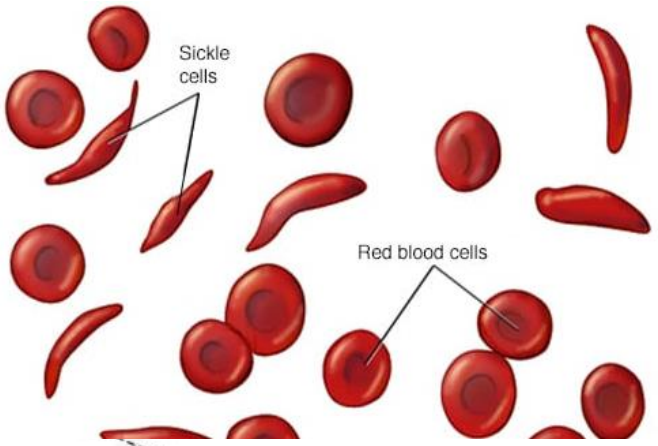


Liability model

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



Effect size

50.0

High

3.0

Intermediate

1.5

Modest

1.1

Low

Rare alleles causing Mendelian disease

Few examples of high-effect **common** variants influencing common disease

Low-frequency variants with intermediate effect

Rare variants of small effect very hard to identify by genetic means

Common variants implicated in common disease by GWA

0.001

0.005

0.05

Very rare

Rare

Low frequency

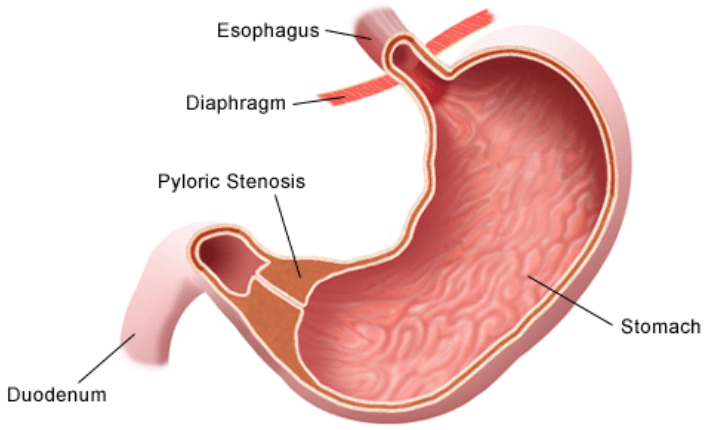
Common

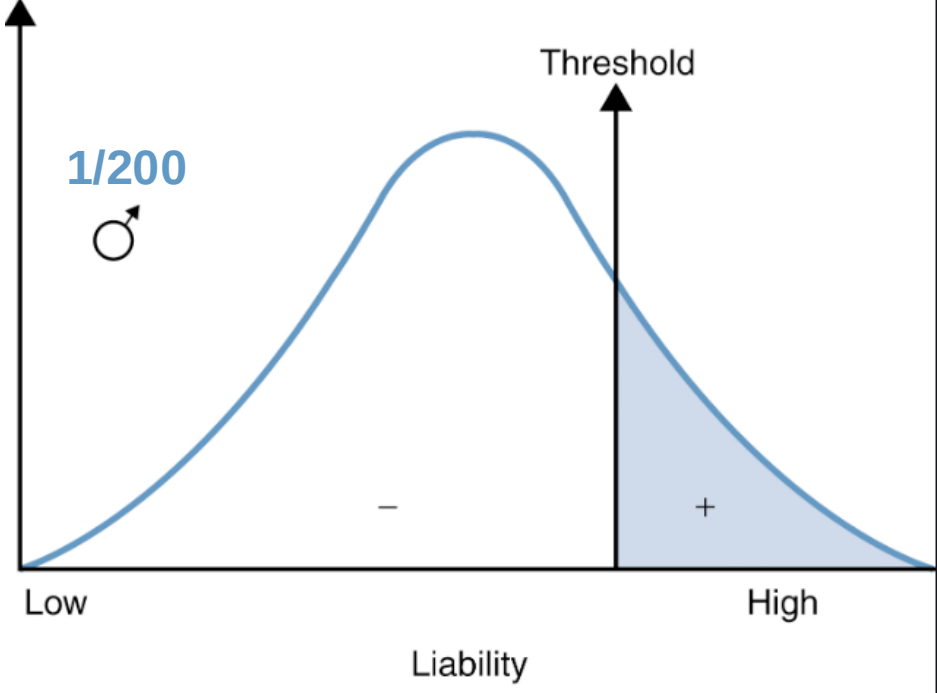
Allele frequency

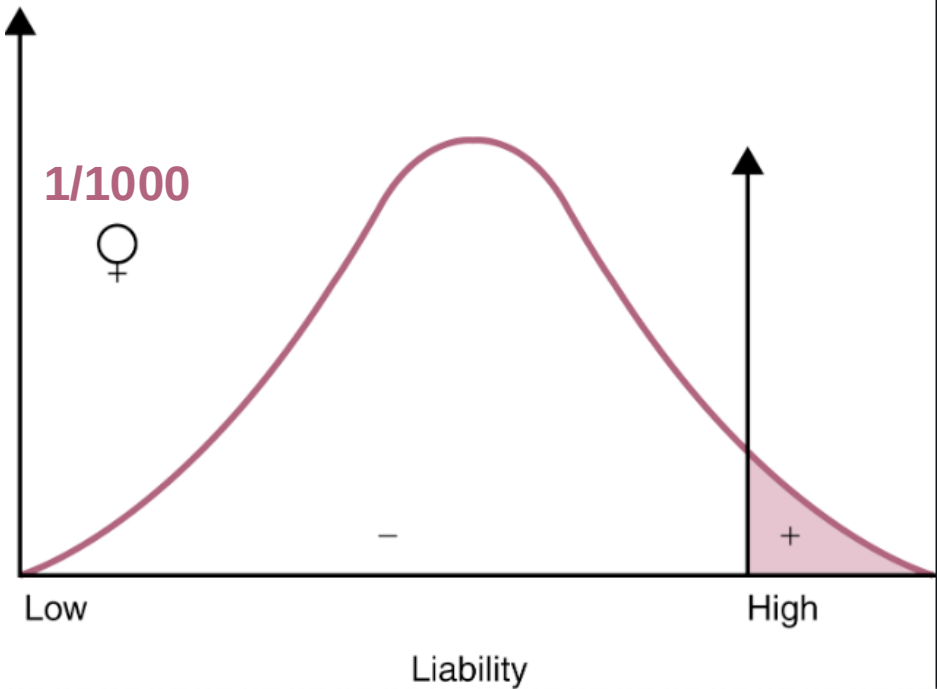
DIFFERENT THRESHOLD VALUES BETWEEN SEXES

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.



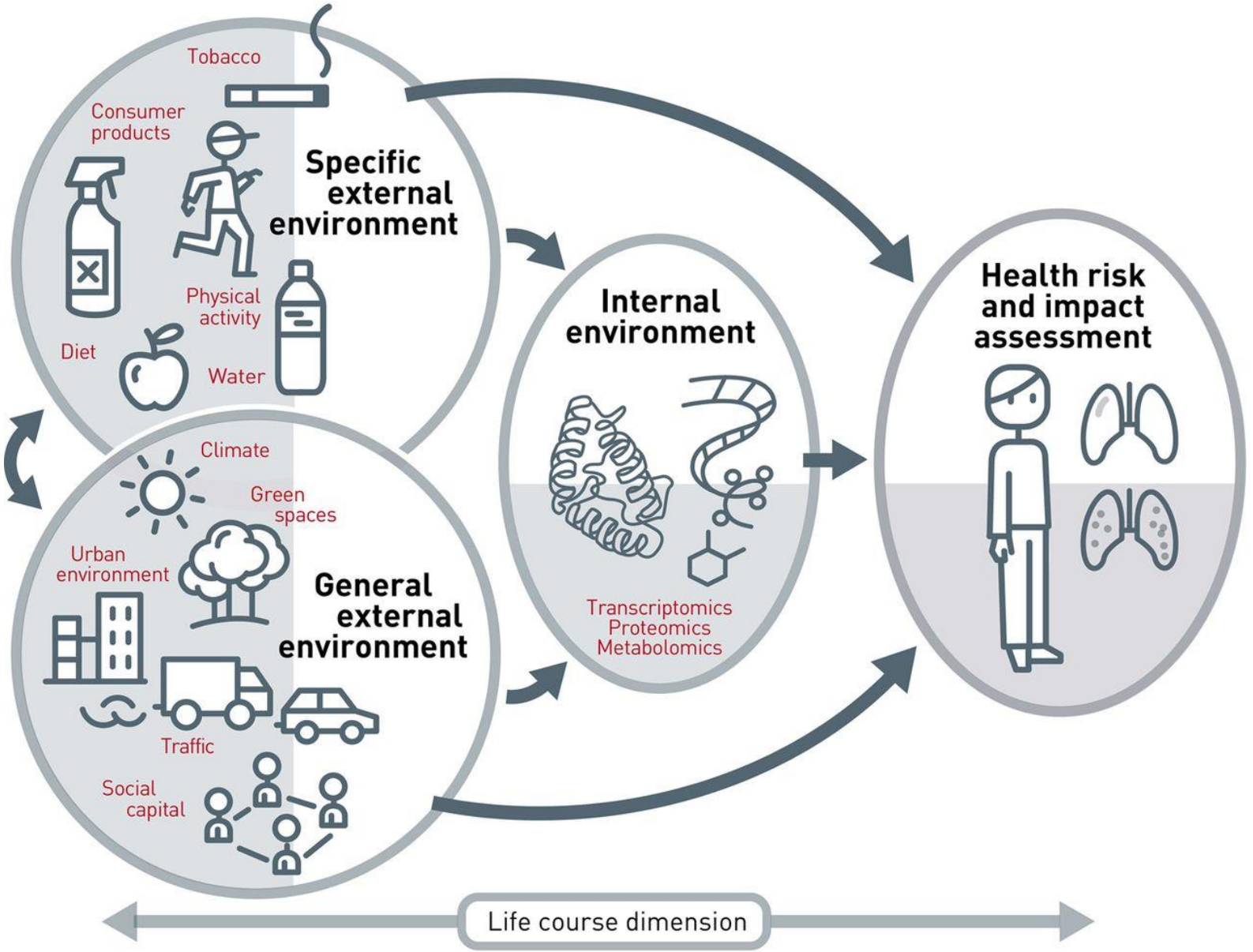




ENVIRONMENTAL EXPOSURE

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

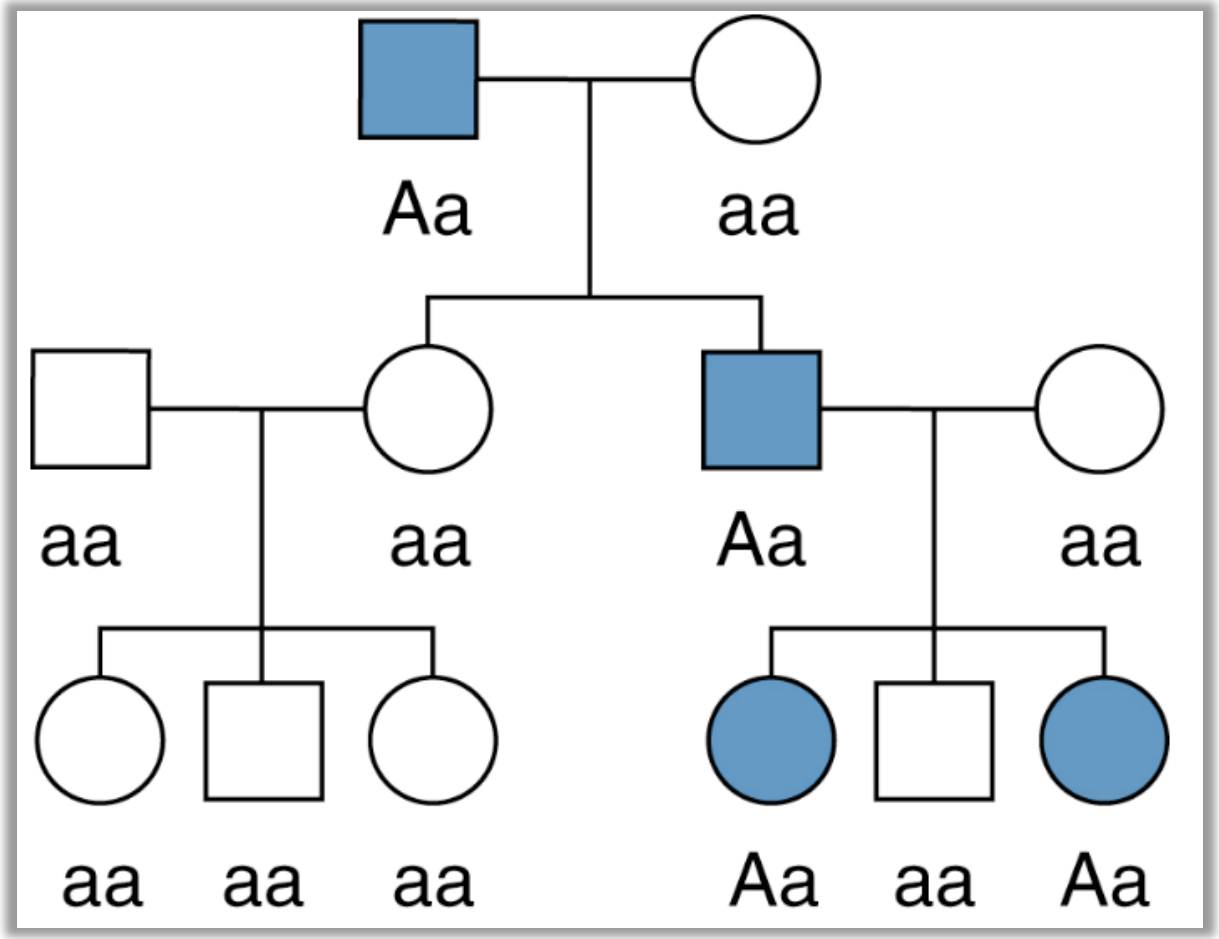
MONOGENIC TRAITS

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 Probands and Relatives*

Relatives	Male Probands		Female Probands	
	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?

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

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How can we test which one is the correct one?

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

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

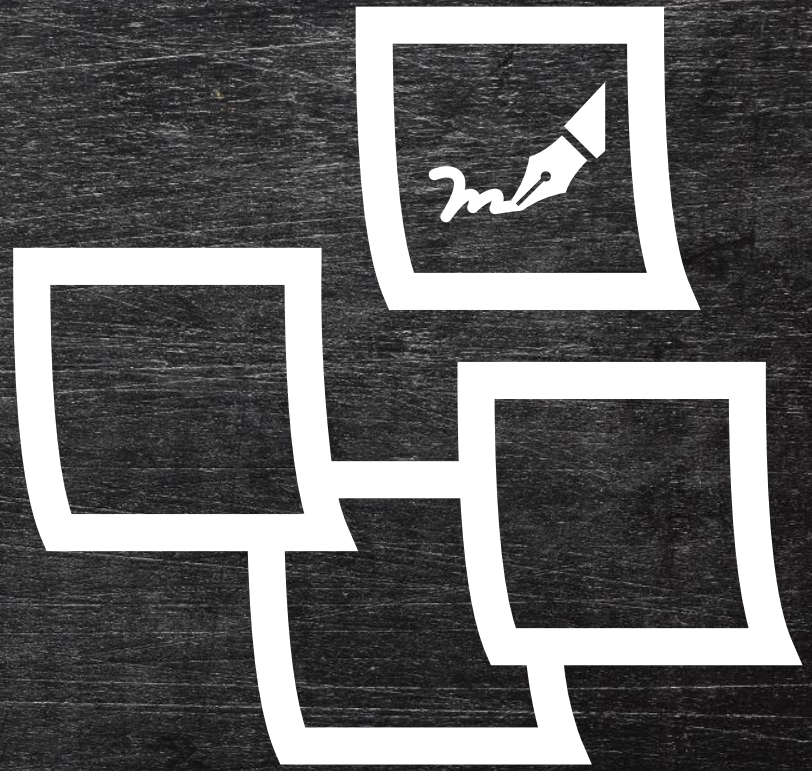
- Types of trait-inheritance
- Liability model
- Recurrence risk
- Environmental exposures modulate outcomes

AGENDA

08:15 – 08:45	Lecture 1 [*Recap + indirect testing*]
08:45 – 09:15	Exercises A + Break
09:15 – 09:40	Lecture 2 [*Multifactorial traits*]
09:40 – 10:00	Exercises B
10:00 – 10:40	Break + Group work
10:40 – 11:15	Lecture 3 [*Quantitative genetic theory*]
11:15 – 11:50	Break + Exercises C
11:50 – 12:00	Evaluation at Moo

GROUP WORK

1) Go into groups of 3
2) Select one complex traits; either one with continous variation or a disease
3) Use the literature to find:
    i. trait characteristics (*age of onset, sex difference, symptons, prevalence, diagnosis, pathology, etc*)
    ii. environmental exposures associated with the trait
    iii. genetic contributions to the selected trait



AGENDA

08:15 – 08:45 Lecture 1 [*Recap + indirect testing*]

08:45 – 09:15 Exercises A + Break

09:15 – 09:40 Lecture 2 [*Multifactorial traits*]

09:40 – 10:00 Exercises B

10:00 – 10:40 Break + Group work

10:40 – 11:15 Lecture 3 [*Quantitative genetic theory*]

11:15 – 11:50 Break + Exercises C

11:50 – 12:00 Evaluation at Moodle

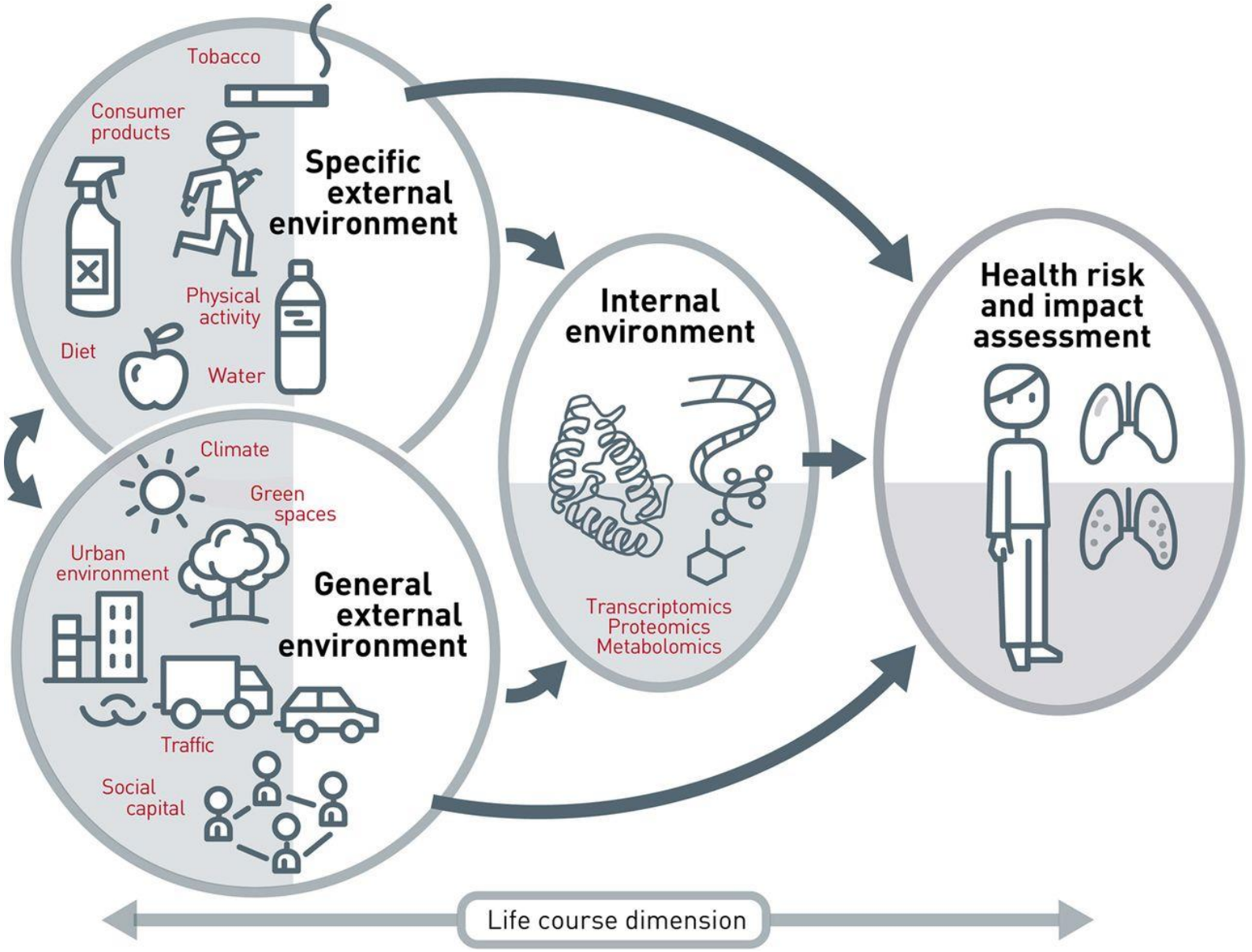
QUANTITATIVE GENETICS

- 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

Genotypic value

Environmental deviation

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

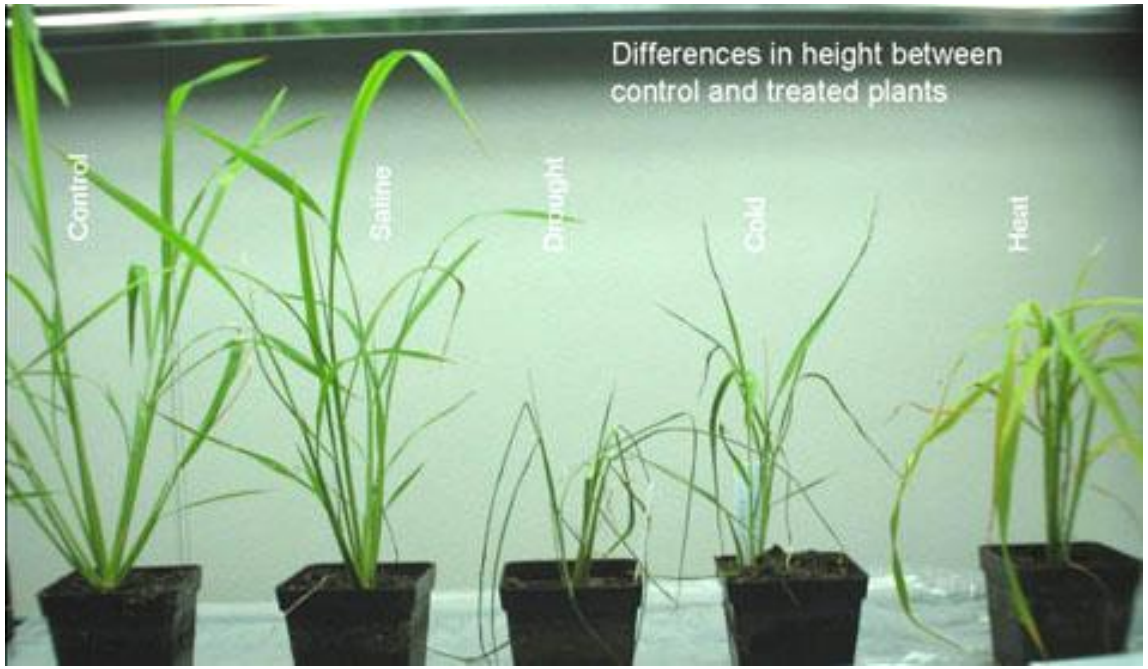
Every individual has a phenotypic value.

ENVIRONMENTAL DEVIATION

$$P = G + E$$

External effects that modulates the phenotypic value.

… or things that we cannot explain



THE GENOTYPIC VALUE

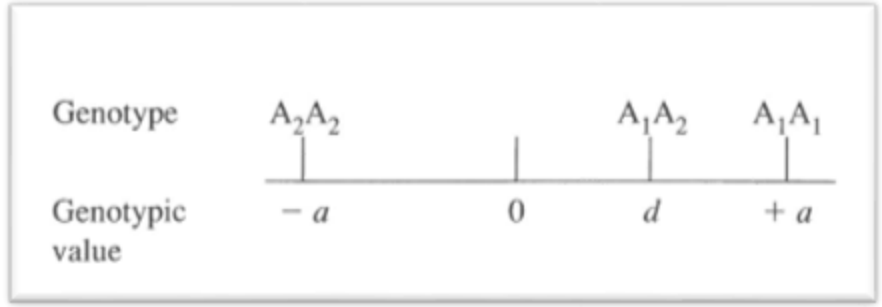
$$P = G + E$$

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:

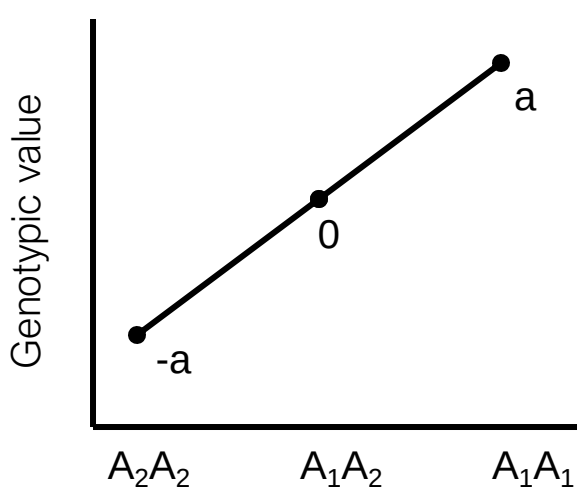
THE GENOTYPIC VALUE

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	$d = a \mid -a$
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)	$d < -a$

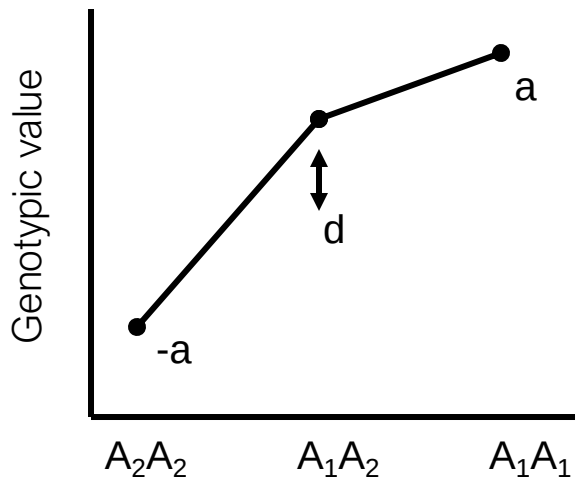
THE GENOTYPIC VALUE



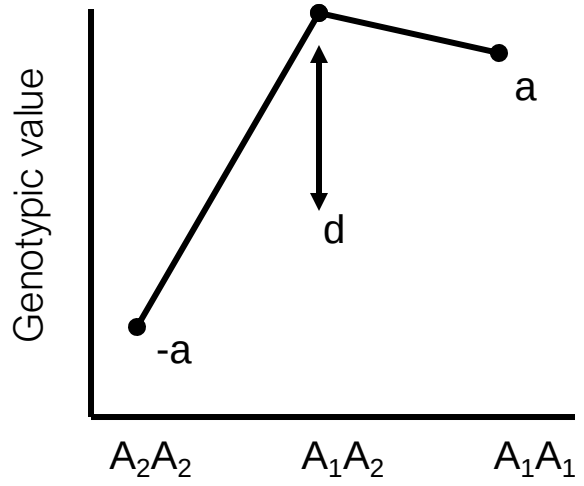
Additive gene effect



Partial dominance

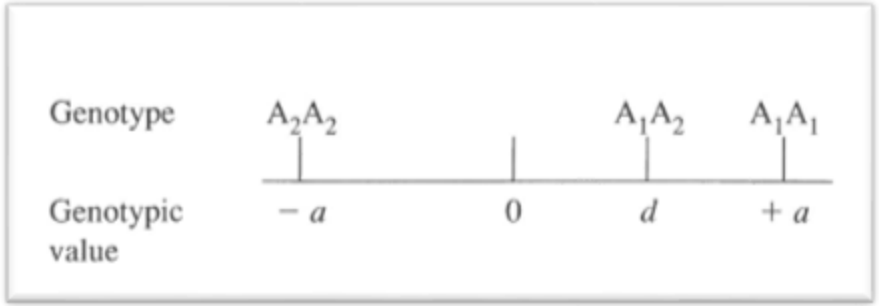


Overdominance



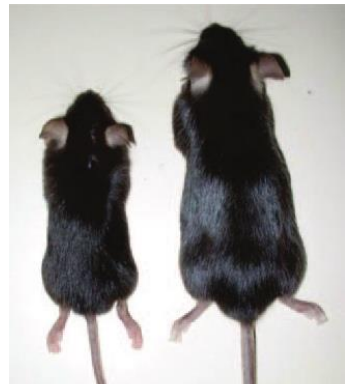
ESTIMATE G

$P = G + E$

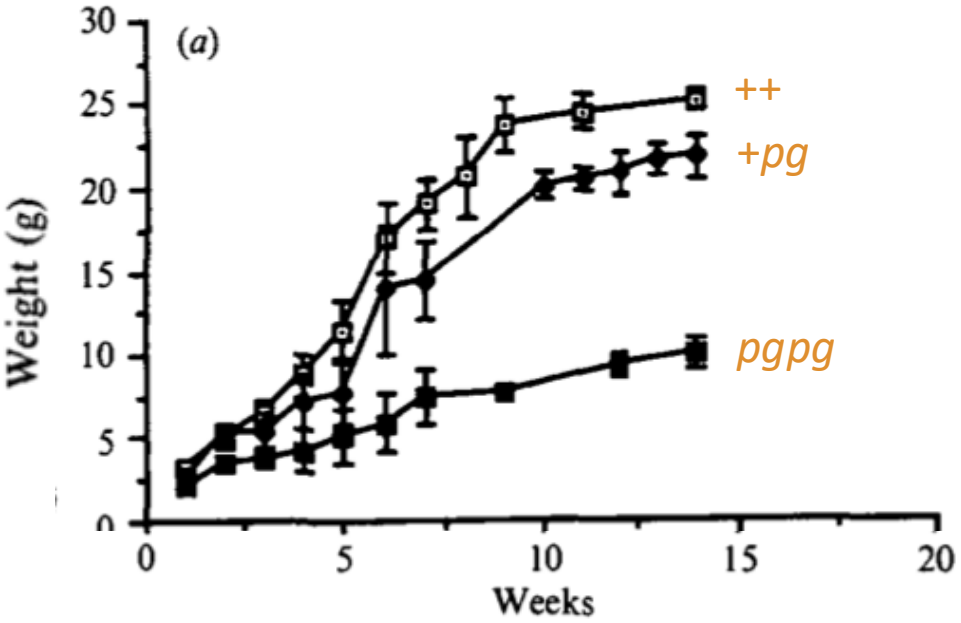


In mice, the gene *pygmy* (*pg*) is strongly correlated with body size.

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:

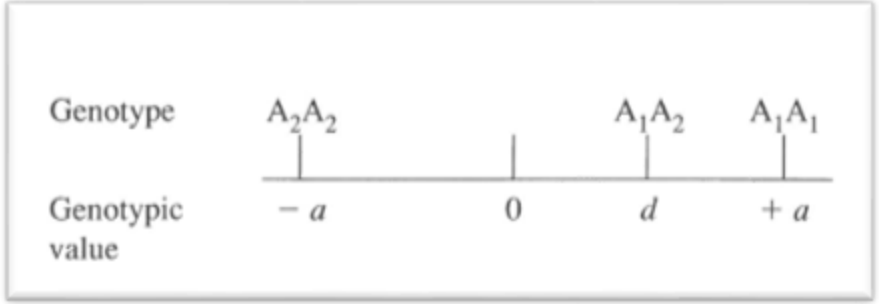
m = (25+10)/2 = 17.5

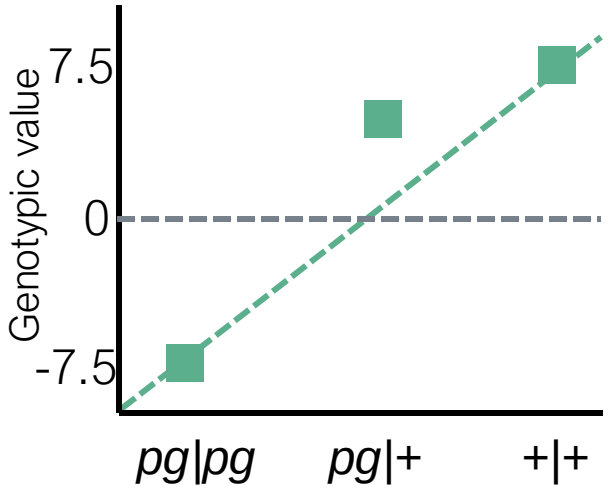
a is the difference between homozygote and m

a = 25 - 17.5 = 7.5

d is the difference between heterozygote and m

d = 22 - 17.5 = 4.5

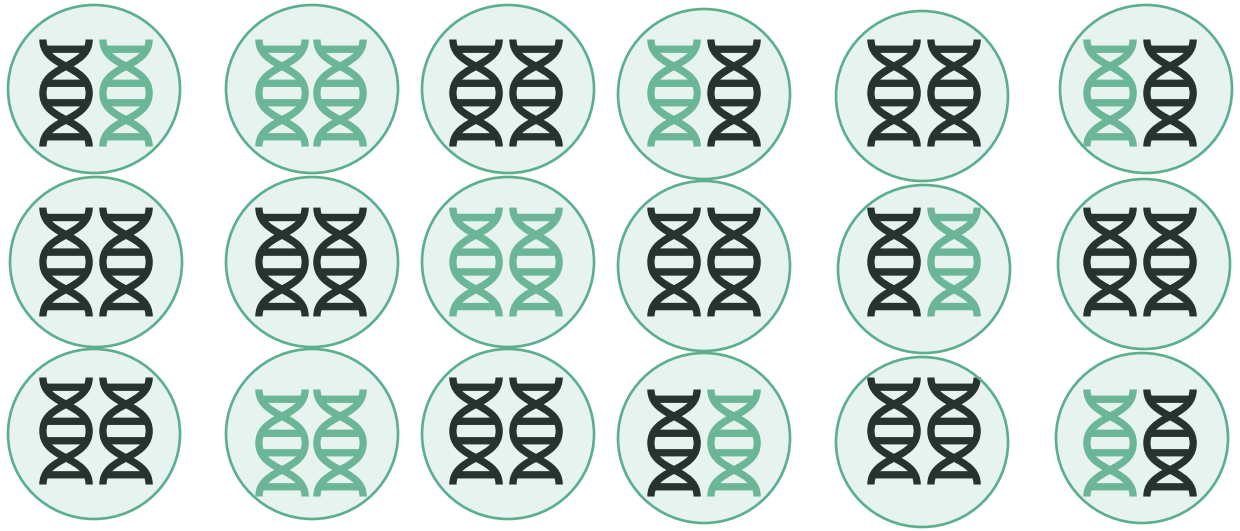




pg does act additive, but with partial dominace

ALLELE FREQUENCY

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



	12	12/36=0.33	*q*
	24	24/36=0.66	*p*
	36		

ALLELE FREQUENCY
CHANGE THE POPULATION MEAN

Allele frequency has an influence on the trait population mean

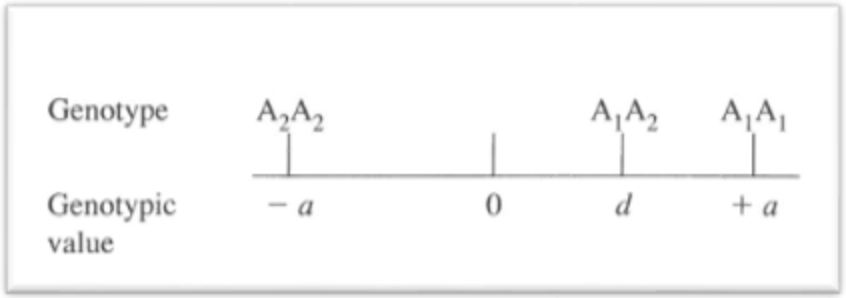
Genotype	*Frequency*	*Value*	*Freq. × Val.*
A_1A_1	p^2	$+a$	p^2a
A_1A_2	$2pq$	d	$2pqd$
A_2A_2	q^2	$-a$	$-q^2a$
		Sum =	$a(p-q)+2dpq$

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 a = 7.5 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

Popoluation mean is then,

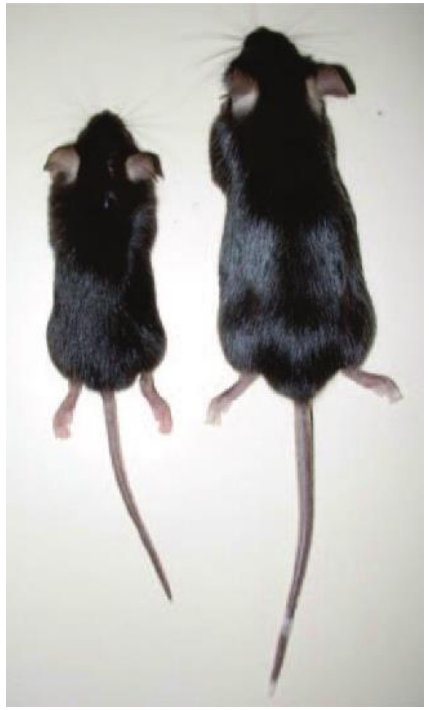
m+M=17.5+6.81 = 24.31

If p = 0.6 and q = 0.4

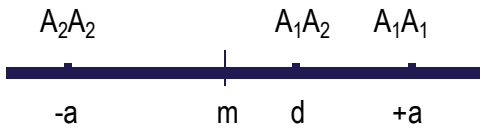
M=7.5(0.6-0.4)+2*4.5*0.6*0.4=3.66

Population mean,

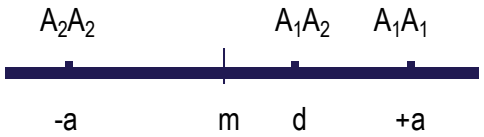
m+M=17.5+3.66 = 21.16

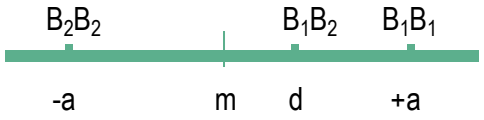


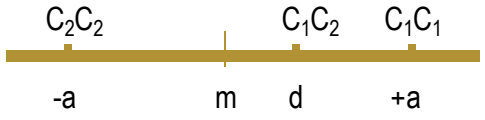
FROM ONE LOCUS TO MANY LOCI

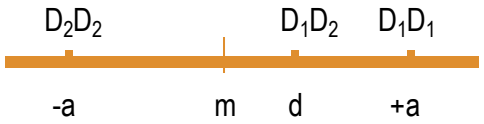


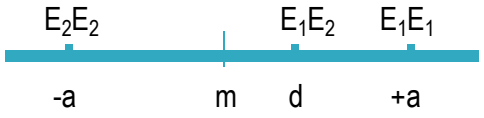
$$M = a(p - q) + 2dpq$$

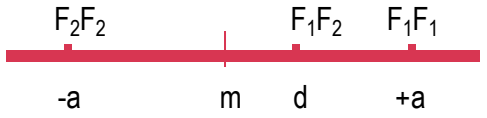












$$M = \sum a(p - q) + 2\sum dpq$$

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 parent 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.

Genotype	*Breeding value*
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 now much of the observed variation that is due to genetic differences among individuals and how much is due to environmental variation.

VARIANCE NOT MEAN

$$P = G + E$$

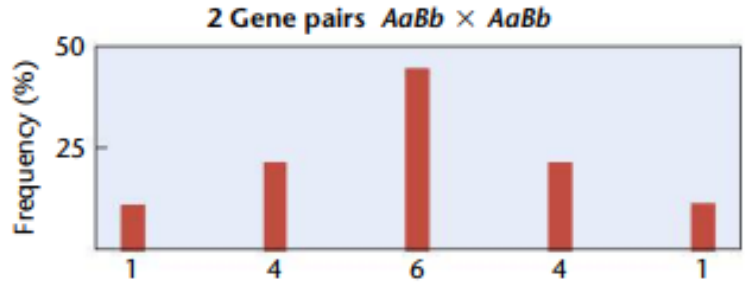
$$V_P = V_G + V_E$$

Phenotypic variance

Genotypic variance

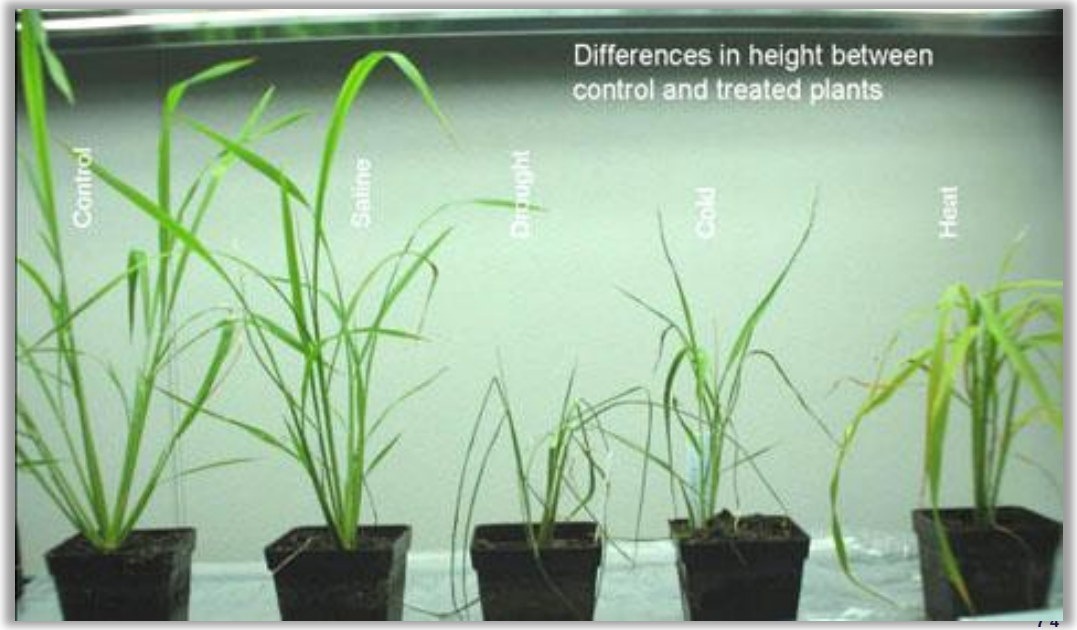
Environmental variance

ENVIRONMENTAL VARIATION



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

→ this blurs the genotypic classes.



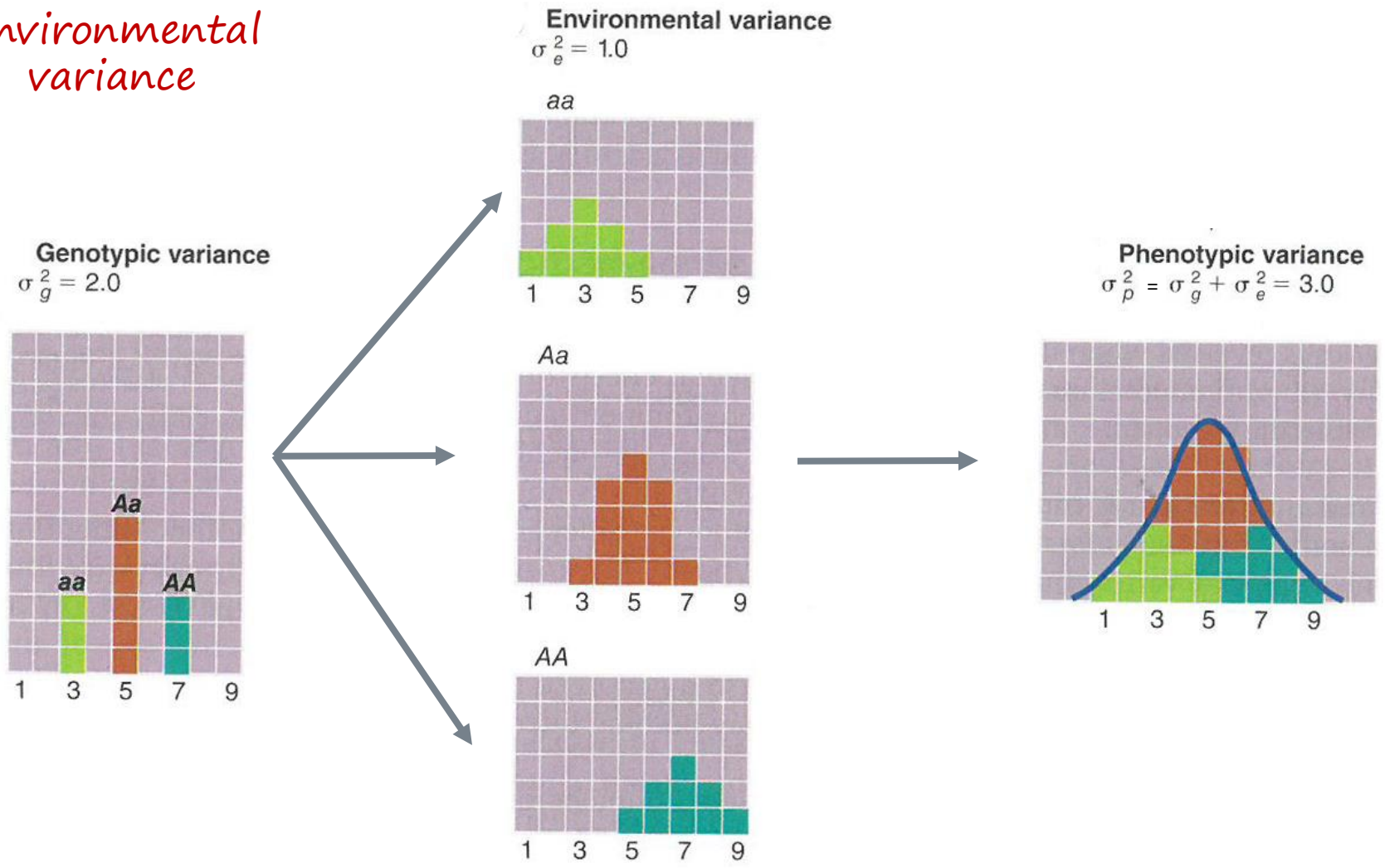
PARTITION OF PHENOTYPIC VARIANCE

Genetic variance

Environmental variance

$$V_P = V_G + V_E$$

Phenotypic variance



GENETIC AND ENVIRONMENTAL VARIANCE

Important…!

$$V_P = V_G + V_E$$

This partition only holds when V_G and V_E are independent:

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

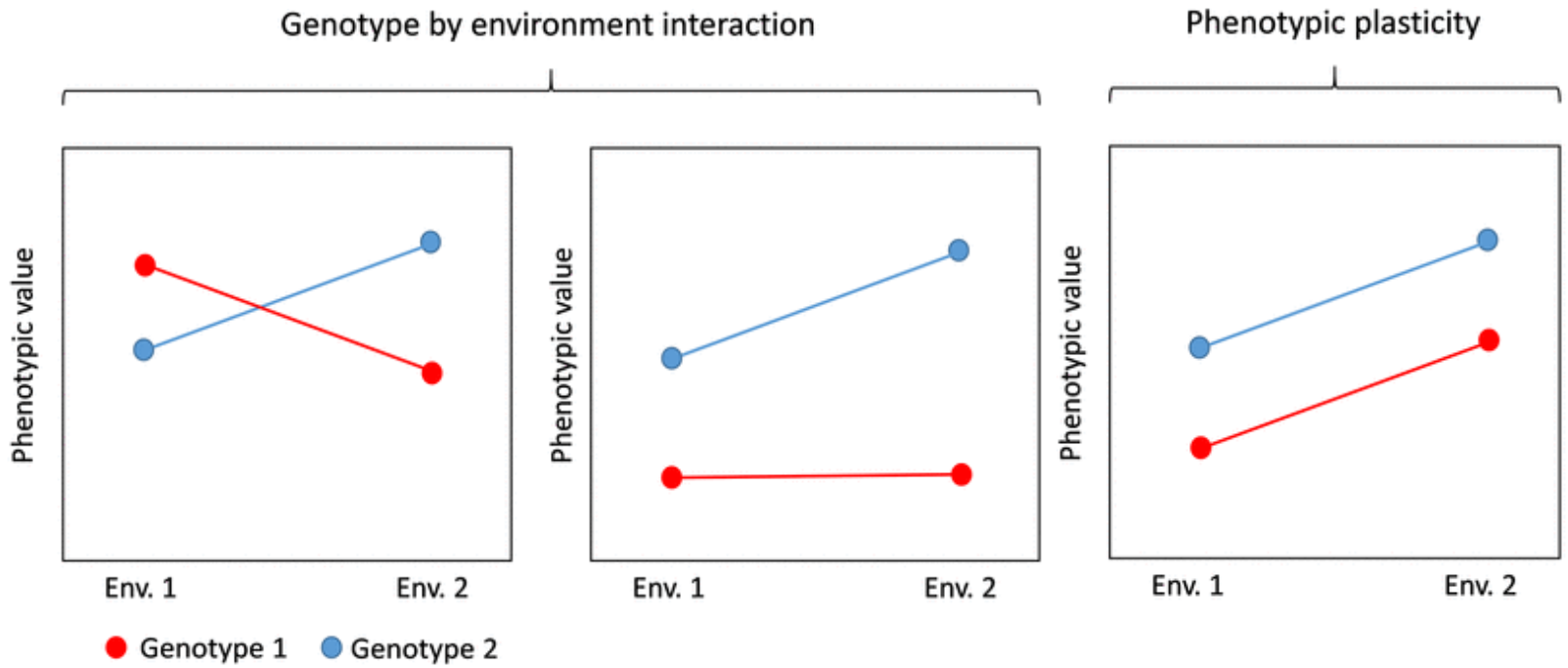
$$Cov(x, y) = 0$$

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

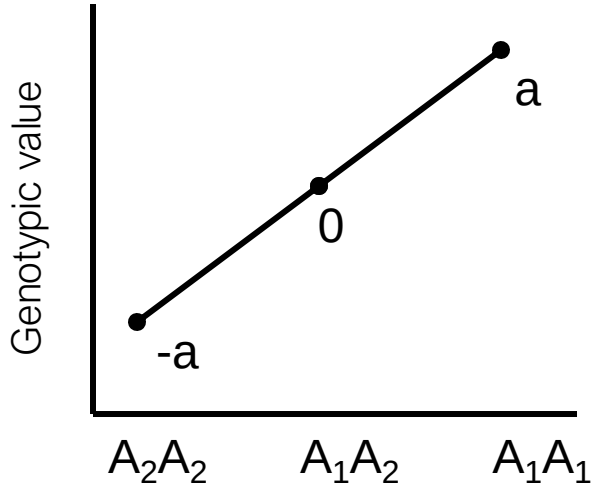
$$V_P = V_G + V_E$$

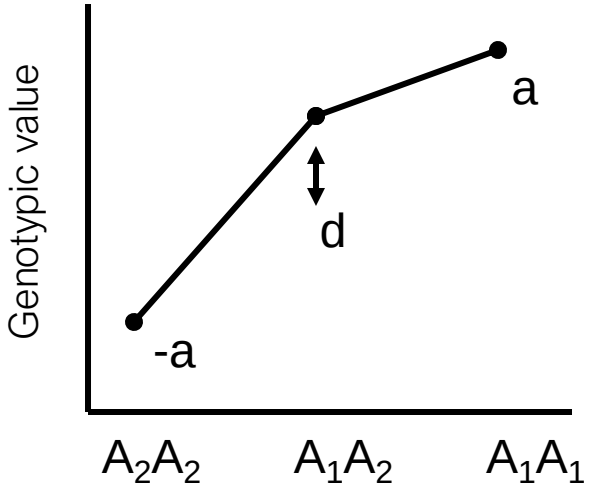
Additive variance

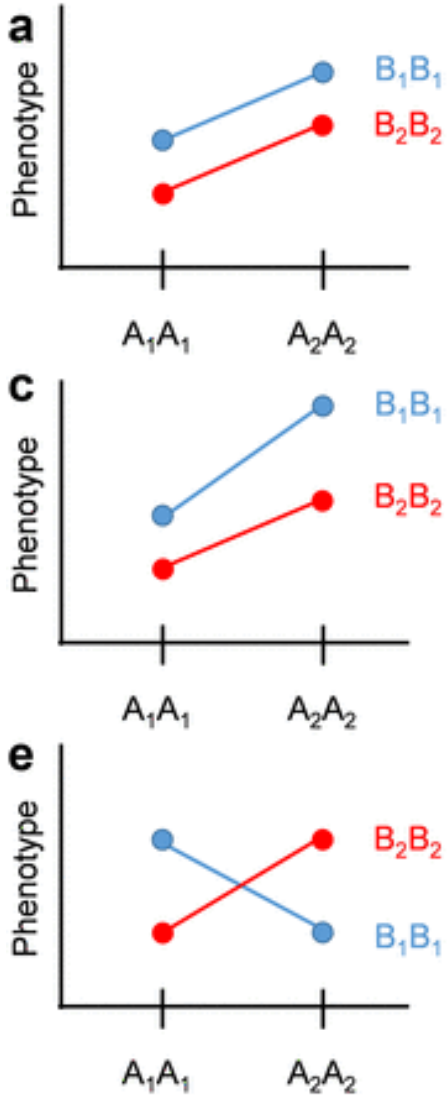
Interaction variance

$$V_G = V_A + V_D + V_I$$

Dominance 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 !** 

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 III

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:

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

$H^2 = 1$→ 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 heritabilitet (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

h^2 is always smaller than H^2

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

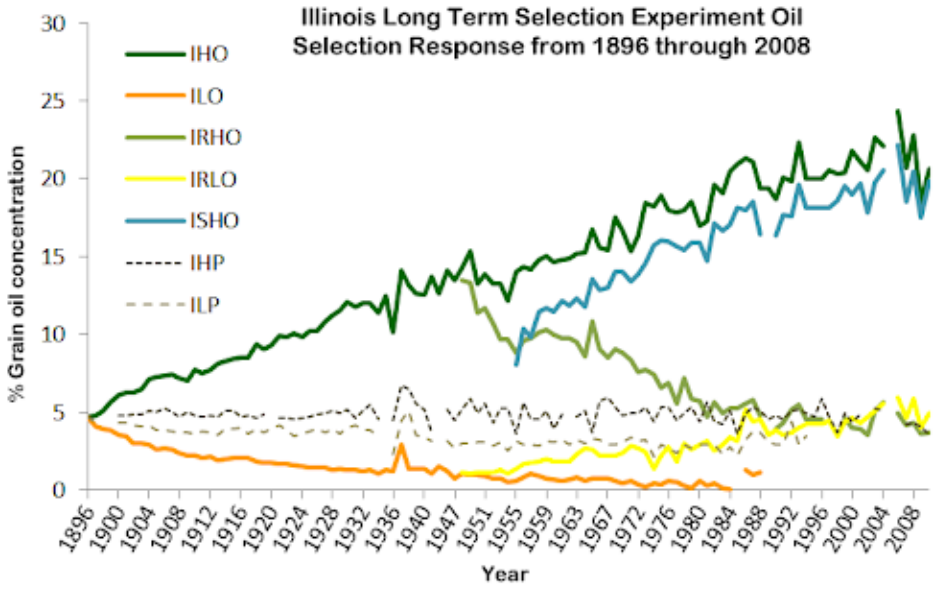
Additive genetic variance: hereditary | one allele from mom, one from dad
Dominance variance: is established after gamete formation
Interaction variance: is established after gamete formation

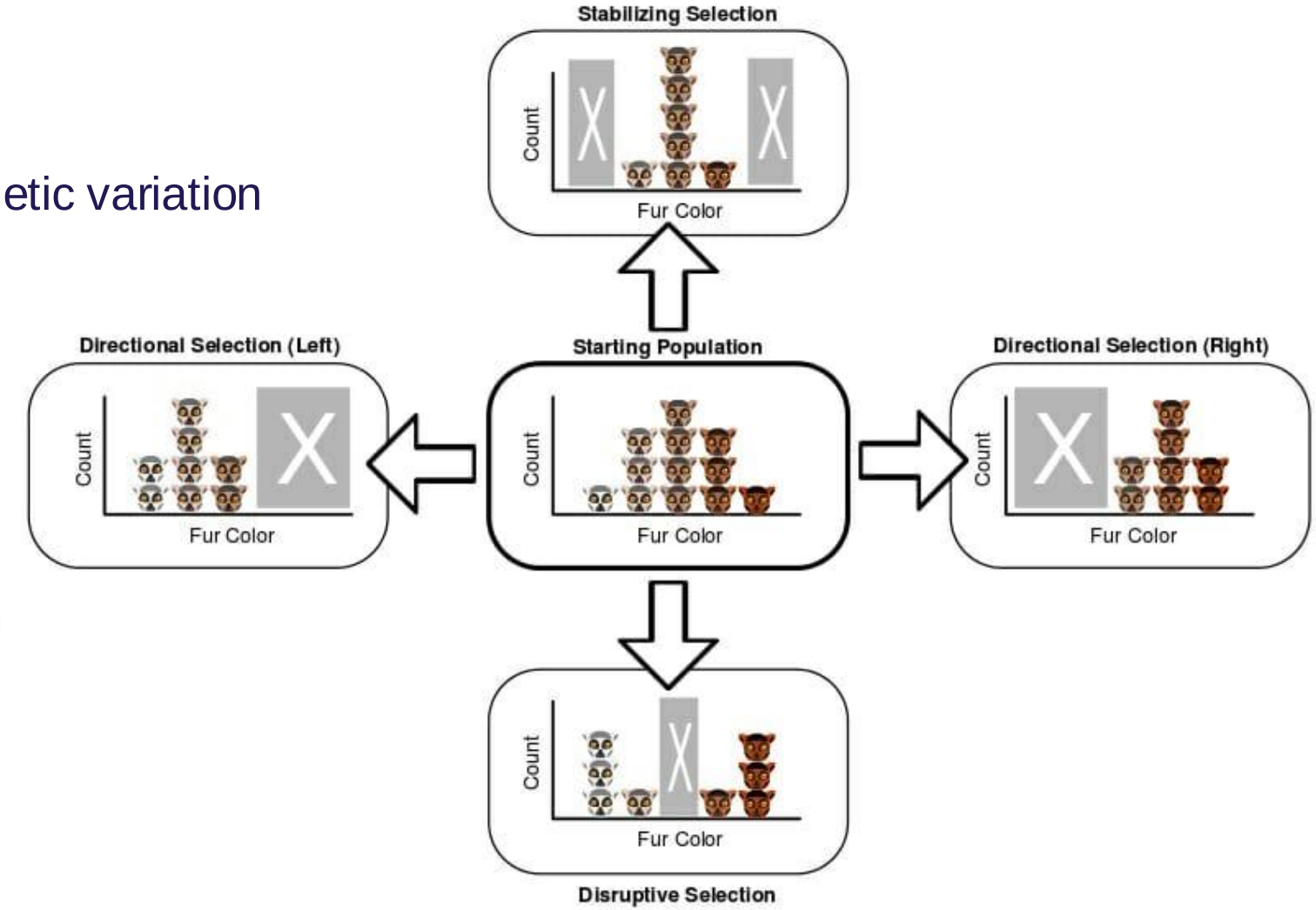
SELECTION AND GENETIC VARIATION

Selection reduces amount of genetic variation

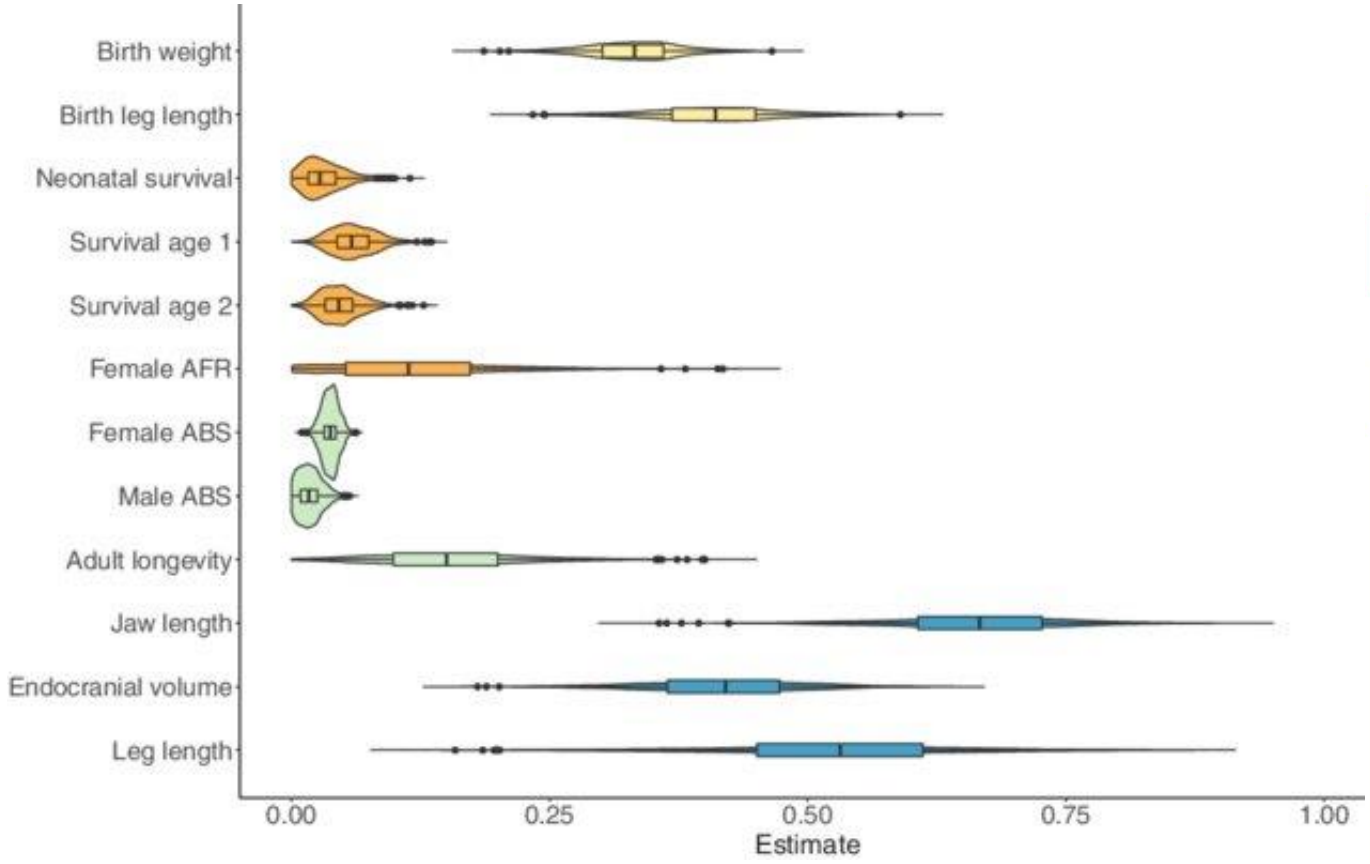
$$V_P = V_G + V_E$$

→ 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

AGENDA

08:15 – 08:45	Lecture 1 [*Recap + indirect testing*]
08:45 – 09:15	Exercises A + Break
09:15 – 09:40	Lecture 2 [*Multifactorial traits*]
09:40 – 10:00	Exercises B
10:00 – 10:40	Break + Group work
10:40 – 11:15	Lecture 3 [*Quantitative genetic theory*]
11:15 – 11:50	Break + Exercises C
11:50 – 12:00	Evaluation at Moo

MOODLE EVALUATION

08:15 – 08:45	Lecture 1 [*Recap + indirect testing*]
08:45 – 09:15	Exercises A + Break
09:15 – 09:40	Lecture 2 [*Multifactorial traits*]
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10:40 – 11:15	Lecture 3 [*Quantitative genetic theory*]
11:15 – 11:50	Break + Exercises C
11:50 – 12:00	Evaluation at Moodle