

(1) Quantitative traits and sequence variation

Lecture objectives

060313
0900:1200

By the end of this lecture you should be able to explain:

- What genetic variation is and where it comes from
- What SNPs are and what type of variation they encode
- The difference between quantitative and qualitative traits (inc. e.g.s)
- Why linkage disequilibrium might help you find important genes

Genetics and variability

- By sequencing genomes from related organisms we can estimate variation among or between species
- Humans share 99.9% of their DNA: only 0.1% is variable!
- The variable part is where we can potentially find an explanation for our phenotypic differences
- Next-gen sequencing = enabling technology
- Alleles and genes



Genetics and variability

- Alleles and genes
 - Alleles (allelomorph) are different forms of a gene occupying the same position (locus) on a chromosome
 - Different alleles are formed as a result of polymorphisms in the genes
- e.g.
- a heterozygous locus will be biallelic, i.e. having both alleles of a gene



Genetics & variation Homozygosis vs. Heterozygosis

Ladies first

Self pollination

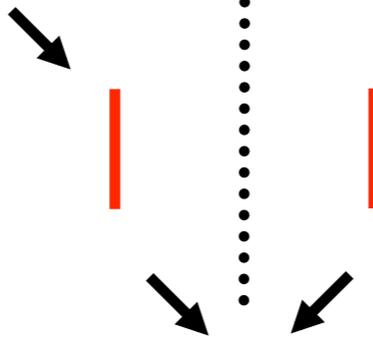
Plant A



e.g. one pair
of chromosomes



pair is split



re-association (F1)



Identical
chromosomes
Identical genes
homozygous

Cross pollination

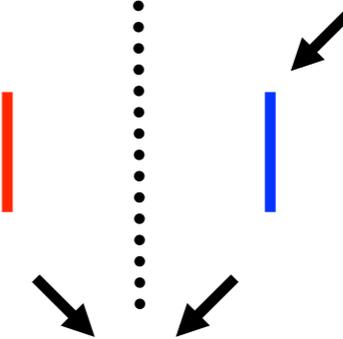
Plant A

x

Plant B



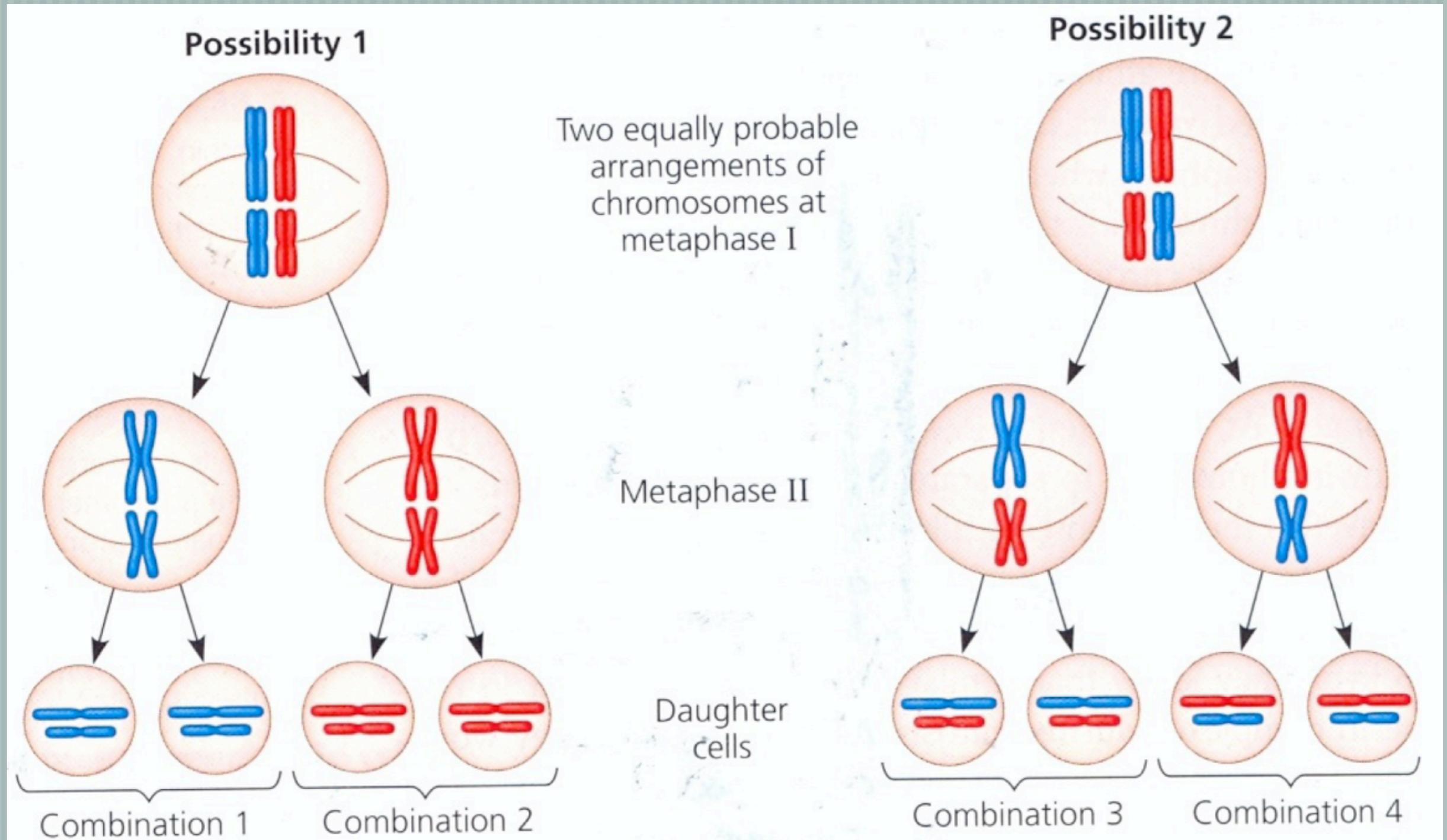
Meiosis



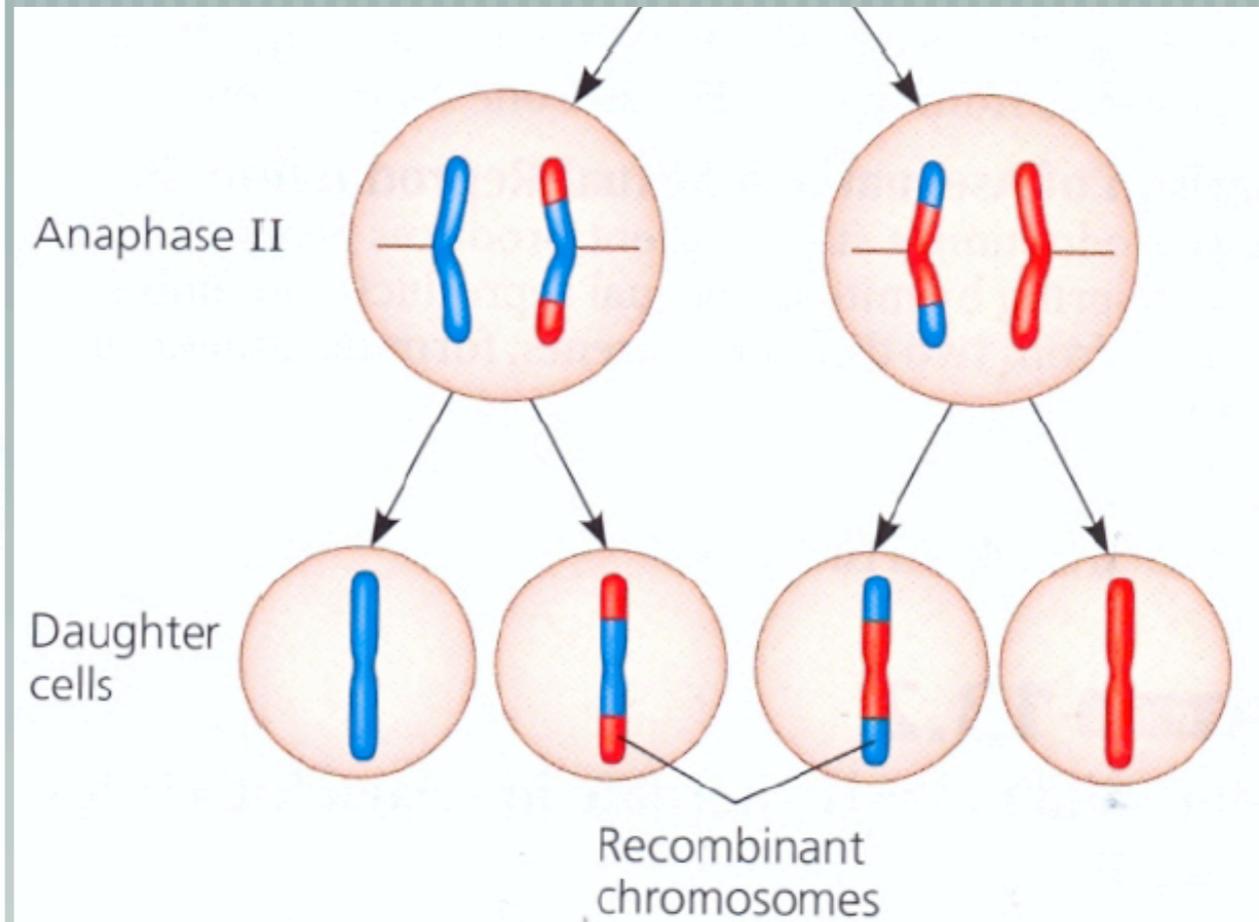
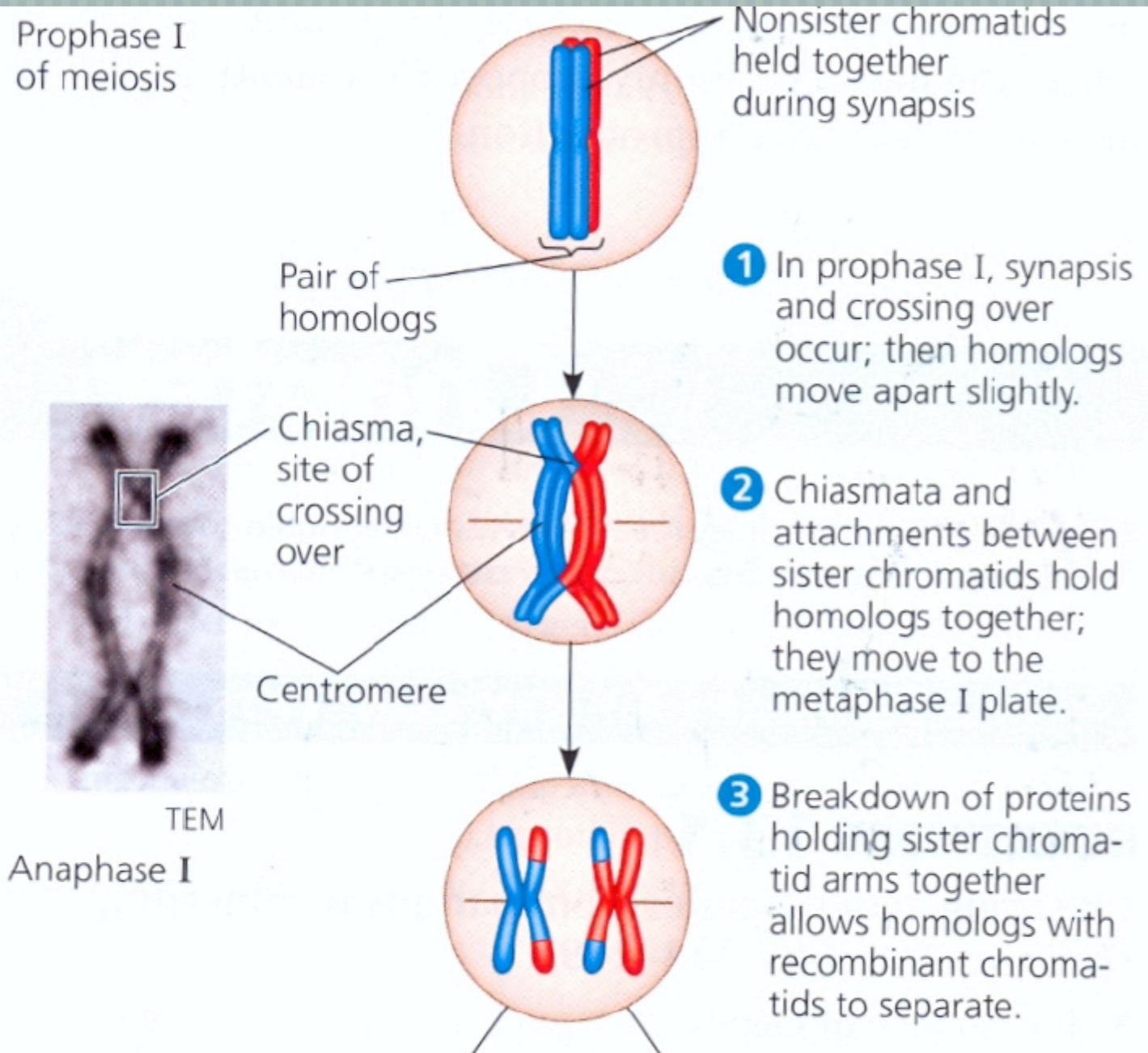
Different
chromosomes
Different genes
heterozygous

Where does variation come from?

Independent assortment of chromosomes

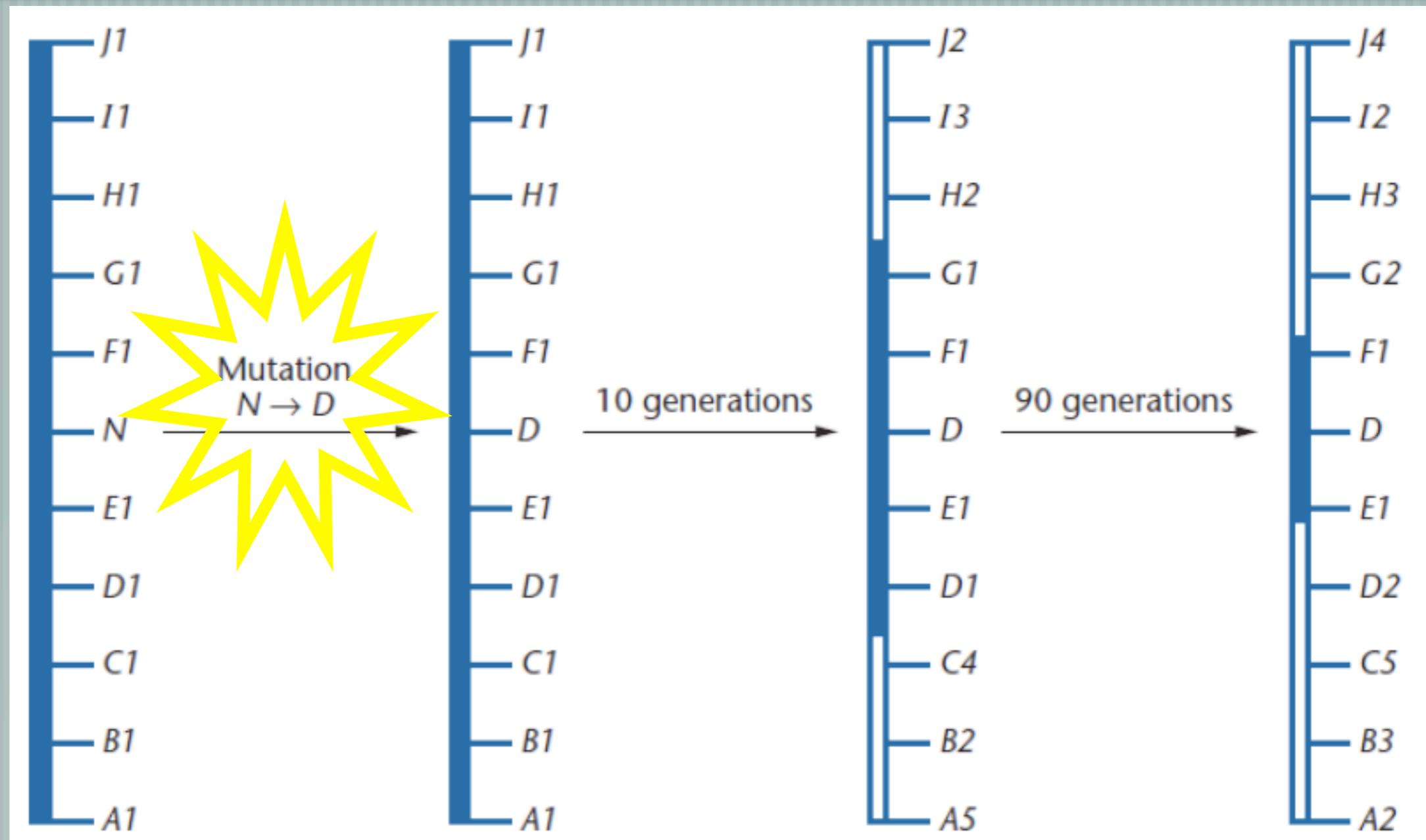


Where does variation come from? Crossing over during meiosis



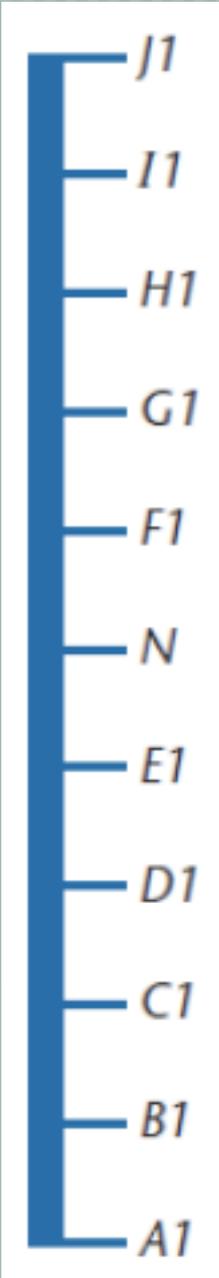
We can use this property to localise the parts of chromosomes involved in a trait

Mutations are maintained in linkage disequilibrium

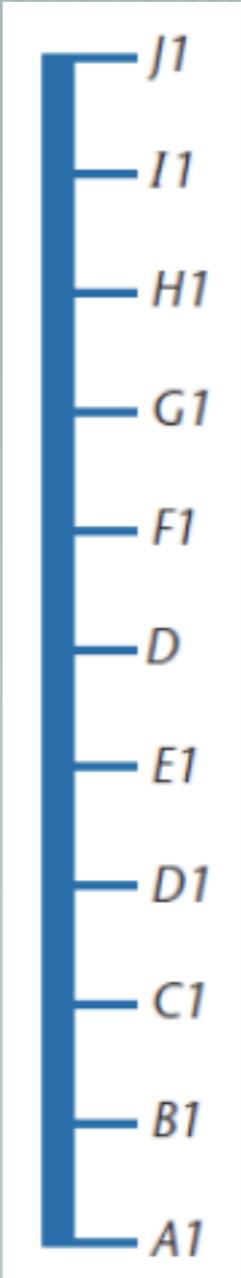


- Linkage: tendency of particular genetic loci to be inherited together
- Linkage disequilibrium: non-random association of particular alleles

Aim: understand the effect of alleles on traits

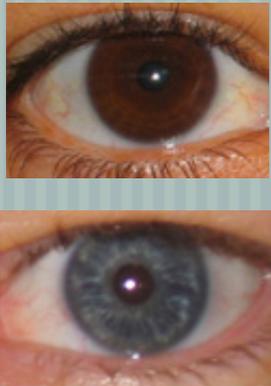


VS



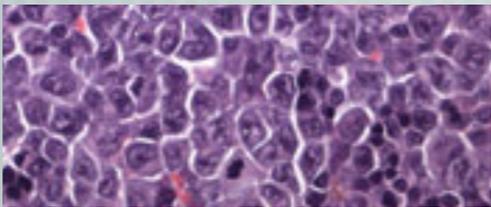
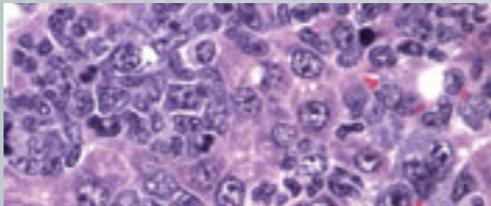
What type of variation is found for traits?

What links these?



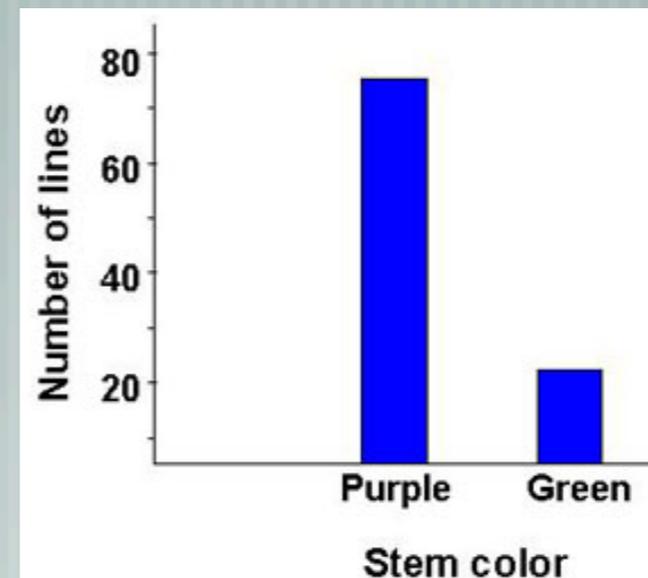
VS

What links these?



Qualitative trait characteristics

- Follow 'Mendelian' inheritance
- Can predict the phenotype from the alleles carried

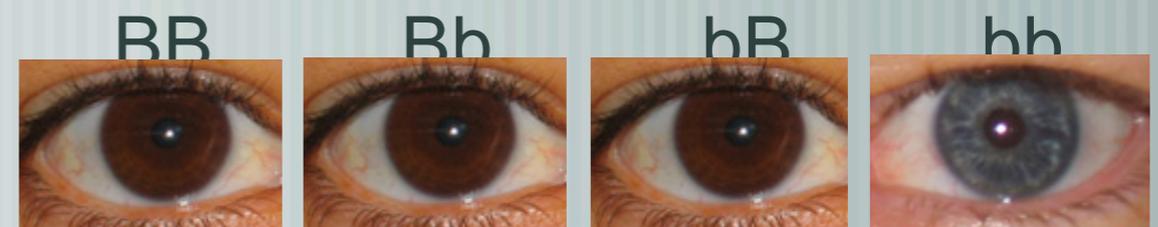


- Often encoded by single genes

e.g. Locus for eye colour with 2 alleles:

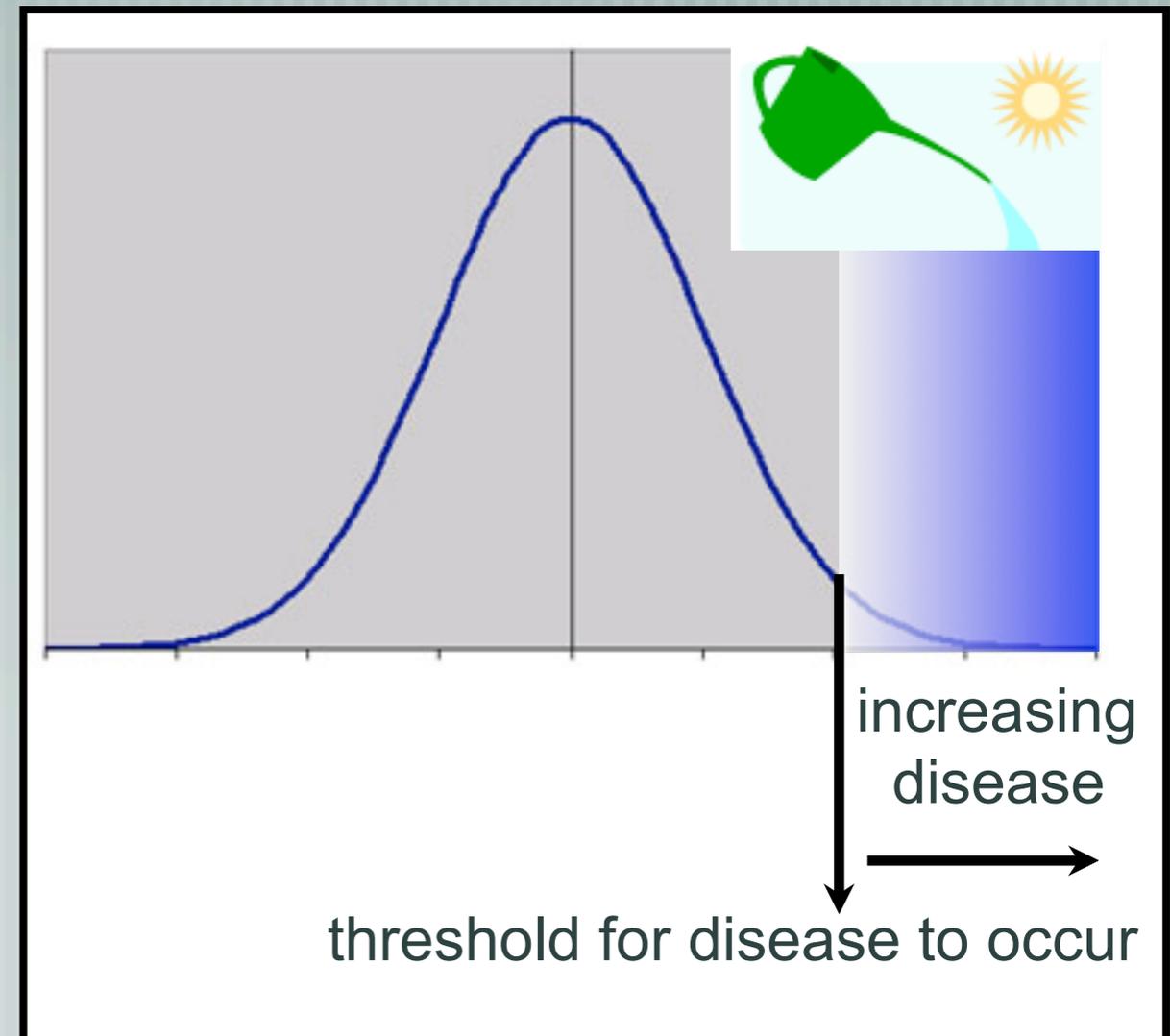
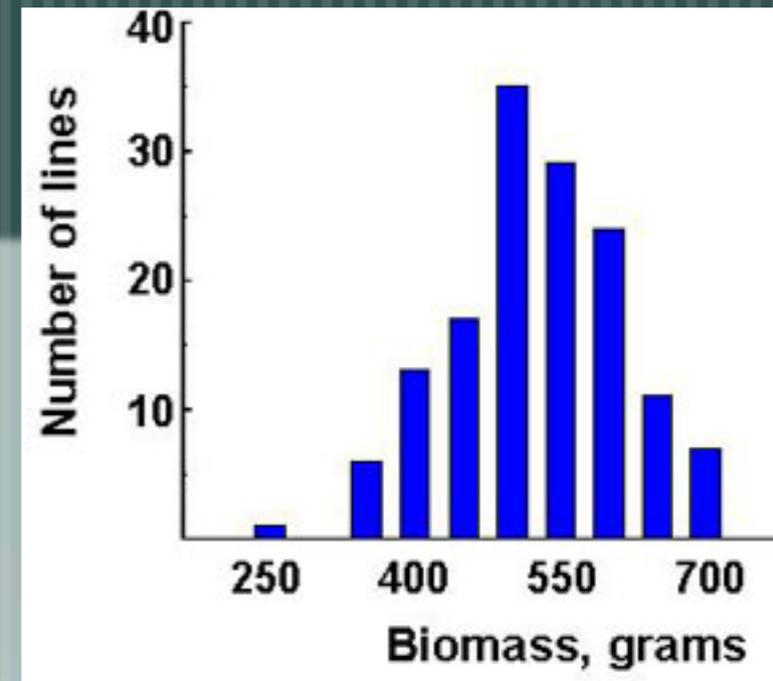
B (dominant allele) and b (recessive allele)

- four possible combinations:



Quantitative trait characteristics

- ‘Infinitesimal model’
- Many genotypes can produce the same phenotype
- Non-Mendelian inheritance
- No typical dominance/recessiveness
- Locus contributions additive (assumed)
= polygenic, or quantitative inheritance



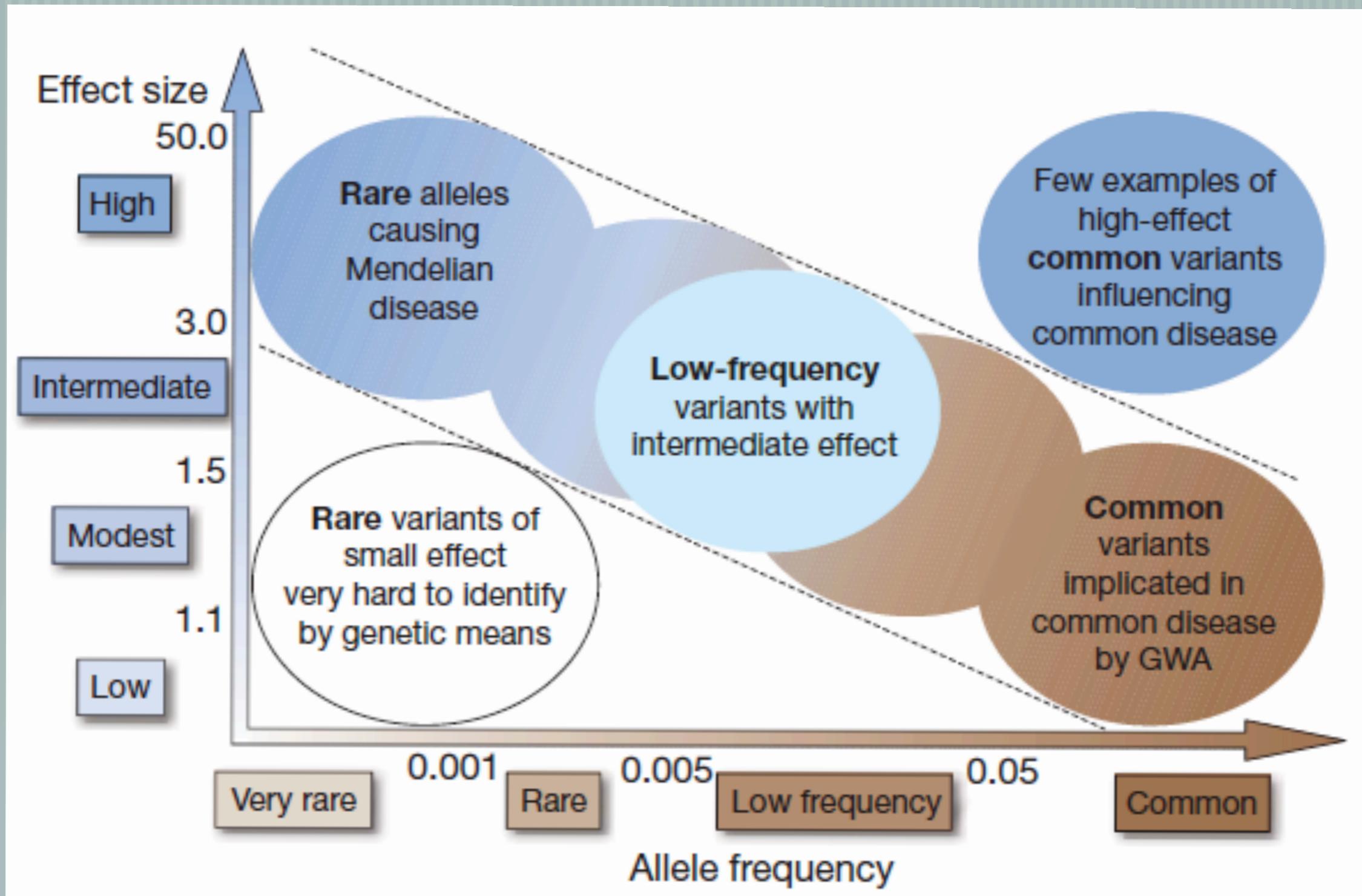
Quantitative trait loci and how to find them

- Complexity of these traits, esp. those involved in adaptation probably arises from segregation of alleles at many interacting loci
- Allelic effects are sensitive to the environment



- Combination of molecular genetics and statistical techniques are needed to identify where these alleles are located

The range of allelic effects

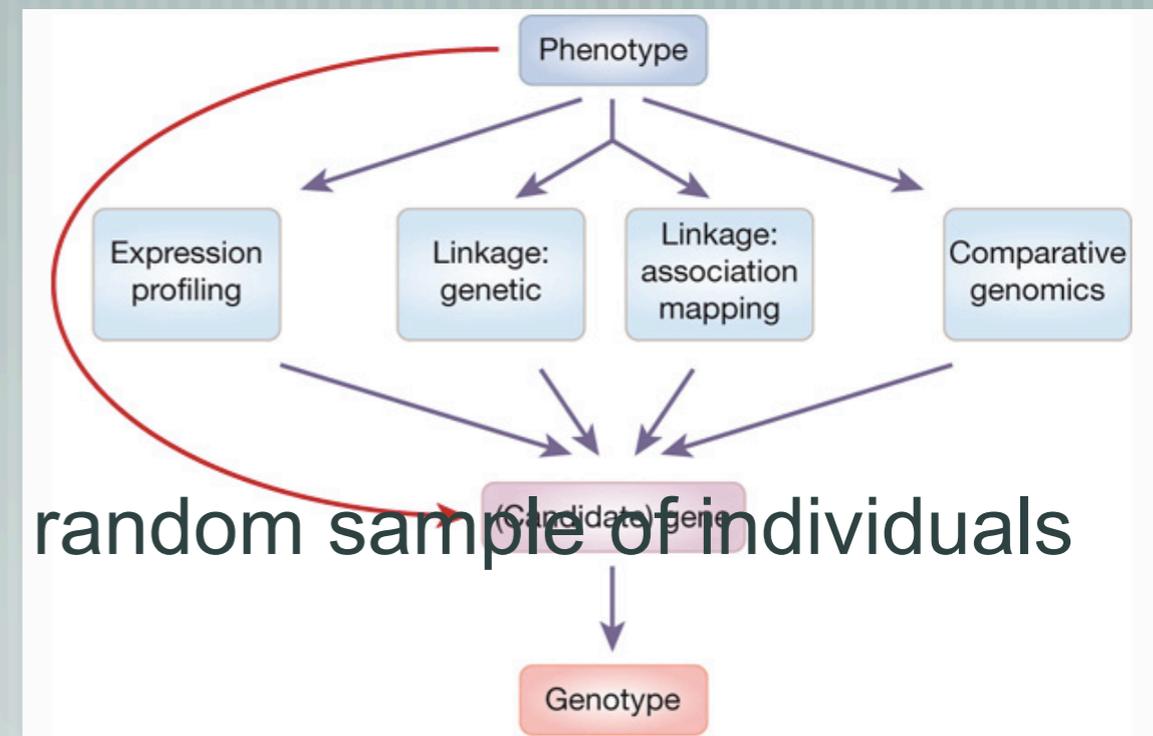


Approaches for discovering the genetic basis of phenotypic variation

- Quantitative trait loci analysis (QTL analysis) & eQTL analysis
 - related populations of organisms generated by a cross
- = recombinant inbred lines

- Genome wide association studies
GWAS

- natural populations of a species
- random sample of individuals



- Statistical methods used to associate genotype (alleles) with trait
- Both rely heavily on accuracy in genotyping, trait measurement

Next time:

(2) Quantitative trait loci and genetic maps

By the end of that lecture you should be able to explain:

- The four main types of information you need to for QTL analysis
- Why understanding recombination & genetic linkage is important for localising genes that control traits
- What a marker-trait association is