- Gregor Mendel's (Australian monk) postulates

Pea plants laid foundation of heredity: traits were inherited through discrete units (genes)
Introduced concept of genes (building blocks of heredity)

- Darwin's theory of natural selection (independent; unknown of Mendel's work)

Origin of species by Charles Darwin: explanation of mechanisms of evolutionary change but lacked understanding of genetic basis of variation & inheritance
Therefore theory open to reasonable criticism in 20th century
Heredity & development were dependant on genetic information residing in genes contained in chromosomes contributing to each individual by gametes= chromosome theory

Chromosomal theory of inheritance: Walter Sutton 1902

- Chromosomes are the carriers of genetic material & genetic factors are located on loci on chromosomes
- Transmission of traits from parent to offspring due to transfer of chromosomes between generations
- Diploid number (2n): each species has a set number of chromosomes
  Humans diploid number = 46 chromosomes comprised of 23 homologous pairs (n)
- Chromosome exists in pairs as homologous chromosomes
- Chromosomes undergo meiosis & mitosis
  Segregation and exchange of chromosomes (crossing over) between the 2 sets of chromosomes in a parent cells
  Meiosis halves the chromosome number so that each gametes (egg/sperm cell) receives 1 copy of each chromosomes = haploid (n) genetic information passed between generations. Mitosis duplicates the chromosomes = 2n
- Mutations located on chromosomes responsible for differences between individuals leading to variation
  Chromosomal rearrangements: translocations & inversions show how mutations affect gene expression = variation
- Provides insight into molecular basis of genetic variation for genetic research

Genetic variation

- Mutation in genes located on chromosomes = new versions of genes (alleles) creating different individuals
- Mutation: any heritable change in DNA sequence & source of all genetic variation
  Inheritance of traits in fruit fly: white-eye variant is an allele of the white gene vs red-eyes allele in Drosophila
- Mutant genes used as markers & geneticist map locations of genes on chromosomes

3. Yellow pea plant with round seeds GgWw crossed with itself, proportion green with round seeds? 3/16 as you have a recessive dominant
4. During which phase is new mutation likely to arise? S phase as it is your duplication phase where changes occur
5. Child has an autosomal dominant phenotype, parents: at least 1 of the parents should have the trait
6. Testing null hypothesis of 1:2:1 genotypic ratios in a cross, what are the degrees of freedom in chi-square test: testing genotypic classes and not phenotypic classes 3 (AA, 2Aa, aa) - 1 = 2
7. Based on which ultimate value do I reject or fail to reject the null hypothesis in chi-square test: P value (set number of class = df & use chi-square test value to get p value which is comparing the observed & expected value. $p>0.05$ fail to reject with no difference and $p<0$ reject as it is not due to chance but a biological entity)

<u>Hardy Weinberg</u>

Frequencies of alleles remain constant in a population over time if no evolutionary influences occur
No selection, no mutation, no migration, large population and random mating
Compare constant population to those evolving populations & the deviation
Frequencies of alleles/genotypes causing diseases compared

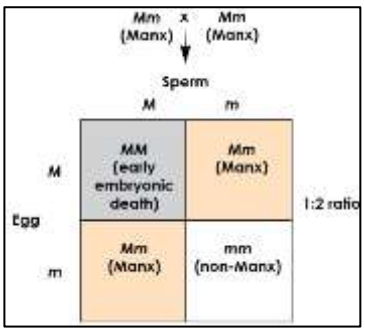
- $p + q = 1$ USED FOR ALLELES
  p is dominant allele and q is recessive allele
  0.6 + 0.4 = 1 (60% and 40%). Frequencies have to be one or another
- $p^2 + 2pq + q^2 = 1$ USED FOR GENOTYPE
  squared as there are 2 alleles in an individual
  p^2 is homozygous dominant; 2pq is heterozygous & q^2 is homozygous recessive

1. Get the missing value from the total in a population if given 1 value
2. Get the number per group/total population = frequency (not whole numbers)
3. Use the recessive genotype frequency as there is only 1 combination [q]
   Don't use dominant genotype frequency as there is more than 1 combination [p]
4. The recessive value (no. recessive/total) = q^2
5. Get q by square rooting for $p + q = 1$ in order to get p by subtracting
6. Get p^2 from solving for p for equation $p^2 + 2pq + q^2 = 1$
7. Therefore you can get the allele & for homozygous dominant, heterozygous etc.

Y is yellow so Yy or YY dominant and y is blue so yy recessive (dominant p = Y and recessive q = y). USE HOMOZYGOUS RECESSIVE as you see the difference
1000 penguins, 12 blue feet

1. Therefore 988 yellow feet (or given yellow and need to find blue to solve further)
2. $12/1000 = 0.012 = q^2$
   Number of penguins with blue is q^2 as there are 2 alleles per individual
3. Square root for q = 0.11 recessive
4. $p + q = 1$ so p = 0.89 dominant

- May act dominantly for a trait and be lethal in the recessive trait



Lethality

- Homozygous lethal dominant combination = die
  Want heterozygous lethal dominant with normal combination = new mutant colour
  If no lethal dominant combination i.e. all normal with no superscript = ordinary
- Homozygous lethal recessive (need both/2 of the alleles) combinations = lethal
  Heterozygous = survive

One allele (A^Y) with 2 actions on 2 different traits

1. Reference to coat colour = dominant action = heterozygous displays mutant phenotype
2. Reference to lethality = recessive action = homozygous lethal & heterozygotes survive

Combination of different modes of inheritance

- Mendel's monohybrid ratio 3:1 changes because of:
  - Incomplete dominance
  - Co-dominance
  - Multiple alleles
  - Lethal alleles
- Combinations of these alleles will also change (9:3:3:1)

QUIZ

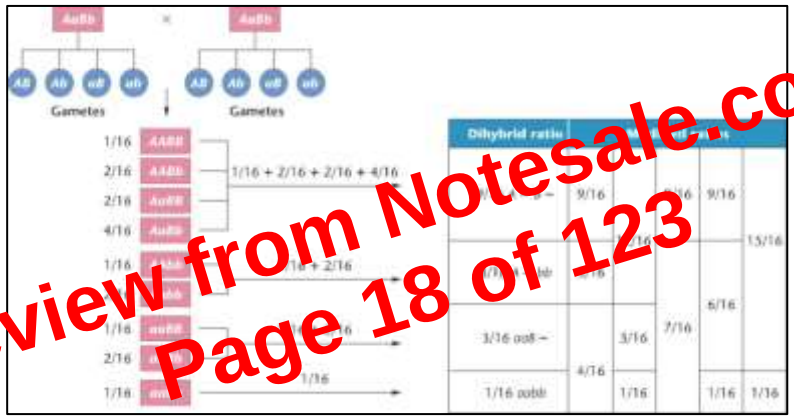
8. In hypercholesterolemia, individuals homozygous for the allele causing disorder lack receptors on liver cells taking up cholesterol. Heterozygotes have one-half of the number of receptors while homozygous for normal allele are phenotypically normal: incomplete dominance. Not co-dominance as not 2 completely different receptors contributing, there is ½ a receptor therefore an intermediate (incomplete)
9. Woman type A blood = type A child, which men could not be the father? None of the answers are correct (A, B, AB, O). Any man can be father, not enough genotypic information as A & B can be homozygous or heterozygous for dominant allele

Gene interactions

- Genes interact with one another with several genes influencing a particular characteristic = developmental biology epigenesis (epistasis/epistatic to a gene)
- Gene 1, gene 2, gene 3, gene 3 = character 3

Epistasis

- Expression of 1 gene pair masks or modifies the effect of another gene pair
- Ratio out of 16 = dihybrid cross but 1 trait investigated not the 2 different traits together as it would be in the classical dihybrid cross (expect 9:3:3:1)
- Ratio's expressed in 16 parts in the study of a single character indicates that 2 gene pairs are interacting during the expression of the phenotype
- Homologous pairs of chromosomes: 1 chromosome = A & B locus with the homologue = A & b locus
  Gene B influences the effect of gene A therefore gene B is epistatic to the gene A
- Gene A with enzyme A changes X white to Y brown but then gene B with enzyme B changes that Y brown to Z black (gene B influences the effect that gene A caused & gene B is epistatic to the gene A)
  AaBb x AaBb = white: brown: black = 9:3:4 (not 9:3:3:1 that would have occurred if gene B didn't change the brown effect to black)
- Epistasis has 2 genes influencing a trait but only 1 trait is investigated (black on the brown trait) looks like dihybrid ratio but 3 combinations (white, brown & -> black) not 2 combinations (white & brown)



Recessive epistasis (focus on a gene with homozygous recessive influencing ratio)

Case 1 - mouse on coat colour

- A- aa
- Second gene pair bb gives albino regardless of genotype at locus A
- Recessive condition for gene B impacts the phenotypic expression
- If homozygous (bb) at albino locus gene B = no pigmentation

bb genotype masks or supresses the expression on A allele = epistasis

- P: AABB x aabb with F1: AaBb
- A-B- 9/16, A-**bb** 3/16, aaB- 3/16, aa**bb** 1/16
- Therefore albino is 3/16 + 1/16 = 4/16
- 9 agouti: 3 black: 4 albino
- 9:3**:3:1** = 9:3**:4**

Dominant epistasis (focus on gene with homozygous dominant/heterozygous influencing ratio therefore other gene shown when the epistatic gene (dominant) is not there i.e. homo recessive)

Case 2 - squash on colour

- Dominant allele at A locus = always white fruit
- aaB = yellow and aabb = green
- B locus only expressed in plant that has the aa genotype (no dominant allele)
- If recessive allele combination at 1st locus A (aa but B) = yellow
  DOMINANT AT 1 LOCUS and if not appearing & recessive = other gene appears
- Recessive at both genes/loci (aa bb) = green

A- genotype marks or supresses the expression on B allele = epistasis

- P: AABB x aabb with F1: AaBb
- **A**-B- 9, **A**-bb 3, aaB- 3, aabb 1
- **9:3**:3:1 = **12** (epistatic gene white): 3 (yellow): 1 (green)

Complimentary epistasis (duplicate recessive)

Case 3 - pea on flower colour

- At least 1 dominant allele at each gene pair (A AND B loci) needed for purple flowers
- Dominant for BOTH genes/loci = purple flowers
- Homozygous recessive or at least 1 dominant allele = white flowers
- P: Aabb x aaBB with F1: AaBb
- **A**-**B**- 9: aaB- 3: A-bb 3: aabb 1
- 9 (purple): 3:3:1 (white) = 9**:7**

Cooperating epistasis (additive/novel phenotype)

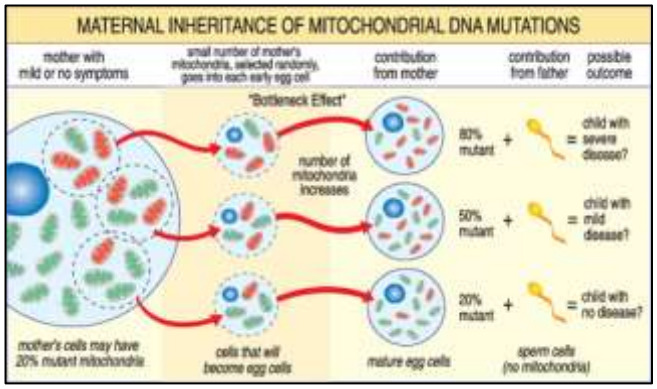
Case 4 - squash on fruit shape

- Cross disc shaped fruit with long fruit = all F1 disc shaped
- F1 self-fertilising both parental types occur in F2 & new shape sphere
- BOTH dominant alleles at both genes = disc
- **1 dominant for either** of the genes = sphere
- Recessive alleles at both genes = elongated
- Both gene pairs influence the fruit shape equally
- P: AABB x aabb with F1: AaBb
- A-B- 9 disc: **aaB**- 3 sphere: **A-bb** 3 sphere: aabb 1 elongated
- 9**:3:3**:1 = 9**:6**:1

For epistasis: the classical ratio is modified & need P1 pure breeding for both = F1 interbreed/self-fertilised = F2 so for deductions on modes of inheritance you need a classical experimental cross all the way to F2

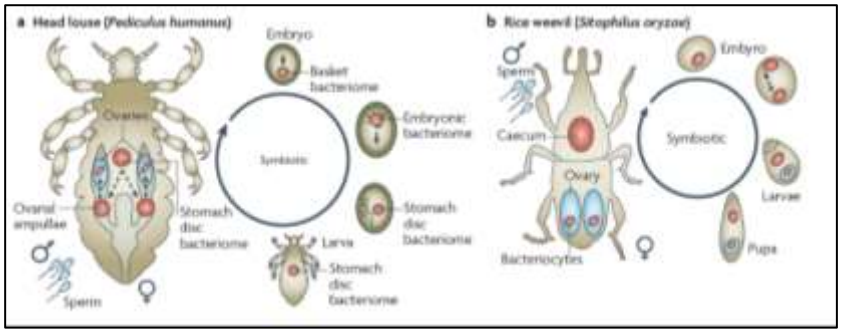
<u>Complementation analysis</u>

of mitochondria in mitosis (gamete formation depends on amount of defectiveness inherited)
  - Mature egg cells = 80%, 50% or 20% mutant = severe, mild & no disease
  - Mature egg cells may inherit more defective mitochondria than other cells in a certain organs i.e. if in muscle tissue = more defective mitochondria inherited = defective muscular issues not neutral



<u>Infectious heredity</u>

- Symbiotic or parasitic association of a microorganism within a host organism affects hosts phenotype = transmission of altered phenotype to offspring
- Invading infectious microorganism exists in symbiotic relationship with host organism so = invader to maternal egg cytoplasm (ooplasm) = affects offspring phenotype when reproduction occurs
  - Strain of microorganism = strain of offspring
- Rhabdovirus Sigma in *Drosophila*
  - Causes carbon dioxide sensitivity
  - Provide carbon dioxide & then decrease the levels to recover
  - Affected flies with virus with not recover normally from CO_2 anaesthesia
- Protozoan in *Drosophila*
  - Affected flies produce predominantly female offspring if reared at 21°C/lower therefore temperature dependant
  - When ooplasm from affected individuals/protozoan itself is injected into oocytes of normal individuals = temperature sensitive altered sex ratios
- Bacterial endosymbionts (intracellular)
  - Head lice: bacteriome exists outside of ovaries but the bacteria migrates to ovaries & infects individual eggs
  - Rice weevil: bacteriocytes inside the weevil migrating to the ovary to be symbiotic with caecum



If offspring are ee and Ee and a parent is ee, the other parent can't be EE as there is no donation from that parent of an e allele to create a recessive offspring of ee therefore that parent is a carrier only
If offspring are Ee and a parent is ee the other parent can be EE or Ee (include both)

- Sex-linked recessive traits/pedigrees: colour-blindness and baldness
- All circles have XX as they females and squares have XY as they males
- Track sex-linked recessive therefore shaded is recessive
- Shaded is r for recessive and R for dominant, the trait can only occur on the X chromosome. Male does not have the ability to mask as there is only 1 X
- A male offspring X^ry gets the Y from the father (X^RY) so just need to decide on mothers alleles. If she is unshaded then it is X^rX^R (carrier) or X^RX^R but has to be the carrier one as the X^r needs to go the male and there are some dominant offspring needed and R. The female unshaded offspring must be either of X^rX^R or X^RX^R as a dominant will come from the father and mother is a carrier so can get either R or r

OFFSPRING NEED TO GET 1 ALLELE FROM EACH PARENT

<u>Why do cells divide</u>

- Growth of a multicellular organism
- Recovery and regeneration of damaged cells
- Reproduction for haploid (gametes) to the double in chromosomes = 2n organism

<u>The cell & genetic information</u>

Is the nucleus the only bearer of genetic information? Occurs mitochondrial DNA (mtDNA) and chloroplastic DNA (cDNA) where extra DNA is maternally inherited, or the DNA circulated in organelle from symbiosis of engulfing eukaryotic cells

- Chromatin: mixture of DNA & proteins that makes the DNA a compact unit to fit in the nucleus = nucelosome which is twisted and coiled = chromosomes into a genome
- Histone proteins assemble the DNA into special structures forming the nucleosome
- It is then folded to configure a chromatin fibre
- Improves the strength of the DNA during cell division, gene expression regulation and DNA replication, and protecting DNA from damage

- Chromosome: condensed chromatin that is compact, thick and thread-like structures of nucleic acids tightly coiled around histone proteins after cellular division/mitosis and meiosis with DNA packaged into a genome
- Made by the condensation of chromatin fibres
- Higher order of DNA organization, where DNA is fully condensed onto itself

See if theoretical combinations (expected) occur in either of the crossover types (observed):

- None of the recombinants as Sbc and sBC of NCO (SBC) expected, occur in observed as there is no dominant S; recessive b; recessive c and recessive s; dominant B; dominant C therefore B as the middle gene as SBC does not occur
- C and S gene could be in the middle as you see recombinants as Bcs and bCs (BCS) & Bsc and bSC (BSC) in SCO2 expected crossover genotypes which occur in observed

Crossing over between **2nd and 3rd** gene (SBC does not work) -> occurring in SCO1

NCO C (BCS) in the centre: B**CS** x b**cs** = B**Cs** and b**cS**
NCO S (BSC) in the centre: BSC x bsc = BSc and bsC

See if theoretical combinations (expected) occur in either of the crossover types (observed):

- None of the recombinants as BCs and bcS of NCO (BCS) expected, occur in observed therefore C as the middle gene as BCS does not occur
- S gene is in the middle as you see recombinants as BSc and bsC (BSC) in SCO1 expected crossover genotypes which occur in observed

5. Correct order is BSC because both SCO1 and SCO2 is theoretically possible to get the genes in relevant combinations
6. Write genes in correct order

SBC = BSC	1828	the 2 NCO classes = highest frequency
sbc = bsc	1779	**83.1%** -> (1828+1779)/4338 as NCO grouped
SBc = BSc	148	2 SCO1 classes
sbC = bsC	139	**6.6%**
SbC = bSC	227	2 SCO2 classes
sBc = Bsc	217	**10.2%**
Total	4338	

7. Schematic representation of DNA with genes indicated & determine distance by looking at crossover types

B 10.2cM S 6.6cM C

To produce SCO1, a crossing over has to occur between S and C [BSC NCO 83.1% -> BSc SCO1 6.6%]. Use frequency of this crossover/recombination to determine distance 6.6% so S-C 6.6cM

To produce SCO2, a crossing over has to occur between B and S [BSC NCO 83.1% -> bSC SCO2 10.2%]. Use frequency of this crossover/recombination to determine distance 10.2 so B-S 10.2cM

Colourless green	92	
Coloured green	12	2 reciprocal SCO classes
Colourless yellow	8	

2. Calculate distances between genes

For NCO: 88 + 92/total 200 = 90% NCO
For SCO: 12 + 8/200 = 10% SCO
Therefore R 10cM Y -> distances refer to crossovers & the 10% is the SCO = 10cM

Coloured yellow 88 and colourless green 92 due to parental **Ry**, **rY** gamete homolog (RrYy) x **ry**, **ry** (rryy) gamete homolog = Rryy & rrYy = **coloured yellow** & **colourless green**

Mapping of 3 genes: maize without DCO

1. Determine order of genes: compare NCO large & DCO small phenotypic class of F_2
2. If no DCO occurs, both SCO1 and SCO2 compared to NCO
3. Determine interlocus distance between genes
4. Draw gene map of 3 genes

Mapping of 3 genes: maize with DCO

In maize the recessive mutant genes (without + as it's wild type):
bm - brown midrib
v - virescent seedling
pr - purple aleurone
bmbmvvprpr x bmbmvvprpr = heterozygous x test cross

*Reciprocal classes occur
Most = NCO and least = DCO

(b) Actual results of mapping cross *

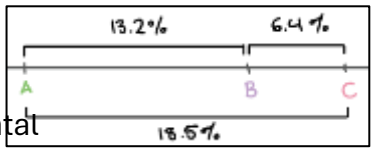
Phenotypes of offspring	Number	Total and percentage	Exchange classification
+ v bm	230	467 42.1%	Noncrossover (NCO)
pr + +	237		
+ + bm	82	161 14.5%	Single crossover (SCO)
pr v +	79		
+ v +	200	395 35.6%	Single crossover (SCO)
pr + bm	195		
pr v bm	44	86 7.8%	Double crossover (DCO)
+ + +	42		

*The sequence pr – v – bm may or may not be correct

3 genes: order & distance and 6 classes of 2 NCO and 4 SCO (2 SCO1 and 2 SCO2)

3 genes: order & distance and 8 classes of 2 NCO, 4 SCO (2 SCO1 and 2 SCO2) and 2 DCO

CONCEPT 2: genetic distance

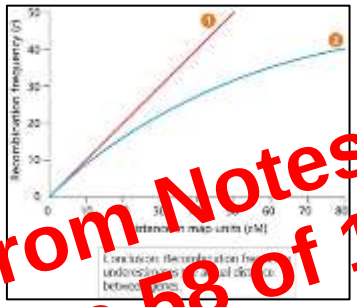


RF (A-B) = 13.2% -> A to B more spread out
RF (B-C) = 6.4% -> B to C closer
RF (A-C) = 18.5% -> largest RF = outermost distance of genes i.e. parental

RF not additive: recombination frequency underestimates actual distance between genes

18.5%/cM -represents the directly measured A-C RF is smaller than map distance calculated from A-B and B-C RFs due to double crossovers
AB + BC = 13.2cM + 6.4cM = 19.6 cM AC whereas AC = 18.5%/cM (difference due to DCO)

Further apart distance (distance increase cM) = increase in recombinant frequencies (r) = straight line linear graph



CONCEPT 3: cis vs trans configuration

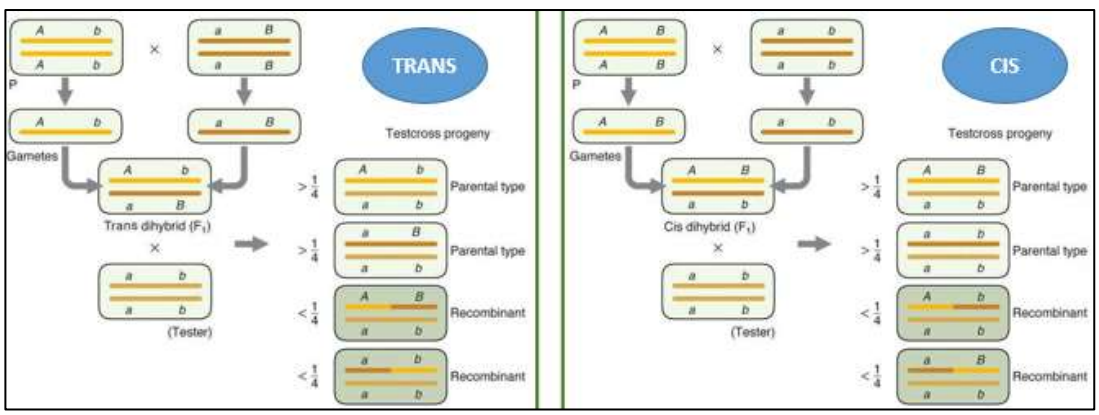
Arrangement of linked loci in dihybrids as AaBb

Trans: parental/non-cross over and recombinants not the same

Ab Ab x aB aB **P1** = F1 and the F1 undergoing a test cross (ab ab) = >1/4 Ab ab >1/4 aB ab, <1/4 AB ab and <1/4 ab ab **F2**
> = parental type and < = recombinant

Cis: parental/non-cross and recombinants can be the same

AB AB x ab ab **P1** = F1 and the F1 undergoing a test cross (ab ab) = >1/4 AB ab, >1/4 ab ab, <1/4 Ab ab and *<1/4 aB ab* **F2**
> = parental type and < = recombinant

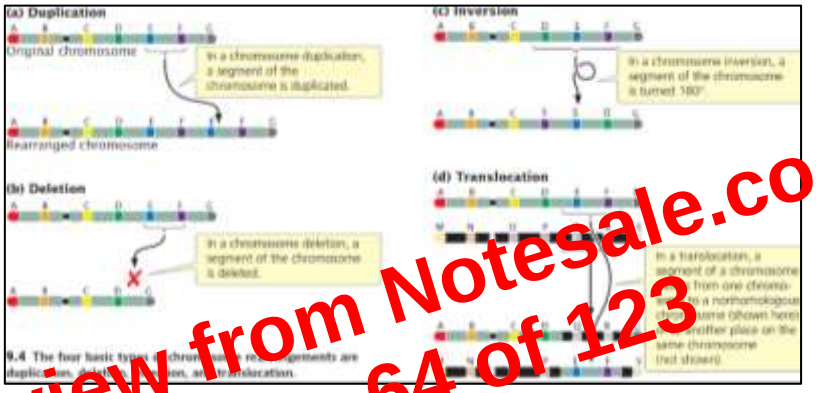


QUIZ

- ✓ Chromosome number is not multiple of a complete set: aneuploidy
  Polyploidy = multiple sets
- ✓ Genetic disease caused by trisomy for chromosome 13: Patau syndrome
- ✓ Gain of extra chromosome sets from individuals of same species: autopolyploidy
- ✓ Cultivated cotton plant is tetraploidly (52 chromosomes), how many chromosomes did ancestral haploid have? Tetra = 4n therefore ancestral haploid = 52/4 = 13

Variation in chromosome structure

Duplication: segment of chromosome is duplicated
Deletion: segment of chromosome is deleted
Inversion: segment chromosome is turned 180 degrees
Translocation: segment of chromosome moves from 1 chromosome to a non-homologous chromosome or to another place on the same chromosome



- If homozygous not sure abnormality
- Heterozygous for abnormality in bivalents during meiosis
- Unusual but characteristic pairing during meiosis
- Used to identify type of change occurred

Deletion

- Lost portion of chromosome due to damage externally (UV) or internally (meiosis) from 1 to many genes deleted depending on size of deletion

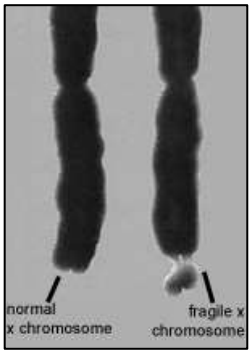
1. Terminal deletion: deletion at end of a chromosome
2. Intercalary deletion: deletion form interior chromosome

- Acentric fragment occurs where a piece of chromosome has no centromere
- Synapsis occurs between deleted chromosome and normal chromosome homologue
- Deficiency compensation loop forms as 1 chromosome is now shorter than the other

Fragile sites

- Fragile X: region on X chromosome where chromosome can break forming a gap
  - Region on chromosome does not stain due to gap on chromosome
- Caused by repetitive elements

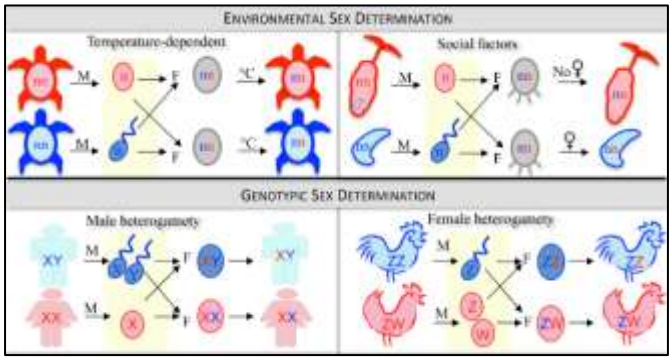
1. Common fragile site: present in all humans and common site for cancer
2. Rare fragile site: present in few people and association with genetic disorders



Martin Bell Syndrome: fragile-X

- More in males due to only having 1 X chromosome therefore if heterozygous i.e. in females you are normal therefore less common due to the masking effect
  - 1/1500 males and 1/8000 females
- Men: mental retardation, enlarged testes and abnormal facial features (long faces and large ears)
- Fragile X syndrome: 2nd most common genetic cause of mental retardation after Down syndrome
- Trinucleotide (CGG) in FMR1 gene (familial mental retardation)
  - FMRP widely expressed cytoplasmic protein abundant in brain & testis
  - CGG 6-55 (normal); 55-200 (pre); >230 (full)
  - Genetic anticipation

SEX CHROMOSOMES AND SEX DETERMINATION - study unit 2



Genotypic influence: sex determined by genotype

Environmental influence: sex determined by internal and external environmental conditions

Sex chromosomes is a pair of heteromorphic chromosomes that characterises 1 sex or other

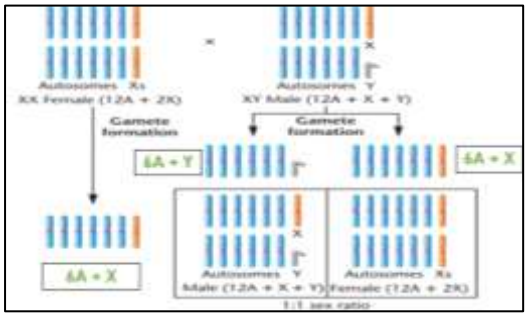
- XX/XO Protenor system: *C. elegans, Protenor* (insect)
- XX/XY Lygaeus system: mammals and *Lygaeus turcicus* (insect) -> XY
- ZZ/ZW system: birds, fish, reptiles, moths and butterflies -> ZW
- Haplodiploidy: bees and ants

Protenor system **XX/XO**

- XX Females (12A + 2X) x XO Male (12A + X) -> no Y present in males just 1 less X = gap
- Female always forms same gamete = only 1 type 6A + X
- Male has 2 gametes = 2 types 6A + X and 6A (the 1 less X)
    - ½ with X chromosome and ½ without X chromosome
- 1:1 sex ratio is reformed with Autosomes Xs Female (12A + 2X) and Autosomes X Males (12A + X)
    - Xs -> more than 1 X chromosome and X -> only 1 X chromosome

Lygaeus system **XX/XY**

- XX Females (12A + 2X) x XY Male (12A + X + Y) -> Y is now present in open gap
- Female always forms same gamete = only 1 type 6A + X
- Male has 2 gametes = 2 types 6A + X and 6A + Y
    - ½ with X chromosome and ½ with Y chromosome
- 1:1 sex ratio is reformed with Autosomes Xs Female (12A + 2X) and Autosomes Y Males (12A + X + Y)

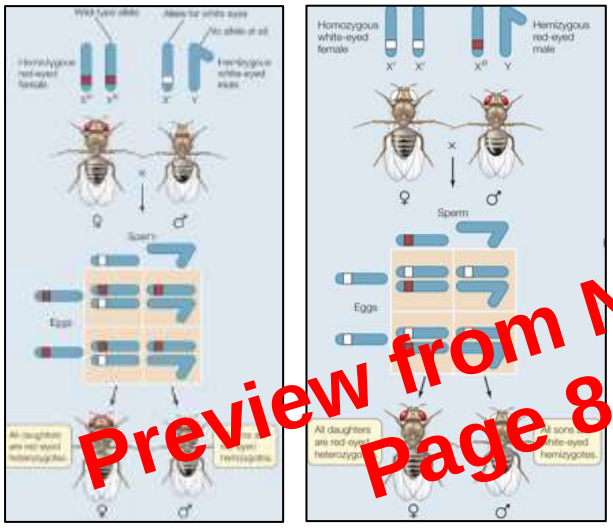


Hetero vs homogametic

- Males are heterogametic sex generating 2 types of gametes = different gametes
    - XY

Expectations from sex linkage

- For determining if sex linked: experimental cross but twice with males and females showing reciprocal phenotypes
- Female: red eyes X^RX^R homozygous red & male: white eyes X^rY hemizygous white
  If X-linked -> all offspring male or female have red eyes because if a female pure breeding for red eyes, red eye allele received and if dominant over white = all offspring red allele = red eyes therefore females red heterozygotes X^RX^r and males red hemizygotes X^RY
  Repeat female: white eyes X^rX^r homozygous white & male: red eyes X^RY hemizygous
  If X-linked -> all female offspring have red eyes as dominant red allele from father masks recessive allele from mother and all male offspring have white eyes as they get Y from father and only white allele from female X^r therefore females red heterozygotes X^RX^r and males white hemizygotes X^rY
- Same cross but outcomes not the same



Autosomal recessive trait

- Appears in both sexes with equal frequency
- Skips generations
- Affected offspring born to unaffected parents
- Both parents heterozygous -> ¼ offspring affected
- More frequently among offspring of consanguine marriages

Autosomal dominant trait

- Appears in both sexes with equal frequency
- Both sexes transmit trait to offspring
- Not skips generations
- Affected offspring must have affected parents unless possess a new mutation
- 1 parent affected as heterozygous & other parent unaffected = ½ offspring affected
- Unaffected parents do not transmit trait

In a plant, height varies from 6cm - 36cm. 6cm and 36cm plants are crossed. All F1 are 21cm. In F2, continuous variation observed with most being 21cm and 3/200 are short as the 6cm P parent

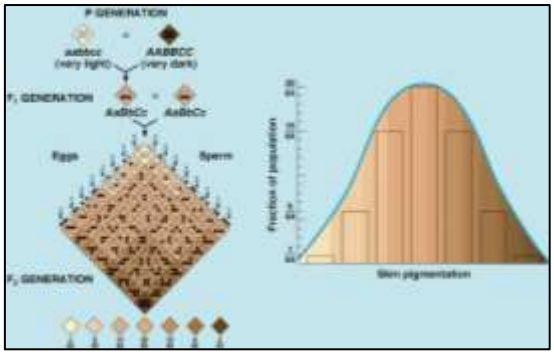
How many gene pairs contribute to the phenotype?
$1/4^n$ number of F2 expressing P phenotype = 3/200 (as that proportion represents at least 1 of the P phenotype as 6cm) = 1/64 ($¼^3$)
Therefore n = 3 as $¼^3$
Therefore 3 genes pairs -> A, B and C each with 2 alleles
2n + 1 = 2(3) + 1 = 7 distinct classes

How much does each additive allele add to the phenotype?
Determine range -> 36-6 = 30cm
3 gene pairs = 6 alleles
Range/(gene pairs x alleles) = range/(gene pairs x 2) = range per additive alleles which is the **average effect per allele** contributing to each phenotype
30/(3 x 2) = 30/6 = 5cm contributing each additive allele to phenotype

Base length with no additive alleles is 6cm. What is the F1 phenotype?
Smallest extreme + (avg. effect of each allele x number add. alleles) = **F1 phenotype**
AABBCC = 6cm + (5x6) = 36cm
AaBbCc = 6cm + (5x3) = 21cm
aabbcc = 6cm + (5x0) = 6cm

<u>Statistical analysis</u>

- Quantitative traits follow normal distribution:
  - 68% of the data occurs within 1 standard deviation about the mean
  - 95% of the data occurs within 2 standard deviations about the mean
  - 99.7% of the data occurs within 3 standard deviations about the mean
- Mean: $\bar{X} = \frac{\sum Xi}{n}$
- Variance: $s^2 = \frac{\sum(Xi - \bar{X})2}{n-1}$
- Standard deviation: $s = \sqrt{s^2}$
- Standard error: $S_{\bar{X}} = \frac{s}{\sqrt{n}}$
- Covariance: $cov_{XY} = \frac{\sum[(X_i - \bar{X})(Y_i - \bar{Y})]}{n-1}$
- Correlation: $r = (cov_{XY})/(s_X s_Y)$



d. What is the narrow sense heritability?
$h^2 = V_A/V_P = 870 / 2620 = 0.33$

e. What is the mean weight of the next generation?
$h^2 = (M2-M) / (M1-M)$
$0.33 = (M2-500) / (600-500)$
M2 = 533g as the predicated variation in next generation (M2) after a selected variation in a population (M1 = 600g) based on a population of 500g

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Formulas

$1/4^n$ = number/proportion **F2** individuals in fractional form expressing 1 parental phenotype
Where n will determine the number of genes involved

- Fraction of F2 phenotype expressing EITHER P extreme phenotype (i.e. all dominant or all recessive) not the in between which would be the continuous scale range

2n + 1 = number of distinct phenotype classes observed

- Determine n from the fraction $1/4^n$ = fraction of extreme phenotype then x2 + 1

Average effect per allele **-> range/(gene pairs x alleles) = range/(gene pairs x 2) = range per add. allele = avg. effect of each allele**
Range/(gene pairs x alleles) = range/(gene pairs x 2) = range per additive alleles which is the average effect per allele contributing to each phenotype

Base length of F1 has no additive alleles
Smallest extreme + (avg. effect of each allele x number additive alleles) = F1 phenotype

$V_P = V_G + V_E$
$V_G = V_A + V_D$
$V_P = V_E + V_A + V_D$ -> $V_P = V_G + V_E$ where **$V_G = V_A + V_D$**

$H^2 = V_G/V_P$

$h^2 = V_A/V_P$
$h^2 = R/S$ where $R = h_2S$
$h^2 = (M2-M) / (M1-M)$

Proportion add. alleles: V_A/V_P where $V_A = (h_2)(V_P)$ due to $h^2 = V_A/V_P = R/S = (M2-M) / (M1-M)$
Proportion non-add. alleles: $H_2 - h_2$ or V_D/V_P because $(V_D + V_I)/V_P$ & $V_I = 0$ where $V_D = V_G - V_A$ due to $V_G = V_A + V_D + V_I$

Oil content in maize due to realized heritability:

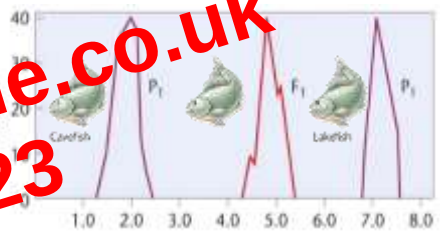
Gene order: Q in the middle of (D disregarded) due to each gene in the middle, crossing them and seeing which F1 showed in the observed DCO table
Q correlates to the intermediate or large eyes

P1: AQB//AQB lakefish x aqb//aqb cavefish
F1: A**q**B & a**Q**b -> double cross over in BC offspring seen in ABd - I and abD -L

Inter-locus distance and map QTL: distance = %SCO + %DCO
A-Q: SCO2 + DCO = 8.9 + 0.97 = 9.87% = 9.87 cM
Q-B: SCO1 + DCO = 20.84 + 0.97 = 21.81% = 21.81 cM
B-D doesn't exist

A 9.87 cM **Q** 21.81 cM B ? D

Defined and different means for cohort P1 cavefish, F1 and P1 lakefish -> V_P limited for each
Discrete mean but variation on each side mean
P1 extreme for small eyes (cavefish) and larger eyes (lakefish -> inbred) therefore **F1 genetic homogeny where $V_G = 0$**
Environmental heterogeneity $V_E \neq 0$ therefore variation is from environment $V_P = V_E$
F1 intermediate with P1 at each extreme
F1 homogenous as it is environmental heterogeneity



F2 mean has the same mean as the F1 offspring
V_P variance is larger expanded where **$V_G \neq 0$** and **$V_E \neq 0$**
Phenotypic range between extreme means of P1
Normal distribution where $V_P = V_G + V_E$

Intimidate eyes = incomplete dominance
Eye size multifactorial or complex trait
Polygenic environmental effects therefore $V_P = V_G + V_E$

Range between F1 and P1 means -> means intermediate
Backcross with lakefish as large eyes = bimodal distribution

Individuals at extreme phenotypes P1: multifactorial trait & polygenic environmental effects
$(Aa)_n$ x $(aa)_n$ -> $(Aa)_n$ & $(aa)_n$ ~1:1 -> bimodal
Aa additive allele and aa non-additive allele
Large eyes associated with non-additive allele

Individuals larger than extreme phenotypes P1 at 8.0: multifactorial trait & polygenic environmental effects
$(Aa)_n$ x $(AA)_n$ -> $(AA)_n$ & $(Aa)_n$ ~1:1 -> not bimodal DUE TO TRANSGRESSIVE SEGREGATION
Transgressive segregation: P1 not all fixed for all additive/non-additive alleles therefore combination with more extreme additive/non-additive allele phenotypes then original extreme phenotypes = smoothing of curve

AABBcc x aabbCC -> AaBbCc
Cavefish AABB more additive alleles than lake fish CC
Smaller eyes P1 cavefish AABBCC. Larger eyes P1 lakefish aabbcc (non-additive alleles)

Basic eye development gene -> loss of function genes for eye development does not support embryonic data as all embryonically develops eyes
Secondary eye growth gene -> loss of function genes for eye growth does not support embryonic data as eyes do not stop growing they only shrink
Third gene responsible for eye degradation -> gain of function that counters exceeding gene action growth of basic and secondary genes to make it smaller

Biogenetic law (recapitulation theory): ontogeny recapitulates phylogeny as the development of animal embryo and young traces the evolutionary development of the species

POPULATIONS & EVOLUTIONARY GENETICS - study unit 3

Variation within and between populations

- There is phenotypic variation within populations
- Frequency with which a certain phenotype occurs changes over time or between different populations
- Response to selection is an indication that genetic variation exists at genes responsible for traits
- Natural theory explains more variation on molecular level than expected
    - More frequency as mutations in molecular level doesn't impact phenotype
- Phenotypic changes: changes frequency of alleles that determine trait phenotypes
- Population genetics is the study of change in allele frequency
- Microevolution gives small changes in allele frequencies and a shift in time enables large changes to evolve = macro-change = macroevolution

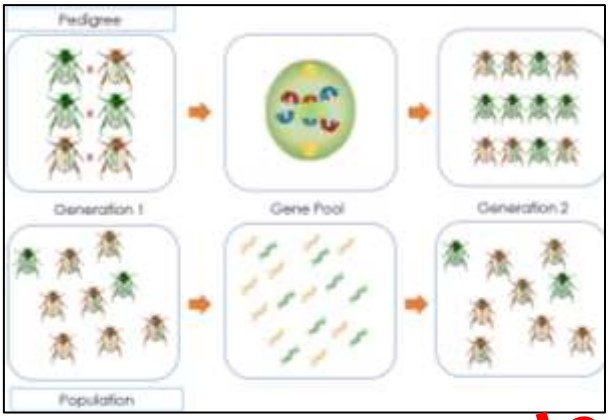
Populations and gene pools

- Population:
    - Group of individuals from the same species that lives in the same geographical area and potentially interbreeds producing
- Gene pool:
    - All gametes (alleles) produced by breeding members of the populations in a single generation
- Single locus in population: different individuals have different genotypes for that specific locus on the homologous chromosomes
    - Homologous pair of chromosomes has a locus for flower colour and different individuals will have allele for purple or white = different genotypes for locus

- Frequencies of different alleles and genotypes occur in a population and frequencies change from one generation to the next
    - Generation 1 75% G and 25% g -> generation 2 71% G and 29% g

Individuals are diploids that contributes gametes to gene pool & mixture of gametes from gene pool = next generation
Traits are passed along in a pedigree & pedigrees are interconnected in a population

Pedigree is a combination of individual mating's & gamete formation needed for offspring in *generation 1* to constitute for the *gene pool* where there is a union of gametes in gene pool forming *generation 2* for a *population*



Hardy-Weinberg law

- Fundamental mathematical model describing allele frequencies and genotypic frequencies in a population from one generation to the next
- If a locus conforms to the model expectation it occurs in hardy Weinberg equilibrium
- Allele and genotypic frequencies remain constant over generations if no external evolutionary forces act at the locus on genes
- Model assumes
    - No selective advantage
    - No mutation: no new alleles created
    - No migration: no external allele imported
    - Infinite population: large so change events have a small impact
    - Random mating: sperm equal probability to fertilise any egg in gene pool

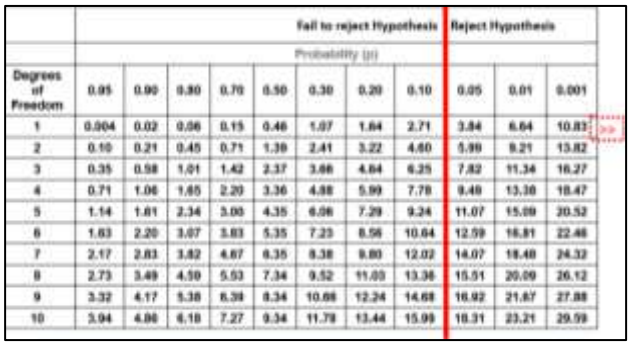
EXAMPLE

Single locus with 2 alleles G and g
Generation 1 -> GG, GG, Gg, Gg and Gg
Gene pool -> donated alleles -> G, G and G, G and G, g and G, g and G, g
Allele frequencies -> G = 7/10 = 0.7 and g = 3/10 = 0.3
Generation 2 -> GG, GG, GG, Gg and gg

Genotypic frequencies in HW equilibrium

$X^2 = \sum(o - e)^2/e$

Df = number of classes (phenotype/genotype) - 1 sampling error - 1 parameter estimation (genotypic frequencies are counted from allele frequencies in sample = assumptions therefore room for error)



Degrees of Freedom	Fail to reject Hypothesis: 0.95	0.90	0.80	0.70	0.50	0.30	0.20	0.10	Reject Hypothesis: 0.05	0.01	0.001
	Probability (p)										
1	0.004	0.02	0.06	0.15	0.46	1.07	1.64	2.71	3.84	6.64	10.83
2	0.10	0.21	0.45	0.71	1.39	2.41	3.22	4.60	5.99	9.21	13.82
3	0.35	0.58	1.01	1.42	2.37	3.66	4.64	6.25	7.82	11.34	16.27
4	0.71	1.06	1.65	2.20	3.36	4.88	5.99	7.78	9.48	13.28	18.47
5	1.14	1.61	2.34	3.00	4.35	6.06	7.29	9.24	11.07	15.09	20.52
6	1.63	2.20	3.07	3.83	5.35	7.23	8.56	10.64	12.59	16.81	22.46
7	2.17	2.83	3.82	4.67	6.35	8.38	9.80	12.02	14.07	18.48	24.32
8	2.73	3.49	4.59	5.53	7.34	9.52	11.03	13.36	15.51	20.09	26.12
9	3.32	4.17	5.38	6.39	8.34	10.66	12.24	14.68	16.92	21.67	27.88
10	3.94	4.86	6.18	7.27	9.34	11.78	13.44	15.99	18.31	23.21	29.59

Population sample of 100

	MM	MN	NN	
Obs.	50	20	30	100
Exp.	36	48	16	100
$X^2 = \sum(o - e)^2/e$	5.44	16.33	12.25	**34.02**

Df = 3 - 1 - 1 = **1**

p > 0.05 reject and p < 0.05 fail to reject
X^2 = 34.02 is way less than 0.05 so p <<< 0.05 -> less than 0.001
Reject null hypothesis

<u>Case study</u>

Resistance to HIV-1 infection

- CCR-5 receptor protein occurs on immune cells
- Deletion in gene makes protein non-functional
- Homozygotes are resistant to HIV-1

Do frequencies of mutant alleles in population remain constant over generations?
How resistant is population to HIV-1?

Observed genotypic numbers & frequencies (count):
+/+ 582 f = 0.827
+/- 114 f = 0.162
-/- 8 f = 0.011
Total = 704

Allele frequencies:
p = f (+) = 0.827 +/+ + ½ (0.162) +/- = 0.908
q = f (-) = 0.011 -/- + ½ (0.162) +/- = 0.092

Expected genotypic frequencies and numbers:
+/+ = p^2 = 0.908 x 0.908 = 580.423
+/- = 2pq = 2(0.908)(0.092) = 117.619
-/- = q^2 = 0.092 x 0.092 = 5.959

Statistical test:

	Observed	Expected	X^2
++	582	580.423	0.00428
+-	114	117.619	0.11135
--	8	5.959	0.69906