

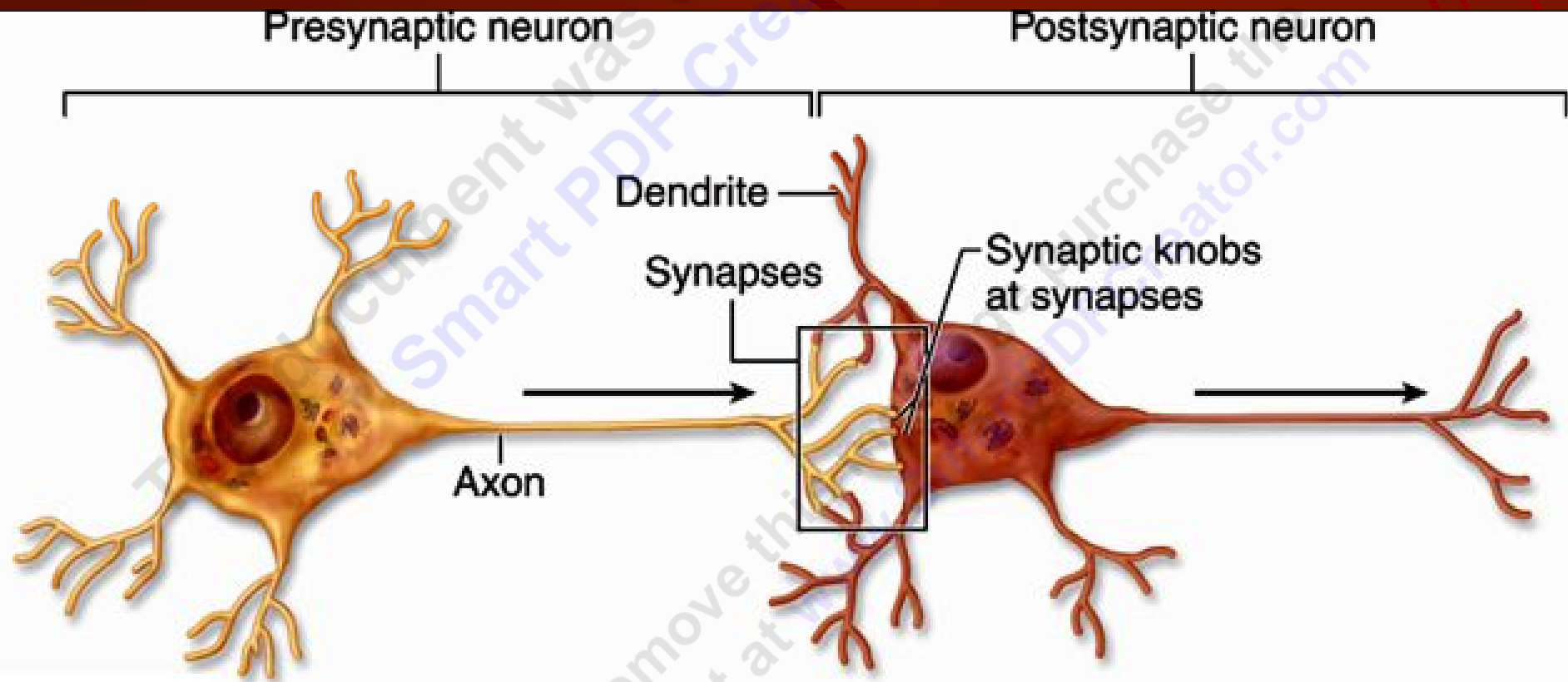
Physiology of Synapses and Synaptic Receptors

المشابك الخلوية و مستقبلات نواقلها الكيميائية

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جامعة الملك سعود

Q: What are synapses ? And where are they located ?



المشابك العصبية Synapses

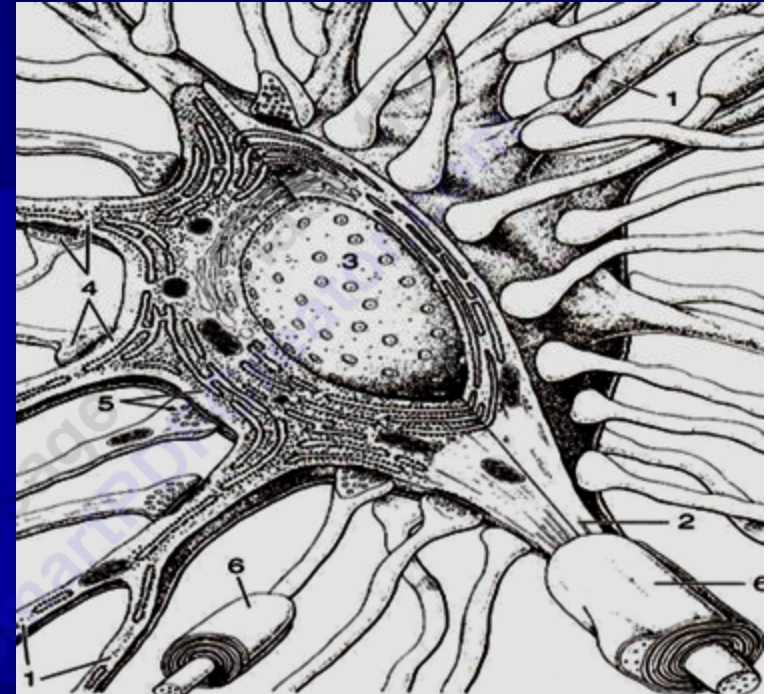
- المشابك العصبية هي أماكن تماس بين العصبونات
- و بواسطتها تتصل العصبونات و تتحاور و تتبادل الرسائل و المعلومات بين بعضها البعض
- وهي الأساس لكل عمليات الجهاز العصبي الدنيا

Lower CNS Functions

- كمثال لذلك المنعكسات Reflexes
- كما هي أيضا الأساس لعمليات المخ و العليا و الراقية

Higher Brain Functions

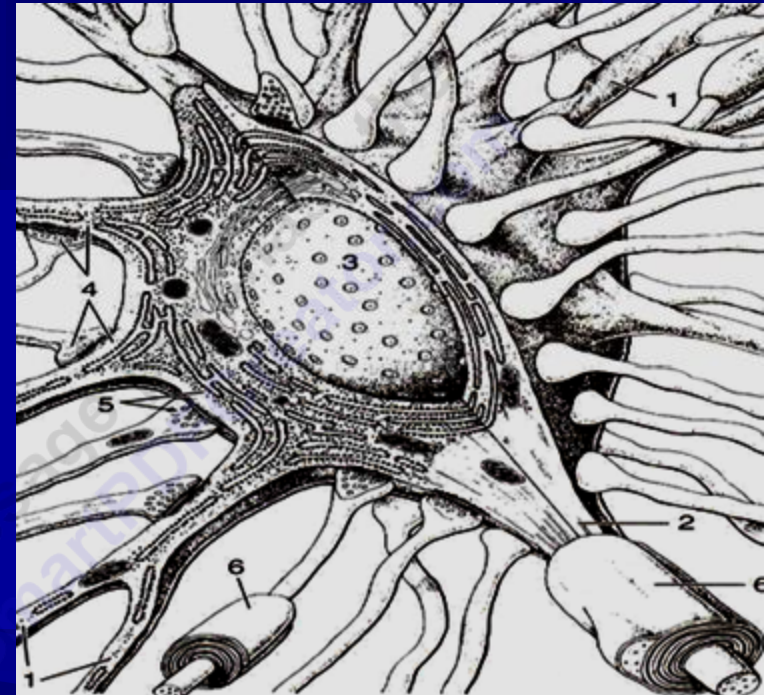
- مثل الفهم و المقدرة علي تحليل المعلومات الواردة ، و حفظها (الذاكرة) وغير ذلك من العمليات الفكرية Cognitive Processes



المشابك العصبية Synapses

■ و بعض العصبونات عليها مشابك قليلة ، و لكن البعض الآخر عليه مشابك كثيرة قد يصل عددها إلى عشرة آلاف أو أكثر

■ Some neurons have , only few synapses on them , but others may have as many as 10,000 synapses on their soma and dendrites.



- Q : What are the parts of a synapse ?
- Q : And what does each part of synapse contain ?

عندما يقترب طرف أو نهاية الآكسون

■ Nerve Terminal or Axon Terminal

■ **Presynaptic Cell** بتاع الخلية السابقة اللي هي
■ **Postsynaptic Cell** من جدار الخلية التاية اللي هي ال

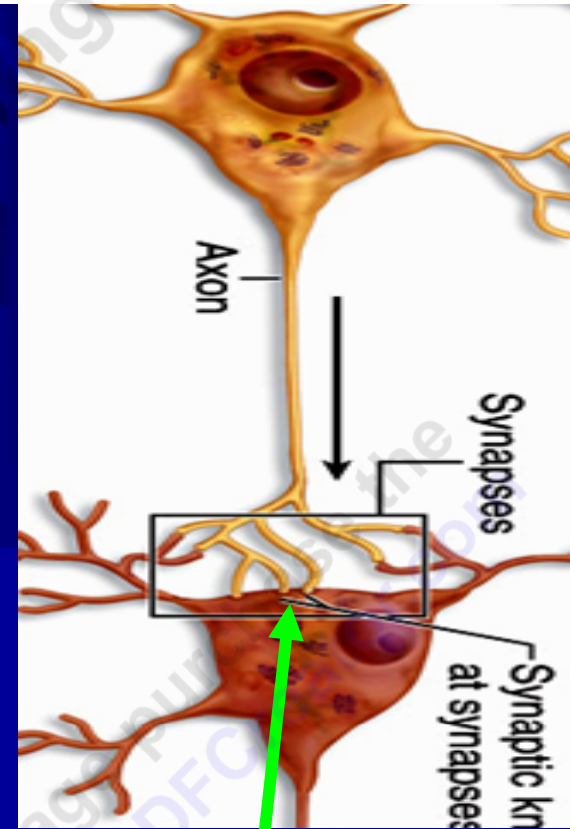
■ يتضخم طرف الآكسون هذا بحيث يستدير ليشبه ممسكة أو
■ مقبض أو أكرة الباب **Door Knob**

■ لذلك يسمونه **Synaptic Knob**

■ و طبعا جدار الخلية بتاعه هو ال **Presynaptic Membrane**

■ بينما جدار الخلية التالية هو ال

■ **Postsynaptic Membrane**



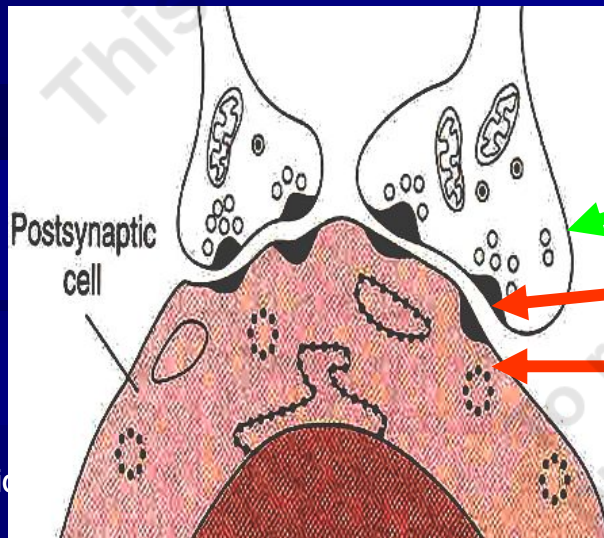
Synaptic knob هي تضخم في نهاية الآكسون

Presynaptic Cell بتاع الخلية السابقة

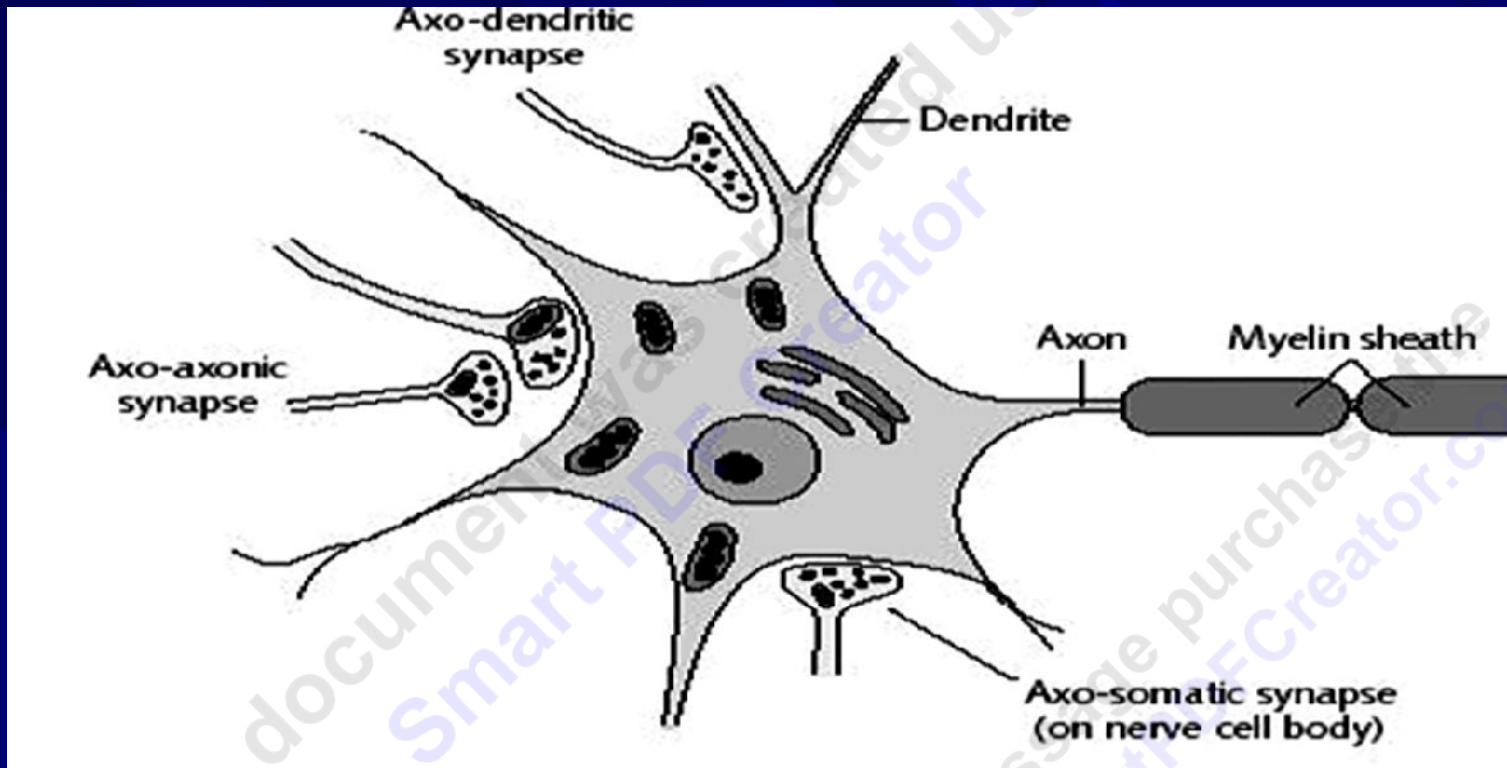
Presynaptic Membrane

Postsynaptic Membrane

وهو طبعا جدار ال (Postsynaptic Cell Neuron)



Classification of Synapses According to Location

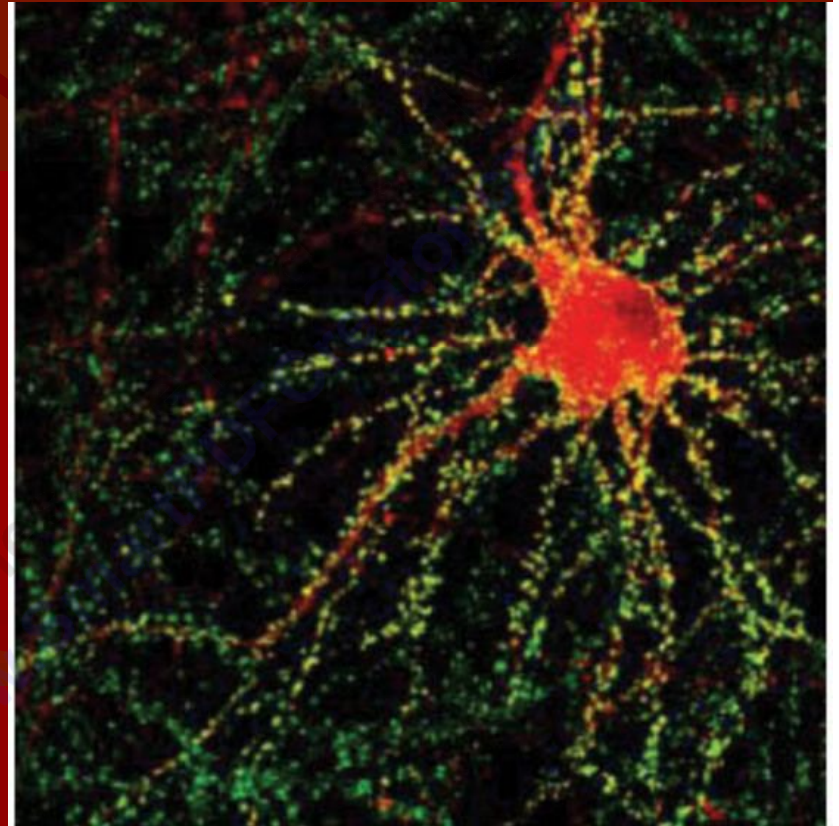


✓ They could be :

- (1) Axo-dendritic , (2) Axo-axonal (axo-axonic) ,
(3) Axo-somatic ,
- & less commonly → (4) Dendro-somatic , (5) Somato-somatic

Q : What is a synaptic transmitter (neurotransmitter) ?

- A neurotransmitter is a chemical substances that is released by a neuron (called presynaptic cell) , crosses the synaptic cleft , and binds to a receptor located on the membrane (postsynaptic membrane) of another cell .



Neurotransmitters (Chemical Transmitters)

الناقلات الكيميائية

■ **الناقلات الكيميائية** هي مواد ترسلها الخلية ما قبل المشبك **Presynaptic cell** ثم تعبر الأخدود المشبكي **Synaptic Cleft** لتتحد مع المستقبلات في الخلية التالية للمشبك **Postsynaptic Cell** لتحفزها أو لتحبطها ، حسب نوع الناقل العصبي (لو كان تحفيزي أو إحتباطي)

- **Neurotransmitters** are chemical substances released by some neurons (called **Presynaptic cell**) , cross the synaptic cleft , and bind to receptors on the dendrites or soma of other neurons (the **Postsynaptic cell**) .

Q : What are the types of transmitters ?

- Excitatory neurotransmitter :
a transmitter that produces excitatory postsynaptic potential (EPSP) on the postsynaptic neuron .
- Inhibitory neurotransmitter :
a transmitter that produces inhibitory postsynaptic potential (IPSP) on the postsynaptic neuron .

Q : What are EPSP and IPSP ?
(Remember from Musculoskeletal block)

■ **What is the nature of these bioelectric responses ?**

A : Graded Potentials (i.e., proportional to the strength of the stimulus) .

■ **In what way do they affect the excitability of the postsynaptic membrane ?** EPSP makes the postsynaptic membrane more excitable (thus more liable to produce AP), & IPSP makes it less excitable

■ **In what ways do they differ from action potentials ?**

■ (1) They are proportional to the strength of the stimulus (i.e., do not obey All-or-None Law)

■ (2) They can summate (add up)

■ Neurotransmitters can be Excitatory or Inhibitory for Synaptic Transmission
تحفيزية/ محفزة / تثبيطية/ مثبطة/ محبطة للنقل المشبكي

➤ Excitatory Neurotransmitter : الناقل المحفزة (التحفيزي)

Is a transmitter that produces Excitatory Postsynaptic Potential (EPSP) تحفيز محلي on the postsynaptic neuron .

➤ The EPSP is a Local Response تحفيز كهربائي محلي ، لا ينتقل بعيدا that decreases the membrane potential of the postsynaptic cell , bringing it closer to the Firing (Threshold) Potential عتبة إنطلاق الأكشن بوتنشال

➤ In other words , the EPSP is a local depolarizing potential that makes the Postsynaptic Cell more liable (easier) to fire (produce) و بالتالي جاعلا إياها مشحونة و أكثر قابلية للأستثارة و بالتالي أكثر Action Potentials قابلية و جاهزية لأطلاق أكشن بوتنشال

- Examples of excitatory transmitters :
- (1) **Acetylcholine** : Opens sodium channels in the Postsynaptic Cell Membrane → depolarization → EPSP .
- (2) **Glutamate** : Produces EPSP by opening of calcium channels .
- (3) **Serotonin (5-Hydroxytryptamine)** Present in high concentration in brain Raphe Nuclei . It is involved in sleep production .

Q : What is Long – Term Potentiation (LTP) ?

- What is the main neurotransmitter involved in LTP ?
- Give example of one of its physiological functions ?

Long – Term Potentiation (LTP)

الاستثارة طويلة الأمد

- Repetitive stimulation makes the postsynaptic membrane more excitable for a longer than normal period of time .
- i.e. it potentiates (facilitates) transfer of information across that synapse → making it easier & longer-lasting
- Glutamate Receptors play important role in this process of **LTP** .a process
- This LTP is a is essential for formation of **memories** in the brain

■ هذه العملية ضرورية لحفظ و تخزين الذكريات (المذاكرة مثلا)

Inhibitory Neurotransmitter

الناقل المثبط و المحبط

- when it combines to its receptors , it produce Inhibitory Postsynaptic potential (IPSP) that hyperpolarizes the post-synaptic cell , thereby making it less excitable (more difficult to excite , more difficult to produce APs) .
- Examples of inhibitory transmitter is
 - **GABA** (which in some places opens chloride channels , and in others opens potassium channels).
 - **Enkephalin** : Inhibitory transmitter . Found in the GIT and spinal cord . In the spinal cord it exerts analgesic activity **مخفف للألم** , reducing the feeling of pain .

Formation of a Transmitter

- Q : In what location of the neuron is the neurotransmitter synthesized ?
- Q : In what location of the neuron is the transmitter vesicle synthesized ?
- How are these processes functionally coupled to produce successful synaptic transmission ?

Q: What happens to the transmitter after it has combined with its postsynaptic receptors and produced its effect ?

In the synaptic cleft there are enzymes that will then destroy the receptor :

In case of :

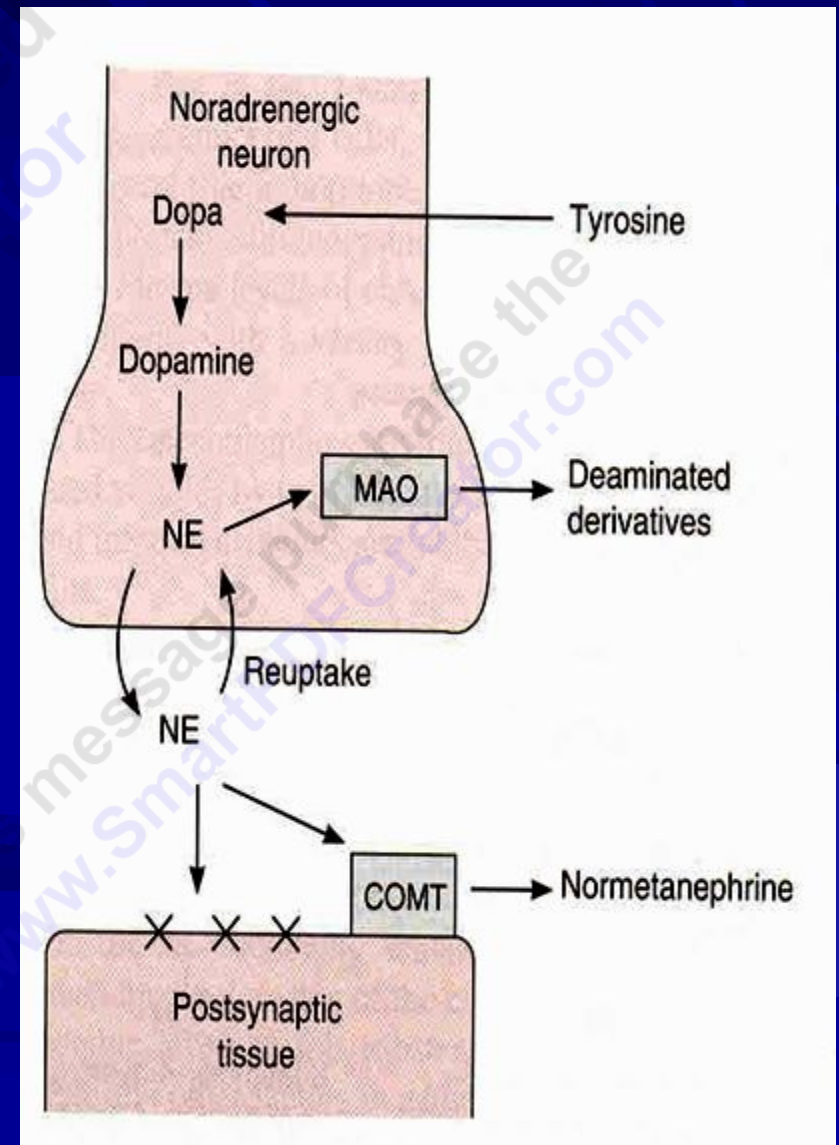
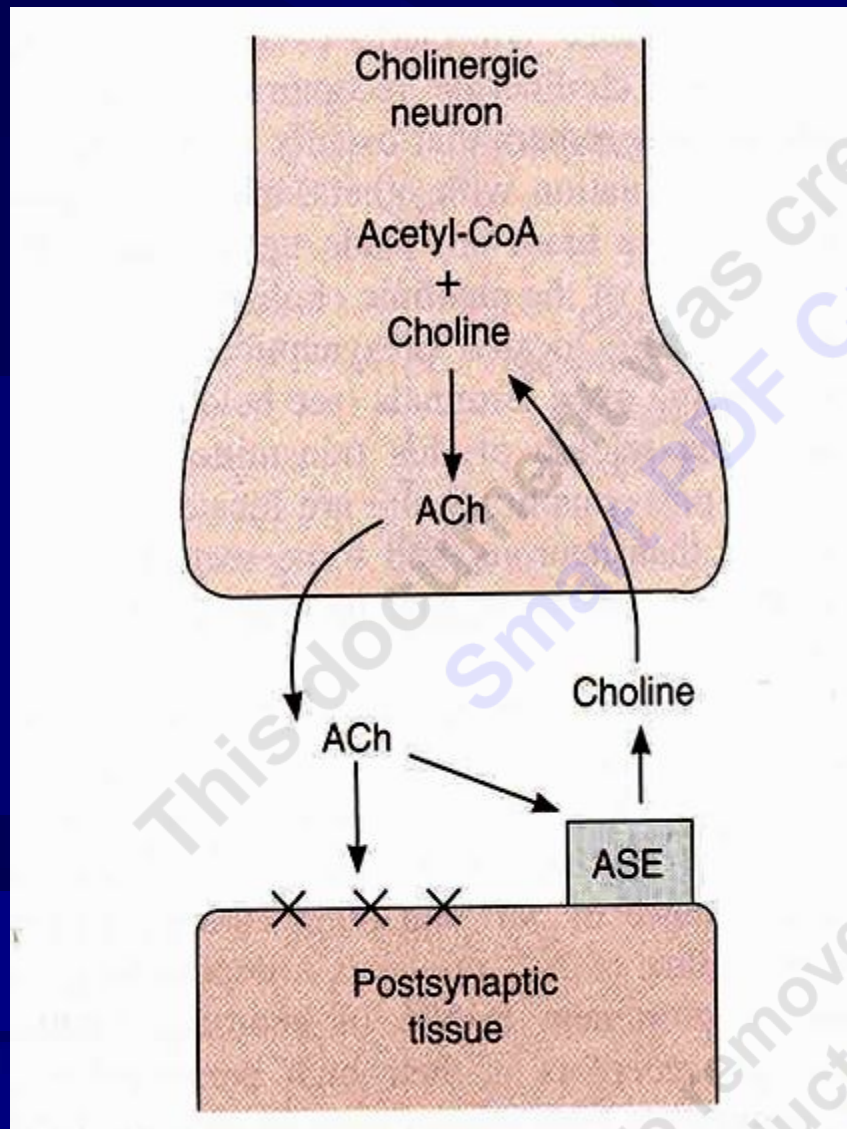
✓ Acetylcholine →

Acetylcholinesterase (ACh-esterase) ;

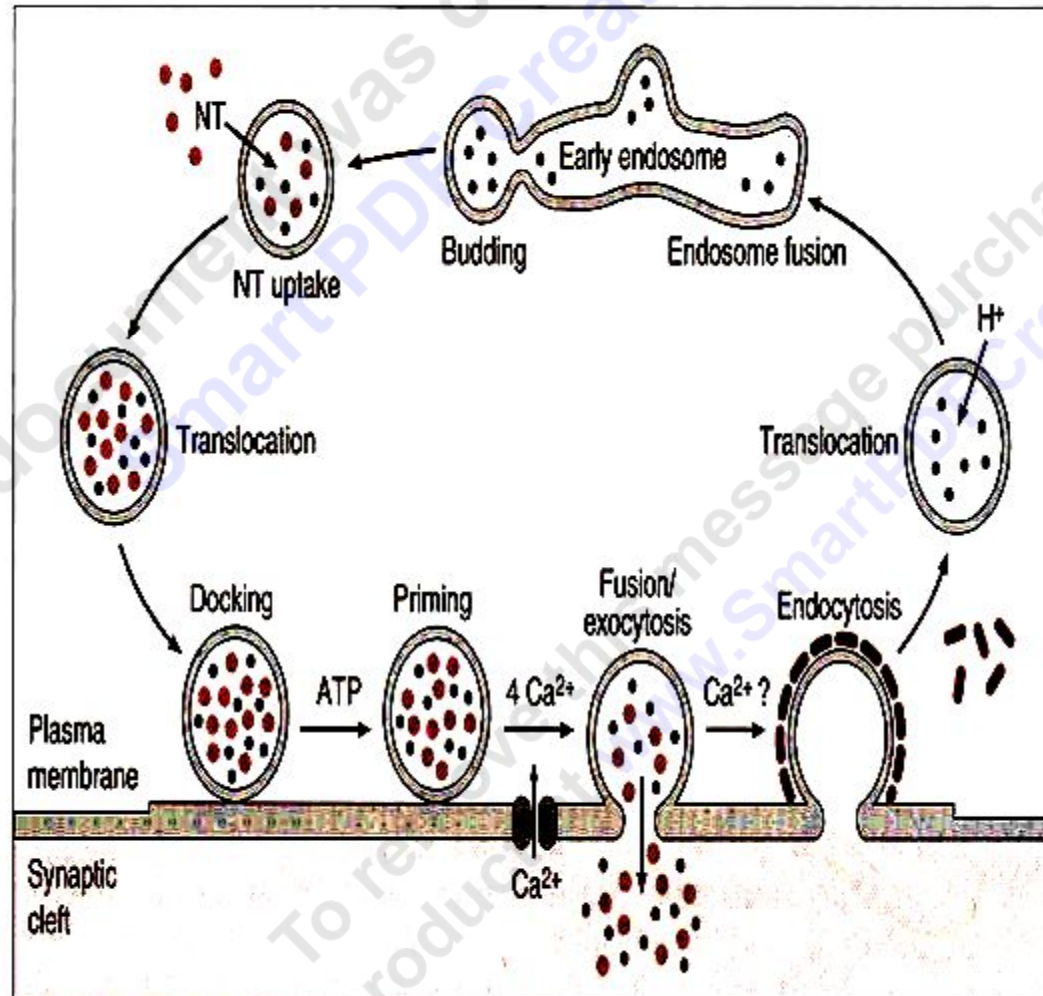
✓ Noradrenaline → it is COMT
(Catechol-O-Methyl Transferase)

Final Fate of Transmitter

- Q : What happens to the transmitter after it has combined with its postsynaptic receptors and produced its physiological effect ?
- In the synaptic cleft there are enzymes that will then destroy the transmitter .
- Examples :
- In case of Acetylcholine → Acetylcholinesterase (ACh-esterase) ;
- In case of Noradrenaline → Catechol-O-Methyl Transferase (COMT)



Vesicle Recycling



Examples of Factors that Affect Neurotransmission

- What is the effect of :
 - Alkalosis ?
 - Hypoxia ?
 - Acidosis ?

Some Properties of Synapses & Synaptic Transmission

PROPERTIES OF SYNAPTIC TRANSMISSION

1/ ONE WAY CONDUCTION

Why ?

2/ SYNAPTIC DELAY

الزمن المستغرق بين التحفيز و ظهور الأستجابة .. ما سبب هذا التأخير ؟

The time taken between stimulation of the pre-synaptic ending and elicitation of the post-synaptic response .

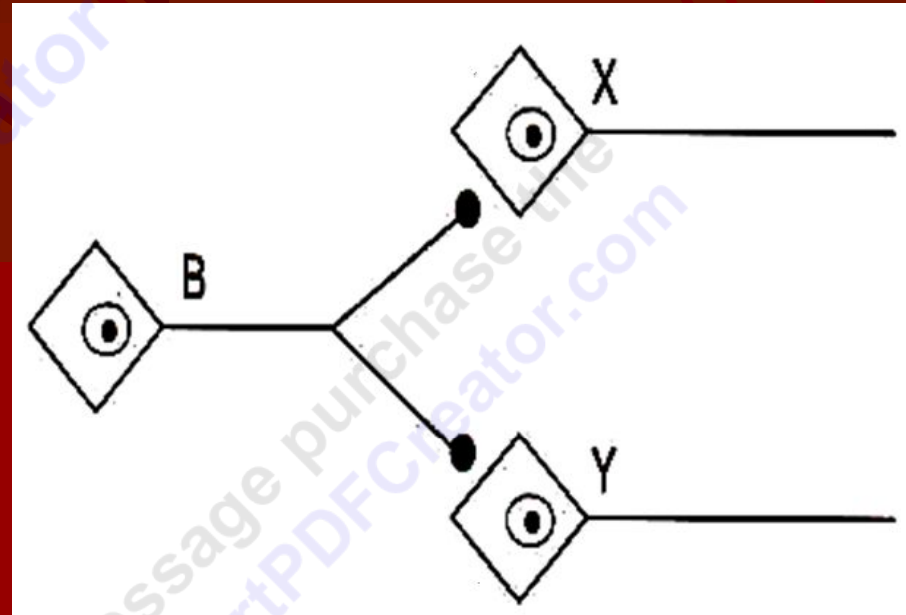
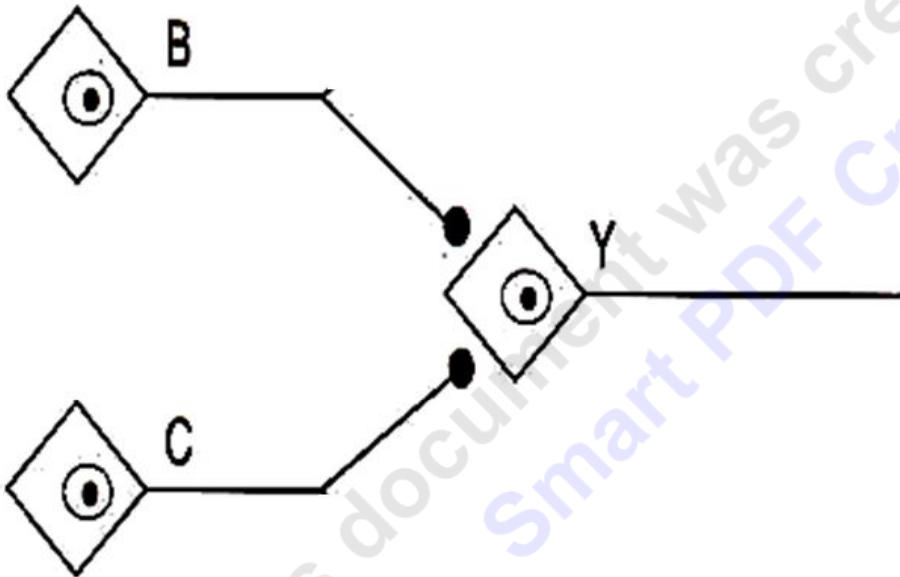
المتوسط عبر كل ساينابس لحاله هو 0.5 millisecond

Average synaptic delay in one synapse = 0.5 ms (0.5 – 0.6 ms).

- ✓ Therefore , in 2 synapses = 1.0 – 1.2 ms,
- ✓ in 3 synapses = 1.5 – 1.8 ms ,
- ✓ in 4 synapses = 2.0 – 2.4 ms , etc

يعني لو سألوك في الاختبار : أقسم الرقم علي 0.5 يجيك عدد الساينابس

3/ Convergence and Divergence



- What is the physiological role of convergence ?
- What is the physiological role of divergence ?

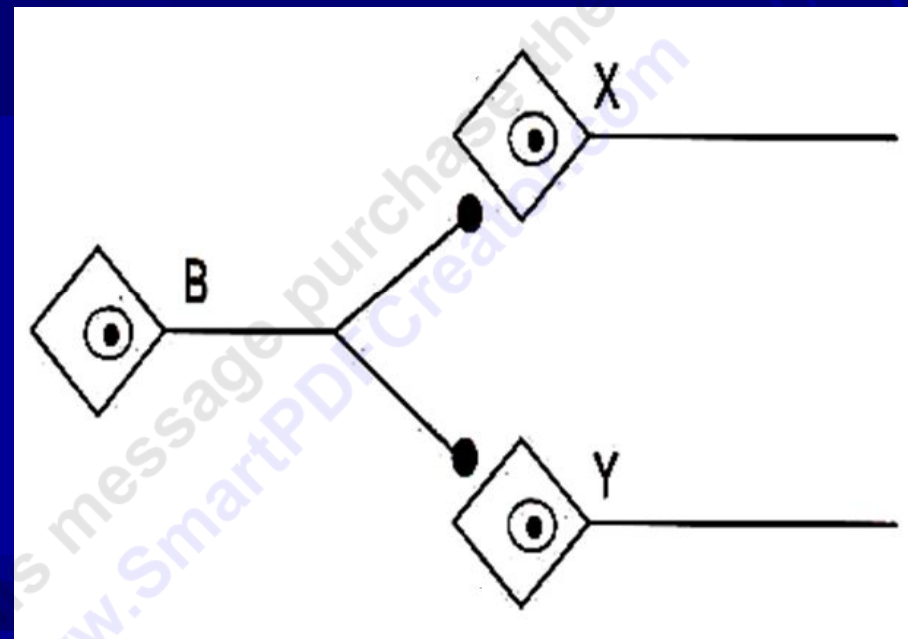
التفرع لنشر الخبر 3/ Divergence

في هذه الشبكة العصبية الأكسون B ينقسم
diverges ليعطي الخليتين X and Y

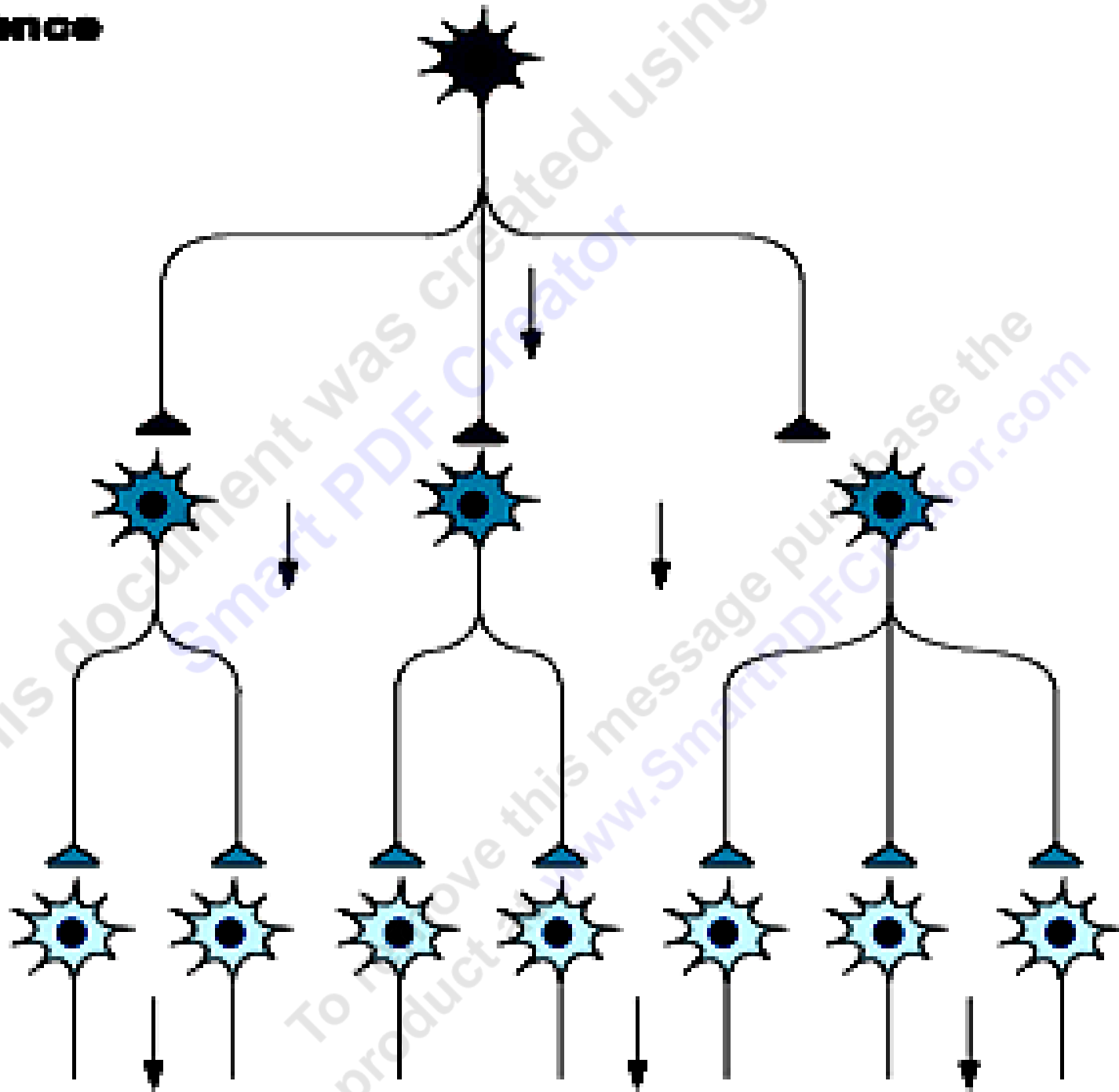
■ Advantages of divergence

- (1) spread of information .
- (2) amplification of the post-synaptic responses .

Example : in the sympathetic system one pre-ganglionic neuron can innervate up to 20 post-ganglionic neurons

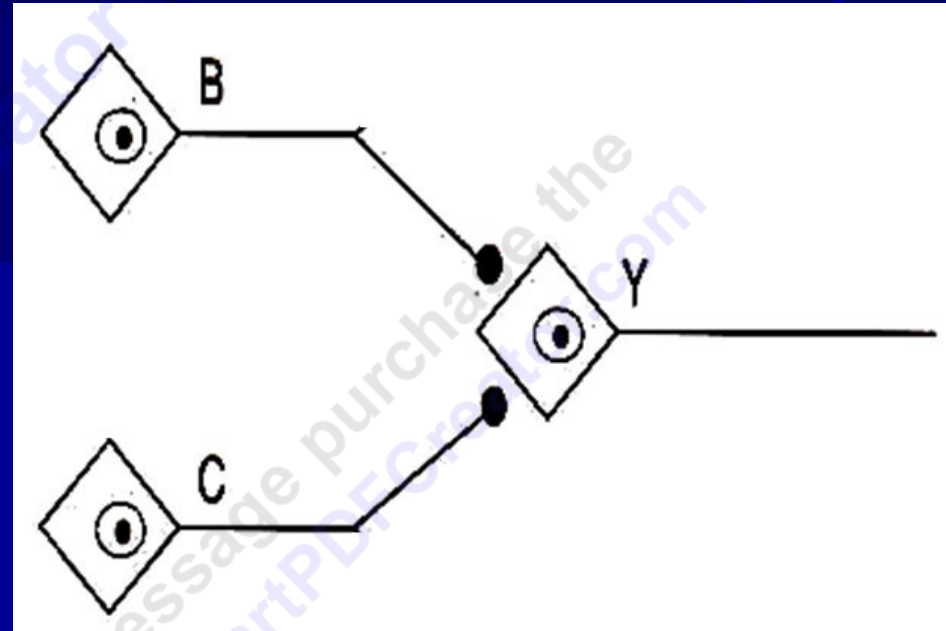


Divergence



Convergence الاجتماع للتشاور

و من ناحية أخرى : فرعان من
الأكسونين B and C
يجتمعان converge
علي الخلية Y



4/ CONVERGENCE

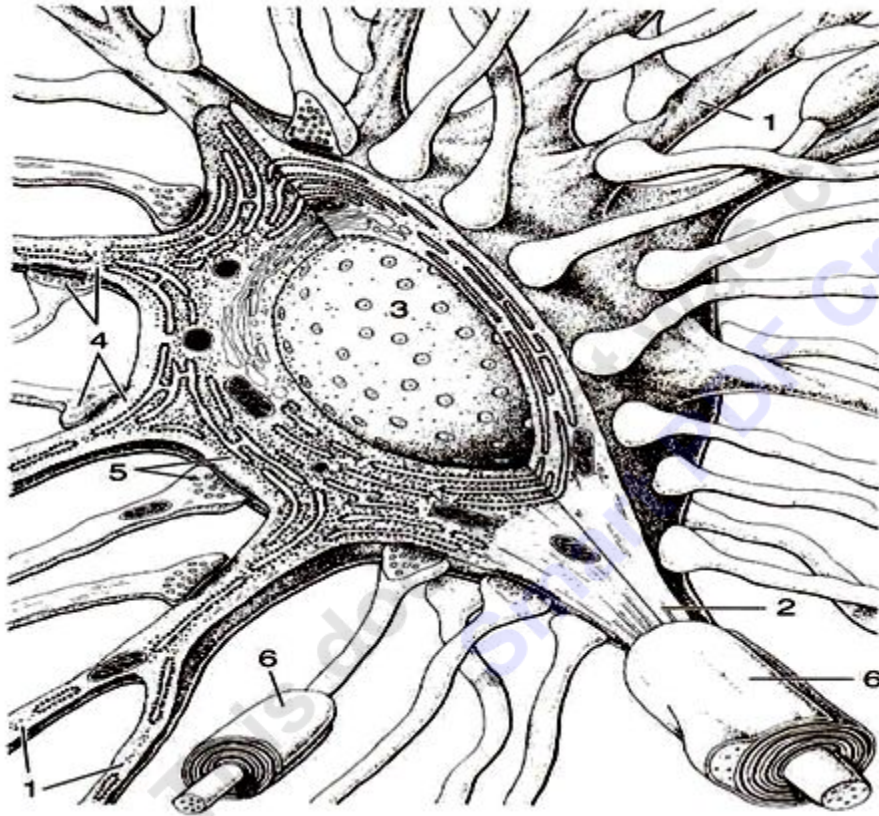
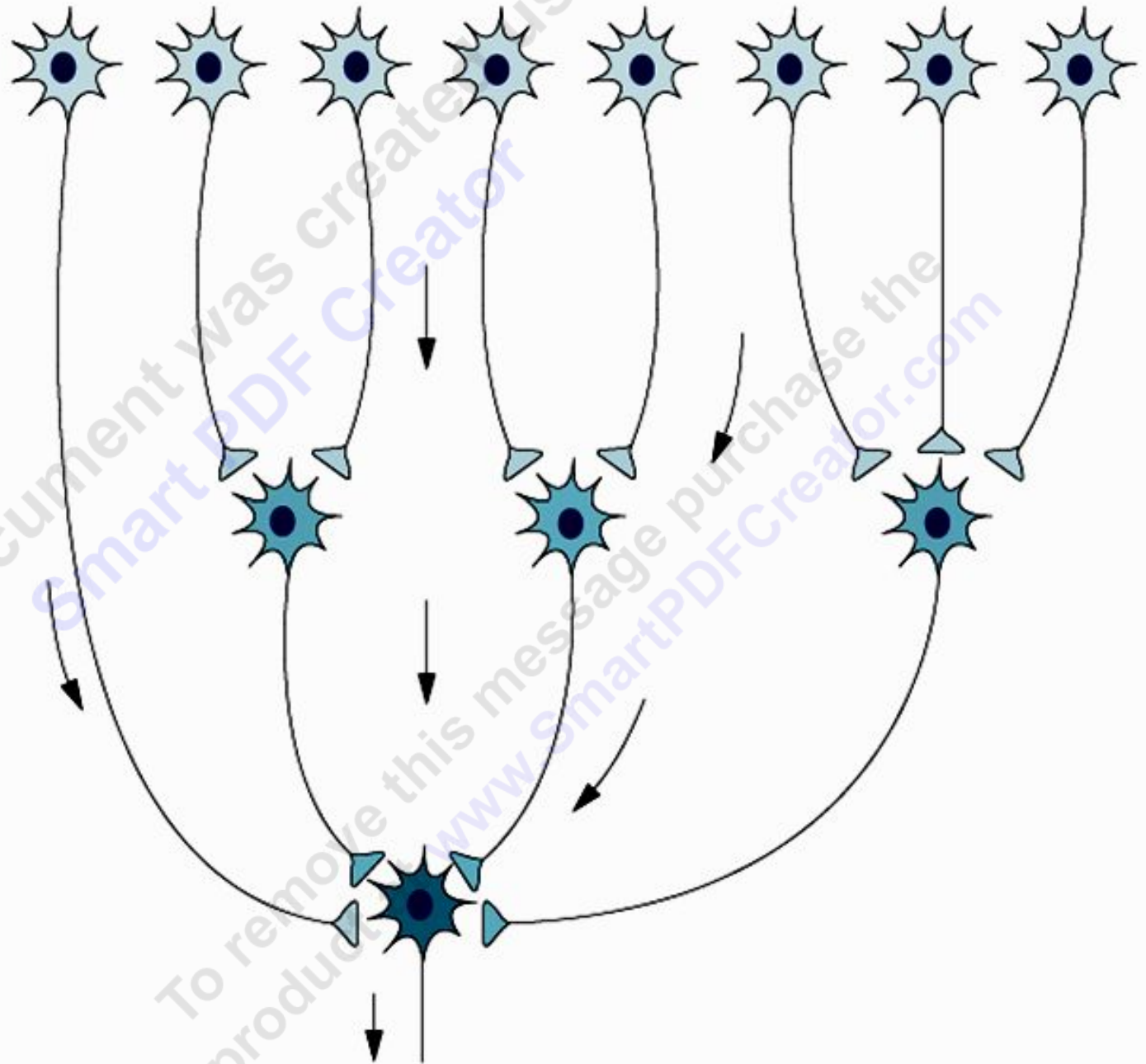


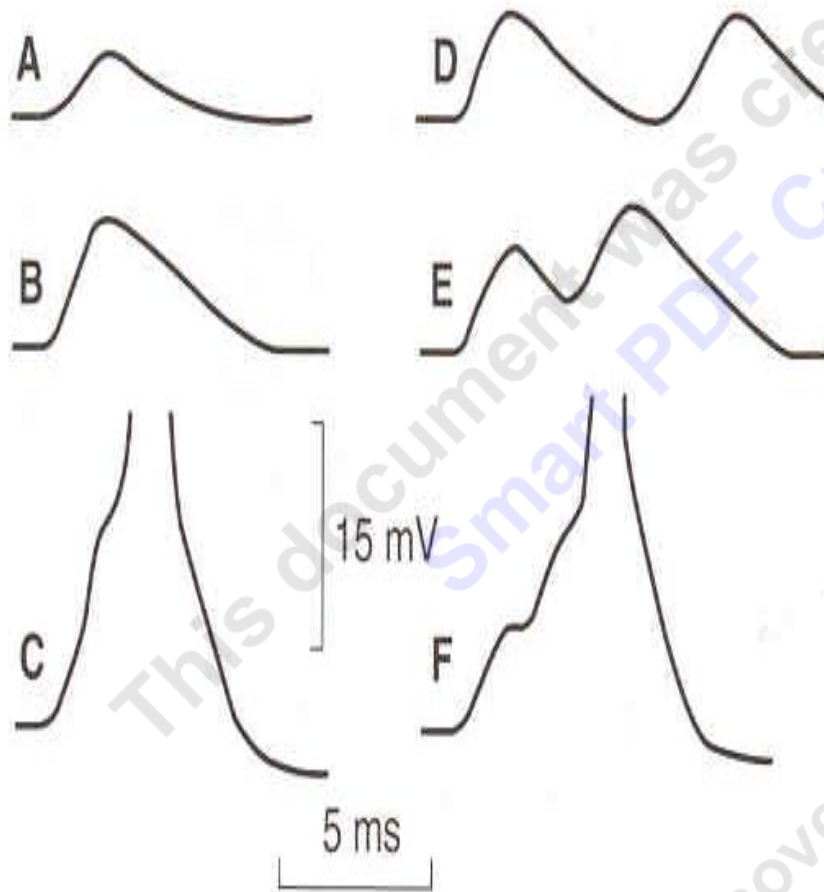
Figure 4-1. Synapses on a typical motor neuron. The neuron has dendrites (1), an axon (2), and a prominent nucleus (3). Note that rough endoplasmic reticulum extends into the dendrites but not into the axon. Many different axons converge on the neuron, and their terminal buttons form axodendritic (4) and axosomatic (5) synapses. (6) Myelin sheath. (Reproduced, with permission,

- Example : the spinal motor neuron (anterior horn cell , AHC) receives between 1000 – 10,000 synaptic inputs : Some of these terminals are excitatory (produce EPSPs).
- And others are inhibitory(produce IPSPs) on the soma or dendrite of the post-synaptic cell.
- Advantage : Helps in (1) Spatial Summation التجميع المكاني, (2) integration and modulation of information .

Convergence



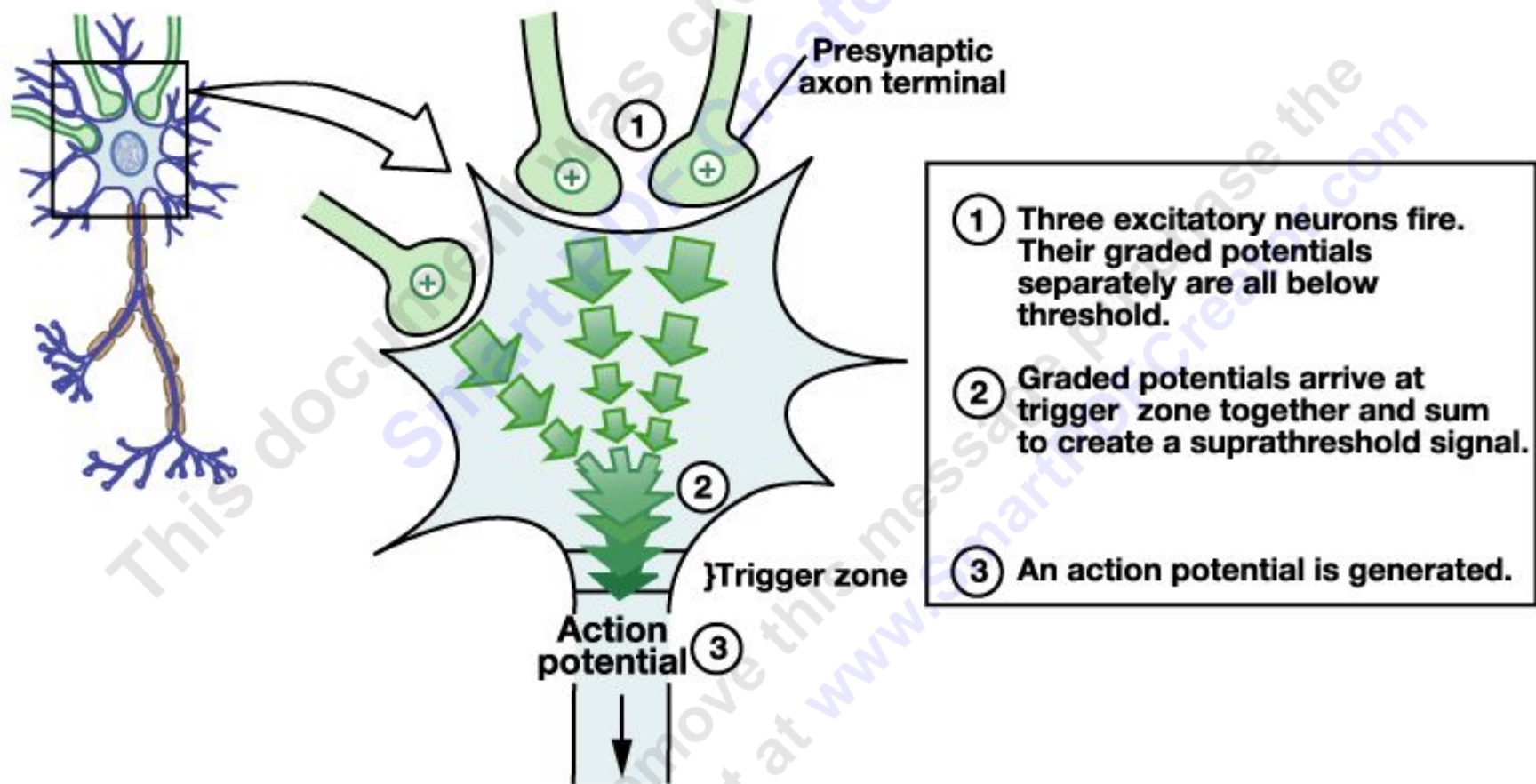
Summation التجميع: Spatial & Temporal



■ Spatial summation التحفيز بالجماعة (التجميع المكاني) : due to adding up of EPSPs produced by more than one synaptic knob . Thus activity in one synaptic knob facilitates activity in another.

■ Temporal summation التجميع الزماني التحفيز بالألحاح في زمن متلاحق ، حتى ولو كان من فرد : Repeated afferent stimuli (even if from a single synaptic knob) cause new EPSPs before previous EPSPs have decayed.

Spatial Summation



5/ Inhibition (1)

- Presynaptic inhibition ?

Where ?

Mediator ?

- Postsynaptic inhibition ?

- Reciprocal inhibition ?

- Inhibitory interneuron ?

Example ? Renshaw cell ?

- Define :

Feed-back inhibition ?

Feed-forward inhibition ?

Lateral inhibition ?

Inhibition (3)

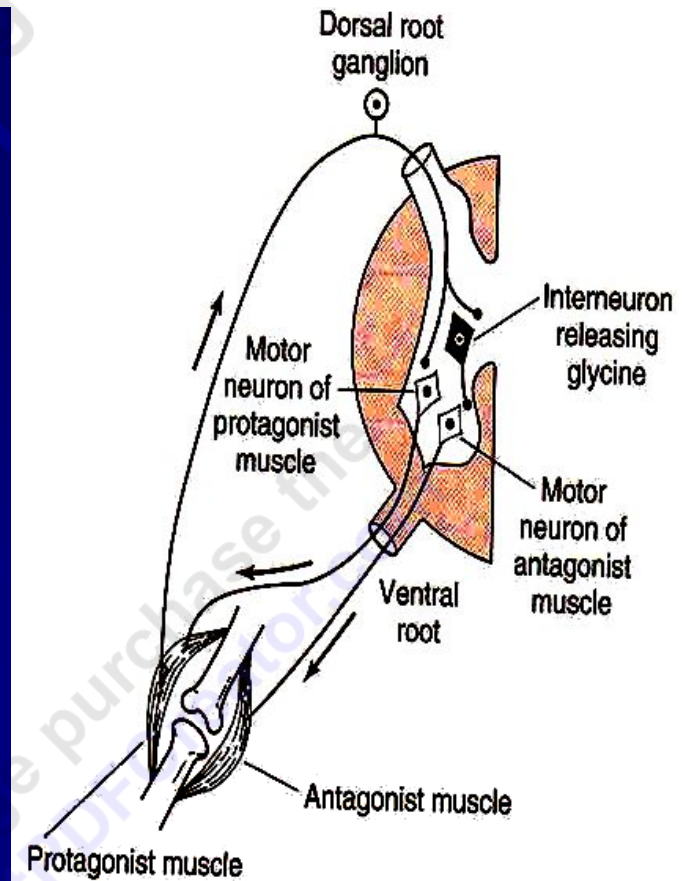
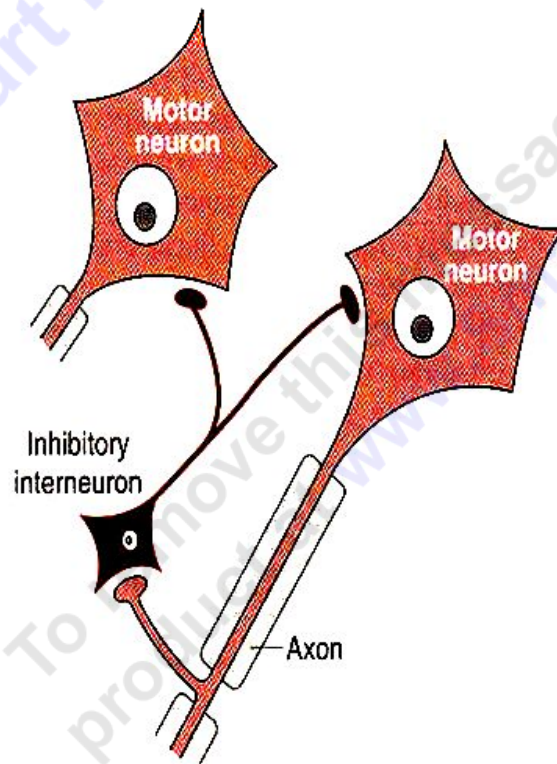
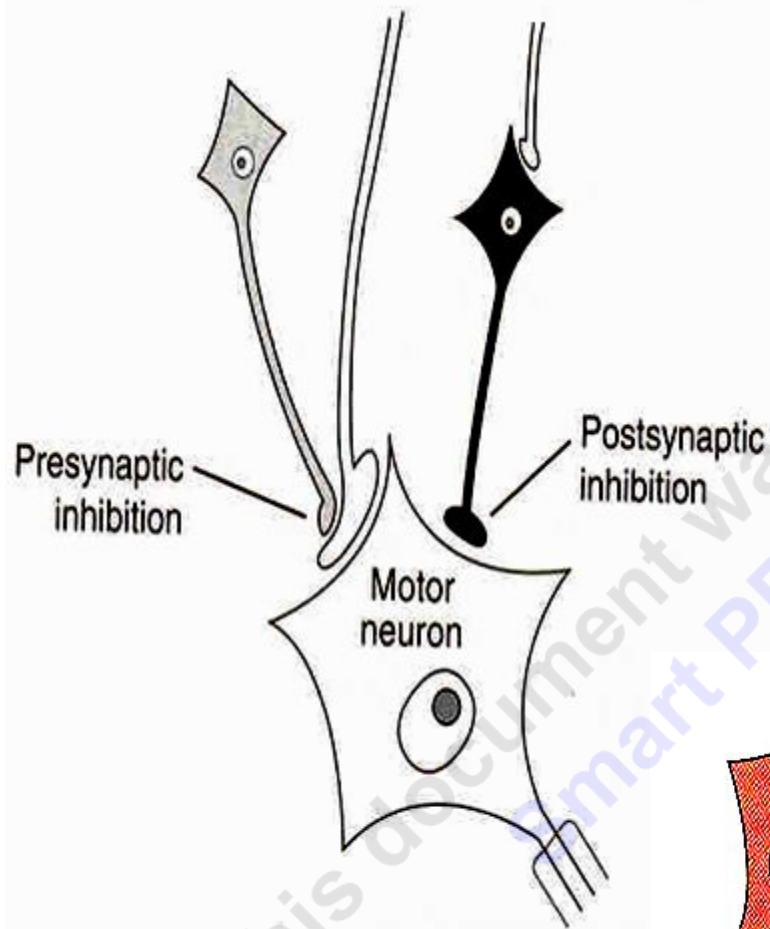
- Define :

Feed-back inhibition ?

Feed-forward inhibition ?

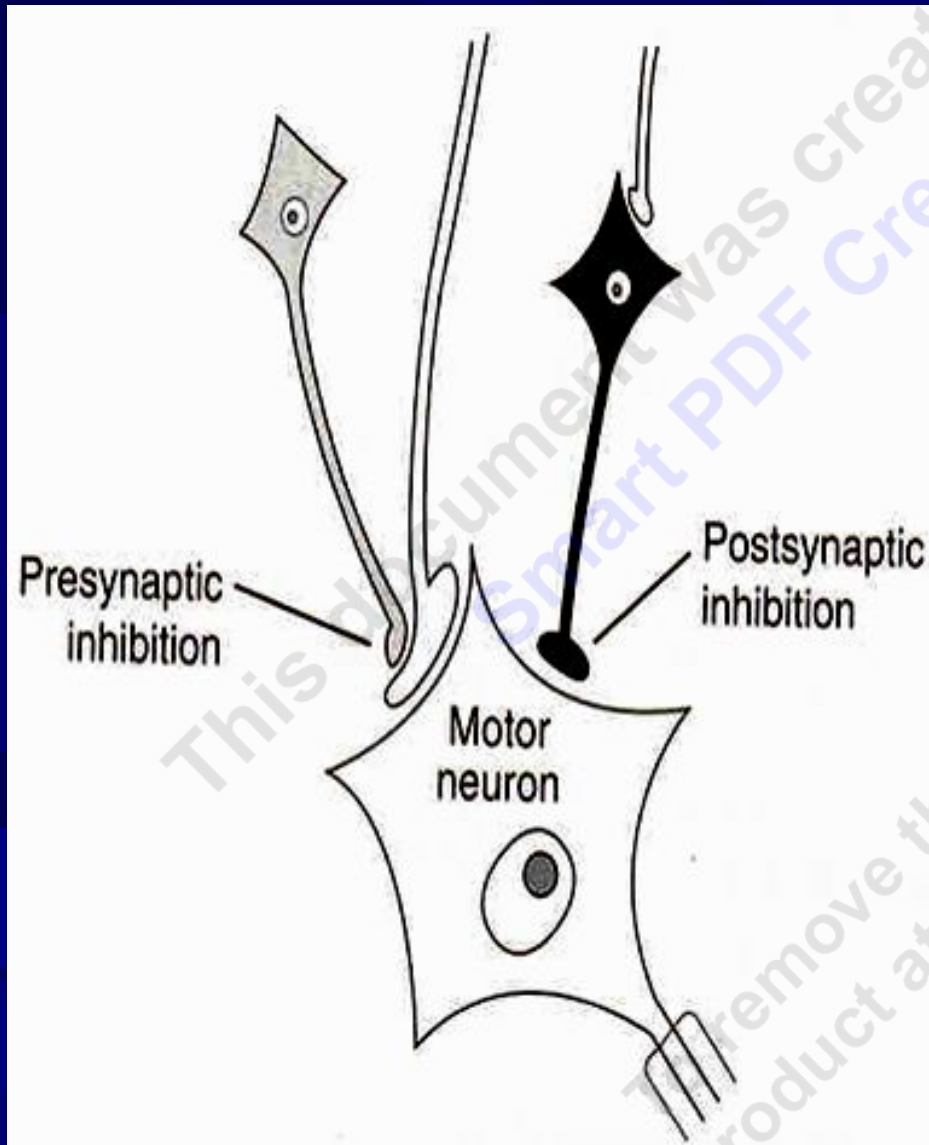
Lateral inhibition ?

- Explain physiological significance of each ?



8/ INHIBITION

A/ Presynaptic Inhibition



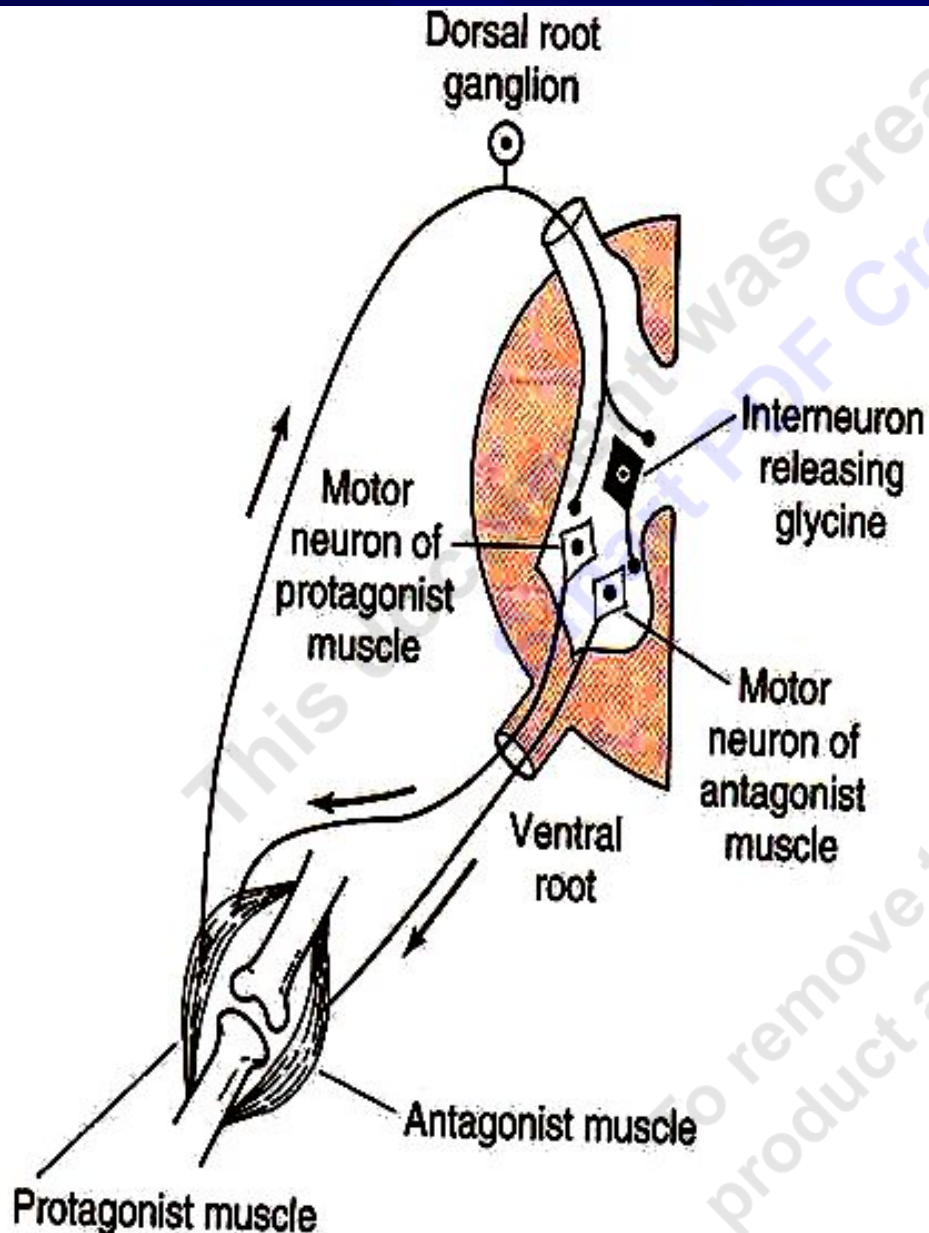
An inhibitory neuron, not acting directly on the target cell, but makes **axo-axonal synapse** on an excitatory ending that ends on the target cell. This inhibitory interneuron releases GABA which acts via either :

- (1) **GABA_A** receptors that increase chloride conductance
→ decreasing calcium entry into the excitatory synaptic knob
→ reduced or absent vesicle release ;

or GABA may act via

- (2) **GABA_B** receptors which, through G-protein → increase potassium conductance, thereby decreasing calcium entry into the synaptic knob of the excitatory neuron.

B/Postsynaptic Inhibition (also called Direct Inhibition)



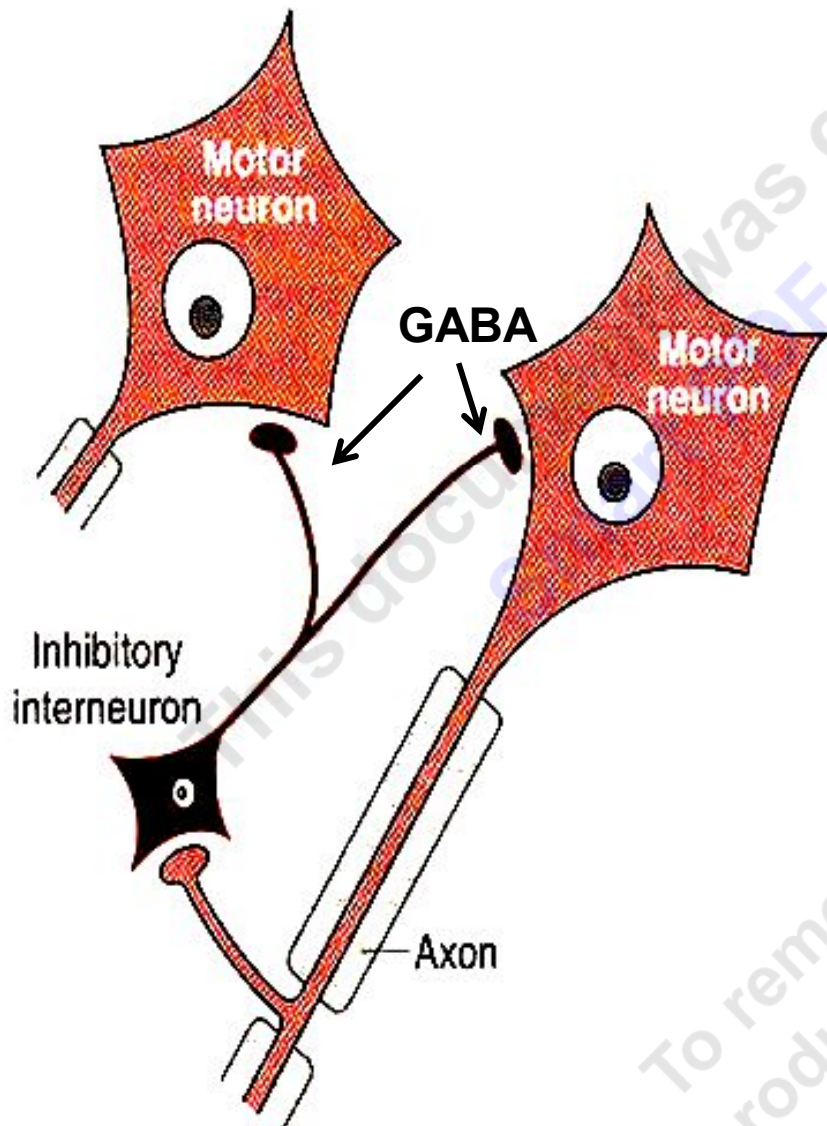
The inhibitory interneuron acts directly on the target cell (and not indirectly upon a cell that acts on the target cell , compare this diagram with the diagram in the previous slide).

Example of this **Direct Inhibition** is **Reciprocal Inhibition** in the spinal cord , which occurs by means **Reciprocal Innervation**

الأحباط المتبادل

→ Activity in spindle afferent , besides exciting the motoneuron supplying the agonist muscle , activates an **inhibitory interneuron** that → directly inhibit the motoneuron supplying the antagonist muscle .

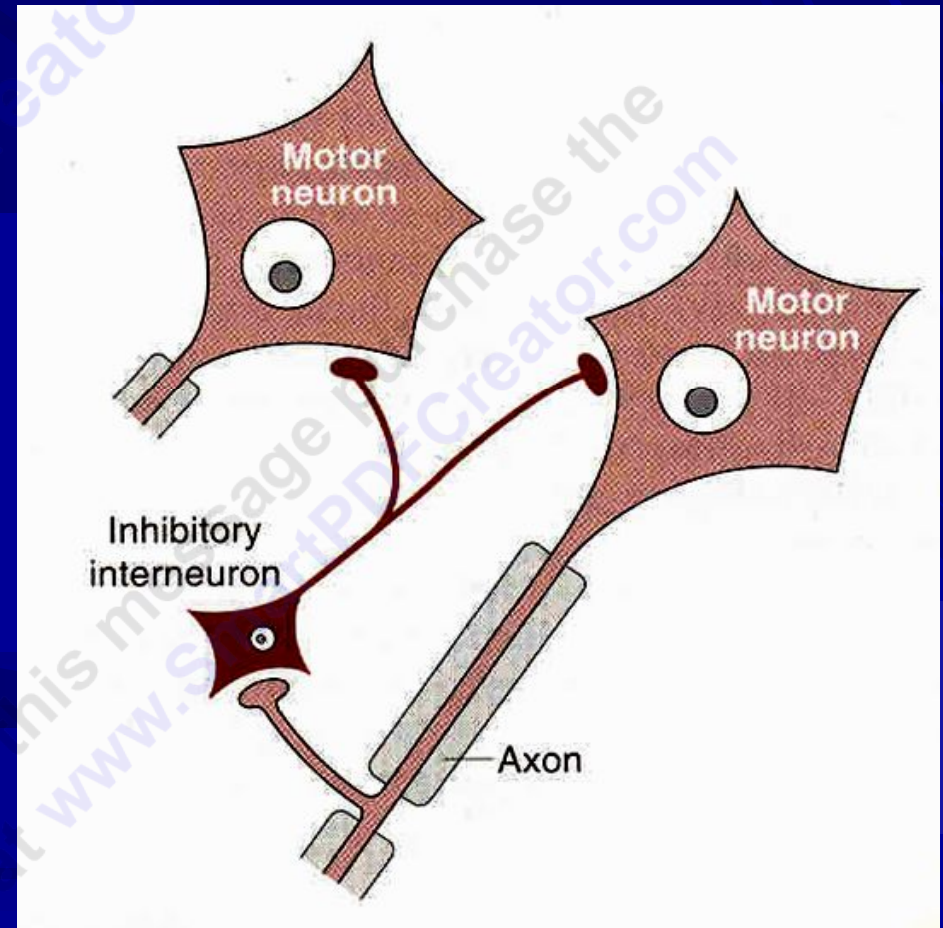
C/Feedback Inhibition (Renshaw Cell Inhibition)



- Neurons may also inhibit themselves in a negative feedback fashion (Negative Feedback inhibition).
- A spinal motoneuron gives a collateral that synapses **Renshaw cell** which is inhibitory interneuron.
- Then **Renshaw cell** , in turn , sends back axons that inhibit the spinal motoneuron .
- These axons secrete an inhibitory transmitter that produces IPSPs on cell-bodies of motoneurons and inhibit them .

7. The Renshaw cell

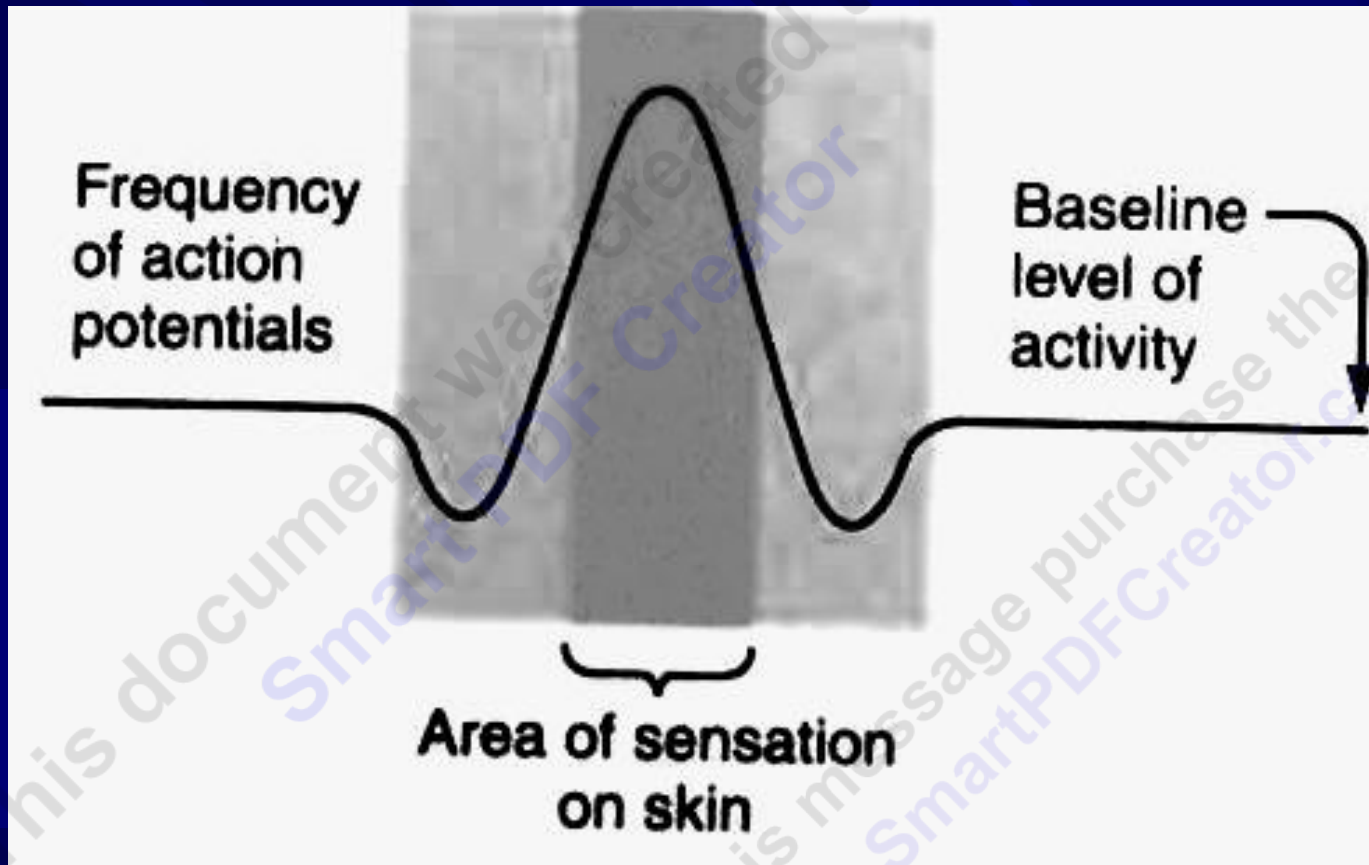
- Is located in anterior horn in close association with motor neurons.
- it is an inhibitory cell excited by collaterals from an alpha motor neuron to project back and inhibit the same motor neuron (negative feedback fashion).



D/ Feed-forward Inhibition

- Example : In the cerebellum → Basket and Stellate cells are excited by Granule cells via the parallel fibers → and their output inhibits the Purkinje cells .

E/ Lateral (Surround) Inhibition



- The best example of this is in the visual cortex → منطقة البصر في الدماغ
Activation of a particular neural sensory unit is associated with Inhibition of sensation of surrounding nearby units (it sends collateral fibers to inhibit its neighbours)

Thanks !