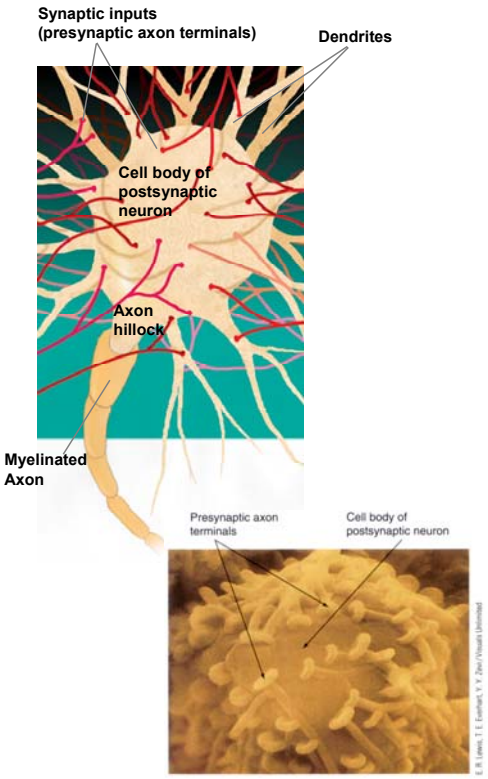
Νευροφυσιολογία και Αισθήσεις

Διάλεξη 5

Συναπτική Μετάδοση (Synaptic Transmition)

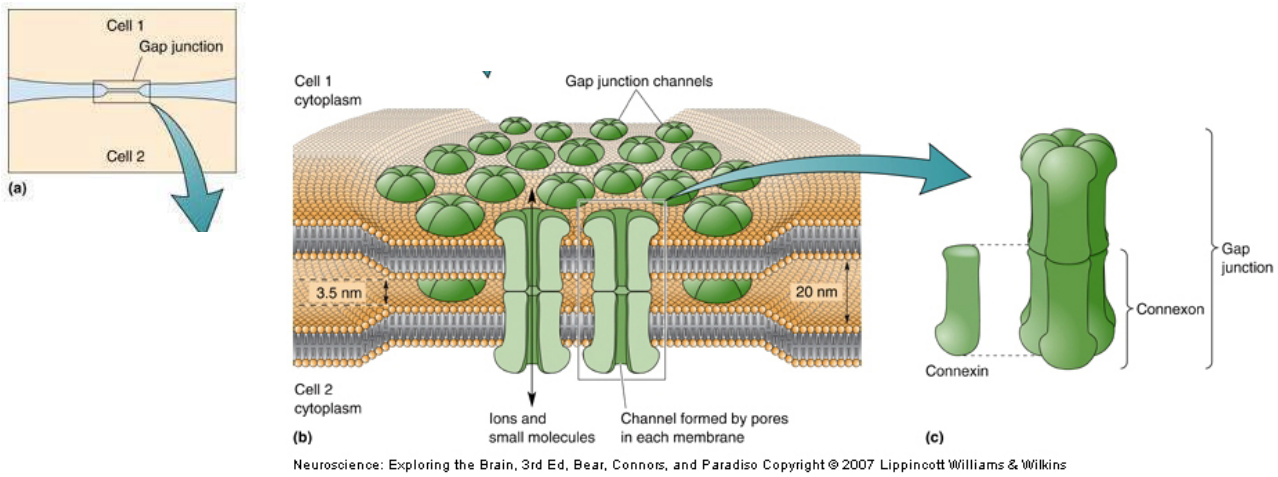
Synapses and Integration

- **A neuron innervates (terminates or supplies) on**
  - Other neurons, Muscle, Gland
- **Synapse**
  - A junction between two neurons
    - First neuron = Presynaptic neuron
      - Synaptic knob at the end of axon
      - Synaptic vesicles with neurotransmitter (chemical messenger molecule)
    - Synaptic Cleft (in chemical synapses)
    - Target cell = Postsynaptic neuron
      - Subsynaptic membrane
  - Most inputs on the dendrites
- **Synaptic Transmission**
  - The process of information transfer at a synapse
  - Plays role in all the operations of the nervous system
  - One-directional signaling: Neuron to target cell



Types of Synapses

- **Electrical Synapses**
  - Gap junction
    - Channel (Connexon- formed by six connexins)
  - Cells are said to be “electrically coupled”
    - Flow of ions from cytoplasm to cytoplasm
  - Very fast transmission
    - Postsynaptic potentials (PSPs)
  - Found where activity coordination is required



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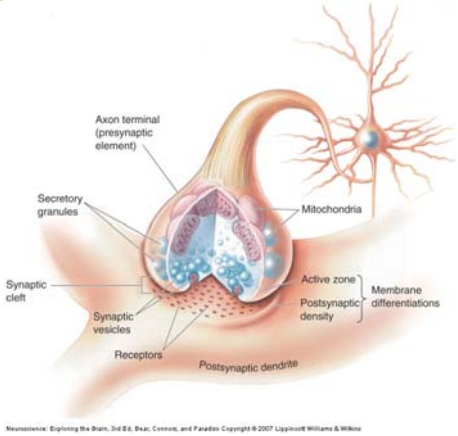
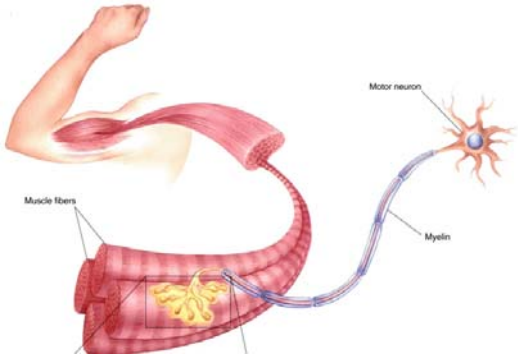
Types of Synapses

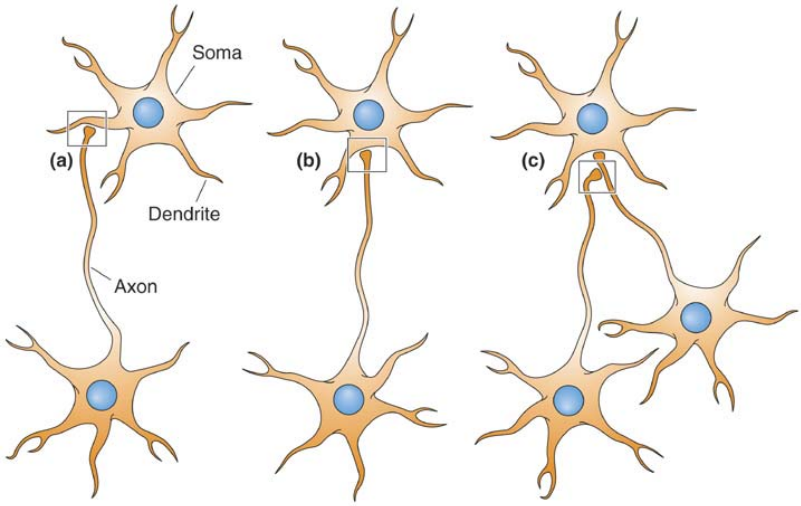
- **Chemical Synapses**
  - No direct ion flow → Chemical signal transmission
  - E.g. Neuron-Neuron
- **The Neuromuscular Junction (NMJ)**
  - Chemical signal transmition
  - Neuron-Muscle
  - Studies of NMJ established principles of synaptic transmission
  - High clinical relevance





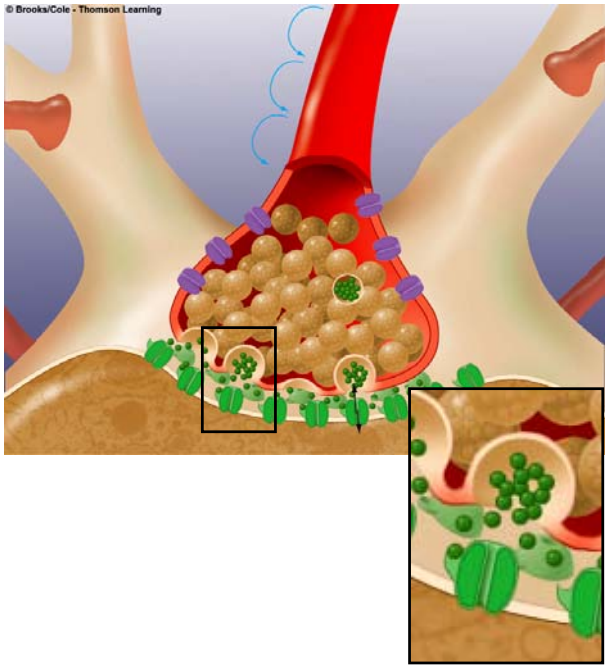
Types of Synapses

- **CNS Synapses (Examples)**
  - Axodendritic: Axon to dendrite
  - Axosomatic: Axon to cell body
  - Axoaxonic: Axon to axon
  - Dendrodendritic: Dendrite to dendrite



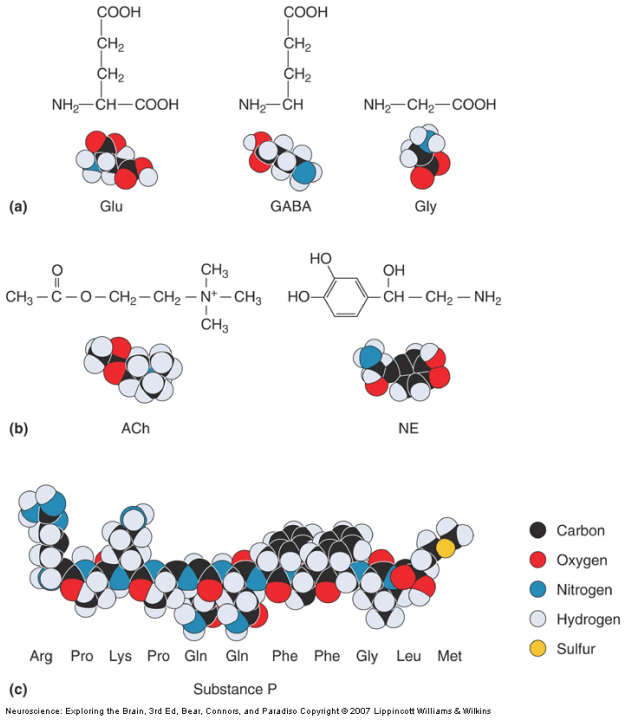
Principles of Chemical Synaptic Transmission

- **AP reaches the synaptic knob**
- **Voltage-gated Ca^{2+} channels open**
- **Ca^{2+} flows into the synapse from the ECF**
- **Ca^{2+} induces exocytosis of vesicles and release of neurotransmitter**
- **Neurotransmitter diffuses across the synaptic cleft to the subsynaptic membrane and binds to specific receptors**
- **Binding triggers opening of ion channels**
  - Each neuron releases one specific neurotransmitter
  - Many different neurotransmitters exist
  - Cause permeability changes of different ions
  - Can be excitatory or inhibitory synapses



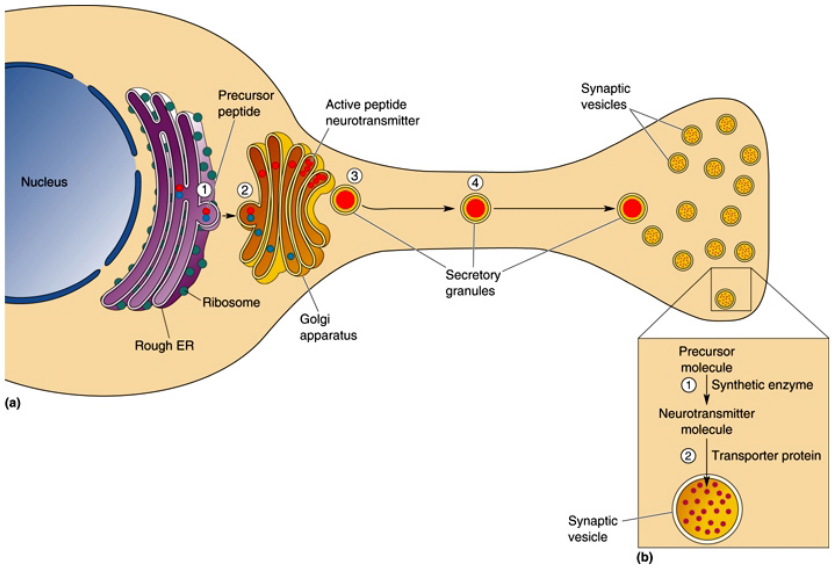
Principles of Chemical Synaptic Transmission

- **Neurotransmitters**
  - Amino acids: Small organic molecules
    - e.g., Glutamate, Glycine, GABA
  - Amines: Small organic molecules
    - e.g., Dopamine, Acetylcholine, Histamine
  - Peptides: Short amino acid chains (i.e. proteins) stored in and released from secretory granules
    - e.g., Dynorphin, Enkephalins



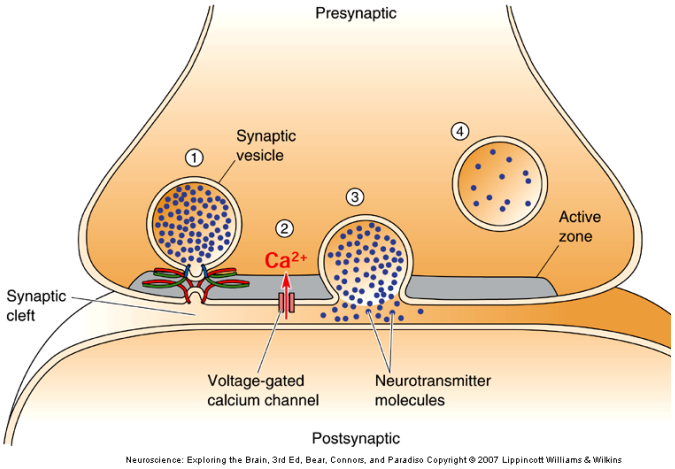
Principles of Chemical Synaptic Transmission

- **Neurotransmitter Synthesis and Storage**
  - Amines, amino acids, peptides
  - Vesicular transportation (???? Speed ????)



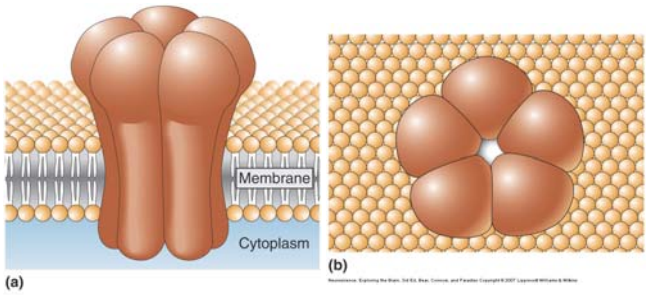
Principles of Chemical Synaptic Transmission

- **Neurotransmitter Release**
  - Exocytosis: Process by which vesicles release their contents
  - Mechanisms
    - Process of exocytosis stimulated by release of intracellular calcium, $[Ca^{2+}]i$
    - Proteins alter conformation - activated
    - Vesicle membrane incorporated into presynaptic membrane
    - Neurotransmitter released
    - Vesicle membrane recovered by endocytosis

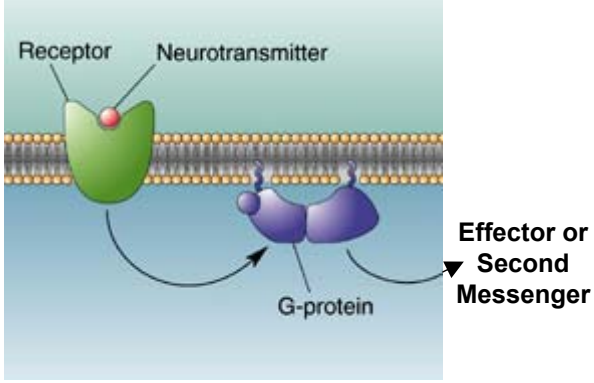


Principles of Chemical Synaptic Transmission

- **Neurotransmitter Receptors and Effectors**
  - Ionotropic: Transmitter-gated ion channels
  - Metabotropic: G-protein-coupled receptor

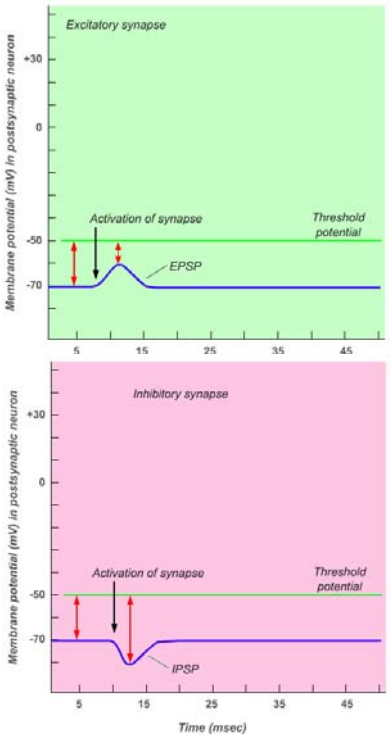


- **Autoreceptors**
  - Presynaptic receptors sensitive to neurotransmitter released by presynaptic terminal
  - Act as safety valve to reduce release when levels are high in synaptic cleft (autoregulation)



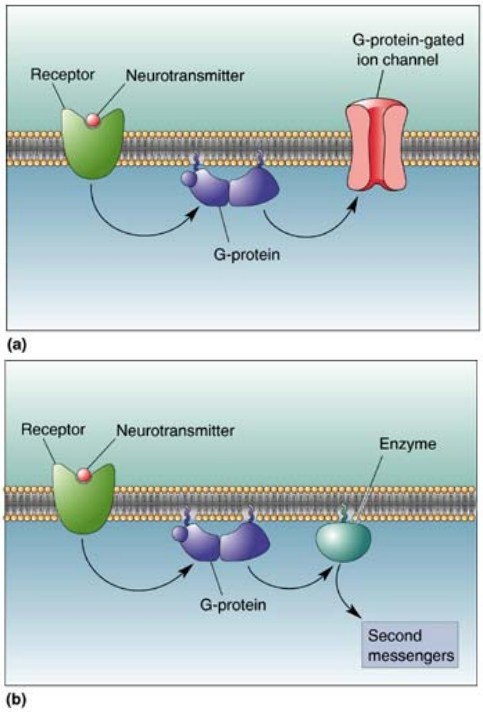
Principles of Chemical Synaptic Transmission

- **Transmitter-gated ion channels**
  - Excitatory Synapses
    - Open non-specific cation channels (both Na^+ and K^+ can pass through)
    - More Na^+ flows into the cell than K^+ flows out
      - Both the chemical and electrical gradients favor Na movement
    - Net result → ***Excitatory Postsynaptic Potential*** (a small depolarization)
    - Usually one EPSP is not enough to trigger an AP
    - Membrane is now more excitable
  - Inhibitory Synapses
    - Different neurotransmitters
    - Open either K^+ or Cl^- channels
    - K+ efflux or Cl- influx → ***Inhibitory Postsynaptic Potential*** (a small hyperpolarization)
  - Synaptic Delay
    - 0.5 to 1 msec
    - Travel through more synapes → ↑Total reaction time



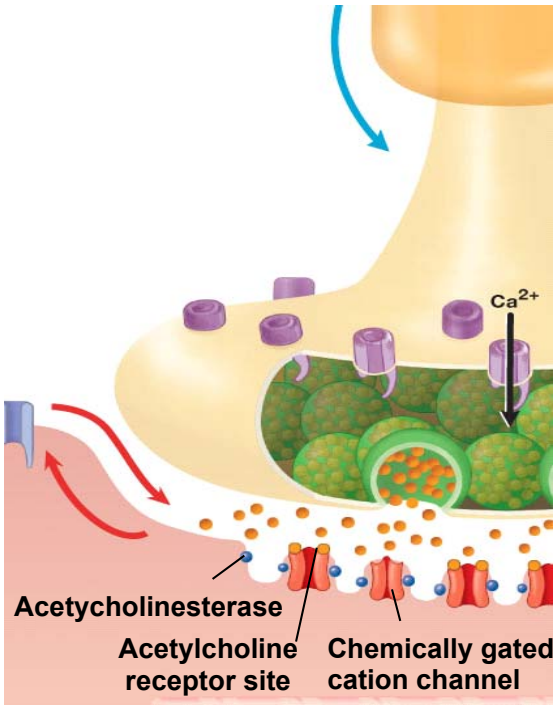
Principles of Chemical Synaptic Transmission

- **G-Protein-Coupled Receptors**
  - Steps of neurotransmitter action
    - Bind to receptor proteins
    - Activate small proteins
    - Activate
      - "Effector" proteins
      - Second messengers
  - Can have metabolic effects →Metabotropic receptors
  - Same neurotransmitter can have different postsynaptic actions
  - ACh Effect
    - Heart → hyperpolarization, slower rythm
    - Skeletal muscle → depolarization, contraction
  - We will discuss the neurotransmitters in the next lecture



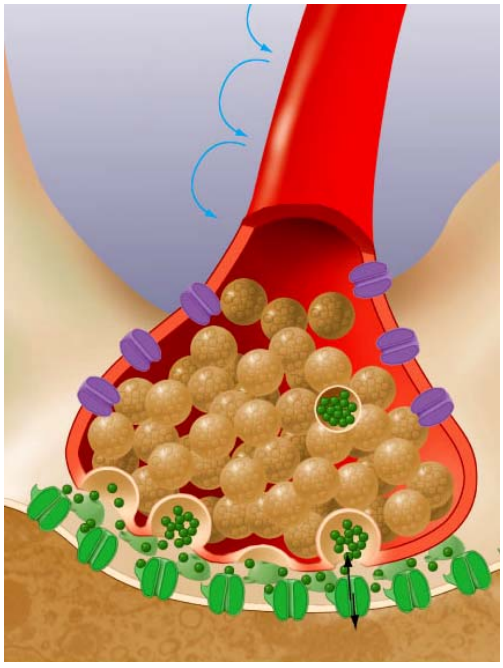
Principles of Chemical Synaptic Transmission

- **Neurotransmitter Recovery and Degradation**
  - Diffusion: Away from the synapse
  - Reuptake: Neurotransmitter re-enters presynaptic axon terminal→ recycling
  - Enzymatic destruction
    - Inside terminal cytosol or
    - Synaptic cleft (by specific enzymes within the subsynaptic membrane)
  - Desensitization: e.g., AChE cleaves Ach to inactive state



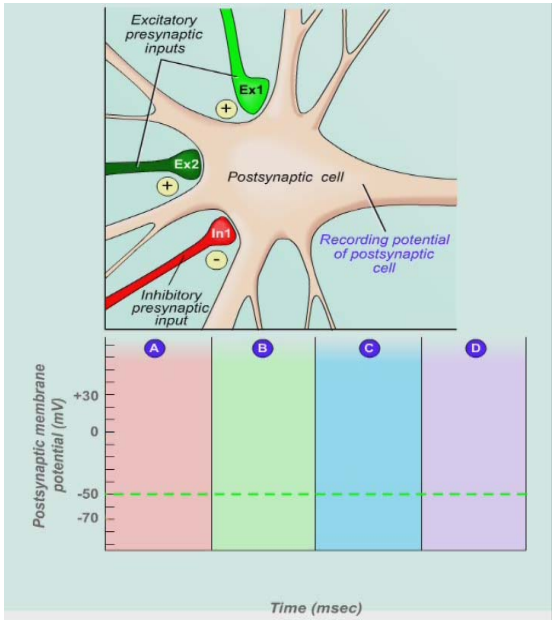
Principles of Synaptic Integration

- **Synaptic Integration**
  - Process by which multiple synaptic potentials combine within one postsynaptic neuron
- **Quantal Analysis of EPSPs**
  - Synaptic vesicles: Elementary units of synaptic transmission
  - Quantum: An indivisible unit
  - Miniature postsynaptic potential (“mini”)
  - Quantal analysis: Used to determine number of vesicles that release during neurotransmission
  - Neuromuscular junction: About 200 synaptic vesicles, EPSP of 40mV or more
  - CNS synapse: Single vesicle, EPSP of few tenths of a millivolt



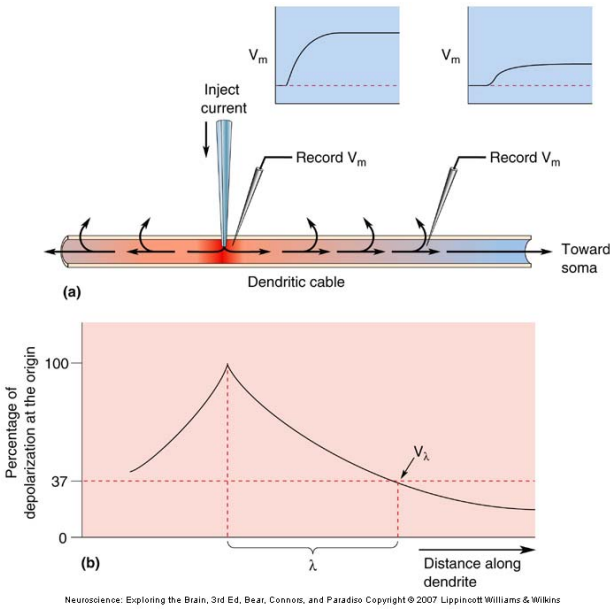
Principles of Synaptic Integration

- **Grand Postsynaptic Potential (GPSP)**
  - EPSPs and IPSPs are graded potentials and can be summed
    - Allows for neurons to perform sophisticated computations
  - Temporal Summation
    - PSPs occurring very close in time can be summed
    - E.g. repeated firing of pre-synaptic neuron because of a persistent input
  - Spatial Summation
    - PSPs from different adjacent synapses can be summed
  - Concurrent EPSPs and IPSPs
    - Cancel each other (more or less) depending on amplitude and location



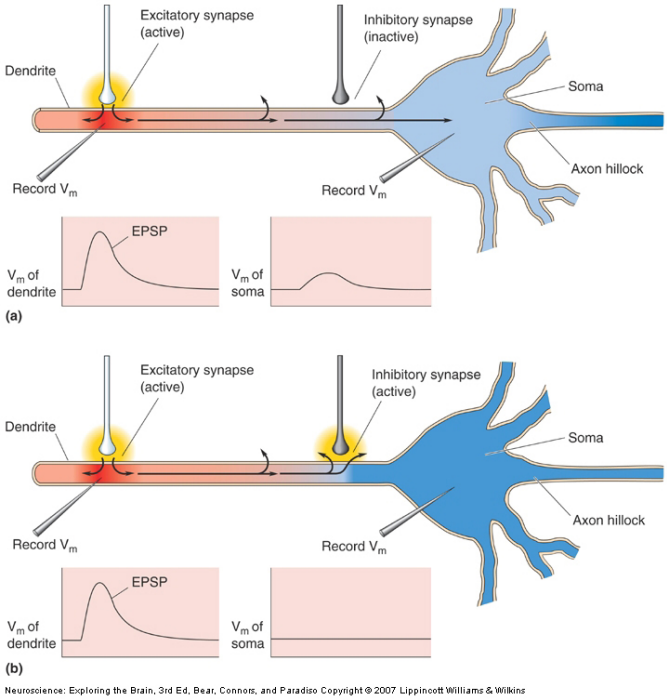
Principles of Synaptic Integration

- **The Contribution of Dendritic Properties to Synaptic Integration**
  - Dendrite as a straight cable
  - Membrane depolarization falls off exponentially with increasing distance
    - $V_x = V_o/e^{x/\lambda}$
  - Dendritic length constant (λ)
    - Proportional to $R_{membrane}/R_{internal}$
  - In reality, dendrites are very elaborate structures that contribute to more complex integrative properties
- **Excitable Dendrites**
  - Dendrites of some neurons have voltage-gated sodium, calcium, and potassium channels
    - Can act as amplifiers (vs. passive)
  - Dendritic sodium channels: May carry electrical signals in opposite direction, from soma outward along dendrites
    - "Informing" dendrites of a relevant AP



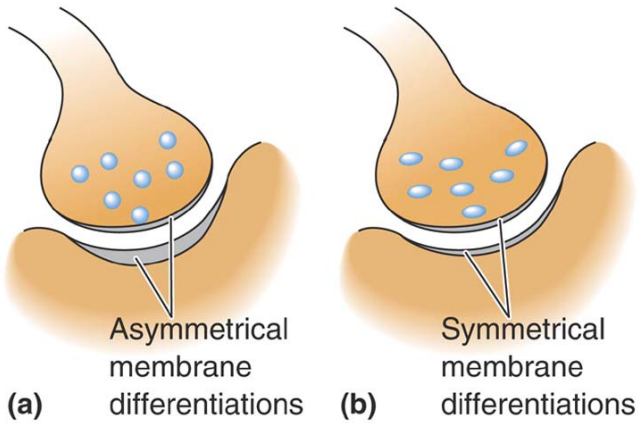
Principles of Synaptic Integration

- **Inhibition**
  - Action of synapses to take membrane potential away from action potential threshold
  - Exert powerful control over neuron output
- **IPSPs**
  - Excitatory vs. inhibitory synapses
    - Bind different neurotransmitters, allow different ions to pass through channels
  - Membrane potential less negative than -65mV → hyperpolarizing IPSP (e.g. K^+ channels)
- **Shunting Inhibition**
  - Inhibiting current flow from soma to axon hillock
  - Shunting of current
    - Flow of Cl^-
  - Membrane potential remains at -65 mV (equilibrium of Cl^-)



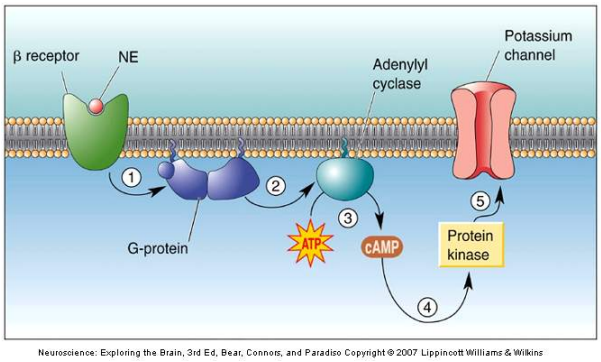
Principles of Synaptic Integration

- **The Geometry of Excitatory and Inhibitory Synapses**
  - Excitatory synapses
    - Gray's type I morphology
    - Clustered on soma and near axon hillock
  - Inhibitory synapses
    - Gray's type II morphology
  - Useful in mapping geometric relations



Principles of Synaptic Integration

- **Modulation**
  - Neuromodulators released by neuron
    - Synaptic transmission that modifies effectiveness of EPSPs generated by other synapses
  - Large molecules which fine-tune a neuron's response
    - Change neurotransmitter production or release
    - Change number of receptors
    - Etc
  - Effect are long term (days, months or years)
  - Example: Activating NE β receptor → reduces K+ conductance



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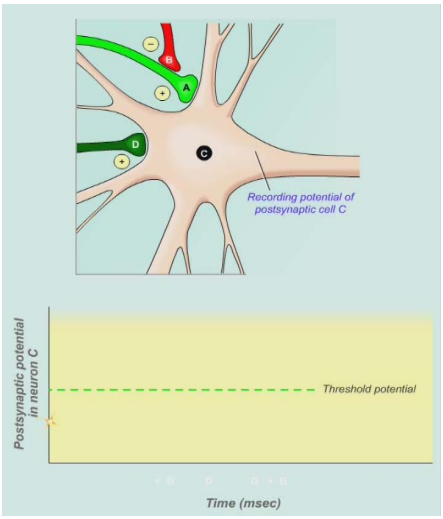
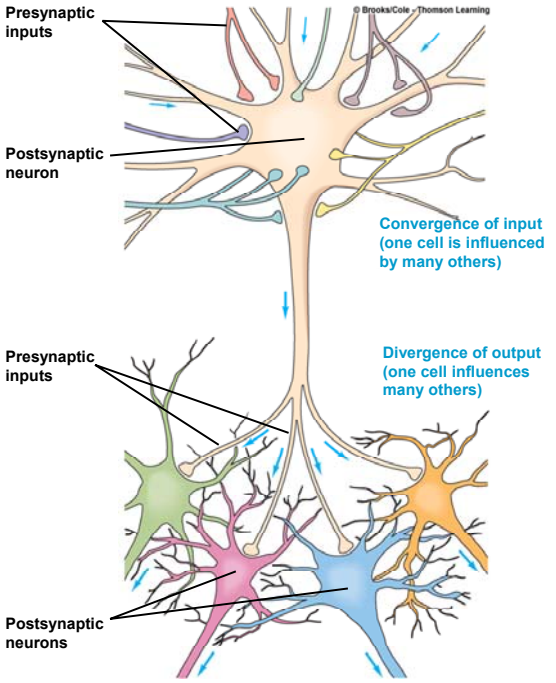
Principles of Synaptic Integration

- **Pre-synaptic inhibition or Pre-synaptic facilitation**
  - Pre-synaptic terminal innervated by modulatory axon terminal
  - Modulatory neuron can inhibit or facilitate the action of a neuron
    - Changing amount of Ca^{2+} entering
  - Does not have any effect on the post-synaptic neuron



Principles of Synaptic Integration

- **Post-synaptic Integration**
  - APs are initiated depending on a combination of inputs
  - Neuron is a complex computational device
    - Synapses = inputs
    - Dendrites = processors
    - Axons/APs = output
  - Signaling and frequency of APs is a result of integration of information from different sources
  - Information not significant enough is not passed at all
  - Neurons are integrated into complex networks (10^{11} neurons and 10^{14} synapses in the brain alone!)
    - Converging
    - Diverging



Arrows indicate direction in which information is being conveyed.

Neuropharmacology

- **Effect of drugs on nervous system tissue**
- **Drug actions may include**
  - Altering the synthesis, axonal transport, storage, or release of a neurotransmitter
  - Modifying the neurotransmitter interaction with the postsynaptic receptor
  - Influence neurotransmitter reuptake or destruction
  - Replace a neurotransmitter with a substitute either more or less powerful

- **Receptor antagonists: Inhibitors of neurotransmitter receptors**
  - Curare→ binds ACh receptors of muscle → prevents contraction
  - Strychnine → blocks the receptor of inhibitory neurotransmitter glycine → convulsions, muscle spasticity
- **Receptor agonists: Mimic actions of naturally occurring neurotransmitters**
  - Phenylephrine → binds α1 receptors → vasoconstriction, releaves hypotension and nasal congestion
- **Block reuptake of neurotransmitter**
  - Cocaine → block dopamine reuptake→ pleasure pathways remain “on”
- **Prevent release of neurotransmitter**
  - Tetanus toxin → prevents release of inhibitory neurotransmitter GABA → muscle excitation unchecked → uncontrolled muscle spasms

- **Defective neurotransmission: Root cause of neurological and psychiatric disorders**

Concluding Remarks

- **Chemical synaptic transmission**
  - Rich diversity allows for complex behavior
  - Provides explanations for drug effects
  - Defective transmission is the basis for many neurological and psychiatric disorders
  - Key to understanding the neural basis of learning and memory

Επόμενη Διάλεξη …

Διάλεξη 6

Νευροδιαβιβαστές (Nerotransmitters)