

Tutorial 9: Excitatory Postsynaptic Potentials

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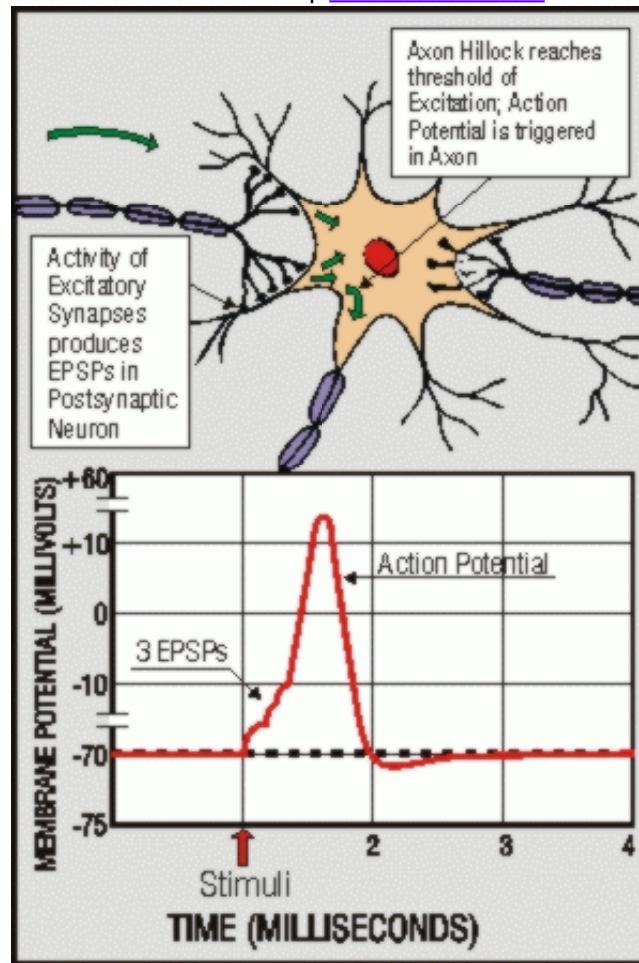


Figure 9: Excitatory Postsynaptic Potentials

[Part 1: Image-Mapped Tutorial](#)

[Part 2: Matching Self-Test](#)

[Part 3: Multiple-Choice Self-Test](#)

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Tutorial 9 describes the process by which information from many neurons becomes integrated to affect the activity of a single neuron; to make the activity of thousands represented by one "whole". This neural integration takes place at the postsynaptic membrane, or along the membrane of a neuron's dendrites and cell body. This is where information converges from the terminal endings of axons from other neurons. As [described previously](#), the direction of information as it flows along a neuron is from dendrite to cell body to axon hillock (where the integration occurs) along the axon to the axon's terminal buttons. The terminal buttons form the presynaptic membrane of the [synapse](#), which forms the site of communication between two neurons.

When an action potential reaches the presynaptic membrane, it triggers the release of chemicals called neurotransmitters. These neurotransmitters can affect the postsynaptic membrane in one of two ways. They either initiate an excitatory postsynaptic potential (EPSP) or an inhibitory

postsynaptic potential (IPSP). EPSPs and IPSPs are graded responses that reflect the nature and magnitude of neurotransmitters released at the synapse at any given point in time. Both EPSPs and IPSPs differ from action potentials in that they are subthreshold responses that decay very rapidly in time and space. Whether or not the acted-on neuron will fire (action potential triggered) depends on the integration of all EPSP and IPSP activity at any given moment at the axon hillock, the initial segment of its axon. Because postsynaptic potentials decay rapidly, the synapses located closest to the axon hillock are dominant in their affect over that neuron's activity.

Excitatory postsynaptic potentials are induced by neurotransmitters that open calcium (Ca^{2+}) channels. Calcium is in higher concentrations outside the resting neuronal membrane. When calcium channels are opened by a neurotransmitter, calcium influx occurs with subthreshold depolarization across the membrane. Because this depolarization is subthreshold, multiple EPSPs are necessary for activation of an action potential.

Inhibitory postsynaptic potentials counteract the depolarization of excitatory postsynaptic potentials via membrane hyperpolarization. This mechanism that involves chloride and / or potassium ions will be discussed in more detail in [Tutorial 12](#).

The calcium ion plays other very important roles in neurophysiology. Calcium ions trigger the migration of synaptic vesicles and release of neurotransmitters in the presynaptic membrane. We will consider these mechanisms in [Tutorial 11](#). They also bind enzymes located within the postsynaptic membrane of dendrites and activate biochemical and structural changes. For example, Ca^{2+} is involved in the growth of dendritic spines that occur with learning.

Advanced

Many recent and exciting avenues of research have been stretching our knowledge of the development, structure, and function of the dendritic trees of neurons and the postsynaptic membranes that define them. These scientific ventures include the study of plastic (changeable) features of developing and mature postsynaptic structures and their response to stimulation (Segal, Korkotian & Murphy, 2000; Sourdret & Debanne, 1999), characteristics that distinguish different populations of neurons, characteristics that appear to be universal, and finely-tuned mechanisms that modulate postsynaptic potentials (PSP's).

Populations of neurons may undergo development that is unique to their primary functions; this unique development involves the mechanisms that are used to regulate the excitability of postsynaptic potentials (Spitzer & Ribera, 1998). Studies of neuronal development indicate that the voltage-dependent ion channels utilized by the postsynaptic membrane differ across populations. Indeed, newly discovered voltage-dependent potassium channels are structurally and functionally diverse (Pongs, 1999). These various channels may determine the occurrence of back propagation of dendritic action potentials, signal to noise ratios in the excitability of the presynaptic membrane, and the responsiveness of the postsynaptic membrane to synaptic input. Since these different K^+ channels are genetically coded, it is possible that inherited disorders involving alterations in neuronal excitability (e.g., epilepsy, heart arrhythmia, hearing loss) are secondary to mutations of the genes that encode the structure of these channels.

New recording techniques allow neurobiologist to measure signal generation simultaneously from multiple points of a single neuron. These techniques involve the use of sharp microelectrodes, patch-clamp recordings from neuronal processes (Stuart & Spruston, 1995) and high-resolution optical recordings of changes in Ca^{2+} concentration (Basarsky, Duffy, Andrew & MacVicar, 1998). Recorded data are subjected to models used to predict the distribution of membrane potentials across the entire dendritic tree. An even more refined technique allows the scientist to record

intracellularly from voltage-sensitive dyes applied to neurons within brain slices (Gelperin & Flores, 1997; Sabatini & Regehr, 1998; Zecevic & Antic, 1998). These approaches allow for spatial analysis of more complex neurophysiological relationships.

Recent studies using these various techniques of multiple recordings indicate that the active electrical properties of different regions of an individual neuron are remarkably complex, dynamic, and for the most part impossible to predict based on our current models. Improvements in multi-site recording will eventually provide a more complete picture of synaptic integration and action potential conduction in the dendrites of individual neurons.

The mechanism of calcium ion influx in the generation of an excitatory postsynaptic potential (EPSP) appears to be universal across populations of neurons. It appears, however, that two additional calcium ion mechanisms contribute to the generation of EPSPs. These newly discovered mechanisms include the release of Ca^{2+} intracellularly from intracellular stores and Ca^{2+} entry via ligand-gated channels. Ligand-gated channels are opened when a specific molecule binds to a channel subunit (Eilers, Plant & Konnerth, 1996). As mentioned previously, it is Ca^{2+} influx via voltage-dependent channels along the presynaptic membrane that triggers the release of neurotransmitters. In addition, when a train of action potentials is sent to the axon terminal of a neuron, Ca^{2+} levels increase overall in the presynaptic cytoplasm.

It is already known that neurotransmitter binding to a receptor site on the postsynaptic membrane serves as the switch for generating an EPSP, the turning on of a neuron. Neurobiologists have recently discovered two enzymes that serve as volume control for EPSP activity (Westphal et al., 1999). Each of these enzymes is associated with a protein that anchors itself to the inside of the neuronal membrane, called yotiao. This protein holds the enzymes close to their site of action, the N-methyl-D-aspartate (NMDA) receptor. NMDA receptors are primary channels through which Ca^{2+} ions flow into the neuron. Glutamate and cyclic AMP, incidentally, are the neurotransmitters specialized for the NMDA receptor. The first enzyme that the yotiao protein holds near the NMDA receptor is called cAMP-dependent protein kinase (PKA). When yotiao releases PKA, the enzyme stimulates the NMDA channel to let in more Ca^{2+} . When yotiao releases the second enzyme, type 1 protein phosphatase (PP1), the enzyme down regulates the NMDA receptor, slowing down the influx of Ca^{2+} . These enzymes are readily available to the NMDA receptor, thanks to yotiao, so they may instantly enhance or dampen the flow of ions to maintain proper firing and recovery.

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Suggestions for further study

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(Protein Studies Reveal Sophisticated Control Of Nerve Communication)

Science Daily Research News

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NMDA receptor blockers and the prevention of neuronal damage due to stroke, epilepsy, Huntington's Disease, and AIDS.

<http://psych.hanover.edu/Krantz/neural/actionpotential.html>

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