LECTURE 3

NERVOUS SYSTEM

NEURONS AND SYNAPSES

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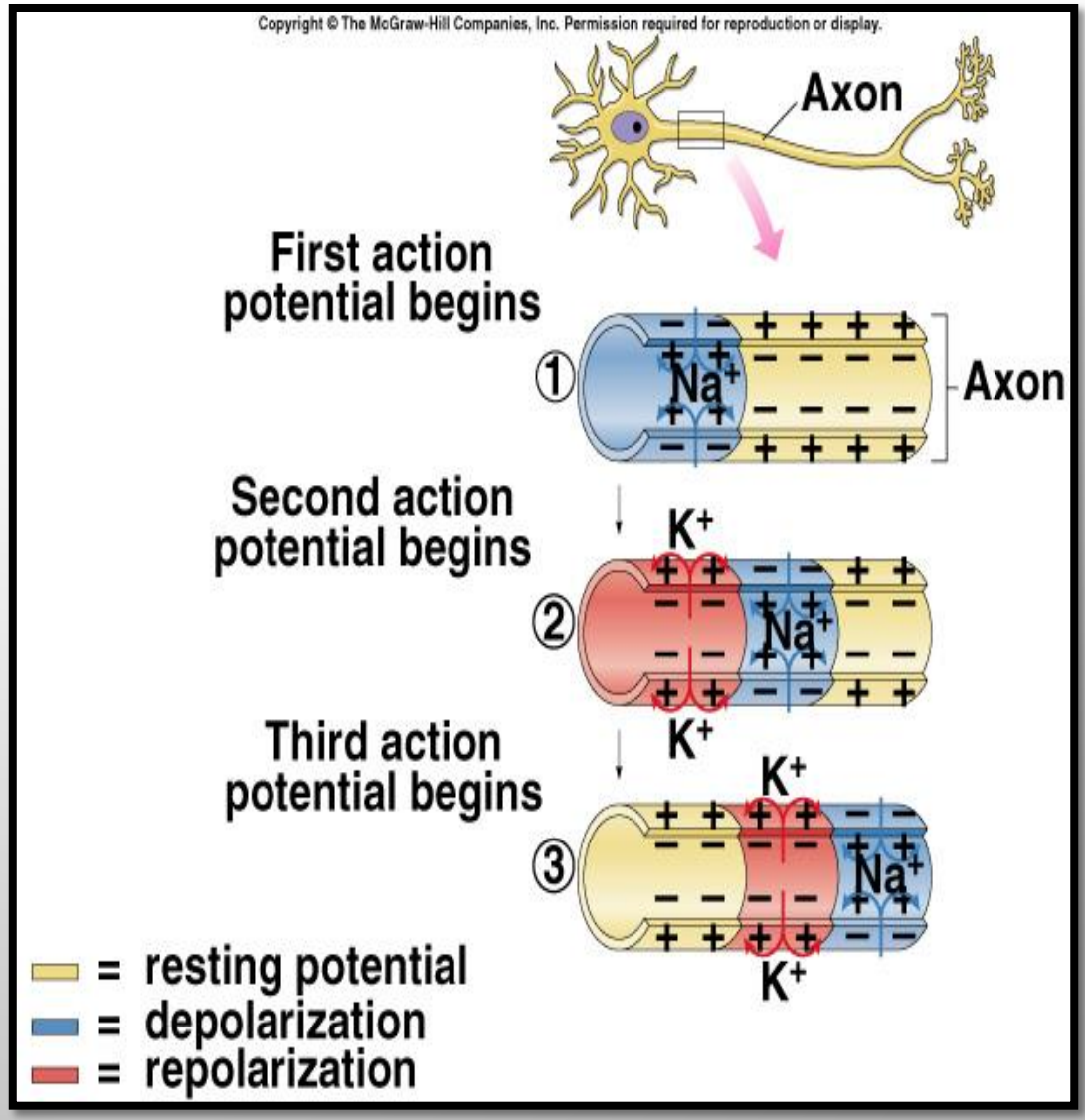
CABLE PROPERTIES OF NEURONS

- **ABILITY OF NEURON TO TRANSMIT CHARGE THROUGH CYTOPLASM.**
- **AXON CABLE PROPERTIES ARE POOR:**
  - **HIGH INTERNAL RESISTANCE.**
  - **MANY CHARGES LEAK OUT OF THE AXON THROUGH MEMBRANE.**
- **AN AP DOES NOT TRAVEL DOWN THE ENTIRE AXON.**
- **EACH AP IS A STIMULUS TO PRODUCE ANOTHER AP IN THE NEXT REGION OF MEMBRANE WITH VG CHANNELS.**

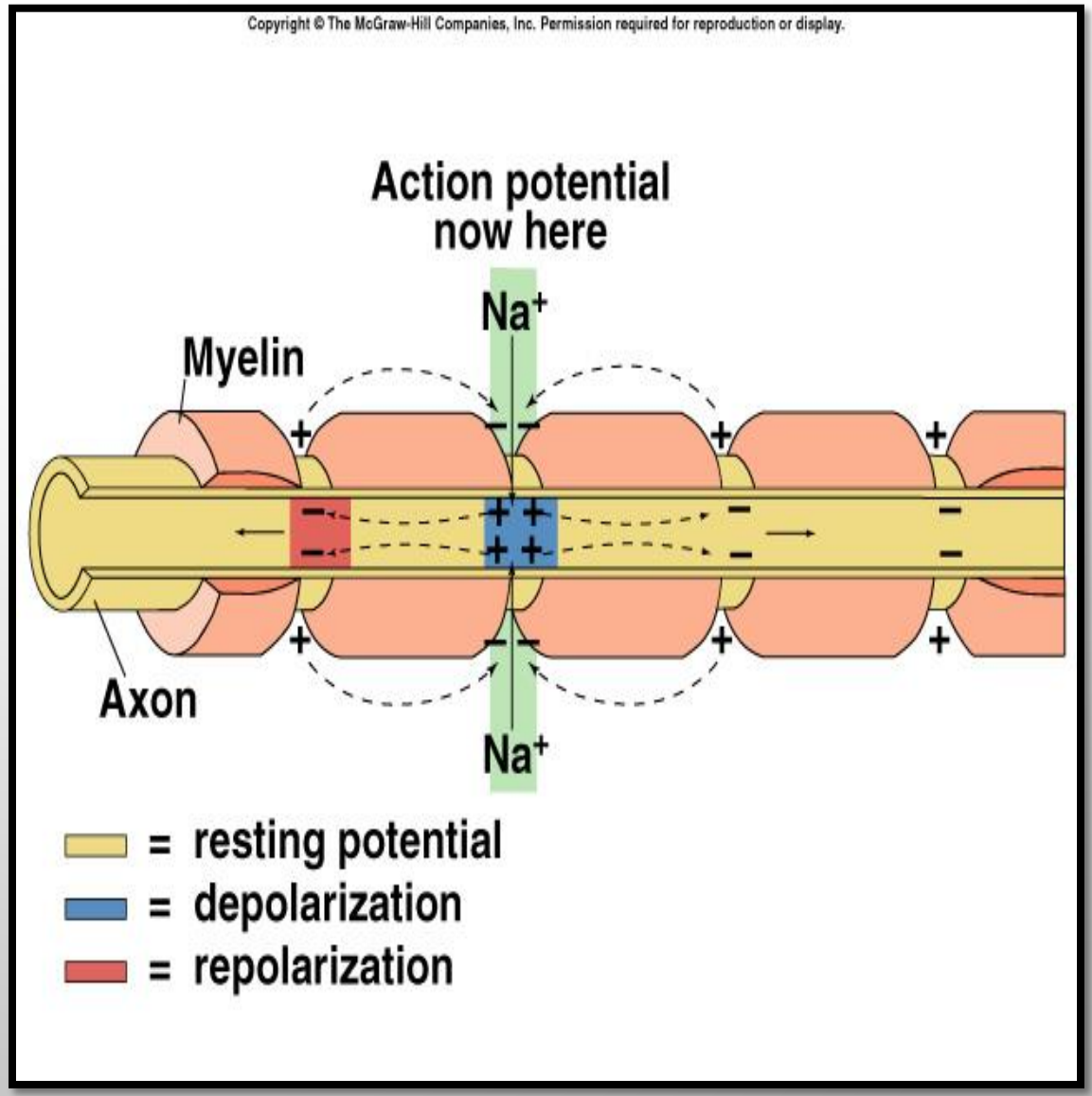
CONDUCTION IN AN UNMYELINATED AXON

- CABLE SPREAD OF DEPOLARIZATION WITH INFLUX OF NA^+ DEPOLARIZES THE ADJACENT REGION MEMBRANE, PROPAGATING THE AP.
- CONDUCTION RATE IS SLOW.
  - AP MUST BE PRODUCED AT EVERY FRACTION OF MICROMETER.
- OCCURS IN 1 DIRECTION; PREVIOUS REGION IS IN ITS REFRACTORY PERIOD.



CONDUCTION IN MYELINATED AXON

- **MYELIN PREVENTS MOVEMENT OF NA^+ AND K^+ THROUGH THE MEMBRANE.**
- **INTERRUPTION IN MYELIN (NODES OF RANVIER) CONTAIN VG NA^+ AND K^+ CHANNELS.**
- **AP OCCURS ONLY AT THE NODES.**
  - **AP AT 1 NODE DEPOLARIZES MEMBRANE TO REACH THRESHOLD AT NEXT NODE.**
- **SALTATORY CONDUCTION (LEAPS).**
  - **FAST RATE OF CONDUCTION.**

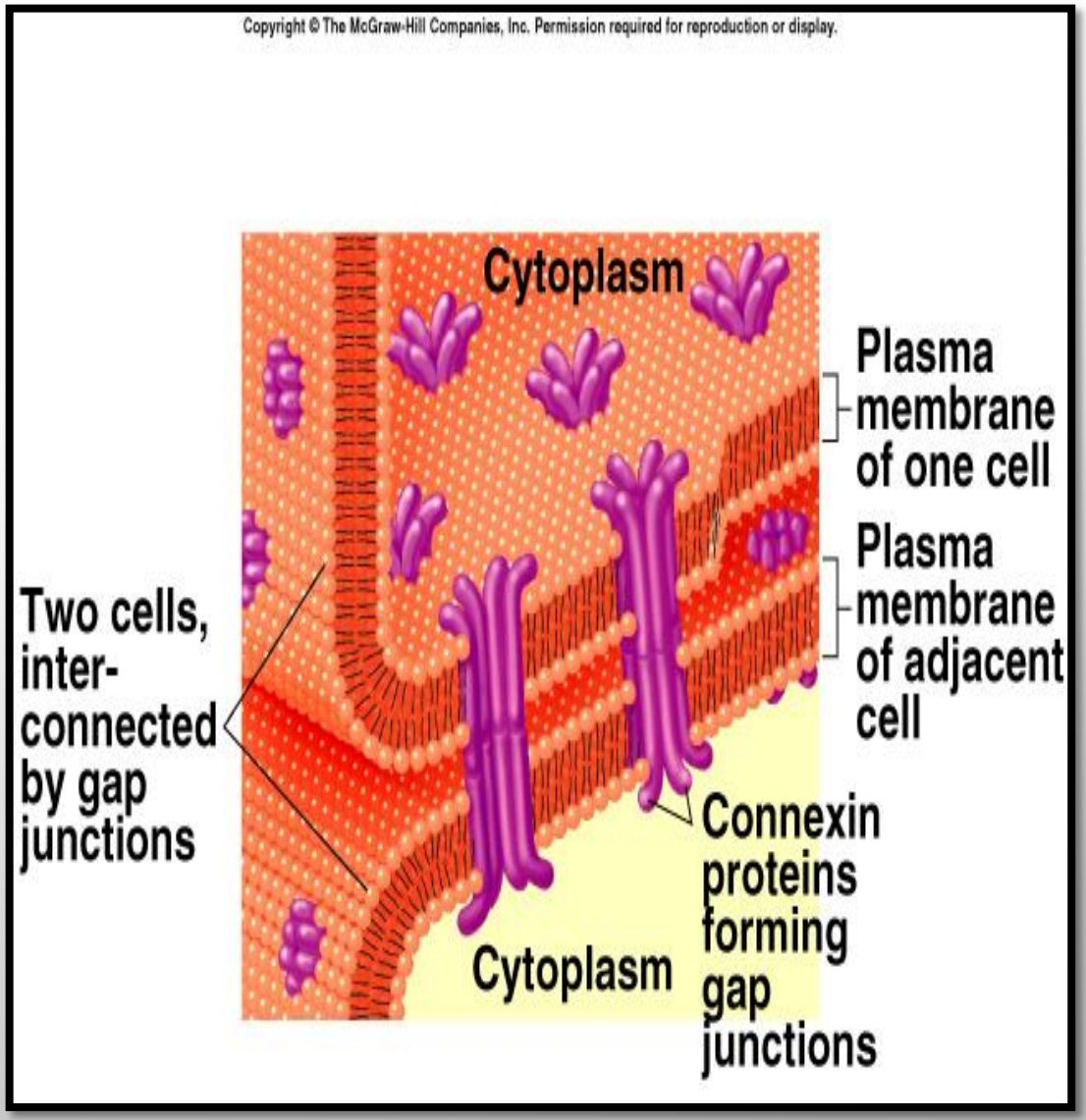


SYNAPSE

- **FUNCTIONAL CONNECTION BETWEEN A NEURON AND ANOTHER NEURON OR EFFECTOR CELL.**
- **TRANSMISSION IN ONE DIRECTION ONLY.**
- **AXON OF FIRST (PRESYNAPTIC) TO SECOND (POSTSYNAPTIC) NEURON.**
- **SYNAPTIC TRANSMISSION IS THROUGH A CHEMICAL GATED CHANNEL.**
- **PRESYNAPTIC TERMINAL (BOUTON) RELEASES A NEUROTRANSMITTER (NT).**

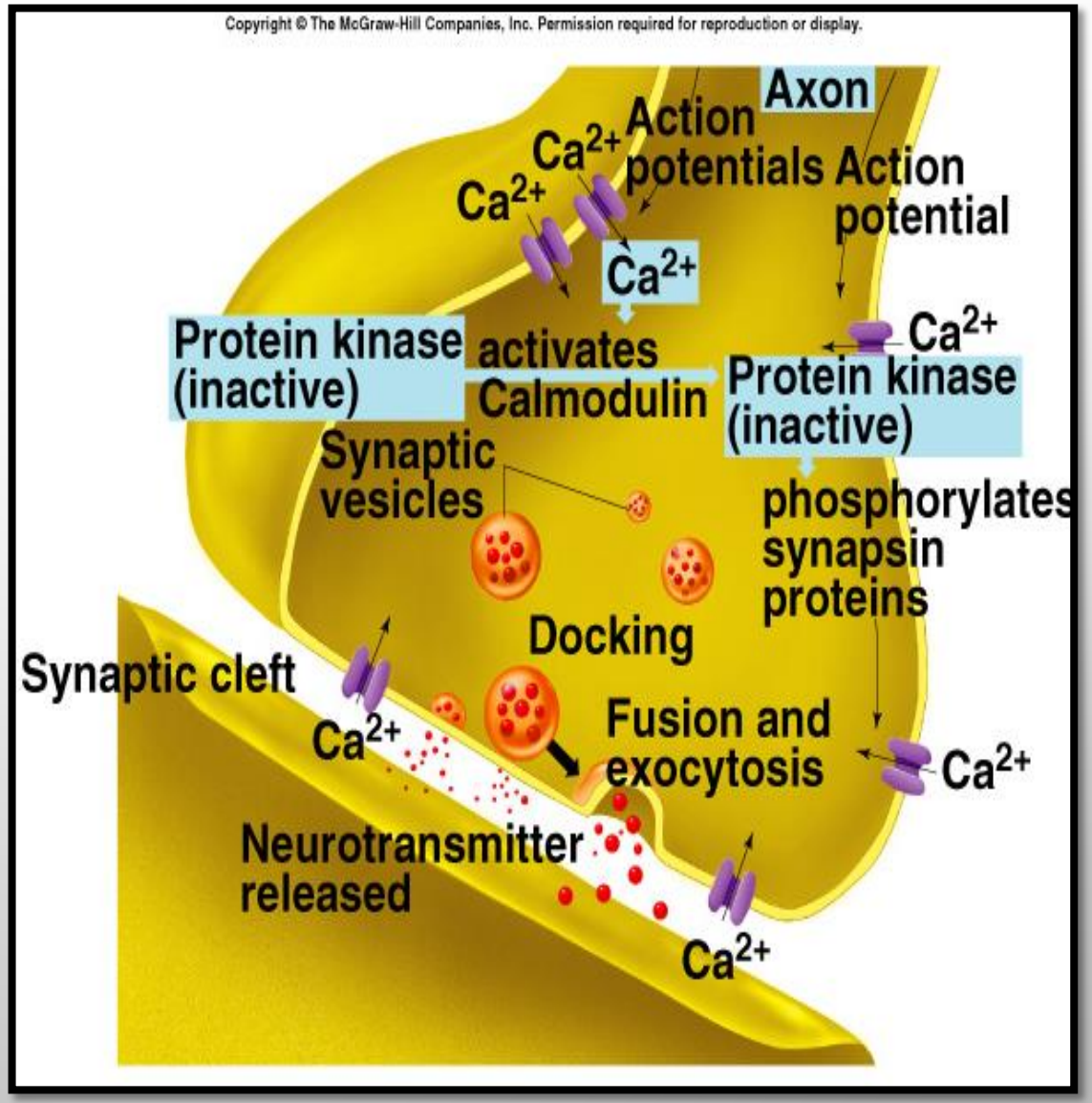
ELECTRICAL SYNAPSE

- **IMPULSES CAN BE REGENERATED WITHOUT INTERRUPTION IN ADJACENT CELLS.**
- **GAP JUNCTIONS:**
  - **ADJACENT CELLS ELECTRICALLY COUPLED THROUGH A CHANNEL.**
  - **EACH GAP JUNCTION IS COMPOSED OF 12 CONNEXIN PROTEINS.**
- **EXAMPLES:**
  - **SMOOTH AND CARDIAC MUSCLES, BRAIN, AND GLIAL CELLS.**



CHEMICAL SYNAPSE

- **TERMINAL BOUTON IS SEPARATED FROM POSTSYNAPTIC CELL BY SYNAPTIC CLEFT.**
- **NTS ARE RELEASED FROM SYNAPTIC VESICLES.**
- **VESICLES FUSE WITH AXON MEMBRANE AND NT RELEASED BY EXOCYTOSIS.**
- **AMOUNT OF NTS RELEASED DEPENDS UPON FREQUENCY OF AP.**



SYNAPTIC TRANSMISSION

1 - NT RELEASE IS RAPID BECAUSE MANY VESICLES FORM FUSION-COMPLEXES AT "DOCKING SITE."

2 - AP TRAVELS DOWN AXON TO BOUTON.

3 - VG CA^{2+} CHANNELS OPEN.

- **CA^{2+} ENTERS BOUTON DOWN CONCENTRATION GRADIENT.**
- **INWARD DIFFUSION TRIGGERS RAPID FUSION OF SYNAPTIC VESICLES AND RELEASE OF NTS.**

4 - CA^{2+} ACTIVATES CALMODULIN, WHICH ACTIVATES PROTEIN KINASE.

5 - PROTEIN KINASE PHOSPHORYLATES SYNAPSINS.

- **SYNAPSINS AID IN THE FUSION OF SYNAPTIC VESICLES.**

SYNAPTIC TRANSMISSION

6 - NTS ARE RELEASED AND DIFFUSE ACROSS SYNAPTIC CLEFT.

7 - NT (LIGAND) BINDS TO SPECIFIC RECEPTOR PROTEINS IN POSTSYNAPTIC CELL MEMBRANE.

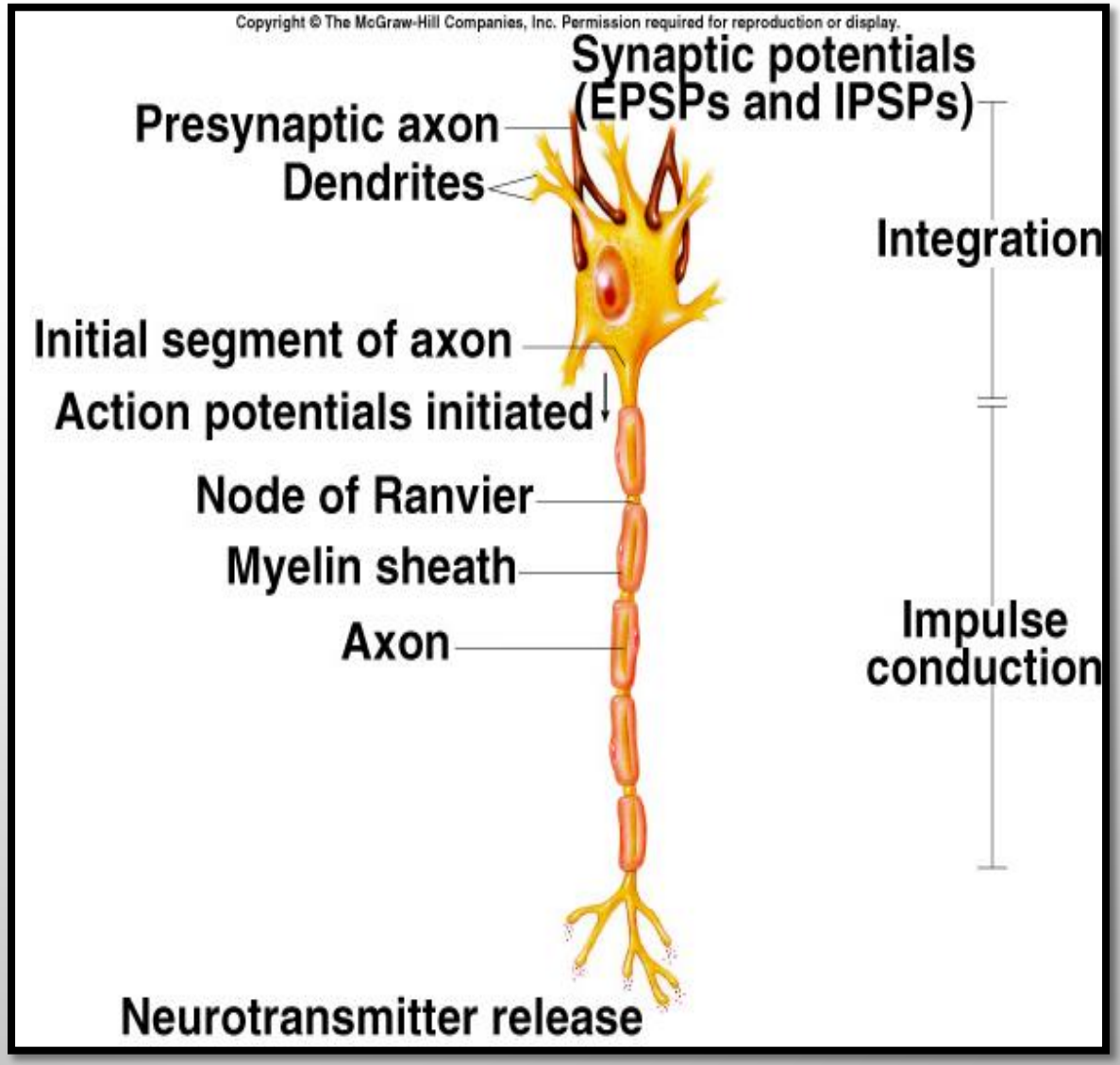
8 - CHEMICALLY-REGULATED GATED ION CHANNELS OPEN.

- **EPSP: DEPOLARIZATION.**
- **IPSP: HYPERPOLARIZATION.**

9 - NEUROTRANSMITTER INACTIVATED TO END TRANSMISSION.

CHEMICAL SYNAPSES

- **EPSP (EXCITATORY POSTSYNAPTIC POTENTIAL):**
  - **DEPOLARIZATION.**
- **IPSP (INHIBITORY POSTSYNAPTIC POTENTIAL):**
  - **HYPERPOLARIZATION**

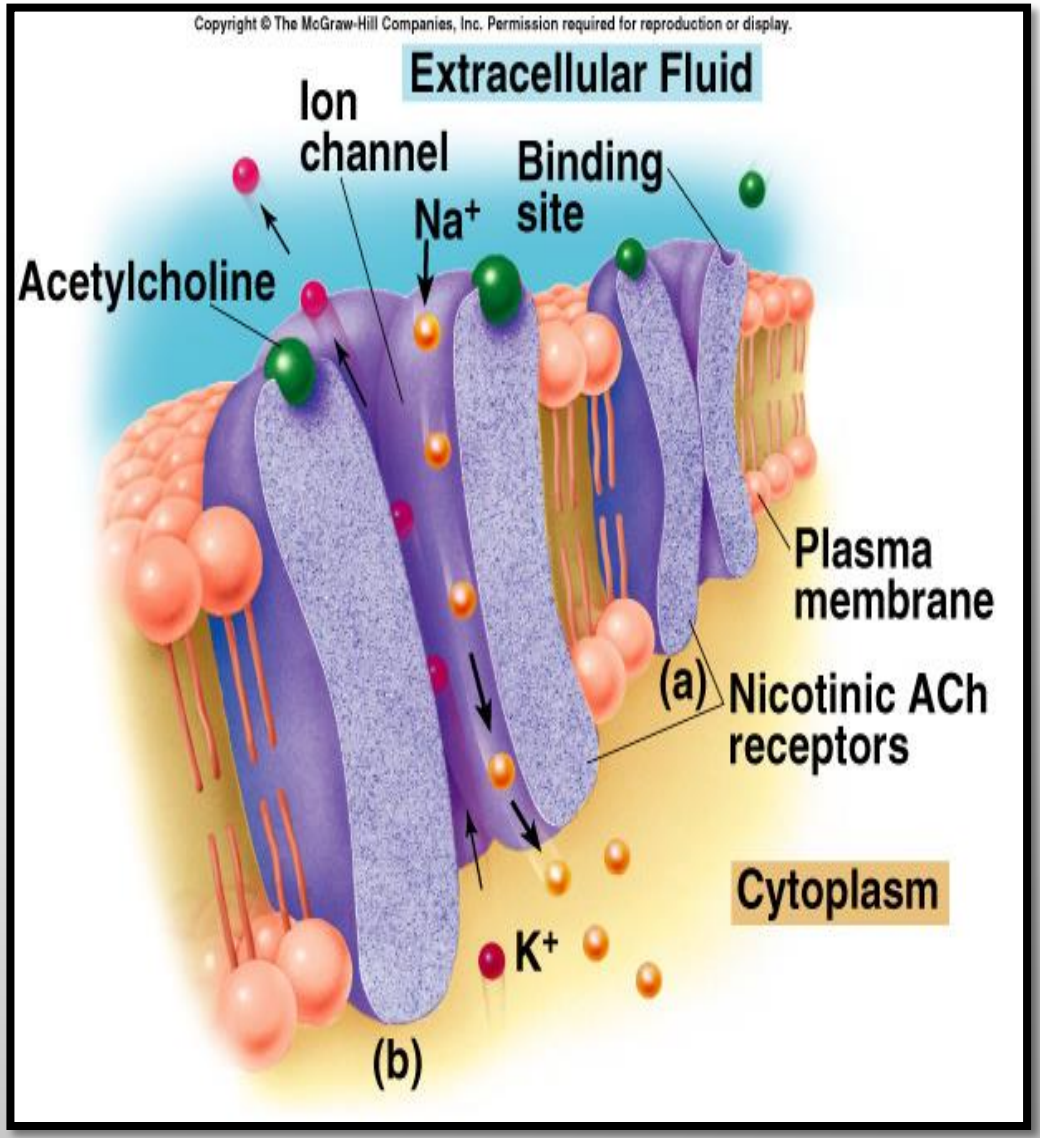


1 - ACETYLCHOLINE (ACH) AS NT

- **ACH IS BOTH AN EXCITATORY AND INHIBITORY NT, DEPENDING ON ORGAN INVOLVED.**
  - **CAUSES THE OPENING OF CHEMICAL GATED ION CHANNELS.**
- **NICOTINIC ACH RECEPTORS:**
  - **FOUND IN AUTONOMIC GANGLIA AND SKELETAL MUSCLE FIBERS.**
- **MUSCARINIC ACH RECEPTORS:**
  - **FOUND IN THE PLASMA MEMBRANE OF SMOOTH AND CARDIAC MUSCLE CELLS, AND IN CELLS OF PARTICULAR GLANDS.**

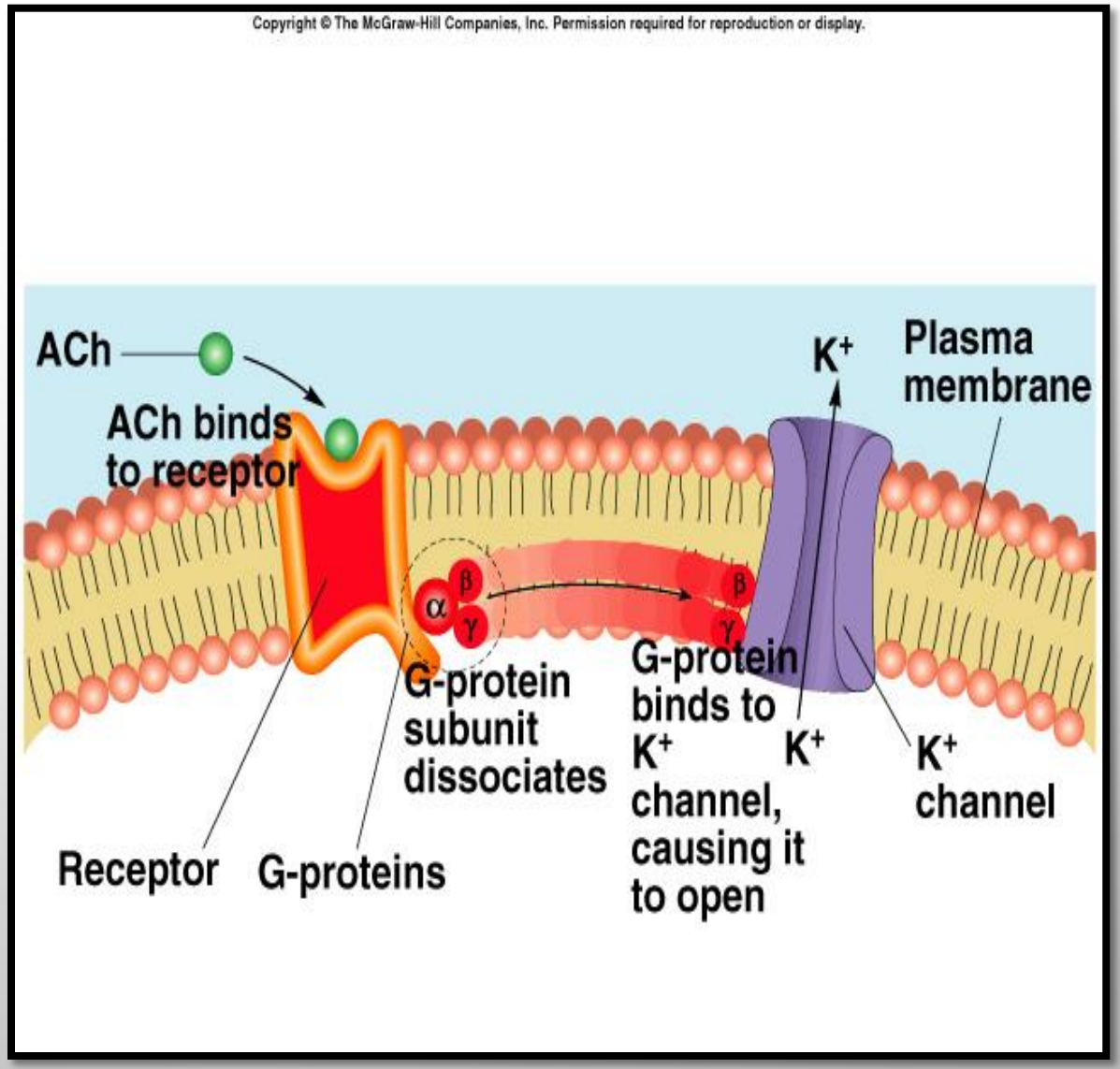
LIGAND-OPERATED ACH CHANNELS

- **MOST DIRECT MECHANISM.**
- **ION CHANNEL RUNS THROUGH RECEPTOR.**
  - **RECEPTOR HAS 5 POLYPEPTIDE SUBUNITS THAT ENCLOSE ION CHANNEL.**
  - **2 SUBUNITS CONTAIN ACH BINDING SITES.**
- **CHANNEL OPENS WHEN BOTH SITES BIND TO ACH.**
  - **PERMITS DIFFUSION OF NA^+ INTO AND K^+ OUT OF POSTSYNAPTIC CELL.**
- **INWARD FLOW OF NA^+ DOMINATES.**
  - **PRODUCES EPSPS.**



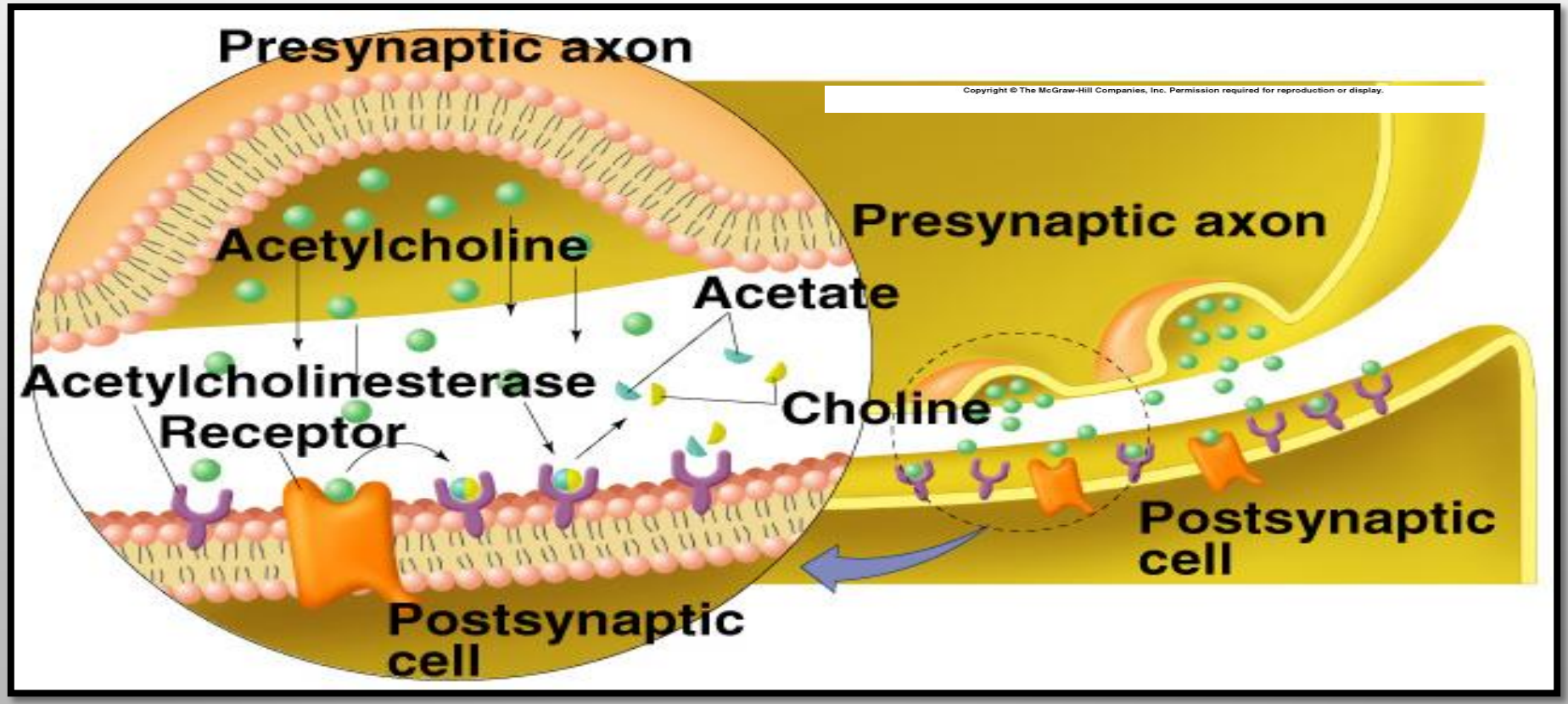
G PROTEIN-OPERATED ACH CHANNEL

- ONLY 1 SUBUNIT.
- ION CHANNELS ARE SEPARATE PROTEINS LOCATED AWAY FROM THE RECEPTORS.
- BINDING OF ACH ACTIVATES ALPHA G-PROTEIN SUBUNIT.
- ALPHA SUBUNIT DISSOCIATES.
- ALPHA SUBUNIT OR THE BETA-GAMMA COMPLEX DIFFUSES THROUGH MEMBRANE UNTIL IT BINDS TO ION CHANNEL, OPENING IT.



ACETYLCHOLINESTERASE (ACHE)

- **ENZYME THAT INACTIVATES ACH.**
  - **PRESENT ON POSTSYNAPTIC MEMBRANE OR IMMEDIATELY OUTSIDE THE MEMBRANE.**
- **PREVENTS CONTINUED STIMULATION.**



ACH IN CNS

- **CHOLINERGIC NEURONS:**
  - **USE ACH AS NT.**
  - **AXON BOUTON SYNAPSES WITH DENDRITES OR CELL BODY OF ANOTHER NEURON.**
- **FIRST VG CHANNELS ARE LOCATED AT AXON HILLOCK.**
- **EPSPS SPREAD BY CABLE PROPERTIES TO INITIAL SEGMENT OF AXON.**
- **GRADATIONS IN STRENGTH OF EPSPS ABOVE THRESHOLD DETERMINE FREQUENCY OF APS PRODUCED AT AXON HILLOCK.**

ACH IN PNS

- SOMATIC MOTOR NEURONS SYNAPSE WITH SKELETAL MUSCLE FIBERS.
  - RELEASE ACH FROM BOUTONS.
  - PRODUCES END-PLATE POTENTIAL (EPPS).
- DEPOLARIZATION OPENS VG CHANNELS ADJACENT TO END PLATE.

EPPS

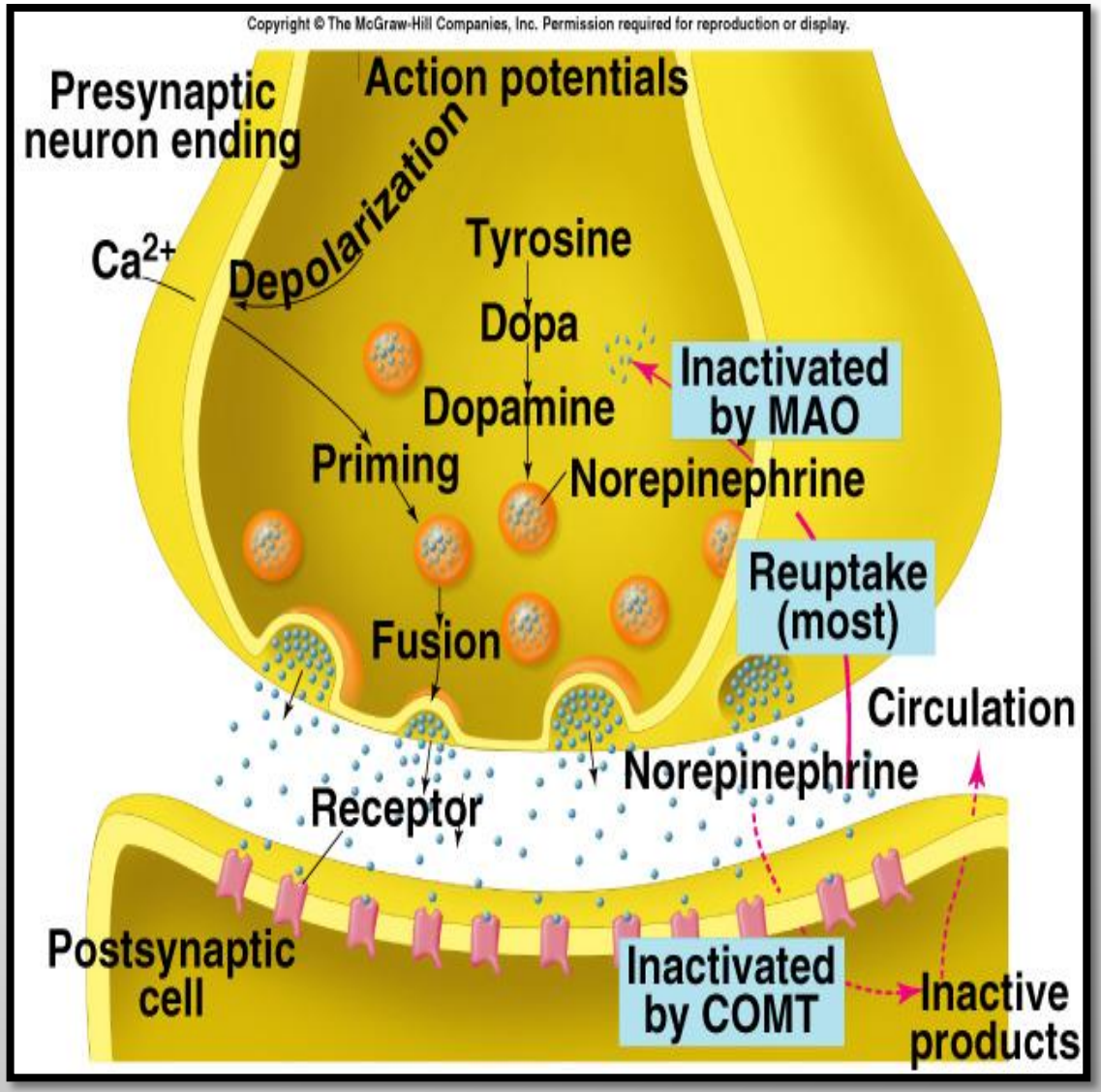
IT'S VOLTAGE WHICH CAUSE DEPOLARIZATION OF SKELETAL MUSCLE CAUSED BY NEUROTRANSMITTERS BINDING TO POSTSYNAPTIC MEMBRANE IN NEUROMUSCULAR JUNCTION.

2 – MONOAMINES AS NT

- **MONOAMINE NTS:**
  - **EPINEPHRINE.**
  - **NOREPINEPHRINE.**
  - **SEROTONIN.**
  - **DOPAMINE.**
- **RELEASED BY EXOCYTOSIS FROM PRESYNAPTIC VESICLES.**
- **DIFFUSE ACROSS THE SYNAPTIC CLEFT.**
- **INTERACT WITH SPECIFIC RECEPTORS IN POSTSYNAPTIC MEMBRANE.**

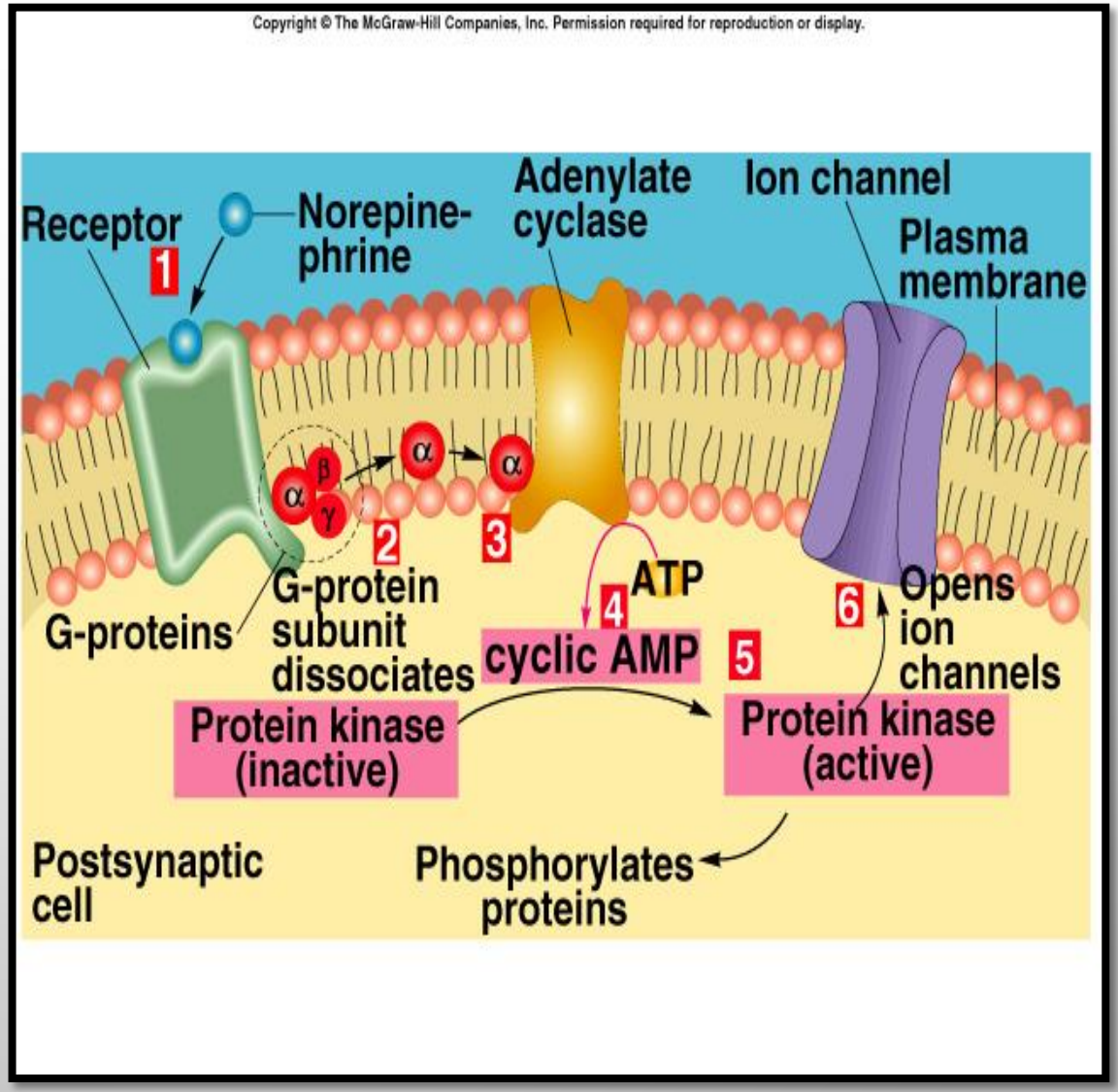
INHIBITION OF MONOAMINES AS NT

- REUPTAKE OF MONOAMINES INTO PRESYNAPTIC MEMBRANE.
  - ENZYMATIC DEGRADATION OF MONOAMINES IN PRESYNAPTIC MEMBRANE BY MAO.
- ENZYMATIC DEGRADATION OF CATECHOLAMINES IN POSTSYNAPTIC MEMBRANE BY COMT.



MECHANISM OF ACTION

- MONOAMINE NT DO NOT DIRECTLY OPEN ION CHANNELS.
- ACT THROUGH SECOND MESSENGER, SUCH AS CAMP.
- BINDING OF NOREPINEPHRINE STIMULATES DISSOCIATION OF G-PROTEIN ALPHA SUBUNIT.
- ALPHA SUBUNIT BINDS TO ADENYLATE CYCLASE, CONVERTING ATP TO CAMP.
- CAMP ACTIVATES PROTEIN KINASE, PHOSPHORYLATING OTHER PROTEINS.
- OPEN ION CHANNELS.



A - SEROTONIN AS NT

- **NT (DERIVED FROM L-TRYPTOPHAN) FOR NEURONS WITH CELL BODIES IN RAPHE NUCLEI.**
- **REGULATION OF MOOD, BEHAVIOR, APPETITE, AND CEREBRAL CIRCULATION.**
- **SSRIS (SEROTONIN-SPECIFIC REUPTAKE INHIBITORS):**
  - **INHIBIT REUPTAKE AND DESTRUCTION OF SEROTONIN, PROLONGING THE ACTION OF NT.**
  - **USED AS AN ANTIDEPRESSANT.**
    - **REDUCES APPETITE, TREATMENT FOR ANXIETY, TREATMENT FOR MIGRAINE HEADACHES.**

B – DOPAMINE AN NT

- NT FOR NEURONS WITH CELL BODIES IN MIDBRAIN.
- AXONS PROJECT INTO:
  - NIGROSTRIATAL DOPAMINE SYSTEM:
    - NUERONS IN SUBSTANTIA NIGRA SEND FIBERS TO CORPUS STRAITUM.
    - INITIATION OF SKELETAL MUSCLE MOVEMENT.
    - PARKINSON'S DISEASE: DEGENERATION OF NEURONS IN SUBSTANTIA NIGRA.
  - MESOLIMBIC DOPAMINE SYSTEM:
    - NEURONS ORIGINATE IN MIDBRAIN, SEND AXONS TO LIMBIC SYSTEM.
    - INVOLVED IN BEHAVIOR AND REWARD.
    - ADDICTIVE DRUGS:
      - PROMOTE ACTIVITY IN NUCLEUS ACCUMBENS.

C – NOREPINEPHRINE (NE) AS NT

- **NT IN BOTH PNS AND CNS.**
- **PNS:**
  - **SMOOTH MUSCLES, CARDIAC MUSCLE AND GLANDS.**
    - **INCREASE IN BLOOD PRESSURE, CONSTRICTION OF ARTERIES.**
- **CNS:**
  - **GENERAL BEHAVIOR.**

3 - AMINO ACIDS AS NT

- **GLUTAMIC ACID AND ASPARTIC ACID:**
  - **MAJOR EXCITATORY NTS IN CNS.**
- **GLUTAMIC ACID:**
  - **NMDA RECEPTOR INVOLVED IN MEMORY STORAGE.**
- **GLYCINE:**
  - **INHIBITORY, PRODUCES IPSPS.**
  - **OPENING OF CL^- CHANNELS IN POSTSYNAPTIC MEMBRANE.**
    - **HYPERPOLARIZATION.**
  - **HELPS CONTROL SKELETAL MOVEMENTS.**
- **GABA (GAMMA-AMINOBUTYRIC ACID):**
  - **MOST PREVALENT NT IN BRAIN.**
  - **INHIBITORY, PRODUCES IPSPS.**
    - **HYPERPOLARIZES POSTSYNAPTIC MEMBRANE.**
      - **MOTOR FUNCTIONS IN CEREBELLUM.**

4 – POLYPEPTIDES AS NT

- **CCK:**
  - **PROMOTE SATIETY FOLLOWING MEALS.**
- **SUBSTANCE P:**
  - **MAJOR NT IN SENSATIONS OF PAIN.**
- **SYNAPTIC PLASTICITY (NEUROMODULATING EFFECTS):**
  - **NEURONS CAN RELEASE CLASSICAL NT OR THE POLYPEPTIDE NT.**