



PHYSIOLOGY

FACULTY OF PHARMACEUTICAL SCIENCES

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LECTURE 5- PARTS (1) & (2)

Objectives

1. Discuss **signal transmission** at **synapses**.
2. Distinguish **spatial and temporal summation of postsynaptic potentials**.

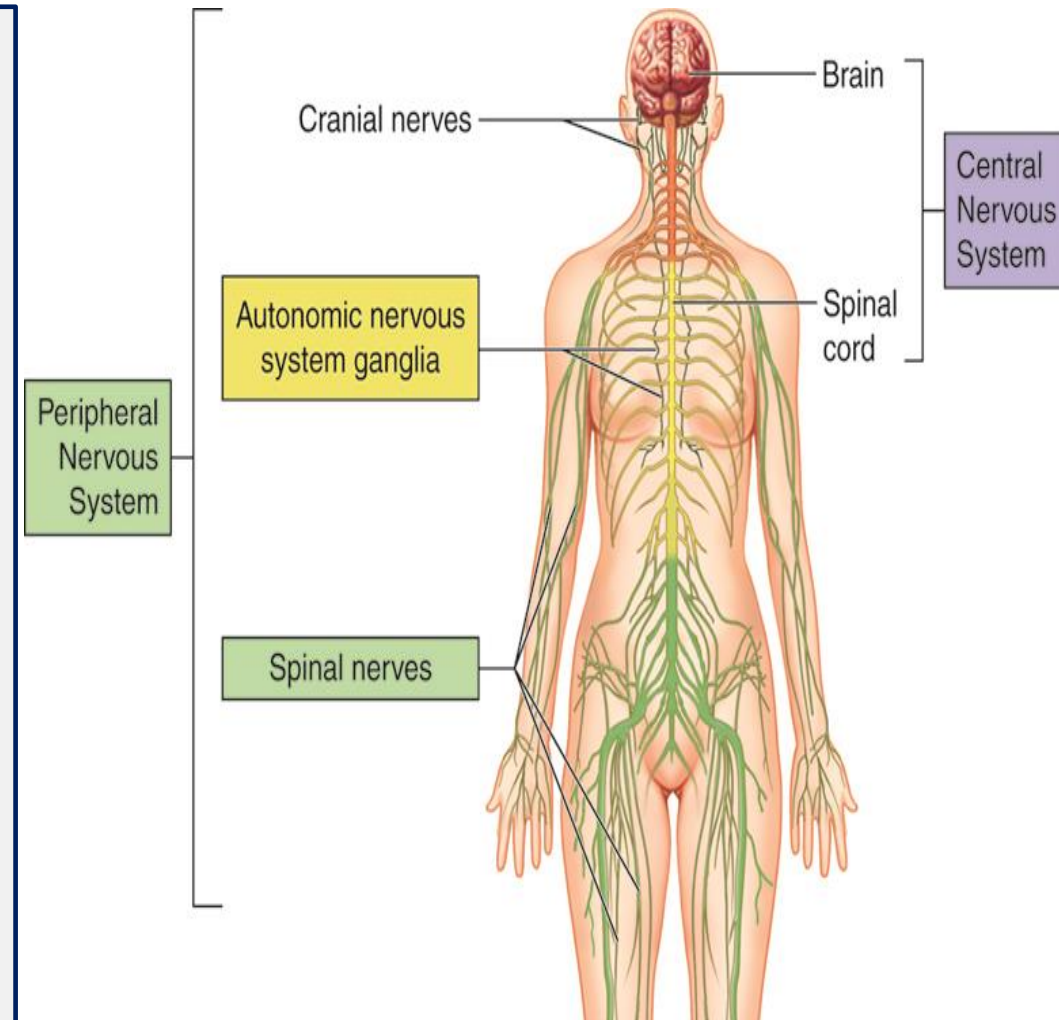
(Pages 424-436 of the reference).

General Overview



NERVOUS SYSTEM

- It consists of **central nervous system (CNS)** and **peripheral nervous system (PNS)**.
- The **CNS** consists of brain (85 billion neurons) and spinal cord (100 million neurons.).
- The **PNS** consists of all nervous tissue outside the CNS, which include nerves, ganglia, enteric plexuses, and sensory receptors.



SIGNAL TRANSMISSION AT SYNAPSES

- ✓ Recall from lecture 3 that **a synapse** is a region where communication occurs between two neurons or between a neuron and an effector cell.
- ✓ The term **presynaptic neuron** refers to a nerve cell that carries a nerve impulse toward a synapse (sends a signal).

synapse

الذي يُفرز neurotransmitter؛

SIGNAL TRANSMISSION AT SYNAPSES

- ✓ A postsynaptic cell is the cell that receives a signal. It may be a nerve cell called **a postsynaptic neuron** that carries a nerve impulse away from a synapse or an **effector cell** that responds to the impulse at the synapse.

SYNAPSES BETWEEN NEURONS

- Synapses may be **electrical or chemical** and they differ both structurally and functionally.

لا يتضمن انتقال السيال العصبي دائماً وجود neurotransmitter في بعض الأحيان يكون هناك روابط بين cells'body يتنقل السيال العصبي مباشرة بينهم اسمها Gap junctions لأن الاستجابات في بعض يجب أن تكون سريعة جداً في بعض organ زي الدماغ والقلب لأن أسرع من chemical synapse

electrical synapse

ELECTRICAL SYNAPSES

- At an electrical synapse, **action potentials (impulses) conduct directly** between the plasma membranes of adjacent neurons through structures called **gap junctions**.

عبارة عن فتحات داخلها
أنابيب بين الأغشية البلازمية
(tubular connexons)
للخلايا تعمل كقنوات أو tunnels

- Each gap junction contains a **hundred or so tubular connexons**, which act like tunnels to connect the cytosol of the two cells directly.

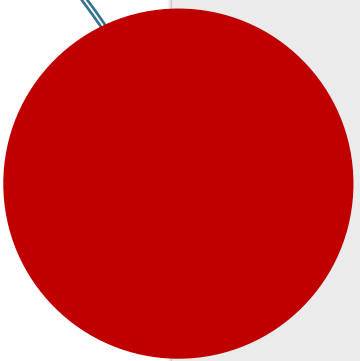
ELECTRICAL SYNAPSES

- Gap junctions are common in **visceral smooth muscle**, **cardiac muscle**, and the **developing embryo**. They also occur in the **brain**.

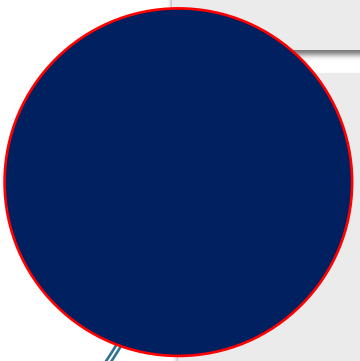
- الخلايا العصبية في هذه المناطق تكون electrical

- أي Synapse بين الجنين وأرام هو electrical

ELECTRICAL SYNAPSES HAVE TWO MAIN ADVANTAGES:

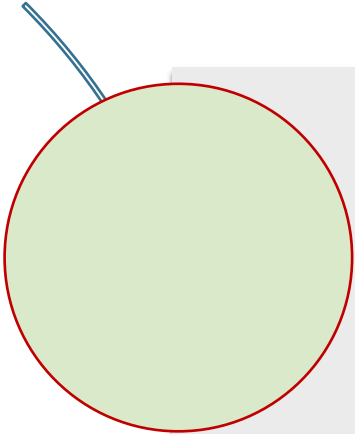


Faster communication (At an electrical synapse, the action potential passes directly from the presynaptic cell to the postsynaptic cell. The events that occur at a chemical synapse take some time and delay communication slightly).

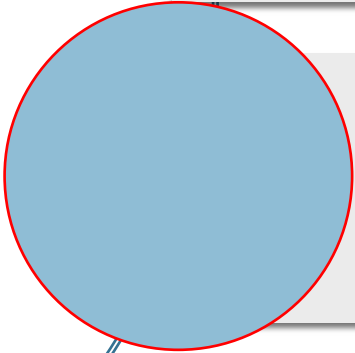


Synchronizati^{تزامن}on (large number of neurons or muscle fibers can produce action potentials in unison^{بكون تأثير AP ماشي على الـ neurons} if they are connected by gap junctions).
(نقل سريع) (فمن الأول للثاني سرعة ١
درجة ممكن انكره بالثاني وهو الثالث فتأثر AP بصل على العصب الأول و الثاني لسرعة انتقاله)
^{تزامن}

CHEMICAL SYNAPSES



The **plasma membranes of presynaptic and postsynaptic neurons** in a chemical synapse are separated by the **synaptic cleft**, a space of 20–50 nm that is filled with interstitial fluid.

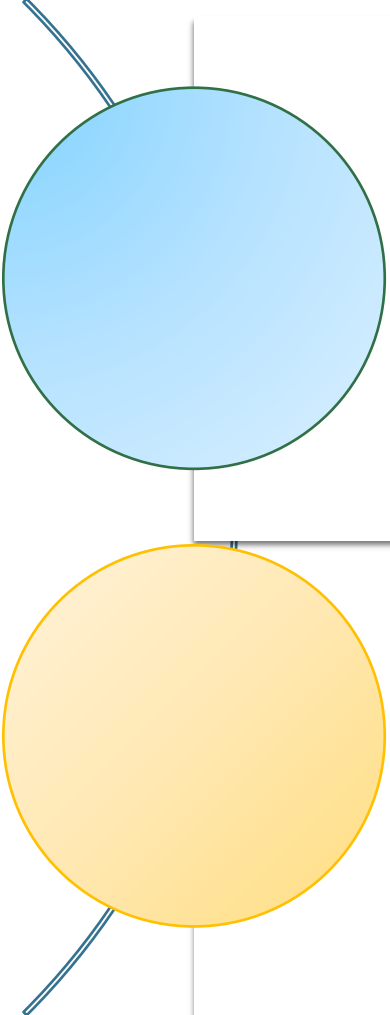


Nerve impulses cannot conduct across the synaptic cleft (**indirect form of communication**).

لا ينتقل AP إلى synaptic cleft الذي يخرج هو neurotransmitter
فيكون indirect communication

ليس فيه تأخير

CHEMICAL SYNAPSES



In **response to a nerve impulse**, the presynaptic neuron releases a **neurotransmitter** that diffuses through the fluid in the synaptic cleft and binds to receptors in the plasma membrane of the postsynaptic neuron.

The **postsynaptic neuron** receives the chemical signal and in turn produces a **postsynaptic potential**, a type of **graded potential**.

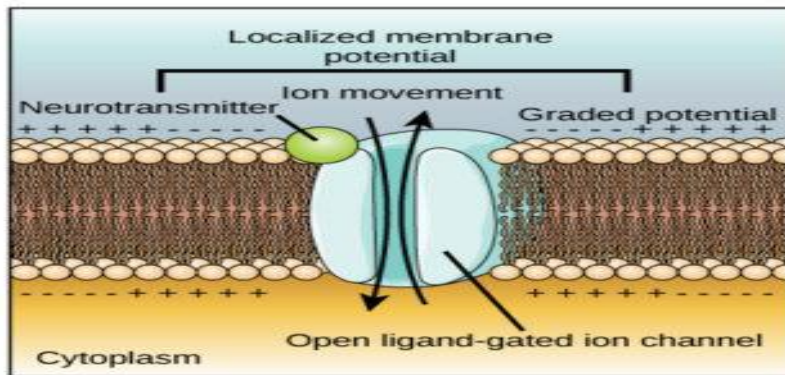
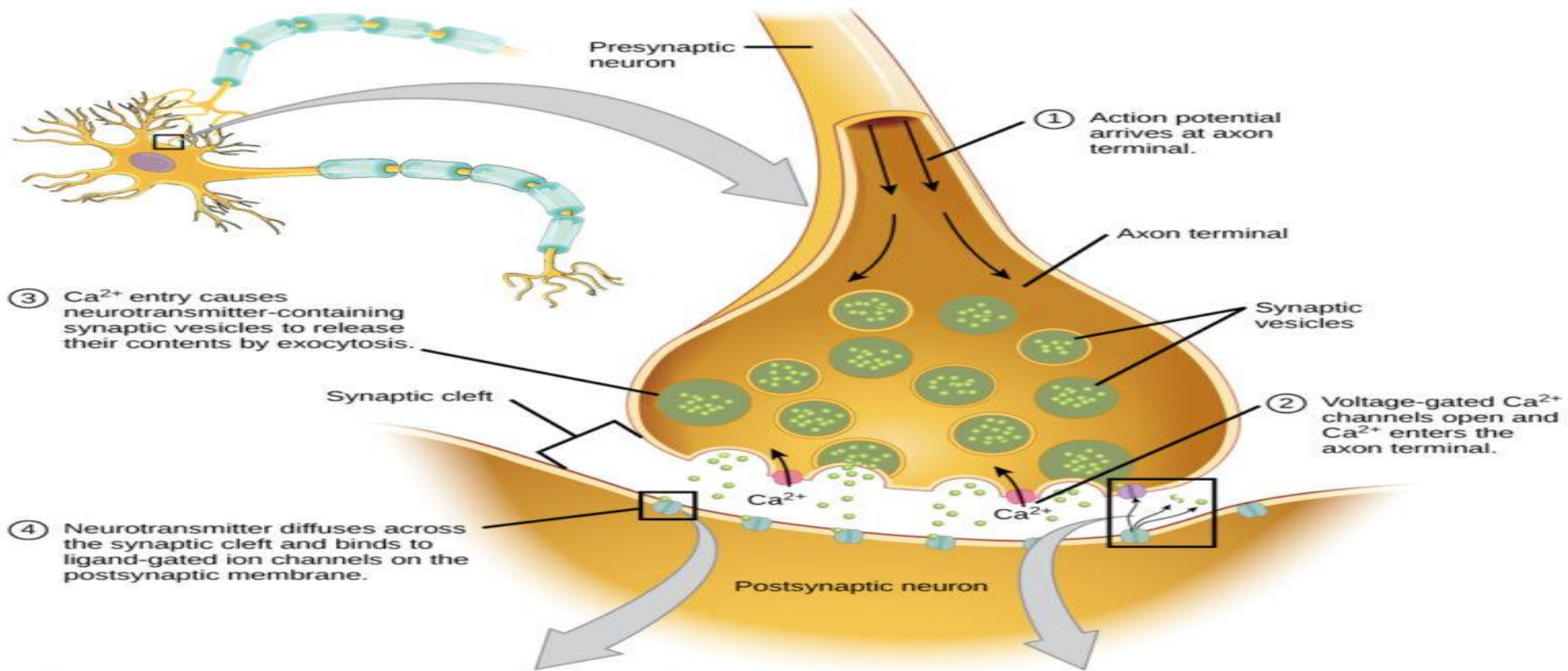
- إذا استقبلت (sensory receptors) neurotransmitter يكون اسم (graded potential)
(receptor potential)

- إذا استقبلت neurotransmitter على sensory neuron يكون اسم (graded potential) (generator potential)
- إذا استقبلت neurotransmitter على dendrites أو cell body يكون اسم (graded potential)
(post synaptic potential)

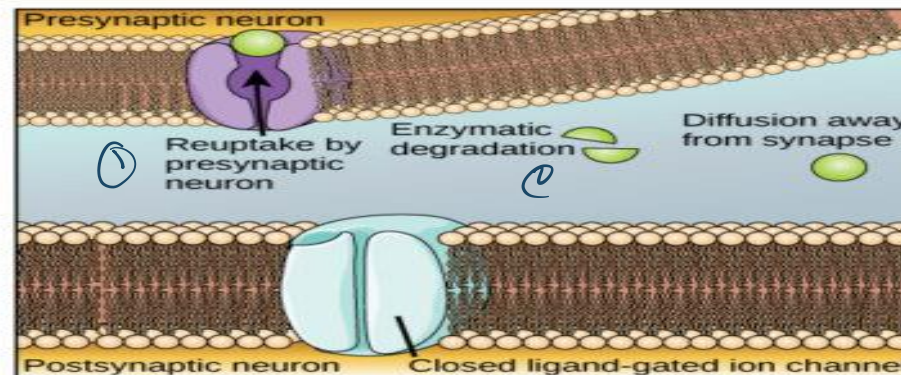
CHEMICAL SYNAPSES

- Thus, the presynaptic neuron converts an electrical signal (nerve impulse) into a chemical signal (released neurotransmitter).
- The time required for these processes at a **chemical synapse**, a synaptic delay of about 0.5 msec, is the reason that chemical synapses relay signals more slowly than electrical synapses.

صبي التأخير عن electrical synapse
لحو أن chemical synapse تستغرق 0.5 msec



⑤ Binding of neurotransmitter opens ligand-gated ion channels, resulting in graded potentials.

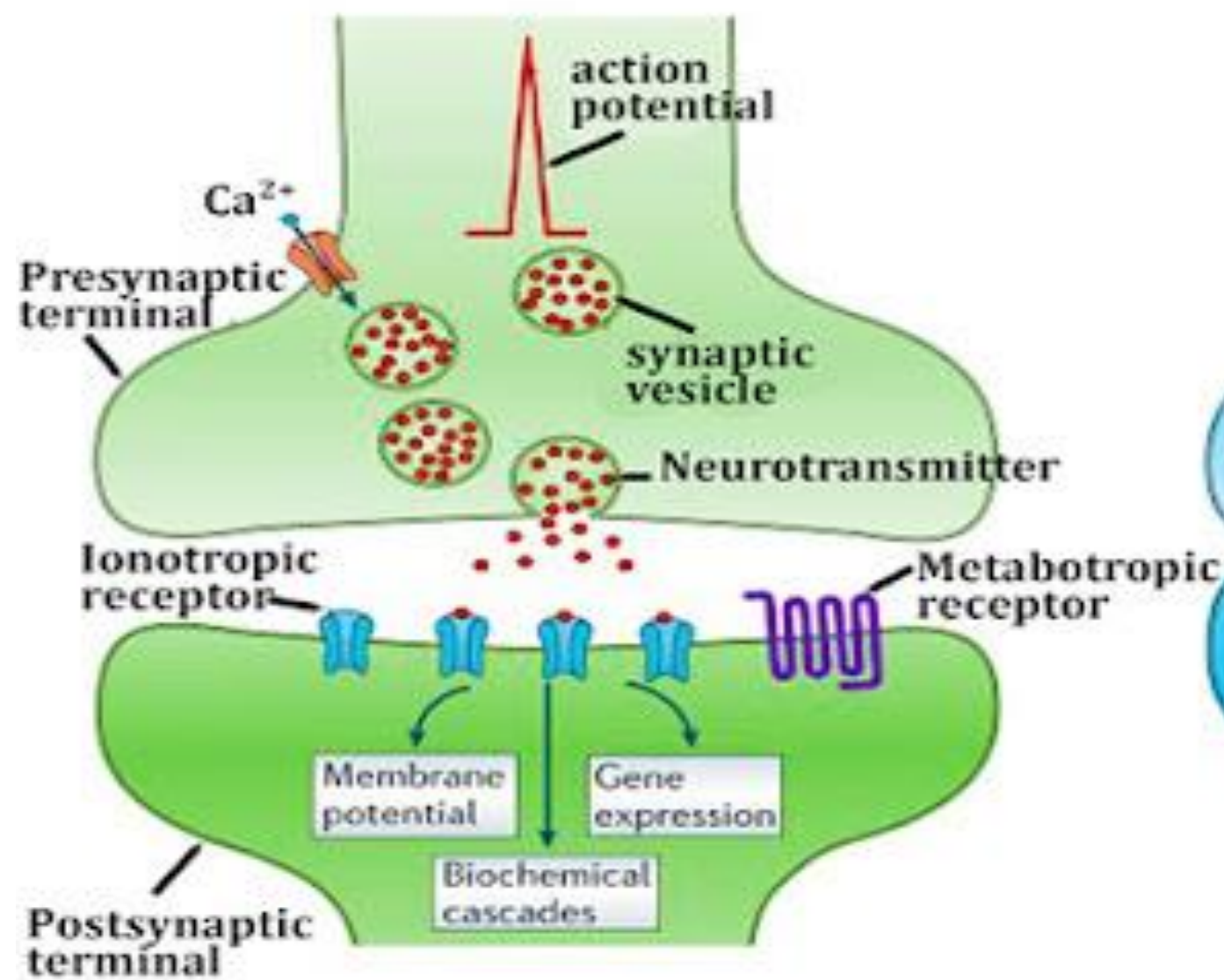


⑥ Reuptake by the presynaptic neuron, enzymatic degradation and diffusion reduce neurotransmitter levels, terminating the signal.

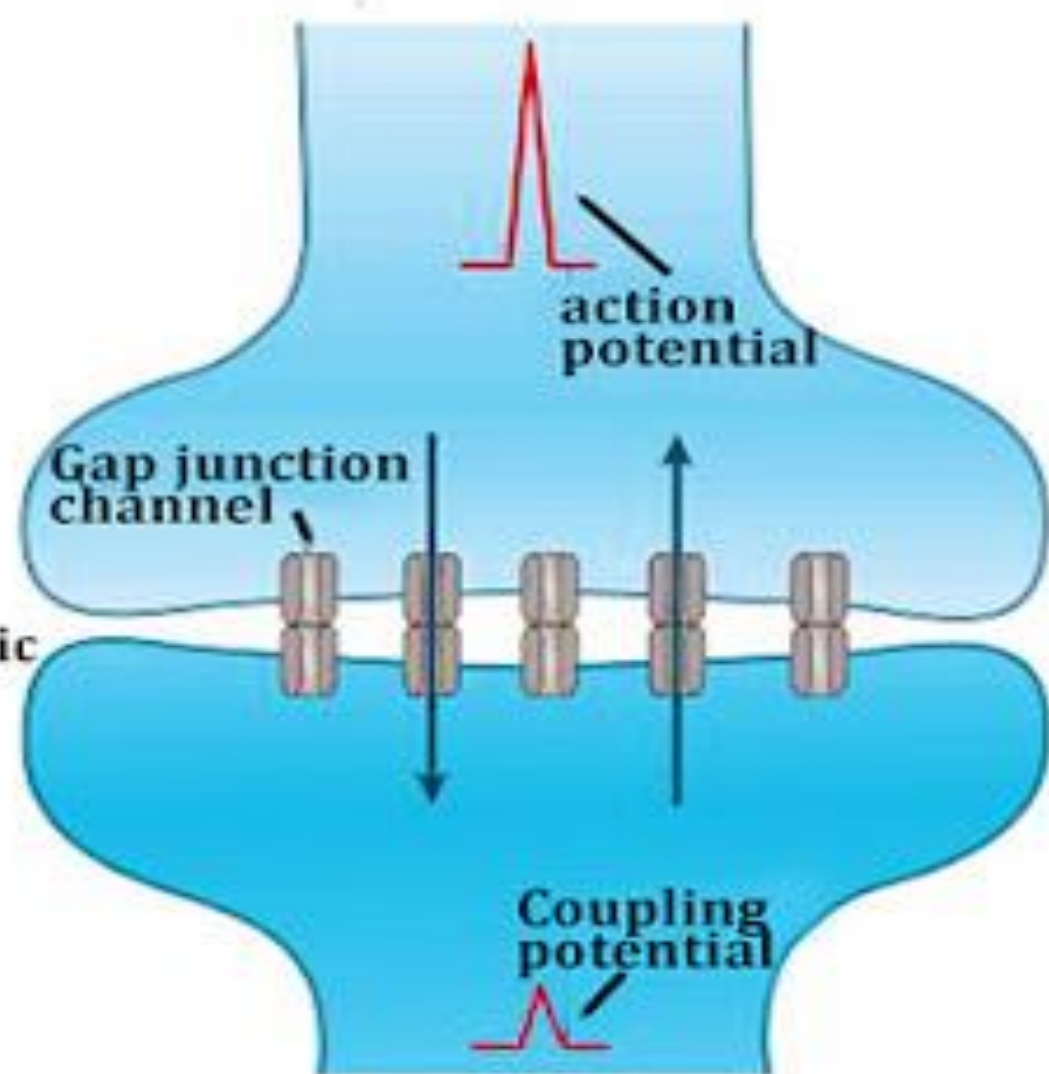
Postsynaptic potential

- Opening of Na^+ ions channels allows inflow of Na^+ ions, which causes depolarization.
- However, opening of Cl^- or K^+ ions channels causes hyperpolarization.
- When a depolarizing postsynaptic potential reaches threshold, it triggers an action potential in the axon of the postsynaptic neuron.

Chemical synapse



Electrical synapse



EXCITATORY AND INHIBITORY POSTSYNAPTIC POTENTIALS

Depolarization of the postsynaptic membrane is excitatory because it brings the membrane closer to threshold. A depolarizing postsynaptic potential is called an **excitatory postsynaptic potential (EPSP)**.

hyper-polarizing inhibition

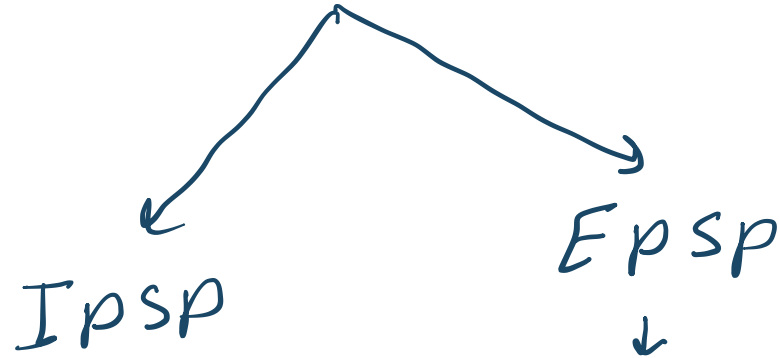
عندما يرتبط ligand
بال receptor تفتح ion channel
وتدخل Na^+ إلى داخل الخلية
فيقوم بعمل depolarization ويصبح جهد
الخلية أقرب لـ threshold ما يجعل
تأثير (post synaptic potential) هو (excitation) لأن
الخلية تنخفض على إنتاج AP

EXCITATORY AND INHIBITORY POSTSYNAPTIC POTENTIALS

During hyperpolarization, generation of an action potential is more difficult than usual because the membrane potential becomes inside more negative and thus even farther from threshold than in its resting state. A **hyperpolarizing postsynaptic potential** is termed an **inhibitory postsynaptic potential (IPSP)**.

عندما يرتبط ligand
بـ receptor تفتح قنوات K⁺
تخرج K⁺ من الخلية أو قنوات Cl⁻ تدخل
Cl⁻ داخل الخلية مما يبعد جهد الخلية
عن threshold فيكون تأثيره postsynaptic
potential هو inhibition لأن ما
داخل الخلية يصبح أكثر سالبة
ونقل قدرة الخلية على إنتاج
AP

potential



IpSP

neurotransmitter

له تأثير الخلية يعني

عمل hyperpolarization

(inhibition)

بعيد عن threshold

EpSP

neurotransmitter

حفر الخلية تعمل EpSP

عمل depolarization اي هي

(excitation)

قريب من threshold

STRUCTURE OF NEUROTRANSMITTER RECEPTORS

Neurotransmitter receptors are classified as either **ionotropic receptors** or **metabotropic receptors** based on whether the neurotransmitter binding site and the ion channel are components of the same protein or are components of different proteins.

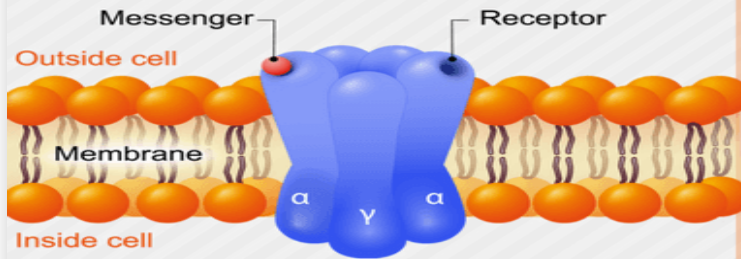
IONOTROPIC vs METABOTROPIC RECEPTORS

WWW.INTERACTIVE-BIOLOGY.COM

IONOTROPIC RECEPTORS

both are ligand-gated transmembrane proteins

Acts quickly.



Ionotropic receptors change shape when they are bound by a ligand. This change in shape creates a channel that allows ions to flow through.

METABOTROPIC RECEPTORS

Takes a little longer depending on the number of steps required to produce a response.

Metabotropic receptors do not have channels.

Metabotropic receptors activate a G-protein that in turn activates a secondary messenger, that in turn will activate something else.

Metabotropic receptor activation may or may not result in the opening of ion channels somewhere else on the membrane.

More on this at www.interactive-biology.com

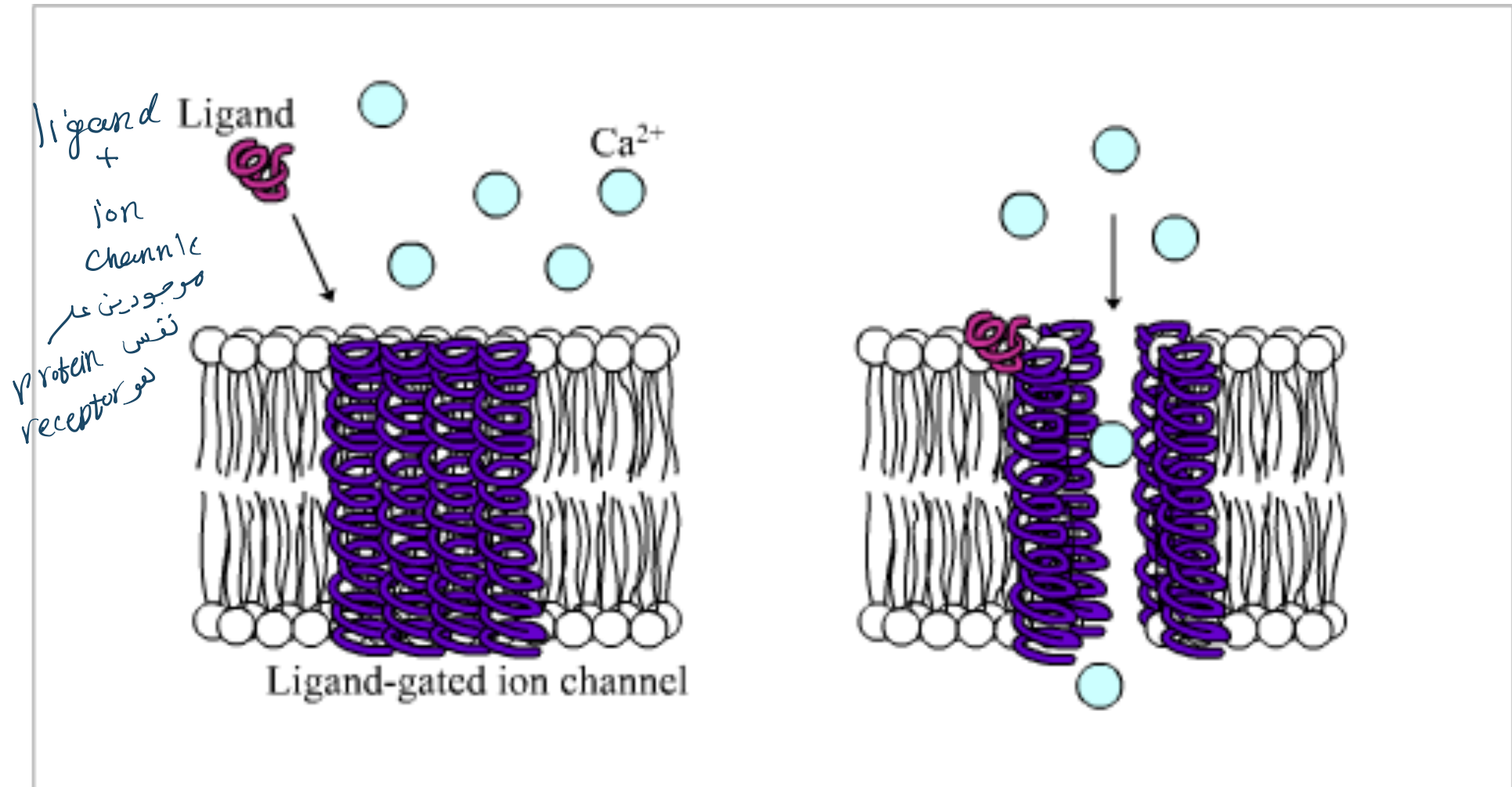
- مش دائما ion channels
بتكون بجانب receptors مرات
بتكون بعيدة عنها

- في منها بتكون ion channels
بجانب receptor (بكونوا على نفس
البروتين) فبجرد ما يرتبط ligand
بال receptor بتغير شكل ion channel
وتغير شكلها بفتح بمرور الأيونات ولها
receptors بسميها (ionotropic receptor)

- إذا كانت ion channels منفصلة
عن receptor (موجودين على بروتينات
مختلفة) يرتبطو ببعض عن طريق بروتين
يسمى G protein والذي عند ارتباط
ligand بال receptor يتحفر ويقوم بتغيير
ion channel بشكل مباشر أو بشكل غير مباشر
عن طريق تحفيز بروتين آخر في (cytosol)
يسمى messenger protein يتفعل G protein
والذي عند تحفزه يفتح ion channel ولها

يسمى (metabotropic receptor) نقد cholinergic و adrenergic باستثناء
receptor مثال على metabotropic receptor
نقد مثال على ionotropic receptor

IONOTROPIC RECEPTORS



IONOTROPIC RECEPTORS

- is a type of **neurotransmitter receptor** that contains a **neurotransmitter binding site** and an **ion channel** (i.e neurotransmitter binding site and the ion channel are components of the **same protein**).

IONOTROPIC RECEPTORS

- *When the correct neurotransmitter binds to the ionotropic receptor, the ion channel opens, and an EPSP or IPSP occurs in the postsynaptic cell.*

METABOTROPIC RECEPTORS

is a type of neurotransmitter receptor that contains a **neurotransmitter binding site** but **lacks an ion channel** as part of its structure. However, a metabotropic receptor is **coupled to a separate ion channel** by a type of membrane protein called a **G protein**.

يكون receptor مرتبط بقناة أيونية منفصلة عن طريق G protein

METABOTROPIC RECEPTORS

- When a neurotransmitter binds to a metabotropic receptor, the **G protein either directly** opens (or closes) the ion channel or it may act **indirectly** by activating another molecule, a “**second messenger**,” in the cytosol, which in turn opens (or closes) the ion channel.
- Thus, a metabotropic receptor differs from an ionotropic receptor in that the neurotransmitter binding site and the ion channel are components of **different proteins**.

REMOVAL OF NEUROTRANSMITTER

- is essential for **normal synaptic function**. If a neurotransmitter could linger in the synaptic cleft, it would influence the postsynaptic neuron, muscle fiber, or gland cell indefinitely.

يجب إزالة neurotransmitter من synaptic cleft لأن
بقاءها لفترة أطول يؤدي إلى تحفيز مستمر للخلية العصبية أو
العضلية أو الغدة مما يؤدي إلى الضرر

REMOVAL OF NEUROTRANSMITTER

1. Diffusion: Neurotransmitters diffuse away from the synaptic cleft.

تفرج من المكان
آخر بغير عن
مكانه الأول

مسؤول عن side effect
للأدوية

2. Enzymatic degradation: Certain neurotransmitters are inactivated through enzymatic degradation.

3. Uptake by cells: Many neurotransmitters are actively transported back into the neuron that released them (reuptake). Others are transported into neighboring neuroglia (uptake).

تفرج من المكان
غريب

الفرق بين *diffusion* و *uptake* ؟

uptake يتكون عن طريق *active transport* ← تحتاج طاقة

diffusion يتكون عن طريق *passive transport* ← لا تحتاج طاقة

SPATIAL AND TEMPORAL SUMMATION OF POSTSYNAPTIC POTENTIALS

- A **typical neuron** in the CNS receives input from 1000 to 10,000 synapses.

أجمع البيانات

- **Integration of these inputs** involves summation of the postsynaptic potentials that form in the postsynaptic neuron. Recall that **summation** is the process by which graded potentials add together.

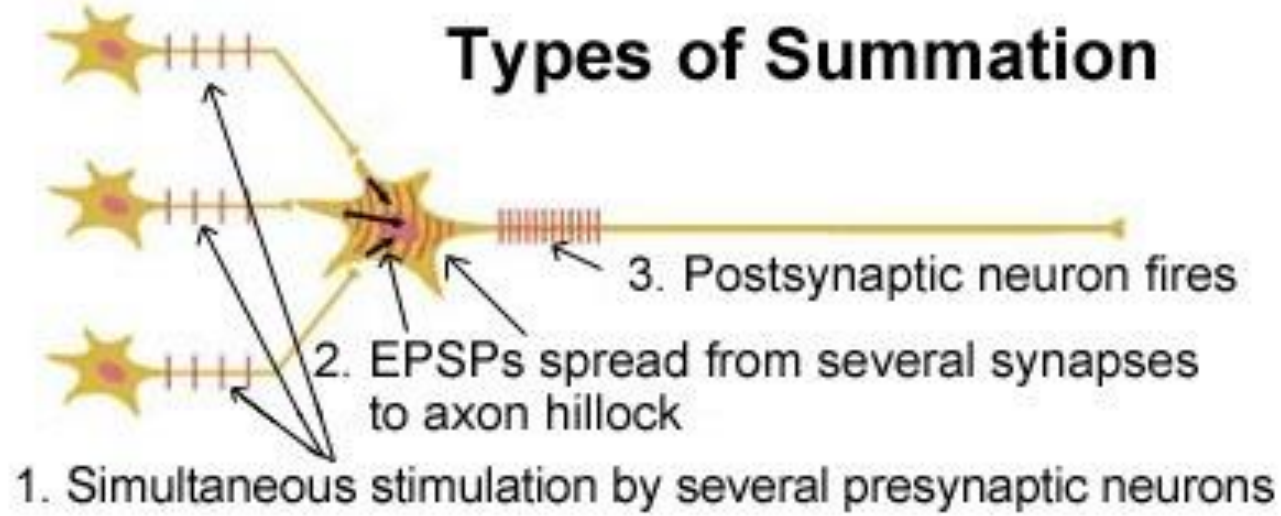
دمج .

SPATIAL AND TEMPORAL SUMMATION OF POSTSYNAPTIC POTENTIALS

- The greater the summation of EPSPs, the greater the chance that threshold will be reached. At threshold, one or more nerve impulses **(action potentials)** arise.

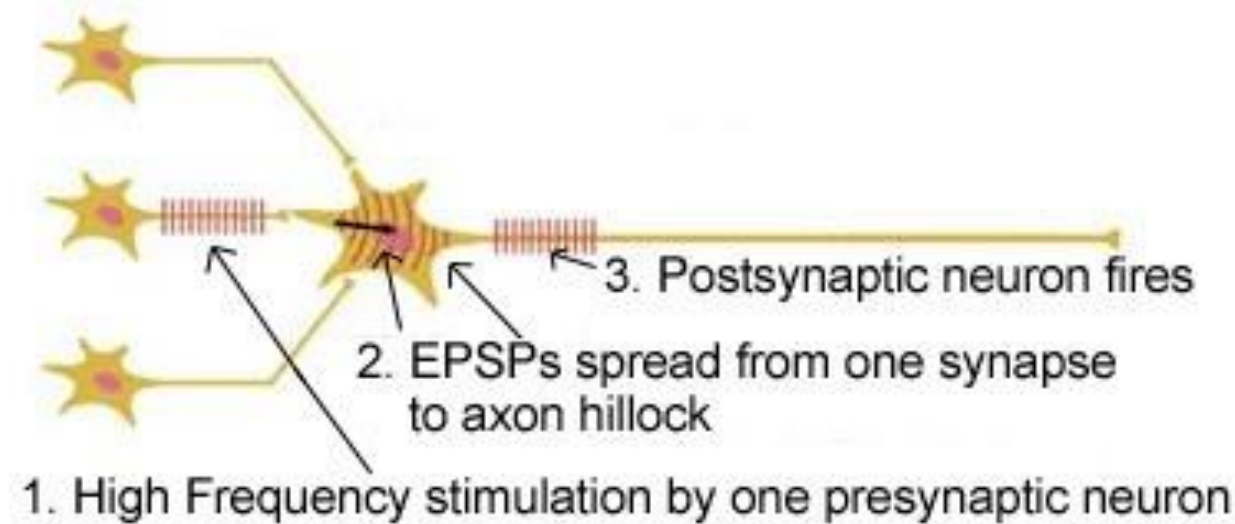
*different
sensory neurons
يتوصل لنفسى اعلاان*

Types of Summation



تحفيز متزامن من اكثر من خلية

Spatial summation



Temporal summation

SPATIAL AND TEMPORAL SUMMATION OF POSTSYNAPTIC POTENTIALS

- There are two types of summation: **spatial summation and temporal summation.**
- **Spatial summation** is summation of postsynaptic potentials in response to stimuli that occur at **different locations in the membrane of a postsynaptic cell at the same time.**

SPATIAL AND TEMPORAL SUMMATION OF POSTSYNAPTIC POTENTIALS

- **Temporal summation** is summation of postsynaptic potentials in response to stimuli that occur at the **same location in the membrane of the postsynaptic cell but at different times.**

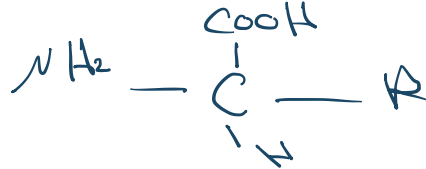
SMALL-MOLECULE NEUROTRANSMITTERS

■ Acetylcholine (ACh)

- Released by many PNS neurons & some CNS neurons.
- Excitatory neurotransmitter on neuromuscular junction (NMJ) but inhibitory neurotransmitter at others.
- Inactivated by acetylcholinesterase.

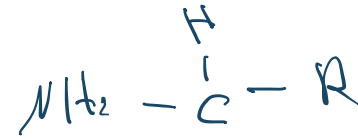
الوصل العصبي العضلي
(Neuromuscular Junction) هو
الموقع الذي يحدث فيه الاتصال بين الخلايا
العصبية الحركية والألياف العضلية

■ Amino Acids



- Glutamate released by nearly all excitatory neurons in the brain - inactivated by glutamate specific transporters
- Gamma-aminobutyric acid (GABA) is inhibitory neurotransmitter (blocking brain signals) for 1/3 of all brain synapses (Antianxiety ^{القلق} drugs such as diazepam ^{مضاد} (Valium) is a GABA agonist -- enhancing GABA's inhibitory effect).

SMALL-MOLECULE NEUROTRANSMITTERS



amino acids تم تعديلها عن طريق
إزالة مجموعة كربوكسيل (COOH-)

■ Biogenic Amines

- Certain amino acids are modified and decarboxylated (carboxyl group removed) to produce biogenic amines .
- They are prevalent in the nervous system include norepinephrine, epinephrine, dopamine, histamine and serotonin.
منتشر
- Biogenic amines may cause either excitation or inhibition, depending on the type of metabotropic receptor at the synapse.

NEURAL CIRCUITS

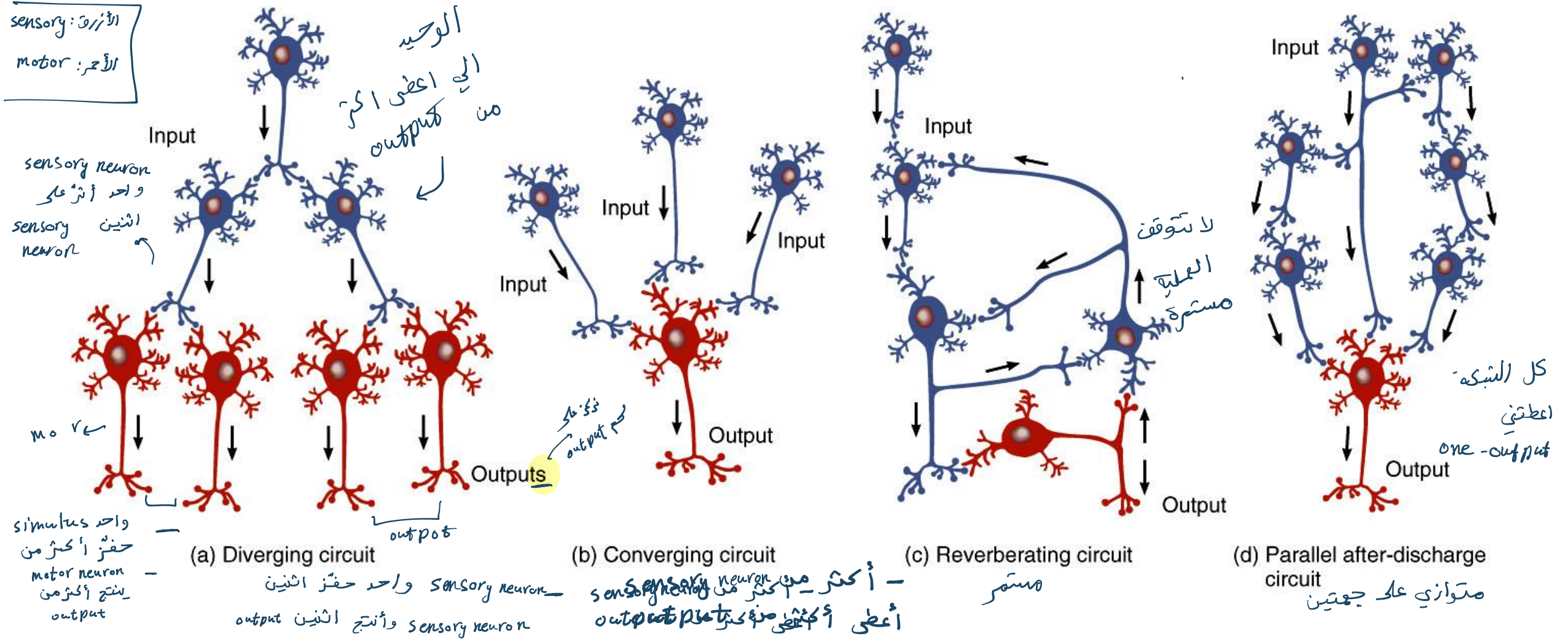
دوائر عصبية

- The CNS contains **billions of neurons organized into complicated networks called neural circuits, functional groups of neurons that process specific types of information.**
مجموعات وظيفية من الخلايا العصبية تتعاون معاً لمعالجة معلومات معينة
- In a **simple series circuit**, a **presynaptic neuron stimulates a single postsynaptic neuron**. The second neuron then stimulates another, and so on.
- The **divergence**, ^{يسوع} permits one presynaptic neuron to **influence several postsynaptic neurons** (or several muscle fibers or gland cells) at the same time.

NEURAL CIRCUITS

- **Convergence**, several **presynaptic neurons synapse with a single postsynaptic neuron**.
- Stimulation of the presynaptic cell causes the postsynaptic cell to transmit a series of nerve impulses. One such circuit is called a **reverberating circuit**. **This arrangement sends impulses back through the circuit again and again.**
- Fourth type of circuit is the **parallel after-discharge circuit**. In this circuit, a **single presynaptic cell stimulates a group of neurons, each of which synapses with a common postsynaptic cell**. A differing number of synapses between the first and last neurons imposes varying synaptic.

NEURAL CIRCUITS





THANK YOU

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