Placental & Marsupial ~~Animals~~ Mammals

- Placental mammals : long-lasting placentas, developed offspring
- Marsupials : pouch , 2 vaginas
- Marsupials found in Australia & America [New World]
- Convergent adaptations of placental & marsupial mammals

Molecular Genetics :

- DNA is now the sole & universal carrier of genetic code
- The code is universal – every organism contains the same cellular machinery for decoding and copying genetic information.
- Strong evidence for common ancestor
- Possible to track evolution by comparing genetic sequences directly / looking at proteins

Molecular Clock : [DNA, RNA, protein can be compared]

↳ pair of species compared for the same protein : Coding differences highly correlated with divergence derived from fossil data. Genetic difference accumulate at a constant rate.

↳ Evolutionary tree of the cytochrome c gene & mitochondrial closely correlates with morphological trees.

Evidence : ① Collagen extracted from tyrannosaur & Mammoth Fossils entirely supports morphological datas

② Birds closer to alligator than to mammals

③ T. rex closer to birds

Falkland Island ~~wolf~~ "Wolf" [Dusicyon australis]

↳ only native mammal on the Falklands
↳ related to fox species on mainland
↳ recent study looked at ancient Dusicyon avus mitochondrial DNA (7800-3000 year BP)
↳ 2 species split around 16,000 years ago, around last glacial
↳ Wolf walked to Falklands.

Speciation and Its Mechanisms

Species — Biological Definition (Mayr, Dobhansky)

↳ a population of reproducing organisms that is isolated from other populations

- Prokaryotes & eukaryotes that are not strictly sexual (eg most plants) fit less easily
- impossible to use with extinct organisms

Requirements of speciation

1. Time
2. Isolation
3. Selection

Speciation

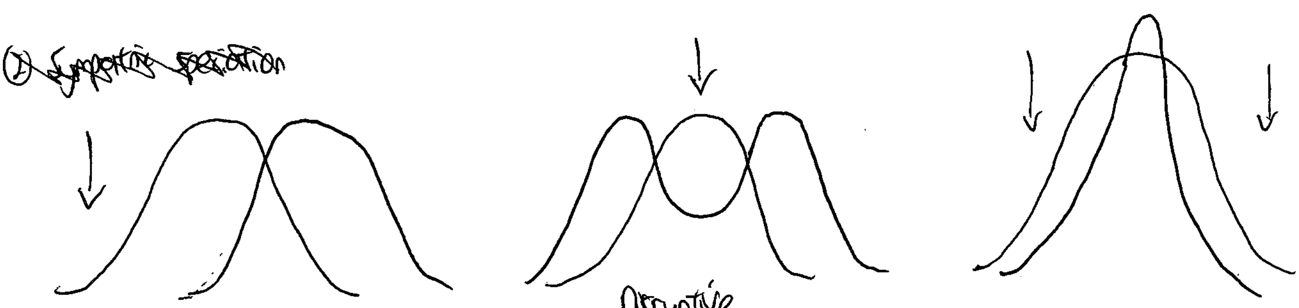
- Appearance of reproductive isolation
- Exploitation of changing ecological niche
- Ecological ~~niche~~ effects (eg predators ↑ diversity)
- Species can appear
  - ↳ in time along a lineage (eg: humans / chimps & our common ancestor)
  - ↳ in space due to isolation eg: animals on an island
  - ↳ various genetic effects (selection, drift, bottlenecks) play a role
  - ↳ these can be identified & by population genetics [measuring allele frequency]

Modes of Speciation:

(1) Allopatric speciation [allo – other & patra – fatherland]

- classic & widespread mode of speciation
- not necessarily diff. selection pressures & adaptations in 2 zones, leading to speciation
- 2 diff. species of antelope squirrels on either side of Grand Canyon can't interbreed
  - ↳ birds show no such effect on either side

(2) ~~Sympatric speciation~~



a) Directional Selection

Disruptive ~~Stabilising~~ Selection

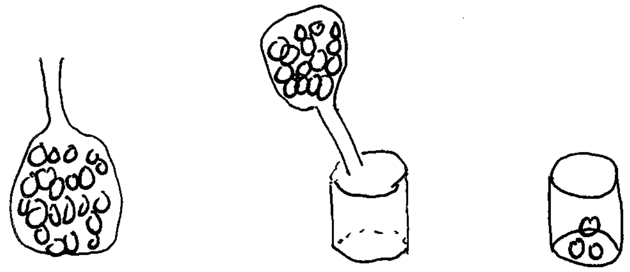
Stabilising Selection

Genetic Drift

↳ In large randomly-mating populations, large fluctuations are unlikely

↳ random effects can cause major changes in small populations

Founder effects / bottlenecks



original Population ⟶ Bottlenecking Event ⟶ Surviving Population

↳ sampling & statistical effects such as drift & bottlenecks, combined with long periods of isolation can lead to speciation

↳ This does not undermine the power of natural selection as the only way to consistently creating adaptations

↳ speciation is X an adaptation, merely an event / a consequence of particular ~~events~~ conditions, which can involve the by-products of subsequent selection

↳ Species are accidents, taking a long time to occur.

↳ Partly because selection is often not directly involved

* SPECIATION IS not the goal of evolution, just a consequence of other events *

↳ 100,000 – 5 million years

Coyne & Orr: mean time taken to go from single individual to 2 reproductively isolated individuals (NOT in bacteria)

↳ Speciation is a branching process — to get 100,000,000 species today, speciation occur every 200,000,000 year

↳ speciation occur more rapidly & frequently than this

Sickle Cell Anaemia

↳ homozygotes are anaemic

↳ Anaemic variant still exist

↳ Heterozygotes less likely to get malaria

↳ Sickle cell anaemia variant of Hb gene is advantageous in malarial zones — only heterozygotes are 'fitter'
— if homozygotes, die of sickle-cell anaemia

What is Selected?

→ evolution is a change in allele frequencies

→ phenotype & genotype often not directly linked, can get selection without evolution

Helena Cronin : genes are being selected

Dick Lewontin : phenotypes being selected

Bill Hamilton :

→ Genes can be linked together — possible to have increased frequencies of deleterious gene due to 'hitchhiking' — physically close to a selected gene

→ Selection operates on individuals who expresses phenotypes not genotypes

→ these individuals interact & transmit their genes differentially

→ where their phenotypes are at least partly determined by genes, there is possibility of EVOLUTION

Where's the Fitness?

↳ Some characters appear to have ~~maladaptive~~ maladaptive and to reduce fitness

↳ in many cases : Sexual Selection

↳ generally female choice

↳ " Runaway sexual selection" up to a point

↳ underlying the character are good genes
  ↳ direct / indirect correlates

↳ Peacock → either survival ('handicap')
  → colours show no parasites

- Virgin / newly mated queen
  - ↳ identical genotype to her workers sisters
  - ↳ Mates, find potential nests, & loses wings

- mates, finds potential nests, loses wings, goes underground & never see light again
  - ↳ male dies, female can live for decades

- Queen raise 1st generation, who then forage

- Larvae fed by their sisters who can be more closely related to them then to their own offspring

Microevolution: evolutionary events within a species / population

↳ gives rise to macroevolution

Macroevolution : 'evolution on a grand scale'

= major evolutionary events above the level of the species

eg : evolution of major animal groups [mammals, birds, reptiles]

Definition

(1) Microevolution → changes in the gene pool of an organism over time

(2) Gene pool is all alleles of all genes of all individuals in a population

↳ represents all of the genetic variation — raw material of evolution within a population

Evolution by natural selection requires...

- Differential reproductive success
- genetic differences between individuals (genetic variation)

Evolution changes the genetic structure of a population / species

Darwin's Problem
- On the Origin of Species by means of natural selection [Charles Darwin, 1859]
- Experiments on Plant Hybridization [Gregor Mendel, 1866]

Early 20^{th} century : Macromutationist vs. Darwinians

↗ JBS Haldane, Sewall Wright & Ronald Fisher

Population Genetics : The study of microevolution ≈ "New Synthesis" or "Neo-Darwinism"

↳ a synthesis of Darwin's theory of evolution by natural selection w/ Mendel's theory of inheritance.

↳ How humans pathogens are evolving?

(1) Bacteria — antibiotic resistance (MRSA)

(2) Viruses — resistance to antiviral drugs (HIV) ↗ drugs "cocktail" mixture given to HIV patient to prevent development of resistance

(3) Emerging new pathogen eg : avian influenza

↳ How humans ~~are evolving~~ have evolved in response to pathogens — resistance to blood borne parasites

α - thalassemia → lack of α-globin

β - thalassemia → lack of β-globin

} Some individuals still have these mutations due to heterozygote advantage

Mitosis : nuclear division associated $\bar{w}$ somatic cells, producing 2 genetically identical daughter cells

NORMALLY in PLANTS:

Haploid multicellular organism [gametophyte]

↳ some gametes undergo mitotic cell division

2n → 2n, 2n

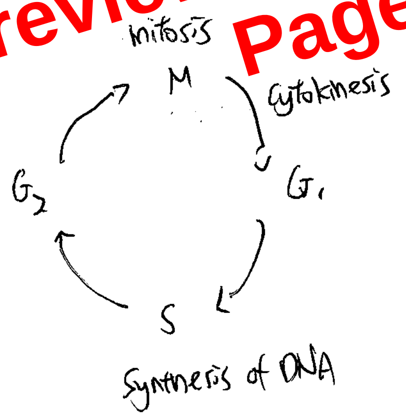
Diploid mother cell → ② Diploid Daughter Cells

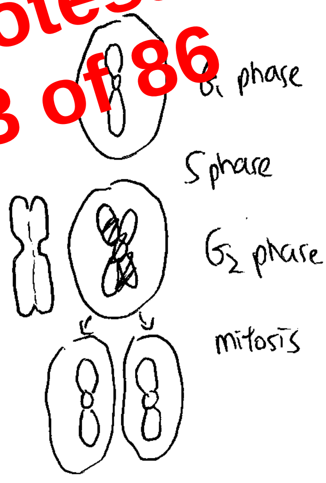
Meiosis : nuclear division that produces cells that develop into gametes

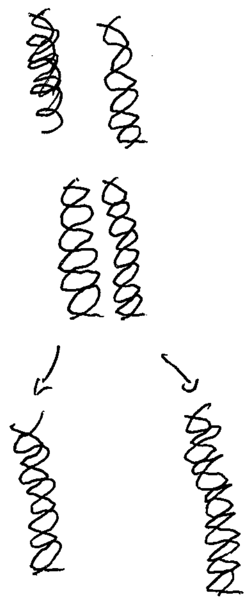
2n → n, n, n, n

4 haploid daughter cells

Duplication & Segregation of chromosomes : the cell cycle



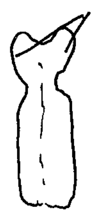




Period between successive mitoses → interphase

[G_1 + S + G_2]

gap① synthetic gap②



sister chromatids attached along their lengths

↓

sister chromatid cohesion

Mendelian Genetics

believed @ ~~[illegible]~~ Darwin's time

How are traits transmitted? Blending vs. particulate inheritance

Mendel's Experimental Approach (1865)

↳ True / Pure breeding

Flower colour	Purple &	White
Flower Position	Axial &	Terminal
Seed colour	Yellow	Green
Seed shape	Round	Wrinkled
Pod shape	Inflated	Constricted
Pod colour	Green	Yellow
Stem length	Tall	Dwarf

Summary of Mendel's Experiment

↳ the monohybrid cross [traits controlled by single gene]

YY (yellow seeds) × yy (green seeds)

3:1 phenotypic ratio in F2 generation

Mendel's 1st law: Principle of Segregation

↳ Alleles of a single gene segregate randomly & equally into gametes.

Dihybrid cross: traits at 2 different gene loci of 2 different chromosomes *

RRyy (round, green seeds) × rrYY (wrinkled, yellow seeds)

9:3:3:1 phenotypic ratio in the F2 generation

Mendel's 2nd Law: Principle of Independent Assortment

↳ Alleles from different gene segregate randomly into gametes

The chromosome theory of inheritance: In 1902-1904, Walter Sutton & Theodor Boveri recognised parallels between Mendel's laws & behaviour of chromosomes during meiosis & fertilisation

[Sutton - ~~Boveri~~ Boveri Theory]

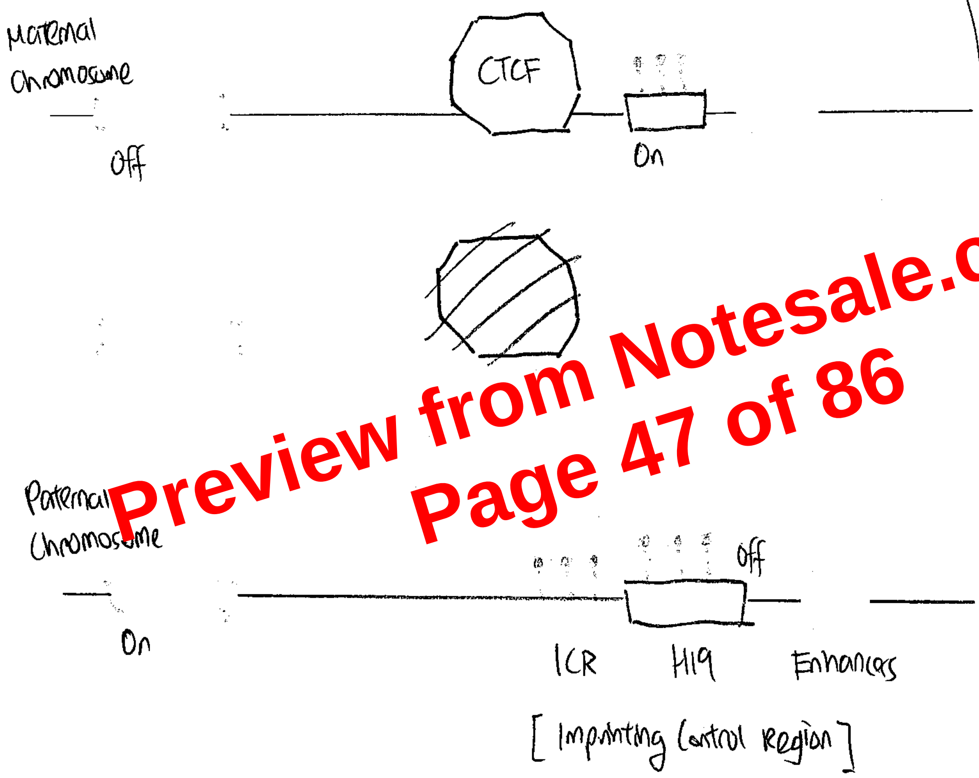
Genomic Imprinting is an Example of epigenetics:

CG

70% of CpG dinucleotides are methylated in vertebrates

CTCF protein bind to a sequence of ICR, preventing enhancers on switching on the mutant Igf2 alleles in maternal chromosome.

Epigenetics: study of heritable changes that are NOT caused by changes in DNA sequence



SRY is a DNA binding protein [transcription factor] thought to regulate expression of genes necessary for testis formation

↳ proteins that bind to DNA

SRY expression occurs after 6th week of pregnancy.

Genital ridge (germ cells & Somatic cells) [Week 4] → Indifferent gonad [Week 6] → ovary

Indifferent gonad $\xrightarrow{\text{SRY expression}}$ testis [week 8]

Sex Determination in Drosophila:

↳ The ratio of X chromosomes to autosome sets (X:A ratio) determines sex in Drosophila

X:A ≥ 1.0 → female

X:A ≤ 0.5 → male

X:A between 0.5 & 1.0 — intersex flies

⤳ Y chromosome has no influence

⤳ sex determination in Drosophila is cell autonomous

Sex chromosome	Autosome sets	X:A ratio	Sex
XX	2	1.0	F
XY	2	0.5	M
XXY	[illegible]	1.0	F
[illegible]	2	[illegible]	M
XX	3	0.67	Intersex

cell autonomous : each individual cell makes its own decision to be either male / female

Sex inheritance

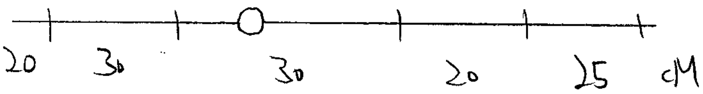
↳ Reciprocal crosses usually give the same results

yellow female x green male
↓
All yellow F_1
↓
3 yellow : 1 green

green female x yellow male
↓
All yellow F_1
↓
3 yellow : 1 green

3 Types of Gene Maps

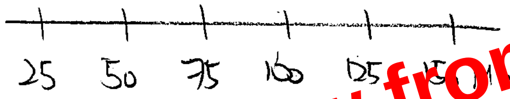
- Physical Maps: show distances between genes / DNA markers based on ~~their~~ the direct measurement of DNA (base pairs, bp)
- Cytogenic maps: indicate gene positions with respect to cytogenic markers eg. banding pattern
- Linkage maps: show the relative position of genes or ~~maker~~ markers on a chromosome based on meiotic recombination frequencies (centiMorgan, cM)



Linkage Map

Cytogenic map ↗ by looking at ~~chro~~ microscope after staining chromosomes

1 centiMorgan (cM) is approximately [illegible] in humans.



Physical map

Physical Map:

- The 1st were made using restriction enzymes that cut DNA at specific sites → restriction enzyme map
- The Human ~~Genome~~ Genome project has provided the ultimate physical map of the human chromosomes → their DNA sequence

From linkage to disease gene: "positional cloning"

Once linkage with ① DNA marker has been found:
↳ repeat linkage analysis w closely spaced DNA markers to obtain linkage to within 1 cM (~1 Mb).

Identify candidate genes by inspection of the human genome sequence
↳ looking for mutations in affected individuals, while mutation is absent in unaffected individual

Extranuclear genomes of mitochondria & chloroplasts

Many prokaryotic features:
- circular dsDNA genomes
- ribosomes of mt & cp diff. from those in cytoplasm & are sensitive to bacterial antibiotics

Endosymbiont theory: Ancestral host cell took up a prokaryote which became mitochondria
↳ to become 'plant cell', chloroplast is took up.

Genes Found in organelle Genomes:
mtDNA ~ remnant of a larger DNA
- components required for translation eg: tRNA, rRNA
- structural genes for proteins involved in oxidative phosphorylation
eg: cytochrome oxidase, NADH-dehydrogenase, ATPase

cpDNA
- genes encoding tRNAs & rRNAs involved in chloroplast translation
- structural genes for proteins involved in photosynthesis eg: large subunit of ribulose bisphosphate decarboxylase
[rubisco = most abundant enzyme]

Heritability

↳ can be useful to know the proportion of the total phenotypic variance due to genes.

~~Herit~~ Heritability (H^2)

$$H^2 = \frac{V_G}{V_P} \qquad 0 < H^2 < 1$$

↓

Broad sense heritability

A more useful measure of heritability is $\underbrace{\text{narrow-sense heritability } (h^2)}_{\text{predicts the response to selection}}$

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

Why is knowledge of heritability of a trait useful?

* ↑ heritability ↑ effect of selection
only narrow-sense heritability shows effect to selection *

· Animal & Plant breeding:
If a trait has a high h^2 then phenotype of an individual more accurately reflects its genotype.
ie. cow with high milk yield → offspring $\bar{w}$ ↑ milk yield
Artificial selection for a trait of economic importance will be faster for traits showing high h^2.

· Medical Genetics:
If a trait has high h^2, then it may be easier to identify genes associated $\bar{w}$ the trait

Estimation of heritability:

h^2 – 1.0 — 100% genes 0% environment
h^2 – 0.5 – 50% " 50% "
h^2 – 0 — 0 " 100% "

regression line: $y = a + bx$

$b = h^2 = \text{gradient}$

Heritability in Humans:
Twin studies:
· Identical (Monozygotic, MZ) twins share their environment & all of their genes / alleles ← ① fertilisation
[relatedness = 1]

Nonidentical twins (dizygotic DZ) ← ② fertilisation
· share their environment but only half of their genes [r = 0.5]

For a trait, if ~~DZ~~ MZ twins resemble each other more than do DZ twins, then genetic factors contribute to variation in the trait, assuming equal environments.

Embryonic stem cells as the basis for advanced genetic approaches in the mouse.

↓

Making targeted knockout of genes using ES cells

↓

Led to Nobel Prize in Medicine in 2007

- Martin Evans
- Oliver Smithies
- Mario Capecchi

Final breakthrough → reprogramming differentiated cells back to a pluripotent embryonic state without having to use nuclear transplantation

Klf-4
Sox-2
Oct 4
Myc

overexpression of these factors in fibroblasts lead to iPS. [Yamanaka factors]

normally fibroblasts

Animal or human individual → 1° cell culture → (Pluripotency genes in suitable vector) most cells receive the gene → (Plate onto feeder cells) Culture in ES medium → Colonies appear

↓ Subculture individual Colonies

Freeze cells for future use ← Carry out tests for bona-fide iPS phenotype

Protocol of induced pluripotent stem cells (iPS) by Shinya Yamanaka

- have adapted the protocol & succeeded in making human iPS cells

Huge implications

1) Can induce pluripotent stem cells from patients suffering from diseases. Model diseases in vitro

2) Can induce pluripotent stem cells from patients from cell replacement therapies

eg: regenerative medicine, no immunological rejection