

Potencial de membrana o reposo

- Concepto de potencial
- Bases iónicas del potencial de reposo
- Permeabilidad de la membrana
- Modelo de circuito equivalente
- El potencial de membrana en reposo viene determinado por los canales iónicos de reposo.
-

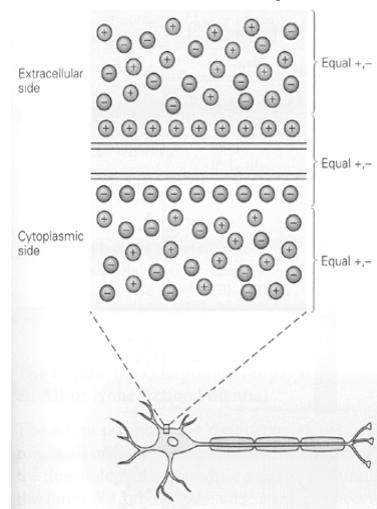
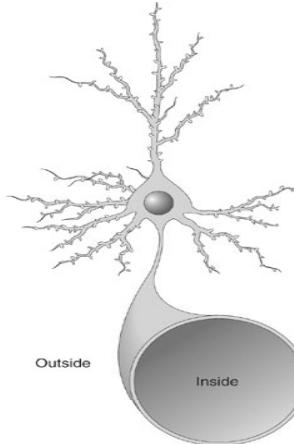


Figure 2-9 The membrane potential of a cell results from a difference in the net electrical charge on either side of its membrane. When a neuron is at rest there is an excess of positive charge outside the cell and an excess of negative charge inside it.

Ecuación de Goldman

$$V = \frac{62 \log P_K[K_2] + P_{Na}[Na]_2 + P_{Cl}[Cl]_1}{P_K[K_1] + P_{Na}[Na]_1 + P_{Cl}[Cl]_2}$$

V = voltaje a través de la membrana
 P = permeabilidad de la membrana al K, Na y Cl
 Entre paréntesis, las concentraciones iónicas



Outside	Inside	Ratio Outside:Inside	E_{ion} (a 37°C)
[K ⁺] _o = 5 mM	[K ⁺] _i = 100 mM	1:20	-80 mV
[Na ⁺] _o = 150 mM	[Na ⁺] _i = 15 mM	10:1	62 mV
[Ca ²⁺] _o = 2 mM	[Ca ²⁺] _i = 0.0002 mM	10,000:1	123 mV
[Cl ⁻] _o = 150 mM	[Cl ⁻] _i = 13 mM	11.5:1	-65 mV

Aproximate ion concentration on either side of a neuronal membrane

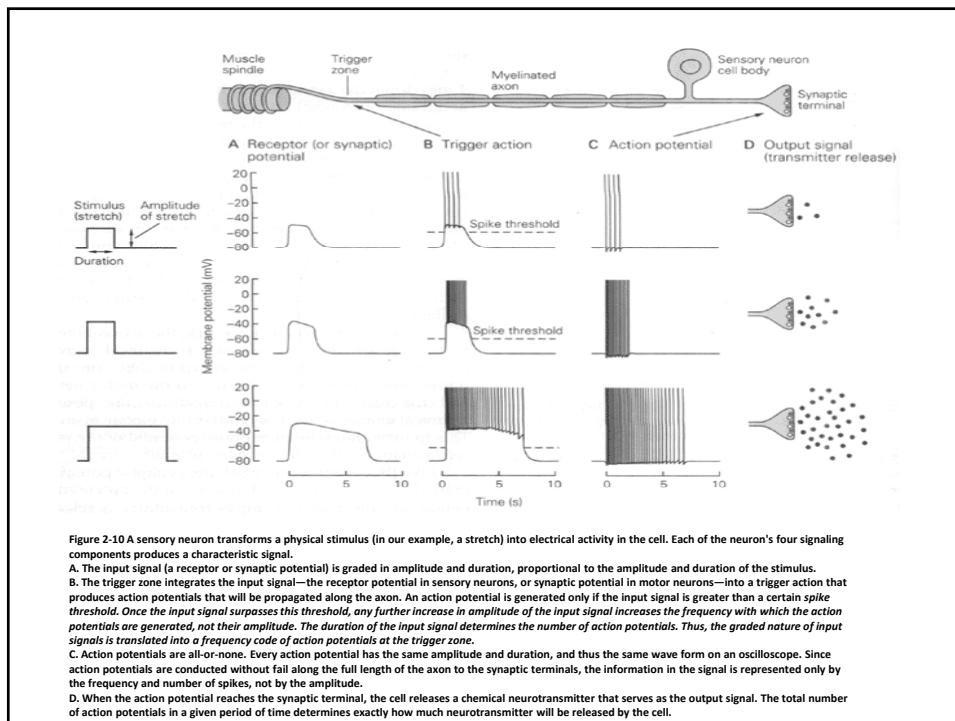
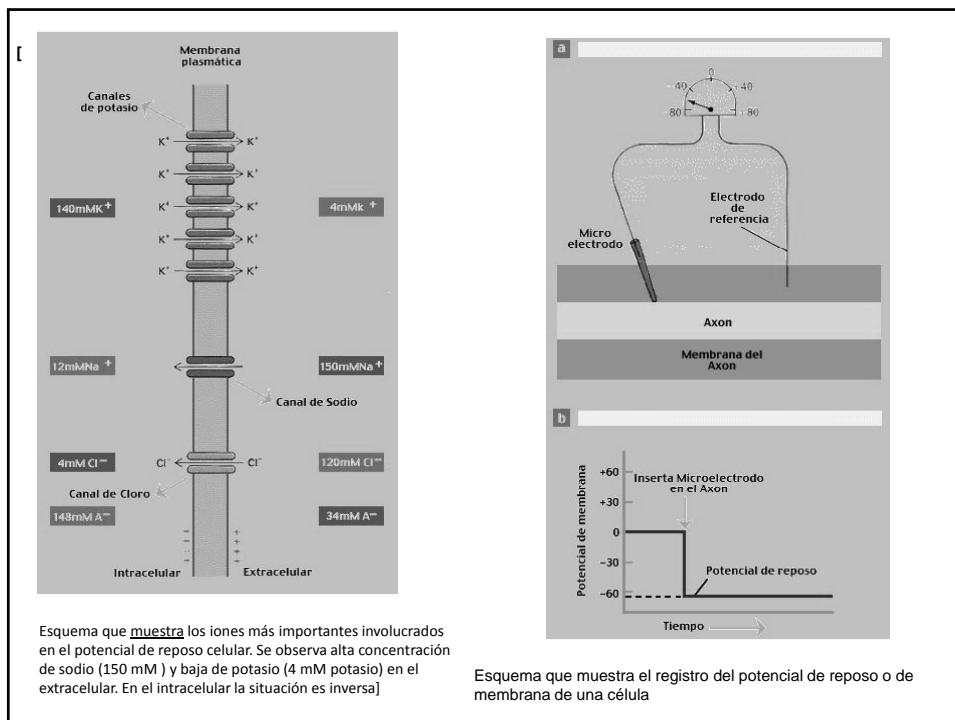
Ecuación de Nernst

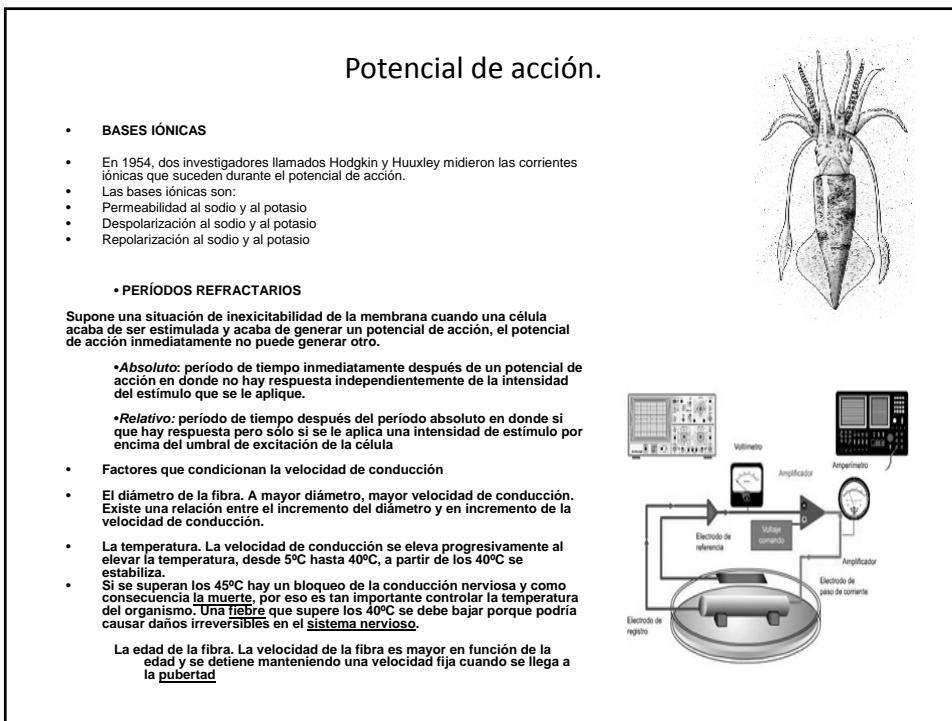
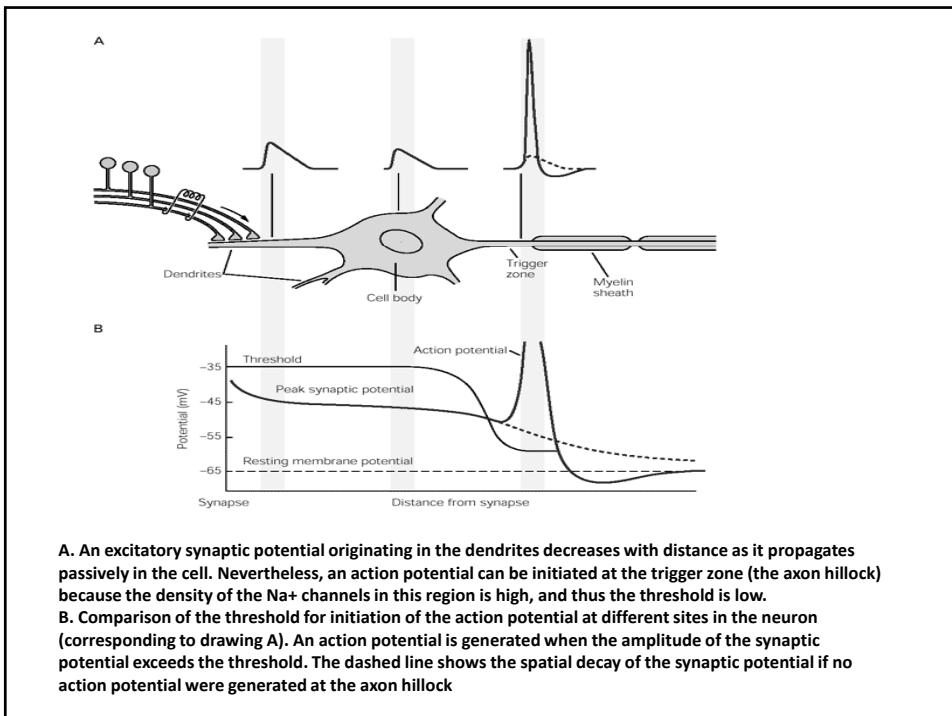
Ecuación de Nernst

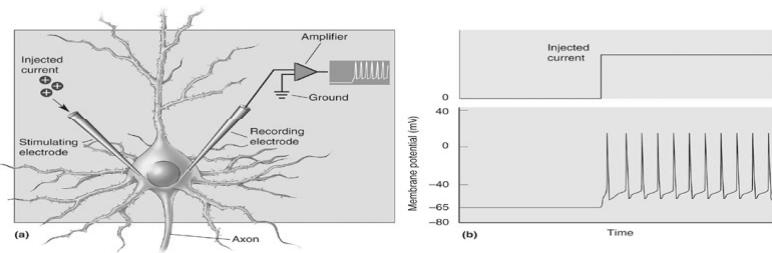
$$E_x = \frac{RT \ln [X]_2}{zF} \frac{}{[X]_1}$$

E = diferencia de potencial en el equilibrio
 R = constante de los gases
 T = temperatura absoluta
 z = carga eléctrica delión considerado
 F = constante de Faraday
 X₁ y X₂ = concentraciones iónicas

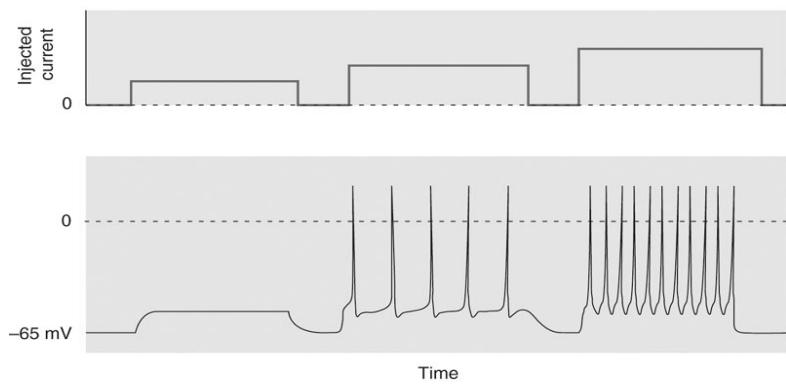
Ion	Potencial de equilibrio
K ⁺	-95 mV
Cl ⁻	-90 mV
Na ⁺	+65 mV
Potencial de reposo celular	-90 mV







The effect of injecting a positive charge into a neuron

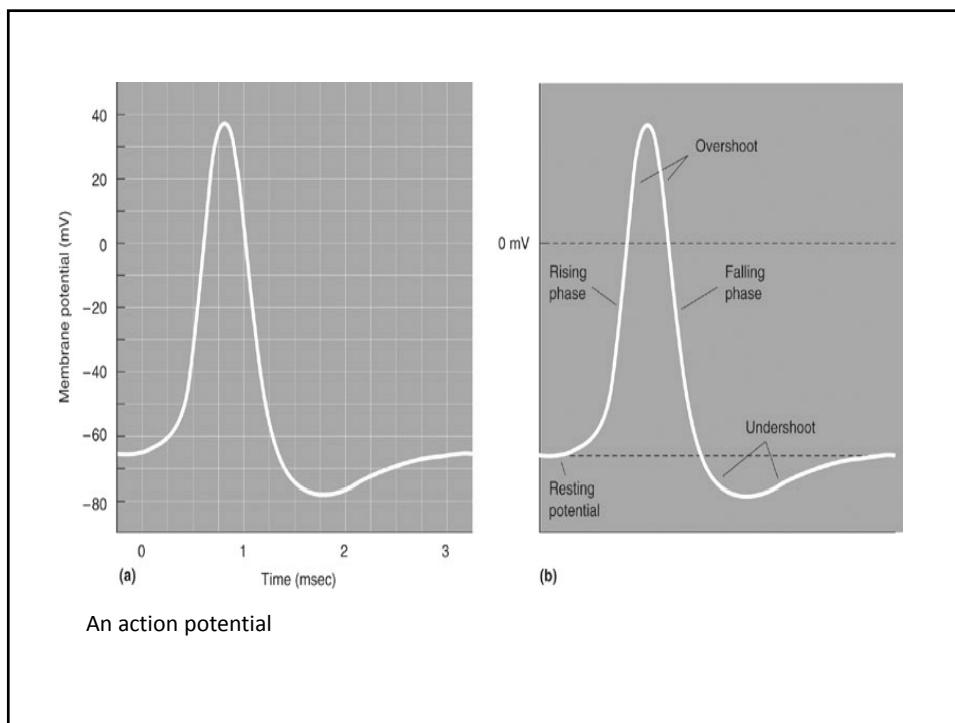
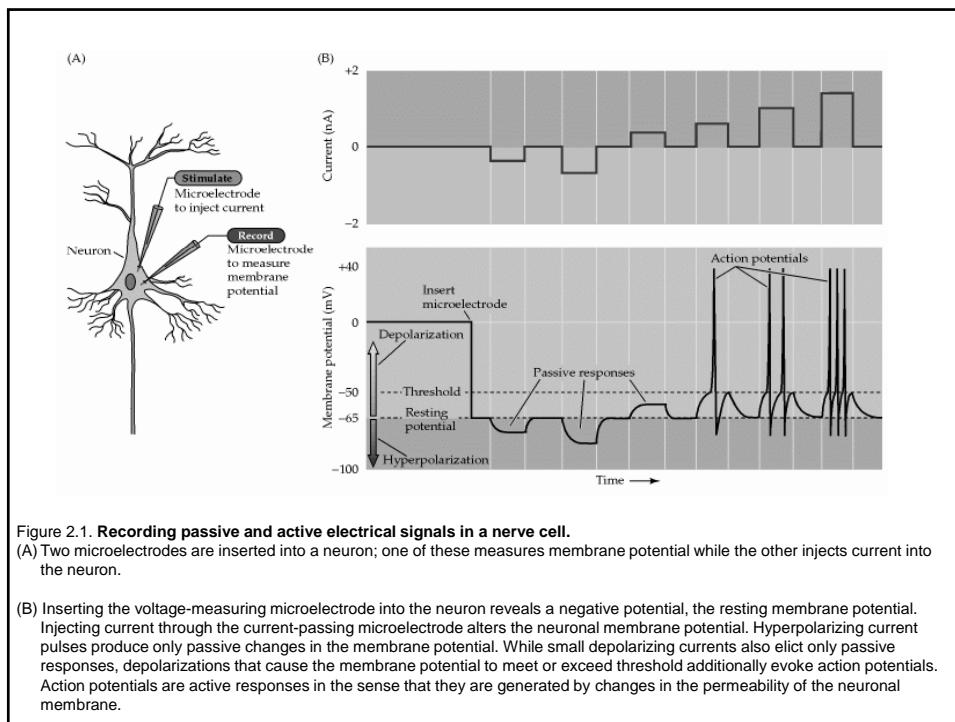


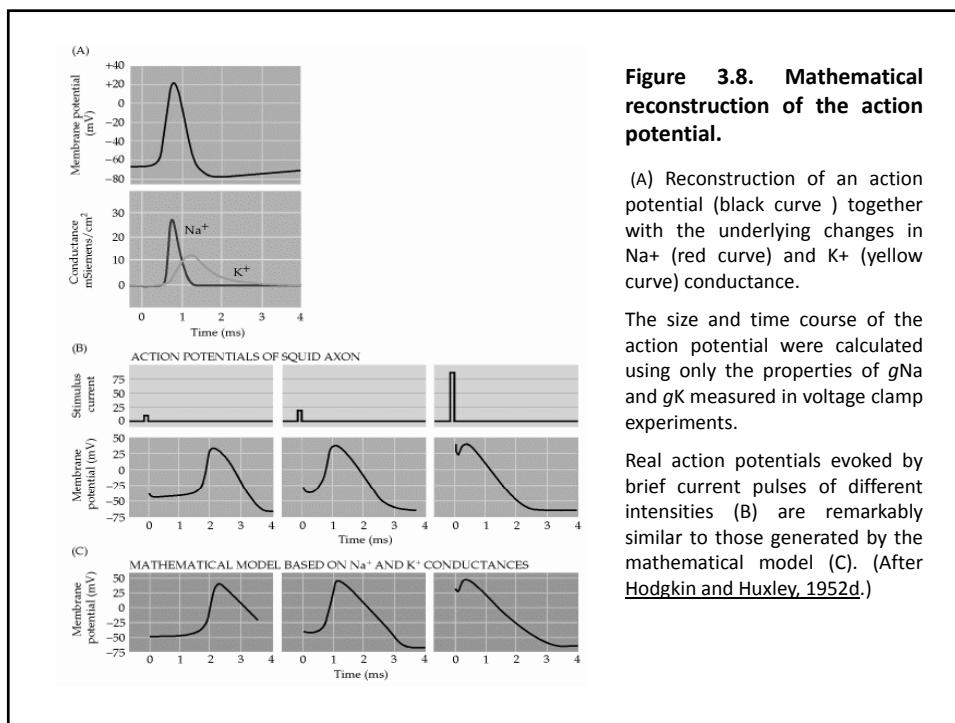
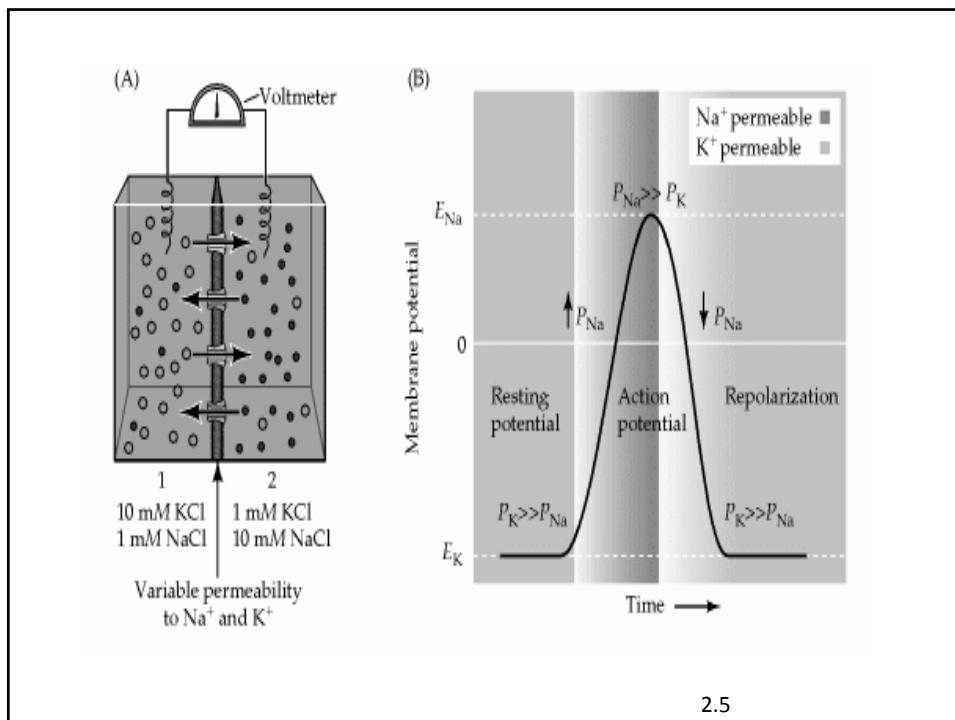
If injected current does not depolarize the membrane to threshold, no action potentials will be generated.

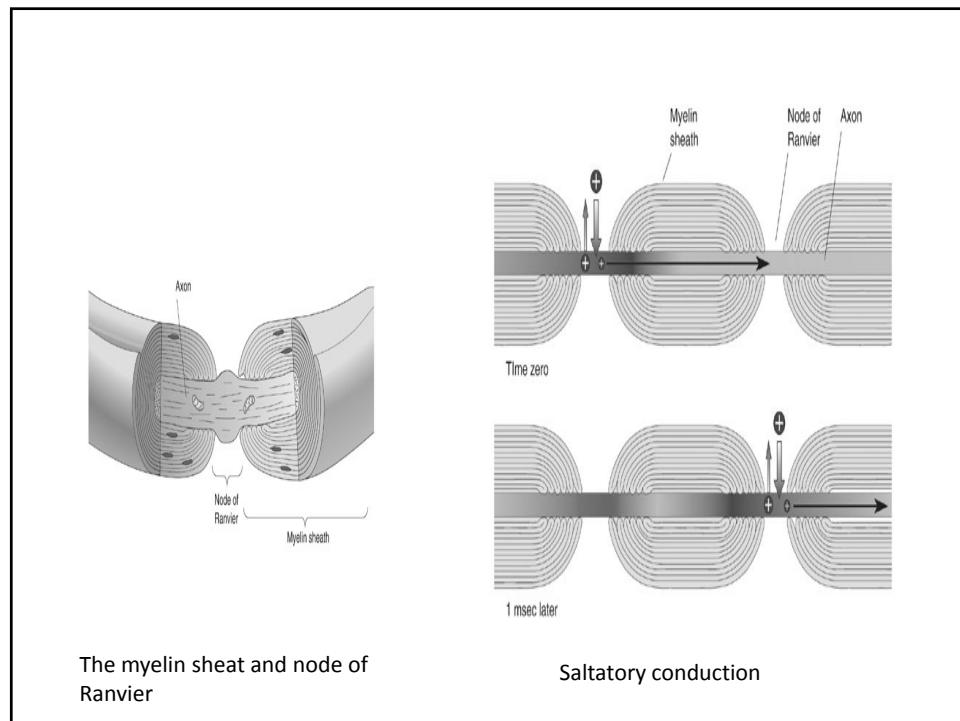
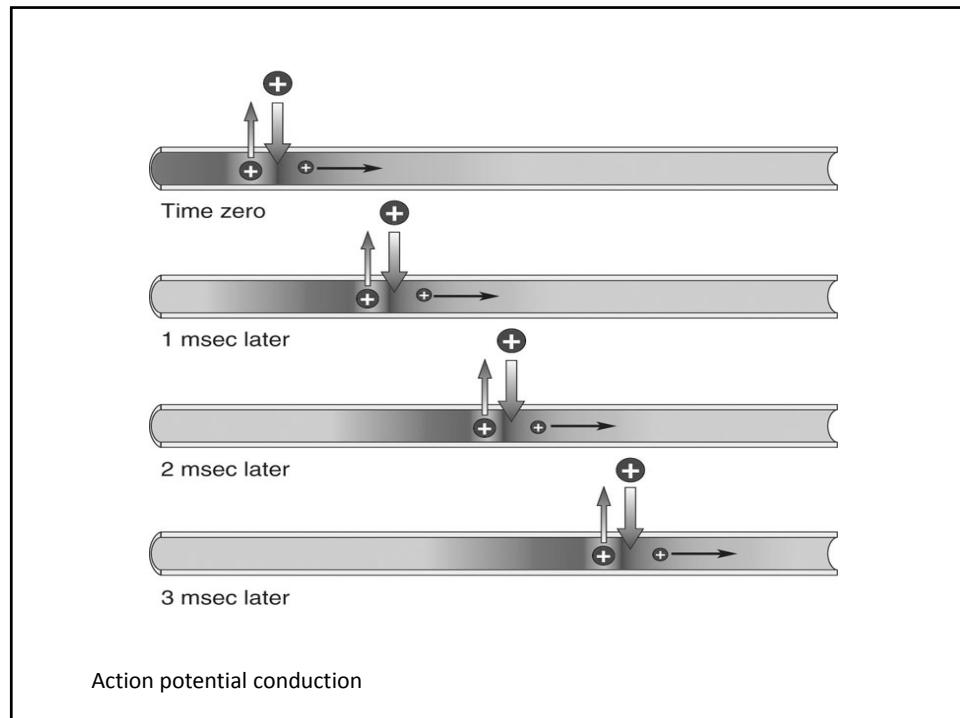
If injected current depolarizes the membrane beyond threshold, action potentials will be generated.

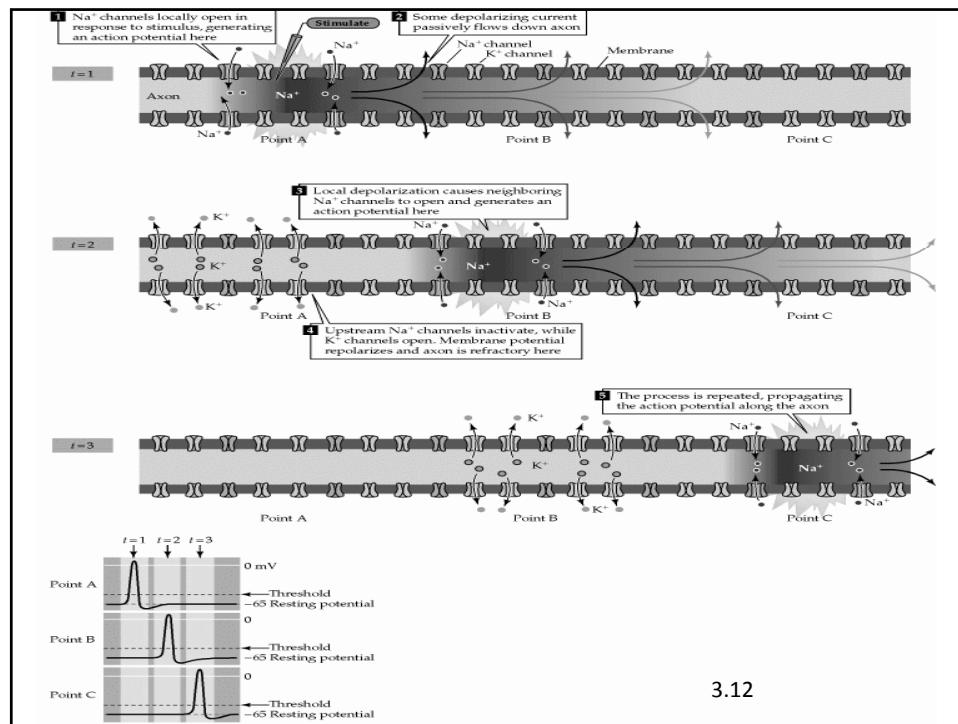
The action potential firing rate increases as the depolarizing current increases.

The dependence of action potential firing frequency on the level of depolarization

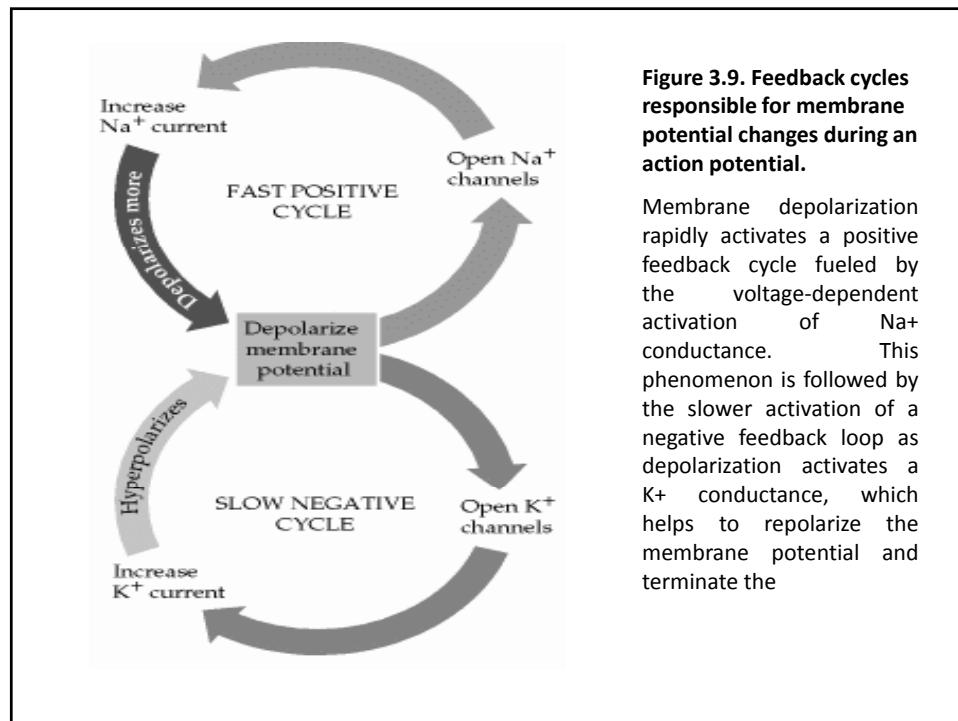


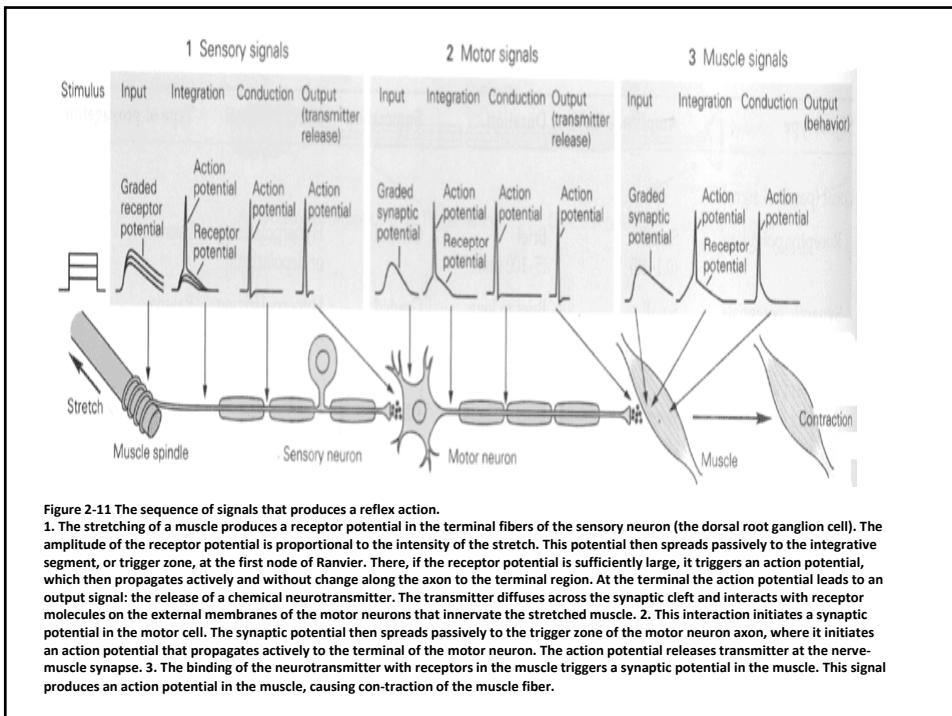






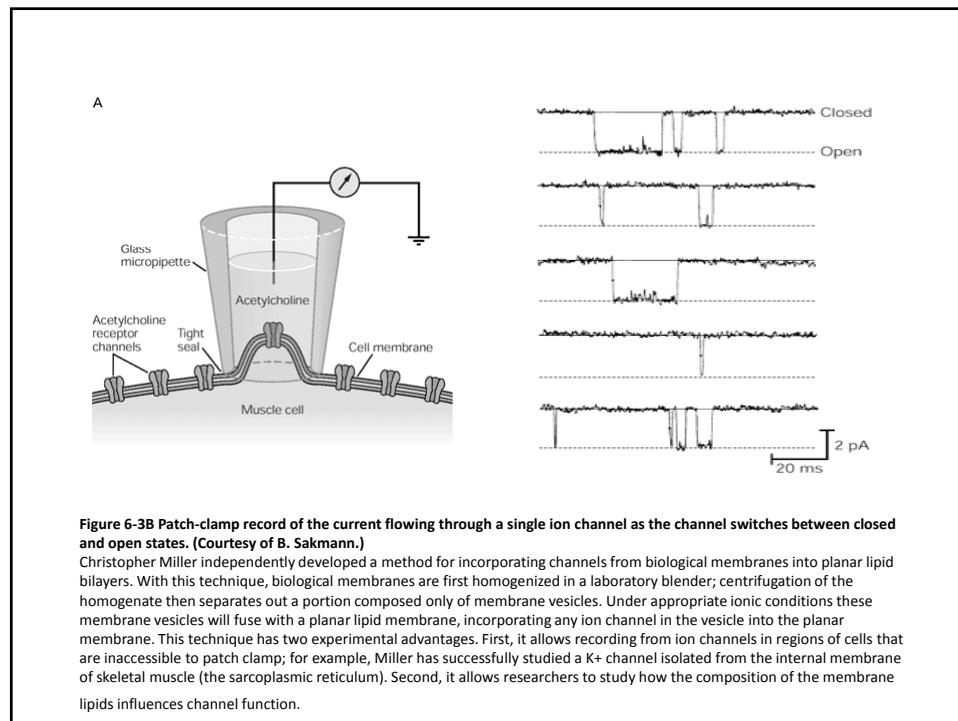
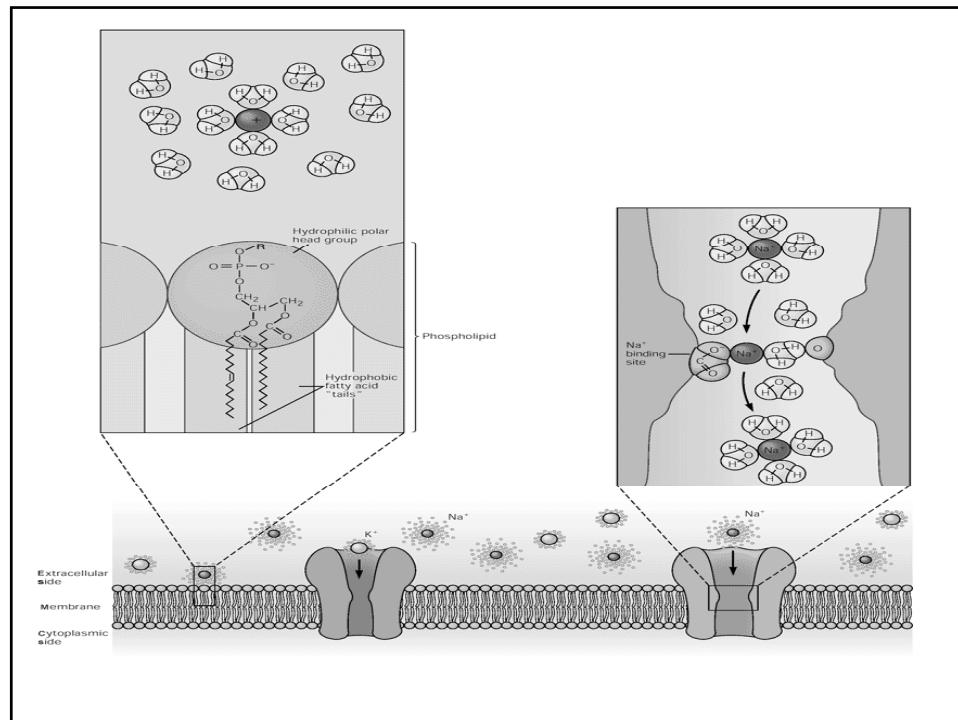
3.12





Canales iónicos

- **Figure 6-1 (Opposite)** The ionic permeability properties of the membrane are determined by the interactions of ions with water, the membrane lipid bilayer, and ion channels
- Ion channels are integral membrane proteins that span the lipid bilayer, providing a pathway for ions to cross the membrane. Phospholipids form self-sealing lipid bilayers that are the basis for all cellular membranes. Phospholipids have a hydrophilic head and a hydrophobic tail. The hydrophobic tails join to exclude water and ions, while the polar hydrophilic heads face the aqueous environment of the extracellular fluid and cytoplasm.
- Left enlargement: Ions in solution are surrounded by a cloud of water molecules (waters of hydration) that are attracted by the net charge of the ion. This cloud is carried along by the ion as it diffuses through solution, increasing the effective size of the ion. It is energetically unfavorable, and therefore improbable, for the ion to leave this polar environment to enter the nonpolar environment of the lipid bilayer. In the illustration, a positively charged ion (red) attracts the electronegative oxygen atoms of the surrounding water molecules. The inset also shows the structure of a phospholipid. It is composed of a backbone of glycerol in which two of its -OH groups are linked by ester bonds to fatty acid molecules. The third -OH group of glycerol is linked to phosphoric acid. The phosphate group is further linked to one of a variety of small, polar, alcohol head groups (R).
- Bottom: A model showing how ion channels are able to select for either K⁺ or Na⁺ ions.
- Potassium channel (left): Although a Na⁺ ion itself is smaller than a K⁺ ion, its effective diameter in solution is larger because its local field strength is more intense, causing it to attract a larger cloud of water molecules. Thus, a channel can select for K⁺ over Na⁺ by excluding hydrated ions whose diameter is larger than the pore.
- Sodium channel (right): Sodium channels have a selectivity filter somewhere along the length of the channel, with a site that weakly binds Na⁺ ions. According to the hypothesis developed by Bertil Hille and colleagues, a Na⁺ ion binds transiently at an active site as it moves through the filter (right enlargement). At the binding site the positive charge of the ion is stabilized by a negatively charged amino acid residue on the channel wall and also by a water molecule that is attracted to a second polar amino acid residue on the other side of the channel wall. It is thought that a K⁺ ion, because of its larger diameter, cannot be stabilized as effectively by the negative charge and therefore will be excluded from the filter. (Modified from Hille 1984.)



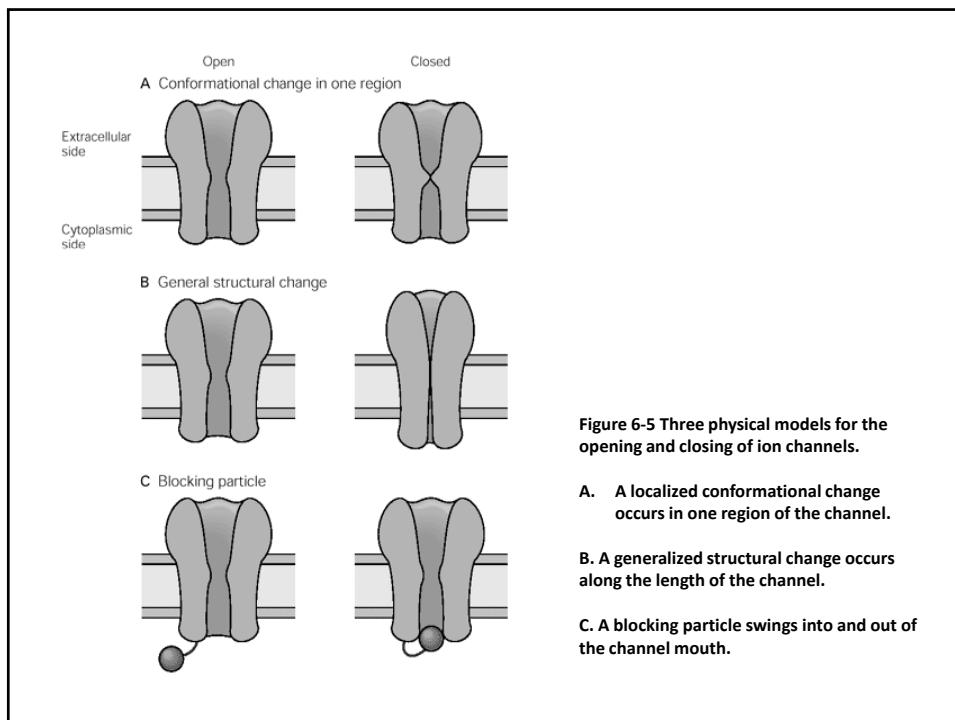


Figure 6-5 Three physical models for the opening and closing of ion channels.

- A. A localized conformational change occurs in one region of the channel.
- B. A generalized structural change occurs along the length of the channel.
- C. A blocking particle swings into and out of the channel mouth.

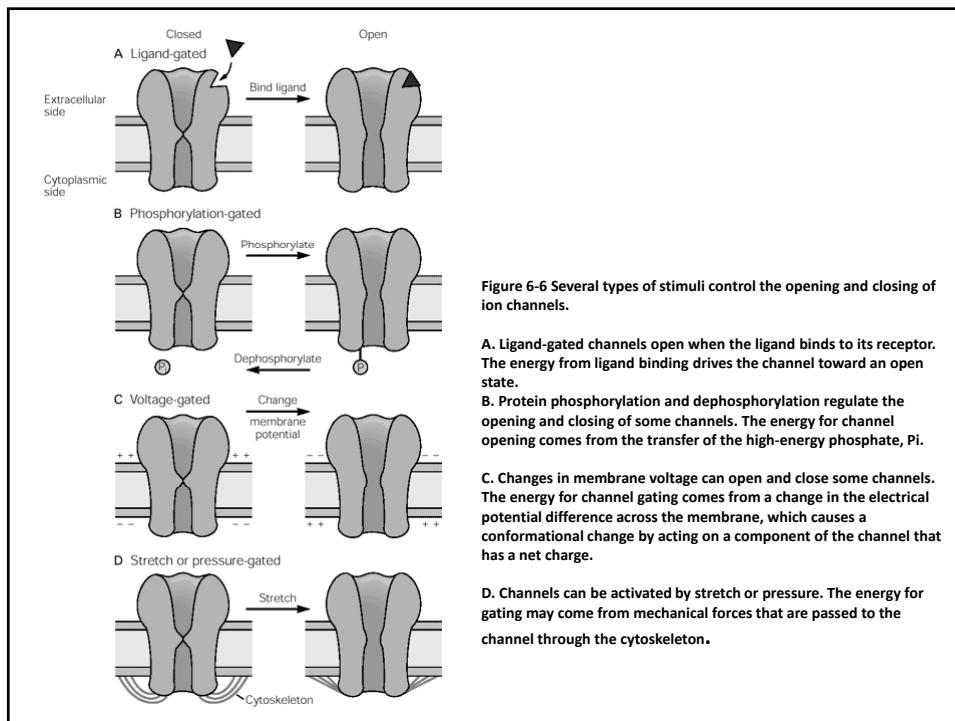
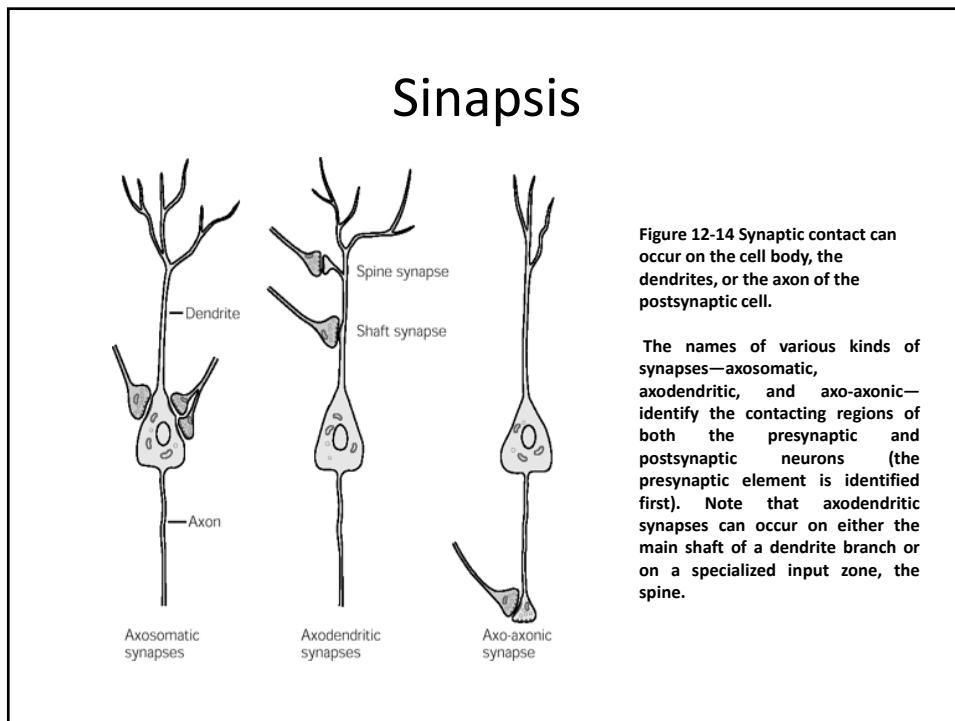
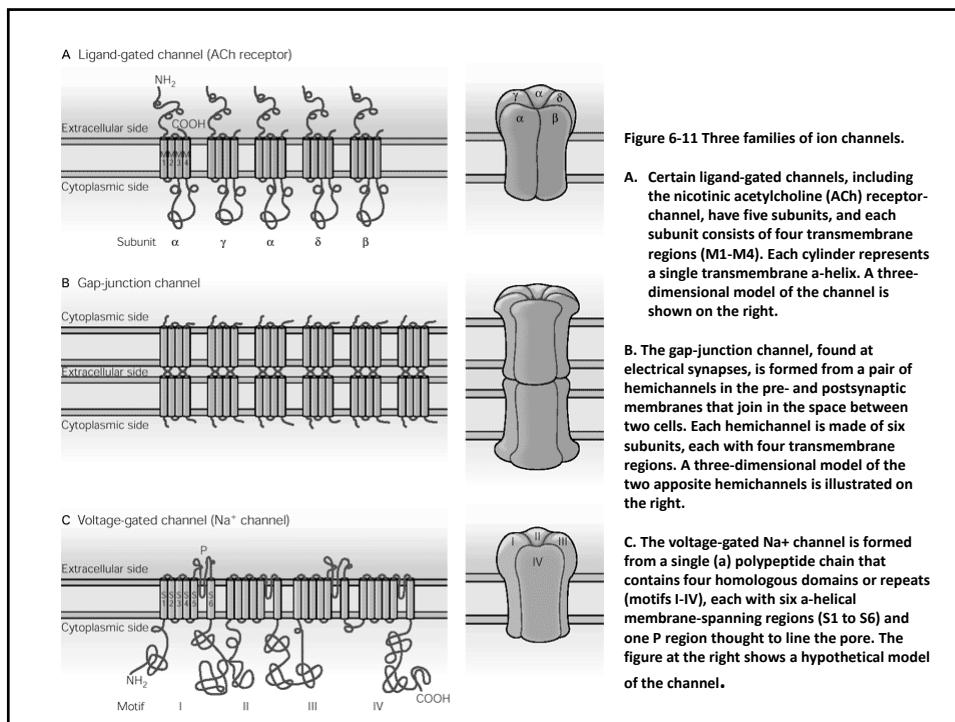
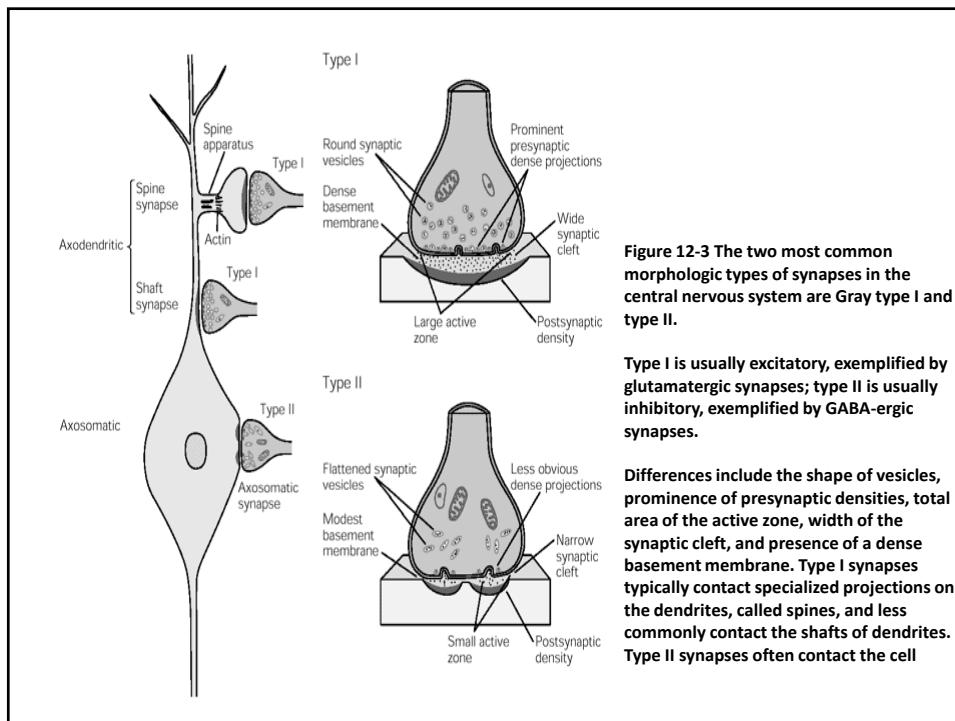
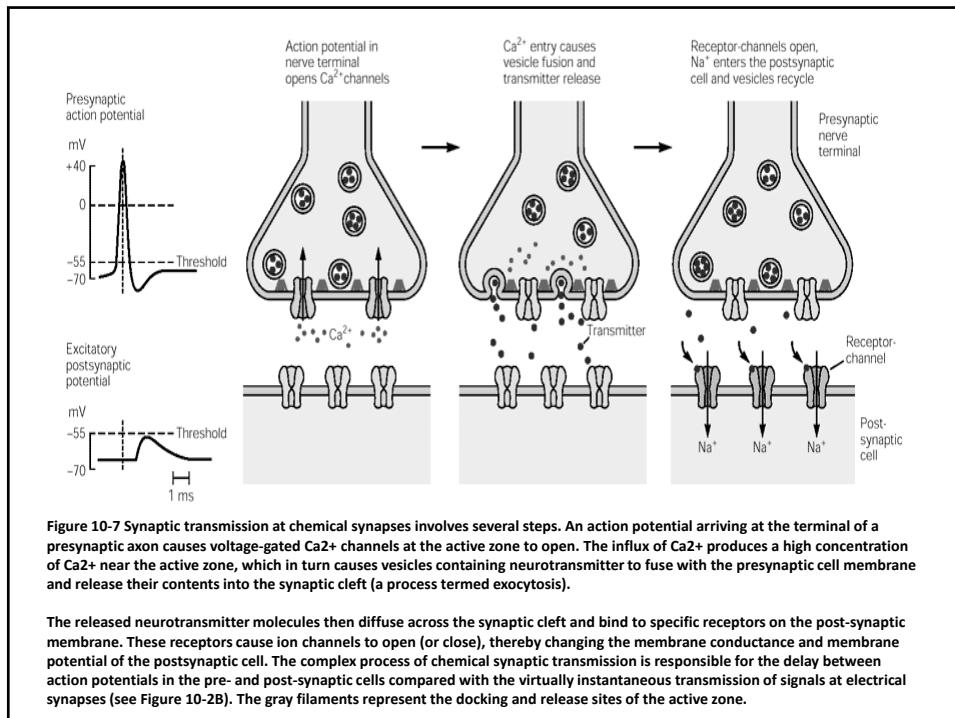


Figure 6-6 Several types of stimuli control the opening and closing of ion channels.

- A. Ligand-gated channels open when the ligand binds to its receptor. The energy from ligand binding drives the channel toward an open state.
- B. Protein phosphorylation and dephosphorylation regulate the opening and closing of some channels. The energy for channel opening comes from the transfer of the high-energy phosphate, Pi.
- C. Changes in membrane voltage can open and close some channels. The energy for channel gating comes from a change in the electrical potential difference across the membrane, which causes a conformational change by acting on a component of the channel that has a net charge.
- D. Channels can be activated by stretch or pressure. The energy for gating may come from mechanical forces that are passed to the channel through the cytoskeleton.





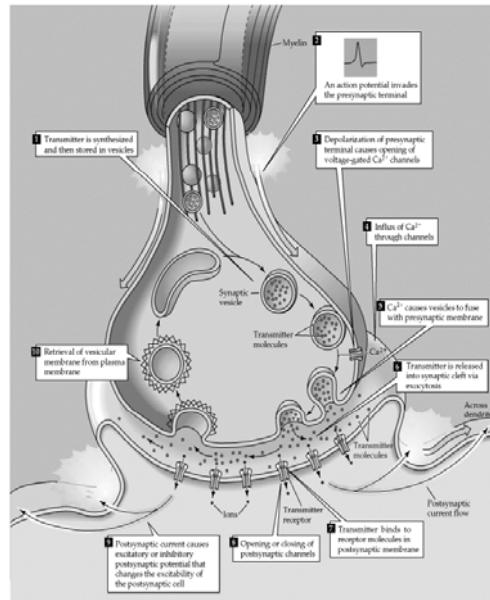


Figure 5.3. Sequence of events involved in transmission at a typical chemical synapse.

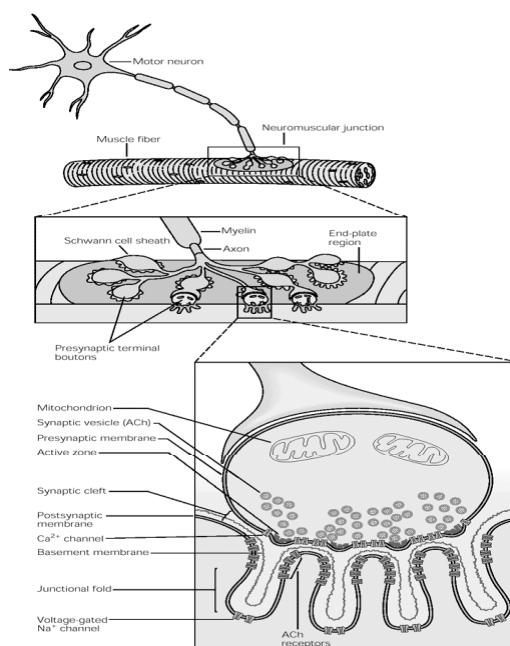
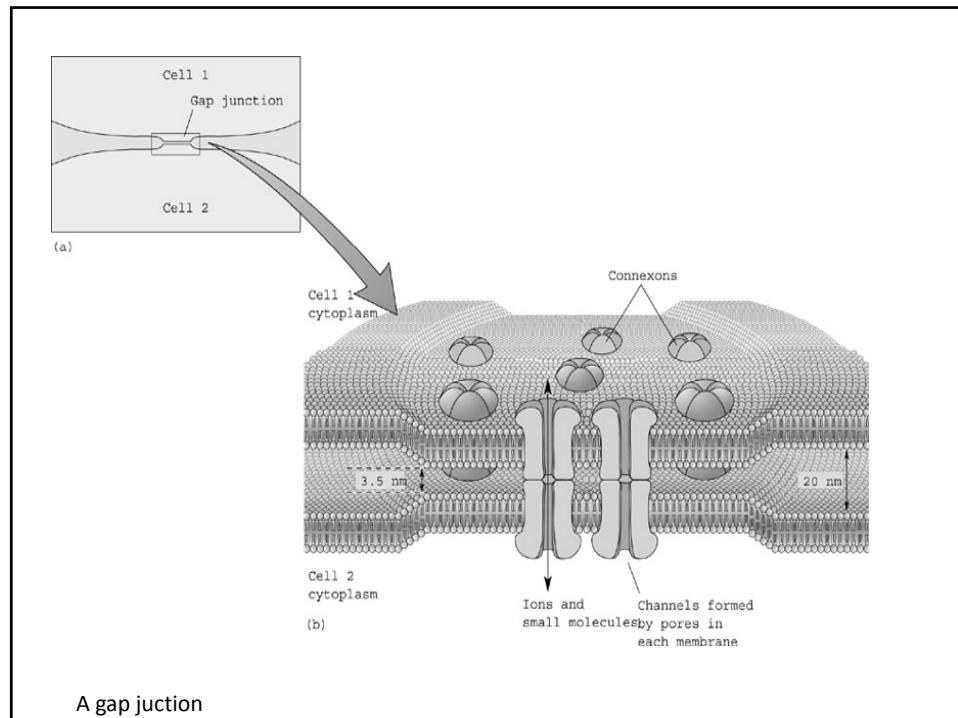
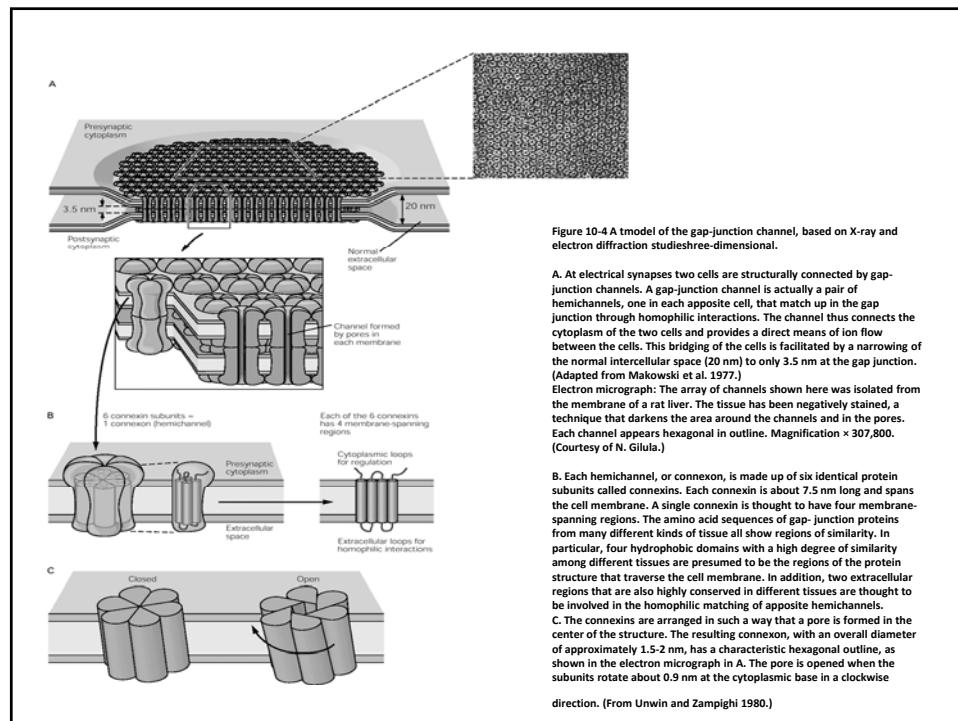


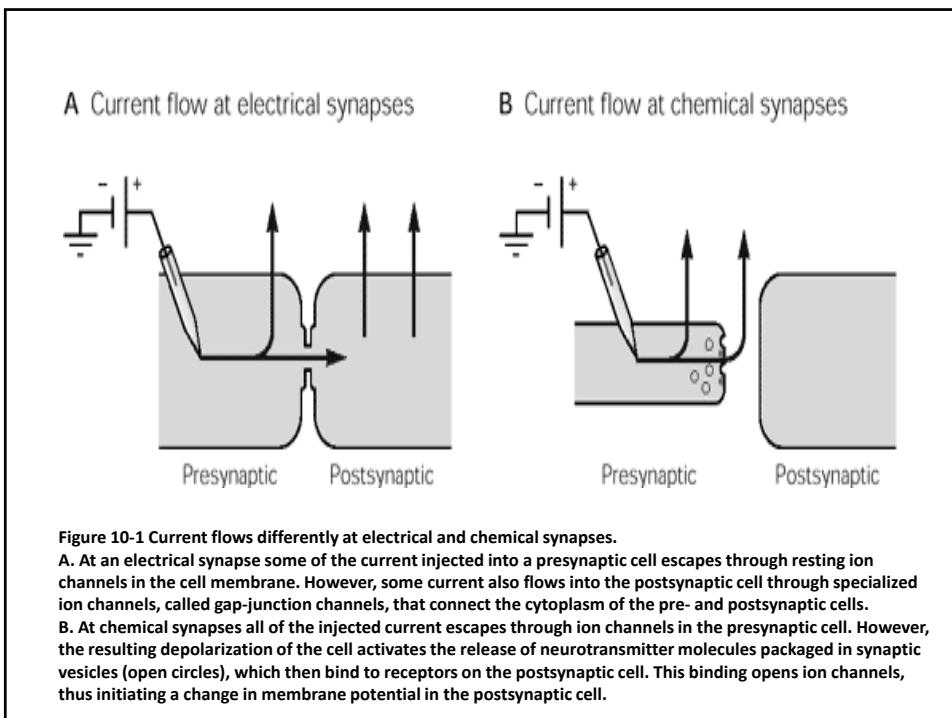
Figure 11-1 The neuromuscular junction is readily visible with the light microscope. At the muscle the motor axon ramifies into several fine branches approximately 2 μm thick. Each branch forms multiple swellings called presynaptic boutons, which are covered by a thin layer of Schwann cells.

The boutons lie over a specialized region of the muscle fiber membrane, the *end-plate*, and are separated from the muscle membrane by a 100 nm synaptic cleft. Each presynaptic bouton contains mitochondria and synaptic vesicles clustered around active zones, where the acetylcholine (ACh) transmitter is released. Immediately under each bouton in the end-plate are several junctional folds, which contain a high density of ACh receptors at their crests. The muscle fiber is covered by a layer of connective tissue, the basement membrane (or basal lamina), consisting of collagen and glycoproteins. Both the presynaptic terminal and the muscle fiber secrete proteins into the basement membrane, including the enzyme acetylcholinesterase, which inactivates the ACh released from the presynaptic terminal by breaking it down into acetate and choline. The basement membrane also organizes the synapse by aligning the presynaptic junctional folds. (Adapted in part from McMahan and Kuffler 1971.)



A gap junction





Neurotransmisores

Neurotransmisores en el SNC	
Moléculas pequeñas	Péptidos
Aminoácidos γ-aminobutirato (GABA) Glicina Glutamato Aspartato Taurina Aminas biógenas Acetilcolina Dopamina Noradrenalina Adrenalina Serotonina Histamina Nucleótidos Adenosina ATP Otros Óxido nítrico Monóxido de carbono	Péptidos opioides β-endorfina Dnororfina Metionina Péptidos neurohipofisarios Vasopresina Oxitocina Taquicininas Sustancia P Casinina Neurocininina Otros Secretina Péptido Intestinal Vasoactivo Glucagón Neuropéptido Y Somatostatina Colescistoquinina Angiotensina

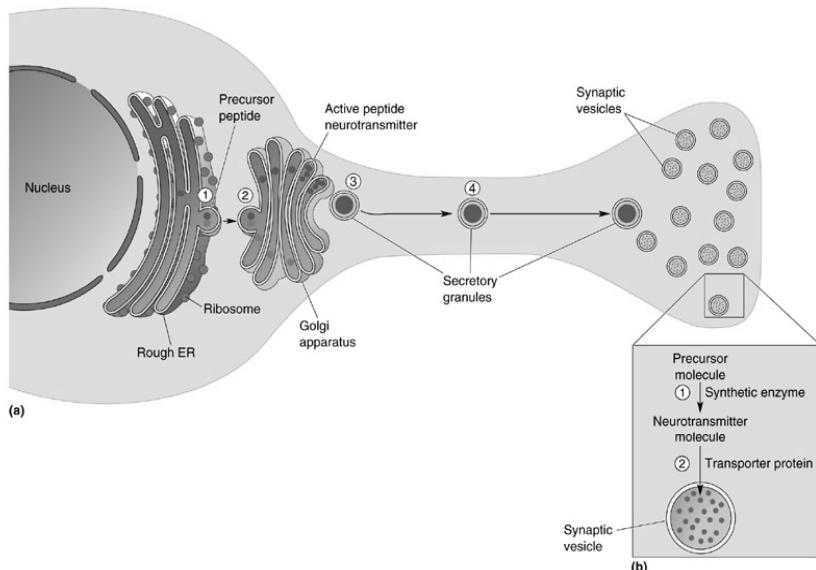
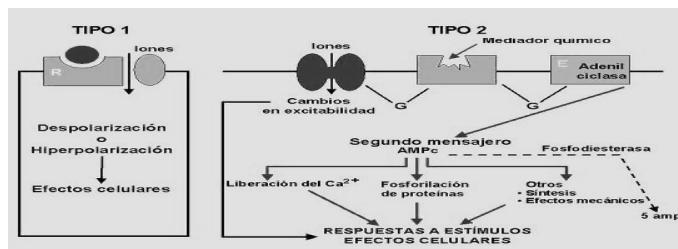
Receptores

- Receptores ionotrópicos:**

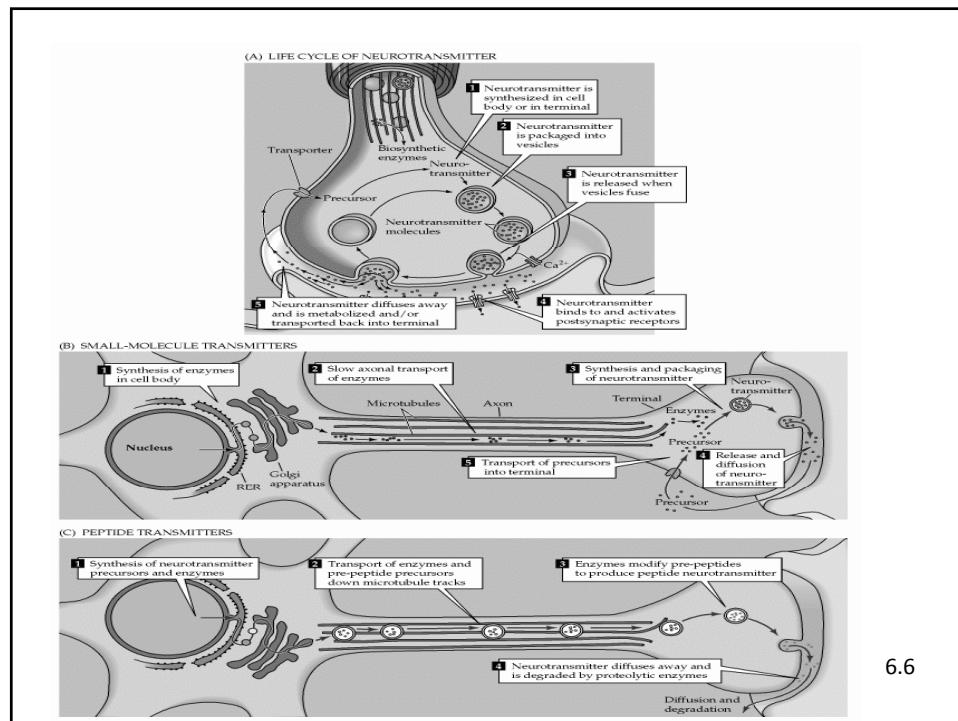
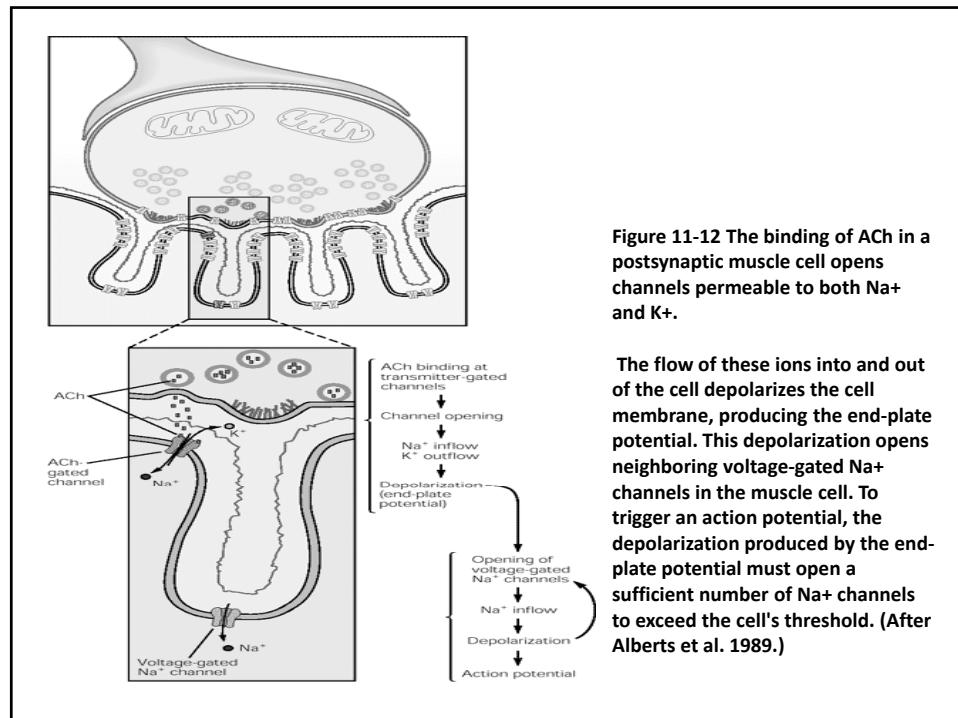
Producen una respuesta rápida al abrir o cerrar canales iónicos, que producen despolarizaciones o generando potenciales de acción o respuestas excitatorias o producen hiperpolarizaciones o respuestas inhibitorias. En el primer caso, actúan canales de cationes monoiónicos como los de Sodio y Potasio, mientras que en el segundo caso, son los canales de Cloruro los que se activan.

- Receptores metabotrópicos:**

Liberan mensajeros intracelulares, como AMP cíclico, Calcio, y fosfolípidos por el mecanismo de transducción de señales. Estos segundos mensajeros activan proteínas quinasas, las cuales, fosforilan activando o desactivando canales al interior de la célula. En el caso de una despolarización, son los canales de Potasio que se cierran, en caso de hiperpolarización, los mismos canales son abiertos produciendo el aumento de cationes intracelulares.



The synthesis and storage of different types neurotransmitter



Drogas y neurotransmisores

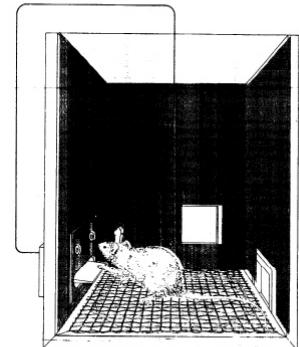


FIGURA 18-4
Aparato para experimentos de autoestimulación. (*Adaptado de Olds.*)

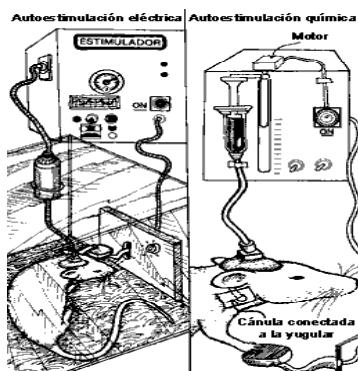
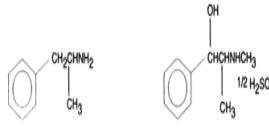


FIGURA VI. *Experimento de autoestimulación. Dispositivo utilizado para la estimulación eléctrica o química del cerebro. Esta puede ser controlada por el investigador, o como se ve aquí, por el mismo animal. La rata busca la "autoestimulación" cuando esta le produce efectos placenteros o le evita el dolor. Apretando el pedal, el animal activa el estimulador eléctrico o el motor que controla la jeringa que contiene la droga.*

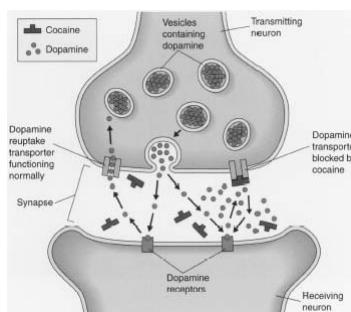
Tipos de drogas

1. DROGAS DOPAMINÉRGICAS-NORADRENÉRGICAS: cocaína

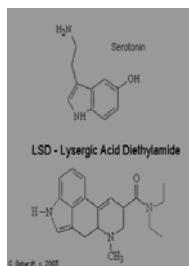


Anfetamina

Efedrina



2. DROGAS SEROTONINÉRGICAS, ALUCINÓGENAS INDOLES: LSD

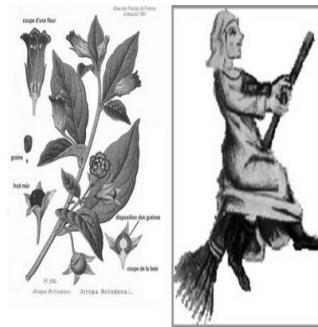


- ENACTÓGENAS/ALUCINÓGENAS NO INDOLES : éxtasis
- Alucinógenos clásicos , DROGAS ANTICOLINÉRGICAS : Belladona



Figura 9. Diversos tipos de pastillas de "éxtasis", decomisadas por la policía.

La MDMA incrementa la liberación de serotonina, dopamina y norepinefrina, inhibe la recaptación de estos neurotransmisores a nivel presináptico e interfiere la acción degradadora de la monoamino-oxidasa, aumentando también la síntesis de dopamina. Todo esto comporta un acumulo de serotonina, dopamina y norepinefrina en los espacios sinápticos intra y extracraeales, dando lugar a los efectos clínicos que se describen posteriormente, y que son parecidos a los que induce la anfetamina y la cocaína



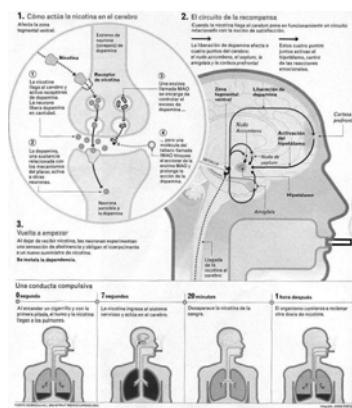
Dada la amplia distribución central y periférica de este receptor, los efectos de estos alcaloides ocurren a muy diversos niveles: sequedad de la boca, taquicardia, aumento de la temperatura corporal, disminución del peristaltismo gastrointestinal (p. ejem., constipación), dilatación pupilar, confusión mental, obnubilación de la conciencia, pérdida de la memoria reciente, y somnolencia, delirio y coma a dosis elevadas. A diferencia de otros alucinógenos, los anticolinérgicos no incrementan la percepción sensorial

USO.....

- DROGAS DISOCIATIVAS, (Anestésicas), ANTIGLUTAMATÉRGICAS, Arilciclohexilaminas, Análogos a la fenciclidina: PCP
- DROGAS COLINÉRGICAS, Alcaloides de núcleo pirídico: nicotina

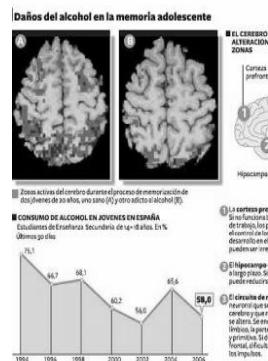


PCP (Phencyclidine) is a dissociative drug formerly used as an anesthetic agent, exhibiting hallucinogenic and neurotoxic effects. It is commonly known as Angel Dust, but is also known as Wet, Sherm, Sherman Hemsley, Rocket Fuel, Ashy Larry, Shermans Tank, Wack, Halk Hogan, Ozone, Hannah, Hog, Manitoba Shlimbo, and Embalming Fluid, among other names.

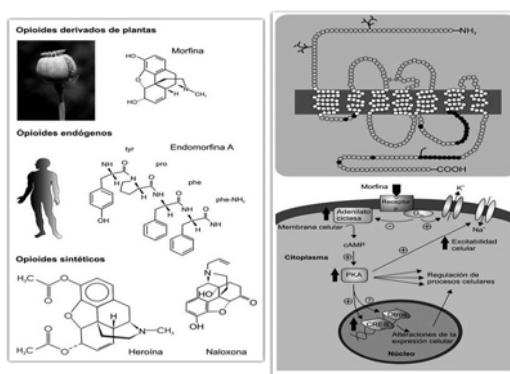


abuso.....

- DROGAS GABAÉRGICAS: alcohol**

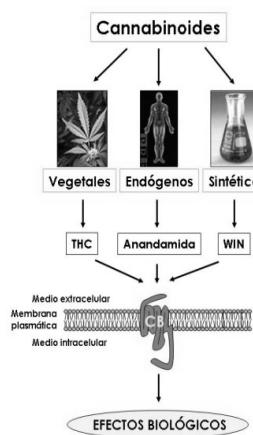


- DROGAS OPIÁCEAS (Analgésicas): morfina**



Y ...Usted que opina?

- DROGAS CANABINOIDES , Inhibición del GABA y el Glutamato: marihuana**



- DROGAS XANTINAS (Estimulantes suaves) : cafeína**

La cafeína existe en un gran número de plantas, como las nueces de kola, hojas de té, semillas de cacao, y, por supuesto, granos de café. La cafeína estimula el cuerpo, afectando el sistema nervioso central. También bloquea la acción de una sustancia neuroquímica conocida como adenosina, cuya función en el organismo es ordenarle que disminuya su ritmo de actividad.



- SOLVENTES E INHALANTES**

Neurotransmisor	Localización	Función
Transmisores pequeños		
Acetilcolina	Sinapsis con músculos y glándulas; muchas partes del sistema nervioso central (SNC)	Excitatorio o inhibitorio Envuelto en la memoria
Aminas		
Serotonina	Varias regiones del SNC	Mayormente inhibitorio; sueño, envuelto en estados de ánimo y emociones
Histamina	Encéfalo	Mayormente excitatorio; envuelto en sueño, humor, temperatura y balance de agua
Dopamina	Encéfalo; sistema nervioso autónomo (SNA)	Mayormente inhibitorio; envuelto en emociones/ánimo, regulación del control motor
Epinefrina	Áreas del SNC y división simpática del SNA	Excitatorio o inhibitorio; hormona cuando es producido por la glándula adrenal
Norepinefrina	Áreas del SNC y división simpática del SNA	Excitatorio o inhibitorio; regula efectores simpáticos; en el encéfalo envuelve respuestas emocionales
Aminoácidos		
Glutamato	SNC	El neurotransmisor excitatorio más abundante (75%) del SNC
GABA	Encéfalo	El neurotransmisor inhibitorio más abundante del encéfalo
Glicina	Médula espinal	El neurotransmisor inhibitorio más común de la médula espinal
Otras moléculas pequeñas		
Óxido nítrico	Inciso	Pudiera ser una señal de la membrana postsináptica para la presináptica
Transmisores grandes		
Neuropéptidos		
Péptido vasoactivo intestinal	Encéfalo; algunas fibras del SNA y sensoriales, retina, tracto gastrointestinal	Función en el SN incierta
Colecistokinina	Encéfalo; retina	Función en el SN incierta
Sustancia P	Encéfalo; médula espinal, rutas sensoriales de dolor, tracto gastrointestinal	Mayormente excitatorio; sensaciones de dolor
Encefalinas	Varias regiones del SNC; retina, tracto intestinal	Mayormente inhibitorias; actúan como opióticos para bloquear el dolor
Endorfinas	Varias regiones del SNC; retina, tracto intestinal	Mayormente inhibitorias; actúan como opióticos para bloquear el dolor

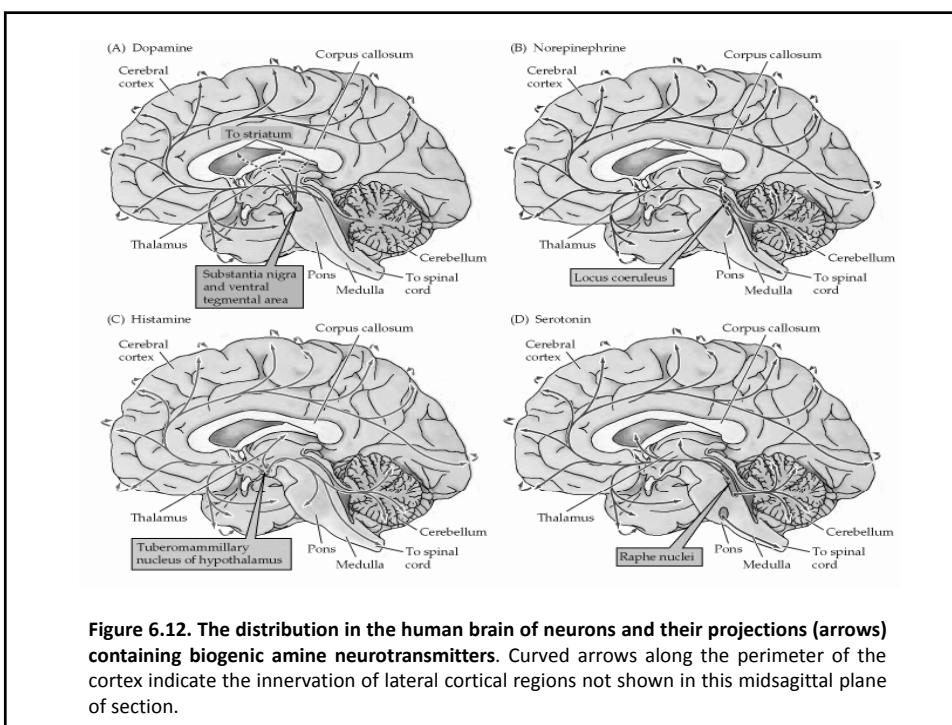


Figure 6.12. The distribution in the human brain of neurons and their projections (arrows) containing biogenic amine neurotransmitters. Curved arrows along the perimeter of the cortex indicate the innervation of lateral cortical regions not shown in this midsagittal plane of section.

Correlación senso-motora

- Sistemas perceptuales
- Sistema motor
- Integración sensorial