BME205 – Fundamentals of Biomedical Engineering

Harder version of grade 12 bio

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[1] *TeX file on GitHub*

Contents

PART

I

The Foundation of Physiology

Section 1

Homeostasis

- internal environment is held relatively constant within an organism
- more of a steady state oscillation instead of equilibrium (equilibrium is more like being dead, nothing chagning)

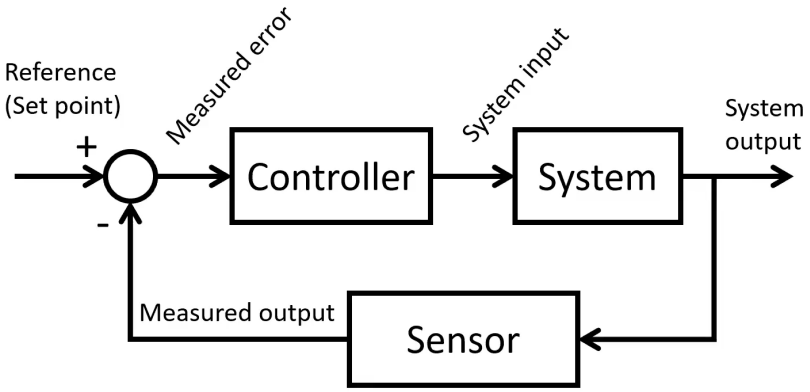


Figure 1. Negative feedback control loop flow diagram

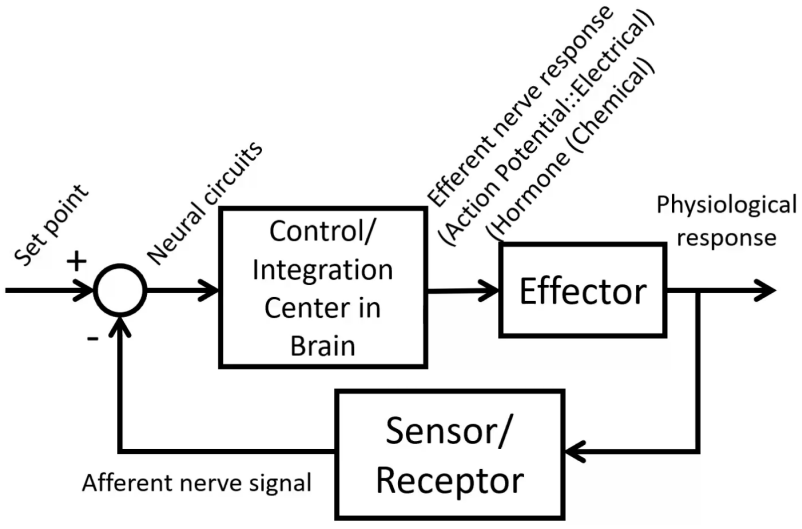


Figure 2. Same control loop but with more physiological terms

- idea is that the negative feedback is equivalent to some difference between a reference point R and some sensor value S :

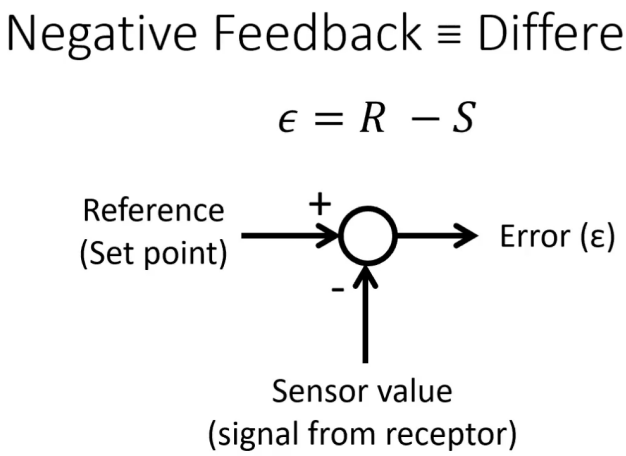


Figure 3.

- example: regulating body temperature

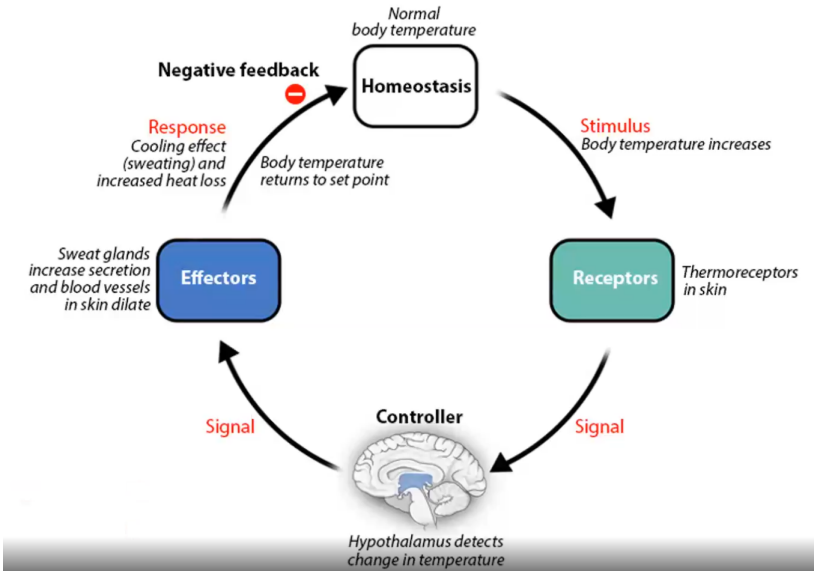


Figure 4.

- for any feedback loop, you should be able to identify:
  - the physiological variable
  - what and where the sensor is
  - where in the brain the control centre is
  - what and where the effectors are

PART II

Cell Physiology

Section 2

Cell Structure

TABLE 2-2 Summary of Cell Structures and Functions

Cell Part	Structure	Function
Plasma membrane	Lipid bilayer studded with proteins and small amounts of carbohydrate	Acts as selective barrier between cellular contents and extracellular fluid; controls traffic in and out of the cell
Nucleus	DNA and specialized proteins enclosed by a double-layered membrane	Acts as control centre of the cell, providing storage of genetic information; nuclear DNA provides codes for the synthesis of structural and enzymatic proteins and serves as blueprint for cell replication
Cytoplasm		
Organelles		
Endoplasmic reticulum	Extensive, continuous membranous network of fluid-filled tubules and flattened sacs, partially studded with ribosomes	Forms new cell membrane and other cell components and manufactures products for secretion
Golgi complex	Sets of stacked, flattened membranous sacs	Modifies, packages, and distributes newly synthesized proteins
Lysosomes	Membranous sacs containing hydrolytic enzymes	Serve as digestive system of the cell, destroying foreign substances and cellular debris
Centriole	Usually paired, small barrel-shaped organelles that consist of nine short triplet microtubules	Site of growth of new microtubules: both cytoplasmic transport microtubules and the microtubules that form the mitotic spindle
Peroxisomes	Membranous sacs containing oxidative enzymes	Perform detoxification activities
Mitochondria	Rod- or oval-shaped bodies enclosed by two membranes, with the inner membrane folded into cristae that project into an interior matrix	Act as energy-producing organelles; major sites of ATP production; contain enzymes for citric acid cycle and electron transport chain
Vaults	Shaped like hollow octagonal barrels	Serve as cellular trucks for transport from nucleus to cytoplasm
Cytosol: gel-like portion		
Intermediary metabolism enzymes	Dispersed within the cytosol	Facilitate intracellular reactions involving the degradation, synthesis, and transformation of small organic molecules
Ribosomes	Granules of RNA and proteins—some attached to rough endoplasmic reticulum, some free in the cytoplasm	Serve as workbenches for protein synthesis
Transport, secretory, and endocytotic vesicles	Transiently formed, membrane-enclosed products synthesized within or engulfed by the cell	Transport and/or store products being moved within, out of, or into the cell, respectively
Inclusions	Glycogen granules, fat droplets	Store excess nutrients
Cytosol: cytoskeleton portion		As an integrated whole, serves as the cell's "bone and muscle"
Microtubules	Long, slender, hollow tubes composed of secretory vesicles	Maintain asymmetric cell shapes and tubulin molecules; coordinate complex cell movements, specifically facilitating transport of secretory vesicles within cells, serving as main structural and functional component of cilia and flagella, and forming mitotic spindle during cell division
Microfilaments	Intertwined helical chains of actin molecules; microfilaments composed of myosin molecules also present in muscle cells	Play a vital role in various cellular contractile systems, including muscle contraction and amoeboid movement; serve as a mechanical stiffener for microvilli
Intermediate filaments	Irregular, threadlike proteins	Help resist mechanical stress

Figure 5. Cell Structures and Functions

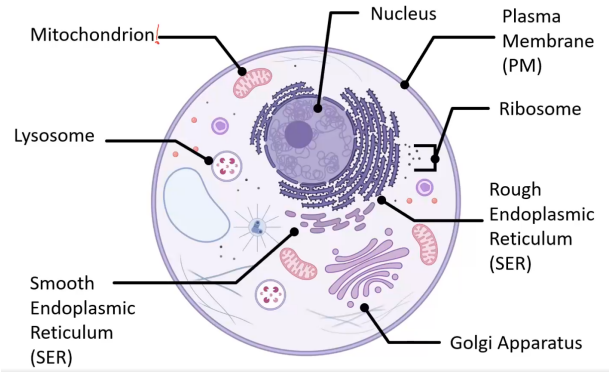


Figure 6. Cell organelles.

2.0.1 The Nucleus

- control centre of cell
- has a nuclear envelope made of two lipid bilayer membranes
- passageways for proteins, called "pores"
- inside nucleus: the nucleolus, responsible for manufacturing RNA (necessary for construction of ribosomes)

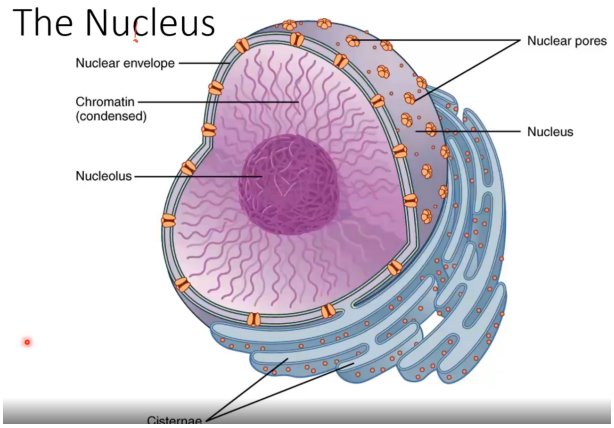


Figure 7. The nucleus.

Section 3

DNA Transcription and Translation

- DNA – double stranded nucleic acid that stores genetic information

Subsection 3.1

DNA Structure

- made from 2 polynucleotide chains

- DNA supercoils into chromosomes
- Levels of complexity of DNA are shown in Figure 8

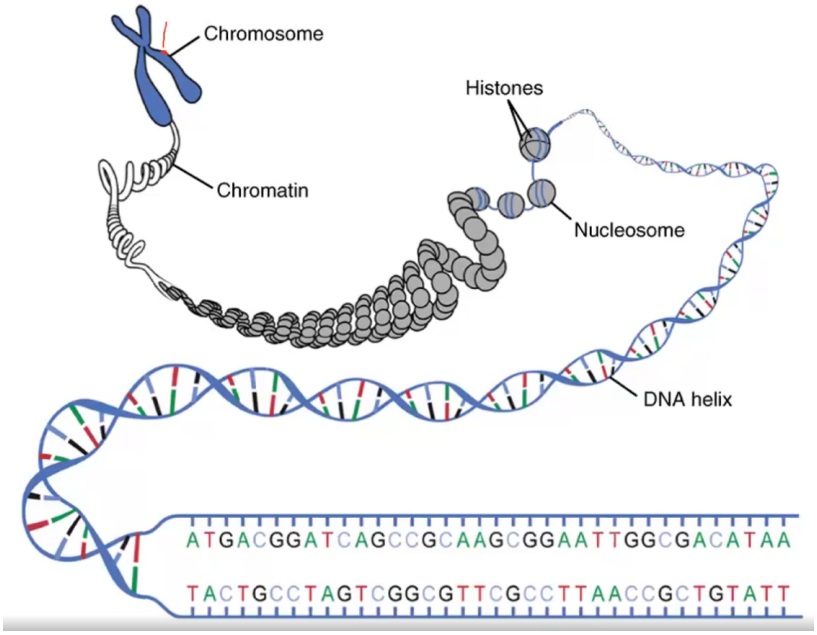


Figure 8. Levels of complexity of DNA.

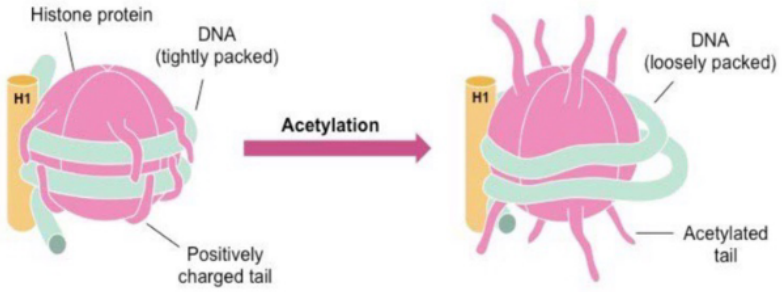


Figure 9. Histone tails trap down the DNA.

- there are different kinds of nucleosome packing: euchromatin for high transcriptional activity, heterochromatin for little to no transcriptional activity
- each nucleotide contains a sugar (deoxyribose), phosphate group, and nitrogenous base
- 4 N-bases: adenine (A), guanine (g), thymine (T), cytosine (C)
  - C and T have one ring structure, G and A have two ring structure
- A-T pair, G-C pair

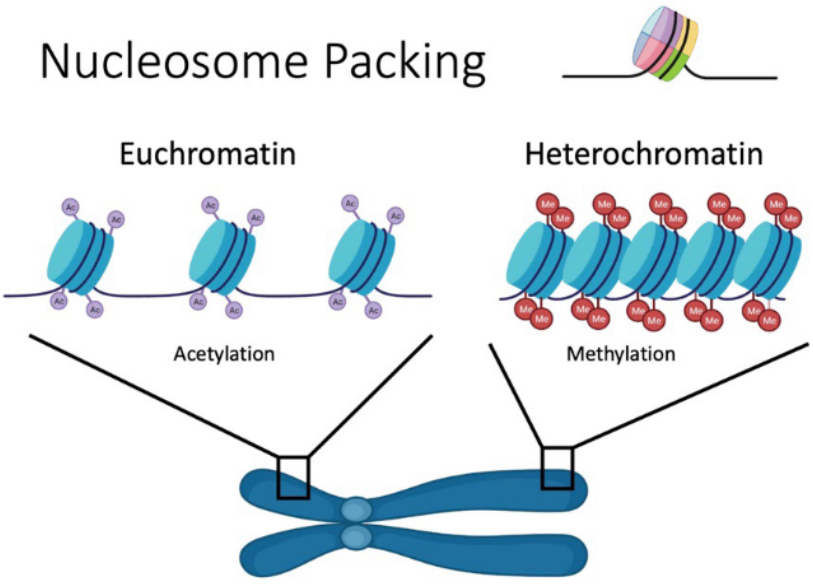


Figure 10. Nucleosome packing.

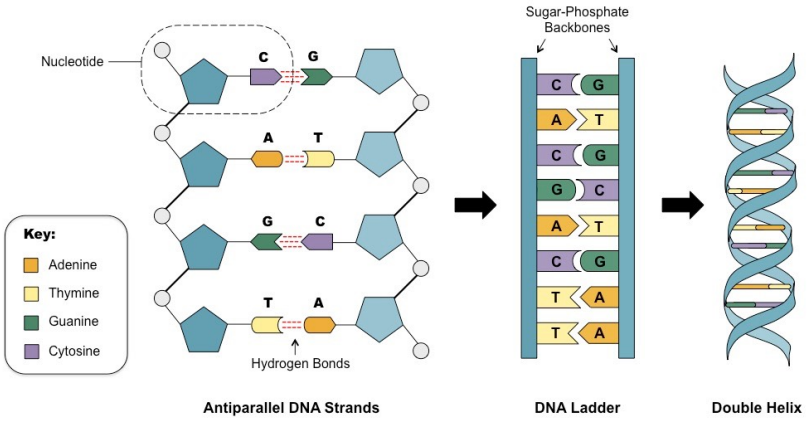


Figure 11. DNA structure.

Subsection 3.2
DNA Transcription

- first step in gene expression: copy gene's DNA sequence to make an RNA molecule
- DNA is used as a template for complementary base-pairing
- performed by enzymes called RNA polymerase – links nucleotides to form an RNA strand using DNA strand as template
- in eukaryotes, RNA must be processed after transcription (spliced and have 5' cap at beginning and 3' poly A tail)

Subsection 3.3
DNA Translation

- DNA translation has 3 stages: initiation, elongation, termination
- Initiation: ribosome joins mRNA and first tRNA to form initiation complex
- Elongation: amino acids are brought by tRNA and linked to form chain
  - protein chain gets longer
- Termination: finished protein is released to do job in cell
  - when 'stop' codon in mRNA (UAA, UAG, or UGA) enters A site, recognized by release factors (proteins)
  - H_2O is added to the acid, causing separation

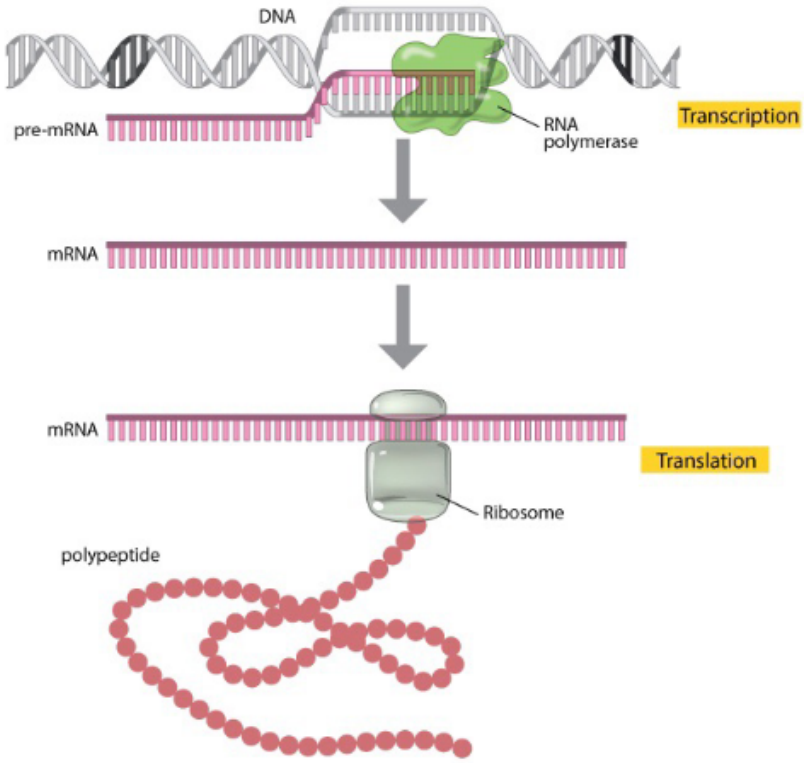


Figure 12. Summary of DNA transcription and translation.

Section 4

Cellular Metabolism

- **intermediary metabolism**: chemical reactions inside the cell that involve degradation, synthesis, and transformation of small organic molecules (e.g. sugars, amino acids, and fatty acids)
  - all of these chemical reactions happen in the cytoplasm
  - most of it happens in the cytosol, which contains thousands of enzymes involved in glycolysis and other intermediary biochemical reactions

- **Anabolic processes**: synthesis of molecules for building up organs and tissues
- **Catabolic processes**: breakdown of complex molecules into simple ones
- cells require energy for anabolic processes (building complex molecules)
- this energy comes from carbon bonds of ingested food
- cells convert this energy into a usable form of energy: high-energy phosphate bonds in **adenosine triphosphate (ATP)**
- to obtain energy from ATP, cells split phosphate bond in ATP, which gives **adenosine diphosphate (ADP)**:

$$\text{ATP} \rightarrow \text{ADP} + P_i + \text{energy for use by the cell.}$$

- chemical pathways for production of ATP involve 3 separate processes:
  1. substrate-level phosphorylation
  2. anaerobic glycolysis
  3. aerobic metabolism
- majority of ATP is generated from sequential dismantling of absorbed nutrient molecules in 4 steps:
  1. glycolysis (both aerobic and anaerobic)
  2. decarboxylation of pyruvate
  3. tricarboxylic acid cycle (TCA; aerobic)
  4. electron transport chain (ETC; aerobic)

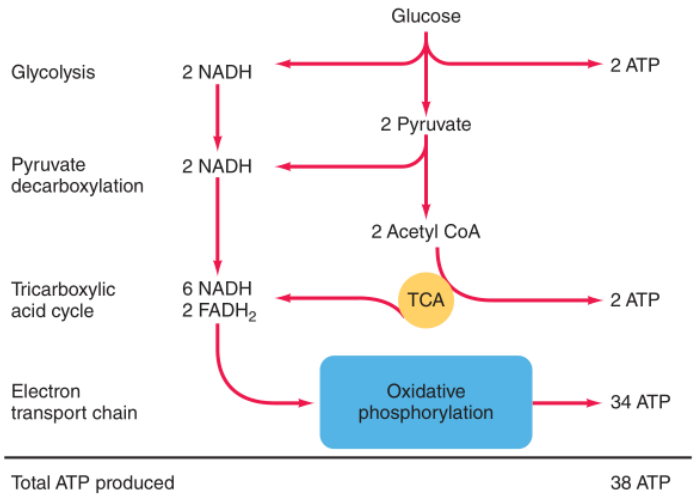


Figure 13. Overview of ATP production. Maximum theoretical yield from 1 glucose is 38 ATP.

4.0.1 Pathways for Production of ATP

Substrate-Level Phosphorylation

- some tissues (skeletal muscle) have low concentrations of ATP – need to have quick ready supply of ATP
- **phosphorylation**: adding phosphate group to an organic molecule
- phosphorylation of ADP using creatine phosphate (CP) generates ATP
- reaction catalyzed by skeletal muscle cell enzyme creatine kinase

$$\text{CP} + \text{ADP} \longleftrightarrow \text{creatine} + \text{ATP}.$$

Glycolysis

- breaks down glucose into 2 pyruvic acid molecules
- occurs in the cytosol
- some of the released energy is directly used to convert ADP to ATP while also producing NADH
- not really efficient at it though: most of the energy is still stored in the pyruvic acid molecules produced (what the mitochondria is for)

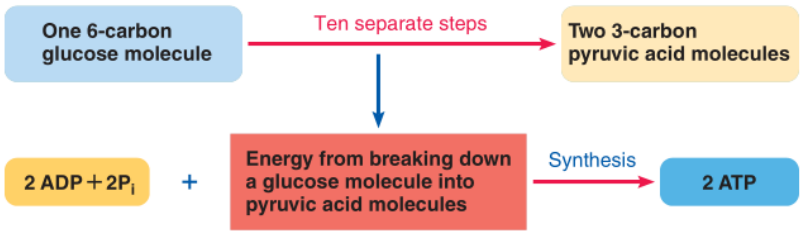


Figure 14. Simplified summary of glycolysis. Net yield of 2 ATP and 2 NADH.

Pyruvate Decarboxylation

- pyruvic acid (produced in cytosol by glycolysis) enters mitochondrial matrix through carrier protein monoccarboxylate transporter (located on inner mitochondrial membrane)
- inside mitochondria: pyruvate is metabolized by pyruvate dehydrogenase complex and decarboxylated
  - Decarboxylation: removal of a carbon, formation of CO_2, and formation of 1 NADH
- pyruvate is converted to acteyl CoA – now ready to enter TCA cycle

Tricarboxylic Acid Cycle

- key purpose of Krebs cycle: produce hydrogens for entry into the ETC, which will be caught by NAD^+ and FAD to form NADH and $FADH_2$
- the 2 carbons from acetyl CoA are converted into CO_2
- oxaloacetic acid accepts acetyl CoA at start of cycle, and is regenerated at the end of cycle for use again
- 1 molecule of ATP is produced for each acetyl CoA

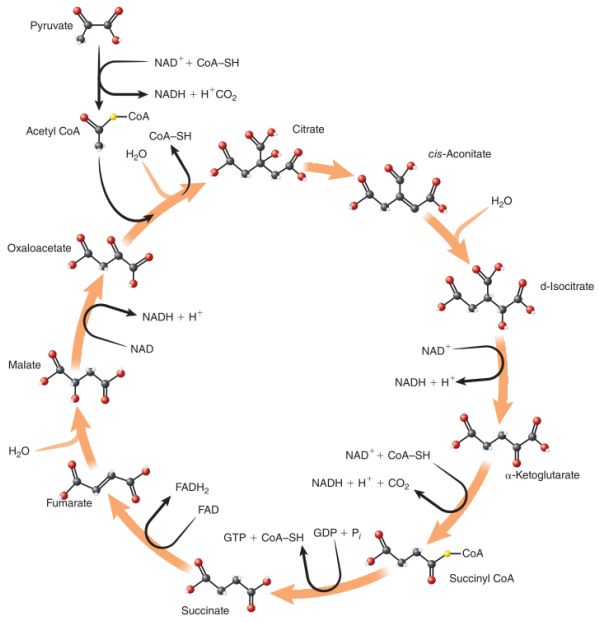


Figure 15. Krebs Cycle.

Electron Transport Chain

- NADH and $FADH_2$ drop off hydrogens at ETC
- hydrogen ions are pumped into intermembrane space – build up high concentration
- the enzyme ATP synthase is activated by the flow of hydrogen ions back to the mitochondrial matrix and makes ATP through oxidative phosphorylation
- NADH enters ETC early, produces 3 ATP; $FADH_2$ enters later, produces 2 ATP

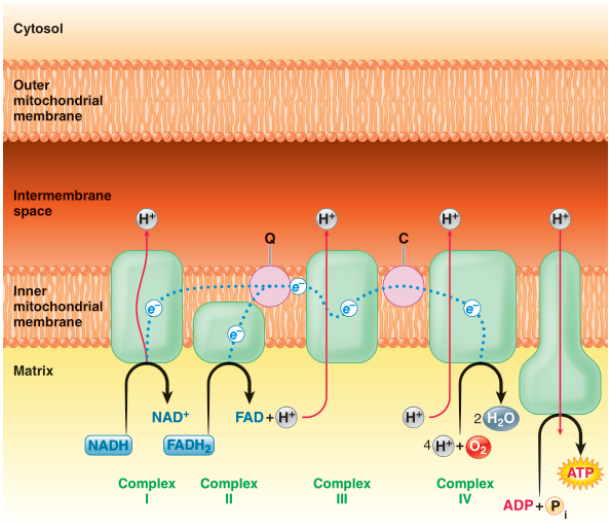


Figure 16. Oxidative phosphorylation at the Electron Transport Chain. ATP synthesis relies on movement of hydrogen ions across inner mitochondrial membrane.

4.0.2 Practical ATP Yield

- theoretical maximum of 38 ATP assumes: (1) NADH produced in glycolysis in the cytosol doesn't need energy to be transported to the ETC, (2) ETC is 100% efficient
  - cells may require ATP to shuttle NADH from cytosol into mitochondria
  - ETC usually produces 2 or 3 ATP from NADH (use 2.5) and 1 or 2 from $FADH_2$ (use 1.5)
- actual yield is around 30 to 32 ATP (depending on how NADH from glycolysis gets to the ETC)

Section 5

The Cell Membrane

- bounds cells
- thin lipid bilayer with interspersed proteins with carbohydrates on outer surface
- cholesterol is tucked in the layer and helps with fluidity and stability of membrane
- bilayer is embedded with proteins with many purposes:
  - channels for passage of small ions across teh membrane
  - carriers for transport of specific substances in or out of the cell
  - docking-marker acceptors for fusion with and subsequent exocytosis of secretory vesicles ????????
  - membrane-bound enzymes that govern specific chemical reactions
  - receptors for detecting and responding to chemical messengers that alter cell function
  - cell adhesion molecules that help hold cells together and serve as a structural link between the extracellular surroundings and intracellular cytoskeleton
- membrane carbohydrates serve as self-identity markers – important for cell to cell interactions

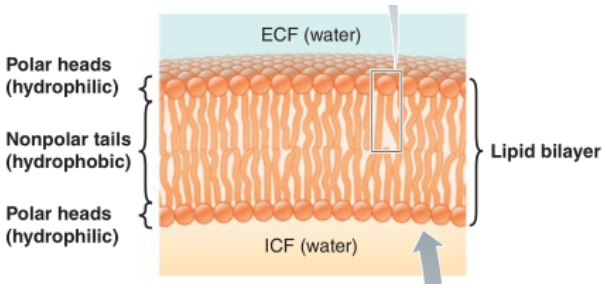


Figure 17. Phospholipid bilayer.

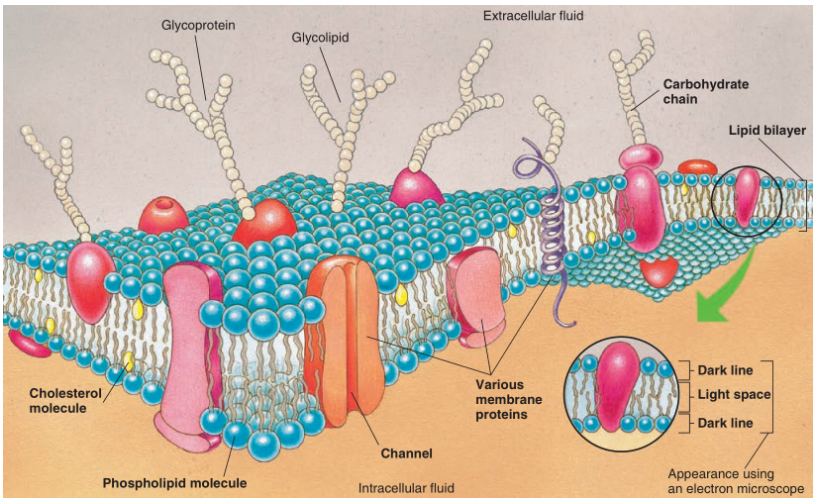


Figure 18. Fluid mosaic model of plasma membrane structure.

Section 6

Cell-to-Cell Adhesions

- some cells need to stay together (cells of the same tissue)
- some cells within given types of tissues are directly linked by gap junctions (specialized cell junction)

Subsection 6.1

Gap Junctions

- communicating junctions between 2 adjacent, but not touching cells
- connected by small tunnels made up of connexons that permit exchange of ions and small molecules between adjacent cells
- important in spreading electrical activity

Section 7

Membrane Transport

- materials can be passed between extracellular fluid (ECF) and intracellular fluid (ICF) by unassisted/assisted means
- transport mechanisms can be:
  - passive – particle moves across membrane without cell expending energy
  - active – cell must expend energy

Section 8

Unassisted Membrane Transport

- for lipid-soluble particles/ions

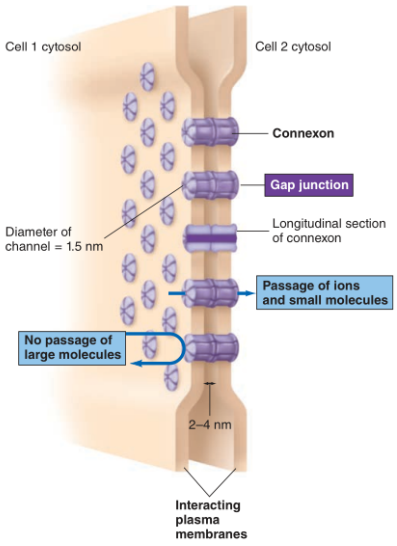


Figure 19. Gap junction.

- **Diffusion**: for non-polar (lipid soluble) moleuclues of any size can dissolve in and pass through bilayer down gradients
  - small ions traverse membrane passively down electro-chemical gradients through specific open protein channels
- **Osmosis** – special case where water passively moves down its own concentration gradient to area with higher solute concentration

Section 9

Assisted Membrane Support

- for small polar molecules and selected ion movements

Subsection 9.1

Carrier-mediated transport

- particle transported by specific membrane carrier proteins
- carrier-mediated transport takes two forms: passive (facilitated diffusion) and active transport
- carriers can move:
  - 1 substance in one direction
  - 2 in opposite direction
  - 2 in same direction

9.1.1 Passive transport

- facilitated diffusion down concentration gradient (high to low concentration)

9.1.2 Active transport

- requires carrier to expend energy to transfer particle against concentration gradient (low to high concentration)

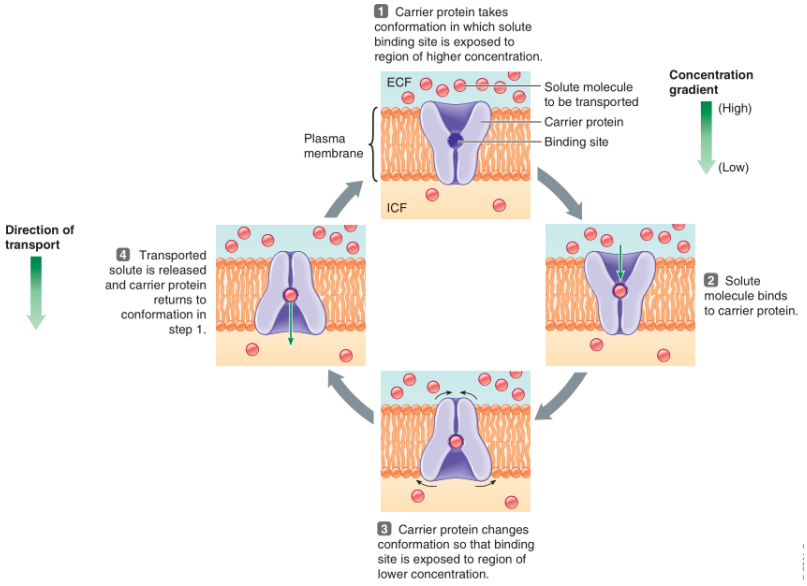


Figure 20. Example of facilitated diffusion.

Primary Active Transport

- requires ATP directly to drive the pump

Secondary Active Transport

- energy is not directly required to run the pump
- uses second-hand energy stored in the form of ion concentration gradient (e.g. Na^+ gradient) made by primary active transport

Subsection 9.2
Vesicular Transport

- for large polar molecules (since some can't permeate the membrane)
- leave (exocytosis) and enter (endocytosis) cell by being wrapped in a piece of membrane to form a vesicle

Section 10
Intracellular Communication

- cells need to communicate with each other to do stuff

Section 11
Membrane Potential

- separation of opposite charges due to relative number of cations and anions in the ICF vs ECF
- enables communication in nervous tissue and muscle

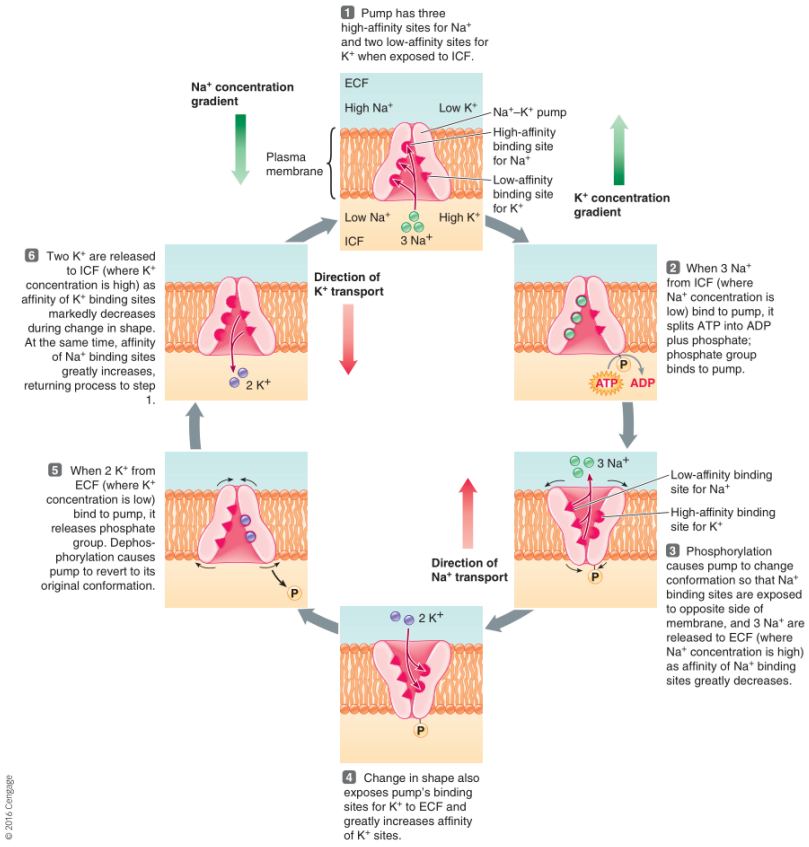


Figure 21. Na^+-K^+ ATPase pump. Important example of primary active transport. It uses energy in the carrier's phosphorylation-dephosphorylation cycle to sequentially transport Na ion out of the cell and K ion into the cell against their concentration gradients. It moves 3 Na out and 2 K in for each ATP split.

TABLE 2-3 Characteristics of the Methods of Membrane Transport

Methods of Transport	Substances Involved	Energy Requirements and Force-Producing Movement	Limit to Transport
Diffusion			
Through lipid bilayer	Nonpolar molecules of any size (e.g., O_2, CO_2, and fatty acids)	Passive; molecules move down concentration gradient (from high to low concentration)	Continues until the gradient is abolished (steady state with no net diffusion)
Through protein channel	Specific, small ions (e.g., Na^+, K^+, Ca^{2+}, and Cl^-)	Passive; ions move down electrochemical gradient through open channels (from high to low concentration and by attraction of ion to area of opposite charge)	Continues until there is no net movement and a steady state is established
Special case of osmosis	Water only	Passive; water moves down its own concentration gradient (water moves to area of lower water concentration, i.e., higher solute concentration)	Continues until concentration difference is abolished or until stopped by an opposing hydrostatic pressure or until cell is destroyed
Carrier-Mediated Transport			
Facilitated diffusion	Specific polar molecules for which a carrier is available (e.g., glucose)	Passive; molecules move down concentration gradient (from high to low concentration)	Displays a transport maximum (T_m); carrier can become saturated

Figure 22. Table of membrane transport methods.

- **equilibrium potential**: the electric potential across the cell membrane when the electrical gradient exactly balances the concentration gradient of the ion

TABLE 2-3 Characteristics of the Methods of Membrane Transport (*continued*)

Primary active transport	Specific ions or polar molecules for which carriers are available (e.g., Na^+, K^+, and amino acids)	Active; ions move against concentration gradient (from low to high concentration); requires ATP	Displays a transport maximum; carrier can become saturated
Secondary active transport	Specific polar molecules and ions for which cotransport carriers are available (e.g., glucose, amino acids, and some ions)	Active; molecules move against concentration gradient (from low to high concentration); driven directly by ion gradient (usually Na^+) established by ATP-requiring primary pump	Displays a transport maximum; cotransport carrier can become saturated
Vesicular Transport			
Endocytosis			
Pinocytosis	Small volume of ECF fluid; also important in membrane recycling	Active; plasma membrane dips inward and pinches off at surface, forming an internalized vesicle	Control poorly understood
Receptor-mediated endocytosis	Specific, large polar molecule (e.g., protein)	Active; plasma membrane dips inward and pinches off at surface, forming an internalized vesicle	Necessitates binding to specific receptor site on membrane surface
Phagocytosis	Multimolecular particles (e.g., bacteria and cellular debris)	Active; cell extends pseudopods that surround particle, forming an internalized vesicle	Necessitates binding to specific receptor site on membrane surface
Exocytosis	Secretory products (e.g., hormones and enzymes) as well as large molecules passing through cell intact; also important in membrane recycling	Active; increase in cytosolic Ca^{2+} induces fusion of secretory vesicle with plasma membrane; vesicle opens up and releases contents to outside	Secretion triggered by specific neural or hormonal stimuli; other controls involved in transcellular traffic and membrane recycling not known

Figure 23. Table of membrane transport methods, continued.

- equilibrium potential for a given ion of differing concentrations across a membrane is given by the **Nernst equation**:

Theorem 1 **Nernst Equation**: used to calculate equilibrium potential of an ion across a membrane

$$E_x = \frac{61}{Z_x} \log_{10} \frac{[C]_o}{[C]_i}$$

- E_x – equilibrium potential
- Z_x – valence (electrical charge for ion) (e.g. Z = 1 for Na ion)
- $[C]_o$ – concentration outside cell
- $[C]_i$ – concentration inside cell

Graphing Electrical-Chemical Gradients

Process:

Step 1: Set up graph with the Electrical Driving Force (V_m) on y-axis and Concentration Driving Force on the x-axis
Step 2: Find E_{ion}
Step 2: Plot, on the y-axis, the equilibrium potential E_{ion}
Step 4: Plot, on the x-axis, a point that is either positive or negative according to the concentration gradient when the potential is zero
Step 5: Connect the two points with a line
Step 6: Determine what the ion will do at the V_m

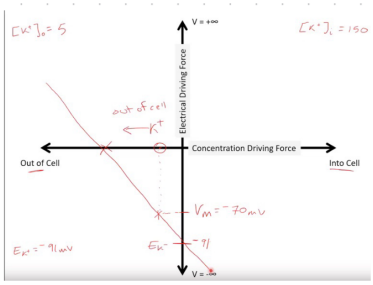


Figure 24. Process of grpahing electrical-chemical gradients.

Equilibrium Potential Balances (Diffusion and Electrical Potential)

$$\Delta G_{chem} = RT \ln \frac{[C]_o}{[C]_i}$$

and

$$\Delta G_{elec} = ZFV_m.$$

- where Z is charge, F is Faraday's constant (96500), V_m is voltage difference
- at equilibrium: $\Delta G_{chem} = \Delta G_{elec}$
- free energy moving out of cell:

$$\Delta G = \Delta G_{chem} - \Delta G_{elec}.$$

  - if $\Delta G < 0$: spontaneous (ion moves out of cell)
  - if $\Delta G > 0$: non-spontaneous (ion moves into cell)

Section 12

Graded Potentials

- local changes in membrane potential that occur in varying grades or degrees of magnitude or strength
- may or may not lead to action potential

Section 13

Action Potentials

- brief, large, rapid changes in membrane potential – potential reverses
- inside of excitable cell transiently becomes more positive than outside

Conduction via a Nerve Fibre

- **Contiguous conduction**: along unmyelinated axons
- **Saltatory conduction**: myelinated axons
- myelin acts like electrical tape with little bits exposed between
- Factors impacting speed of propogation:
  - amount of myelination
  - axon diameter
  - temperature

Section 14

Synapses

- **axon** (nerve fibre): conducts action potentials in undiminished fashion from axon hillock to terminals
- **synapse** (neural junction): site of transmission of electrical nerve impulses between 2 nerve cells (neurons)
- **synaptic cleft**: small space between neurons
- **presynaptic neuron**: sends signal
- **postsynaptic neuron**: receives signal
- chemical signals (neurotransmitters) packaged in vesciles and sent over

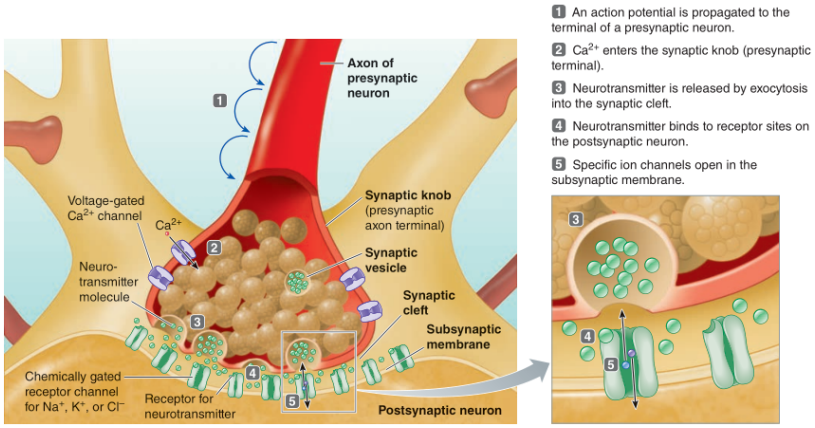


Figure 25. Synaptic structure and function. The events that occur at a synapse.

PART

III

The Central Nervous System

Section 15

Organization of the Nervous System

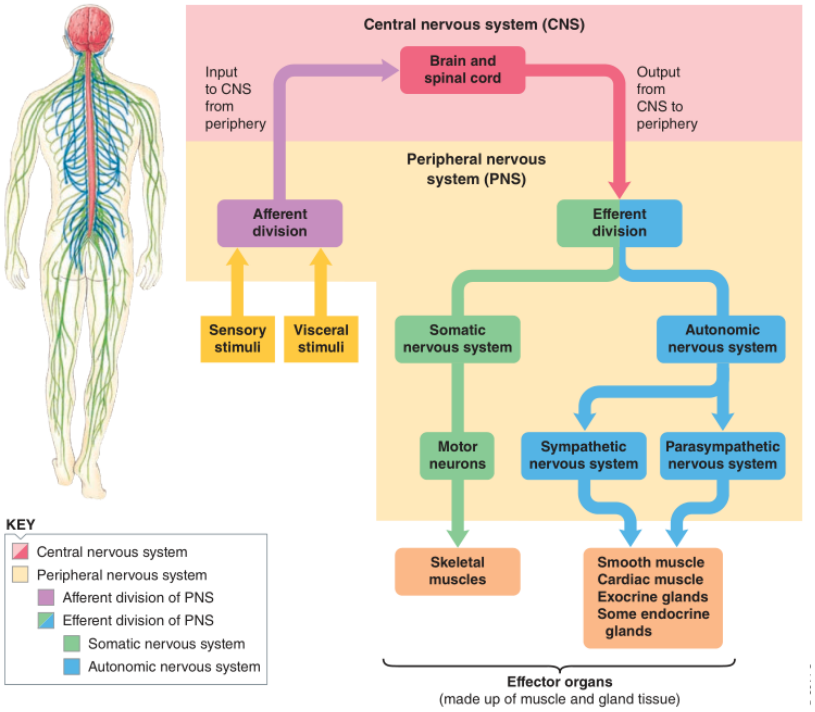


Figure 26. Organization of the Nervous System

- Central nervous system (CNS) consists of the brain and spinal cord
- Peripheral nervous system (PNS) consists of fibres that carryinformation between the CNS and other body parts
- the PNS is divided into the afferent and efferent divisions
- afferent – carries information to the CNS
- efferent – carries signals from the CNS to the effector organs
  - 2 subdivisions in efferent division:
    1. Somatic nervous system: consists of nerve fibres of the motor neurons that control skeletal muscles (conscious control)
    2. Autonomic nervous system consists of nerve fibres that innervate glands, cardiac muscles, and smooth muscles (unconscious control)
       * further subdivided into sympathetic (for fight-or-flight) and parasympathetic (inhibits overworking) nervous system

Subsection 15.1
Three Functional Classes of Neurons

- afferent, efferent, and interneurons

Afferent

- in the afferent division
- shaped differently from the other two
- has a sensory receptor at its peripheral ending
  - which generates action potentials in response to a stimulus (e.g. touch)
- soma (cell body) is devoid of dendrites and adjacent to the spinal cord
- peripheral axon (afferent fibre) extends from the receptor to the soma
- a short central axon passes from the soma to the spinal cord
- action potentials go from receptor (distal end) to the spinal cord (proximal end)

Efferent

- receive signals from interneurons in the CNS and innervate its target

Interneurons

- connect signals from afferent to efferent
- makes up 99% of neurons (100 billion)
- more complex actions require more interneurons between afferent and efferent

Subsection 15.2
Glial Cells

- glial cells (or neuroglia) make up about 90% of cells in the CNS
- they don't initiate or conduct nerve impulses, but do communicate using chemical signals and maintain homeostasis
- serves as the connective tissue of the CNS
- maintains adequate extracellular composition for neuron activity
- modulates synaptic function, so they are considered nearly as important to memory as neurons
- 4 major types of glial cells: Astrocytes, Oligodendrocytes, Microglia, Ependymal cells
  - astrocytes: induce formation of blook-brain barrier, take up exxcess K ions to maintain homeostasis, and degrade released neurotransmitters into raw materials for the synthesis of more neurotransmitters (most common too)
  - oligodendrocytes: form myelin sheaths in CNS (in contrast to Schwann cells in PNS)
  - microglia: play defense as phagocytic scavengers

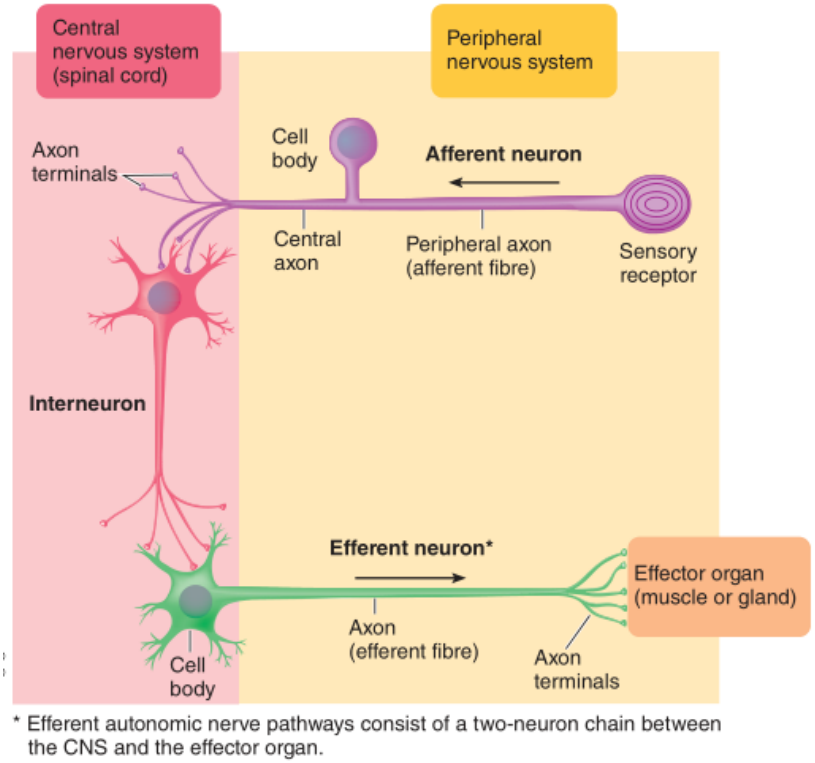


Figure 27. Organization and function of the three classes of neurons.

  - ependymal: line internal cavities of brain and spinal cord, contribute to cerebrospinal fluid formation and act as stem cells that can form new neurons and glial cells

- learning occurs when myelin sheaths lengthen or new ones are created
  - makes it more likely for APs to traverse the entire neuron
  - neuroplasticity – neurons that fire together, wire together; neurons that fire out of sync, fail to link

Subsection 15.3
Cerebrospinal Fluid

- has greater electrochemical gradient – makes action potentials easier

Subsection 15.4
Anatomical Landmarks in the Brain and Spinal Cord

- cerebral cortex controls sensory perception, voluntary movement, personality, and sophisticated mental events like memory
- hypthalamus regulates temperature, thirst, urine output, food intake, and other homeostatic functions
  - role in sleep-wake cycle
  - emotion and basic behaviour

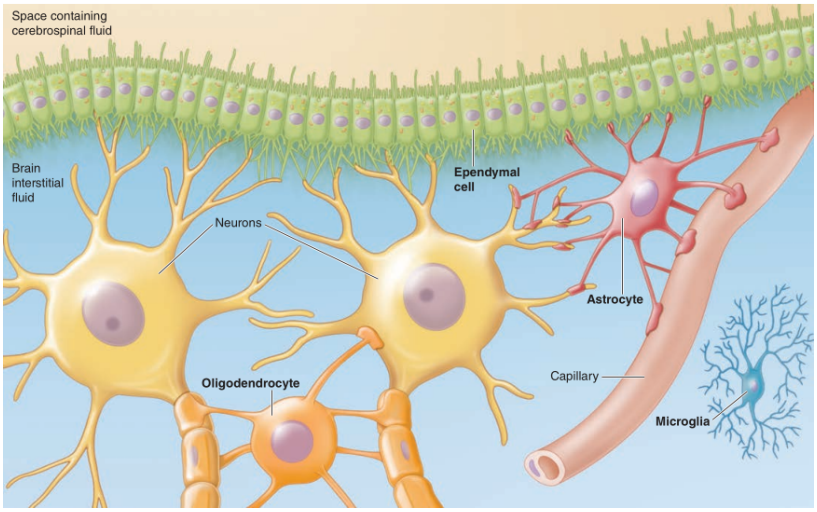


Figure 28. Glial cells of the central nervous system.

  - important link between nervous and endocrine systems
- cerebellum maintains balance and coordination
- brainstem is control centre for cardiovascular, respiratory, and digestive systems

Subsection 15.5
Spinal Cord

- descends through vertical canal and is surrounded by the vertebral column
- spinal nerves are paired neurons that emerge from the spinal cord
- from head to toe:
  - 8 cervical (neck) nerves
  - 12 thoracic (chest) nerves
  - 5 lumbar (abdominal) nerves
  - 5 sacral (pelvic) nerves
  - 1 coceygeal (tailbone) nerve

15.5.1 Spinal Cord in Cross-Section

- grey matter in spinal cord forms an inner butterfly-shaped region surrounded by white matter
- cord grey matter consists primarily of neuronal cell bodies and their dendrites, interneurons, and glial cells
- white matter consists primarily of myelinated neurons
  - organized into tracts (bundles of nerve fibres/axons of long interneurons)
  - ascending tracts go from cord to brain while descending tracts go brain to cord

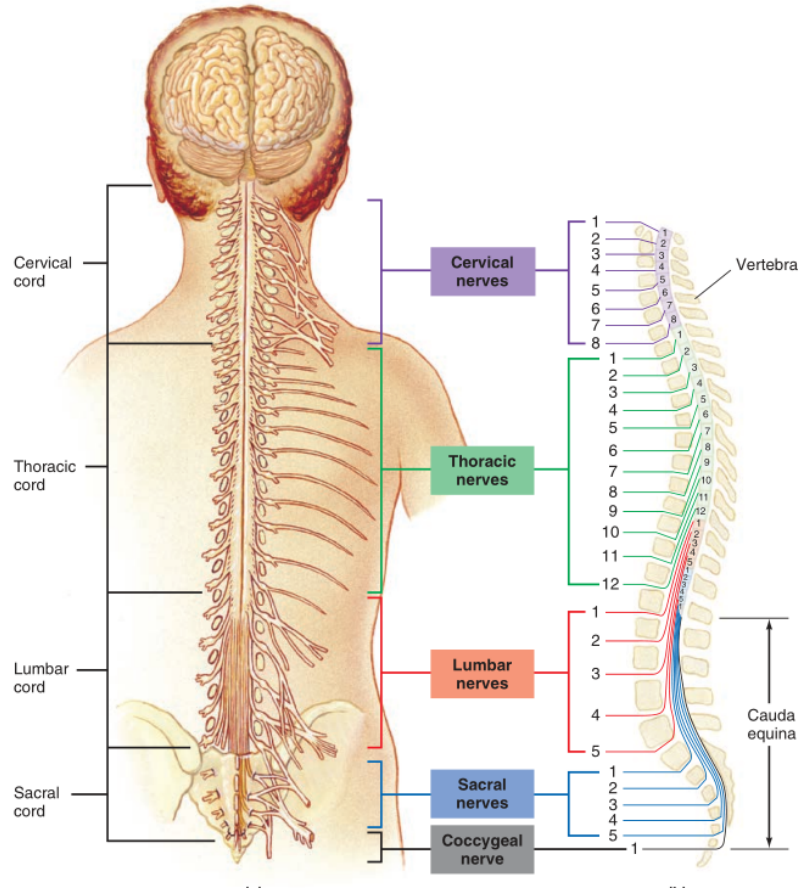


Figure 29. Spinal nerves.

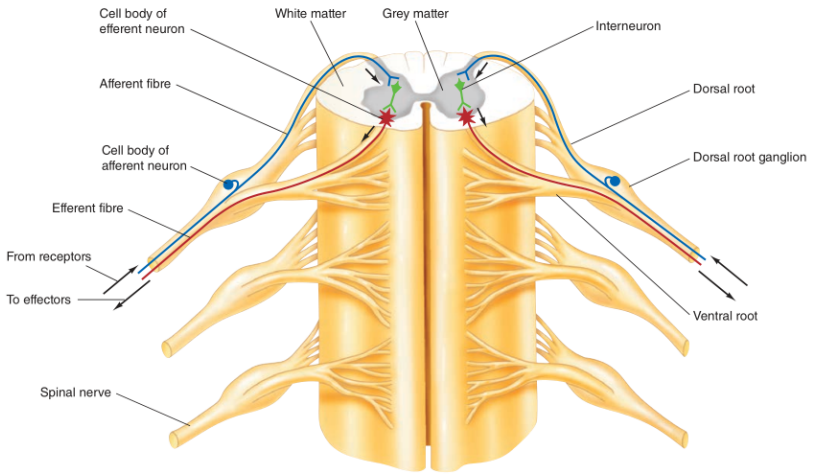


Figure 30. Spinal cord in cross section.

- sensory pathways have afferent neuron connect to an interneuron in the grey matter region, which then enters an ascending tract in the white matter region
  - enters grey matter through dorsal root

- motor neurons have interneuron travel down descending tract, goes from white matter to grey matter, connects to an efferent neuron, and exits out of the spinal cord through the ventral root

Subsection 15.6
Reflexes

- reflex: any response that occurs automatically without conscious effort
- nerve impulses that enter the spinal cord on the same side from which nerve impulses leave it are called reflex arcs
  - a neural pathway that controls an action reflex
- stretch reflex: involves an afferent neuron originating at a stretch-detecting receptor in a skeletal muscle (causing stretch)
  - terminates on the efferent neuron innervating the same skeletal muscle
    - causes counteracting contraction
    - reciprocal innervation
- stretch reflex is caused by a reflex arc
- stretch reflex is a mono-synaptic reflex (no interneurons) (e.g. knee jerk)
- polysynaptic reflexes have interneurons between the afferent and efferent neurons (e.g. withdrawal reflexes)

Subsection 15.7
Cranial Nerves

- most fibres pass through the brain stem
- these include the 12 pairs of cranial nerves
  - all but the vagus nerve of the cranial nerves supply structures in the head and neck with sensory and motor fibres
    - vagus nerve supplies organs in the thoratic and abdominal cavities
    - is the major nerve of the parasympathetic nervous system
  - includes glossopharyngeal nere – controls the pharynx and hypoglosal nerve (which controls the tongue)

Subsection 15.8
Cerebral Cortex

- the cerebrum is divided into left and right cerebral hemispheres
  - connected by the corpus callosum
- each hemisphere has a thin outer shell of grey matter (cerebral cortex) covering a thick core of white matter
- grey matter acts like comuter and white matter acts like wires
- 4 major lobes
  - occipital, temporal, parietal, and frontal (back, side, middle top, front)

- sensations from the body surface (touch, pressure, pain, etc.) are somaesthetic sensations
  - information is projected to the somatosensory cortex (front of parietal lobe)
    * responsible for processing of somaesthetic and proprioceptive (awareness of body position) input
    * representation by body parts (to show what body parts are controlled where in the cortex) is the sensory homunculus

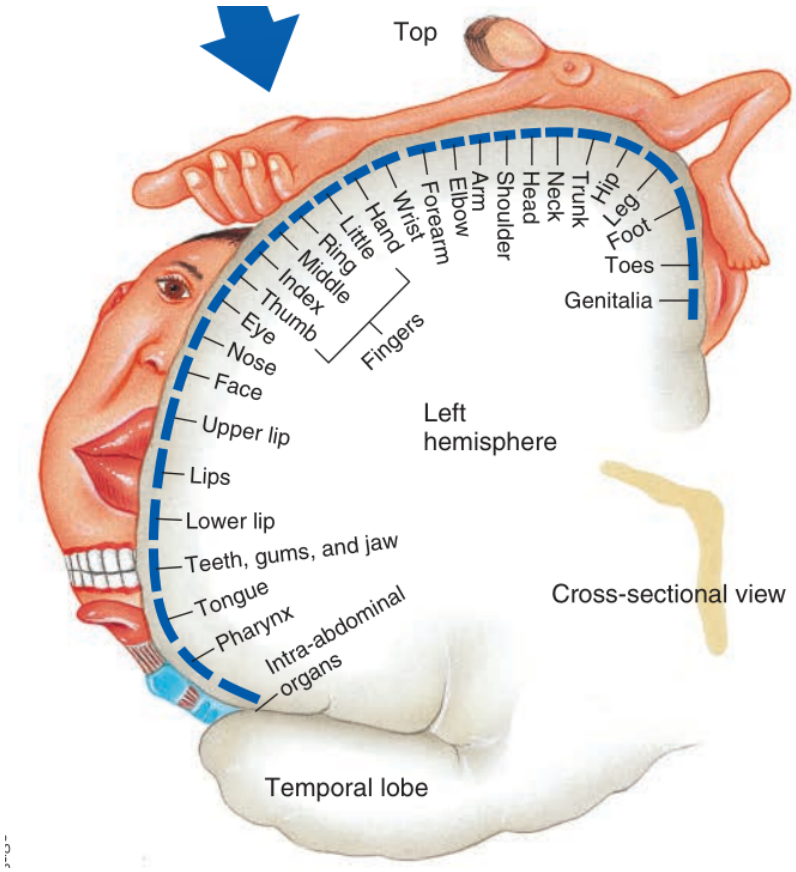


Figure 31. Sensory homunculus.

- control of motor functions of skeletal muscles is done in the primary motor cortex
  - back of frontal lobe, in front of somatosensory cortex
  - representation by body parts is the motor homunculus
- note that left side of the brain tends to control right side of the body and vice versa
  - means nerves cross from one side to the other in the brain

PART

IV

The Peripheral Nervous System

Section 16

Afferent Division

- carry nerve impulses (action potentials) from receptors or sense organs to the central nervous system (CNS)
- the nerves, including in the efferent division, are neurons bundled up into fascicles
- afferent neurons have a single long dendrite, a short axon, and a smooth rounded cell body
- just outside the spinal cord, thousands of afferent cell bodies are aggregated in the dorsal root ganglion

Section 17

Receptor Physiology

- afferent neuron has a receptor at its peripheral ending that responds to stimulus from the internal and external environment
  - stimuli are detectable body changes that meet a minimum threshold
- there are many types of receptors:
  - somatosensory receptors such as free nerve endings consisting of a neuron with an exposed receptor
  - special senses receptor turns a mechanical stimulation (non-neural) into a neural signal by synapsing onto a sensory neuron
  - conversion of chemical/mechanical energy into electrical energy for action potential is transduction
- CNS can differentiate the stimuli from several properties including (MILD):
  - modality
  - intensity
  - location
  - duration
- **modality** is the type of stimulation a neuron responds to
  - nociceptors (pain), photoreceptors (light), chemoreceptors (chemicals in smell), thermoreceptors (heat), mechanoreceptors (mechanical energy)

- **intensity** is modelled by frequency coding (increased firing rate increases intensity) and population coding (increased number of activated receptors increases intensity)
- **location** referes to where neurons are activated
  - lateral inhibition can occur where an excited neuron can reduce the activity of neighbouring neurons
- **duration** refers to the length of the membrane potential, and correspondingly the action potential, during a stimulus
  - phasic receptors have membrane and action potentials at the beginning and end of the stimulus only (gets used to it)
  - tonic receptors have the potentials last for the entire stimulus (doesn't get used to it)
  - putting a shirt on and getting accustomed to it would use phasic receptors

Subsection 17.1
Receptor Potentials to Action Potentials

- if a receptor potential has sufficient magnitude, it may initiate an action potential in the afferent neuron membrane next to the receptor
  - done by triggering the opening of Na^+ channels
  - the manner by which opening is done depends on whether the receptor is a separate receptor cell or a specialized afferent ending
    - for a separate receptor cell, a receptor potential triggers the release of chemical messengers, which then travel across a gap to open the chemically gated Na^+ channels in the afferent neuron (similar to a synapse)
    - for a specialized afferent receptor ending, the potential created by teh stimulus trhoguh receptor specific channels opens voltage gated Na^+ channels
- if the magnitude of the resulting ionic flux is big enough to reach threshold, an action potential is generated that travels from the afferent neuron to the CNS
- note that afferent neurons have action potentials generated next to the receptor while they occur at the axon hillock for interneurons and efferent neurons
- larger receptor potential does not increase action potential magnitude (all-or-none law), but can increase the frequency of action potentials

Section 18
Neuromuscular Junctions (NMJ)

- recall that when an action potential arrives at a presynaptic neuron, it activates voltage gated ion channels
  - this allows Ca^{2+} to enter the neuron and allows for acetylcholine to exit the neuron via exocytosis and is released into the NMJ
  - when 2 ACh binds to each receptor of the post-synaptic neuron, sodium (in) and K (out) channels open, the end plate potential is lowered

  - this depolarization generates a potential called the **end plate potential** (EPP)
  - now the action potential spreads along the muscle cell (instead of axon in nervous system) and activates other voltage gated channels to excite the whole muscle
  - once ACh is no longer being secreted, another enzyme on the surface of the muscle cell called **acetylcholinesterase** removes any excess ACh to bring the muscle back to a relaxed state
    * no ACh removal means you will not be able to relax

Subsection 18.1
Vulnerability of NMJs

- **Black widow spider venom**: explosive release of ACh causes muscle spasms
- **Botulism Toxin**: blocks release of ACh causing muscles to depress and not function as expected and could cause choking
- **Curare**: ACh receptor antagonist – reversible binds to ACh receptor sites (blocks action of ACh at receptor sites)

PART V

Muscle Physiology

Section 19
Skeletal Muscle Structure

- skeletal muscle is attached to bones through tendons
- muscle cells are also known as muscle fibres
- muscle fibres are made of myofibril
- lots of mitochondria and nuclei in muscle cells
- muscle fibres are bundled together into muscle fascicles
  - fascicles have blood vessels, veins, nerves, etc. as well
- the sarcolemma/myolemma is the cell membrane of the muscle cell

Subsection 19.1
Myofibrils

- myofibrils are the predominant structural feature of a skeletal muscle fibre (main working component of the muscle cell)
- made of myofilaments (thick is myosin, thin is actin)

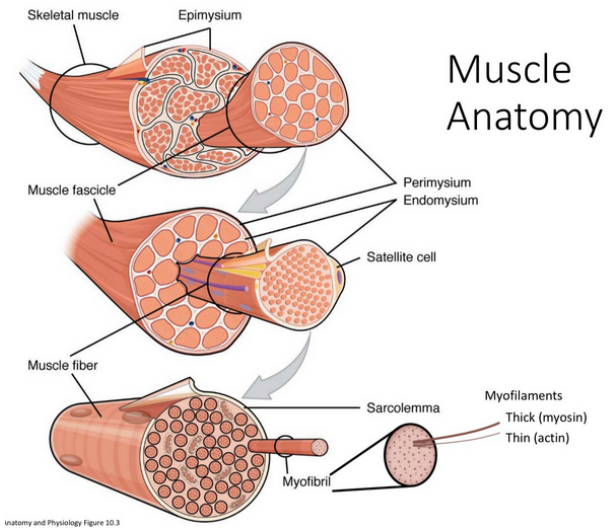


Figure 32. Muscle anatomy.

19.1.1 A and I Bands

- the A-band is Anisotropic, made up of a stacked set of thick filaments along with portions of thin filaments (produced by actin) that overlap on both ends of thick filaments (produced by myosin)
- the I-band consists of the remaining portion of the thin filaments that do not project into the A-band
- the H-zone is the lighter area (known as the "heller") within the middle of the A band where the thin filaments do not reach
- the M-line is known as the "middle line"
- the Z-line is in the middle of each I-band – area between two Z-lines is called a **sacromere**
- the stringy line things that holds myosin to the Z-line is a highly elastic protein called **titin**
- muscle fibres function by having myofilaments sliding acros each other – titin contracts and pulls thin filaments while thick filaments remain the same
- when muscles contract and relax, the H-zone and I-bands contracts and expands since titin is contracting/expanding
  - the titin can be thought of as a spring that contracts and expands to move the muscle
- this movememnt causes the overall sacromere to expand or contract

Section 20

Skeletal Muscle Function (Excitation-Contraction Coupling)

- since nerves only interact with the outside of muscle fibres and there are many myofibrils inside a muscle fibre, how does the signal get to each myofibril?

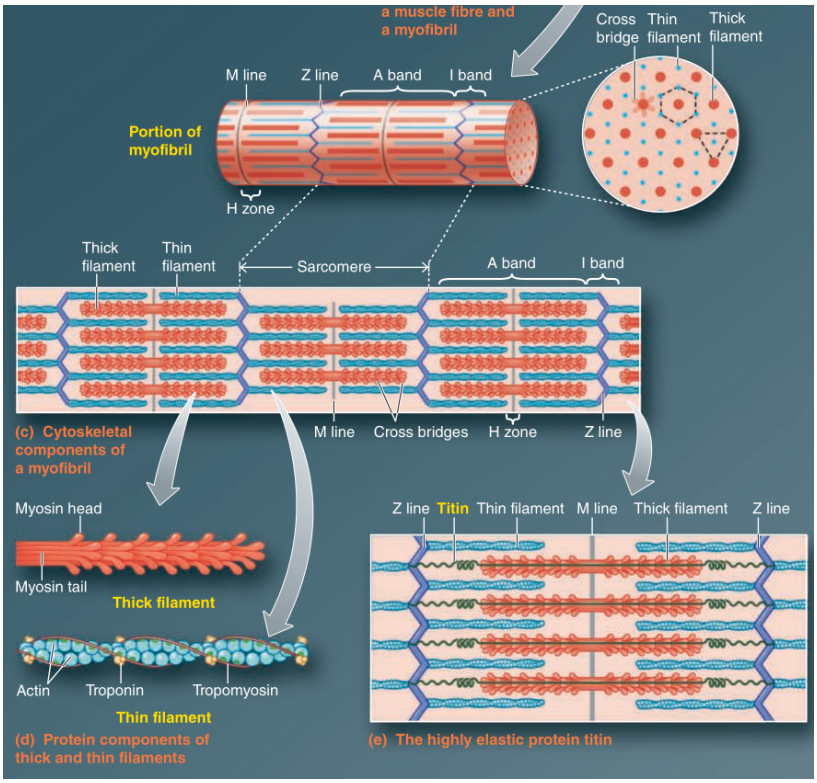


Figure 33. Myofibril.

- NMJ depolarizes the sarcolemma and then t-tubules allow electrical signal to travel down to myofibrils

- terminal cisternae (lateral sacs) are like reservoirs for calcium and are part of the sacroplasmic reticulum (SR)

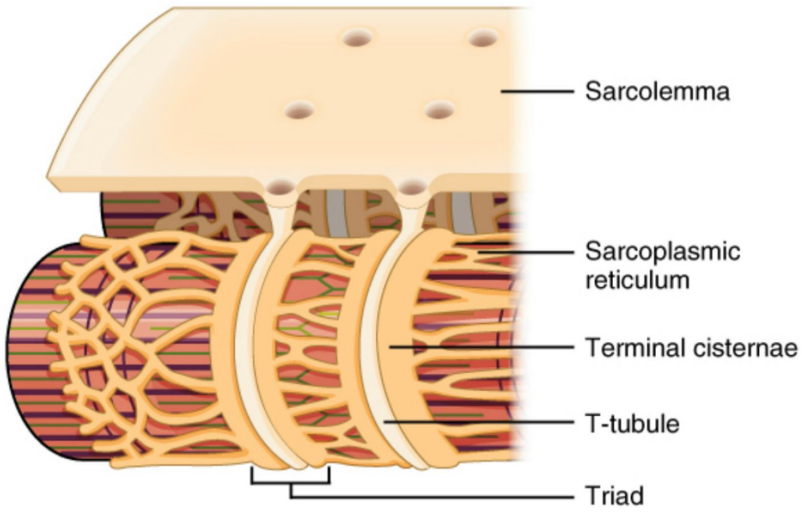


Figure 34. Terminal cisternae (lateral sacs).

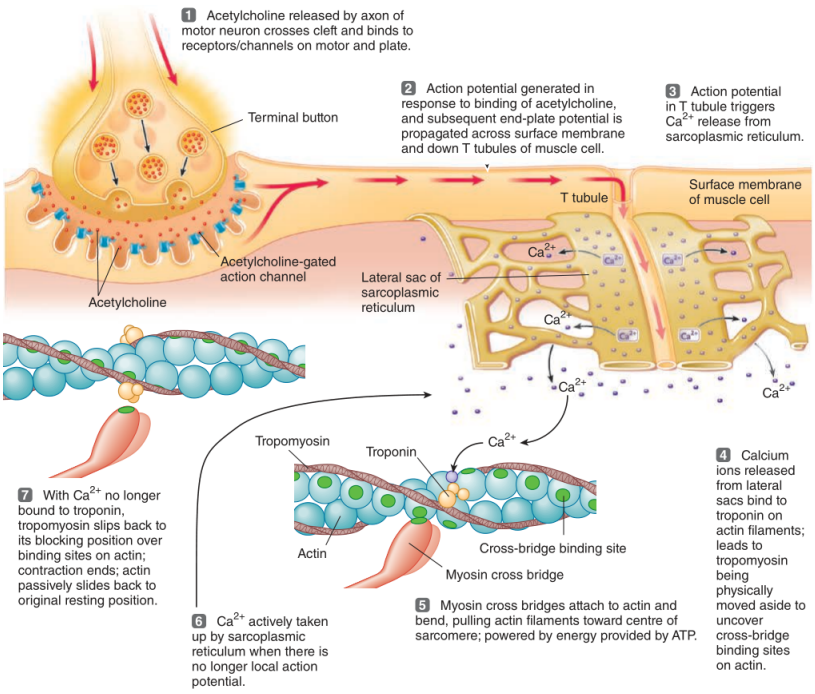


Figure 35. How muscles contract on a molecular level.

- neuron to muscle mapping is 1 neuron to 1 motor group (a few muscle cells)
- EPP travels down into t-tubules
- signal travels to sarcoplasmic reticulum (SR)
- allows calcium to be released into sarcoplasm
- calcium causes some stuff that leads to the whole muscle contracting

Subsection 20.1

Energy Supply to Skeletal Muscles – Cross Bridge Cycling

- what happens when calcium is released into sarcoplasm – how it causes muscle contraction
- the **cross-bridge link** is a secure structure that provides energy to muscle cells

1. Energized stage: the myosin head brings ADP and inorganic phosphate but is bent slightly away from the thin filament
2. Binding stage: the head bends to bind with the muscle fibre and forms the cross-bridge link
3. Bending stage: the head bends even more (power stroke, applying 5 pN of force), releasing the phosphate first and ADP second
4. Detachment stage: the head takes ATP formed by the released ADP and phosphate and detaches from the muscle fibre
    - if no ATP, the myosin head is frozen on the thin filament

5. Reattachment: ATP is broken down into ADP and phosphate (hydrolyzed/dephosphorylated)

- note that in the case of no ATP, the muscle cell is frozen – **rigor mortis**
- calcium moves the troponin complex out of the way
- pulls the tropomyosin latch open
- exposes all the cross-bridge binding sites located on the actin (thin filament)
- to relax, the reverse steps happen

Section 21

Skeletal Muscle Mechanics

- rebar is to concrete as muscle is to bone (functionally)
- types of contractions:
  - concentric – muscle contracts
  - eccentric – muscle elongates
  - isometric – muscle contracts but stays in place

Subsection 21.1

Tension Developed by Each Fibre

21.1.1 Action Potential Frequency

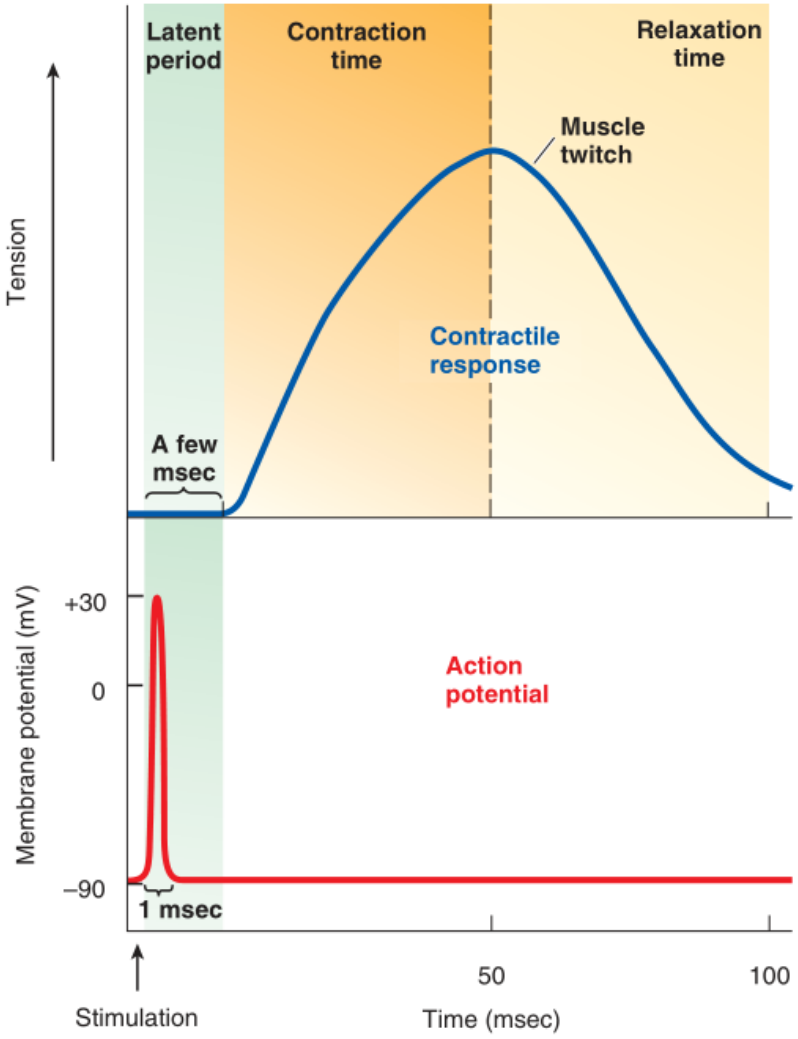


Figure 36. Relationship between action potential and resultant muscle twitch.

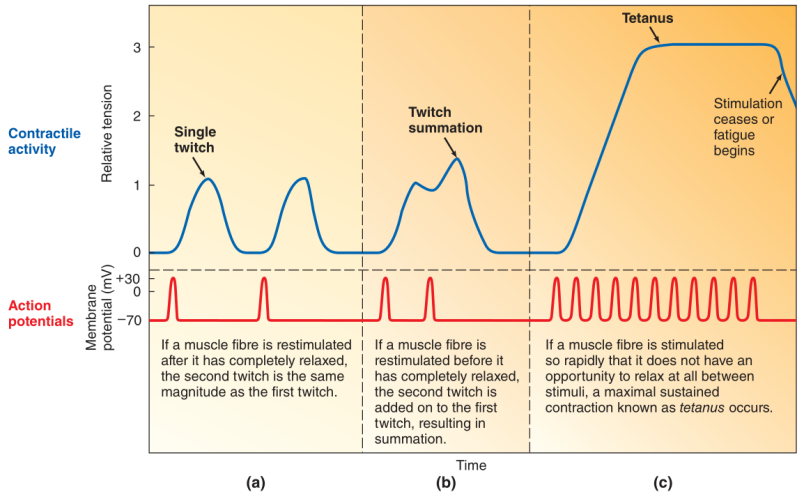


Figure 37. Summation and tetanus.

- after a high enough stimulation frequency, it causes twitch summation and there is a tetanic maximum that a muscle can contract to
- around 100 Hz is what causes tetanus

21.1.2 Fibre Length

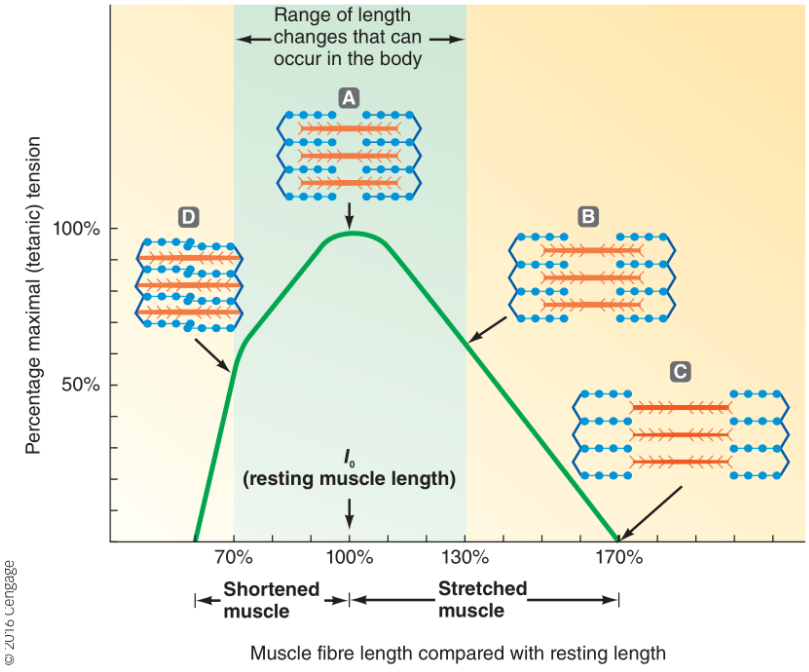


Figure 38. Length-tension relationship.

- there is also some passive length-tension due to titin being stretched or compressed

21.1.3 Fibre Diameter

- fibre hypertrophy – bigger myofibrils (swole) caused by growing bigger Z disc
- fibre splitting or hyperplasia – more myofibrils (ripped) caused by tearing Z disc
- smaller diameter = less force, larger diameter = more force

21.1.4 Fatigue

- type 1 fibres don't fatigue very much (can sustain tension for long time)
- type 2A fatigues quickly
- type 2X fatigue very quickly
- factors that influence muscle fatigue:
  - ADP interferes with cross-bridge
  - Accumulation of lactic acid (interferes with making more ATP)
  - increased extracellular K (stops depolarization)
  - depletion of glycogen energy reserves

21.1.5 Fibre Type

- mitochondria: many in slow twich (type 1), less in fast twitch (type 2)
- capillaries: many in slow and type 2A, few in type 2X
- myoglobin content: high in slow and 2A, low in 2X
- contraction velocity: slow in slow, fast in 2A, fastest in 2X
- size of motor neuron innervating fibre: smaller in slow, larger in fast, largest in type 2X

Subsection 21.2

Number of Active Fibres

21.2.1 Number of fibres per motor unit

- more muscle fibres recruited = more power

21.2.2 Number of active motor units

- different motor neurons control different motor units (slow twitch, fast twitch)

Section 22

Smooth Muscles

- smooth muscles are found in STOVE:
  - Skin
  - Tracts (such as gastrointestinal tract)
  - Hollow Organs (e.g. stomach)
  - Vessels
  - Eyes

Subsection 22.1
Structure of Smooth Muscles

- in the relaxed state:

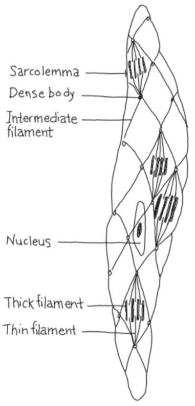


Figure 39. Relaxed smooth muscle.

- in the contracted state:

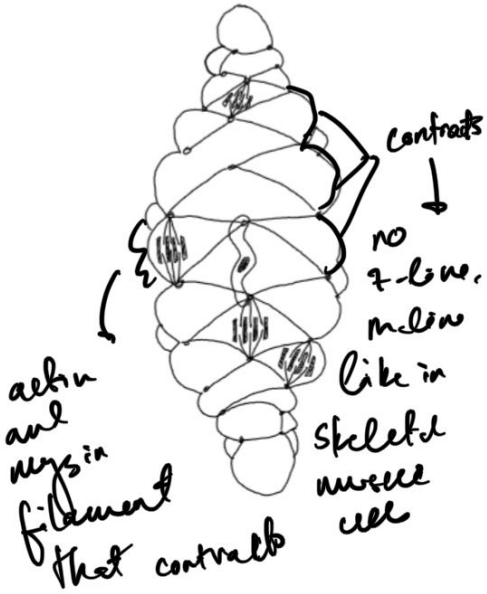


Figure 40. Contracted smooth muscle.

- these are innervated by the autonomic nervous system
- they can be initiated either by neurogenic or myogenic causes

- nervous stimulation can modify contraction, excite or inhibit, and contribute to gradation
- gradation is accomplished mainly via varying number of muscle fibres, varying cystolic Ca^2+, as well as autonomic, hormonal, mechanical stretch, and metabolites
- these are affected by hormones and have poorly developed sarcoplasmic reticulum
- they also have gap junctions
- main source of Ca is ECF

Subsection 22.2
Types of Smooth Muscle

- Single-unit and multi-unit smooth muscles
- multi-unit muscles consist of multiple discrete units that function independently of one another
  - separately stimulated by nerves to contract (similar to skeletal muscle) – neurogenic
  - multi-unit muscles do not have gap junctions between the muscle cells and have more motor neurons to control precisely how each fibre contracts and expands
- single unit muscles contract as a single unit
  - single unit muscle fibres are electrically linked by gap junctions

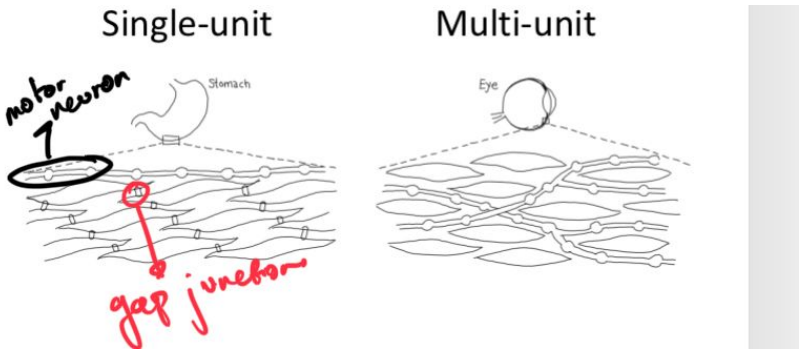


Figure 41. Single and multiunit smooth muscles.

PART
VI

Cardiac Physiology

Section 23
Cardiac Muscle

- cardiac muscle is wrapped in curvy circular ways

Table 1. Differences between skeletal and cardiac muscle.

Skeletal Muscle	**Cardiac Muscle**
Innervated using the somatic nervous system	Innervated using the autonomic nervous system
Initiated due to neurogenic causes	Initiated due to myogenic causes – initiated by muscle cells
Initiates contraction and achieves gradation	Modifies contraction through excitement and inhibition
Gradation accomplished by number of motor units, frequency summation	Gradation by varying length of muscle fibres and Ca^2+ amount in cytosol
Not affected by hormones	Affected by hormones
Well developed sarcoplasmic reticulum	Moderately developed sarcoplasmic reticulum (mainly gets Ca from ECF)
No gap junctions	Has gap junctions

- there is significant variation in the type of cardiac muscles depending on where they are
- both skeletal and cardiac muscles are **striated** (has alternating dark and light bands – repeating sacromeres)
  - they have the actin and myoactin mechanisms for function with the push and pull mechanism for motion
  - cardiac muscle is involuntary, skeletal muscle is voluntary
- calcium plays a role in depolarization in the heart

Section 24

Electrical Activity of the Heart

- cardiac muscle has a much higher concentration of mitochondria – needs to constantly open and close ion channels to keep heart beating
- electrical activity starts in right atrium, travels in this order: sinoatrial node, atrial muscle, atrioventricular node, Purkinje fibres, ventricular muscle
- in a skeletal muscle fibre, Na^+ comes into the cell upon initiation of an action potential with a delayed inflow of K^+ due to the slow initiation for the voltage gated channels
- in the heart, different types of muscles have different polarization patterns
  - these patterns spread due to the gap junctions between cardiac fibres

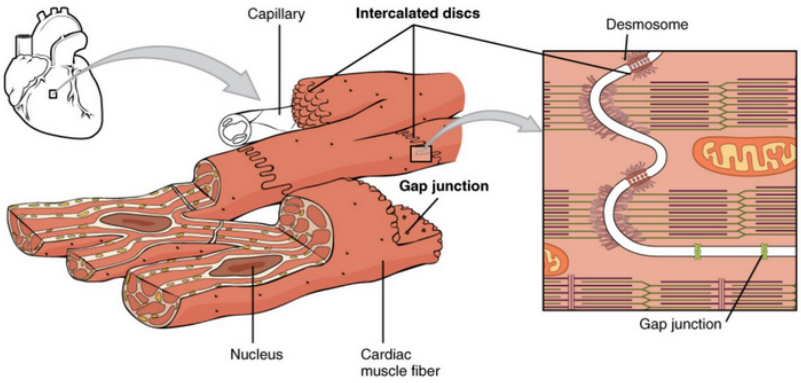


Figure 42. Gap junctions between cardiac fibres.

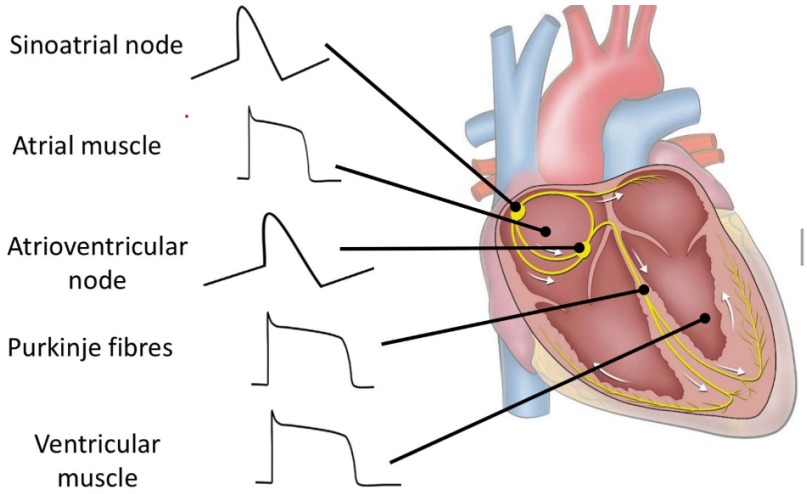


Figure 43. Different polarization patterns for different types of muscles in the heart.

Subsection 24.1

Ventricular Myocyte Action Potential

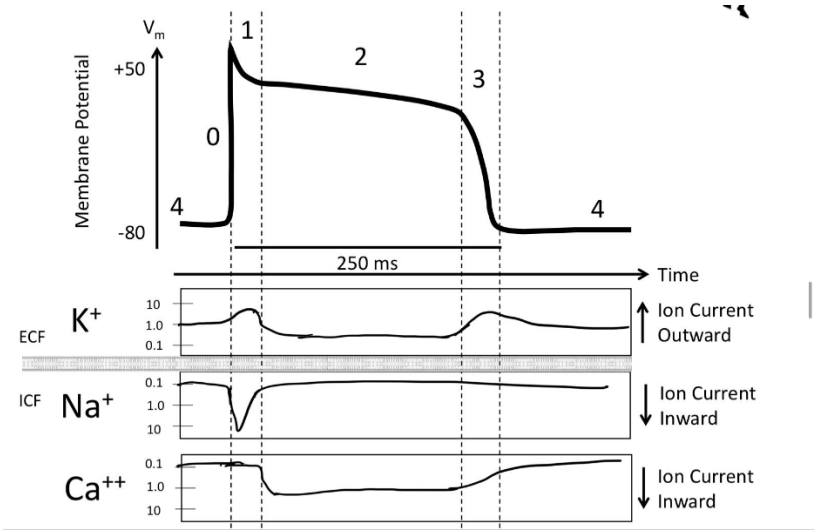


Figure 44. Action potential in ventricular muscle cells.

- Phase 4 – normal resting state (resting membrane potential)

- Phase 0 – rapid depolarization which while not instantaneous, is very very quick

- Phase 1 is caused due to K channels which cause a slight depolarization

- Phase 2 – K^+ going out while Ca^{2+} going in causes a plateau

- Phase 3 – more K^+ channels open, which expel these ions, causing a rapid depolarization

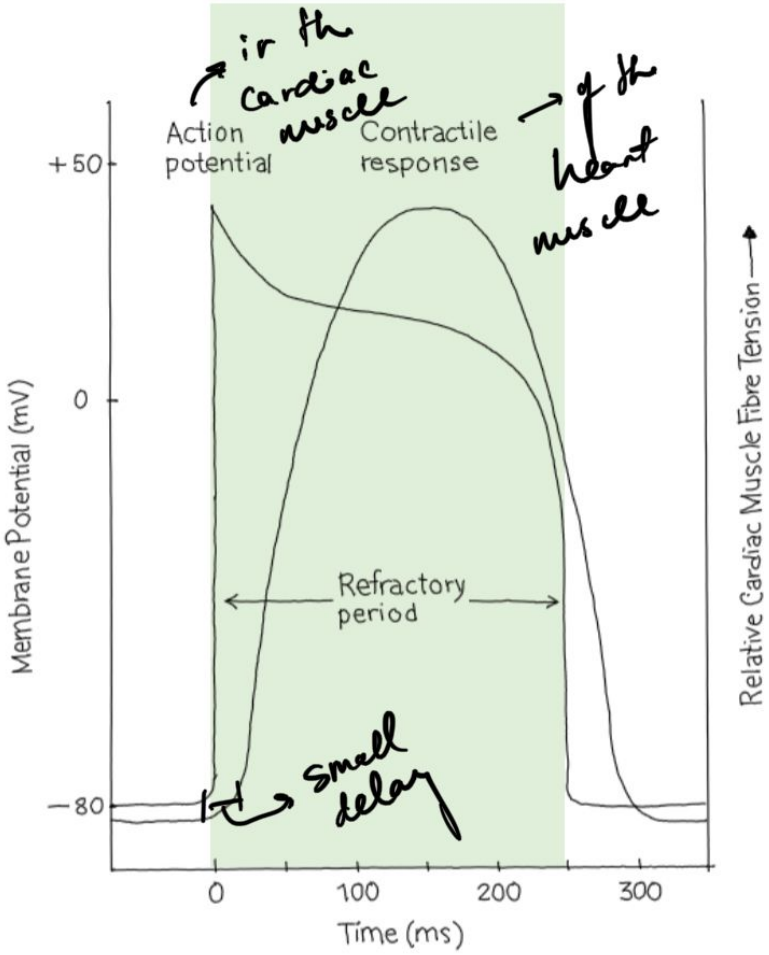


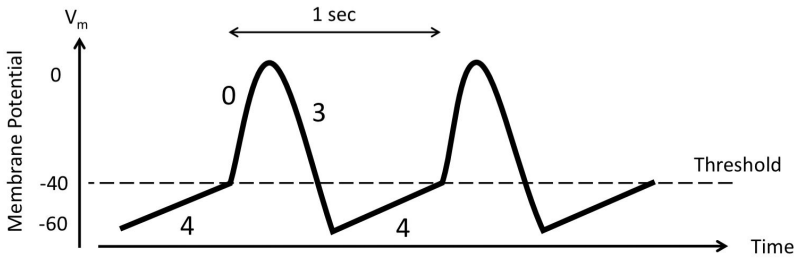
Figure 45. Relationship of an action potential and the refractory period to the duration of the contractile response in cardiac muscle.

- the refractory phase prevents frequency summation and allows the muscle to relax
  - without this the muscle would not be able to expel or take in blood

Subsection 24.2

Pacemaker (Nodal) Cells

- Calcium causes the depolarization (instead of the sodium in ventricular muscles)
- transient channels are known as **T channels** while longer lasting channels are known as **L channels**
- heartrate modulation:
  - rate of depolarization: decreased rate causes a lower heart rate (takes longer to reach threshold)
  - more hyperpolarized: requires more time to reach threshold (decreases heart rate)
  - shift in threshold: a lower threshold causes a longer time to depolarize and hence a lower heart rate; higher threshold causes higher heart rate



Phase 4: Resting membrane potential

Phase 0: Membrane depolarization

Phase 3: Repolarization

Figure 46. Pacemaker activity of cardiac autorhythmic cells.

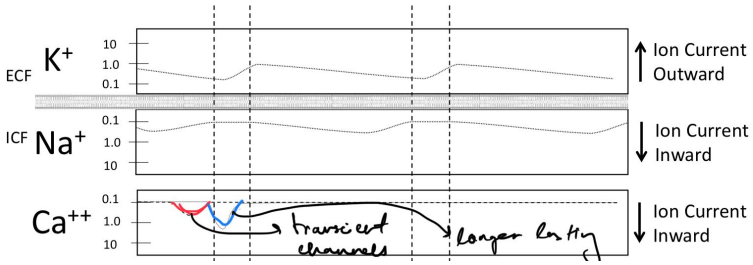


Figure 47. Ion concentrations during pacemaker activity.

Subsection 24.3

Electrocardiogram (ECG)

- positive deflection on ECG can be depolarization moving toward electrode or repolarization moving away from electrode
- direction of electrical activity:
  - depolarize atria (P wave): sinoatrial node, atrial pathways, atrioventricular node
  - depolarize septum from left to right (Q, R, and S wave): atrioventricular node, Bundle of His, Purkinje system (faster conduction velocity)
  - depolarize ventricular muscle: Purkinje system, ventricular muscle, endocardium, epicardium
  - repolarization occurs in reverse order (ventricular first) (T wave)
- physical trauma to the heart during the T wave may cause ventricular fibrilation – could trigger another depolarization

24.3.1 Matching ECG to Pumping Actions

- major events of cardiac cycle:
  - ventricular diastole
    - passive filling

    - atrial ejection
  - ventricular systole
    - isovolumic ventricular contraction
    - ventricular ejection
  - ventricular diastole
    - isovolumic ventricular relaxation

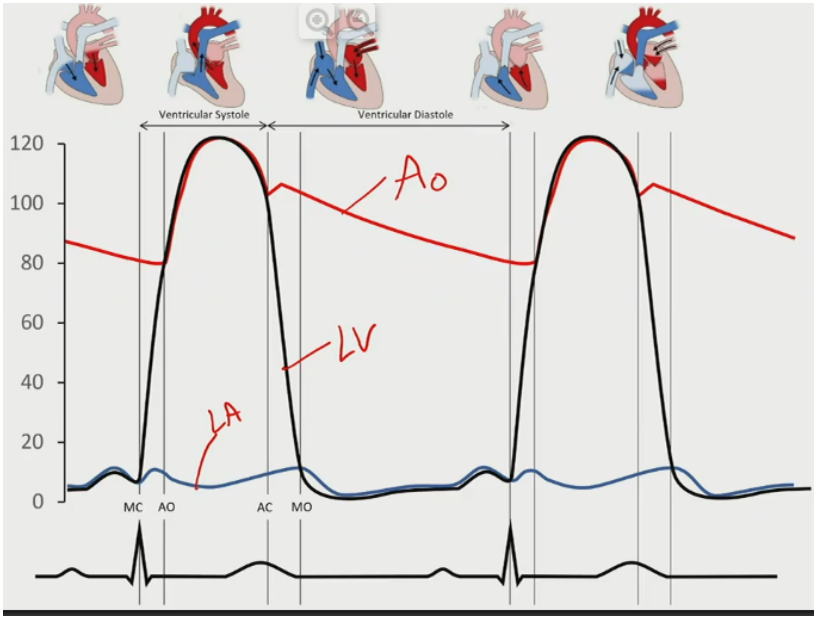


Figure 48. Matching ECG to pumping actions.

24.3.2 Volume of Blood Inside Heart

- left ventricular stroke volume (typically around 70mL) is given by:

$$SV = EDV - ESV.$$

- where EDV is end diastolic volume (135 mL), ESV is end systolic volume (65 mL)

Section 25

Cardiac Regulation

- cardiac output (L/min) is given by the product of stroke volume and heart rate:

$$CO = SV \cdot HR.$$

- SV and HR are the two main factors that influence cardiac output

Subsection 25.1

Heart Rate

- autonomic effects on the heart

- cardiovascular center in the medulla sends signals to heart
- vagus nerve triggers atrial muscle (parasympathetic stimulation)
  - the vagus nerve releases ACh that increases the permeability of the SA node to K by slowing the clsure of K voltage-gated channels
  - this lowers the minimum diastolic potential – depolarization takes longer to reach back to threshold
  - also decreases the rate of depolarization – enhanced K permeability opposes the pacemaker current (resulting from Na and K currents) responsible for the gradual depolarization
- sympathetic nerves trigger ventricular myocytes
  - sympathetic nerves releases norepinephrine (NE) that binds to the $\beta 1$ adrenergic receptors, that functionally increase the HR
  - increases the pacemaker current – increases rate of depolarization and reaches threshold faster
  - increases Ca currents makes Ca voltage-gated channels more active and threshold potential is lowered – takes less time to reach threshold
  - greater sympathetic stimulation increases calcium permeability which increases conduction velocity for the AV node and Purkinje fibres
- need vagal and sympathetic tone (how much ACh or NE is dripping out from the nerves) to decrease/increase your heart rate

Subsection 25.2

Stroke Volume

25.2.1 Intrinsic Control of SV

Theorem 2 **Frank-Starling Law**: the more you stretch the heart muscle, the more force it develops

25.2.2 Extrinsic Control of SV

- sympathetic nerves are the only ones that go to the ventricular muscles
- increased Ca permeability increases Ca currents and availability in cytosol of ventricular myocytes
- this increases the force developed by ventricular myocytes and force of ventricular contraction
- ultimately increases SV

PART

VII

Vascular Physiology