

Topic 8: NEURONAL PHYSIOLOGY: GRADED AND ACTION POTENTIALS

I Introduction

- A All cells possess a membrane potential related to the non-uniform distribution of and differential permeability of Na⁺, K⁺ and large intracellular ions.
- B Neurons and muscle cells are excitable cells that make use of this potential
- C Graded potentials are short distance signals
- D Action potentials are long distance signals

II Graded Potentials

- A Local changes in membrane potential
- B Magnitude of change is related to magnitude of triggering event
- C Triggering event
 - 1 stimulus
 - 2 interaction of chemical messenger with receptor
 - 3 spontaneous change
- D How it works
 - 1 triggering event causes a flow of ions across the membrane
 - 2 leads to localized change in membrane potential (e.g. flow of Na⁺ into cell will make the membrane potential more positive/less negative)
 - 3 w/o out constant triggering event, graded potentials will die out
 - 4 current is local – does not spread very far; and is small, <10mV change

III Action Potentials: Mechanisms

- A Terms
 - 1 Polarization: separation of charges
 - 2 Depolarization: reduction in potential (usually this means becoming more positive/less negative)
 - 3 Hyperpolarization: increase in potential (becoming more negative/less positive)
 - 4 Repolarization: return to resting potential
 - 5 Voltage-gated (voltage-regulated) channels: ion channels that open or close in response to changes in membrane potential

B Events in an Action Potential

- 1 Resting Potential
- 2 Triggering event
- 3 Slow depolarization from -70 to -50
- 4 -50 is threshold; explosive depolarization to +30 mV
- 5 repolarization
- 6 frequently overshoots: hyperpolarization (-80)
- 7 in nerve takes 0.001 seconds

C Mechanisms of Action Potential Events

- 1 At rest (-70 mV) many K^+ channels open, most Na^+ channels closed; these **Na^+ channels are voltage regulated channels**
- 2 As depolarization begins (we will discuss how this all begins in more detail in the next lecture), some Na^+ channels open
- 3 Na^+ concentration and electrical gradients are into cell, so Na^+ starts to move into cell
 - a This causes more depolarization, which opens more Na^+ channels
 - b **Positive** feedback loop established
- 4 At threshold (-50 mV) “all” Na^+ channels are open
 - a membrane far more permeable to Na^+ than K^+
 - b Na^+ rushes in, and inside of cell becomes positive (+30 mV)
- 5 Two things help repolarize:
 - a Voltage-sensitive Na^+ channels close at +30 mV
 - b K^+ channels are also voltage-sensitive; when membrane voltage is +30, “all” K^+ channels open; K^+ rushes out of cell along both concentration and electrical gradient.
 - c Positive charges leaving with K^+ repolarizes membrane.
- 6 K^+ rushing out can take out too many positive charges = a slight hyperpolarization

D Restoration of Gradients

- 1 At completion, membrane potential restored, but concentrations of Na^+ and K^+ not.
- 2 Very few K^+ and Na^+ cross membrane during AP compared to total available, so concentration not changed much.
- 3 Na^+/K^+ ATPase pump.

IV Action Potentials: The Neuron

A Neuron Structure (review)

- 1 Three parts
 - a cell body
 - i nucleus and organelles
 - b dendrites
 - i numerous extensions from cell body
 - c axon or nerve fiber
 - i single elongated tubular extension
 - ii conducts action potentials away from cell body
 - iii may give off side branches or collaterals
 - iv has highly branched endings called axon terminals
 - d first portion of axon + region of cell body from which it leaves is called axon hillock
- 2 Can range in length from less 1 mm to over 1 meter

B Conduction of Action Potential

- 1 Initiated in axon hillock
- 2 conduction by current flow down axon
- 3 resting potential in adjacent inactive area depolarized to threshold
- 4 first action potential triggers next one in adjacent area
- 5 is a self perpetuating cycle: All or None – once AP starts, it will be conducted down the entire axon

C Myelination

- 1 Myelin is composed of lipids
- 2 Surrounds portion of axon, like rubber insulation around a wire
- 3 In CNS myelin forming cells are called oligodendrocytes
- 4 In Peripheral NS, myelin formed by Schwann cells.
- 5 Gaps between myelin are called Nodes of Ranvier
- 6 Impulse jumps from Node to node
- 7 Increases speed of action potential conduction
- 8 MS is caused by destruction of myelin

D Refractory Period

- 1 Prevents AP from moving in both directions on axon
- 2 Absolute refractory period: Na⁺ channels are closed and inactivated
- 3 Relative refractory: AP can occur, but stimulus must be much larger than normal to get one started (K⁺ gates are still open during this time)
- 4 SO: ensures unidirectional movement of AP, and sets an upper limit on frequency of AP.

Topic 9: NEURONAL PHYSIOLOGY: SYNAPSES AND NEUROTRANSMITTERS

I Synapse Structure

- A Synapse is site of communication between nerve cells
- B Axon terminals of one junction with some part of another
 - 1 dendrites of another (axo-dendritic synapse)
 - 2 soma of another (axo-somatic synapse)
 - 3 axon of another (axo-axonal synapse)
- C Convergence = one neuron may have 1000's of others input
- D Divergence = one neuron may synapse on several others
- E Synapse anatomy
 - 1 presynaptic neuron
 - a synaptic knob
 - b synaptic vesicles
 - c neurotransmitter
 - 2 postsynaptic neuron
 - 3 synaptic cleft

II Synapse Function

- A Action Potential reaches axon terminals
- B Action Potential triggers voltage-regulated Ca^{++} channels to open
- C Influx of Ca^{++} triggers fusion of synaptic vesicles with plasma membrane = synaptic release
- D Neurotransmitter diffuses across synaptic cleft and binds to a receptor on the postsynaptic membrane
- E Causes some change in the postsynaptic cell (usually a local change in membrane potential by opening an ion channel)
- F Neurotransmitter is removed from synaptic cleft

III Synapse Function – postsynaptic neuron (# D and E, above, in more detail)

- A Excitatory Postsynaptic Potential (EPSP)
 - 1 Neurotransmitter binds to receptor
 - 2 Na^+ channels open (or Ca^{++} channels)
 - 3 Lots of Na^+ in
 - 4 With net influx of +, membrane depolarizes a little
 - 5 Membrane is closer to threshold

- B Inhibitory Postsynaptic Potential (IPSP) – also a graded potential
 - 1 Neurotransmitter binds to receptor
 - 2 K⁺ or Cl⁻ channels open
 - 3 K⁺ leaves or Cl⁻ comes in
 - 4 Results in hyperpolarization of membrane
 - 5 Membrane is further from threshold

- C How receptors can open channels
 - 1 ionotropic: receptor is itself an ion channel
 - 2 metabotropic: receptor activates second messenger system which later results in some effect on an ion channel

- D Grand Postsynaptic Potential (GPSP)
 - 1 Sum of all EPSP and IPSP = GPSP
 - 2 Temporal Summation
 - a frequent excitatory potentials more likely to reach threshold than infrequent
 - 3 Spatial Summation
 - a multiple excitatory potentials from various postsynaptic sites more likely to reach threshold than a single EPSP
 - 4 If GPSP at axon hillock is at threshold, an action potential will result

- IV Neurotransmitter removal (#II F in more detail)
 - A Inactivated by enzymes
 - B Actively pumped into synaptic knobs
 - C Diffuses away

Neurotransmitters & Neuropeptides

- A Neurotransmitters
 - 1 small molecules (size of amino acid)
 - 2 “fast-acting”
 - 3 synthesized in cytosol of synaptic knob
 - 4 Neurotransmitter examples:
 - i inhibitory neurotransmitters: glycine, GABA (open Cl⁻ channels)
 - ii excitatory neurotransmitters: glutamate (open Na⁺ channels)
 - iii others: acetylcholine (found at neuromuscular junction -- opens Na⁺ channels), dopamine, serotonin, etc. (most of these are

metabotropic receptors)

- B Neuropeptides
 - 1 larger molecules (2-40 amino acids)
 - 2 can be slow-acting
 - 3 synthesized in rough ER of cell body then transported in vesicles to synapse along microtubules
 - 4 usually change effectiveness of synapses (act as neuromodulators)
 - 5 Neuropeptide examples
 - a enkephalin, endorphin
 - b substance P

- VII Ways to modify synapse function using drugs
 - A Mimic the neurotransmitter (e.g. morphine mimics endorphins)
 - B Other interaction with a neurotransmitter receptor
 - 1 anti-anxiety drugs (such as Valium) interact with the GABA receptor
 - C Block re-uptake of neurotransmitter
 - 1 Cocaine blocks the reuptake of dopamine
 - 2 Fenfluramine blocks reuptake of serotonin
 - 3 fluoxetine (Prozac) is also a serotonin reuptake inhibitor
 - D Block enzyme pathways that degrade neurotransmitters
 - 1 several anti-depressants block an enzyme that degrades serotonin, dopamine, epinephrine, and norepinephrine