Lecture#12

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We will complete talking about muscle cells

*In general, cells can go through:

1-Hypertrophy: increase in the cell's size.

* We can notice it on the people who do weight lifting (muscular people).

*How could hypertrophy happen to muscle cells ??

Answer: By exercising, skeletal muscle cells produce more actin and myosin, as a result the myofibril becomes larger, which results in increasing of the size of the muscle cell as a whole.

2-Hyperplasia: increase in the number of the cells.

***Note: The more highly differentiated the cells are, the harder it is for them to undergo mitosis.**

* Skeletal muscle cells can't undergo mitosis because they are highly differentiated, but in certain cases skeletal muscle cells may undergo hyperplasia due to the presence and fusion of satellite cells, still this hyperplasia is limited because skeletal muscle cells have few number of satellite cells (regeneration is poor).

So, skeletal muscle cells can undergo hypertrophy and has limited ability to undergo hyperplasia.

-Skeletal muscle is composed of skeletal muscle fibers, some of these skeletal muscles fibers, which are located in the middle of the muscle, are special type of muscle cell fibers, they are smaller than other muscle cell fibers and they are called muscle sensory receptors or proprioceptors or muscle spindle or stretch receptors or intrafusal muscle fibers.

*****for example, we have sensory receptors in our skin for heat and cold (thermoreceptors), pain (nociceptors), touch and pressure (mechanoreceptors). These sensory receptors are able to transform the external stimulus into electrical impulses (action potential).
Proprioceptors are sensory receptors in the skeletal muscle that provide information about changes in muscle length; they can detect any changes in the length of the muscle.

***remember:** The muscles have to be innervated by motor nerves in order to contract.

*Features of proprioceptors:-

1-Few number of muscle cells

2-surrounded by a thick perimysium (capsule), and because they are capsulated, these fibers are also called intrafusal fibers.

Note that the standard skeletal muscle fibers that produce contraction and make up large mass of muscle are called extrafusal muscle fibers

3-their nuclei are usually located in the middle of the muscle cell, unlike extrafusal muscle fibers where their nuclei are peripherally located.

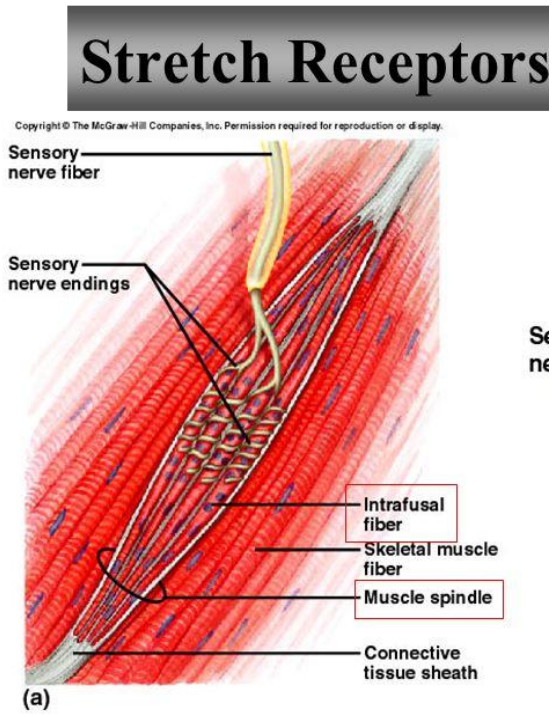
4-sensory nerves wrap around these muscle fibers in order to transfer electrical impulses towards our central nervous system

5- They are called stretch receptors because they can detect any changes in the length (stretch) of the muscle.

-stretch receptors mechanism is considered protective, how is that?

Answer: If the muscle is overstretched, these proprioceptors will send messages to our central nervous system and our central nervous system will send motor impulses in order to contract the muscle.

*The muscle spindle tells our nervous system the position of our muscles in space without looking at them.



Types of Muscle fibers

We have 3 different types of skeletal muscle fibers in our body:

1. Slow fibers (Red Muscles)
2. Fast fibers (White Muscles)
3. Intermediate fibers.

The main difference between types is how they produce ATP. The color of the muscle is different (Grossly not histologically)

First: Slow Fibers (Red Muscles):

1. They produce the ATP needed to perform their contraction by Oxidative phosphorylation using the Mitochondria, which produces high amounts of ATP in a long time (slow) (Aerobic = Oxygen is used)
2. The fuel for the production of ATP is Fatty acids (mainly), fatty acids are produced by metabolism of fats, so in order to burn fat in the body, you need to work aerobically

(Aerobic exercises are called so because people are activating their red muscles to burn fats. These exercises are usually preceded with warm up exercises, to supply the muscles with high amount of oxygen)

3. They look red because:
a. they have high amount of mitochondria
b. they are highly vascularized
c. They contain high amounts of Myoglobin (Hemoglobin like protein, has heme (iron), and is an oxygen binding protein)
4. The ATPase activity of their myosin's heads is low, so the contraction is slow.
5. This slow contraction is prolonged (for a long time but slow).
6. They don't Fatigue easily.

Examples: Spinal muscles, muscles of the back, hip flexors (postural muscles are mainly red fibers)

Second: Fast Fibers (White Muscles)
1. They are white in color, because they don't have high amounts of myoglobin and mitochondria.
2. They don't need Oxygen to produce ATP (Anaerobic).
3. Glycolysis: production of ATP without the need of oxygen, it occurs in the cytoplasm directly and quickly.
4. They are called Fast fibers because:
a. They produce ATP quickly within the cytoplasm by glycolysis, they produce fast contractions
5. The ATPase activity of their myosin's heads is high
6. They are larger than red fibers.
7. They produce fast and strong contraction but for short time.
8. Activated in weight lifting activities, for example if you are carrying a heavy object, you give maximum force but this contraction will not last for a long time

For Example: people who sprint (run at maximum speed for short distance) produce very strong contractions for a short period of time (white fibers), while Marathon runners have higher amount of red fibers, they run long distance for a long period of time without getting fatigue (their speed is moderate).

9. They store high amount of glycogen

10. They get fatigue easily because one of the byproducts of Glycolysis is Lactic acid (it causes burning sensation but it will soon be absorbed).
11. The fuel for these muscles is: Glucose.

Third: Intermediate Fibers:
They have characteristics between both the white and the red

***Cardiac muscles:**

- ✓ Cardiac muscle is striated (composed of repeated units of sarcomeres inside the myofibril as in skeletal muscle)
- ✓ Self excitatory and electrically coupled: this means that these cardiac muscle cells are able to initiate contraction without nerve input (no motor end plate). this is called **Myogenic activity of the cardiac cells**

***Myogenic activity** they generate their own electrical impulses (pacemaker)

- ✓ Rate of contraction is modulated by autonomic nervous system (sympathetic and parasympathetic)(only to control the force of contraction not to initiate it).
  Sympathetic: increase the force of contraction.
  Para sympathetic: decrease the force of contraction.
- ➢ Remember that skeletal muscles are not self-excitatory and they need to be innervated to contract.

The main similarities between cardiac and skeletal muscle are:

1. Both are striated.
2. Both are composed of myofibrils, each myofibril is surrounded by a network of sarcoplasmic reticulum
3. Almost the same contraction mechanism.

The main differences between cardiac and skeletal muscle are:

1. The cardiac muscle cell is also called muscle fiber, but compared with the skeletal fibers, cardiac muscle is shorter and interconnected (branched).

2. Cardiac muscle cell is single nucleated but sometime it is binucleated while skeletal muscle cell is multi-nucleated.

3. The one nucleus in the cardiac muscle cell is located in the center, while the multi-nuclei of skeletal muscle are found under the sarcolemma in the periphery.

4. the striations of cardiac muscle are less distinct (obvious), while it‘s more obvious in skeletal muscle. ***Why***?

> Because cardiac muscle cells have higher amount of mitochondria than skeletal muscle, these mitochondria are located between the myofibrils. In addition, heart muscle cells store glycogen so the higher amount of mitochondria, glycogen, lipid inside the cytoplasm results in less obvious striations, while in the skeletal muscle, the sarcomeres are arranged above each others, so it appears uniformly striated, more obvious than the cardiac muscle. (but both skeletal and cardiac muscle are striated)

** (the stored lipids and glycogen are used as a fuel for the cardiac muscle cells)

**The heart muscle contract all time so it need large amount of mitochondria (up to 40% of cell volume) in order to produce ATP for muscle contraction.

5. The sarcolemma of the cardiac muscle also has invaginations. T-tubules also surround each myofibril, but instead of having triads (as in case of skeletal muscle) we have diads. Diad is one T-tubule with one tubular end of SR. The sarcoplasmic reticulum in the case of cardiac muscle is less extensive (smaller in size and less branched) than in skeletal muscle.

**In general T tubules in cardiac muscle are larger and occur near to the Z line of sarcomere.

6. Diads are found near the Z line but triads are found in the skeletal muscle at the junction between the A and I bands.

Intercalated discs:

Zigzag- like structure, Step-Like structure connecting two cardiac muscle cells together, it has two parts:

1. Horizontal Part

2. Vertical part

It contains 3 types of junctions:

A. **Gap junctions** (not exclusive to epithelial cells, we have them also between cardiac muscle cells). Gap junctions are located in the horizontal part of intercalated disk. Gap junctions allow movement of ions between cardiac muscle cells, this allows contraction of whole muscle uniformly as one unit (although its composed of many cells)

B. It also contains **desmosomes** and **fascia adherens** (Located in the vertical part of intercalated disk), to anchor cardiac cells together mechanically and prevent detachment and pulling apart of cells when the heart is contracting.

NOTE: The fascia adherens has the same concept as Zonula adherens which are found between epithelium cells.

In epithelium it is called zonula because it forms a belt like structure around epithelial cells. But between the heart muscle cells, it forms spot-like areas like the desmosomes)

The difference between desmosomes and fascia adherence: (desmosomes are associated with intermediate filaments, while fascia adherens are associated with actin filaments).

- ✓ Cardiac muscles don't contain satellite cells therefore these cells are not able to regenerate in case of injury
- ✓ Hyperplasia doesn't happen in cardiac muscles, cardiac muscle cells don't regenerate, they have No satellite cells (skeletal muscles have limited ability to regenerate because they contain few satellite cells).
- ✓ Note that satellite cells are undifferentiated stem cells (myoblasts) and they remain in the skeletal muscle tissue after differentiation,

- ✓ They are trying to use stem cells inside the heart in order to regenerate cardiac cells to replace the damaged area of the heart, instead of cardiac implant (stem cell technology).
- ✓ The cardiac muscle cells can undergo hypertrophy (increase in the cell size).

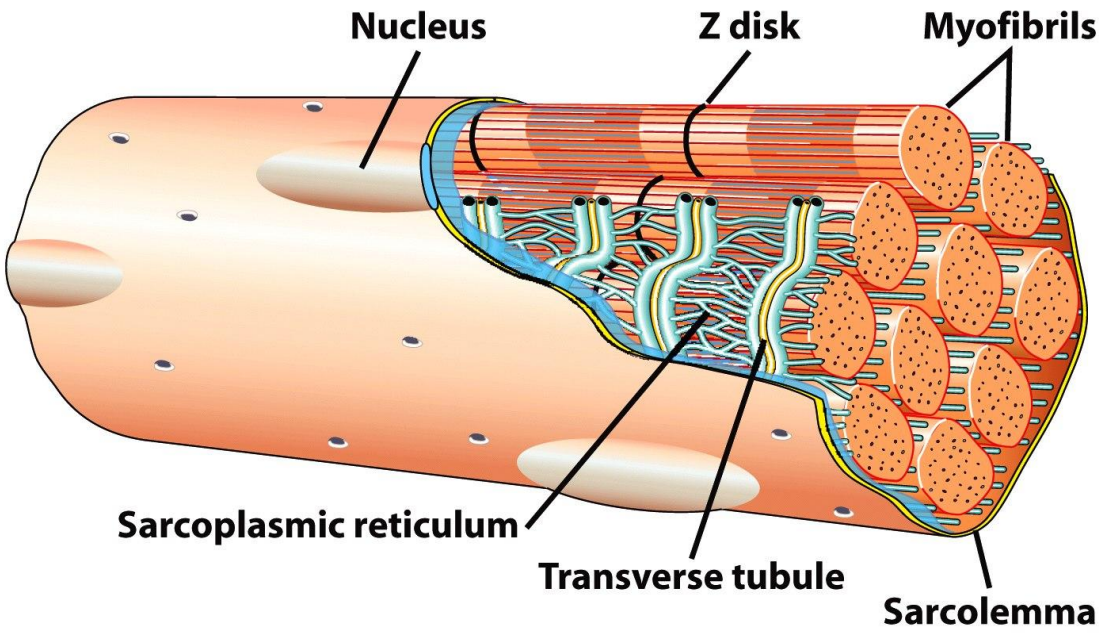
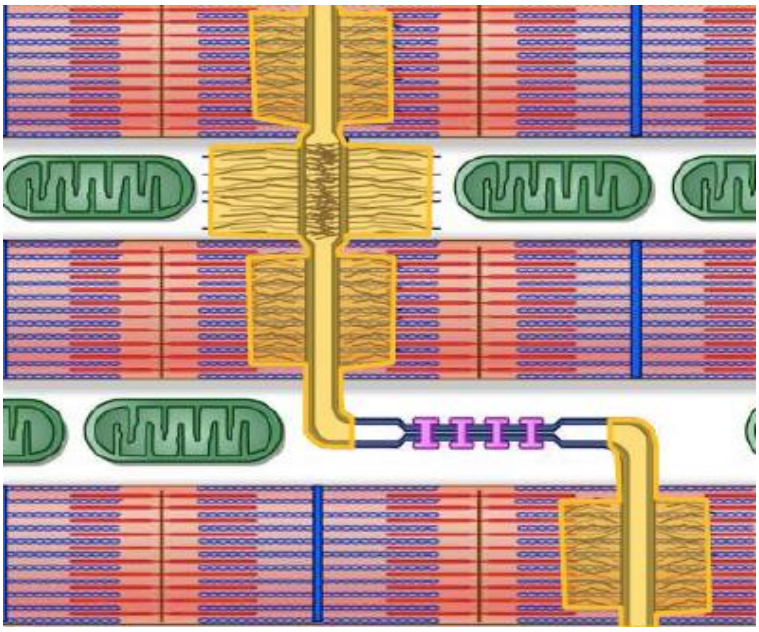


Figure 17-32a
Molecular Cell Biology, Sixth Edition



*Now we will talk about smooth muscles

- ➢ Smooth muscles are found inside the walls of hollow organs and tubes like stomach, intestine, urinary bladder, blood vessels ….etc.

- Smooth muscles are spindle/fusiform in shape (central area is wide and peripherally it is narrower and the nucleus is in the center).

- Smooth muscles are singly-nucleated (one nucleus in the middle of the cytoplasm).

- Smooth muscles are smooth because they don't show striations (sarcomeres), but as all muscle cells they do contain actin and myosin in their cytoplasm, but they are not arranged in a highly regular manner to give the overall striated appearance as in sarcomeres.

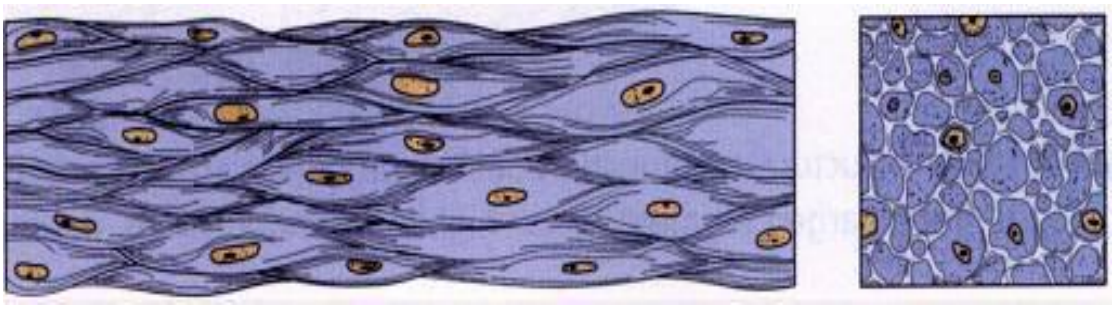
- Usually, these muscles are arranged over each other to form sheets that are tightly packed with small amount of extracellular connective tissue (endomysium), the wide area of one cell overlaps the narrow area of another cell and so on.

- The sheets are perpendicular to each other, one layer is **circular**, the other is **longitudinal**.

- If we look at a longitudinal section across the long axis of the smooth muscles, the previous features (spindle-shaped and singly-nucleated) will be visible.(Notice the figure)

- If we take a cross section through a smooth muscle, we will see different profiles with different sizes, some contain the nucleus and some do not (each cell contains a nucleus, but it depends on the location of the cut, if it's in the **middle** of the cell, The nucleus will be visible, if it's in the **periphery**, we won't see the nucleus).

*__Note:__ if the section is in the **middle** of the cell, the circle will be **big**, but if it's on the **periphery**, the circle would be **small**.



*__How can smooth muscles be stimulated (activated)?__

Answer: By nerves / By local hormones / By mechanical stimuli like stretching. When stretching happens in the urinary bladder due to the accumulation of urine, the reflex of the muscles is to contract.

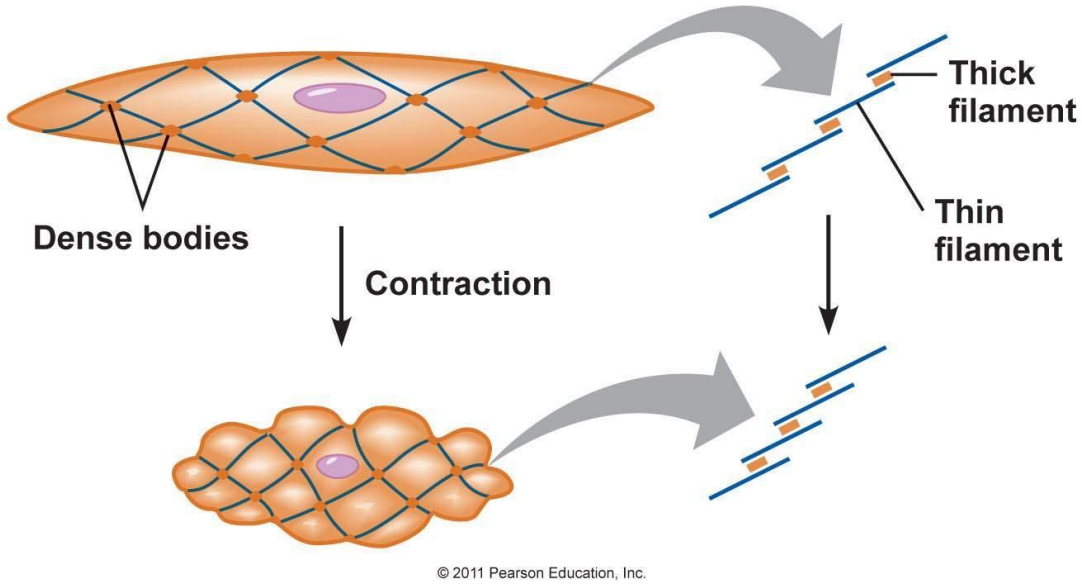
- We find what's called "dense bodies" in the cytoplasm of smooth muscles which appear as dense areas under electron microscope and they are analogous to Z-lines which anchors the actin filaments in the skeletal muscles.
- Dense bodies are composed of α- actinin.
- Dense bodies are the sites where the actin filaments are attached to.

* Dense bodies have two locations:

1- Dense bodies attached to the inner site of plasma membrane, called "sub-membranous dense bodies ".

2- Dense bodies within the cytoplasm, called " intra-cytoplasmic dense bodies".

- Instead of having Z-lines, we have dense bodies, actin filaments are attached to dense bodies and in between we find myosin filaments.
- When the cell contracts, the overlap between actin and myosin increases, this brings dense bodies closer to each other
- When the cell contracts, it becomes rounded with scalloped surface.(notice the figure)



- Intermediate filaments (desmin) anchored two dense bodies together.
- To sum up, dense bodies are connected together by intermediate filaments, actin filaments are attached to these dense bodies and in between these dense bodies there are myosin filaments.
- **<u>Note:</u> no troponin in actin filaments of smooth muscle (instead they have calmodulin-Calcium binding protein)**

- On the plasma membrane of smooth muscle cells, we find pores called caveolae, caveolae are short and shallow invaginations of the plasma membrane of the smooth muscle.

***What is the importance of these caveolae?**

Answer: Increase the surface area of the smooth muscles sarcolemma. Caveolae have high concentration of receptors (because these cells can be controlled by hormones, so we find this high concentration of receptors that have several functions in signal transduction and act as stretch receptors that can sense the stretching and respond by a contraction).

* Smooth muscles can undergo **Hypertrophy and Hyperplasia.**

-Example: the wall of the uterus, which is composed of smooth muscle cells, undergoes both hypertrophy and hyperplasia during pregnancy

*** Smooth muscles are the only type that has high regeneration power. Why?**

The reason is not the presence of high amount of satellite cells. The reason is because these cells are less differentiated cells and can undergo mitosis

** When the cells are less differentiated, they are able to divide as we said before. Skeletal muscle cells are highly differentiated (can't undergo division) and if regeneration of skeletal muscles occurs, it would be because of the satellite cells.

***** Which type of muscles can undergo Hypertrophy? Answer: All types

*Which type of muscles can undergo Hyperplasia? Answer: Smooth muscles

The nervous tissue

-Example: when you see a glass of water, you develop a sensory input (visual input), this stimulus will be converted to an electrical impulse, then it goes to the brain (central nervous system)(CNS), in the brain there is integration of this information ,then taking a decision, if you decide to drink, motor impulses arises from your CNS to your muscles in order to pick up the glass and drink.

- Neurons respond to environmental Changes (stimuli) by altering the ionic gradient across the plasma membrane

*****What are the functions of the nervous tissue:-

1-Sensory function

2-Integration (ex. taking decision)

3-motor function

- Anatomically the nervous system is divided into:

1. Central nervous system: Brain and spinal cord/ responsible for the integration of information, interpretation, making memory and taking decisions.
2. Peripheral nervous system: peripheral nerves ex: (radial, ulnar, axillary nerves……)/ (anything rather than the brain and spinal cord).

- The peripheral nerves are classified according to their origin:

1-from the brain: cranial nerves.

2-from the spinal cord: spinal nerves.

- The peripheral nervous system has two divisions:

1. Somatic: the nerve is going to a voluntary muscle (skeletal muscle) and brings sensation to the CNS from the skin.
2. Autonomic: the nerve is going to involuntary muscle (cardiac or smooth muscle) or a gland (in general to a structure that is not under our conscious control), it regulates the internal environment of our bodies/brings sensations to the CNS from the viscera (lining of your stomach etc.).

- The neurons can be classified (functionally) :

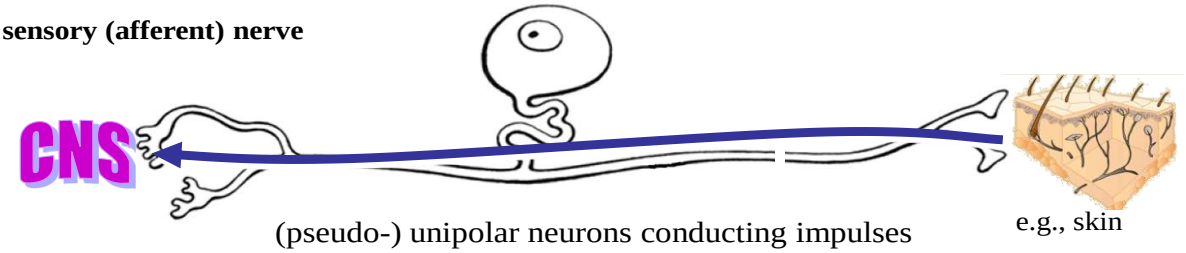
1- Afferent neuron (sensory): our skin, for example, contains sensory receptors (ex. nerve endings) and when stimulated by a stimulus such as pressure/heat, these receptors are going to generate an electrical impulse that goes from the periphery to the CNS.
2- Efferent neuron (motor): an electrical impulse goes from the CNS to a gland or muscle whether it is skeletal or cardiac or smooth.

- The shape of neurons is different between the afferent and the efferent.

*Notice the figure:-

Sensory (Afferent) vs. Motor (Efferent)

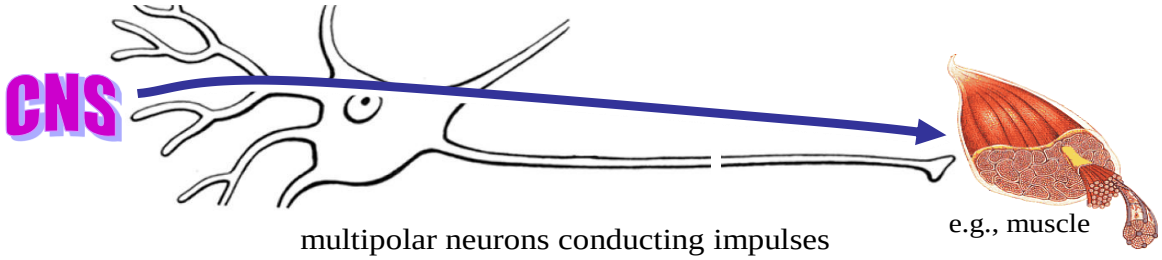
sensory (afferent) nerve



e.g., skin

(pseudo-) unipolar neurons conducting impulses
from sensory organs to the CNS

motor (efferent) nerve



e.g., muscle

multipolar neurons conducting impulses
from the CNS to effector organs (muscles & glands)

Gray's Anatomy 38 1999

The structures of the neuron:

- The Neuron is composed of a cell body (Soma/ perikaryon) and this body has many processes.

- The short and branching processes are called Dendrites
- The long single process is called axon
- Axon at the terminal part gives many branches and the terminations of these branches have button like structures (swelling areas/knobs)
- The cell body contains large nucleus with prominent nucleolus which indicates the activity of the cell (in histological sections this appearance is very specific to neurons) ' Like an eye looking at you (owl eye) or fried egg'

- Dendrites: as you go away from the cell body, these processes become smaller and thinner in diameter (like a tree), they are multiple processes. "profuse branching"
- Axon: it does not branch profusely, it branches at its terminals
- The axon is surrounded by a cell with nucleus and a sheath called myelin (The myelin is mainly composed of lipids), the myelin does not form a continuous layer around the axon, there are spaces (nodes) between the myelin segments. These nodes are called nodes of Ranvier.
- The area of contact between the terminal knob of the axon and the next neuron is called (synapse).

- These neurons are able to convert the stimulus into electrical signal and this electrical signal passes from dendrites to cell body to axon ((Unidirectional propagation of electrical impulses)).

The Histology of the neuron:

- The cytoplasm of the cell body has dots which appear basophilic under the L.M. Basophilia within the cytoplasm means rough endoplasmic reticulum and ribosomes, these dots were called (Nissl bodies) at the beginning as they did not know the ultra structure of these dots, so the cytoplasm of the neuron is full with rough endoplasmic reticulum and ribosomes which again indicates the high synthetic activity of the cell. (Don't forget that these cells synthesize neurotransmitters)
- Also cell body has mitochondria, smooth ER, golgi apparatus (it's important for packaging proteins from the rough ER).
- There are no organelles in the axon and dendrites (except the proximal part of dendrites); they are mainly composed of microtubules, microfilaments and intermediate filaments (neurofilaments), which give the shape of the neuron.
- The microtubules are also important for the movement of the organelles/vesicles within the cell.
- The proximal part of the dendrites contains some nissl bodies but the distal part of the dendrites has no organelles (Similar to the axon)
- We can also find in the cell body lipofuscin pigment, this pigment appears in long-lived cells and it's yellow-brownish in colour. The pigment represents the residual bodies of the lysosomes (Residual bodies= undigested material)
- lipofuscin pigment can be seen in neurons and muscle cells.
- The neurons are highly differentiated cells, they do not undergo mitosis (long-lived cells), so we expect to find things that are related to age changes > lipofuscin pigment.

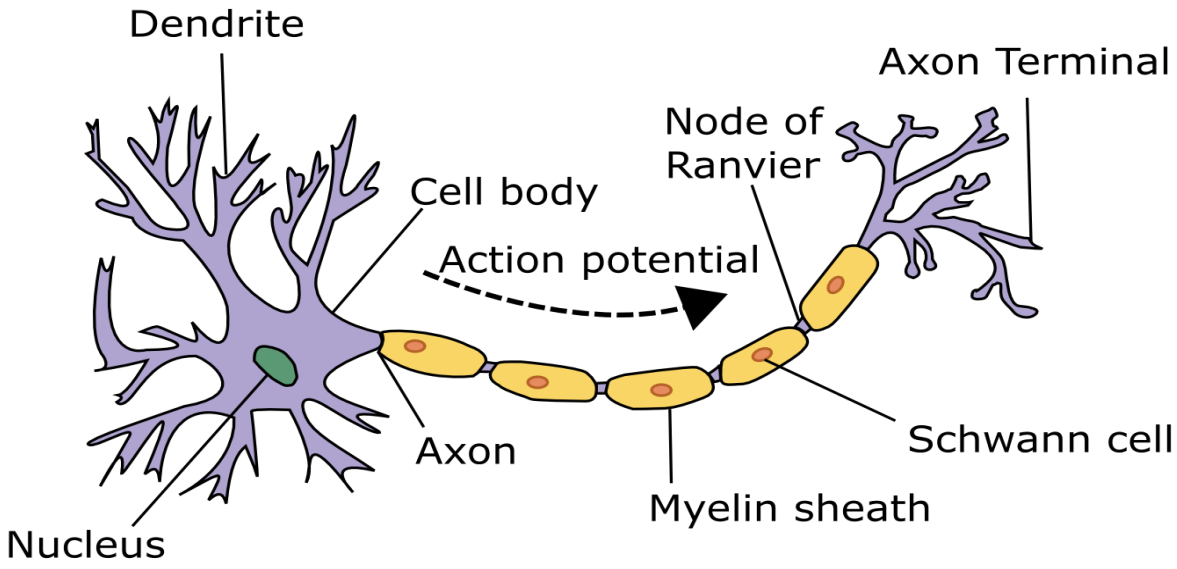
Terminologies of neurons:

- Axoplasm = cytoplasm
- Axolemma = plasma membrane
- Axon hillock = the beginning of the axon from the cell body, it is triangular in shape and unmyelinated. This area is the start point of the action potential.
- Synaptic buttons/knobs= at the terminal site of the axon there are terminal branches, at the end of these branches, the buttons are located; they represent a bulbous area containing vesicles for neurotransmitters.
- The axon has constant diameter except in the terminal part where it starts to branch, unlike the dendrites where they become thinner as you go away from the cell body

- Axons are longer than dendrites their length can reach 1 meter, for example the nerves of the lower limb, their cell bodies extend from the lumbar area to the big toe
- Axon bifurcates at multiple points along its length (axon collaterals).
- The axon is mostly myelinated and it can be unmyelinated whereas the dendrites are never myelinated.
- The axoplasm of the axon contains mitochondria, microtubules, neurofilaments, smooth ER but No Rough ER, no ribosomes and no golgi apparatus.
- Where could we find mitochondria inside the axon?

The terminal part of the axon, in order for the synaptic vesicles to perform exocytosis into the synaptic cleft, this process needs energy and calcium so we expect to find mitochondria and smooth ER inside the axonal terminals.

- Therefore, if there is a cut in the axon, distal segment of the axon degenerates because the axon depends on the cell body for its maintenance. The cell body is the trophic center of the neuron, if the axon is separated from the cell body it will die because it cannot synthesize its own proteins. Therefore, the cell body is important for the vitality of the axon.



- **Myelin:** lipoprotein surrounding the axon for insulation and protection and increasing the velocity of the propagation of the action potential along the axon (The same concept as the rubber around the wire.)

AXONAL TRANSPORT

At the terminal part of the neuron, there are a lot of vesicles containing neurotransmitters, but how these vesicles reach the axonal terminals? by a process called axonal transport, using microtubules and motor proteins.

Axonal transport has two types:

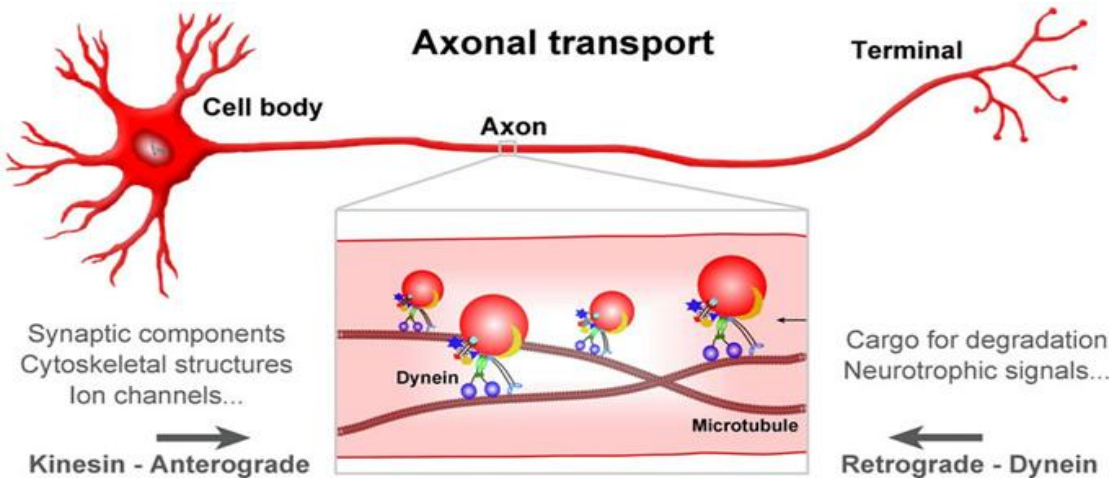
- Anterograde transport: movement of the vesicles from the cell body to the axon terminals, and its motor protein is kinesin
- Retrograde transport: is the movement of the vesicles from the axon terminals toward the cell body (for recycling), and its motor protein is dynein

The nervous tissue is composed of two types of cell:

1-neurons: excitable cells. Neurons are simply us, they perceive, think, sense, and remember. They control muscle activity and regulate the gland secretion.

2-neuroglia : important for supporting ,nourishing and protecting neurons which is vital for establishing an appropriate microenvironment for the neurons to work, plus forming a glue-like structure between the neurons.

- Neurons do not divide (have no centrioles) and they are long-lived cells, while neuroglia can divide, they are supporting cells not neurons so they undergo mitosis.
- neuroglia are smaller in size but larger in number compared to neurons.
- Neurons have high metabolic activity. The cell body has many processes (these processes are difficult to be seen using ordinary stains (H&E)
- Neurons are excitable cells; they receive stimuli and convert them into electrical impulses. (but this function cannot be done by the neuroglia!!



''Wherever the art of medicine is loved, there is also a love of humanity.''

- Hippocrates

*This sheet is done by : Omar Al-Sahily