Drug Effects on End Plate Potential

- Inhibitors -

1. Balk widow spider venom

2.Organophosphates

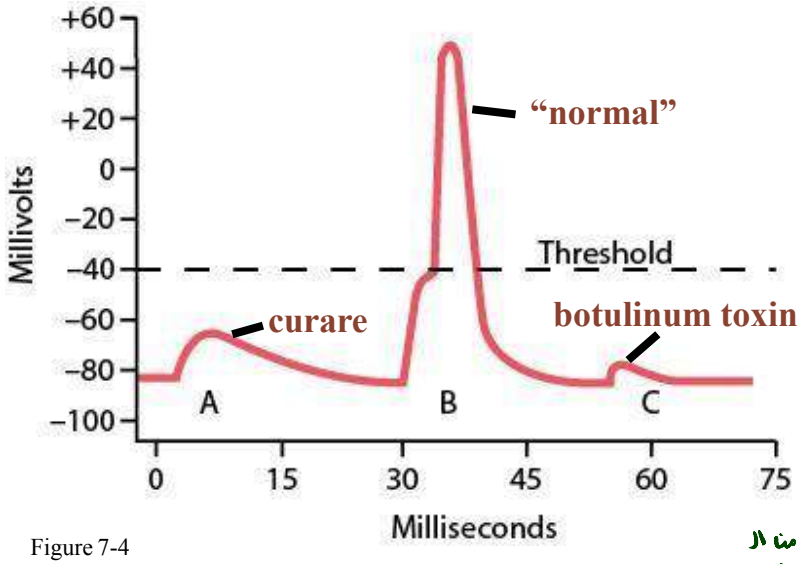


Figure 7-4

Curariform drugs (D-turbocurarine)

- block nicotinic ACh channels by competing for ACh binding site
- reduces amplitude of end plate potential therefore, no AP

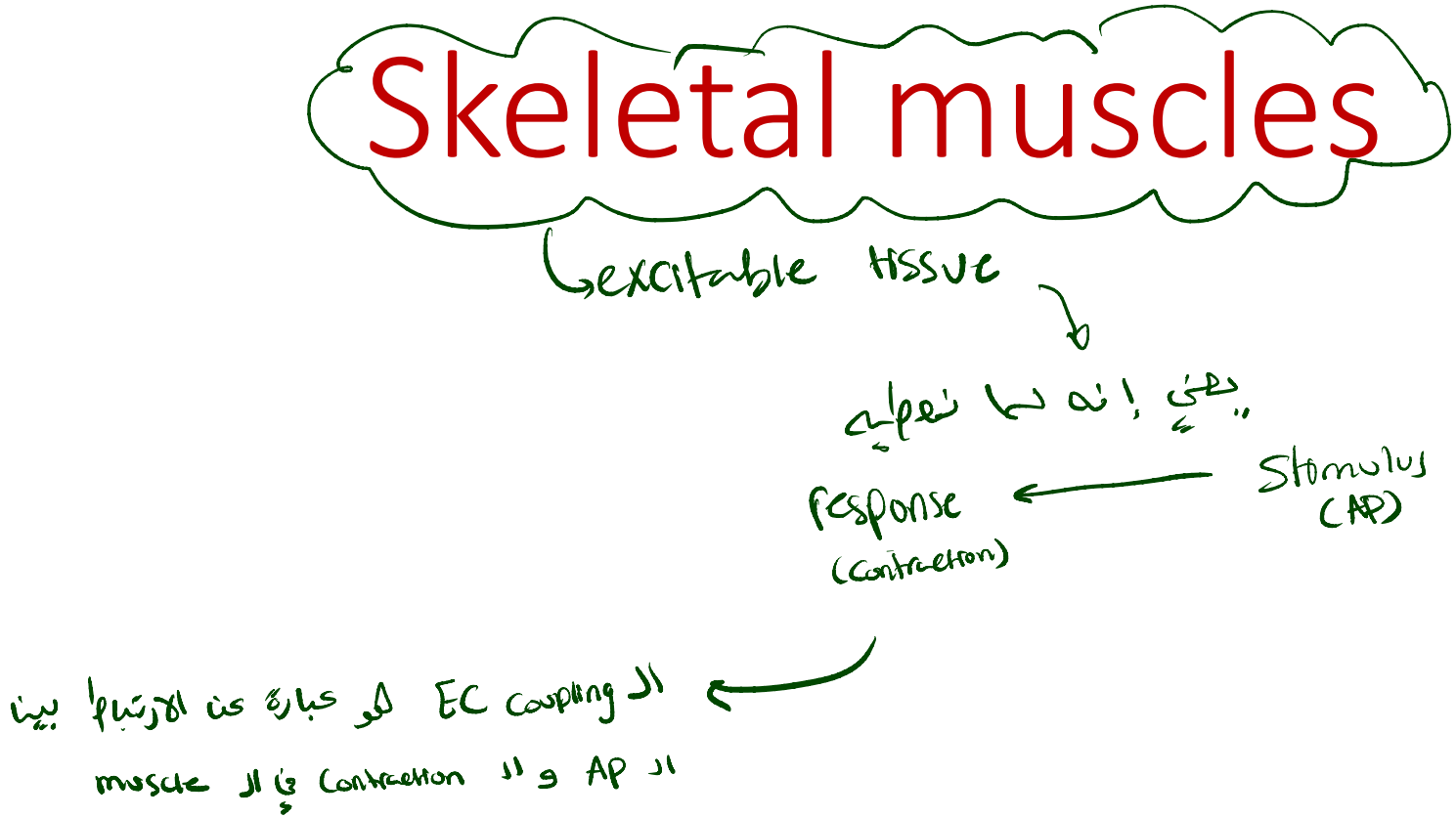
Botulinum toxin

- decreases the release of Ach from nerve terminals
- insufficient stimulus to initiate an AP
- Causes muscle paralysis

Drug Effects on NMJ

- Black widow spider venom : Causes explosive release of Ach at all cholinergic synapses
- Prolonged depolarization May cause respiratory failure
- Acetylcholine esterase inhibitor
  - Organophosphates, insecticides, and nerve gas agents as a weapon.
- Theses substances are anticholinesterase agents thus prolong the action of acetylcholine at cholinergic synapses
- Symptoms of toxicity include :
  - increased saliva and tear production, diarrhea, nausea, vomiting, small pupils, sweating, (autonomic effects), muscle tremors, and confusion.
  - The onset of symptoms is often within minutes, and it can take weeks to disappear

Excitation contraction coupling in Skeletal muscles



Transverse Tubule–Sarcoplasmic Reticulum System In Skeletal Muscles

T-tubules:

- Invaginations of the **sarcolemma** filled with extracellular fluid
- Penetrate the muscle fiber, branch and form networks
- Transmit AP's deep into the muscle fiber

Sarcoplasmic Reticulum:

- terminal cisternae and longitudinal tubules
- **terminal cisternae** form junctional "feet" adjacent to the T- tubule membrane
- intracellular storage compartment for Ca^{2+}

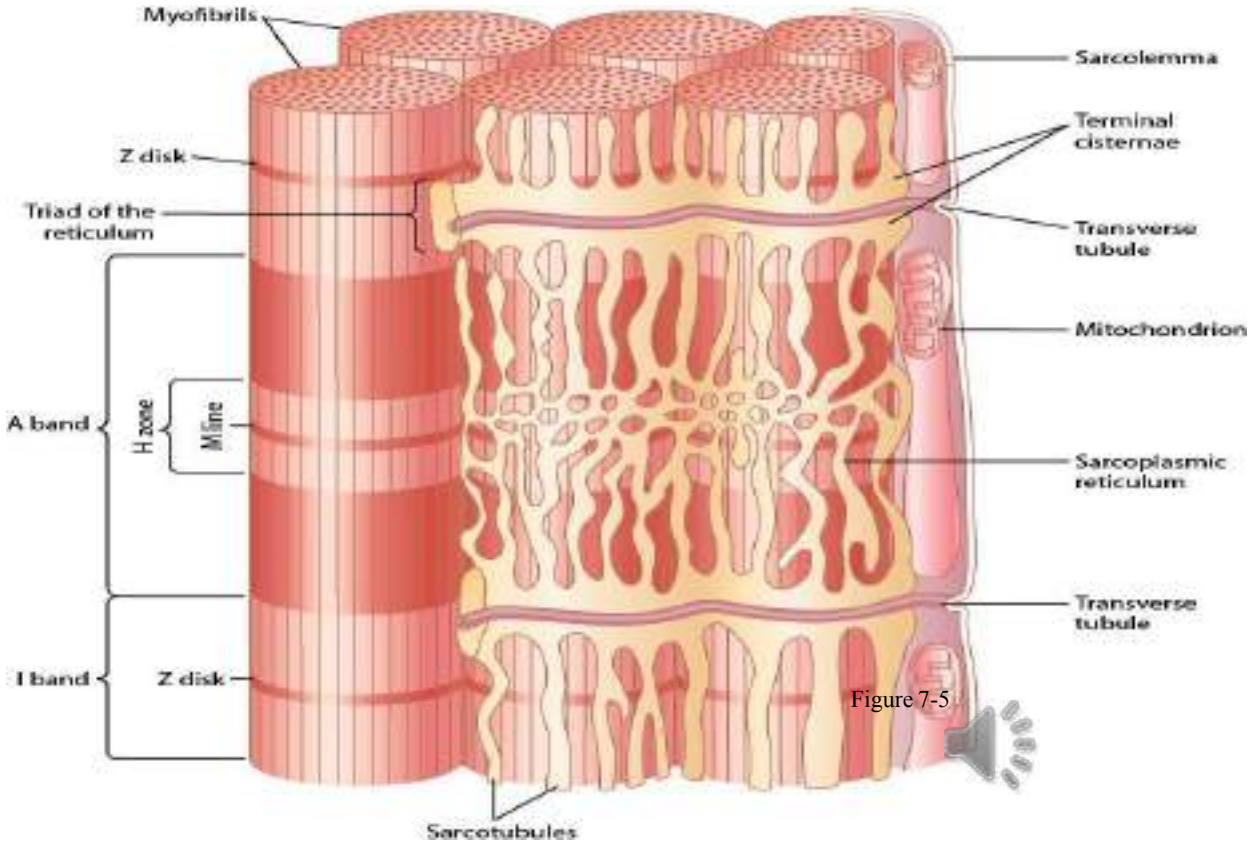


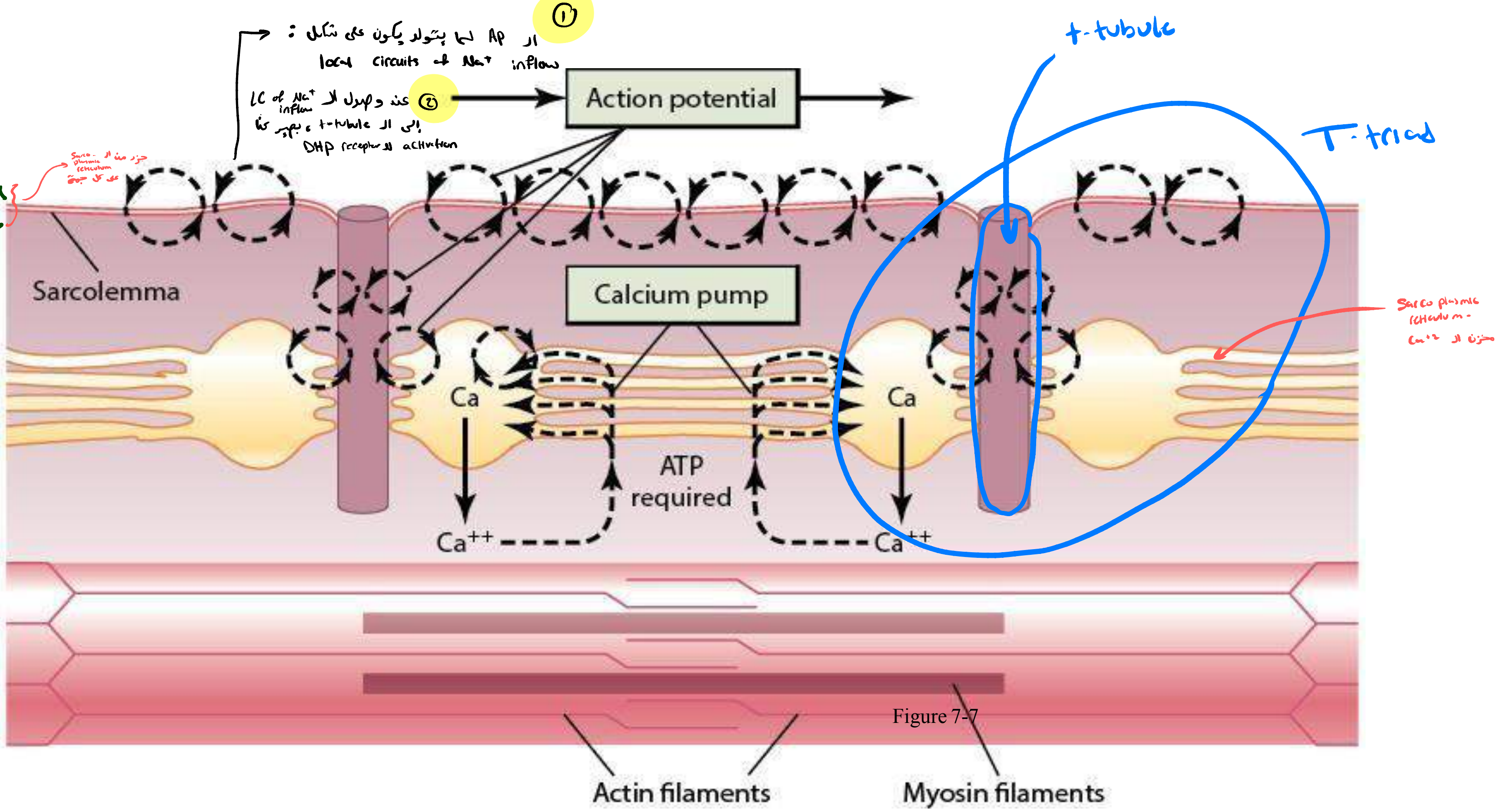
Figure 7-5

The spread of muscle action potential to through the triad and release of Ca during excitation contraction coupling

T-tubules: invagination (تجاويف) of sarcolemma, connects sarcolemma with sacroplasmic reticulum (cisternae)

The "Triad" → 3T → T-tubule; 2,3 terminal cisterae

The junction between two terminal cisternae and a T-tubule



③ لما يصير في activation for DHP receptors ، بيصير ال RyR receptor عن طريق الخيط المشبوك بينهم

④ بفتح جيدويها على ال Sarcoplasmic reticulum ← Ca^{+2} channels ← Ca^{2+} release from SR into cytoplasm

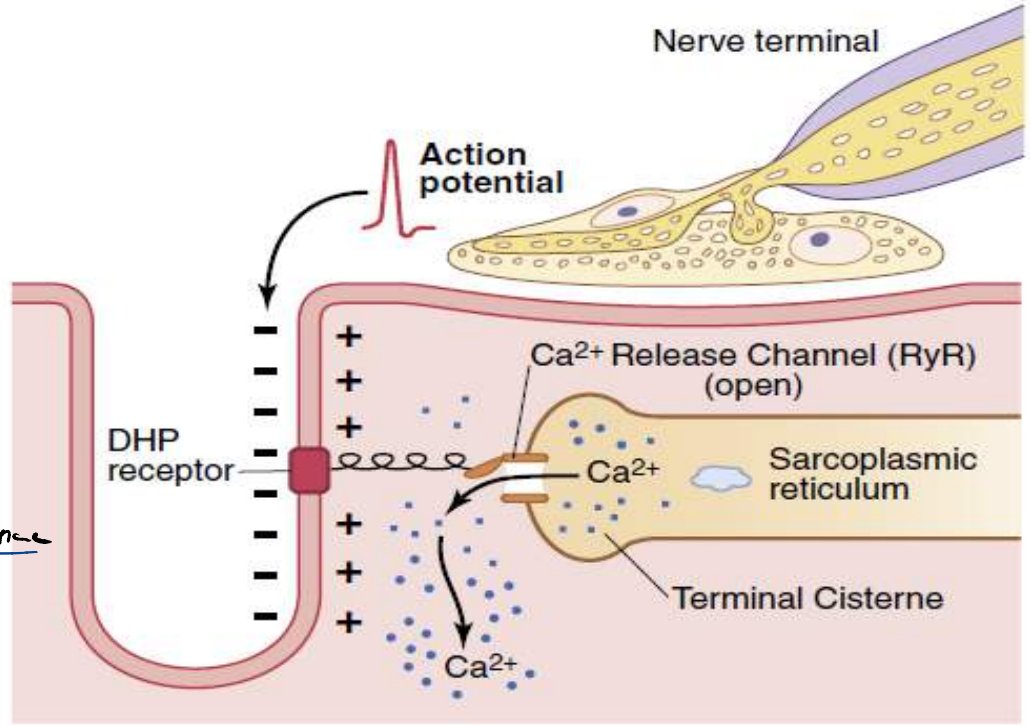
→ ↑↑ intracellular Ca^{+2} → contraction

* الدول ال 4 خطوات هم ملخص ال EC coupling *

EC Coupling – *Skeletal muscle*

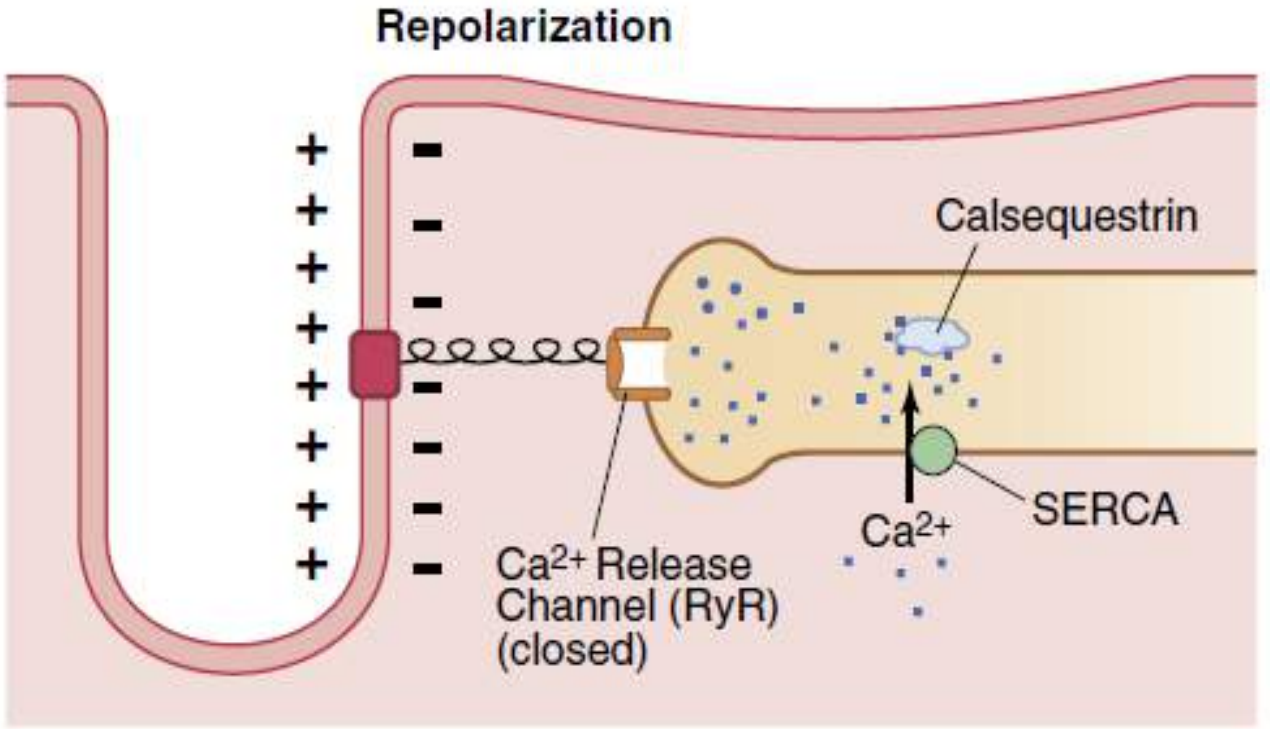
Following the excitation of muscles cells by acetylcholine release, an action potential in the transverse tubule that causes a conformational change in the voltage-sensing dihydropyridine *(DHP)* receptors, opening the Ca++ release channels in the terminal cisternae of the sarcoplasmic reticulum and permitting Ca++ to rapidly diffuse into the sarcoplasm and initiate muscle contraction

found on the terminal cisternae



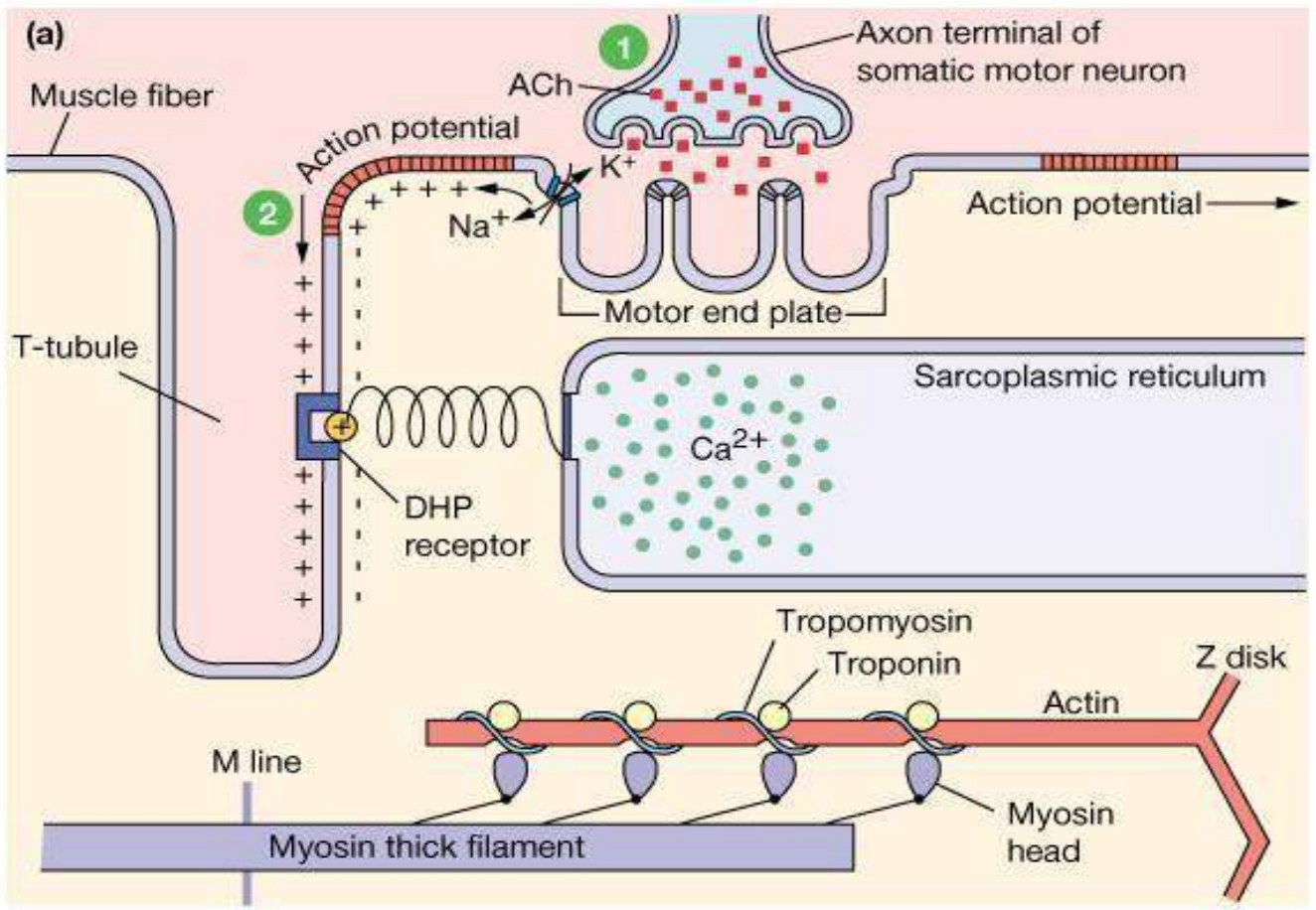
Reuptake of Ca ions released and termination of contraction

During repolarization (the conformational change in the DHP receptor closes the Ca++ release channels and Ca++ is transported from the sarcoplasm into the sarcoplasmic reticulum by an adenosine triphosphate–dependent calcium pump



* في نهاية الـ repolarization، بسكر القنوات DHP
إلي فتحها ← بترجع على الـ Sarcoplasmic reticulum ← بتقلل Ca^+ intracellularly
↳ Contractions stop → muscle relaxation

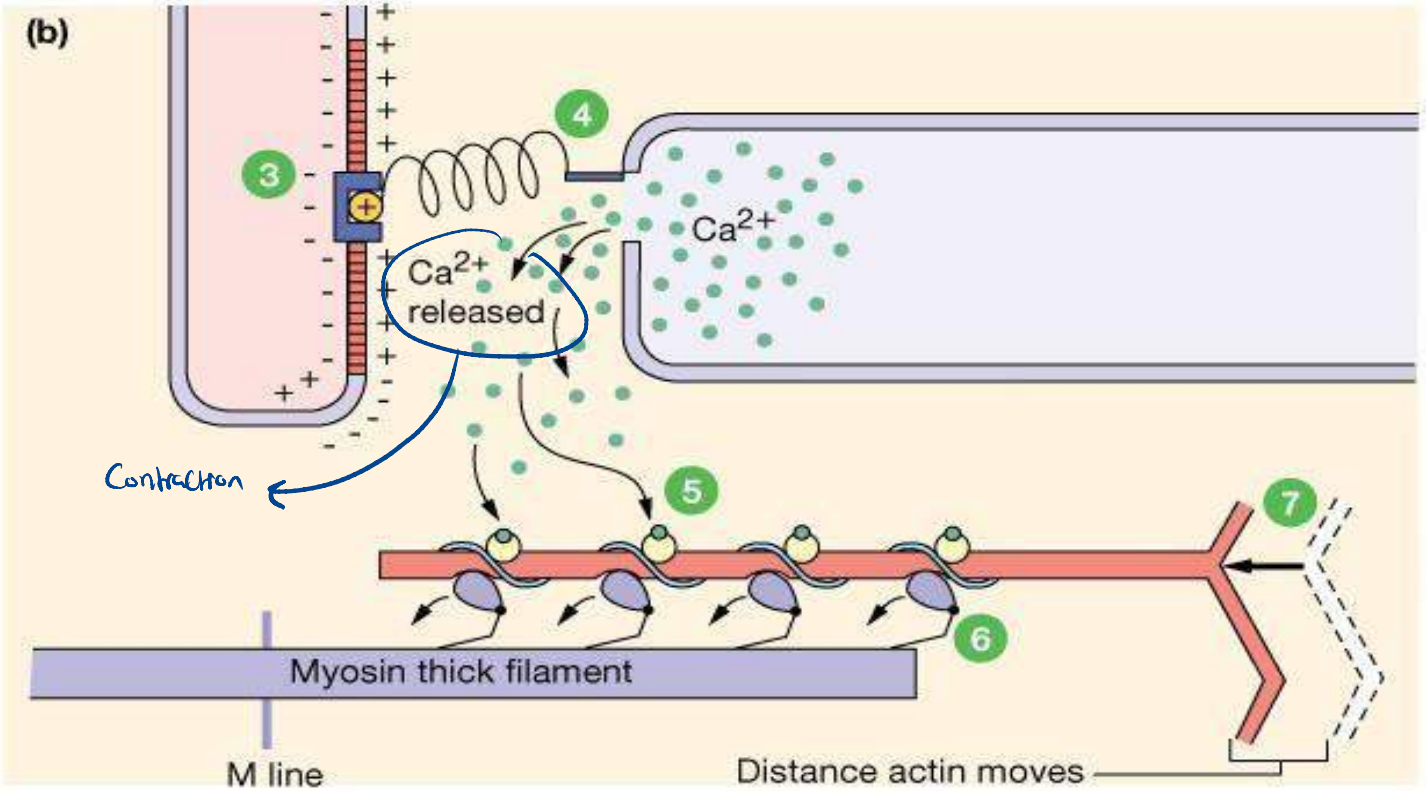
Excitation contraction coupling summary



1. Somatic motor neuron releases ACh at neuro-muscular junction.

2. Net entry of Na^+ through ACh receptor-channel initiates a muscle action potential.

Summary and Steps of Excitation Contraction Coupling



3 Action potential in t-tubule alters conformation of DHP receptor.

4 DHP receptor opens Ca^{2+} release channels in sarcoplasmic reticulum and Ca^{2+} enters cytoplasm.

5 Ca^{2+} binds to troponin, allowing strong actin-myosin binding.

6 Myosin heads execute power stroke.

7 Actin filament slides toward center of sarcomere.

2 pathological cases :

①

Myasthenia Gravis

مرض مناعي

معيقة لو أثر على عضلات التنفس

- **symptoms:**
  - paralysis - lethal in extreme cases when respiratory muscles are involved
- **Cause:**
  - autoimmune disease characterized by the presence of antibodies against the nicotinic ACh receptor which damages or destroys them This results in weak end plate potentials
- **Treatment:**
  - usually ameliorated by anti-AChE (neostigmine) The drug increases amount of ACh in NMJ

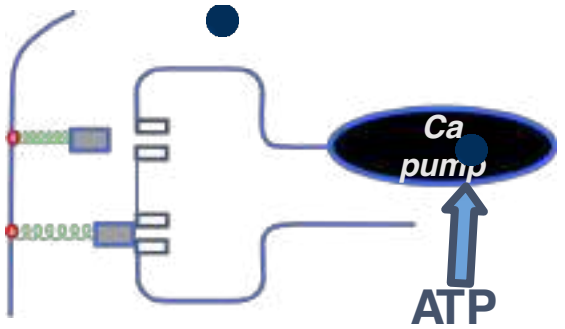
Malignant Hyperthermia

Symptoms:

- increased body temperature
- skeletal muscle rigidity
- lactic acidosis *(hypermetabolism)*

Cause:

- triggered by halogenated anesthetics (isoflurane, halothane)
- familial tendency - can be tested for by muscle biopsy
- constant leak of SR Ca^{2+} through ryanodine receptor



Why is so much heat generated?

Ans: our bodies are only about 45% energy efficient, 55% of the energy appears as heat.