Synaptic Integration

Dr. Simge Aykan

Department of Physiology

Summation of Postsynaptic Potentials

- The cell body of a postsynaptic neuron may receive inputs from hundreds or thousands of synaptic terminals
- A single EPSP is usually too small to trigger an action potential in a postsynaptic neuron
- *Synaptic integration* is the process by which multiple synaptic potentials combine within one postsynaptic neuron

Quantal Analysis of EPSPs

- The postsynaptic membrane of one synapse may have from a few tens to several thousands of transmitter-gated channels
  - how many of these are activated during synaptic transmission depends mainly on how much neurotransmitter is released

- Vesicles each contain about the same number of transmitter molecules (several thousand)
  - *Quantum*: The elementary unit of neurotransmitter release – content of a single synaptic vesicle –

- Spontaneous release of a single vesicle causes a *miniature postsynaptic potential* (mini)

Synaptic Junctions Outside the CNS

- The Neuromuscular Junction
  - Transmission is fast and reliable
    - An action potential in the motor axon always causes an action potential in the muscle cell it innervates
      - One of the largest synapses in the body
      - The postsynaptic membrane of the folds is packed with neurotransmitter receptor

- At the neuromuscular junction, single action potential in the presynaptic terminal triggers the exocytosis of about 200 synaptic vesicles, causing an EPSP of 40 mV or more.

- At many CNS synapses, the contents of only a single vesicle are released in response to a presynaptic action potential, causing an EPSP of only a few tenths of a millivolt

Summation of Postsynaptic Potentials

- Individual postsynaptic potentials can combine to produce a larger potential in a process called *summation*
  - At the axon hillock (high number of Na+ channels)

Summation of Postsynaptic Potentials

- In *spatial summation*, EPSPs produced nearly simultaneously by different synapses on the same postsynaptic neuron add together

- If two EPSPs are produced in rapid succession (1-15 msec) by the same synapse, an effect called *temporal summation* occurs

The Spread of Current Through Neurons

- The effectiveness of an excitatory synapse in triggering an action potential, therefore, depends on how far the synapse is from the action potential-initiation zone and on the properties of the dendritic membrane.
- Passive spread of current

  $\Delta V_x = \Delta V_0 e^{-x/\lambda}$

  λ = square root (r_m/r_a)

  - Lambda is the "*length constant*"
  - At a distance lambda, the membrane depolarization (V), is 37% of that at the origin
  - Actual length constants are 0.1 - 1.0 mm

- Dendrite membranes are electrically passive –lacks voltage gated channels

- Exception; apical dendrites of pyramidal cells of the cerebral cortex

Synaptic Inhibition

- Most synaptic inhibition is mediated by GABA-gated Cl- channels
  - E_{Cl-} is -65 mV
  - If membrane potential is less negative than -65mV, GABA mediates hyperpolarizing IPSP
- Two Mechanisms
  - Hyperpolarization
  - Shunting Inhibition: Inhibiting current flow from dendrites and soma to axon hillock

Shunting Inhibition: Inhibiting current flow to axon hillock

- Increasing membrane conductance will decrease membrane length constant
- Opening any channel will cause an EPSP to decay over a shorter distance
- *Shunting inhibition:* It prevents depolarizing current from reaching the axon hillock and eliciting an action potential.
- *the inward movement of negatively charged chloride ions, is equivalent to outward positive current flow*

Synaptic Modulation

- Synaptic transmission that modifies effectiveness of EPSPs generated by other synapses

- Activating NE β-receptors
  - Close K^+ Channels

  - Decreasing the K^+ conductance increases the dendritic membrane resistance and therefore increases the length constant

  - Distant or weak excitatory synapses will become more effective in depolarizing the spike-initiation zone beyond threshold; the cell will become more excitable

Synaptic Plasticity

Synaptic Plasticity

- The strength of a synapse can change; it is “plastic”
  - A neuron can therefore select its own synapses
- Synaptic plasticity is thought to be the main mechanism of learning and memory

Learning

- Glutamate is the most common excitatory neurotransmitter in nervous system

- Ionotropic glutamate receptors
  - AMPA
    - Rapid influx of Na+
  - NMDA
    - Slow and longer lasting influx of Na+ and Ca^{2+}
    - Requires previous depolarization

- At rest NMDA receptors are blocked by Mg2+
- Depolarization by AMPA removes Mg2+ block
- Na+ and Ca2+ influx through NMDA
- Celular and gene changes triggered by Ca2+
- By repeted high-frequency stimulation the magnitude of the postsynaptic response is enhanced (long term potentiation-LTP)

- Now, the postsynaptic cell is more sensitive to glutamate because it has more receptors to respond to it. Additionally, there are thought to be signals that travel back across the synapse to stimulate greater levels of glutamate release. All of this makes the synapse stronger and more likely to be activated in the future.

- This process is also associated with changes in gene transcription in the neuron, which can lead to the production of new receptors or modifications to the structure of the cell. These changes seem to be important for making the increased responsiveness of LTP long-lasting.

After repeated stimulation stronger postsinaptic potential by increase in the number of AMPA receptors

Neural Circuits

- Complex neural circuits are possible because of associations such as convergence and divergence

Convergence

- A single neuron is affected by converging signals from two or more presynaptic neurons
    - Allows CNS to integrate incoming information from various sources

Divergence

- A single presynaptic neuron stimulates many postsynaptic neurons
  - Allowing widespread effect

Reverberating Circuits

- Important in
  - rhythmic breathing
  - mental alertness
  - short-term memory

- Depend on positive feedback
  - new impulses generated again and again until synapses fatigue

Interaction of Heredity and Environment

- Genes → Hardware
  - Anatomical structures; functional differentiaition and migration process through a series of programmed protein functions
- Environment → Software
  - Experience determines the development of basic working models and makes fine adjustments to make the anatomical formations, especially the connections between nerve cells
- Reciprocal interaction of genes and environment

Generational increases in measured IQ

- Performance on IQ tests has steadily increased over generations
- Tests are renormed periodically with new standardization groups so that the mean IQ always remains at 100

- Flynn Effect
  - Studies on 20 nations
  - IQ performance has been rising steadily all over the industrialized World since 1930s
  - The performance today would earn you an average score of 100 would have earned you an 125 back in 1930s

- World's gene pool could not have changed in 70 years (compared to evolution of life in 3.7 billion years)

- Effect of environmental factors

Intelligence

- Genetically determined limits (reaction range)
  - Hundreds of genes with small effects

- Environmental factors determines where individuals fall within these limits