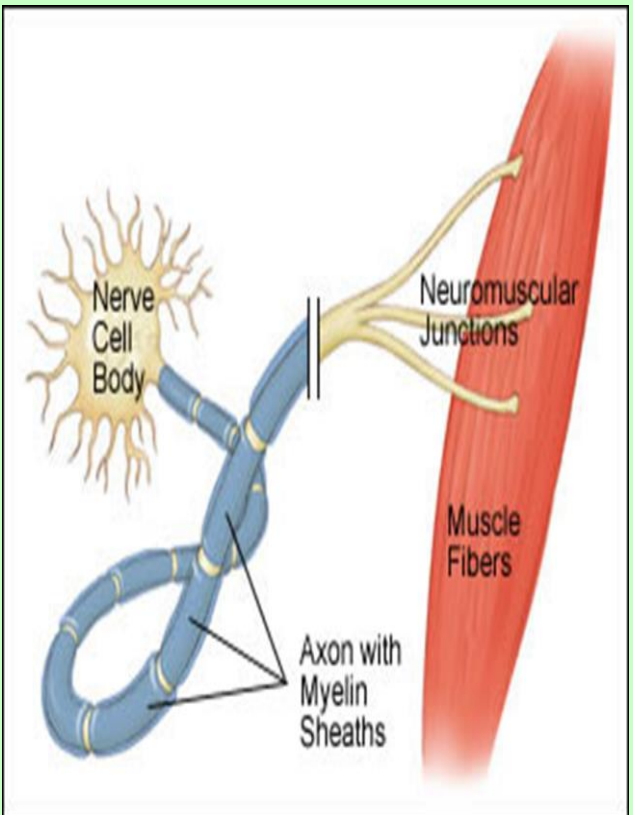


NEURO MUSCULAR JUNCTION



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Objectives

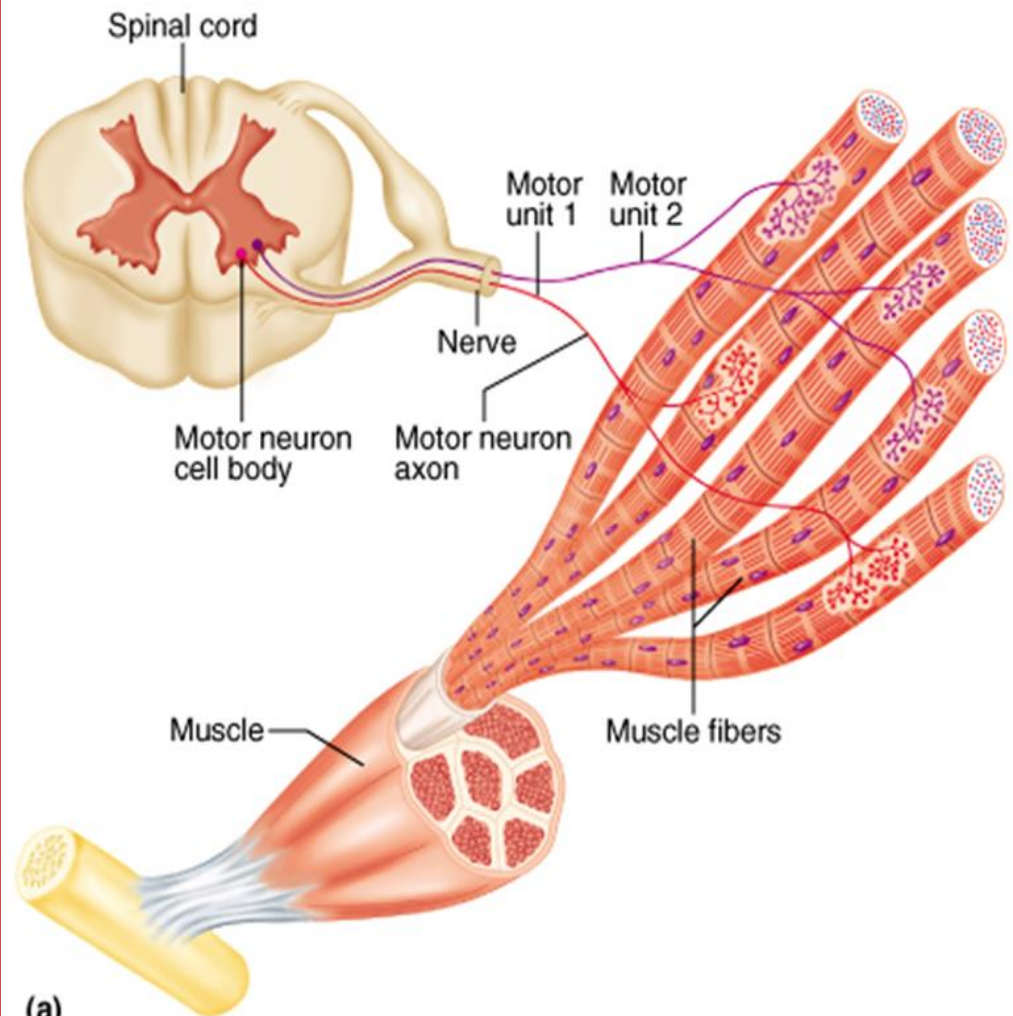
1. **Functional anatomy of the neuromuscular junction.**
2. **Mechanism of neuromuscular transmission.**
3. **Properties of neuromuscular transmission.**
- 4- **Myasthenia gravis**

Neuromuscular junction

The skeletal ms. fibers are innervated by thick myelinated nerve fibers (α)

Motor unit

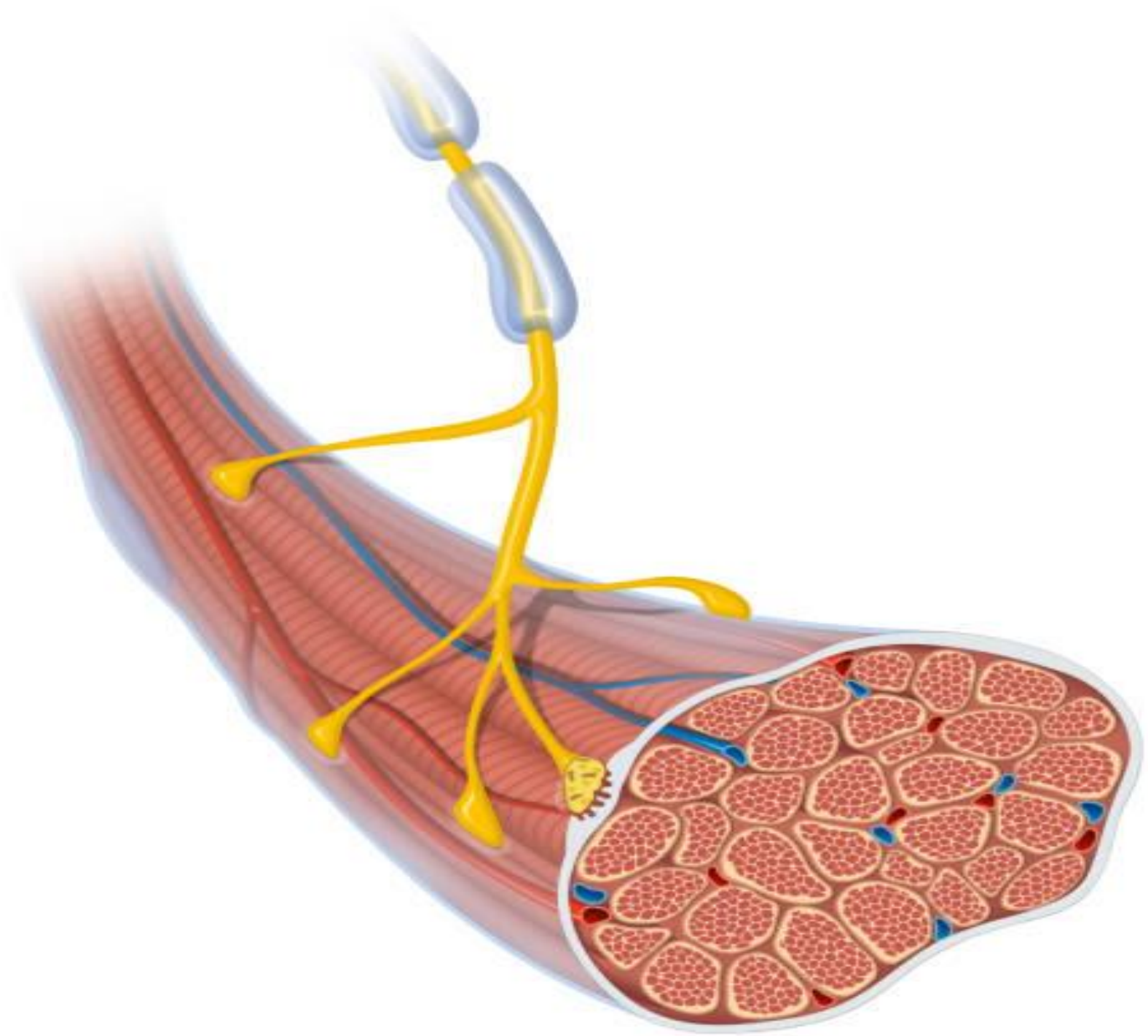
It consists of a motor neuron and the ms. fibres supplied by it.



Functional anatomy of the neuro-muscular junction

-When the nerve fiber approaches the muscle fiber, it loses its myelin sheath and divides into many terminal branches which end in synaptic knobs.

- Each branch forms a junction with a single muscle fiber near its middle.



Neuromuscular junction

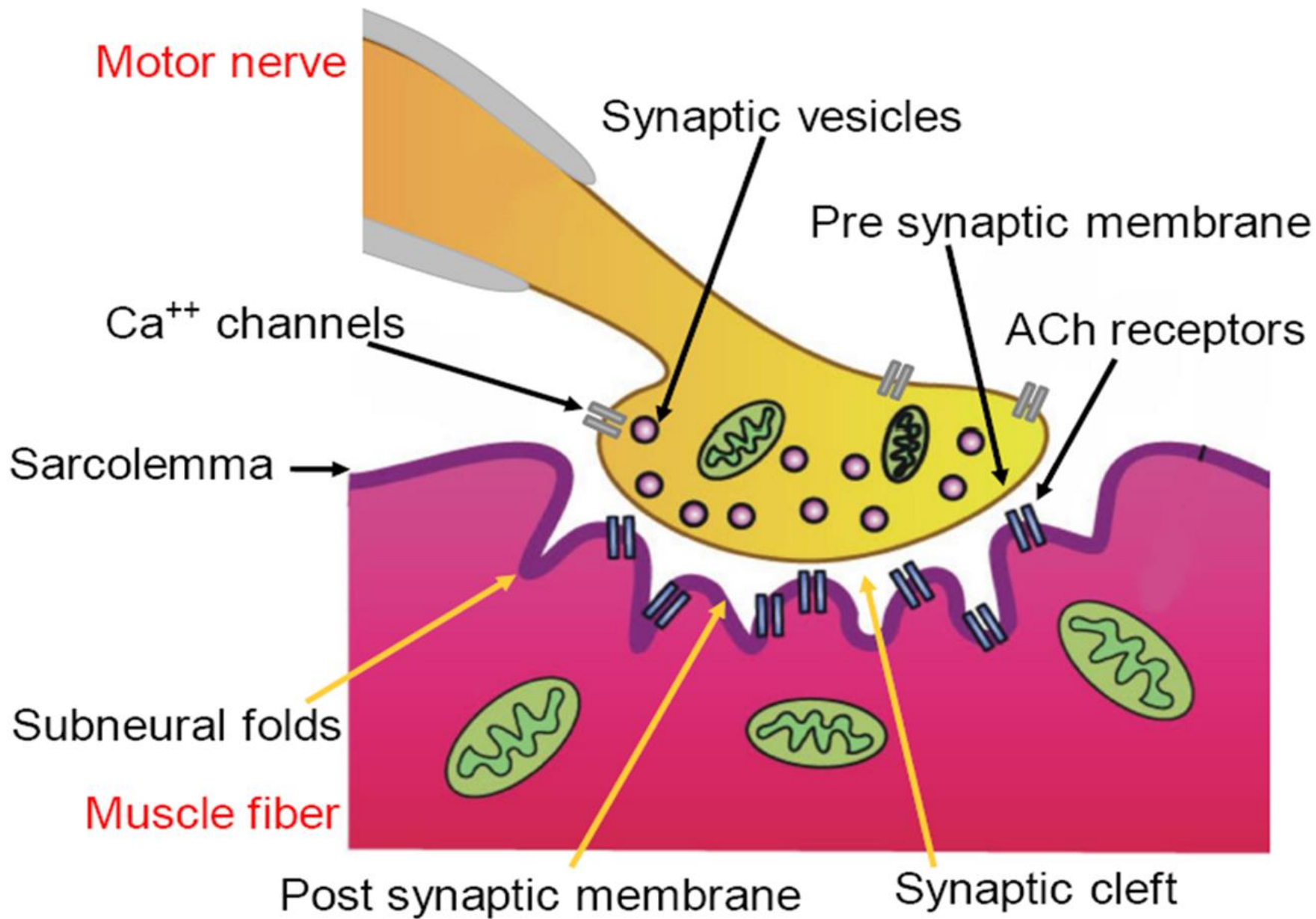
-Neuromuscular junction is the area of contact between motor nerve fiber and a muscle fiber.

Parts:

1-Axonal terminal of motor nerve or presynaptic terminal

2-Motor end plate of muscle or postsynaptic membrane

3-Synaptic cleft



Neuro-muscular junction is composed of:

1) Pre-synaptic membrane :

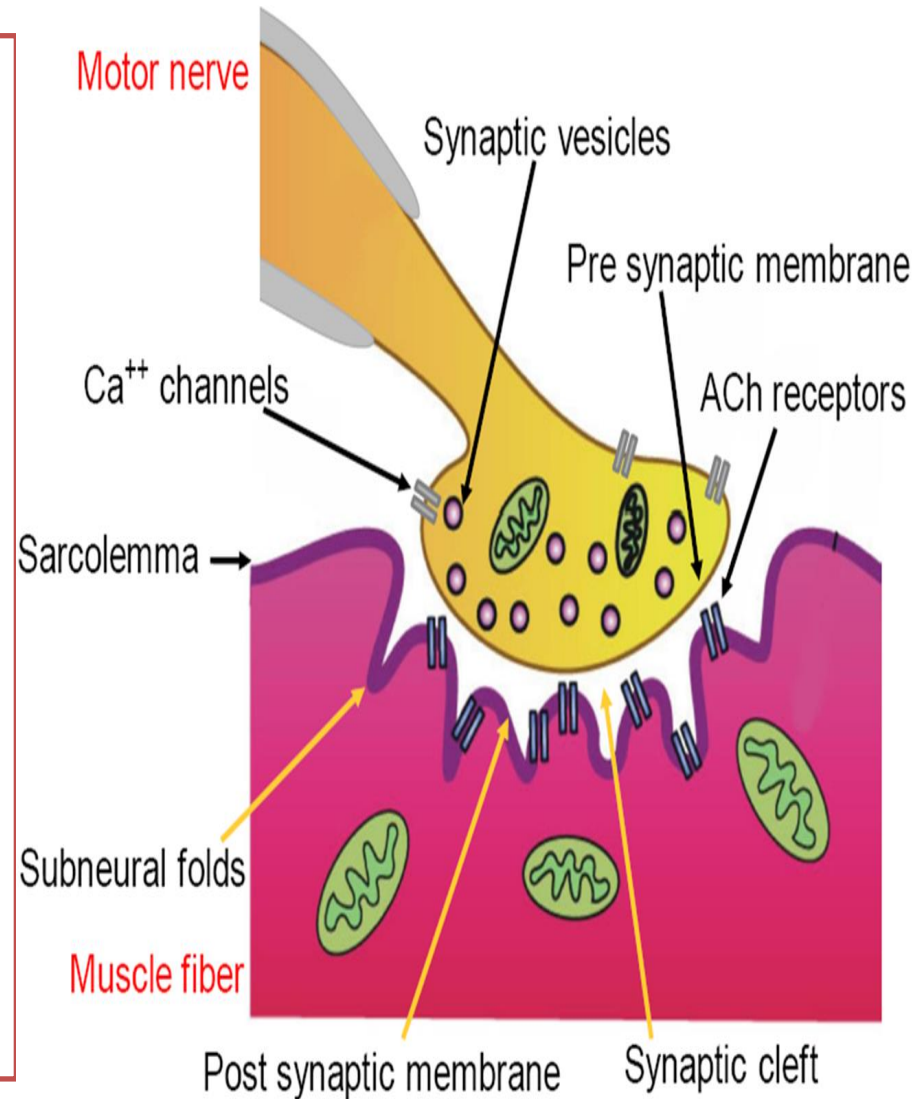
(Synaptic Knob)

which contains:

- **Acetylcholine vesicles.**
- **Multiple voltage gated Ca^{++} channels.**

2) Synaptic cleft(20-30nm)

It is the space between the nerve and muscle membrane.



Neuro-muscular junction is composed of:

3) Post-synaptic membrane = Motor end plate:

- It is the muscle fiber plasma membrane under the synaptic knob.

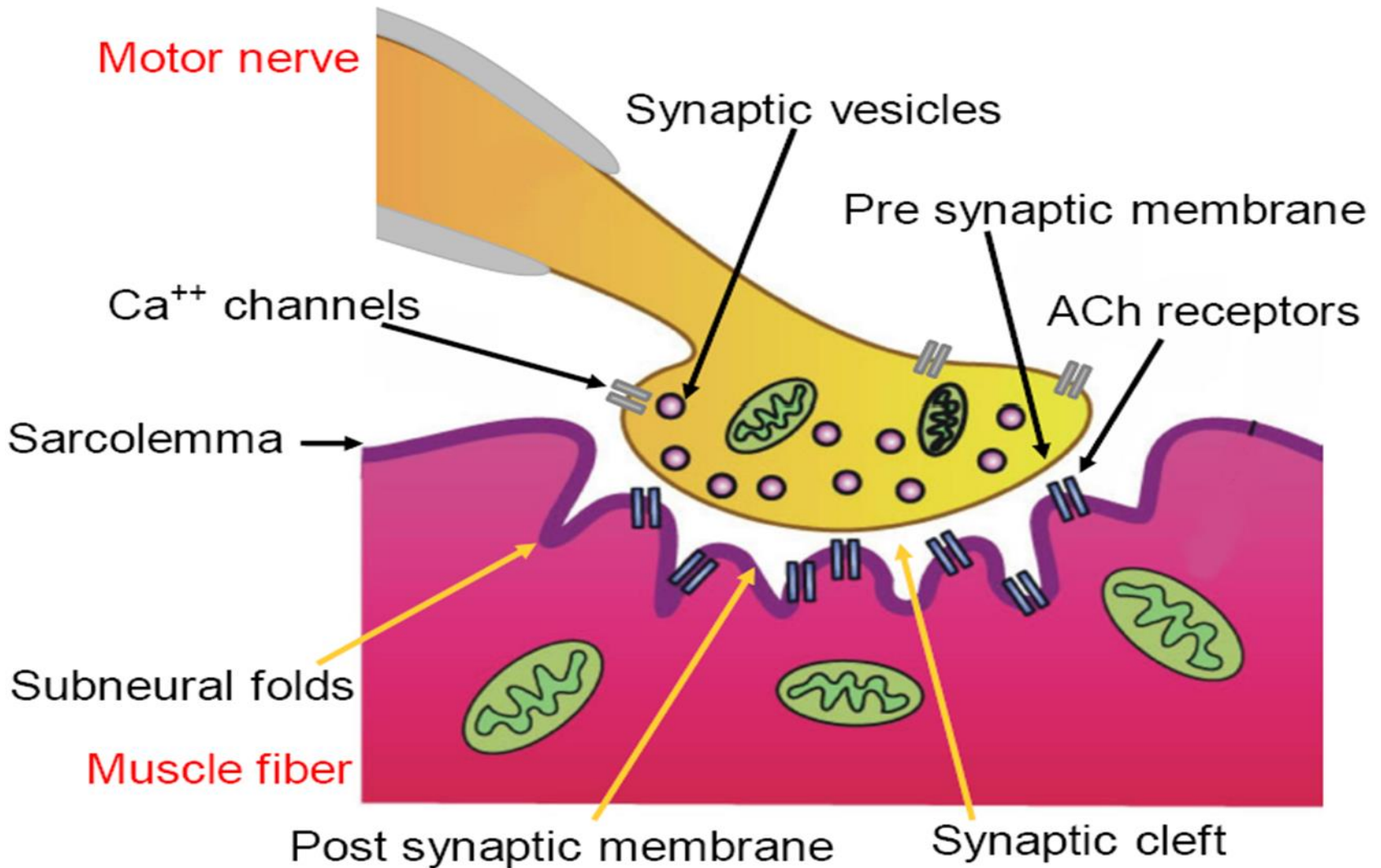
It is thrown into folds to increase the surface area for A.ch. action

It contains:

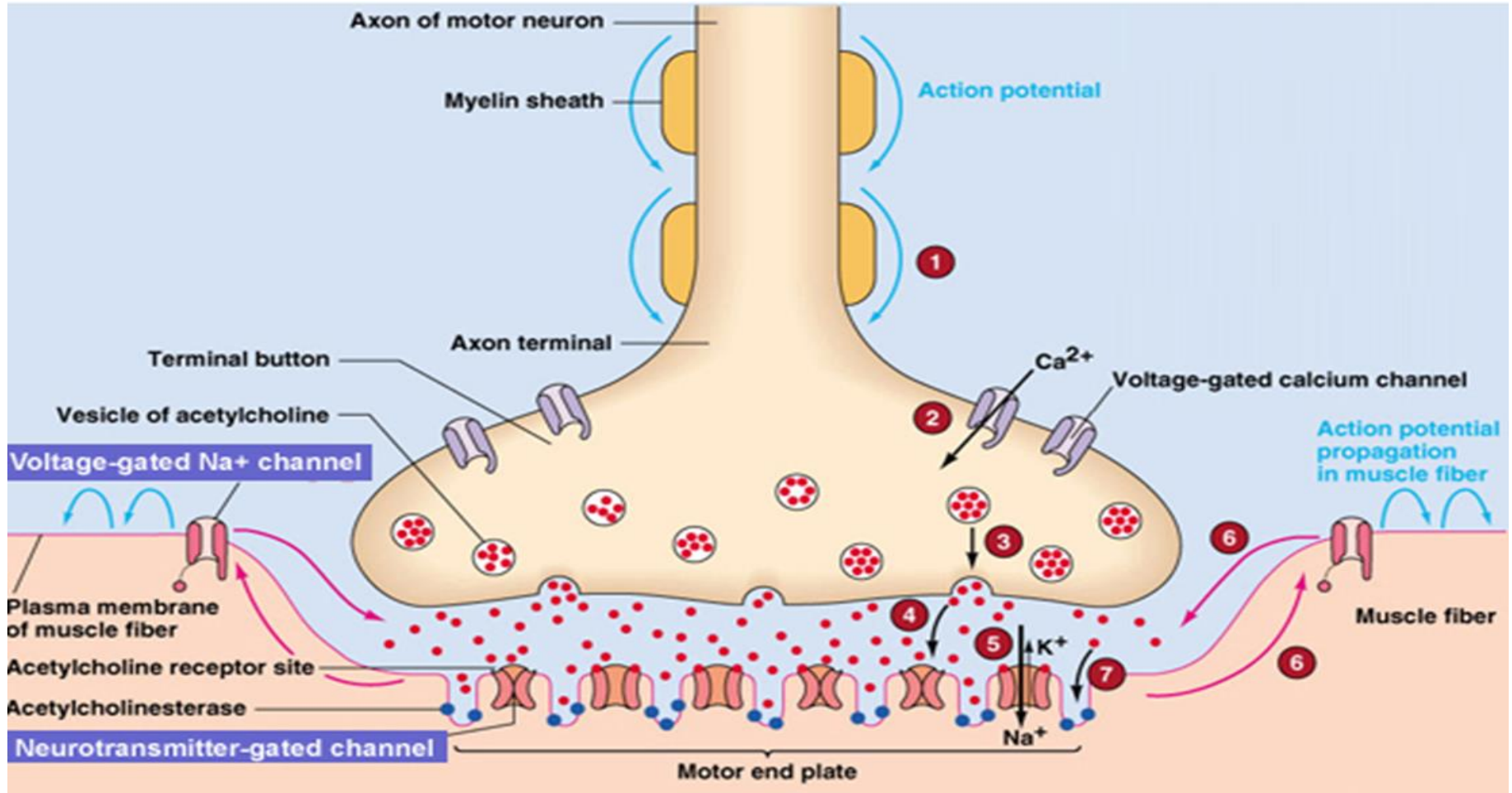
1-Acetylcholine receptors.:Nicotinic receptors, which are ligand gated ion channels

2-Choline-esterase enzyme : which breaks down acetylcholine to an inactive form once it has done its action.

Neuromuscular junction



Mechanism of Neuro-Muscular Transmission



Mechanism of neuromuscular transmission:

- 1) When a nerve impulse reaches the axon terminal, it opens voltage gated Ca^{++} channels.
- 2) thus allowing calcium influx. this leads to movement and fusion of A.ch. vesicles with the presynaptic membrane, rupture of these vesicles and release of A.ch. by exocytosis into synaptic cleft.

Mechanism of neuromuscular transmission:

- 2) A.ch. diffuses across the cleft to the motor end plate
- 3) A.ch. binds with the receptors leading to increase in Na^+ and K^+ permeability at the same time.
- 4) Na^+ influx is greater than K^+ efflux so action potential is produced and propagated along the muscle fiber.
- 5) Once A.ch. produces its action, it is rapidly hydrolyzed with choline-esterase enzyme, to prevent occurrence of multiple contractions

Properties of neuromuscular junction

1) One way conduction

- NMT occurs only from the nerve to the muscle.

because A.ch vesicles are present only in the nerve terminal

(2) Synaptic delay: - It is the time interval between the arrival of nerve impulse to the NMJ and the AP generated in muscle.

- **Causes:** Release of Ach from the presynaptic terminals, and its diffusion across the synaptic cleft , Combination of Ach with the receptors which open the channels leading to diffusion of ions, and generation of action potential.

Properties of neuromuscular junction

3) Synaptic fatigue

- **NMT shows fatigue: -**
- **Fatigue of NMT** due to depletion of the Ach vesicles **due to rapid repeated stimulation of the motor nerve.**
- **O₂ lack facilitates the onset of fatigue because it** decreases the metabolic reactions needed to reform A.ch

Properties of neuromuscular junction

4) Effect of ions:

- a) **Ca ions:** - It helps NMT by causing rupture of the Ach vesicles → so ↓Ca ions near the axon terminal will prevent the release of Ach and ↓NMT.
- b) **Mg ions:** - It inhibit NMT by stabilizing the Ach vesicles → prevent the release of Ach and therefore ↓es NMT.
- c) **K ions:** - It has anticholinergic action on the motor end plate

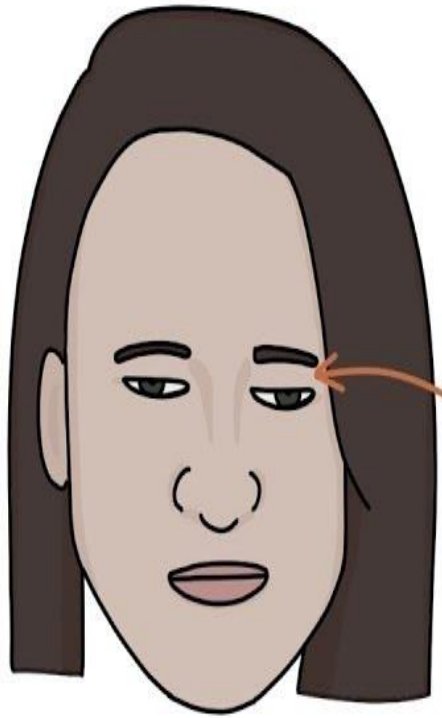
Myasthenia gravis

Def:

-It's an auto-immune disease **that affect the muscle**
characterized by muscle weakness and rapid onset of
fatigue.

Incidence: 1/ 20,000 usually female.

MYASTHENIA GRAVIS

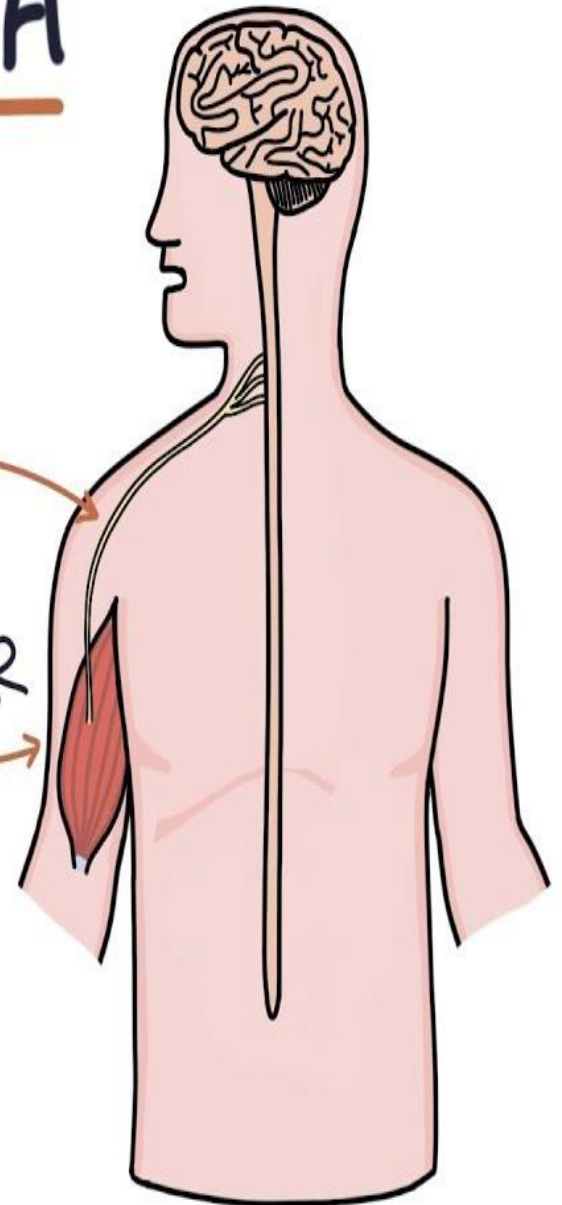
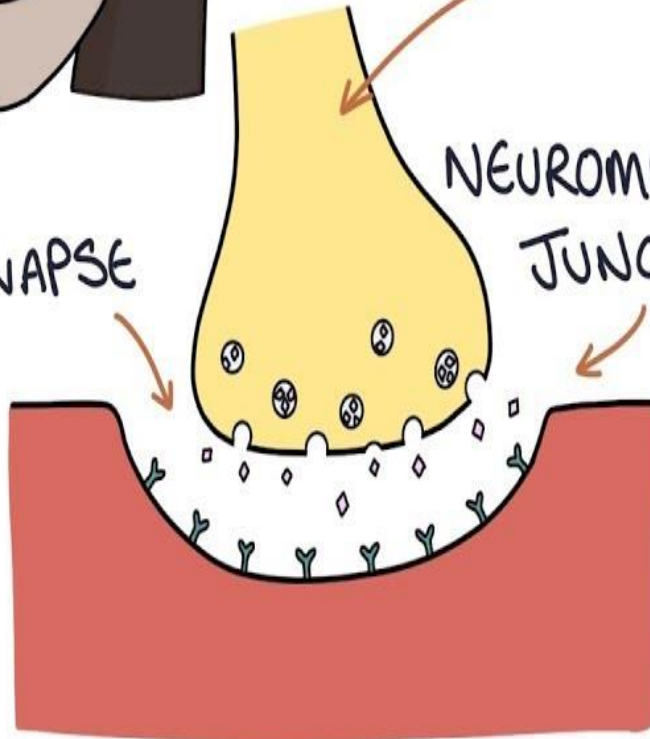


PTOSIS

AXON

NEUROMUSCULAR
JUNCTION

SYNAPSE



Myasthenia gravis

Cause:

- 1- ↓ number of acetyl choline vesicles in the axon terminal.
- 2- ↓ A. Ch content in the vesicles
- 3- widening of the synaptic cleft.
- 4- ↓ junctional folds thus decreasing the surface area.
- 5 - ↓ number of A.ch. receptors on the postsynaptic membrane .

Myasthenia gravis

Clinical picture:

The motor end plate potential is very weak and the ms. fails to contract.

- The first muscles to be affected are those supplied by cranial nerves e.g eye ms
- In severe cases there is general ms. Weakness. death may occur due to respiratory ms. Paralysis.

Diagnosis: 1- Electromyogram. 2-Therapeutic test: the patient is given a dose of prostigmine if improved this confirms the diagnosis.

Summary

- 1. Neuromuscular junction** is the junction between a nerve terminal fibre and a muscle fibre.
- It consists of
 - a- presynaptic part.**
 - b- synaptic cleft.**
 - c- post synaptic part**
 - a-The presynaptic part contain acetylcholine vesicles and calcium channels.**

Summary

2-Passage of nerve impulse causing:

a. Ca entry into presynaptic terminal .

b. Rupture of the synaptic vesicle.

c. Release of acetyl choline.

d. Binding of acetyl choline with the cholinergic receptors.

Summary

e-Muscle action potential.

f-Ca entry into the muscle fibre.

j-Muscle contraction.

5- properties of neuromuscular Transmission includes :

- **One way conduction.**
- **Synaptic delay**
- **Synaptic fatigue**

6- Myasthenia gravis is a disease characterized by muscle weakness due to defect in neuro muscular transmission.

MCQ

1- About neuromuscular transmission ,which of these channels is present in the presynaptic membrane and is responsible for rupture of acetyl choline vesicles?

- a) Voltage gated Na channels.**
- b) K channels.**
- c) H ATPase channels.**
- d) Voltage gated ca channels.**
- e) Chloride channels.**

MCQ

2-Which of these disease is characterized by muscle weakness and occurs due to defect in neuromuscular transmission?

- a) Multiple sclerosis.
- b) Myasthenia gravis .
- c) Lupus erythematosus.
- d) Rheumatoid arthritis.
- e) Rigor mortis.

MCQ

3-As a property of neuromuscular transmission:one way conduction is caused by which of these items?

- a) The presynaptic terminal contains mitochondria.
- b) The presynaptic terminal contains voltage gated ca channels.
- c) The presynaptic terminal contain acetyl choline vesicles.
- d) The post synaptic membrane contain choline esterase enzyme.
- e) The post synaptic membrane contain Na channels.

4- Which of these ions inhibits neuromuscular transmission?

- a) Ca^{++}
- b) Mg^{++}**
- c) Na^+
- d) Cl^-
- e) H^+

5-Which is the type of receptors present in postsynaptic membrane of neuromuscular junction?

- a) B1 adrenergic
- b) Alpha adrenergic
- c) Muscarinic cholinergic
- d) Nicotinic cholinergic**
- e) B2 adrenergic

Short essay questions

- 1) Mention 3 properties of neuromuscular transmission
- 2) Describe functional anatomy of neuromuscular junction
- 3) Describe mechanism of neuromuscular transmission
- 4) Discuss myasthenia gravis as regard definition ,incidence ,clinical picture and diagnosis

