Neurophysiology

Membrane Potential

- Body is electrically neutral
- There are small differences in electrical charge between inside and outside of cell membranes
  → Due to differences in + and – ions on inside and outside of cell membrane
- Differences in charge = potential (stored energy)
- Potential difference is measured as voltage
- For body cells voltage is measured in millivolts: 1mV = 0.001 V
- Resting cells (all cells in body) have potential difference = -50 to -200 mV
  → Muscle and nerve cells -40 to -90 mV
  → Average: -70 mV

The flow of charge = current
- In wires: flow to produce current = electrical
- In neurons: ions flow to produce current = electrochemical impulses

In response to specific stimuli → still down a conc gradient, no ATP required

b. Active transport (solute pumping)

- Moving ions through membrane UP a concentration gradient using specific protein carrier and ATP

Resting Membrane Potential

- Created by 3 major processes:
  1. There are different kinds and concentrations of ions inside and outside cell membranes:
     - Inside cell: negative ions: proteins, PO4^3-, SO4^2-
       positive ions: K^+
     - Outside cell: negative ions: HCO3-, Cl
       positive ions: Na^+
       → There are more negative ions inside cell → especially proteins
       → Negative ions (esp proteins) generally can’t cross membrane
  2. Both Na^+ and K^+ can diffuse across cell membrane by facilitated diffusion via leakage channels
     → Both diffuse across membrane going down their concentration gradient
     → But more permeable to K^+ than to Na^+
  3. Active transport restores concentration gradients of some of these + ions:
     → More Na^+ outside cell
     → More K^+ inside cell
     → Sodium/Potassium pump pumps Na^+ out/K^+ in
       → But pumps 3 Na^+ out for every 2 K^+ in

These characteristics create a resting potential:
  → More negative ions inside cell
  → More positive ions outside cell

Cell membrane is polarized
  → It has a potential for flow of charge
  → That potential ~ -70mV
  → Resting Potential

In nerve and muscle cells this resting potential can be changed by moving ions across the cell membrane
Changing the Resting Potential

A change in resting membrane potential can be produced by anything that changes membrane ion permeability → ie. opens or closes ion gates.

These changes are mediated mainly by gated channels → proteins can change shape to open or close channel in response to specific stimuli → still down a conc gradient, no ATP required → gates can be opened in 3 ways:

i. chemically gated → stimulated by specific chemicals eg. neurotransmitter receptors

ii. voltage gated → stimulated by changes in membrane potential eg. Na⁺, K⁺ and Ca²⁺ channels in axons

iii. mechanically gated → open by physical distortion of membrane surface; eg touch, pressure, vibration sensory receptors

two kinds of potential changes:
1. graded potentials
2. action potentials

1. Graded Potentials

small to large changes in membrane potential due to opening and closing of chemical gates

graded potentials are created when something happens to open gated ion channels (chemical gates)

**depolarization:** membrane potential decreases moves toward "0" becomes less negative

**hyperpolarization:** membrane potential increases moves more negative moves away from "0"

in receptor region of dendrites and cell bodies of neurons these changes are graded potentials → depend on intensity of stimulus

is a very local phenomenon: 
→ dissipates with distance from stimulus

very short lived 
→ quickly returns to resting potential

2. Action Potentials

complete depolarization and repolarization of membrane
due to sequential opening and closing of several voltage gates and active transport

Generation of an Action Potential

1. resting state
active channels closed
at resting membrane potential → + in; - out (-70mv)

2. Stimulus above threshold
(graded potential change to ~ -55-50 mV)

3. Depolarization
Na⁺ gates open
axon membrane becomes 1000’s x’s more permeable to Na⁺ →20,000 Na⁺ enter/gate
-70mV to +30mV (b of ~100mV)
self limiting, lasts ~ 1 ms; till potential reaches ~ +30 mV
then Na⁺ gates close

4. Repolarization
K⁺ gates open
K⁺ rushes out of cell
membrane potential undershoots resting potential (slight hyperpolarization)

5. Return to Resting Potential
Na⁺/K⁺ Pump restores ion concentrations to normal

6. Refractory Period

**Absolute refractory period**
when generating action potential the neuron is incapable of generating another action potential for the first 2 ms regardless of strength of stimulus

Absolute ~2 ms

**Relative Refractory period:**
most of hyperpolarization period
only an exceptionally strong stimulus can trigger another action potential
relative ~3-5 ms

AP’s only created when the stimulus is above some minimum amount (ie. threshold)
(eg. typical threshold ~ -60mv)

voltage gates will only open above threshold

neuron: receptor region – dendrite and cell body chemically gated graded potentials
conducting region - axon voltage gated creates action potential transition at axonal hillock
= trigger zone

only axons of a neuron can create action potentials

**Action Potential Propagation**

depolarization at one location triggers voltage gates in area next to it to depolarize
   → creates a new AP in adjacent area

as new area is depolarizing, original area is repolarizing

at any one time action potential occurs at only one small area of axon

this area appears to travel down axon

= **nerve impulse**: a self propagating wave of action potentials moving down an axon

**Characteristics of a Nerve Impulse**

1. **nerve impulse** is all-or-none (like AP)
   
   above threshold – fires
   
   below threshold – doesn’t fire

2. does not decrease in strength as AP moves along axon
   
   since new AP is created at each point along the way

3. each neuron has its own frequency of firing
   
   frequency of firing usually varies between 10-500 impulses/sec

   **refractory period** determines how quickly a neuron can fire:

   eg. short rp can fire more rapidly than one with longer rf

4. a **stronger stimulus** increases **frequency** of nerve impulse

   not its amplitude

5. **Velocity** of Nerve Impulse is independent of stimulus intensity

   speeds range from ~.5 m/sec to 150 m/sec

   (=2 to 300mph)

   **Velocity** depends on:

   1. **axon diameter**
      
      larger → faster

   2. **thickness of myelin sheath**
      
      unmyelinated = slower
      
      myelinated = faster

3. **Distance between Nodes of Ranvier**

   jumps from node to node (1-2 mm apart)

   where most voltage gates are located

   = **saltatory conduction**

   in terms of velocity; nerve fibers in **PNS** can be:

   **A fibers**

   largest diameter

   thick myelin

   saltatory conduction

   shortest refractory period

   → up to 130 m/sec

   in axons of some large sensory neurons

   eg. touch, pressure, joint positions, heat, cold, etc

   → generally, those that detect “danger”

   all somatic motor neurons (to skeletal muscles)

   → effectors that can do something about the danger

   (reflex arcs)

   **B fibers**

   medium diameter

   thick myelin

   saltatory

   medium refractory period

   → ~10 m/sec

   sensory neurons; some from skin and viscera

   all autonomic (visceral) motor neurons from CNS to ganglia

   **C fibers**

   smallest diameter

   unmyelinated (=thin myelin)

   no saltatory conduction

   longest refractory period

   → ~0.5 m/sec

   neurons that conduct impulses from skin

   all autonomic motor neurons from ganglia to effectors (smooth muscle and glands)

6. a number of physical and chemical substances can affect the generation of a nerve impulse mainly by affecting permeability to specific ions:

   a. **Calcium ions**

      needed to close sodium channels during generation of action potentials

      low Ca++ → repeated transmission of AP

      → muscle spasms

      eg. decrease of Ca++ in blood of pregnant women

      sometimes produces spasms

      eg. spasms can also be produced by diarrhea, vit D deficiency, etc.

   b. **Potassium ions**

      large increases in extracellular K+ causes hyperpolarization

      impulses not triggered → paralysis

   c. **Alcohol, sedatives, anesthetics**

      all block nerve impulses by reducing membrane permeability to ions, mainly Na+

      → No Na+ → no action potential

   **Characteristics of Action Potential**

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   **refractory period** determines how quickly a neuron can fire:

   eg. short rp can fire more rapidly than one with longer rf

   **absolute refractory period** depends on diameter of an axon:

   lg diameter → 1/2500th sec (~0.4ms)

   → up to 2500 impulses/sec

   small diameter → 1/250th sec (~4ms)

   → up to 250 impulses/sec

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d. Cold Temperature
interrupts blood flow
block delivery of oxygen and glucose to neurons
impairs their ability to conduct impulses
cold → numb

e. Continuous Pressure
interrupts blood flow as well
eg. foot goes to sleep
when relieved impulses begin
create prickly feeling

f. Drugs with general effects on Synapses:
1. Dilantin
used to treat epilepsy
epilepsy a too rapid firing of certain brain cells
subsides only when NT supply runs out
dilantin increases effectiveness of Na+ active transport to stabilize resting potential
2. Caffeine
stimulant
generally lowers threshold at synapses

provides quick transmission, no NT
but cannot integrate and make decisions
very common in embryonic brain,
much less common in adults;
get replaced by chemical synapses
eg. brain: rapid stereotyped eye movements
eg. rhythmic contractions of smooth muscle
eg. intercalated discs of cardiac muscle
chambers contract as single cells

2. Chemical Synapses
most common kind of synapse
actual gap or space between nerve cells
one direction only (= unidirectional)
prevents direct transmission of action potential
requires release of a chemical messenger
= neurotransmitter

What Happens at Chemical Synapse:
1. AP travels down axon of presynaptic neuron to axonal end bulb
2. AP causes Ca++ gates to open and Ca++ enters presynaptic neuron
3. Ca++ activates enzymes in axonal end bulb which stimulates exocytosis of neurotransmitter
   [synaptic vesicles move to surface of cell and release NT]
4. NT diffuses across synaptic cleft
5. NT binds to specific receptor molecules in membrane of postsynaptic neuron
   (dendrite or cell body)
6. causes chemical gates to open allowing some ions in
   can cause partial depolarization or hyperpolarization depending on gates
7. termination of NT occurs when:
   a. it is degraded by enzyme on postsynaptic neuron or in synapse
   b. it returns to presynaptic neuron and is reabsorbed
   c. or it diffuses away from synapse
whole process takes 0.3 – 5.0 ms
Above is general idea of what happens at a synapse
There are different kinds of chemical synapses:
1. **excitatory** → produce EPSP's
2. **inhibitory** → produce IPSP's

1. **Excitatory Synapses**

NT binding causes partial depolarization of post synaptic membrane
- Na\(^+\) and K\(^+\) ions diffuse *simultaneously* in opposite directions
- but more Na\(^+\) in than K\(^+\) out
  → **depolarization**
  → produces EPSP's

Lasts only a few milliseconds
then membrane returns to resting potential

2. **Inhibitory Synapses**

NT binding induces hyperpolarization of membrane:
- becomes more permeable to K\(^+\) (out)
  and/or more permeable to Cl\(^-\) (in)
  → **hyperpolarization**
  → produces IPSP's

Remember, each postsynaptic neuron may synapse with 10,000's of presynaptic neurons (=neuronal pools)
some of these synapses are **excitatory**
some are **inhibitory**

**Summation:**
- **Temporal summation**
  1 or more neurons transmit impulses in rapid sequence

- **Spatial summation**
  large # of terminals are stimulated at the same time
  → axonal hillock acts as a "bean counter"
  it totals all the effects
  may or may not trigger AP

**Potentiation:**
can also get **potentiation** (facilitation)
→ doesn't fire but easier to fire next time.

Finally, there are literally 100's of different kinds of neurotransmitters;
some excitatory,
some inhibitory
bind to specific receptors in specific parts of nervous system
can produce a variety of effects on post synaptic neurons
also can get various additional modifications of

**Reflex Activity**

many of the body’s control systems occur at the most basic functional level of neural activity
→ **reflexes**

**reflex** = a rapid, automatic, predictable motor response to a stimulus
unlearned
unplanned
involuntary
→ “hard wired” into our neural anatomy

reflexes can be categorized according to effectors involved:

**somatic reflexes**
→ involve skeletal muscles
we are aware of them (after the fact)
eg. **stretch reflex**
  knee-jerk reflex
  hitting patellar ligament stimulates muscle spindle
  → pulls quadriceps
  → afferent impulses [L- L+]
  → efferent impulse \[
  → contraction of quadriceps

eg. **withdrawal reflex**
  touching hot skillet
  pain receptors in skin
  effectors cause us to pull away from heat

eg. **deep tendon reflex**
  crossed extensor reflex
autonomic (visceral) reflexes
→ nonconscious
usually no awareness;
most internal homeostatic mechanisms
eg. blood pressure, heart rate,
vasodilation, etc
or by nerves of PNS that transmit the signal:

cranial reflexes
→ reflexes that involve cranial nerves

spinal reflexes
→ reflexes that involve spinal nerves

some more complex “reflexes” are learned
involve more complex circuits in several areas of
the brain
eg. riding bike, driving skills, swimming
piano or musical instruments
gymnastics, etc

reflex arc = simplest functional circuit in
nervous system

components of a reflex arc:
receptor
sensory neuron
integration center (CNS)
single or multiple synapses
motor neuron
effector

very few complete neural circuits are simple reflexes
remember each neuron synapses with 10,000 other
neurons
neuronal pools
complex circuits
serial circuits
parallel circuits

serial circuits
= input travels along a specific pathway to a
specific destination
whole circuit works “all-or-none”
eg. spinal reflexes → specific stimulus
always causes the same motor
response

parallel circuits
= inputs are segregated into many different
pathways
information is delivered by each pathway
and dealt with simultaneously
eg. "smelling a pickle”
→sensation
→like/dislike
→remember to buy some
→memory of pickles
→think of your grandmother, whom your
grandfather called “pickles”

Diseases of Nervous Tissue

1. Multiple Sclerosis
autoimmune disease possibly triggered by a virus in genetically
susceptible individuals
oligodendrocytes and myelin sheaths of CNS deteriorate and are
replaced by hardened scar tissue
occur esp between 20–40 yrs of age
nerve fibers are severed
& myelin sheaths in CNS are gradually destroyed
→ short circuits; loss of impulse conduction
affects mostly young adults
common symptoms:
visual problems
muscle weakness
clumsiness
eventual paralysis

2. Tay-Sachs Disease
hereditary disorder seen mainly in infants of Eastern European
Jewish ancestry
abnormal accumulation of a certain glycolipid (GM₂)in myelin
sheath
as it accumulates it disrupts conduction of signals
results in blindness, loss of coordination, dementia
symptoms appear before 1 yr of age, death by 3 or 4