Biology 1201A Final Exam Notes: Full Course

EVOLUTION
Chapter 17: The Development of the Theory

Venus Flytrap – a leaf specialized to trap insects and edges lined with bristles, black trigger hairs (trichomes) that spring the trap and the red colour that attracts prey

Australian Sheep Bowflies occur throughout Australia in habitats ranging from urban to rural settings, in semi-arid open lands & forests and have spread throughout the world, including eastern Canada

- Female fly lays eggs in open wounds on livestock such as sheep
- Eggs hatch into maggots and eat flesh and damage wool
- Organophosphate insecticides are effective because they affect the nervous system and kill both adult flies and maggots
- Some bowflies have a mutation that makes them resistant to insecticides
    - Selection associated with the pesticide changes the population structure of sprayed flies, eliminating nonresistant ones

This is an example of how the combination of genetic-based changes and strong selective pressure has altered the population over time (Evolution)

Biological Evolution: gradual change of populations or organisms over time, measuring time in generations rather than years

17.2 Pre-Darwin Knowledge of the Natural World

Aristotle

- Observer of nature and natural history
- Believed that both inanimate objects and living organisms had fixed characteristics
- Created a ladder-like classification of nature from simplest to most complex – minerals→plants→animals→humans→spiritual gods
    - Scala Naturae/Great Chain of Being
- 14th century
    - Aristotle's classification merged with biblical accounts of creation
    - Europeans believed all different organisms had been created by god and could never change or become extinct
    - Biological research dominated by natural theology – all of god's creation

Francis Bacon (1561-1626)

- English philosopher – established the importance of observation, experimentation and finding evidence to support theory
  (inductive reasoning)

The collective work of – Nicolaus Copernicus, Galileo Galilei, Rene Descartes, Sir Isaac Newton – gave rise to 3 new disciplines

- Biogeography, Comparative Morphology, & Geology

Biogeography

- Global explorations in the 15th -17th Centuries provided naturalists with thousands of unknown plants and animals from around the world
- **"Study of world distribution of plants and animals"**

Comparative Morphology

- Morphology (anatomical structure)
- Natural theologians stated that the body plans were perfect and there was no need to invent a new plan for every species

- **George-Louis Leclerc** (le Comte de Buffon) was puzzled by the existence of body parts with no apparent function
    - Proposed that some animals must have *changed* since their creation
    - Vestigial structures = useless parts (eg. Wisdom teeth)
    - Recognized that species were conceived by nature and produced by time

Geology

- **Georges Cuvier** – French zoologist realized that the layers of fossils he found represented organisms that had lived in the past
    - Suggested that abrupt differences between geological layers indicated shifts in environment
    - Developed theory of "Catastrophism" – each layer of fossils represented the remains of organisms that had died in a local catastrophe such as a flood

17.3 Our View of Earth Changes

- **Bishop James Ussher** – theologian, calculated the age of the earth by counting the number of generations mentioned in the bible
    - Came up with the year 4004 BCE as the year of creation
- **Dr. John Lightfoot** – Cambridge University, continued this research to come up with a more precise time
- He concluded that the earth had been created on October 23rd 4004, BCE
- In 1975**, James Hutton** argued that slow and continuous physical processes, acting over long periods of time produced Earth's major geologic features
    - "Gradualism": the view that Earth changed SLOWLY over history, contrasts with catastrophism
- **Charles Lyell** – extended Hutton's ideas in an influential series of books (Principles of Geology)
    - Argued that geologic processes sculpted earth's surface overlong periods of time earthquakes, volcanoes, movement of glaciers etc.- are the same as the processes we observe today → "Uniformitarianism"

17.3b Biological Evolution

- **Jean Baptiste Lamarck** – proposed the first comprehensive theory of biological evolution based of specific mechanisms
    - Proposed that metaphysical "perfecting principle" caused organisms to become better suited to their environments
        - Simple organisms evolved into complex ones, moving up the ladder of life
    - According to his theory of *use and disuse*, body parts grow in proportion to how much they are used
    - *The inheritance of acquired characteristics* – changes that an organism acquires during its lifetime are inherited by its offspring
        - *Today we know that these mechanisms do not cause evolutionary change – structural changes acquired by organism are NOT inherited by the next generation*
- Lamark DID however make **4 important contributions** to evolution
    1. Proposed all species change through time
    2. Recognized that changes are passed through generations
    3. Suggested organism change in response to environment
    4. Hypothesized existence of specific mechanisms that cause evolutionary change

17.4 Darwin

- 1831, Darwin set sail on "The Beagle" – voyage lasted nearly 5 years
- Darwin read Charles Lyell's Principles of Geology and began to see rock formations through Lyell's eyes
- Hypothesized that plants and animals of the Galapagos were descended from south American ancestors & that appearance of some changed after being isolated on a particular island
- Began collecting a variety of Finches from different islands – wrongly assumed that all birds belonged to the same species

- *Developing the Theory of Natural Selection*
  - Knew that offspring resemble parents and understood selective breeding
  - Artificial selection = selective breeding/breeding to produce specific trait in offspring
  - Evolutionary Divergence = natural selection causing a population to become different over time
  - **NATURAL SELECTION** = principle by which each slight variation of a trait, is useful, is preserved
    - **Favors adaptive traits**
- Major observations
  - Individuals in populations vary in size, form, color, behavior etc
  - Variations are passed on parent to offspring
  - Some inherited variations enable some to survive better than others
  - If next generation is subjected to same process of selection – trait will become even more common

Evolutionary Biology Since Darwin

- Early 20th century – Thomas Hunt Morgan determined that genes are carried on chromosomes
  → Population Genetics: importance of genetic variation as the raw material of evolution – constructed mathematical models that applied to simple and complex traits
- 1930/1940's = **Modern Synthesis** – integrated biogeography, comparative morphology, comparative embryology, genetics, paleontology and taxonomy within evolutionary framework
  - Focused on evolutionary change within populations
  - Tried to link 2 levels of evolutionary change that Darwin identified
    - Microevolution: small scale genetic changes
    - Macroevolution: large scale changes (many small changes)

Further Evolutionary Research

- Adaption by Natural Selection
  - Ex. Wings of birds that have been modified over millions of years to help them reproduce
- The Fossil Record
  - Provides clear evidence of ongoing change in biological lineages
- Historical Biogeography
  - Study of geographical distributions of plants and animals in relation to their evolutionary history is consistent with Darwin's theory
- Comparative Morphology
  - Analysis of living and extinct organisms based on *homologous* traits (homo=same)
- Convergent Evolution = independent evolution of similar traits in unrelated species, such as wings of insects, birds and bats

INHERITANCE OF SAMENESS

Chapter 12: DNA Structure, Replication, and Organization

- In the first half of the 20th Century, scientists believed that proteins were the most likely candidates for hereditary molecules because they appeared to offer greater opportunity for information coding than nucleic acids
  - Proteins → 20 types of AA's
  - Nucleic Acids → 4 types of AA's

12.2: DNA Structure

- Watson and Crick (1935) discovered the structure of DNA
- Each nucleotide consists of:
  - A five-carbon sugar deoxyribose (carbon atoms on deoxyribose are numbered with primes 1' – 5')
  - A phosphate group
  - One of the four nitrogenous bases:
    Adenine (A), Guanine (G), Thymine (T), Cytosine (C)
    - A and G are purines – built from a pair of fused rings of carbon and nitrogen
    - T and C are pyrimidine's – built from a single carbon ring
- **Chargaff's Rule**
  - Number of purines = number of pyrimidine's
  - A=T & G=C

- Phosphodiester Bond: in polynucleotide chain – phosphate linkage between deoxyribose sugars (5 carbon sugar)

- Polynucleotide Chain has Polarity (ends are different)
  - One end 5' – phosphate group is bound to 5' carbon of deoxyribose sugar
  - Other end 3' – hydroxyl group is bonded to the 3' carbon of deoxyribose sugar

Maurice H.F. Wilkins → used X-Ray diffraction to study the structure of DNA

- X-Shaped pattern suggested that DNA has a helical structure
- New model proposed that 2 polynucleotide chains wind into a DNA double helix
- Distance between each pair = 0.34nm
- 10 base pairs per turn of the helix

Complementary Base Pairing: purine-pyrimidine base pairs A-T and G-C

- Hydrogen bonds form between base pairs

12.3 DNA Replication

Watson & Crick's Semi-Conservative Model

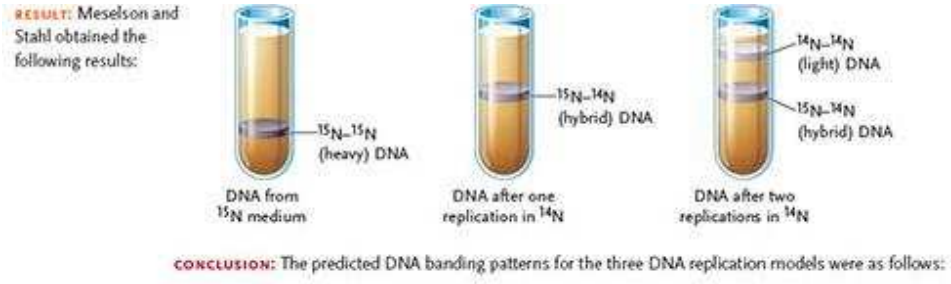
- Each old Strand is a template for the addition of bases
- Result is two DNA helices that are exact copies of the parental DNA molecule with one "old" strand and one "new" strand
- Called "Semiconservative replication"

3 Theoretical Models for DNA replication

- ***Semi-conservative***: parental strands unwind and each is a template for synthesis of new strand – after replication, each double helix has one old strand and one new strand
- ***Conservative***: parental strands unwind and each is a template for a new strand - after replication parental strands pair up again
- ***Dispersive*****:** original double helix splits into double stranded segments, which form new double stranded segments – new form segments form into two double helices and are a mixture of new and old

Meselson & Stahl: Showed that DNA Replication is Semiconservative

- Used a nonradioactive "heavy" nitrogen isotope to tag parental DNA – molecules containing the isotope will be denser than molecules containing regular nitrogen



DNA Polymerases are Primary Enzymes of DNA replication

- Assemble complementary nucleotide chains during replication
- Deoxribonucleoside triphosphates are the substrates for polymerization reactions
- Because four different bases are found in DNA – A,G,C,T – four different deoxyribonucleoside triphosphates are used for DNA replication (d=deoxyribose)
    - dATP
    - dGTP
    - dCTP
    - dTTP

DNA strand antiparallel nature → 5' end of one strand is opposite the 3' end of the other

- DNA Polymerases can add a nucleotide only to the 3' end of an existing nucleotide chain
- DNA polymerases are then said to assemble in the 5' → 3' direction
- Template strand in "read" in the 3' → 5' direction

Polymerases shape resembles a partially closed human right hand, in which template DNA lies over the "palm" in a groove formed by "fingers" and a "thumb"

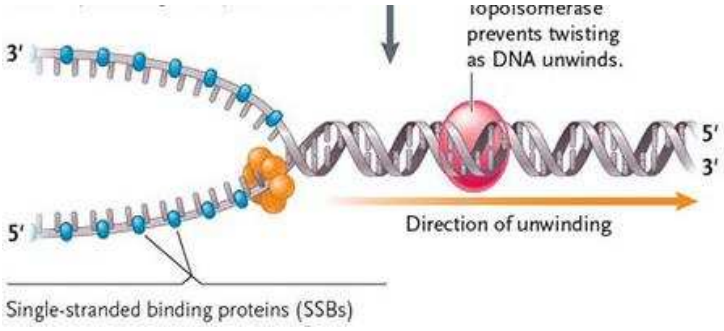
- Template strand does not pass through the tunnel formed by thumb and fingers – instead the template strand and the 3-OH of the new strand meet at the active site for polymerization (palm)
- Nucleotide is added to the new strand when an incoming dNTP enters carrying a base complementary pair to the
- DNA polymerase moves along the template strand, one nucleotide at a time extends the new DNA strand

<u>Key Molecular events of DNA replication:</u>

- Two strands of DNA unwind
- DNA polymerase can add nucleotides only to an existing chain
- The overall direction of new synthesis is in the 5'→3' direction (direction of the template strand)
- Nucleotides enter into a newly synthesized chain according to Chargaff's rule

DNA Helicase – catalyze unwinding

- Unwinding produces a Y shaped structure called a **replication fork**
- **Single-Stranded Binding Proteins (SSB's)**: coat and stabilize single-stranded DNA preventing the strands from reattaching
- **Topoisomerase:** prevents twisting as DNA unwinds



RNA Primers – provide starting point for DNA polymerase; short nucleotide chain made of *RNA* that is laid down as the first series of nucleotides in a new DNA strand

- Primase: an enzyme that assembles the primer for a new DNA strand during DNA replication
- RNA primers are removed and replaced with DNA later in replication

One DNA Strand is Synthesized *Continuously*, The Other *Discontinuously*

- Polymerization can only occur in the 5'→3' direction only allowing synthesis of the top strand – continuously
- Polymerase make the bottom strand in short lengths called **Okazaki Fragments** – produced by *discontinuous replication* – then covalently linked into a single continuous polynucleotide chain
- **Leading strand**: DNA strand assembled in the direction of DNA unwinding

DNA Polymerase III (Main polymerase): extends the primer by adding DNA nucleotides

DNA Polymerase I: removes the RNA primer at the 5' end of the Okazaki fragments, replacing the RNA nucleotides one by one with DNA

Sliding Clamp: Tethers DNA polymerase III to the DNA template making replication more efficient

DNA Ligase: seals nick left between adjacent bases after RNA primers with DNA

- Unwinding at an Ori within a DNA molecule produces two replication forks; two Y's shapes formed together to make a replication bubble – in eukaryotes there are many (sometimes hundreds) of origins or replication along chromosomes

Telomerases – when primers are removed a gap is left in it's place at the 5' end – telomeres bind to the single stranded 3' end and synthesize new telomere DNA using telomerase as an RNA template

- Telomerase moves to the 3' end and synthesizes for DNA
- Telomerase then leaves the extended template strand and a primer is added by primase
- Leaving a longer 5' end after the primer is removed
- And whatever remains is lost causing no effect
- Telomerase is only active in rapidly dividing cells

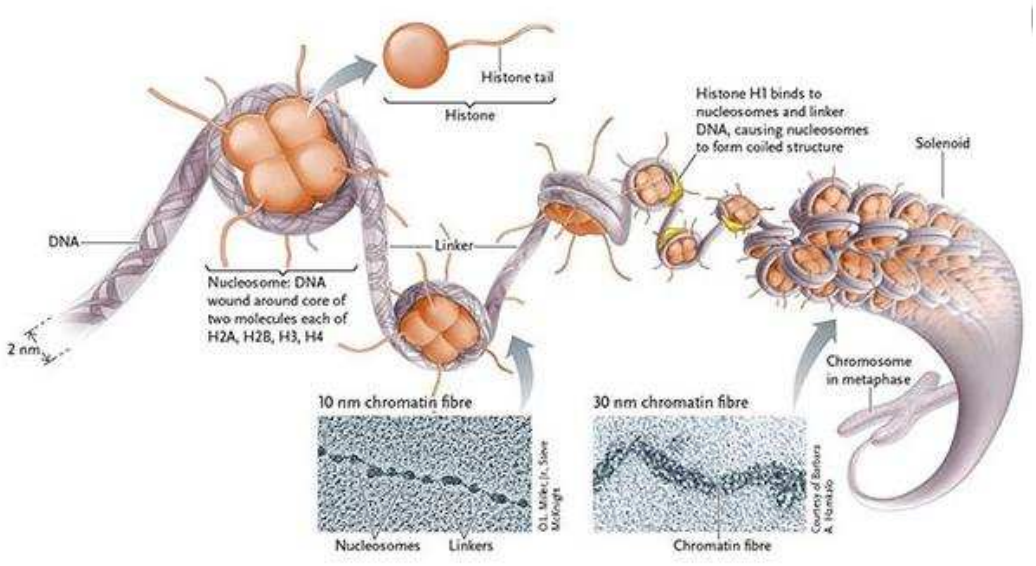
<u>12.4 Replication errors</u>

- DNA polymerases make a few errors called: base-pair mistmatches
- *Proofreading mechanism* depends on ability of DNA polymerases to reverse and remove mismatched bases
    - *Rarely,* DNA polymerase adds a mis-paired nucleotide
    - *Polymerase* recognizes, reverses and removes mismatch and replaces with correct base pair
- DNA repair corrects errors that escape proofreading

- The rare replication errors that remain after proofreading and DNA repair are a primary source of mutations

12.5 Eukaryotic vs. Prokaryotic

- Histones: are a class of small positively charged proteins that are complexed with DNA in the chromosome of eukaryotes – histones link to DNA by an attraction between their positive charges and the negatively charged phosphate groups
    - 5 types exist: H1 H2A H2B H3 H4
    - one function is to pack DNA molecules into narrow confines of the nucleus



- chromatin is distributed between eurochromatin, a loosely packed region in which genes are active in RNA transcription – a heterochromatin, densely packed masses in which genes (if present) are inactive
- nonhistone proteins help control the expression of individual genes

Chapter 8: Cell Cycles

Three Cellular Processes:
DNA Replication, Dynamically changing cytoskeleton, Cell cycle "check-points"

8.2 The Cell Cycle in Prokaryotic Organisms

- Entire mechanism for prokaryotic cell division is called **Binary Fission** – splitting or dividing into two parts, can be thought of in 3 periods – B C D
- (B Period) Cells grow for some time before initiating DNA synthesis
- (C Period) once the chromosomes are replicated and separated to opposite ends of the cell, the membrane pinches together between them to make two daughter cells (D Period)
- When nutrients are abundant, prokaryotic cells have no need for a B Period since they grow quickly enough to divide their cytoplasm as soon as DNA is replicated – under optimal conditions E. Coli can double every 20 minutes
- Replication of the bacterial chromosome happens at a specific region called the *origin of replication* (ori)
    - In the middle of the cell, where enzymes for DNA are located
    - Once ori has been duplicated, the two new origins migrate toward the two opposite ends (poles) of the cell as replication continues
    - New plasma membrane and cell wall material is assembled to divide into two equal parts
- Binary Fission works well because prokaryotic organisms have only a single chromosome – thus, if a daughter cell gets at least one copy of the chromosome, genetic information is complete

- By contrast, genetic information of eukaryotes is divided among several chromosomes

Mitosis - has evolved from an early form of binary fission

- One of the central innovations of the evolution of mitosis is the ability to hold the two newly created molecules of double stranded DNA
  (now called chromatids) together during DNA synthesis

8.3 Mitosis and the Eukaryotic Cell Cycle

Three interrelated systems:

1. A master program of molecular checks and balances ensures an orderly and timely progression through the cell cycle
2. Within the overall regulation of the cell cycle, a process of DNA synthesis replicates each DNA chromosome into two copies with almost perfect fidelity
3. A structural and mechanical web of interwoven spindles and motors of the cytoskeleton separates replicated DNA into daughter cells

Apoptosis: Planned cell death

However

- At a particular stage of the life cycle of sexually reproducing organisms a cell division process called **meiosis** produces some cells that are genetically different from the parent cells
- ***Meiosis*** produces daughter nuclei that are different in that they have one half the number of chromosomes the parental nucleus had
  - The cells that are products of meiosis may function as gametes in animals (fusing with other gametes to create a zygote) and as spores in plants and fungi

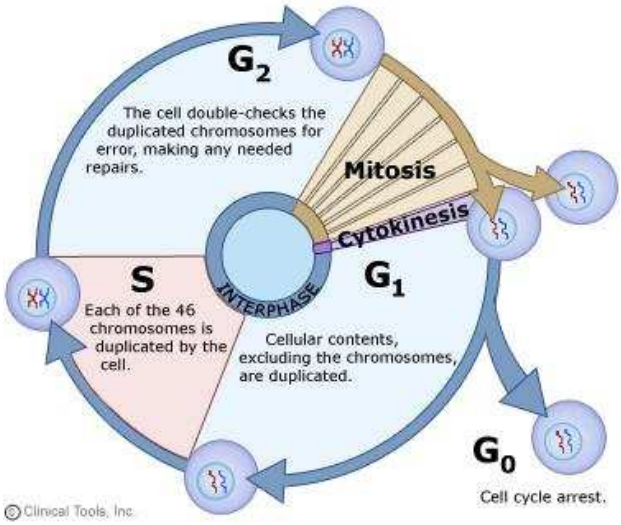
→ Chromosomes are the genetic units divided by Mitosis

- Hereditary information of the nucleus is distributed among several linear, double-stranded DNA molecules
- DNA molecules combine with proteins to stabilize the DNA, assist with packaging during cell division and influence the expression of genes
- Each chromosome in a cell is composed of one of these DNA molecules and its proteins
- Most eukaryotes have two copies of each type of chromosome in their nuclei and their chromosome complement is said to be **diploid, or 2n**
  - Humans have 23 different pairs of chromosomes for a diploid number of 46 (2n = 46)
- Other eukaryotes may have only one copy of each type of chromosome in their nucleus – so, their chromosome complement is **haploid or n**
- The number of chromosome sets is called the **Ploidy** of a cell or species
- Before a cell divides in mitosis, duplication of each chromosome produces identical sister chromatids
  - Held together by sister chromatid cohesion – in which, proteins called cohesions encircle the sister chromatids, during mitosis cohesion is removed and sister chromatids are pulled apart
  - BEFORE replication, one chromosome is composed of one DNA molecule
  - AFTER replication, one chromosome is composed of two DNA molecules

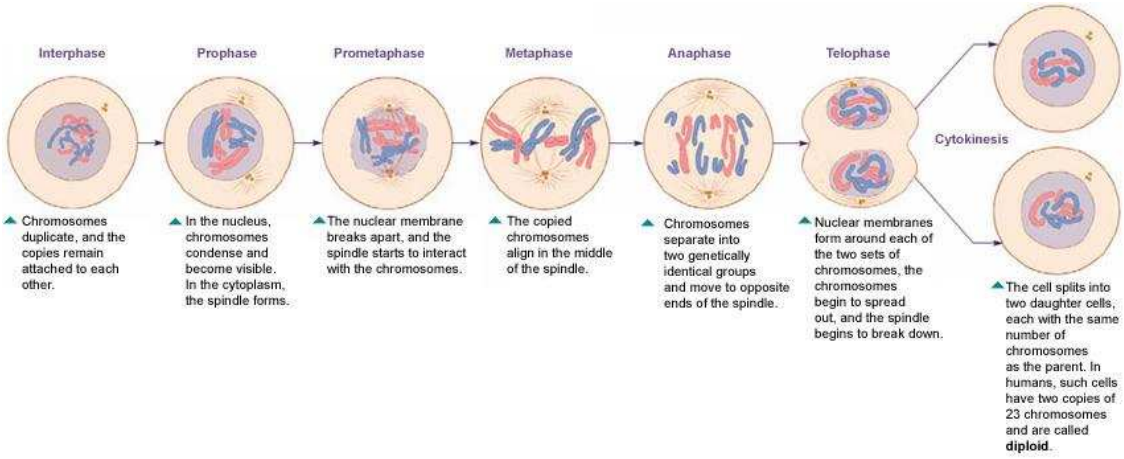
Interphase: 3 stages

1. **G1 Phase**: cell carries out its function and in some cases grows
2. **S Phase**: DNA replication and chromosome duplication occur
3. **G2 Phase**: brief gap in cell cycle – cell growth continues and cell prepares for mitosis
   G0 Phase → cells are not destined to divide immediately; cell in G0 may start dividing again by reentering G1; some cells never resume the cell cycle

   S Phase = 10-12 hours
   G2 Phase = 4-6 hours
   Mitosis = 1 hour or less



Mitosis Proceeds in 5 Stages (After Interphase)



Pro – before → Meta – between → Ana – back → Telo – end

- Few chromosomes actually look like an X, this is because only chromosomes with their centromere near the middle can actually take on the shape
  - Only during (pro)metaphase are chromosomes condensed enough to take on any shape at all
- The complete collection of metaphase chromosomes, arranged according to size and shape forms the **Karyotype** of a given species

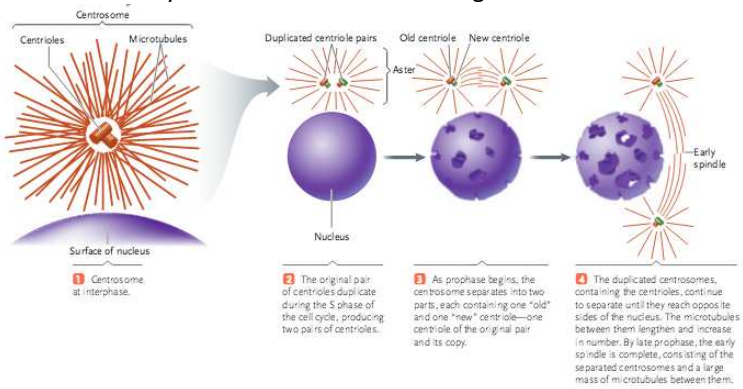
Cytokinesis - furrowing

- In animals, cleavage furrow
- In plants, cell plate

8.4 Formation and Action of the Mitotic Spindle

- Spindle is made up of microtubules and their proteins
- In animal cells, the centrosome divides and the two parts move apart – as this happens, microtubules of the spindle form between them
- In plant cells with no centrosome, the spindle microtubules assemble around the nucleus

- In the spindle, kinetochore microtubules run from the poles to the kinetochores of the chromosomes, and nonkinetochore microtubules run from the poles to a zone of overlap at the spindle midpoint without connecting to the
- Primary function of centrioles is to generate the microtubules needed for flagella/cilia

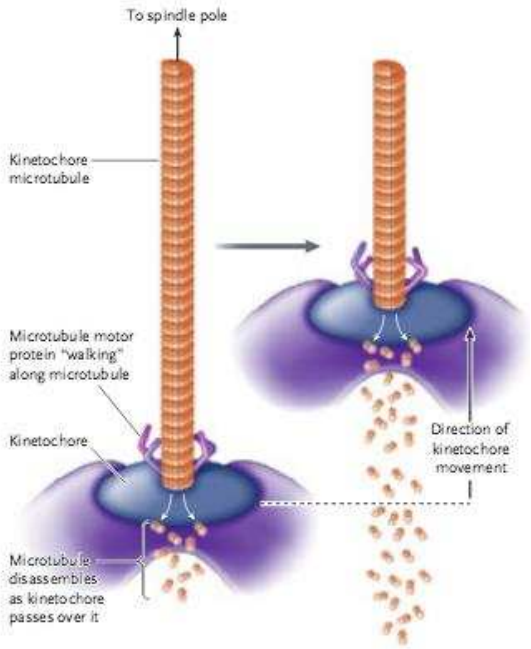


Mitotic Spindles may move chromosomes by a combination of two mechanisms

- **Kinetochore Microtubules**: connect the chromosomes to the spindle poles
- **Nonkinetochore Microtubules**: extend between the spindle poles without connecting to chromosomes; at spindle midpoint

→ The exact mechanism by which chromosomes move is still uncertain; at one time it was believed that microtubules pulled the chromosomes toward the poles of dividing cells - however data suggests that chromosomes walk themselves to the poles along stationary microtubules (pulling yourself up a rope)

→ Chromosomes can also move toward the poles by a mechanism in which motor proteins at the spindle poles pull kinetochore microtubules pole-ward →



<u>8.5 Cell Cycle Regulation</u>

- The cell cycle is controlled by complexes of cyclins and a cyclin-dependant protein kinase (Cdk) – a Cdk is activated when combined with a cyclin and then adds phosphate groups to target proteins, activating them
- The activated proteins trigger the cell to progress to the next cell cycle stage

GENERATING DIVERSITY
Chapter 13: Gene Structure and Expression

Intro: The marine mussel Mytilus clings to rocks pounded by surf daily, constantly in danger of being torn to pieces by predators – resistant to disturbance, nearly impossible to pry off even with a knife

- Fibres holding the mussels to rocks are proteins secreted by muscular foot – include keratin etc to form tough adhesive called byssus
- Fascinates doctors as possible way to hold repaired body parts together

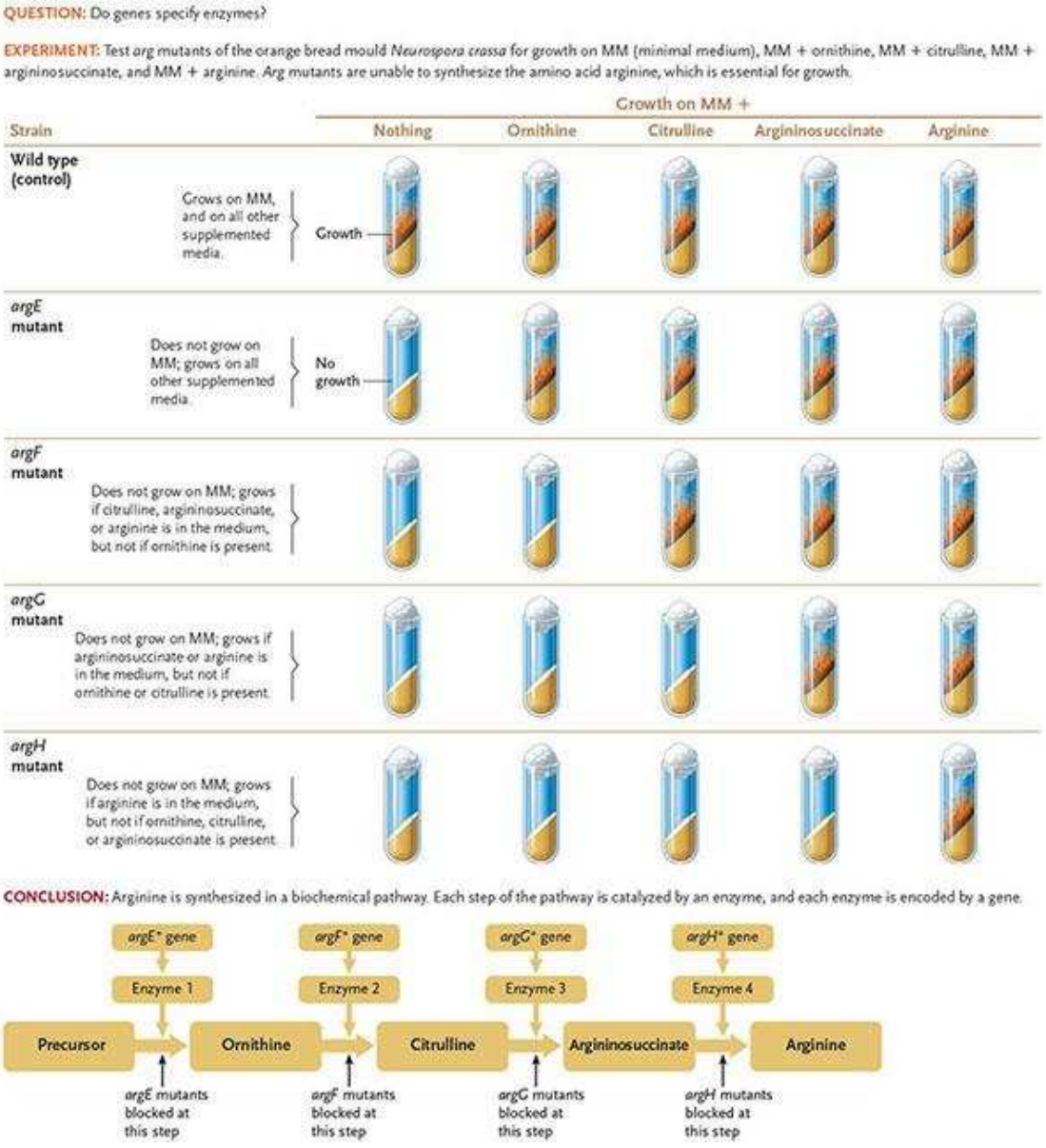
Every protein is assembled on ribosomes according to instructions dictated by genes coded in DNA

13.1 Connection between DNA, RNA, and Proteins
How do we know genes encode?
1896 – Archibald Garrod, an English physician, studied "alkaptonuria" a human disease that does little harm but patients urine turns black when exposed to oxygen

- Inherited trait – also found that people with alkaptonuria excrete a compound called homogentisic acid in their urine
- Normal people are able to metabolize acid and people with disease can't
- Shows relationship between genes and metabolism

1940's – George Beadle, Edward Tatum working with orange beard mould Neurospora crassa

- Collected data showing a direct relationship between genes and enzymes
- Haploid fungus with simple nutritional needs
- Grows readily on a minimal medium (MM) inorganic salts, sucrose & a vitamin
- Exposed spores to X-rays that caused mutations
    - Found that some treated spores wouldn't grow unless MM was supplemented with additional nutrients, such as amino acids or vitamins
    - Mutant strains that are unable to grow on MM are call auxotrophs
- Hypothesized that each auxotrophic strain had a defect in gene coding for enzyme needed to synthesize
- Discovered which specific nutrient each mutant strain needed to grow therefore which gene defect it had
- (argE, argF, argG, argH) each of these show a different pattern of growth
- In sum, Beadle and Tatum had shown a direct relationship between genes and enzymes which they put forward as the **one gene-one enzyme hypothesis**



- Proteins consist of more than one subunit – each of these subunits is a separate molecule called a polypeptide, that is coded by a separate gene
- Polypeptides can assemble to create a functional cluster of molecules called a protein
    - Eg. Protein hemoglobin is made up of four polypeptides, two of an a-subunit, and two of a b-subunit
- Beadle and Tatums hypothesis was later restated as **one gene-one polypeptide hypothesis**
- Keep distinctions between:
    - Protein – the functional collection of polypeptides
    - Polypeptide – molecule encoded by a gene

13.1b Pathway from Gene to Polypeptide involves Transcription & Translation

Transcription: mechanism by which the information encoded in DNA is made in a complementary RNA copy – info from one nucleic acid type is transferred to another
Translation: use of information encoded in RNA to assemble amino acids into a polypeptide – info in nucleic acid, in form of nucleotides is translated (converted) into a different kind of molecule (AA's)

→ 1956 – Francis Crick gave the name "*The Central Dogma"* to the flow of information from DNA to RNA to Protein

Transcription

- Enzyme RNA polymerase (catalyzes assembly of nucleotides into an RNA strand) creates an RNA sequence that is complementary to the DNA
- Process follows same rules as complementary base pairing and nucleic acid chemistry
- One DNA strand or template strand is read by RNA polymerase
- RNA transcribed from a gene encoding polypeptide is called messenger RNA (mRNA)

Translation

- mRNA associated with a ribosome (particle on which amino acids are linked into polypeptide chains)
- As ribosome moves along the mRNA, the amino acids specified by the mRNA are joined one by one to form the polypeptide encoded by the gene

→ Processes are similar in prokaryotic and eukaryotic cells
→ One key difference – prokaryotic cells can translate and transcribe a given gene simultaneously whereas eukaryotic cells transcribe and process mRNA in nucleus before exporting it to cytoplasm for translation on ribosomes

13.1c Genetic Code Written in 3-Letter words using a 4-Letter Alphabet
→ A T G C represents the four nucleotide bases
→ A U G C represents the four RNA bases

- T in DNA is replaced with U in RNA (uracil)
- There are 4 RNA bases and 20 amino acids

Breaking the code

- Genetic code = nucleotide information that specifies the amino acid sequence of a polypeptide
- 4 bases in an mRNA AUGC would be used in combinations of at least three to provide capacity to code for 20 amino acids
- Three letter word (triplet) is called a **codon**
- Genetic info in DNA is first transcribed into complementary 3 letter RNA codons

*Non-template strand in always read 3→5 direction (bottom)

How do Codons correspond to the Amino Acids?

- Marshall Nirenberg and Philip Leder of the NIH in US established identity
- Found that short, artificial mRNAs, artificial mRNAs of codon length (3) could bind to ribosomes in a test tube and cause a single transfer RNA (tRNA), with its linked amino acid to bind to the ribosome
- They then made 64 of the short mRNA's each consisting of a different, single codon
- They added the mRNAs one at a time to a mixture in a test tube containing ribosomes and all the different tRNAs (with AA's)

- Idea was that from mixture, each single codon mRNA would link to the tRNA carrying the amino acid corresponding to the codon – experiment worked for 50 of the 64 codons - allowing those codons to be assigned to amino acids definitively

Another approach…

- Used long artificial mRNA molecules containing only one nucleotide repeated continuously or different nucelotides in repeating patterns
- Each mRNA was added to ribosomes in a test tube and the sequence of amino acids in the polypeptide chain made by ribosomes was analyzed

Features of Genetic Code

- Scientists write the codons in the 5' → 3' direction as they appear in mRNA's, substituting U for T of DNA
- Of 64 codons, 61 specify amino acids
- AUG is the first codon translated in any mRNA in prokaryotes and eukaryotes – AUG is called a start or initiator codon
- 3 codons that don't specify amino acids – UUA,UAG,UGA are stop codons, also called nonsense or termination codons that act as periods of sentence
- Tryptophan and methionine are the only AA's specified by a single codon
- There are many synonyms in the nucleic acid code – feature known as degeneracy (UGU and UGC both represent cysteine ex)
- Commaless – code is sequential, therefore in order to be read correctly, must start in the right spot
- The code is universal – consistency in code makes genetic engineering possible

Chapter 16: Genomics

- Genomics = is the characterization of whole genomes, including their structures (sequences), functions and evolution
- Complete sequencing of the approx. 3 billion base-pair human genome (HGP) began in 1990
- Task was completed in 2003 by Celera Genomics/Craig Ventor

16.2 Genome Sequence Determination and Annotation

- Obtaining the sequence of bases in a genome using DNA sequencing techniques and then analyzing the sequence data using computer-based approaches to identify genes and other

Whole Genome Shotgun Sequencing

- Genomic DNA is isolated and purified, and that DNA is broken into thousands of millions of random overlapping fragments
- Each fragment is amplified to produce many copies and then the sequence fragment is determined
- Genome sequence is determined by computer algorithms

DNA sequencing methods have in common, the following steps:

1. DNA purification
2. DNA fragmentation
3. Amplification of fragments
4. Sequencing each fragment
5. Assembly of fragment sequences into genome sequences

16.2b Genome Landscapes Vary Markedly in Size, Gene Number and Gene Density

- Density of genes = how widely spaced they are

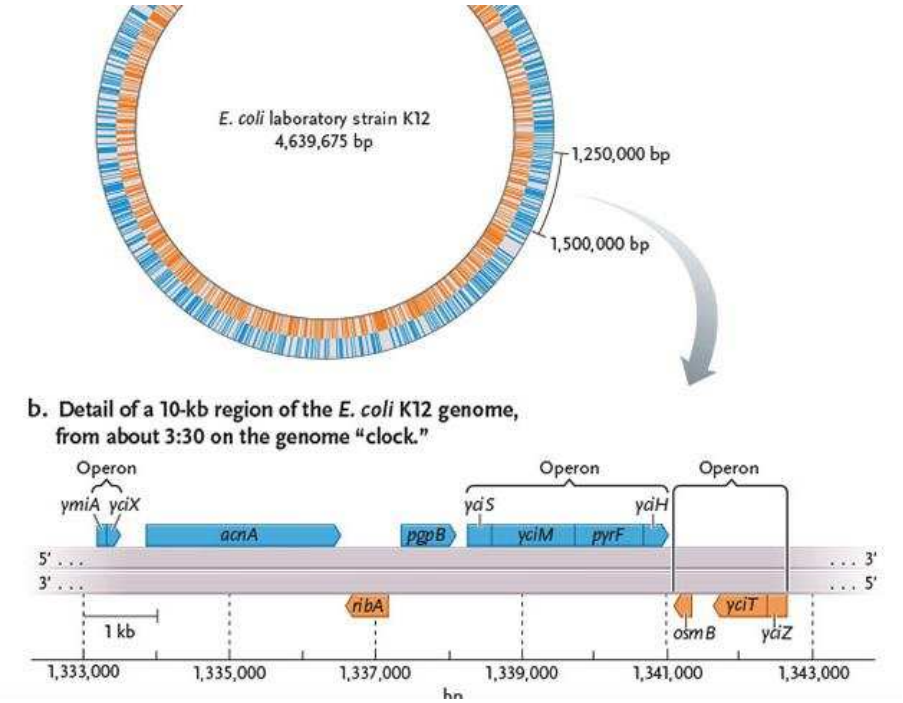
Domain and Organism	Genome Size (millions of base pairs, Mb)	Protein-Coding Genes
Bacteria		
Mycoplasma genitalium	0.58	475
Escherichia coli	4.6	4 146
Archaea		
Thermoplasma acidophilum	1.56	1 484
Methanosarcina acetivorans	5.75	4 540

General Conclusions

- Bacteria and Archaea have genomes that vary widely in size, in addition genes are densely packed in their genomes, with little noncoding space between them
- Thus, the larger genomes of organisms in these two domains tend to reflect increased gene number

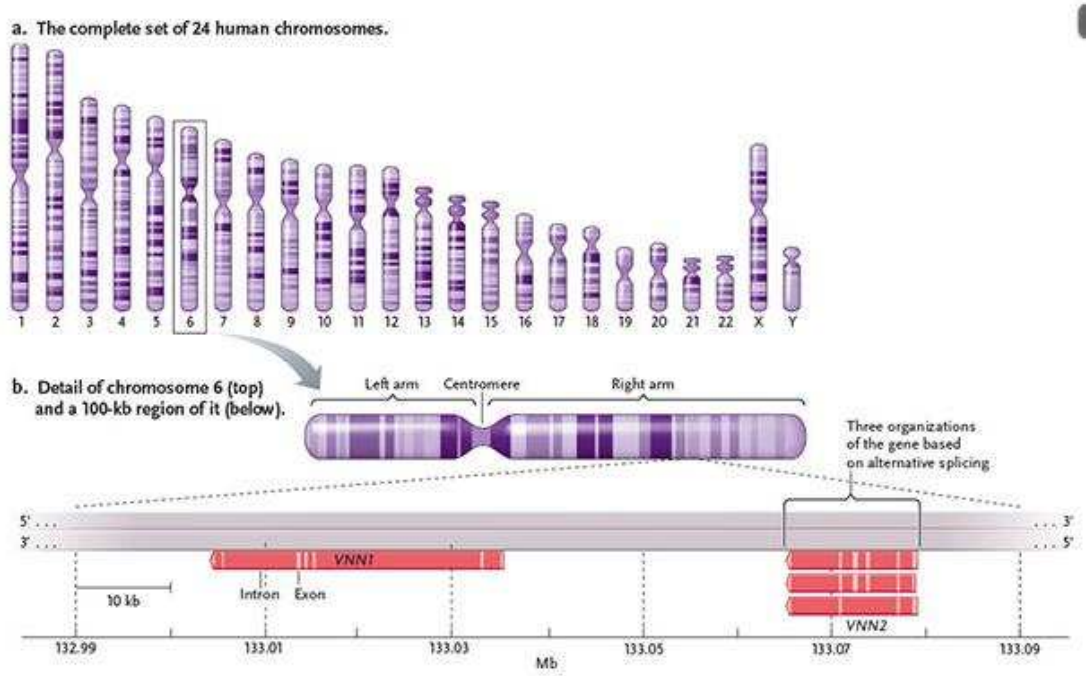
Profile of the E. Coli Genome

- In circular bacterial genomes – you may assume one strand is used as a template for all genes but this is incorrect as both strands used for some of each genes
- Typically there is one origin of replication
- 85-92% of the DNA code for proteins, there is a mixture of operons and single-gene transcription units, some genes are transcribed using template strand, others use leading strand
- relatively few transposable elements or repetitive sequences
- half is organized into operons



Profile of Human Genome

- about 3.2 billion base pairs
- human has 23 pairs of chromosomes (men 24 different chromosomes, 22 autosomes and the X and Y) (women have23, with 22 autosomes and the X chromosome)



- Comparatively, the human genome is much more spaced out,
- Eukaryotic cells rarely organized in operons – single transcription unit

- Exon = parts of DNA that are converted into mature mRNA
- Introns = part of genes that don't directly code for proteins – the more introns the more complex organism
- 20,500 protein-coding genes – avg of 8 exons per gene, introns make up about 95% of the average transcription unit
- since about 2% of genome consists of protein coding sequences, introns represent about 20-25%
- 45% of genome is transposable element sequences, 10% are viruses (JUNK DNA = 75% of genome)

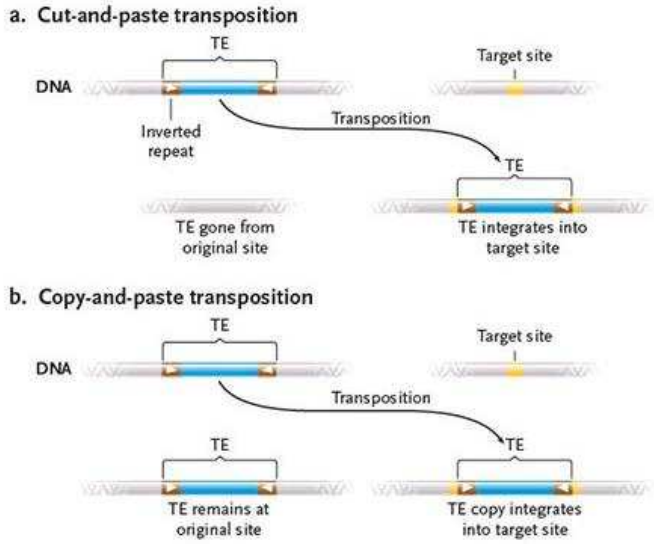
Single-Nucelotide Polymorpisms (SNPs)

- variation in DNA sequence of different human genomes is a change of a single nucleotide

GENERATING DIVERSITY II

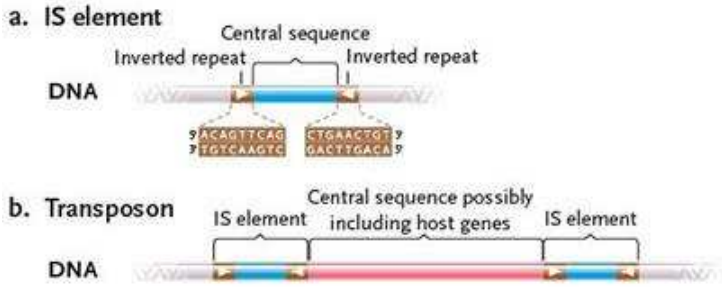
9.4 Mobile Elements

- Particular segments of DNA that can move from one place to another; they usually cut and paste DNA backbones using a type of recombination that does not require homology
- Also known as **transposable elements (TE's)** and their mechanism of movement, involving nonhomologous recombination is called **transposition**
    - Occurs at low frequency in one of two ways depending on element
        - **Cut and paste**: TE leaves original location and transposes to a new location
        - **Copy and paste**: copy of TE transposes to a new location leaving the original TE behind
- Jumping genes is innacurate – Te's are never "in the air" between one location and another
- Important because of the genetic changes they cause – increase genetic variability



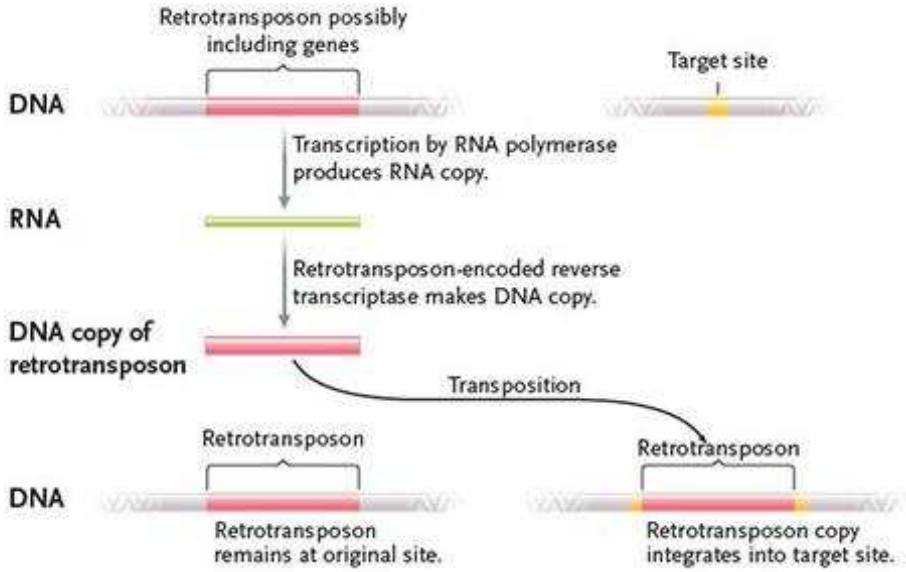
2 Major types of Bacterial TE's **are insertion sequences (IS's)** and **transposons**

- IS's are simplest, relatively small and contain only genes for their transposition – *transposase* (enzyme that catalyzes some reactions for inserting and removing the TE from DNA)
    - At each end of an IS is a short **inverted repeat** sequence – enables the transposase enzyme to identify the ends of the TE when it catalyzes transposition
- Transposons have an inverted repeat sequence at each end, enclosing a central region with one or more genes
- In a number of bacterial transposons the inverted repeat sequence is an IS which provide movement of the element – additional genes in the central region typically code for antibiotic resistance – originating from bacteria or from plasmids
- Over the years, many antibiotics have lost their effectiveness due to the resistance genes carried in transposons



Transposable elements first discovered in Eukaryotes

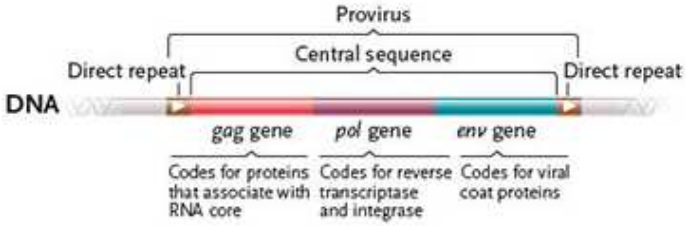
- Barbara McClintock, 1940's found in corn
- Classified as **transposons** or **retrotransposons** in Eukaryotes
- Eukaryotic transposons similar to that of bacteria
- Retrotransposons – however, transpose by a unique copy and paste mechanism
    - Transposition occurs via an intermediate RNA copy of TE
    - First – retrotransposon integrates into DNA and transcribes an RNA copy
    - Next – an enzyme called reverse transcriptase, uses the RNA as a template to make a DNA copy of the retrotransposon
    - DNA copy is then inserted at a new location, leaving original in place – this involves breaking and rejoining DNA backbones
- Once TE's are inserted they become more or less permanent residents, duplicated and passed on during cell division
    - Can be inherited in reproductive cells



Retrotransposons are similar to Retroviruses – The RNA to DNA reverse transcription is similar in both

<u>Retroviruses</u> – infects host cell, reverse transcriptase carried in virus copies RNA into DNA copy and is inserted into host DNA (by genetic recombination)

- Inserted viral DNA is known as **provirus**
- Retroviruses and retrotranspons occupy some 40% of the human genone



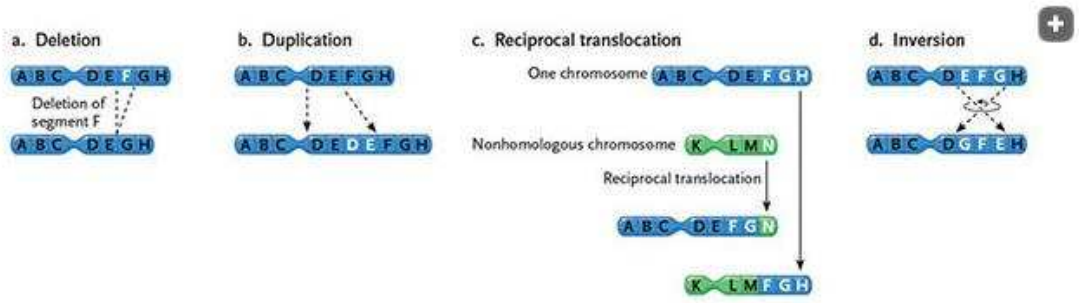
- Many retroviruses do not produce infectious virus particles, they do sometimes cause DNA rearrangements such as deletions and translocations that may alter position of DNA sequence on chromosome and disturb regulation of gene expression – can cause overgrowth and lead to cancer

11.3a Deletions, Duplications, Translocations and Inversions

- Most common chromosomal alterations

Deletion – if a broken segment is lost from a chromosome
Duplication – if a segment is broken from one chromosome and inserted into its homologue – in receiving its homologue, the alleles in inserted fragment are added to the ones already there
Translocation – if a broken segment is attached to a different non-homologous chromosome
Inversion – if a broken segment reattaches to the same chromosome from which it was lost, but in reversed orientation, so that genes are reversed

Chromosome **(a)** deletion, **(b)** duplication, **(c)** translocation (a reciprocal translocation is shown), and **(d)** inversion



- To be inherited, alterations must occur in cells of germ line leading to eggs and sperm

Deletions and Duplications

- Deletion may cause severe problems if missing segment contains genes that are essential for normal development or cellular function – example: one deletion from human chromosome 5 leads to cognitive impairment and a malformed larynx – baby crying sounds like a meow [cri-du-chat] = Cat's cry
- Duplications may have effects harmful or beneficial, depending on genes involved – example: mammals have genesthat encode several types of hemoglobin that are not present in vertebrates such as sharkd that evolved earlier, likely due to duplications followed by mutations – created new and beneficialforms of hemoglobin

Translocations and Inversions

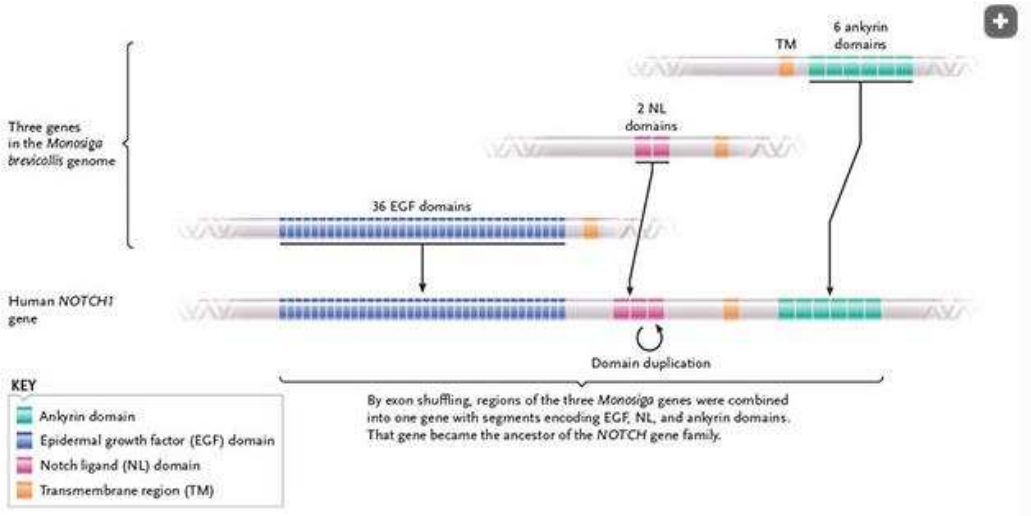
- Translocation, segment breaks from one chromosome and attaches to other non-homologous chromosome
    - In many cases translocation is reciprocal meaning that 2 non-homologous chromosomes exchange segments
    - Resembles genetic recombination, except that two chromosomes involved in the exchange don't contain the same genes (non-homologous)
    - Cancer of the human immune system, lymphoma for example is caused by a translocation that moves segment of chromosome 8 to the end of chromosome 14
        - Translocated segment contains gene that influences cell division – normal at regular location, but overexpressed in new location
- In an inversion, segment breaks and then reattaches to the same chromosome but in reverse
    - Usually same effect as translocation, genes may be broken internally with loss of function or they may be transferred intact to a new location within chromosome that can be harmful or beneficial
    - Important factors in evolution of plants and animals - chromosome pairs in human show inversions and translocations that are not present in our nearest primate relatives goriillas – therefore changes must have occurred after the gorilla human evolutionary lineages split

16.4b New Genes Evolve by Duplication and Exon Shuffling

- New genes are a rare event – much less common than mutation

Exon Shuffling: molecular evolutionary process that combines exons of two or more existing genes to produce a gene that encodes a protein with an unprecedented function

- An exon shuffling occurred early in evolution of animals (700mya) that produced a new gene coding for a protein that that plays a key role in signalling between cells in animal tissues
- Evidence comes from comparing genome sequence of the choanoflagellate Monosiga Brevicollis with the sequences of a number of animal genomes, including humans
- Choanoflagellate are single celled or colonial protists that are thought to be related evolutionarily to animals – evolution of multicellularity in the first animals is thought to have involved molecular mechanisms that enable organism to communicate with one another so they could specialize in performing different functions
- Organism lacks a gene homologous to the gene for the Notch protein – hypothesized that through exon shuffling sequences encoding domains in the three genes were combined in one gene producing the ancestor of the NOTCH gene family
- At some point, a duplication of the sequence coding for NL domain occurred, since Mb gene has sequences coding for only two copies of that domain, while animal notch proteins have sequences coding for three copies



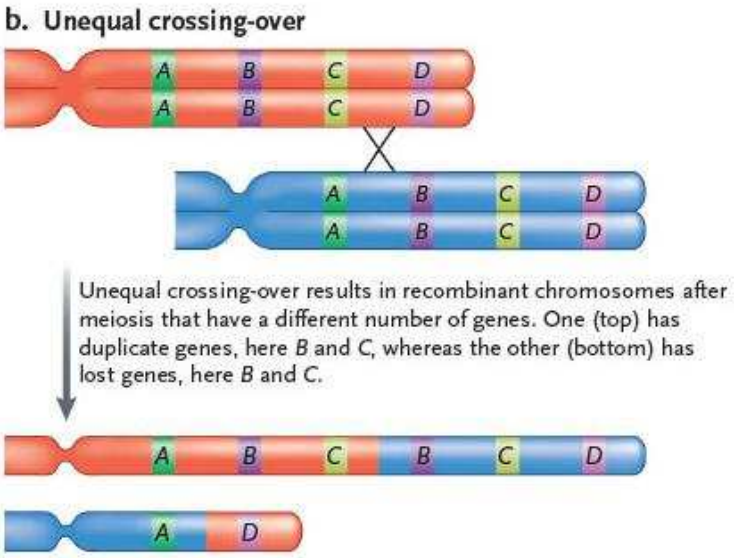
Gene Duplication – any process that produces two identical copies of a gene in an organisms' genome
3 Main Mechanisms:

1. Whole-genome duplication (WGD)
2. Unequal crossing over of homologous chromosomes during meiosis
3. Replication of transposable elements

Widespread failure of chromosome partitioning in meiosis and mitosis can result in zygotes and daughter cells having double the normal number of chromosomes – give rise to polyploidy organisms with WGD (relatively rare – though there are many species with more than 2 sets of chromosomes)

Unequal crossing over is a rare phenomenon in meiosis in which instead of crossing over occurring at the same point on each homologue of pair, crossing over occurs at different points

- The result is that one recombinant chromosome is missing one or more genes while the other has duplicate copies
- Produces tandem duplication of genes, with the duplicate copies clustered in the same region on the chromosome



Gene Duplication may occur as mistake when a transposable element copies itself and splices the DNA copies elsewhere in the genome

- Rarely, transposable elements copy adjacent DNA in addition to their own, producing duplicate copies of any genes in that DNA
    - Produces *dispersed duplication* of genes, meaning that the copies of the gene are found in different places in the genome – often on two different chromosomes
    - At first duplicate copies of a gene have the same protein-coding sequences and encode identical proteins – two genes are functionally redundant, meaning that one could be eliminated from the genome with no loss of biological functioning
    - Often one is mutated into a pseudogene or lost by deletion but if both remain functional they will evolve differently as mutations occur
- Example: nitric oxide synthase enzymes catalyze a reaction that produces nitric oxide (NO) – molecule cells use to communicate
    - In human genome there are 3 different NO synthase enzymes – one expressed in neurons, one in endothelial cells and the third in liver and in a type of white blood cell (macrophage)
    - Homologues of all 3 are found in other mammals as well as birds and reptiles so the gene duplications by which these evolved must have happened over 200mya
    - Evolution of each gene must have involved mutations to regulatory sequences that control transcription
    - Evolution of these genes also involved mutations to the protein-coding sequences
    - 3 genes are found on 3 different chromosomes which suggest that they evolved by dispersed duplication

Production of Multigene Families

Multigene Family – family of homologous genes in a genome that have all evolved from one ancestral gene and therefore have similar DNA sequences and produce proteins with similar structures and functions

- NO example above exhibits a small multigene family

GENERATING DIVERSITY III

Chapter 9: Genetic Recombination

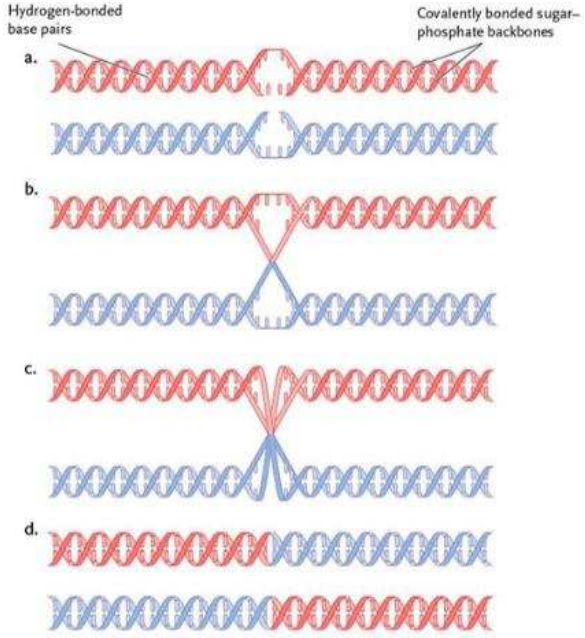
The ultimate source of genetic diversity is mutation of the DNA sequence, often resulting from errors during DNA replication. Since mutations are relatively rare, diversity is amplified through various mechanisms that shuffle existing mutations into novel combinations. This process of literally cutting and pasting DNA backbones into new combinations is called – **genetic recombination**

9.1 Mechanism of Genetic Combination

In general, genetic recombination requires the following:

- Two DNA molecules that differ from one another
- A mechanism for bringing DNA molecules into close proximity
- A collection of enzymes to "cut", "exchange" and "paste" the DNA back together

Simplified model of genetic recombination



a) 2 molecules of DNA with similar sequence are brought into close proximity
b) Enzymes nick DNA backbones, exchange ends, reattach them
c) And
d) In this case, final result is 2 recombined DNA molecules

DNA Double Helix: Sugar phosphate backbone of double helix is held together by strong covalent bonds, whereas the bases pair with their partners through relatively weak hydrogen bonds

Figure above - makes up a single recombination event

- *Cutting and pasting four DNA backbones results in one recombination event*

9.3 Genetic Recombination in Eukaryotes: Meiosis

- Sexual reproduction – the production of offspring through the union of male and female gametes (haploid cell; egg or sperm – haploid cells fuse during sexual reproduction to form a diploid zygote)
- Sexual reproduction depends on meiosis – process of cell division that recombines DNA sequences and produces cells with half the number of chromosomes present in the somatic (body cells) cells of a species
- At fertilization, nuclei of an egg and sperm cell fuse producing a cell called the zygote (fertilized egg) (chromosome number typical of species – diploid – is restored)

9.3a Meiosis Occurs in Different places in Different Organismal Life Cycles

- May assume that gametes are made by meiosis – only true for yourself and other animals
- In life cycle of house plants and some of the fungi, the haploid products of meiosis are spores, not gametes – spores divide by mitosis to form multicellular bodies that make gametes by mitosis
- Many organisms make gametes by mitosis

Animals

- Follow the pattern in which the diploid phase dominates the life cycle, haploid phase is reduced and meisosis is followed directly by gamete formation
- In male animals, each of the four nuclei produced by meiosis is enclosed in a separate cell by cytoplasmic divisions & each differentiates into functional sperm cells
- In females, only one of the four nuclei becomes functional as an egg cell nucleus
- Fertilization restores the diploid phase of life cycle – thus animals are haploid only as sperm or eggs and no mitotic division occurs during the haploid phase of the life cycle

Most plants & some fungi

- Organisms alternate between haploid and diploid generations in which, depending on the organism – either generation may dominate life cycle and mitotic division occurs in both phases (both diploid and haploid can be multicellular)
- Fertilization produces the diploid generation called **sporophytes**
- After sporophytes mature by mitotic division some of their cells undergo meiosis, producing haploid, genetically different, reproductive cells called **spores**
- Spores are not gametes; they germinate and grow by mitotic division into a generation of haploid **gametophytes**
- Develop into egg or sperm nuclei – all identical, produced by mitosis

Most fungi

- Diploid phase is limited to a single cell, the zygote, produced by fertilization
- Immediately after fertilization the diploid zygote undergoes meiosis to produce the haploid phase
- During fertilization two haploid gametes usually designated as (+) and (-) because they are similar in structure, fuse to form a diploid nucleus which, immediately enters meiosis producing four haploid cells

Zygotes arising from fertilization contain DNA from two different parents in close proximity so that recombination may occur – it is not this single celled zygote that undergoes recombination – its only after many rounds of replication by mitosis that certain cells in the resulting multicellular body divide by meiosis (this is when recombination occurs)

<u>9.3b Meiosis changes both chromosome number and DNA sequence</u>

Mitosis = SAMENESS

Meiosis = DIFFERENCE

- Halved chromosome number and recombined chromosomal DNA sequence
- Products of meiosis are not intended to contribute to the body of the organism that makes them

<u>9.3c Meiosis produces **four** genetically different daughter cells</u>

- Cells that are destined to divide by meiosis (called meiocytes) move through their last turn of the cell cycle as usual, replicating DNA and making more chromosomal proteins during S phase
- The resulting G2 cells carry replicated chromosomes, each composed of two identical sister chromatids
- Following the premeiotic interphase, cells enter the first of the two meiotic divisions: meiosis I and meiosis II
    - Meiosis I: chromosomes behave dramatically differently than they do during mitosis – homologous chromosomes find their partner and pair up in a process called **synapsis** – during this pairing *recombination* occurs, and chromosomal segments are exchanged

- Meiosis II: the four sister chromatids are separated into different cells, further reducing the amount of DNA in each – 4 haploid cells with a collection of alleles, is the final result of the two meiotic divisions

Meiosis has same stages of division of mitosis: Prophase, prometaphase, metaphase, anaphase, and telophase
→ A brief interphase called **interkinesis** separates the two meiotic divisions, no replication occurs during this phase

Prophase I: two chromosomes of each homologous pair come together and line up side by side in a zipperlike way; **called pairing or synapsis**

- Fully paired homologues are called **tetrads**

Prometaphase I: nuclear envelope breaks down and the spindle enters the former nuclear area - kinetochore microtubules from one pole attach to both of one duplicated chromosome (Full X)

Metaphase I: align tetrads in the equatorial plane – metaphase plate

Anaphase I: separate two chromosomes of each homologous pair to opposite sides

Telophase I: old spindles disassembles and two new spindles form for second division

Interkinesis

Prophase II → Metaphase II → Anaphase II → Telophase II → 4 daughter cells

Failure in Chromosome Segregation

- **Nondisjunction**: at either meiosis I or meiosis II – the spindle fails to separate the chromosomes of the tetrad and one pole receives both chromosomes and the other has no copies of that chromosome
  - Meiosis II will proceed to separate the chromatids of the extra chromosome as usual, resulting gametes either too few or too many chromosomes
  - **A failure at Meiosis II –** chromatids don't separate to opposite poles, results in gametes with abnormal number of chromosomes
    - **Zygotes** with extra chromosome will have 3 copies – most of this kind do not result in live birth – one exception, is Down Syndrome which can result from 3 copies of chromosome 21

Sex Chromosomes

- Female = XX, Male = XY

BPA & the Grandmother Effect

- Aneuploid – organsims or cells that have more or less the number of chromosomes than they should – agents that promote the problem are known as aneugens
  - Bisphenol A, used in making plastic is an aneugen
  - In pregnant women produces aneupleud gametes

Major Outcomes of Meiosis: the generation of genetic variability and the reduction in chromosome number

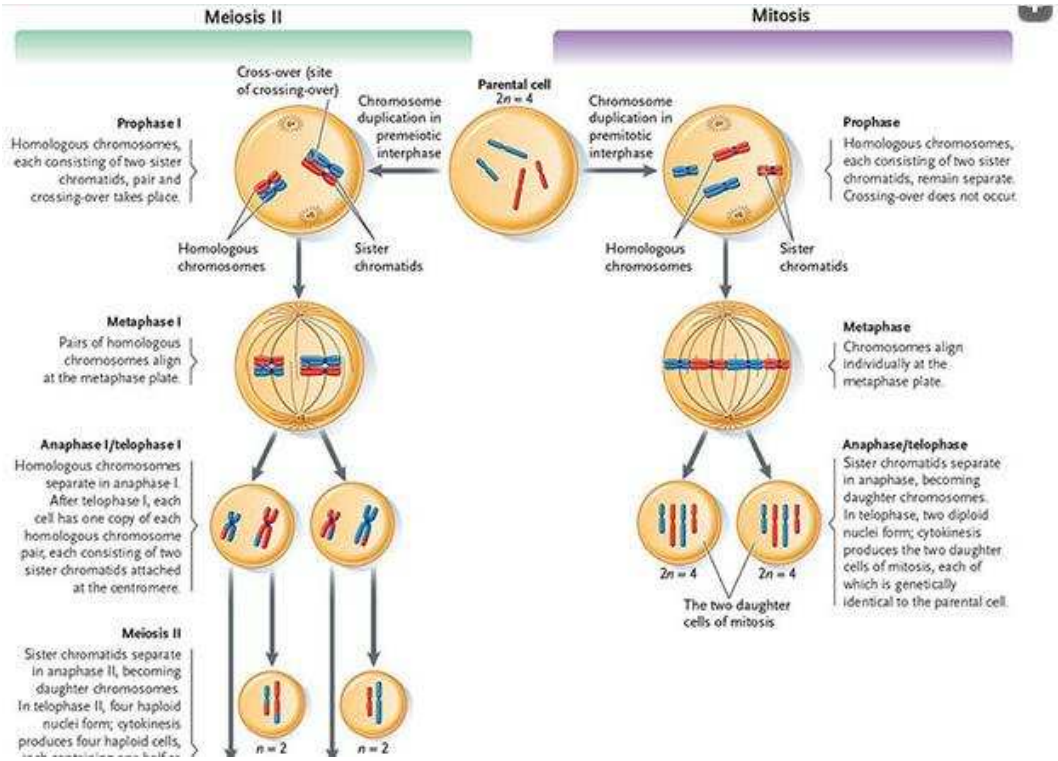
<u>9.3d Several mechanisms contribute to genetic diversity</u>

- Variability increases the chance of survival by offspring and changing environments
- Some argue that meiosis exists to also generate "repaired" chromosomes to be passed on to the next generation

Genetic Variability Arises from four sources:

1. Genetic Recombination of homologous chromosomes
2. Differing combinations of maternal and paternal chromosomes segregated to poles during Anaphase I

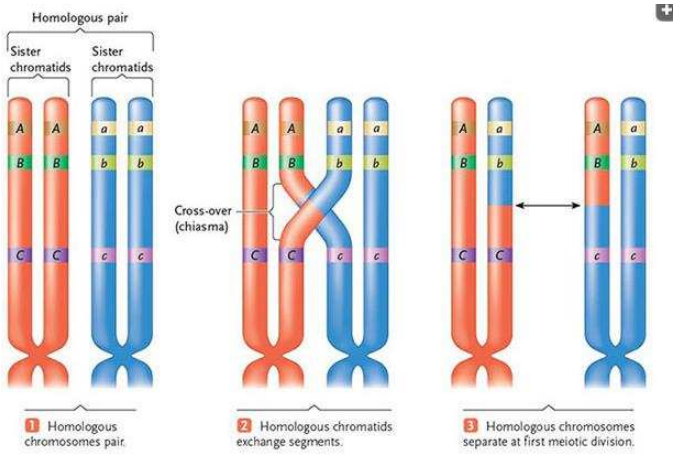
3. Differing combinations of recombinant chromatids segregated to the poles during anaphase II
4. The particular sets of male and female gametes that unite in fertilization



- Regions in which non sister chromatids cross one another (cross-overs) or chiasmata/chiasma clearly show that two of the four chromatids have exchanged segments
- Chromatids participating in recombination are shown side by side but are actually on top of one another – either one can cross over

Random Segregation of chromosomes of maternal and paternal origin accounts for the 2nd major source of genetic variability – all maternal could go to one side and all paternal to the other, or in a more likely scenario a random combination of maternal and paternal chromosomes segregate

- The number of possible random combinations depends on the number of chromosome pairs in a species – for example 39 chromosomes in dogs allow 2^39 different combinations



FAMILY LEVEL INHERITENCE

Chapter 10: Mendel, Genes and Inheritance

Gregor Mendel

- Scholarly monk used garden peas to study patterns of inheritance
- Bread generation after generation of pea plants and observed the patterns by which parents transmit traits to their offspring
- Discovered fundamental rules that govern inheritance

Characters = heritable characteristics

Traits = particular variation in genetic or phenotypic character

Blending Theory of Inheritance – Believed until 1900 (not true)

- Hereditary traits blend evenly in offspring through mixing of parent's blood – much like mixing coffee and cream

Experiment

- Chose garden peas for research because plan could be easily grown in monastery garden without much equipment
- Pea plants self fertilize (self-pollinate) – however for experiment he prevented self pollination so that pollen then had to come from a different plant causing
  "Cross-pollination" or a cross
- Chose True-breeding pea plants: when self-fertilized they pass traits without change from one generation to the next

First worked on single-character crosses

- Purple flowers and white flowers – took pollen from purple flower and placed in white flowers and vice versa
- Seeds were the result of the crosses – each containing, a zygote, or embryo
- The plants that develop from those seeds are the F1 generation (F=filial=son)
- The plants used in initial cross are the parental, or P generation
- Plants that grew from the F1 seed all formed purple flowers, no white, no blending

→ Then, purple flowered F1 plants were left to self-produce seeds that represent the F2 generation

- When the F2 seeds were planted, white flowers reappeared along with more purple
- 705 plants with purple
- 224 plants with white
- 3:1 ratio or about 75% purple flowered plants and 25% white-flowered plants

Mendel's 3 Hypotheses

1. **Genes** - Adult plants carry a pair of factors that govern the inheritance of each character – organism inherits one factor from each parent (correct)
2. **Dominance** – if an individual's pair of genes consist of different alleles, one allele is dominant over the other – recessive allele
3. **Principle of Segregation** – the pairs of alleles that control a character segregate as gametes are formed; half the gametes carry one allele, half carry the other – zygote receives one allele from mom and one from dad

Homozygous = same (PP) or (pp) Heterozygous = different (Pp) or (pP)

Monohybrid (mono = one, hybrid = offspring of parents with different traits) (Pp x Pp)

Genotype = genetic constitution of an organism (Pp)

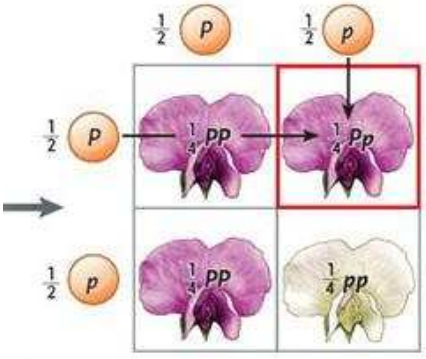
Phenotype = outward appearance (colour)

→ Genotype: Pp & PP = Phenotype: Purple flowers

Probability = possibility that an outcome will occur

- Scale of 0 to 1 (will not happen = 0, will happen = 1)
- **Product Rule**: probability is found by multiplying individual probabilities
  - **Probability that A and B will both occur = A x B**
  - Example: rolling a 4 on dice A is 1/6 and rolling a 4 on dice B is 1/6 so, you multiply 1/6 x 1/6 = 1/36
- **Sum Rule**: when several events all give same outcome, that either A or B or C will occur = probability of A + B + C
  - **Example**: probability of rolling a 7 → 1/6 x 1/6 = 1/36
  - 1/36 + 1/36 + 1/36 + 1/36 + 1/36 +1/36 = 6/36 = 1/6

Punnett Square

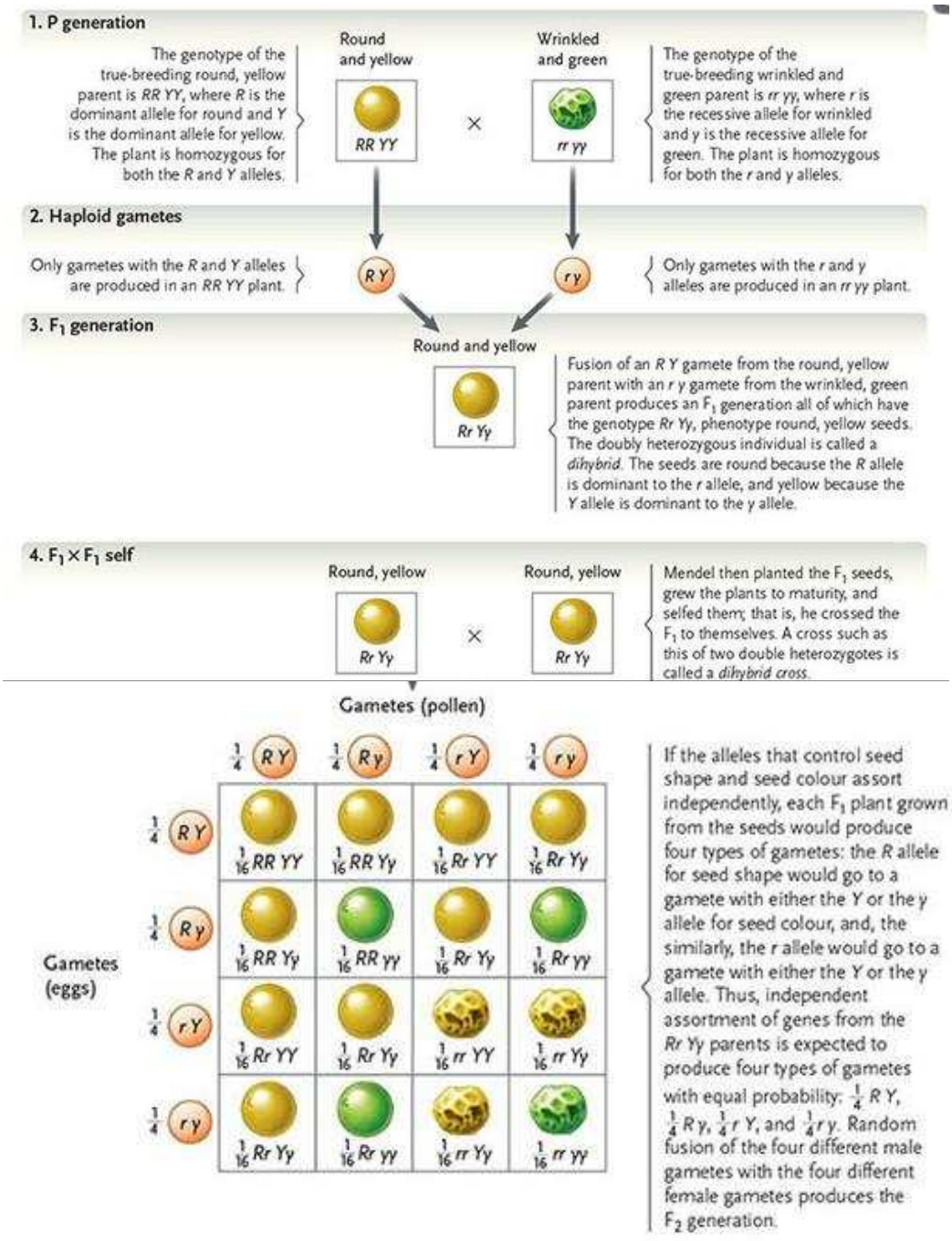


Mendel used a Testcross to check the validity of his hypothesis

- Testcross = cross between an individual with the dominant phenotype and a homozygous recessive individual

Dihybrid Cross

- Crossed parental stocks that had differences in **two** of the hereditary characters he was studying: RR YY x rr yy (shape and seed colour)



Added one further Hypothesis:

- **Independent Assortment**: The alleles of the genes that govern the two characters segregate independently during formation of gametes
- Meaning, the allele for seed shape has no influence on allele for colour and vice versa

Sutton's Chromosome Theory of Inheritance – related Mendel's genes to chromosomes:

- Chromosomes occur in pairs in sexually reproducing, diploid organisms, as do the alleles of each gene
- The chromosomes of each pair are separated and delivered slightly to gametes, as are the alleles of a gene
- The separation of any pair of chromosomes in meiosis and gamete formation is independent of the separation of other pairs, as in independent assortment

- Finally – one member of each chromosome pair is derived in fertilization from male parent and one from female parent
- Sutton Concluded: that genes and their alleles are carried on the chromosomes, known today as the "**Chromosome Theory of Inheritance"**

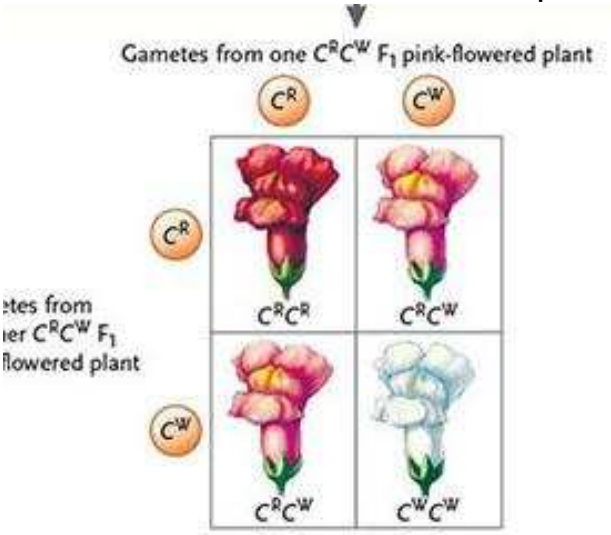
Locus = Particular site at which a gene is located (loci, plural)

- Particular DNA sequence that encodes a protein or RNA product responsible for the phenotype controlled by the gene

In humans, a number of easily seen traits show inheritance patterns – albinism, webbed fingers, achondroplasia (short limb dwarfism), as well as some that cannot be seen – cystic fibrosis

Incomplete Dominance: when dominant alleles do not completely compensate for recessive alleles

- Example: flower colour in snap dragon – if true breeding red-flowered and white-flowered snapdragons are crossed all the F1 offspring have pink flowers
- May make it appear that pure red and white colors have blended – however when two F1 plants are crossed, the red and white traits both reappear in the F2 generation – which has red, pink and white flowers in 1:2:1 ratio
- **Two dominant alleles blend when both parents are homozygous dominant**



CRCR (red) x CWCW (white) = CRCW(pink)F1

- When pink plants are crossed again, red and white colours reapperar together with the pink colour in F2
- Some human disorders show incomplete dominance – for example: Sickle cells disease is *homozygous for a recessive allele* that encodes a defective form of one of the polypeptides of the hemoglobin molecule
    - Individuals heterozygous for that recessive allele and the normal allele have a condition known as sickle cell trait
    - HETEROZYGOUS = Rr x Rr

Familial Hypercholesterolemia → is another example of incomplete dominance

- The gene involved encodes the LDL receptor, a cell membrane protein responsible for removing excess cholesterol from the blood – individuals are homozygous for defective LDL receptor gene – produce no LDL receptors – have 6x the normal level of cholesterol in blood and are prone to heart attack and stroke

Tay-Sachs Disease

- Children who are homozygous recessive do not have a functional version of an enzyme that breaks down gangliosides – type of membrane lipid. – as a result, gangliosides accumulate in the brain leading to mental impairment and eventually death
- Heterozygotes are without symptoms of the disease, even though they have a copy of recessive allele – at a biochemical level – reduced gangliosides can be detected in heterozygotes

Phenylthiocarbamide (PTC)

- Tastes intensely bitter to some people (brussel sprouts) and tasteless to others (20-30% of population)

Codominance - Effects of different alleles are equally detectable in heterozygotes

- Occurs when alleles have approximately equal effects in individuals making two alleles equally detectable in heterozygotes
    - Inheritance of human blood types M, MN, and N is an example of codominance (from ABO bloodtypes)
    - If LmLm would mean M
    - LnLn would mean N
    - LmLn would mean MN

In multiple alleles, more than 2 alleles of a gene are present in a population

- One of mendels major and most fundamental assumptions was that alleles occur in pairs in individuals; in pairs – alleles may be same or different
- MULTIPLE alleles may be present if all the individuals of a population are taken into account
- For example: gene B – could be B1, B2, B3….
- Although any one individual can have only 2 alleles of the gene, there are more than two alleles in the population as a whole
- Multiple alleles of a gene contain nucleotide differences at one or more locations in their DNA sequence – often cause detectable alterations in the structure and function of gene
- Despite the presence of multiple alleles, each diploid individual still has only 2 of the alleles

Human ABO Blood Group (Karl Landsteiner, 1901)

Attempts to transfer whole blood from one person to another were sometimes fatal – only certain combinations of blood types designated A, B, AB and O can be mixed safely in transfusion

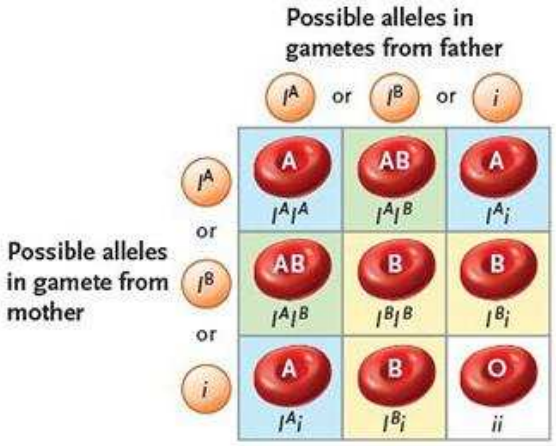
- Real example of multiple alleles – exhibits dominance and codominance

Blood Type	Antigens	Antibodies	Blood Types Accepted in a Transfusion
A	A	Anti-B	A or O
B	B	Anti-A	B or O
AB	A and B	None	A, B, AB, or O
O	None	Anti-A, anti-B	O

- Four blood types, A, B, AB and O are produced by different combinations of 3 alleles of a single gene I – the three alleles IA, IB and i produce the following blood types:

$I^A I^A$ = type A blood
$I^A i$ = type A blood
$I^A I^B$ = type AB blood
$I^B I^B$ = type B blood
$I^B i$ = type B blood
ii = type O blood

In addition, Ia and Ib are codominant alleles that are each dominant to the i allele



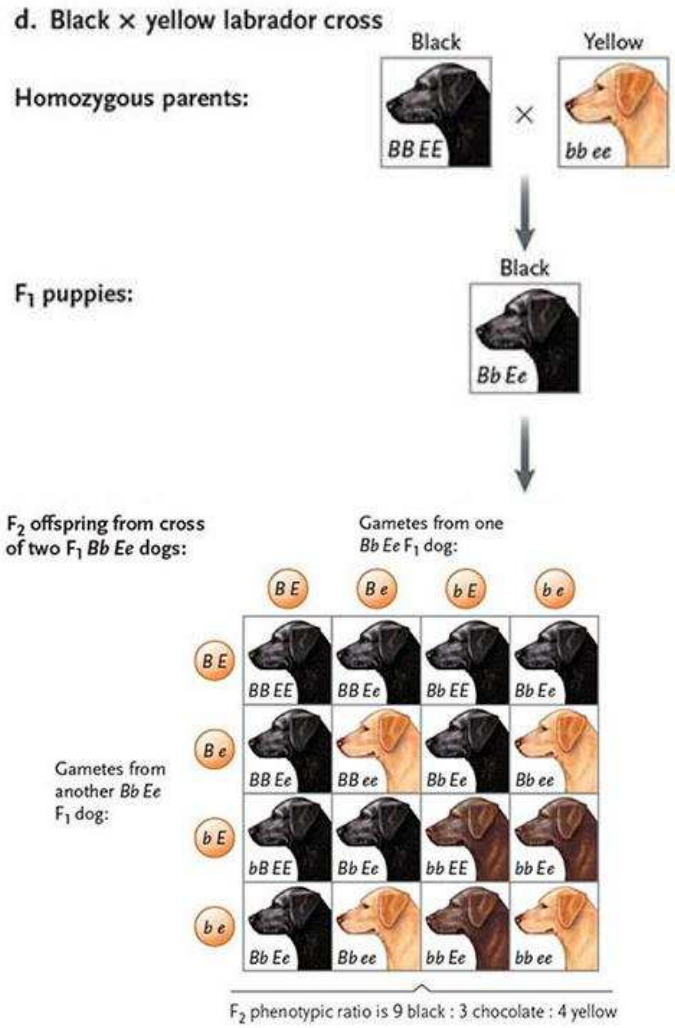
10.2d Epistasis

- Genes intereact with the activity of one gene influenceing the activity of another gene
- Inhibiting or masking the effects of one or more alleles of a gene at a different locus
- Result = some expected phenotypes do not appear among offspring

Labrador Retriever Fur Color example

Dominant Black = B
Recessive Chocolate Brown = b
2nd Dominant Tan = E

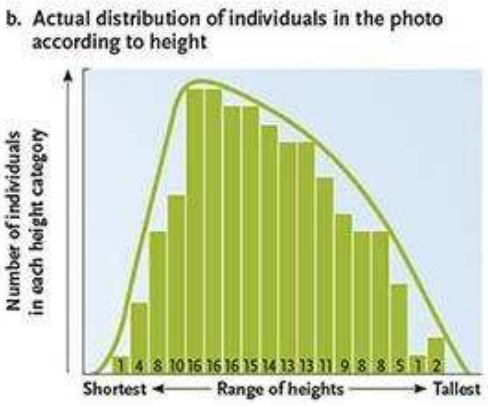
- This other E gene at a different locus determines whether the black or chocolate color appears at all by controlling the deposition of pigment in hairs
- Permits pigment deposition so that the black color in BB or Bb or chocolate in bb actually appears in the fur
- **Pigment disposition is almost completely blocked in homozygous recessive ee individuals so fur lacks melanin and has a YELLOW color whether the genotype for the B gene is BB, Bb or bb – thus E is said to be epistatic to the B gene**
- Epistasis by the E gene eliminates some of the expected classes crosses among labs



- Epistasis is believed to be an important factor in determining an individual's susceptibility to common human diseases – different degrees of susceptibility are a result of different gene interactions in the individuals
    - Ex. Insulin resistance

Polygenic inheritance: several/many different genes contribute to the same character

- More or less a gradation of types, forming a continuous distribution rather than on or off
    - Ex: shorter and taller people – height ranges
    - Skin color and body weight
    - These are known as **Quantitative traits** – character that distributes continuous distribution of the phenotype involved
- Polygenic inheritance can be detected by defining classes of variation, such as human body height of 180 in one class and 181cm in next class and so on
- Number of individuals in each class is then plotted as a graph – producing a bell-shaped curve



Expression of a genetic phenotype can be influenced by environment; particularly common with traits like body size
- Ex poor nutrition influences body size or height- good nutrition can have opposite effect

Pleiotropy: single genes affecting more than one character of an organism (opposite polygenic inheritance)

- Sickle cell disease for example – caused by recessive allele of a single gene that affects hemoglobin structure and function – WHICH in turn affects other aspects, blood vessel blockage, which in turn may damage tissues and organs, producing fatigue, nausea etc – domino effect

Chapter 11: Genes, Chromosomes, and Human Genetics

- Progeria = genetic disorder characterized by accelerating aging and reduced life expectancy
    - Caused by a genetic error that occurs 1/8 million people

11.1 Genetic Linkage and Recombination

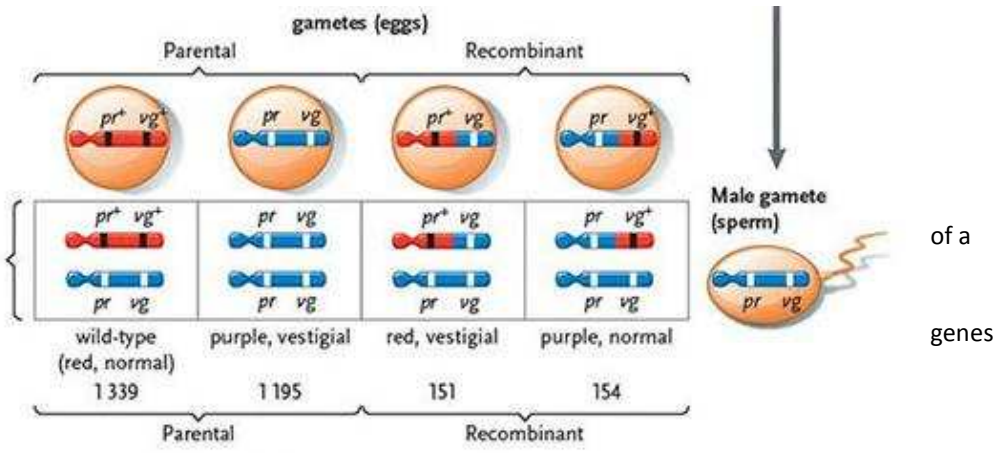
- Chromosomes contain many genes, with each gene at a particular location, or locus – genes located on different chromosomes assort independently during meiosis because the two chromosomes behave independently of one another during as they line up on the metaphase plate
- Genes located on the same chromosome may be inherited together in genetic crosses (not assorted independently) because the chromosome is inherited as a single physical entity in meiosis
- Linked genes = genes on the same chromosome
    - Phenomenon called **Linkage**

Principle of Linkage and Recombination were Determined with *Drosophila (fruit fly)*

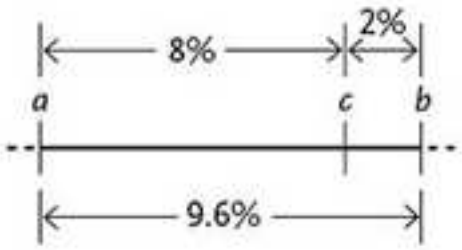
- Thomas H Morgan's group determined relative order of genes on chromosomes and estimated distance between them
- They reasoned that genes sitting far apart on a chromosome would be more likely separated from one another during meiotic crossing over than genes lying closer together
- Geneticists working with fruit flies have all agreed on a "normal" or "wild-type" genotype; any change from wild type is a mutant
- Mutant alleles are name based on the altered phenotype
    - Names for dominant mutant alleles are written with the first letter in uppercase, and recessive alleles written with first letter lowercase
    - Example:
        - Dominant mutant transforming an antenna into a leg is called **A**ntennapedia (Antp)
        - Recessive mutant allele altering eye color is called **v**ermilion (v)
        - The notion for a wild type allele is always by my adding a (+) plus sign to the mutant allele notation
        - Ant p+ refers to then a recessive allele giving a normal phenotype when homozygous

Suggested that two genes are linked genetically – physically associated on the same chromosome (linked) and further hypothesized that the behavior of these linked genes is explained by chromosome recombination during meiosis – further then, proposed that the frequency of this recombination is a function of the distance between linked genes

Linkage Map: map of a chromosome showing the relative locations of genes based on recombination frequencies



- Assume 3 genes, a b and c are carried together on the same chromosome
  - Crosses reveal a 9.6% of recombinants for a and b, an 8% frequency for a and c, and a 2% frequency for b and c
  - Frequencies allow genes to be arranged in one sequence on chromosome:



- Map Unit: unit of a linkage map, equivalent to a recombination frequency of 1% (mu) (centimorgan)

Widely separated linked genes sort independently – even though genes are linked, they are so far apart that they assort independently and show no linkage

Max frequency of recombinant offspring frequency is 50%

11.2 Sex-Linked Genes

- In many organisms – one or more pairs of chromosomes are different in males than females – sex chromosome are called sex-linked genes
- Autosomes = chromosomes other than sex chromosomes (chromosomes 1-22)
- Females = XX, Males = XY
- First discovered in drosophila – mutant eye color caused by recessive allele of a sex linked gene on X chromosome

Human sex determination depends on the SRY gene
SRY = Sex-determining Region of the Y

- Appears to be the master switch in determining development of maleness
- After 6-8 weeks of embryonic development SRY gene becomes active in XY embryos

Pedigree = a chart that shows all parents and offspring for as many human generations as possible

- females are represented by a circle, males by square
- solid square or circle indicates presence of trait

- Color blindness – sex linked trait in which individual is unable to distinguish between red and green
- Hemophelia – sex linked recessive trait that causes blood clotting defect (bleed uncontrollably if they are injured
    - Queen Victoria of England

Inactivation of one X chromosome evens out gene effects
Theoretically products from genes on the X chromosome could be equalized in males and females if:

1. Expression of genes on male X chromosome were doubled
2. Expression of genes on both female x chromosome were halved
3. One x chromosome were “turned off” in females

All of these compensation mechanisms are known in nature but mammals use the latter; females with two X chromosomes inactivate most genes on X chromosome or the other in most body cells

- As a result of equalizing mechanism, the activity in most genes carried on the X chromosome is essentially the same in the cells of males and females
- Inactivation occurs by condensation – packs chromatin of one of 2 X Chromosomes into tightly coiled state
- Inactive condensed X chromosome can be seen within the nucleus in cells of females as a dense mass of chromatin called the Barr Body

POPULATION GENETICS

Microevolution: small-scale genetic changes within populations, often in response to shifting environmental circumstance or chance events (humpback whales)

18.1a Phenotypic Variation
Phenotypic variation: differences in appearance or function among individuals of a population

Quantitative Variation: variation that is measured on a continuum (such as height in humans) rather than in discrete units or categories
Qualitative Variation: variation that exists in two or more discrete states, with intermediate forms often being absent (such as blue or white feathers)

Polymorphism: the existence of discrete variants of a character among individuals in a population (polymorphic traits) → snail shells are polymorphic in background colour, number of striple and colour of stripes, or human blood type

- We describe phenotypic polymorphisms quantitatively by calculating the percentage or frequency of each trait
- If you counted 123 blue snow geese, and 369 white snow geese in a population of 492 geese
    - Freq of blue would be 123/492 = 0.25 and white would be 369/492 = 0.75

Phenotypic variation is caused by genetic differences, and environmental factors, or an interaction of the two is important because only genetically based variation is subject to evolutionary change - It is the phenotype of an individual organism rather than its genotype that is successful or not (ex. Hydrangea in acidic soil = purple flowers, in regular soil = pink flowers)

Basically – Natural selection operates on the phenotype, not the genotype – and it operates on whole phenotype, not just one gene at a time

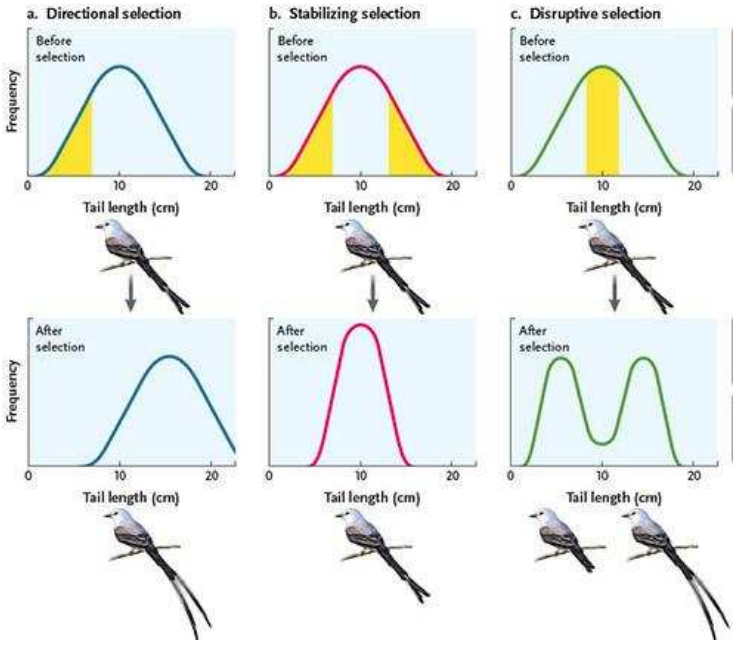
How can we determine whether phenotypic variation is caused by environmental factors or by genetic differences?

- Test for an environmental cause by changing one environmental variable and measuring its effects on genetically similar subjects

18.1c Natural Selection and Phenotypic Variation
3 Modes of Natural Selection

1. Directional Selection
    - Individuals near one end of the phenotypic spectrum have the highest relative fitness
    - After selection the trait's mean is higher or lower than before and variability in trait may be reduced
    - Example: predatory fish promote directional selection for larger body size of guppies when they feed on the smallest individuals
2. Stabilizing Selection (most common)
    - Individuals expressing intermediate phenotypes have the highest relative fitness
    - By eliminating phenotypic extremes, this reduces genetic and phenotypic variation and increases the frequency of intermediate phenotypes
    - Example: very small and very large newborns are less likely to survive than those born at an intermediate weight
    - Can result from multiple selective forces acting on the same trait but in opposite directions (gall's talked about in class that grow on stems – wasps eat small galls, birds eat large galls)
3. Disruptive Selection
    - When extreme phenotypes have higher relative fitness than intermediate phenotypes

- Alleles producing extreme phenotypes become more common, promoting polymorphism
- Under natural conditions, much less common than directional and stabilizing



18.2a Genetic Structure of Populations

gene pool = the sum of all alleles at all gene loci in all individuals in a population

- To describe structure of gene pool, scientists identify the genotypes in a sample and calculate **genotypic frequencies** = percentage of individuals possessing each genotype
- Then can calculate **allele frequencies** = the relative abundance (commonness) of different alleles
- For a locus of two alleles, scientists use *p* to identify frequency of one allele and *q* for the other

Table 18.1 **Calculation of Genotype Frequencies and Allele Frequencies for the Snapdragon Flower Colour Locus**

Because each diploid individual has two alleles at each gene locus, a sample of 1000 individuals has a total of 2000 alleles at the C locus.

Flower Colour Phenotype	Genotype	Number of Individuals	Genotype Frequencies *	Total Number of C^R Alleles *	Total Number of C^W Alleles *
Red	C^RC^R	450	$450/1000 = 0.45$	$2 \times 450 = 900$	$0 \times 450 = 0$
Pink	C^RC^W	500	$500/1000 = 0.50$	$1 \times 500 = 500$	$1 \times 500 = 500$
White	C^WC^W	50	$50/1000 = 0.05$	$0 \times 50 = 0$	$2 \times 50 = 100$
	Total	1000	$0.45 + 0.50 + 0.05 = 1.0$	1400	600

To calculate allele frequencies, use the total of $1400 + 600 = 2000$ alleles in the sample:

$$p = \text{frequency of } C^R \text{ allele} = 1400/2000 = 0.7$$
$$q = \text{frequency of } C^W \text{ allele} = 600/2000 = 0.3$$
$$p + q = 0.7 + 0.3 = 1.0$$

18.2b The Hardy-Weinberg Principle

→ an evolutionary rule of thumb that specifies the conditions under which a population of diploid organisms achieves genetic equilibrium (point where neither allele frequency, or genotype frequency in a population change in succeeding generations)

- Work showed that dominant alleles need not replace recessive ones, and that shuffling of genes in sexual reproduction does not in itself cause allele or genotype frequencies to change

Genetic equilibrium is possible only is all of the following conditions are met:

1. No mutations are occurring
2. Population is infinite in size (no genetic drift)
3. Population is closed to migration from other species
4. All genotypes in population survive and reproduce equally well
5. Individuals in population mate randomly with respect to the trait being considered

If all conditions are met, allele frequency of population for gene locus will never change and genotype frequencies will stop changing after one generation

18.3 Evolutionary Agents

Mutation: Heritable change in DNA
Gene Flow: Change in allele frequencies as individuals join a population and reproduce
Genetic Drift: Random changes in allele frequencies caused by chance events – reduces genetic variation
Natural Selection: differential survivorship or reproduction of individuals with different phenotypes
Nonrandom Mating: choice of mates based on their phenotypes and genotypes

18.3a Mutations

Mutation: is a spontaneous and heritable change in DNA; rare events

- Because it creates entirely new genetic variations, a mutation can be a major source of heritable variation
- For most animals, only mutations in the germ line (production of gametes) are heritable
- On plants, mutations may occur in meristem cells which eventually produce flowers as well as nonreproductive structures – in such cases a mutation may be passed to next generation and influence gene pool

Deleterious mutations – alter an individuals structure, function or behavior in harmful ways

- In mammals for ex. Collagen is essential, simple mutations in humans' cause Ehlers-Danlos syndrome – a disruption of collagen synthesis that may result in loose skin, weak joints, or sudden death

Neutral mutations are neither helpful or harmful

18.3b Gene flow

- Organisms or their genetic material sometimes move from one population to another
- If the immigrants reproduce, they may introduce alleles into a population, shifting its allele and genotype frequencies = gene flow
- Shows that populations are not completely closed and can be open to migration
- Common in some animal species – baboons, fish eggs pushed by ocean currents, pollen being carried by the wind etc
- Movement alone is not sufficient to foster gene flow, individuals must also reproduce

18.3c Genetic Drift

- Random fluctuations in allele frequencies as a result of chance events
- **Population Bottleneck** = dramatic reduction in population size due to a stressful factor such as disease, starvation or drought
- **Founder Effect** = phenomenon in which population that was established by just a few colonizing individuals has only a fraction of the genetic diversity seen in the population from which it was derived
- Genetic drift is more pronounced in small populations than in large ones
    - Tossing a coin 20 or 30 times will produce a more unequal ratio
    - Tossing a coin 500 or 5000 times will produce a ratio closer to 50:50
- Conservation Implications
    - Endangered species experience severe population bottlenecks, resulting in the loss of genetic variability

18.4 Maintaining Genetic and Phenotypic Variation

Diploidy – reduces the effectiveness of natural selection on harmful recessive alleles – such alleles are disadvantageous in the homozygous state, may have little or no effect on heterozygotic individuals; thus recessive alleles can be protected from natural selection by the phenotypic expression of the dominant allele

18.4b Balanced Polymorphisms

balanced polymorphism - Two or more phenotypes are maintained in fairly stable proportion over many generations

Heterozygote Advantage – individuals that are heterozygous at a particular locus have higher relative fitness than either homozygote; perhaps by responding effectively to environmental variation

- Sickle cell anemia examples
    - Homozygous HbS/HbS individuals often die of disease before reproducing whereas heterozygous make up 25% of many populations
    - Common in areas where malaria is present, heterozygotes have greater resistance

Selection in Different Environments – snail shell example

18.5 The Evolution of Adaptive Traits

- Adaptive trait – any product of natural selection that increases relative fitness of an organism in its environment
- Adaptation – accumulation of adaptive traits over time – for example water retaining structures in desert plants
    - For adaption to occur, must be phenotypic variation for selection to act on

18.5b Factors Constraining Adaptive Evolution

- No organism can be perfectly adapted because environments change over time
- Natural selection preserves alleles that are successful under the prevailing environmental conditions; thus each generation is adapted to conditions in which its parents lived and will therefore always be behind if environment changes
- Natural selection is not an engineer creating new organisms from scratch, rather it acts on existing structures by making small modifications

17.3e Impact of Theory of Evolution by Natural Selection

- Darwin argued that all organisms that have ever lived arose through descent with modification
- Envisioned the history of life as a tree
- Four characteristics distinguish Darwin's theory from earlier explanations of biological diversity and adaptive traits
    1. Darwin provided purely physical explanations for origins of diversity (opposed to spiritual)
    2. He recognized that evolutionary change occurs in groups rather than individuals
    3. He described evolution as a multistage process – variations arise within groups, natural selection eliminates unsuccessful variation and continues in next generation
    4. He understood that evolution occurs because some organisms function better than others in a particular environment

SPECIATION

Chapter 19: Species and Macroevolution

Species – population of organisms capable of interbreeding and producing fertile offspring – genetically distinct from other species

- Variation in reproductive patterns complicates the application of the species concept, as does hybridization – which is reproduction involving more than one species

19.1a Naming Species

- Carl von Linne (Carolus Linnaeus) was first modern practitioner of taxonomy – the science that identifies, names and classifies new species
- Binomial nomenclature – species are assigned a two-part name, a species name or binomial
    - The first part identifies genus – group of species with similar characteristics
    - Second part is the specific epithet
    - First letter of first name is always capitalized and entire binomial is italicized
    - Homo Sapiens, can shorten to H. Sapiens

19.1c The Taxonomic Hierarchy

- Comprises a series of formal categories – domain, kingdom, phylum, class, order, family, genus, species and subspecies
- Organisms included within any category comprise a taxon

19.2a The Morphological Species Concept

- Biologists often describe new species on the basis of visible characteristics

19.2b The Biological Species Concept

- Emphasizes dynamic nature of species
- Biological species as defined by Ernst Mayr "groups of interbreeding natural population that are reproductively isolated from [do not produce fertile offspring with] other such groups"
- In principle, if two populations interbreed and produce fertile offspring under NATURAL conditions, they belong to the same species
- Notes genetic cohesiveness of species, as well as genetic distinctiveness of each species
- Explains why individuals of the same species look alike
- Does not always apply to forms of life that produce asexually including most bacteria, fungi etc

19.2c The Phylogenetic Species Concept

- Using both morphological and genetic sequence data, scientists first construct evolutionary tree & then define a phylogenetic species as a cluster of populations – tiniest twigs on tree of life
- One advantage – can apply to any group of organisms including those that are extinct
- Critics argue that morphological and genetic distinction on tree of life reflect the absence of gene flow

19.3 Maintaining Reproductive Isolation

Reproductive isolating mechanism – any biological characteristic that prevents the gene pools of two species from mixing – 2 categories:

1. Prezygotic isolating mechanisms – exert effects before production of fertilized egg
2. Postzygotic isoloating mechanism – opposite

Not mutually exclusive – two or more may operate – considered macroevolution

Timing Relative to Fertilization	Mechanism	Mode of Action
Prezygotic ("premating") mechanisms	Ecological isolation	Species live in different habitats
	Temporal isolation	Species breed at different times
	Behavioural isolation	Species cannot communicate
	Mechanical isolation	Species cannot physically mate
	Gametic isolation	Species have nonmatching receptors on gametes
Postzygotic ("postmating") mechanisms	Hybrid inviability	Hybrid offspring do not complete development
	Hybrid sterility	Hybrid offspring cannot produce gametes
	Hybrid breakdown	Hybrid offspring have reduced survival or fertility

19.4 The Geography of Speciation

subspecies – local variants of a species (may differ in colour, patterns – snake example)

Ring species – species with a geographic distribution that forms a ring around inhabitable terrain

- Differentiated to a point where there can no longer exchange genetic material directly
- Does this make them subspecies or different species?

Clinal Variation – when species is distributed over a large, environmental diverse are some traits may exhibit a cline (pattern of smooth variation along a geographical gradient)

- Example – many birds and mammals in the north hemisphere show clinal variation in body size and length of appendages – colder environments have larger bodies to conserve body heat
- Result of gene flow

Allopatric Speciation (allo = different, patria = homeland) – evolution of reproductive isolating mechanism between two populations that are geographically separated

- May happen when physical barrier (natural disaster) divides large population or when a small population separates from main geographical place
- Occurs in 2 stages
    1. Two populations become geographically separated, preventing gene flow
    2. Populations experience mutations as well as different patterns of natural selection and genetic drift they may accumulate differences that isolate them reproductively – most common mode of speciation
- Over time accumulated genetic difference may cause reproductive isolation
- Species cluster = group of closely related species descended from a common ancestor
- Sometimes allopatric populations re-establish contact when a geographical barrier is eliminated
    - "Secondary contact" tests whether or not populations have diverged into separate species

Reinforcement

1. The enhancement of reproductive isolation that had begun to develop while populations were separated
2. Encouraging or establishing a pattern of behavior using a positive or negative stimulus

Parapatric Speciation – speciation between populations with adjacent geographic distributions

- May occur is hybrid offspring have low fitness
- Organisms whose ranges do not overlap but are immediately adjacent to each other; occur together in a narrow contact zone

Sympatric Speciation – speciation that occurs without the geographic isolation of populations

- New species evolve from a single ancestral species while inhabiting the same geographic region
- Often occurs in plants through polyploidy (extra copies of entire haploid complement of chromosome)
    - Because large genetic changes may prevent polyploidy individuals from breeding with those of the parent species

<u>9.5 Genetic Mechanisms of Speciation</u>

Genetic Divergence in Allopatric Populations

- How much genetic divergence is necessary for speciation to occur?

Polyploidy

- **Autopolyploidy** = Can arise through chromosome duplications within a single species or – error in mitosis or meiosis (called unreduced gametes)
    - Diploid pollen can fertilize diploid ovules of a self-fertilizing individual or it may fertilize diploid ovules on another plant with unreduced gametes
- **Allopolyploidy** = through hybridization of different species
    - Closely related species hybridize and form polyploidy offspring – are sterile if parents have diverged enough that chromosomes don't pair properly during meiosis
    - If chromosome number is doubled, hybrid can produce gametes
    - Rapid compared to genetic divergence
- Both result in doubling chromosomes, but timing of doubling is different
- Autoploidy timing = meiosis
- Alloploidy timing = after a hybrid offspring is produced

Speciation from Chromosome Alterations

- Closely related species have a number of chromosome differences due to translocation, deletion etc.
- May foster postzygotic isolation – can be identified by comparing banding patterns in stained chromosomes