BIOL1003

Molecular Basis of inheritance

Genes in 1940-50

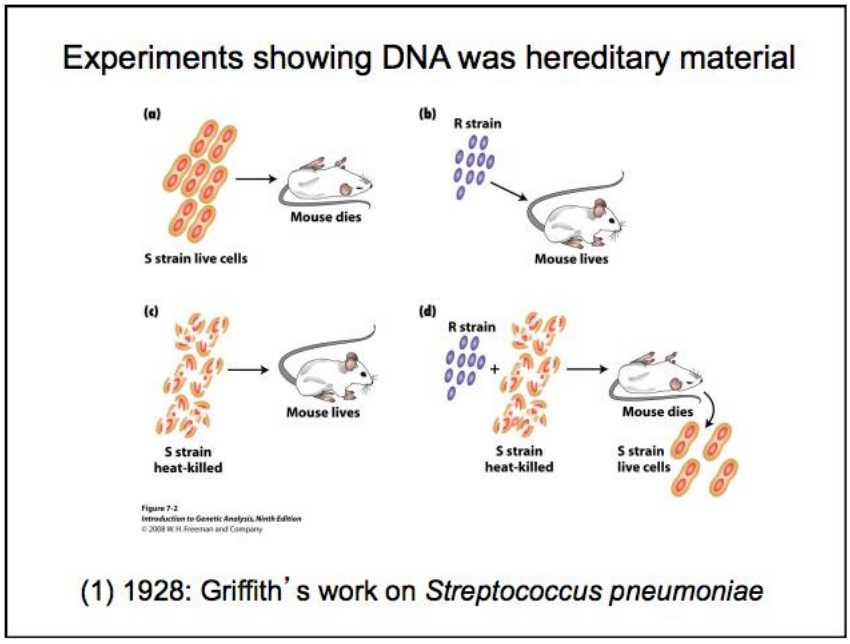
- Genes are hereditary factors causing different traits; their physical nature was unknown
- Genes were carried on chromosomes
- Chromosomes consist of protein and DNA
- Proteins: known as key components of the body; 20 amino acids known
- DNA known to consist of four nucleotides, but structure not known
- How are genes copied? How does mutation occur? How do genes create an organism

Linus Pauling

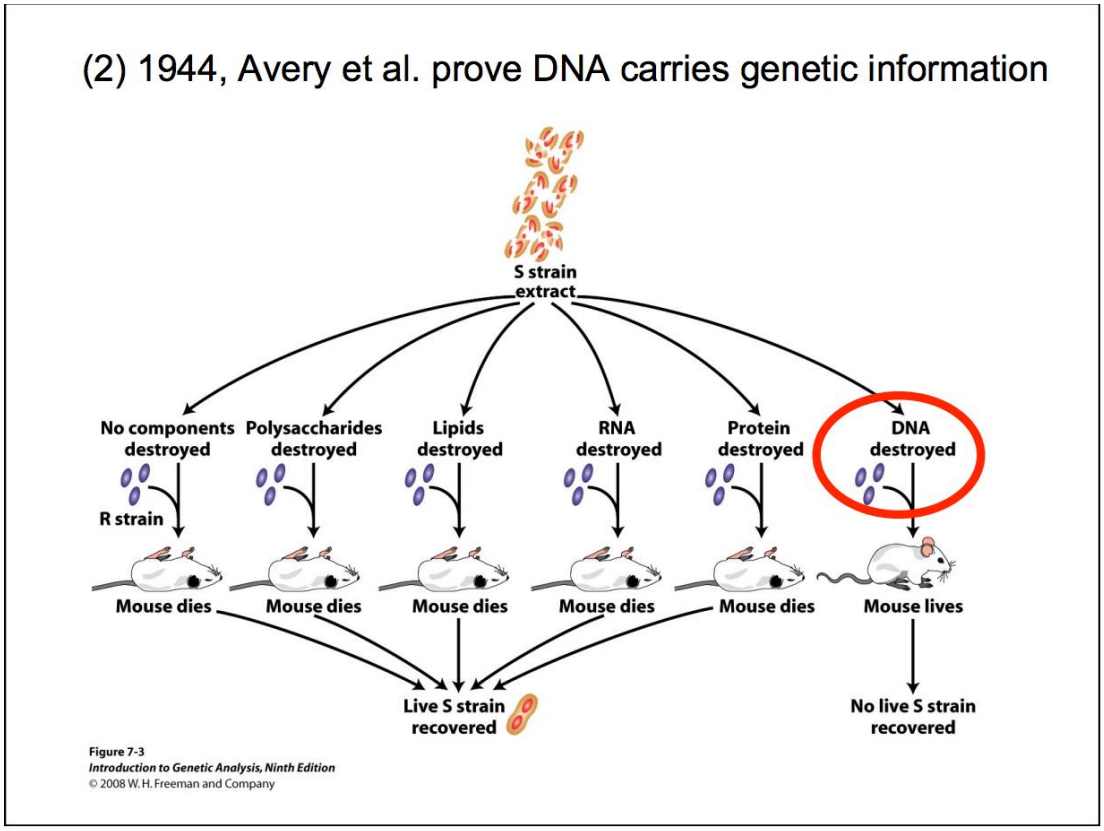
- Theorised that because DNA only has 4 nucleotides it would be too simple to encode proteins
- Proteins contain 20 AAs. Make diverse + complex materials eg hair, skin, enzymes
- Protein likely to be hereditary material

Experiments showing DNA was hereditary material

- 1928 - Griffith used pneumococcus bacterium of two strains, the S(virulent) strain which had a polysaccharide coat, and the R strain which did not. He found that
  - S strain killed mice (bacterium found in mice)
  - R strain mouse lived
  - S strain (heat killed) mouse lived
  - S strain (heat killed) + R strain mouse dies (bacterium found in mice)
- Griffith concluded that the live R strain bacteria must have absorbed genetic material from the dead S strain bacteria, and since heat denatures protein, the protein in the bacterial chromosomes was not the genetic material



- 1944 – Avery + colleagues take heated S strain extract and the R strain and destroy various components of the bacterium eg polysacchiarides, lipids one at a time. What they found was that only when the DNA was destroyed from the S strain did the mouse live, and that no live S strain was recovered when the DNA was removed. – **PROVED THAT DNA WAS HEREDITARY MATERIAL**



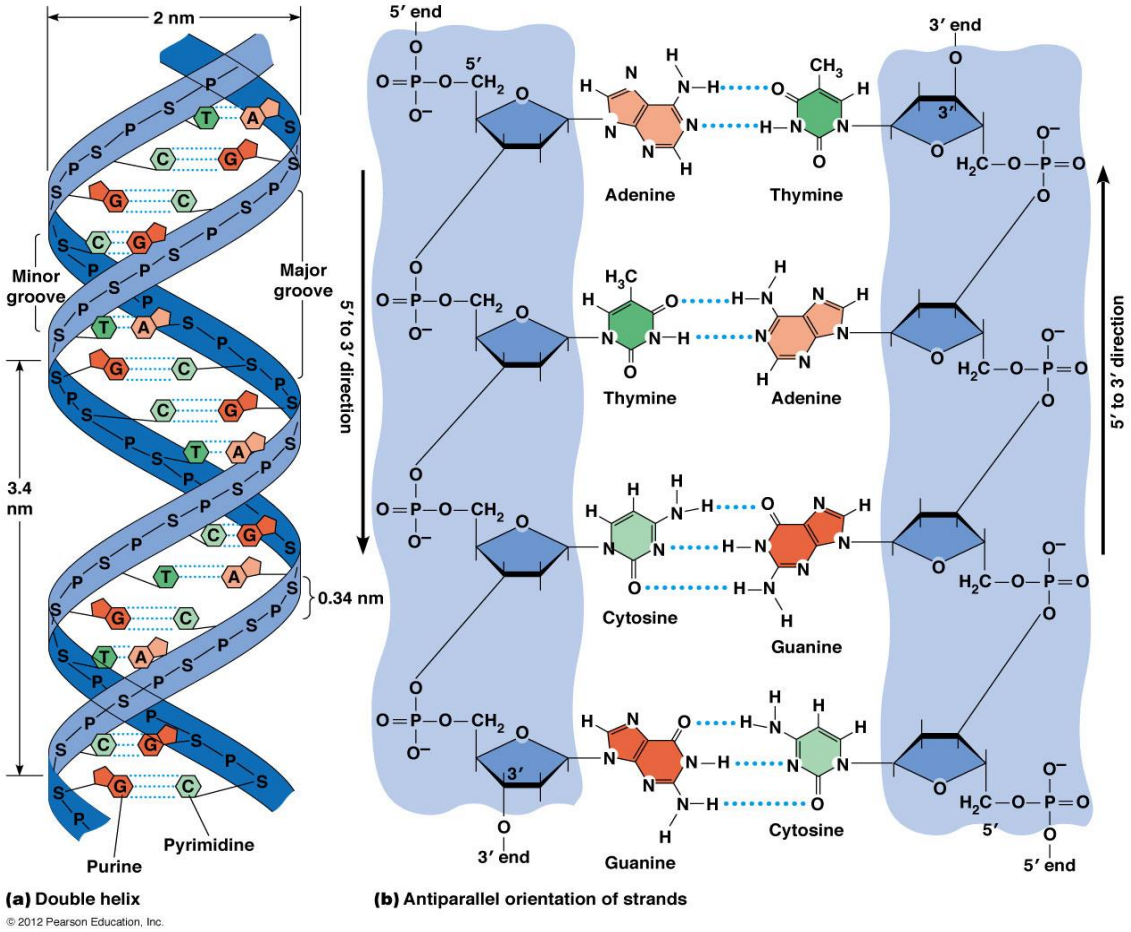
Structure of DNA

- Linus Pauling - Began to accept DNA as hereditary material: published "triple helix" model
- Watson and Crick – used modeling, chemistry, physics to try and understand DNA structure
- They had information available to them

  1. The structure of a nucleotide which comprised of a nitrogenous base attached to a sugar-phosphate backbone. The nitrogenous base was connected to the first carbon of the sugar, phosphate connected to the 5th carbon of and there is a hydroxyl group attached to the 3rd carbon.

  2. Chargaffs rules of base composition that
  Adenine = Thymine
  Guanine = Cytosine

  3. Rosalind Franklin's key experiment – used X ray crystallography to get photos of crystallised DNA fibres. Maurice Wilkins showed Watson and Crick without her knowing – this provided them with final evidence for double helical structure of DNA and they published their findings in 1953.



The Double Helix

- The complementary bases are connected via hydrogen bonding
- It could replicate (complementary base laws) for new cells, hold genetic information, and was stable(could self-repair)
- Could also mutate occasionally

DNA replication

- The process of DNA replication consists of the following steps:
  1. The DNA double helix is unwound by the enzyme, DNA helicase
  2. The DNA unzips forming two single strands
  3. Free nucleotides in the nucleoplasm are added to the single strands by DNA polymerase according to base pair rules resulting in two identical strands of DNA.
- The process is semi-conservative, as each double stranded molecule contains half of the original DNA strand
- Leading and Lagging Strands
  - Leading strand there is continuous DNA synthesis as nucleotides are continuously added to the 3 prime end
  - Lagging strand works in Okazaki fragments, it is discontinuous. The nucleotides have to wait until the two template strands have been opened enough to synthesize the daughter strand
- Mutation occurs with an altering of the base sequence, mistakes can be made and this genetic material can be passed on.

Gene expression

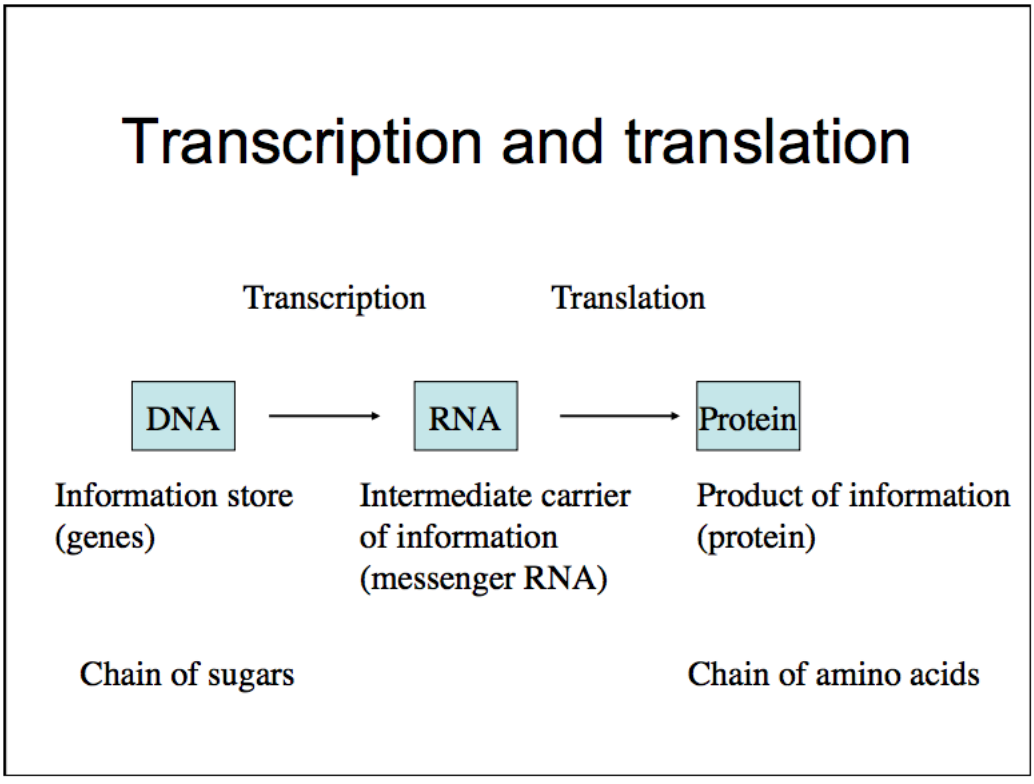
- 20 amino acids – 3 nucleotides are needed for one amino acid as 64 different combinations (overlapping)
- AUG – start codon
- 3 nucleotides = codon
- Typical protein is 300 amino acids long

Genetic Code

- Universal across all phyla
- Suggests a common origin of all life
- Some minor codon usage changes eg insect mitochondria AGG = lysine instead of arginine

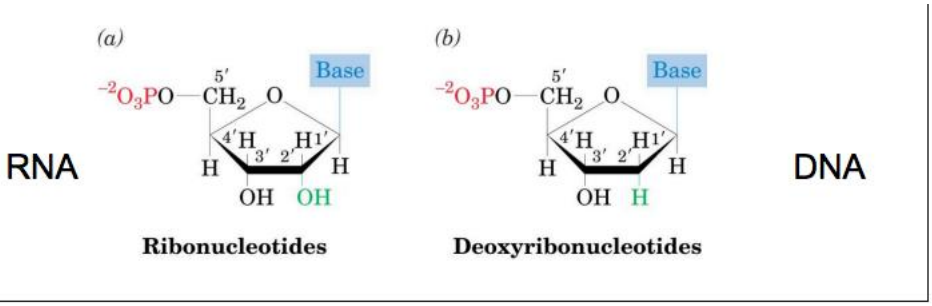
Transcription and translation

- Transcription
  - DNA in the nucleus 'unzips', exposing unpaired nitrogen bases. Messenger RNA then copies the code in the nucleus. Introns are then removed giving a strand of mRNA
- Translation
  - The mRNA then moves from the nucleus to a small and large ribosomal subunit in the cytoplasm and attaches itself. Transfer RNA molecules carry a 'triplet' of bases and specific amino acids match up with their complementary base triplets on the mRNA. This codes for a start codon followed by a determined number of amino acids which are held together by peptide bonds. Eventually a chain of amino acids is formed which fold to form a 3D protein (polypeptide) structure. This is known as translation.



RNA vs DNA

- RNA Uracil replaces Thymine
- RNA exists as a single strand
- Sugar backbone of RNA made of ribonucleotides not deoxyribonucleotides
- Hydroxyl group on second carbon in RNA rather than just hydrogen.



Eukaryotic Protein Synthesis

- In the cell nucleus, RNA polymerase transcribes RNA from DNA (nucleotides still added to 3 prime end)
- Direction of transcription depends where 3 prime end is, if it is left the direction is left
- Introns (non coding sections) are excised from the RNA transcript, the remaining exons are spliced together, producing mRNA.
- mRNA is transported out of the nucleus. In the cytoplasm, ribosomal subunits bind to the mRNA
- tRNA molecules become attached to specific amino acids with the help of activating enzymes. Amino acids are brought to the ribosome in the order directed by the mRNA
  - A P and E site
- tRNAs bring their amino acids in at the A site on the ribosome. Peptide bonds form between amino acids at the P site, and tRNAs exit the ribosome from the E site.
- The polypeptide chain grows until it is completed

mRNA reading frames

- Three ways of reading one strand of mRNA
  - 1st 2nd or 3rd nitrogenous base
- Look for one that doesn't have stop codon in it
- Sensible transcript – start codon, few hundred or more codons, then stop codon

The Cell Cycle and Mitosis

Mitosis and Cytokinesis

- Mitosis is a process of nuclear division by which replicated copies of a cells DNA are organized into chromosomes. The identical copies of DNA are then divided equally between two daughter cells
- Mitosis has four stages:
- Prophase
  - The nuclear membrane and nucleolus begin to break down
  - The DNA condenses to form chromosomes
  - The mitotic spindle, made up of proteins called microtubules or centromeres, begins to form and attaches to the kinetochores on each chromosome

- Metaphase
  - The chromosomes are moved to the centre of the cell by the mitotic spindle

- Anaphase
  - Centromere divides and the mitotic spindle, attached to the kinetochores of the chromosomes, begin to shorten drawing the chromatids of each chromosome to opposite ends of the cell
  - The unattached microtubules on the spindle elongate stretching the cell

- Telophase
  - The chromatids, now called chromosomes, reach the poles of the cell as the unattached microtubules continue to elongate
  - nuclear envelope begins to reform and the nucleoli reappear and chromosomes relax as the DNA unwinds

- Following telophase, cytokinesis occurs or division of the cytoplasm resulting in two daughter cells

The Cell Cycle

- Most eukaryotic cells follows a process of growth and division called the cell cycle
- Throughout interphase the cell is engaged in growth and metabolic activities. Interphase can be further broken down into 3 phases called G1 S and G2
- G1 Phase (first growth)
  - Normal cell functions occur as well as cell growth
  - Chemical checkpoint that controls whether a cell will divide, delay division or enter a resting stage

- S phase (synthesis)
  - DNA replicates producing 2 copies of each chromosome

- G2 phase
  - cell continues to prepare for cell division
  - success of DNA replication is assessed, if good it enters the mitosis phase

- This is then followed by mitosis
- Cells are the fundamental unit of life and they need to behave like entire organisms. They must take in nutrients, perform metabolic functions, release products, grow and reproduce. Control of growth and reproduction in cells is necessary for organisms to function. Uncontrolled growth causes cancer.

Cell structures and Function

Levels of Organisation

- Atoms → Molecular (DNA) → Cellular → Tissue → Organ → Organ system → Organism
- Epithelial Tissue, muscle tissue, connective tissue, nerve tissue
- Nerve tissue – function to allow communication

- Organs form organ systems, which work together to form organisms

Cell Theory

- A cell is the basic structural and functional unit of living organisms. When you define cell properties you are defining the properties of life eg waste, reproduce – applies to the whole organism.
- The activity of an organism depends on both the individual and the collective activities of its cells. – for organ systems to work cells need to work
- According to the principle **of complementarity of structure and function**, the biochemical activities of cells are dictated by the relative number of their specific subcellular structures(organelles) – function of cell type determined by what organelles are present
- Continuity of life from one generation to another has a cellular basis (sperm + egg)

Typical structures of eukaryotic (animal) cells

- Eukaryotic – membrane bound nucleus and membrane bound organelles
- Prokaryotic – do not have a membrane bound nucleus

	Structure	Function
Cytoplasm	Fluid which fills the cell, where organelles 'float' (actually in fixed positions	Allows the movement of molecules throughout the cells
Centriole	Part of the cytoskeleton (not an organelle)	Cell division
Ribosome	Not membrane bound (though considered organelles), made up of 2 protein subunits and rRNA	Protein synthesis (read RNA)
Cell membrane	A dynamic(moving) Phospholipid bilayer; two layers of lipids: the hydrophobic tails facing inward and the hydrophilic heads on the outside of the membrane	Regulates the movement of substances in and out of the cell
Protein Channels	- Passive, allow movement across a gradient, high to low concentration - Active, requires energy to move ions across the membrane - Can determine cell type by looking at surface proteins	- Allow substances in and out of the cell
Nucleus	- Porous membrane, allows molecules in and out - Nucleolus is where ribosomes are assembled, once formed they migrate to the cytoplasm – some go to endoplasmic reticulum others float freely	- Contains genetic information - Regulates cell activities – the control centre of the cell
Smooth Endoplasmic Reticulum (sarcoplasmic reticulum)	- network transport system in the cell	- Assembles lipids and detoxifys poisons eg drugs and alcohol - Liver cell would have high concentration of smooth
Rough	-network transport system in the	- For protein synthesis, packages

Endoplasmic Reticulum	cell with ribosomes	the polypeptide sequence - (Synthesizes protein for secretion, insertion into the plasma membrane, and lysosomal enzymes.)
Golgi Apparatus		- Process and package proteins – determines the destination of the protein - Lipids and carbs can be added, more folding - Hormones, channel proteins
Lysosomes		- Digest waste particles - Cells defence - contain digestive enzymes - Endocytosis – when a cell takes in molecules - Exocytosis – vesicle where products are taken to cell membrane, vesicle fuses with membrane and toxins are released - Macrophage – removes waste and dead cells (high concentration of lysosome)
Mitochondria		- Produces ATP (energy) - Cellular respiration - Theory mitochondria were bacteria and evolved into cell organelle
Cytoskeleton		

ENDOMEMBRANE SYSTEM

The Skeletal System

Bone

- Living tissue
- 206 bones
- Grouped according to shape
  - long eg femur
  - short eg tarsals, metatarsals
  - flat eg skull, clavicle
  - irregular eg vertebrae
- 25% organic, collagen
- 50% inorganic, calcium and phosphate
- 25% water
- Used for support, structure, to protect organs, production of blood cells and storage of inorganic calcium and phosphorus salts

Bone Cell types

- Osteoblasts (build bone)
- Osteocytes (maintain bone)
- Osteoclasts (breakdown bone)

Long bone

- End of any long bone = epiphysis
- Shaft of long bone = diaphysis

Compact Bone

- Solid matrix – strength and rigidity
- Haversian systems/canals
  - made up of concentric circles
  - central canal allows blood circulation (ie the vein/artery to pass through)
- Lamella layers are directly around the central canal and a few radiate away from the central canal
  - In each lamella there are lacunae (cavities) which hold the osteocytes (maintain the bone)
  - Canaliculi are lines radiating from the central canal or ridges in the bone matter, they allow osteocytes to make contact with each other. Nutrients from the artery can pass from one osteocyte to another and remove waste.
- Periosteum – outside connective tissue layer of the bone, has blood vessels which feed to the central canal. Contain osteogenic stem cells, the cells that will differentiate into osteoblasts/cytes.

Cancellous or spongy bone

- Honey comb matrix
- Endosteum covers the trabeculae
- Endosteum contains blood cells and osteogenic stem cells
- Trabeculae – holes in spongy bone, surrounded by osteoblasts and osteocytes toward the centre, osteoclasts too
- Gaps of branches are filled by bone marrow
- When a baby is born, babies bones are filled with red marrow (red blood cells, white blood cells, and blood substances), this recedes to the epiphyses by puberty and is replaced by yellow marrow (fat cells)

Bone formation – ossification

- Embryo (3 months)
- Modelled on connective tissue
- Intramembranous ossification is when a membrane is used as a template to build the bone, used in the formation of flat bone
- Endochondral ossification uses a cartilage as a template to build the bone
  - After the third month, the Periosteum is developed – its osteoblasts infiltrate the blood vessels bringing with them haemopoitic stem cells and osteoclasts then shape the bone (central canal, epiphysis, spongy bone).
  - The growth of the bone changes from the shaft to the epiphysis and the growth plates continue to differentiate into the osteoblasts until the end of puberty

Bones are continuously remodeled

- Appositional growth – the formation of new bone on the surface of older bone or cartilage. While you are building you have to break down, after a 6 month period you are replenished with new bone.

- Osteoblasts are stimulated by stresses on the bone

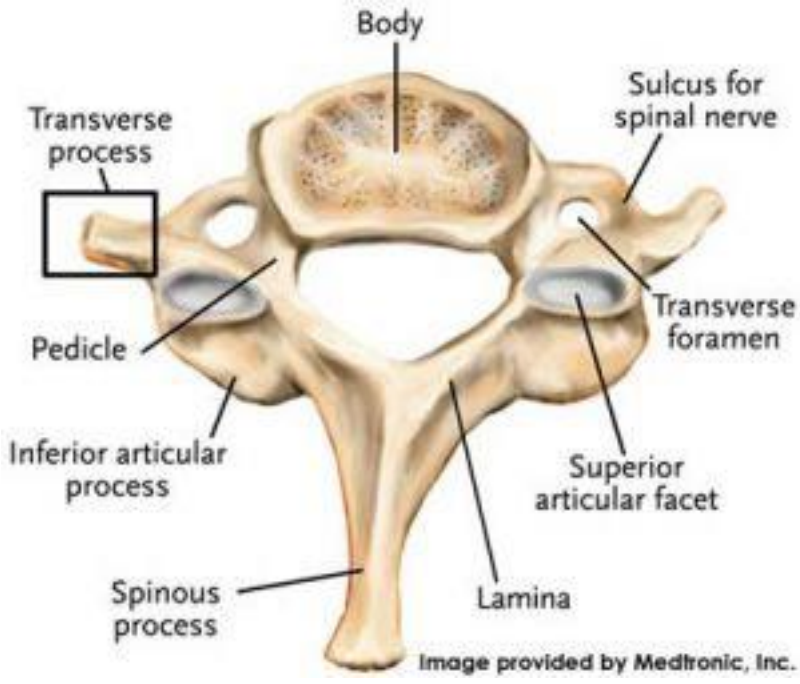
Calcium Homeostasis

- Diagram
- Low blood calcium, receptor in brain which sends a signal down to the parathyroid gland (located posterior to the thyroid gland), releases parathyroid hormone PTH, 3 effects
  - stimulate osteoclasts to break down bone, release it into the blood
  - promotes kidneys to reabsorb calcium from urine
  - stimulate vitamin D formation in kidneys → stimulates calcium reabsorption from digestive system
- High blood calcium stimulates thyroid gland (anterior), produce calcitonin which inhibits osteoclast activity (expand?)
- Increase PTH = Increase blood calcium
- Increase Calcitonin = decrease blood calcium

Vertebral column

- The functions of the vertebral column are to protect the spinal chord, attach ribs and pelvic girdle, and for flexibility

- Transverse process
  - sticks out of vertebrae and attaches to ribs
- Foramen
  - hole for blood vessels to neck and brain
- Spinous process
  - Sticks out back
- Articular facets
  - joints in the spine that allow motion, one pair faces upward and one downward
- Intervertebral discs
  - shock absorber, protect the vertebrae and nerves. Found in between vertebrae
- Body
  - major area of bone



Cervical vs Thoracic

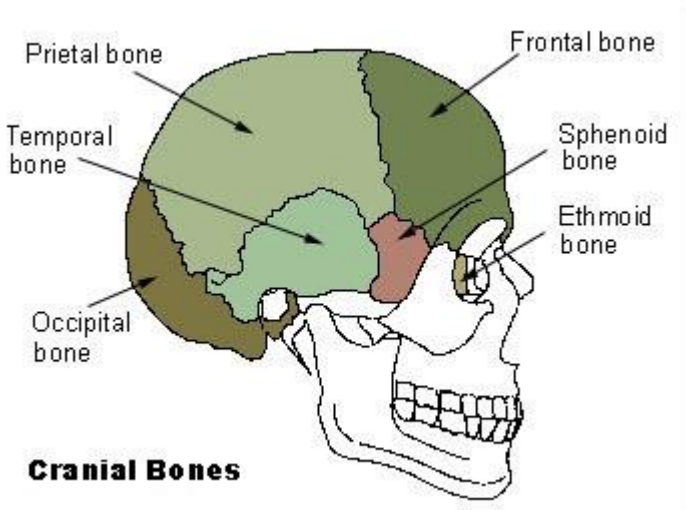
- Cervical 1-7, much smaller
- Cervical has transverse foramen, no transverse process
- Thoracic has transverse process, no transverse foramen

Atlas(C1) vs Axis(C2)

- Axis has dens(process), a spinous process and a kidney shaped vertebral foramen
- Atlas has large vertebral foramen and is round

Skeletal system

- Bones from prac/online
- Axial skeleton (3)
  - Skull (frontal, parietal, temporal, occipital)



-
  - vertebral column (cervical, thoracic, lumbar, sacrum, coccyx)
  - Ribs and sternum
- Appendicular Skeleton
  - Pectoral girdle bones, scapula and clavicle
  - Pelvic girdle, coxal bones
  - Upper limb, humerus, radius, ulna, carpals, metacarpals, phalanges
  - Lower limb, femur, patella, tibia, fibula, metatarsals, phalanges

Types of joints

- Fibrous joints (fixed)
  - Sutures between skulls
  - Jaw and teeth
  - joined by dense regular connective tissue
  - Most stable and least mobile
- Cartilingous joints (slight movement
  - Ribs and the sternum, bones joined by cartilage eg between adjacent vertebra, between coxal bones
  - Joined together by cartilage

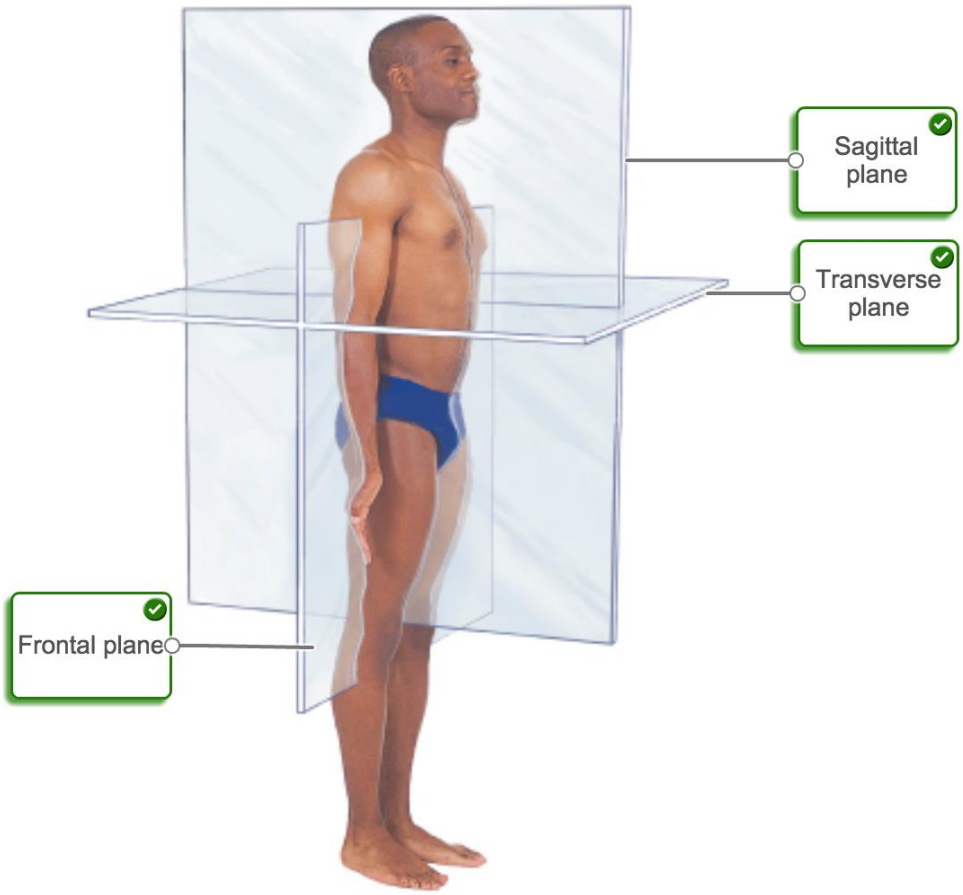
- Synovial joints (free movement)
  - Capsule surrounding articulating bones filled with synovial fluid eg elbow, shoulder, hip and knee
  - Cartilage and synovial fluid
  - Most mobile and least stable

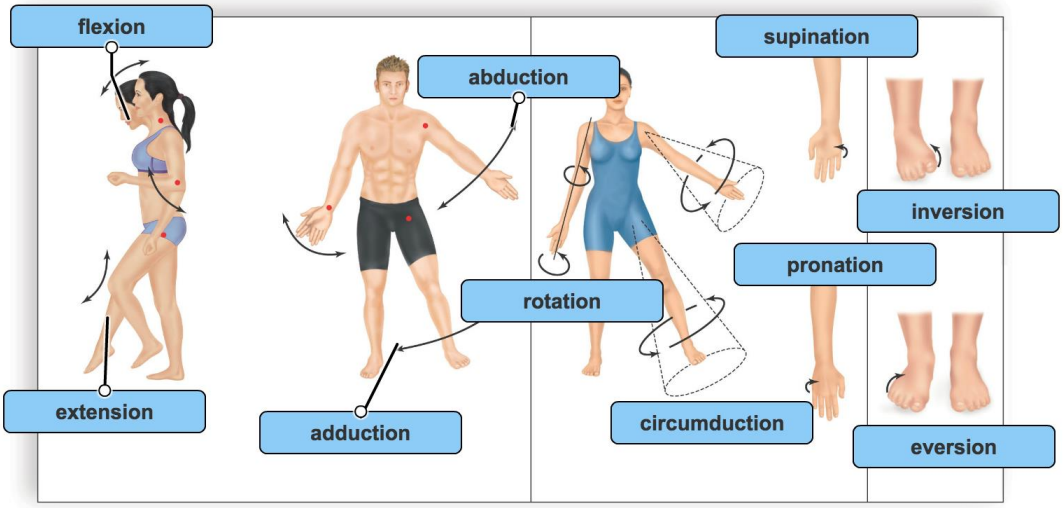
Anatomical terms and relationships

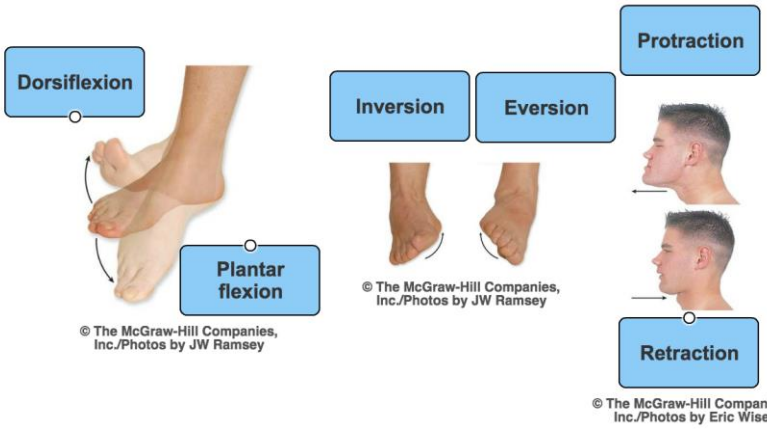
- Superior (top)
- Inferior (bottom)
- Anterior (front) – also known as ventral
- Posterior (back) – also known as dorsal
- Medial – toward middle
- Lateral – toward side
- Proximal – toward trunk
- Distal – toward extremities
- Prone – chest down back up
- Supine – back down chest up
- Abduction – movement of a limb away from the midline of the body
- Adduction – movement of a limb toward the midline of the body

Planes of The Body

- The coronal plane lies side to side through the body
- The sagittal plane passes from front to back
- The midsagittal passes from front to back through the midline of the body
- The transverse plane passes through the long axis of the body, dividing it into top and bottom
- Oblique plane is one that is slanted through the body


Sagittal plane
Transverse plane
Frontal plane


flexion
extension
abduction
adduction
rotation
circumduction
supination
inversion
pronation
eversion


Dorsiflexion
Plantar flexion
© The McGraw-Hill Companies, Inc./Photos by JW Ramsey
Inversion
Eversion
© The McGraw-Hill Companies, Inc./Photos by JW Ramsey
Protraction
Retraction
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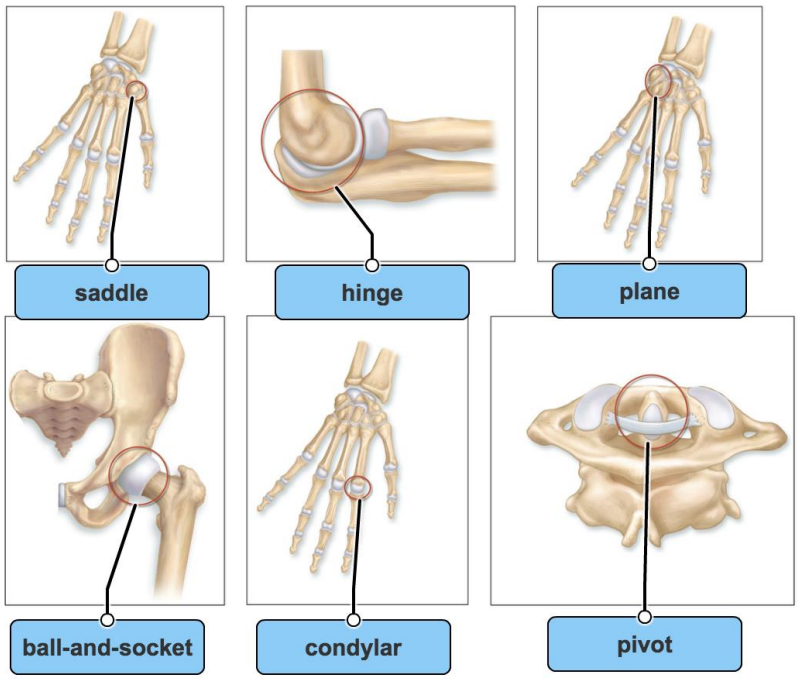
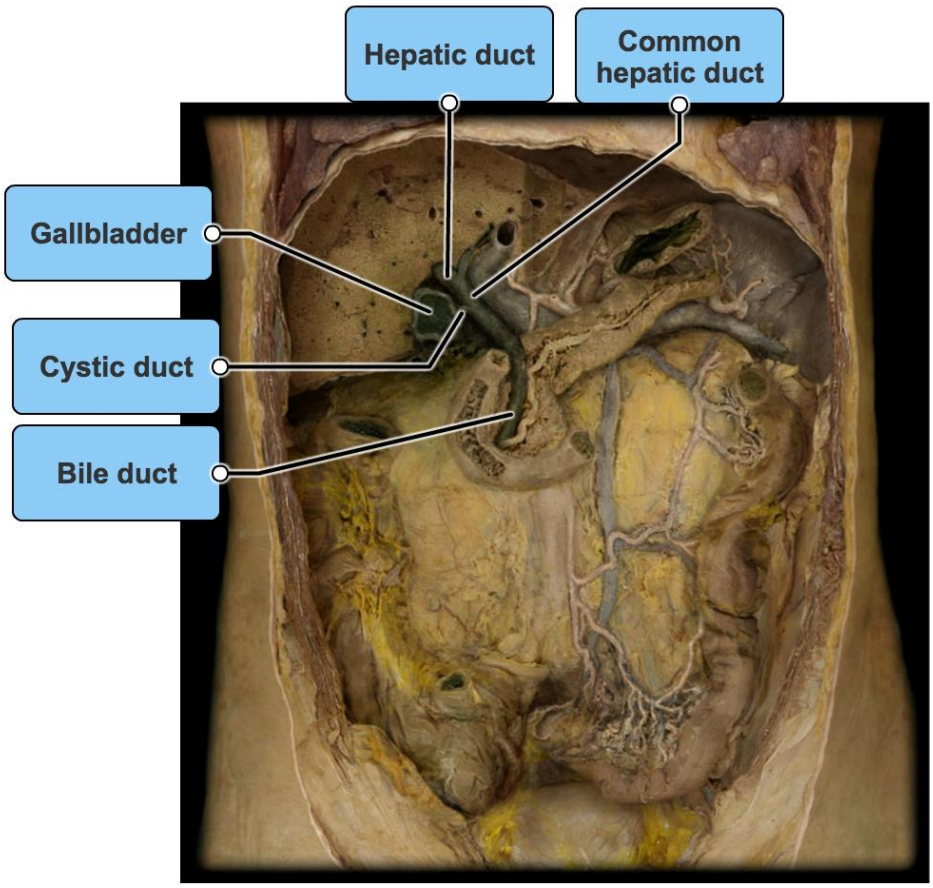
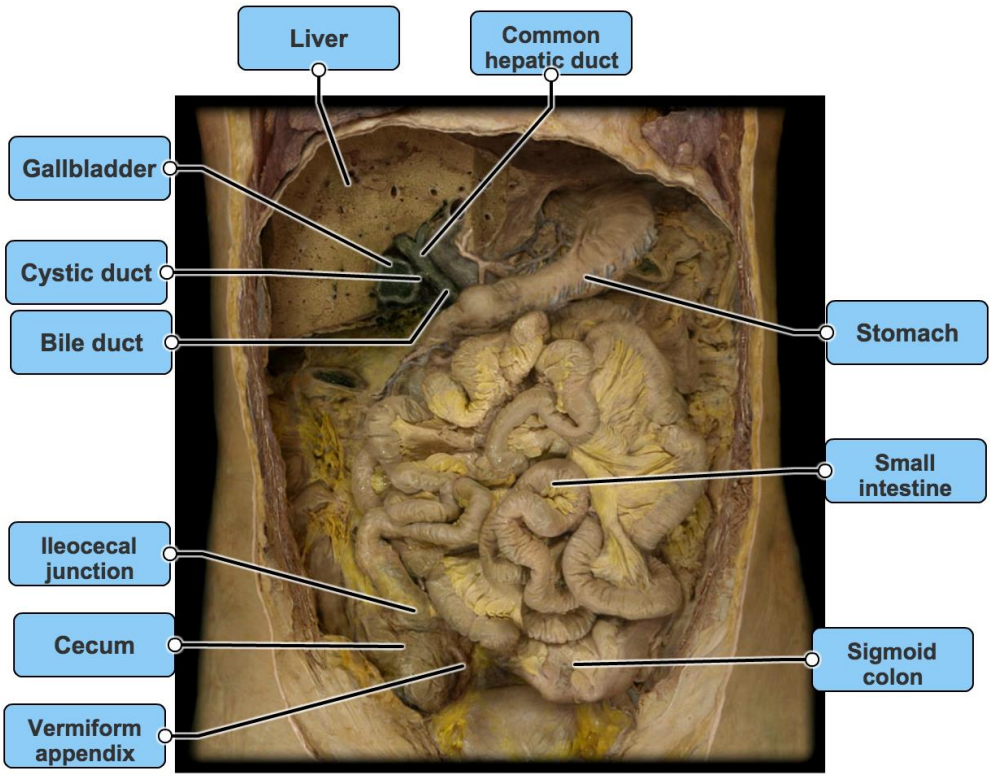
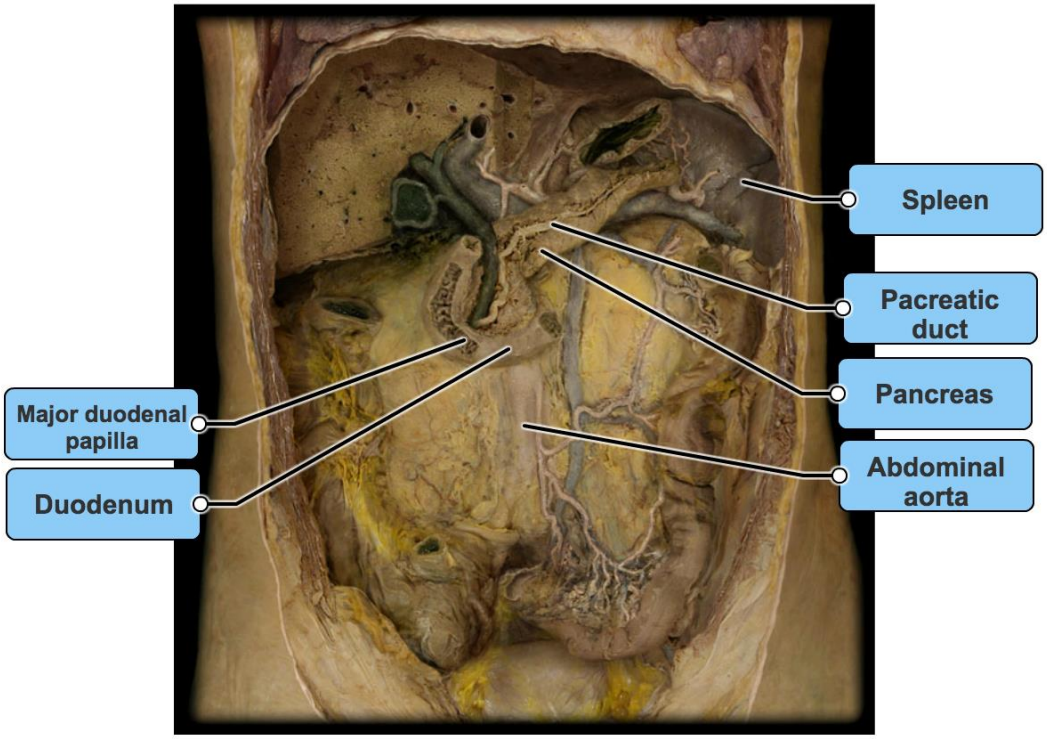
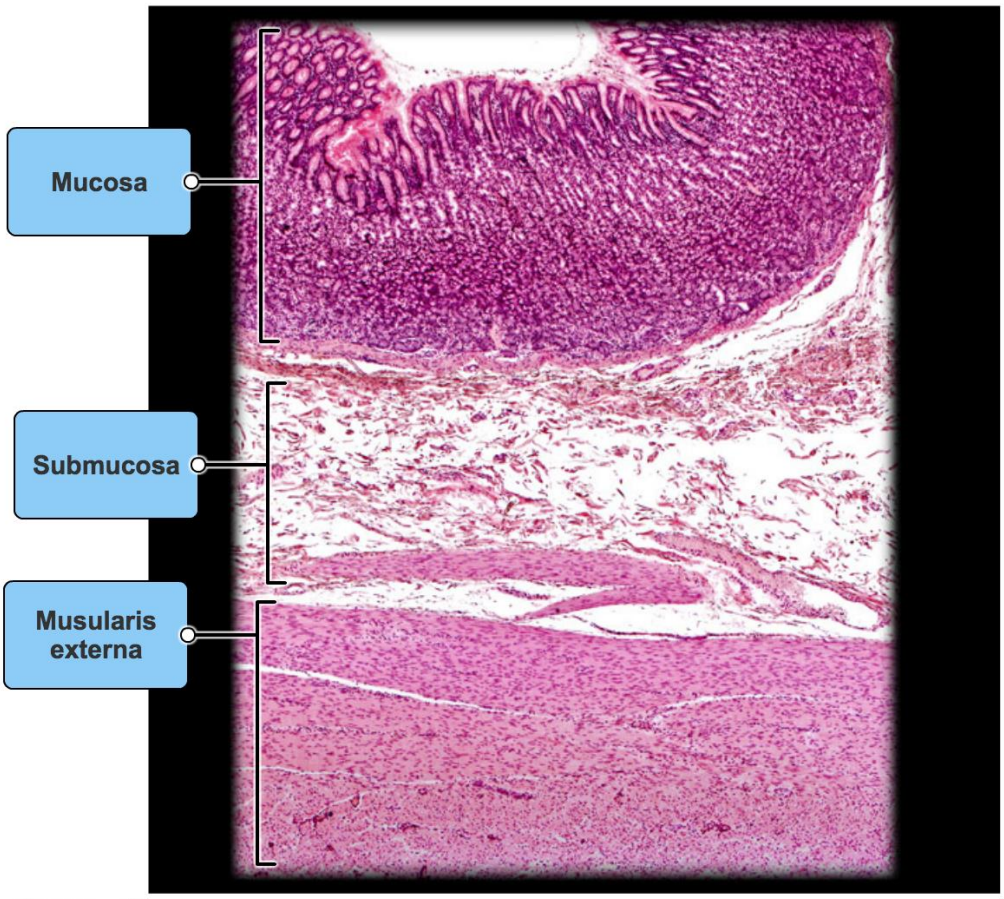

saddle
hinge
plane
ball-and-socket
condylar
pivot

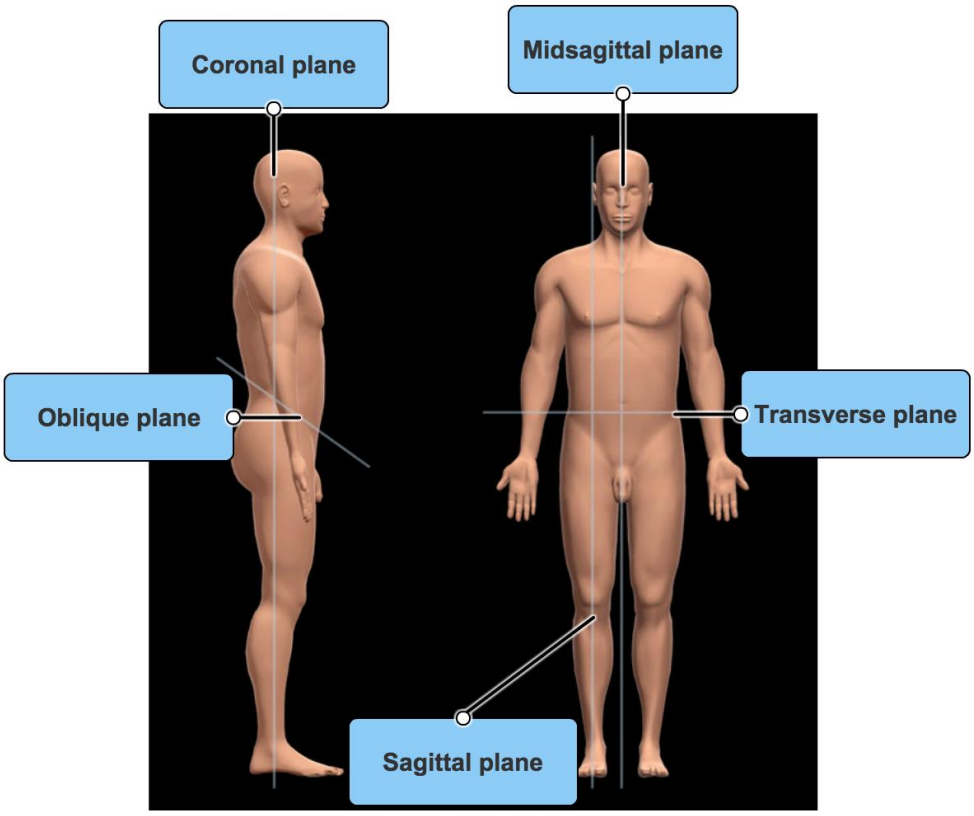

Hepatic duct
Common hepatic duct
Gallbladder
Cystic duct
Bile duct


Liver
Common hepatic duct
Gallbladder
Cystic duct
Bile duct
Stomach
Small intestine
Ileocecal junction
Cecum
Sigmoid colon
Vermiform appendix


Spleen
Pacreatic duct
Pancreas
Abdominal aorta
Major duodenal papilla
Duodenum


Mucosa
Submucosa
Musularis externa

Reset Zoom


Coronal plane
Midsagittal plane
Oblique plane
Transverse plane
Sagittal plane