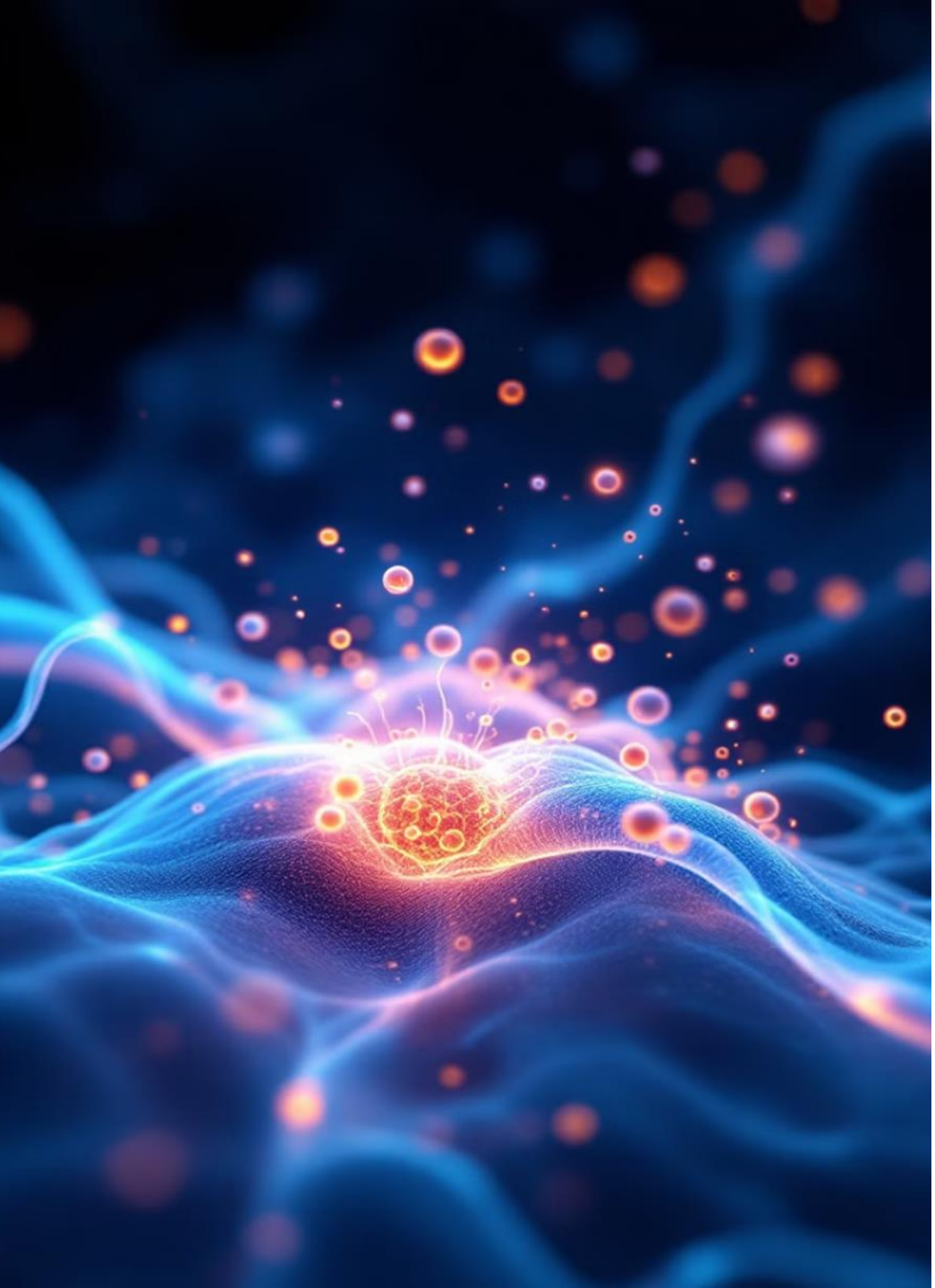


Neuromuscular Junction

Lec.5

Neuromuscular junction

* The central nervous system ultimately controls skeletal muscle contractions, with motor neurons delivering to the muscles commands telling them when to contract and when not.
* Moreover, input from motor neurons always has an excitatory effect on muscle cells and serves to trigger contraction of those cells. The connection between a motor neuron and a muscle cell, referred to specifically as a neuromuscular junction, is fundamentally similar to an “ordinary” synapse between two neurons in the nervous system.

* From simple actions like blinking to complex athletic feats, this vital connection transforms thought into action through an elegant biological mechanism.

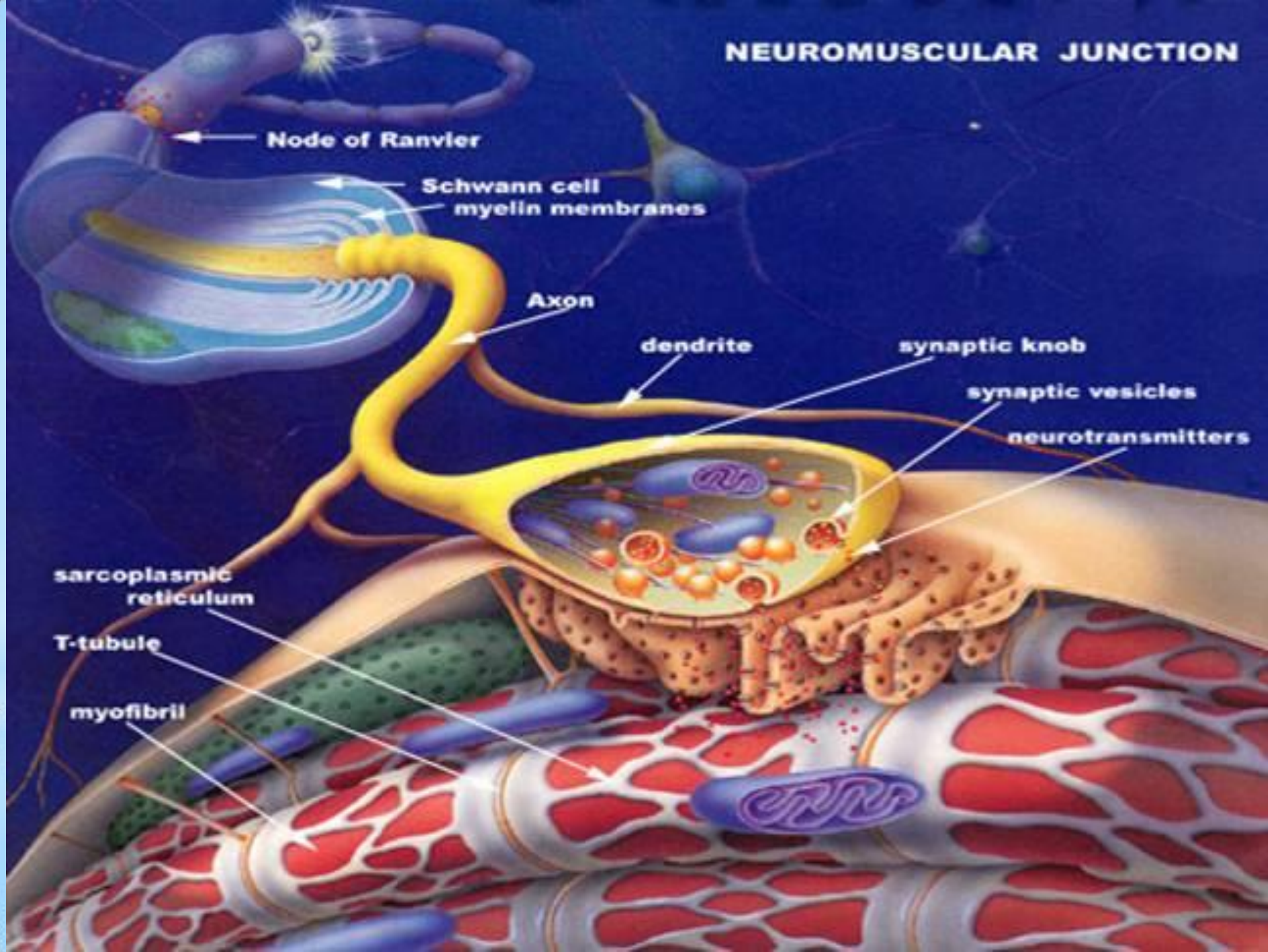
* When a muscle cell receives input from a motor neuron, the cell depolarizes and fires an action potential that then stimulates contraction. The sequence of events that links the action potential to the contraction is referred to as **excitation-contraction coupling.**

Anatomy of the Neuromuscular Junction

* As the axon supplying a skeletal muscle fiber approaches its termination, it loses its myelin sheath and divides into a number of terminal boutons, or endfeet. The endfeet contain many small, clear vesicles that contain acetylcholine, the transmitter at these junctions.
* **Presynaptic terminal**: The motor neuron ending contains synaptic vesicles filled with acetylcholine neurotransmitters.

* **Synaptic cleft:** This narrow gap allows acetylcholine to diffuse across to the acetylcholine receptor in the muscle fiber. The synaptic cleft contains acetylcholinesteras estrase (the enzyme that degrades the acetylcholine neurotransmitter).

* **Post synaptic membrane** : The muscle fiber membrane contains many acetylcholine receptors in junctional folds.

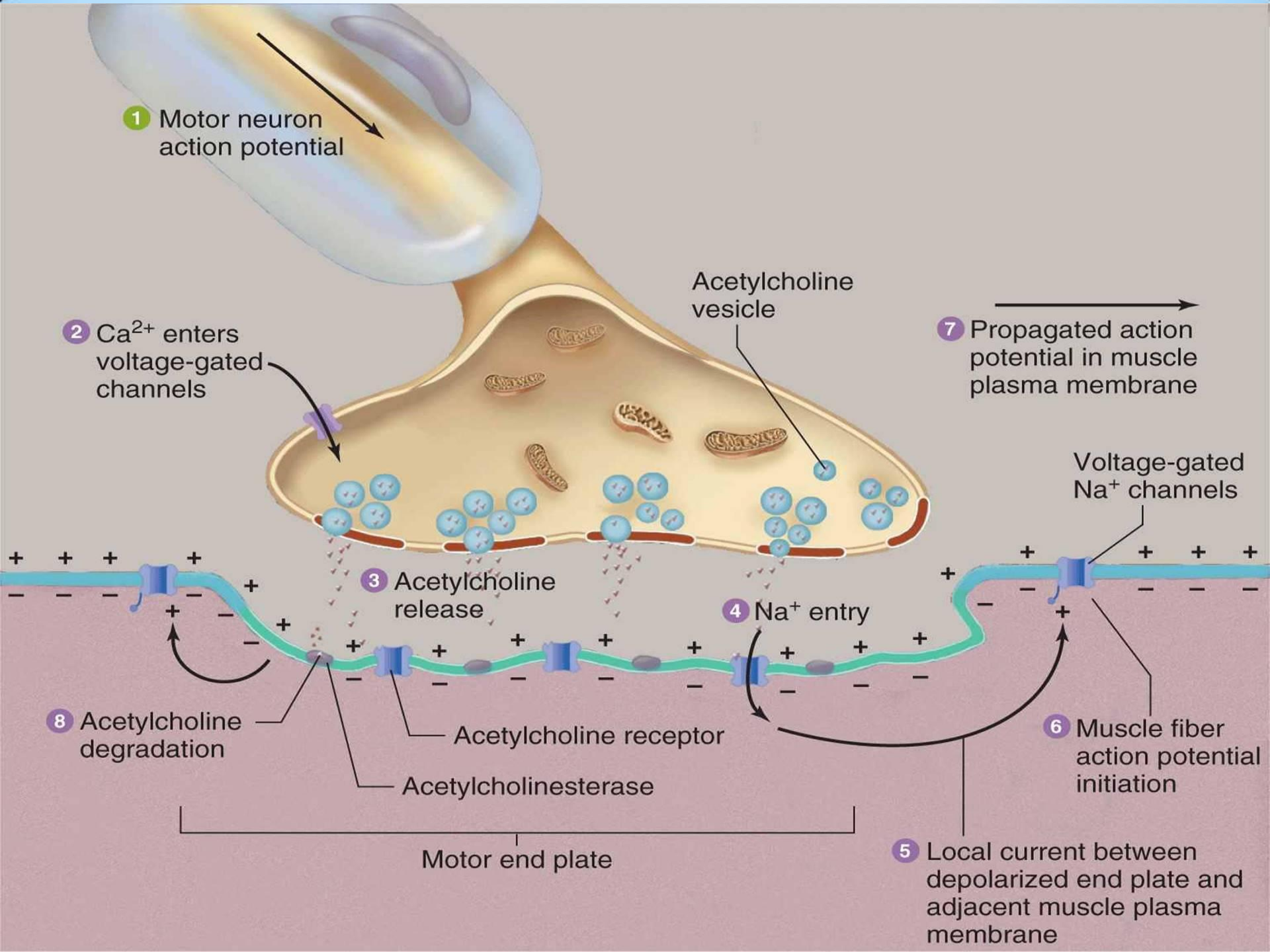

NEUROMUSCULAR JUNCTION
Node of Ranvier
Schwann cell
myelin membranes
Axon
dendrite
synaptic knob
synaptic vesicles
neurotransmitters
sarcoplasmic reticulum
T-tubule
myofibril

The Role of the Neuromuscular Junction in Excitation-Contraction Coupling

* When an action potential spreads over the terminal end feet of an axon , Ca+ channels open and allow calcium ions to diffuse from the synaptic space to the interior of the nerve terminal.
* The Ca+ activate the release of acetylecholine from nerve terminal into synaptic cleft by exocytosis.
* After release acetyl choline diffuses through the synaptic cleft to the muscle membrane (sarcolemma) and attach to the muscle-type nicotinic acetylcholine receptors, which are concentrated at the tops of the junctional folds of the membrane of the motor end plate.

- After binding to its receptor, acetylcholine causes the voltage-gated Na^+ channel to open and firing of an action potential in the muscle, which will lead to depolarizing potential, **the end plate potential**. eventually into skeletal muscle contraction
- Although a motor neuron typically branches and innervates more than one muscle cell, each muscle fiber receives input from only one motor neuron.

* At the neuromuscular junction, the motor neuron's terminal boutons, or endfeet fan out over a wide area of the sarcolemma. Opposite these boutons is a specialized region of the sarcolemma called the motor end plate, which is highly folded and contains a high density of acetylcholine receptors.


1 Motor neuron action potential
2 Ca^{2+} enters voltage-gated channels
Acetylcholine vesicle
7 Propagated action potential in muscle plasma membrane
Voltage-gated Na^+ channels
3 Acetylcholine release
4 Na^+ entry
8 Acetylcholine degradation
Acetylcholine receptor
Acetylcholinesterase
6 Muscle fiber action potential initiation
Motor end plate
5 Local current between depolarized end plate and adjacent muscle plasma membrane

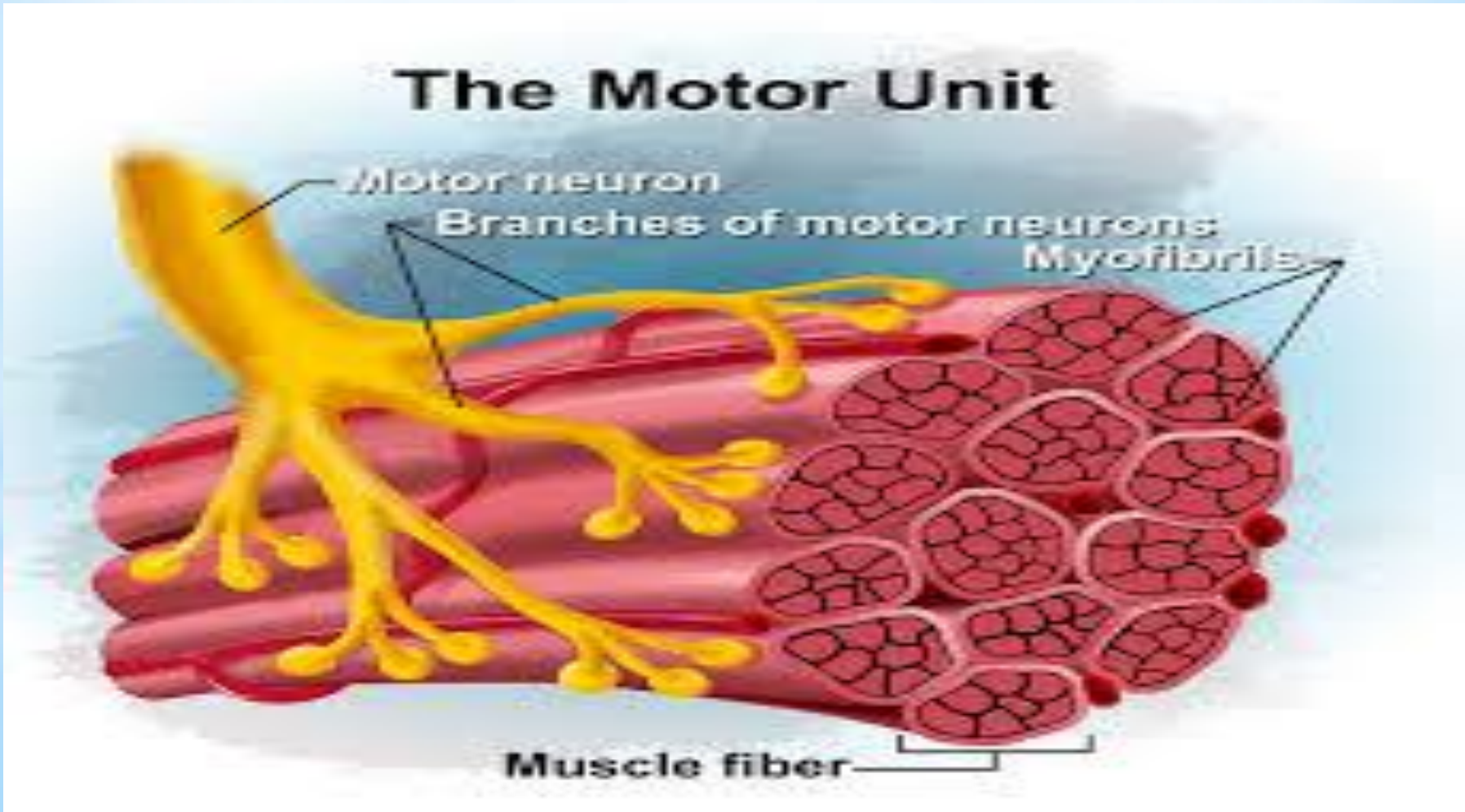
*The Motor Unit

*Single nerve cell body and its axon plus all muscle fibers innervated by the axon's branches. All the muscle fibers of a motor unit are of the same fiber type. Each motor unit has a different amount of muscle fibers.

*The motor unit muscle function depends on the innervation of muscle fibers. Multiple muscle fibers that make up the motor unit are supplied by a single motor neuron in the spinal cord.

*Within muscles like the hand and eye muscles (i.e., muscles involved in tiny, graded, precise action), each motor unit innervates just a small number of muscle fibers (about three to six).

*However, human leg muscles can have up to 600 muscle fibers per motor unit.



*Properties of Neuromuscular Transmission:

1. **Unidirectional** : one direction only from the nerve to the muscle
2. **Delay** : about 0.5 m sec. for release of Ach
3. **Easily fatigued**: due to repeated stimulation(Muscle fatigue is a commonly experienced phenomenon that limits athletic performance and other strenuous or prolonged activity).
4. **Effect of ions:** The number of rupture vesicle is directly proportional with Ca++ions. The number of rupture vesicle is inversely proportional with Mg++ ions (Magnesium paralyzes skeletal muscle dose-dependently by competing with calcium on the presynaptic membrane and inhibiting calcium-dependent acetylcholine release).

5. Effect of Drugs :

* Drugs that increase release of acetylecholine directly e.g carbachole ,small dose of nicotine.
* Indirectly prevent degredation of acetylcholin like neostigmin (reversibly).
* Drugs that decrease acetylcholine release like Botulinum toxin. It acts by blocking the release of acetylcholine from the presynaptic terminal of the neuromuscular junction.