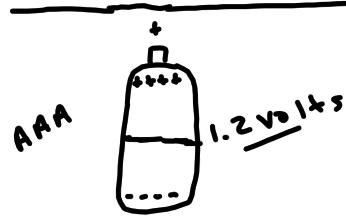
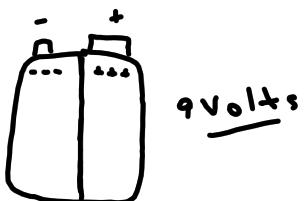


Voltage = Potential



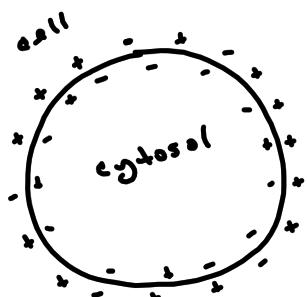
1.2 Volts



9 Volts

separation of
charge generates
voltage

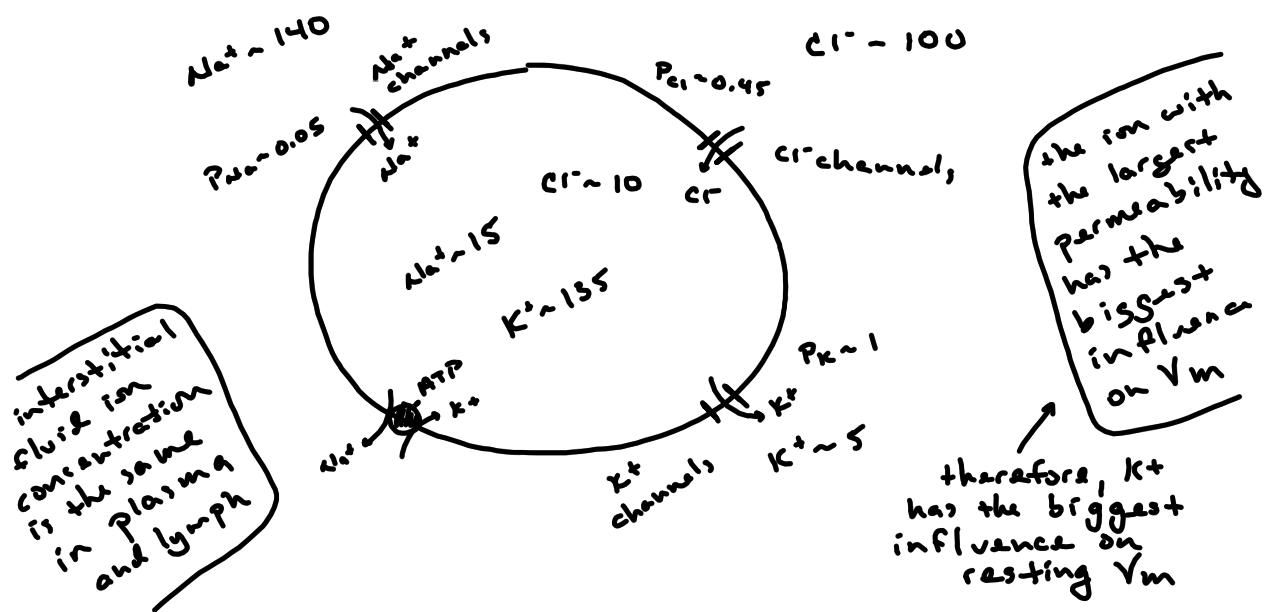
interstitial
fluid

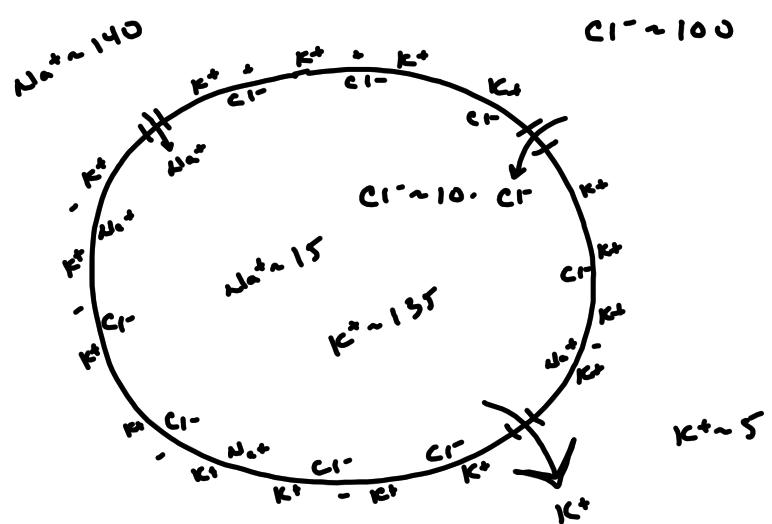


just the
charge on
either side
of the
membrane
that
generates
Vm

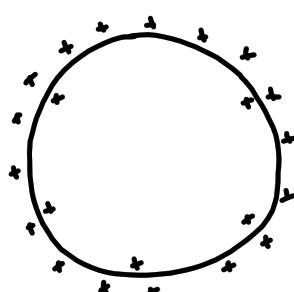
cell membrane
separates charge
and generates
membrane potential
(Vm)
Vm measured
in mV

Resting Membrane Potential



Resting Vm

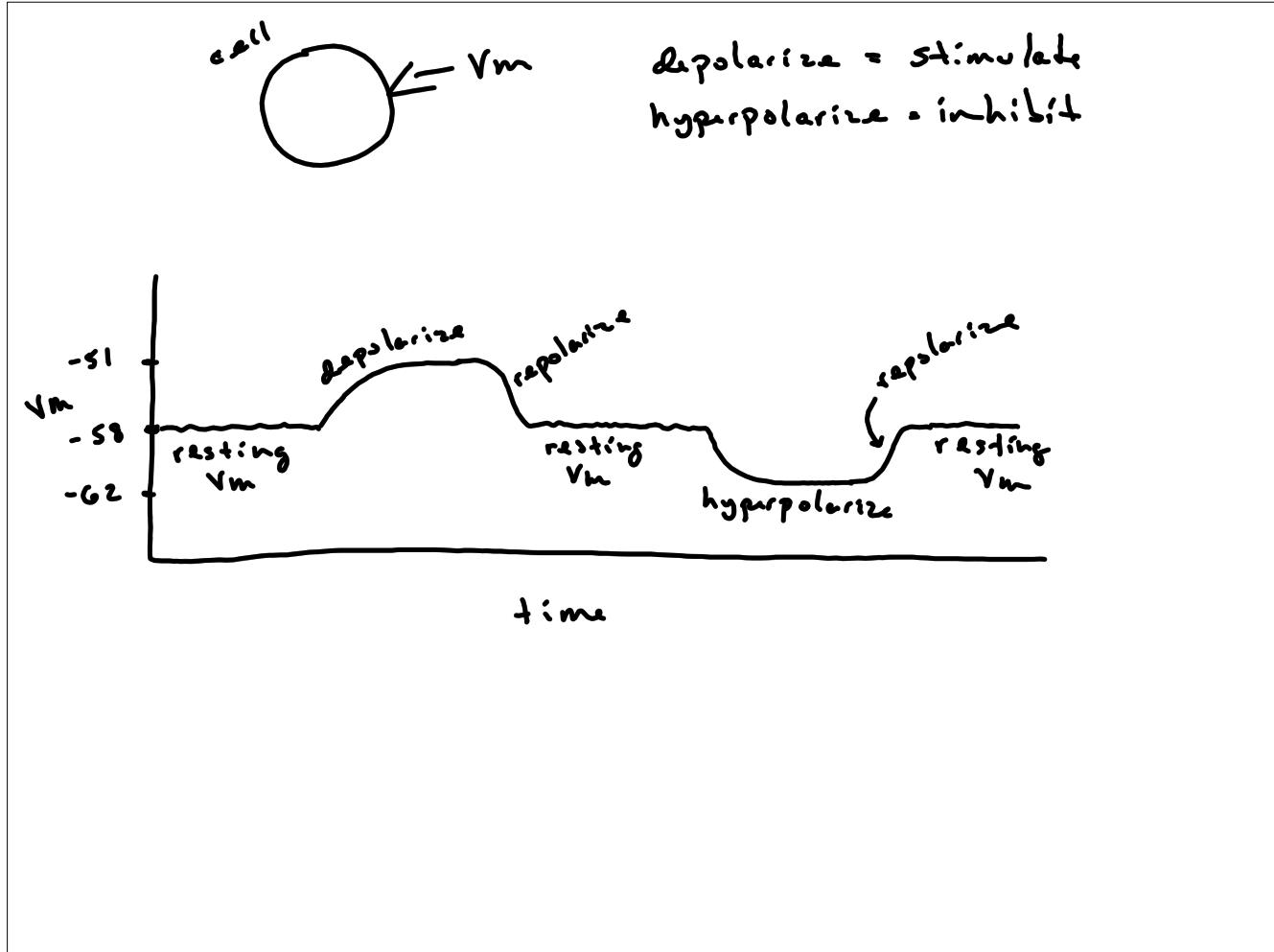
Resting V_m is negative



outer membrane is
more positive than
the inner membrane

∴ inner membrane
is more neg than
the outer membrane

resting V_m is anywhere from
 -40 mV to -90 mV



* How is V_m changed?

↳ change the transport of ions

* How is ion transport changed?

↳ change [ion] gradient

- \uparrow [ion] gradient \rightarrow \uparrow transport

- \downarrow [ion] gradient \rightarrow \downarrow transport

↳ change ion permeability

- \uparrow ion permeability \rightarrow \uparrow transport

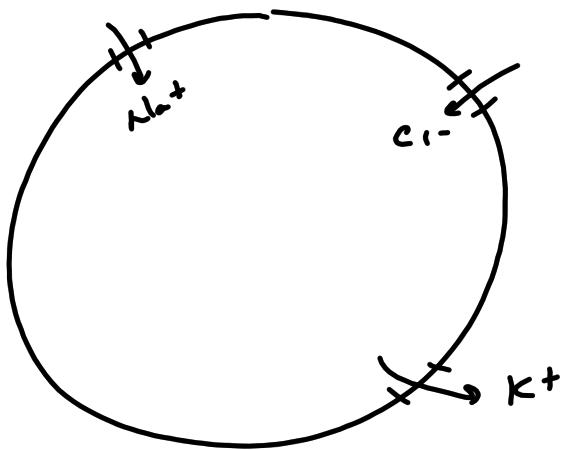
↳ open more ion channels

↳ have more ion channels

- \downarrow ion permeability \rightarrow \downarrow transport

↳ close ion channels

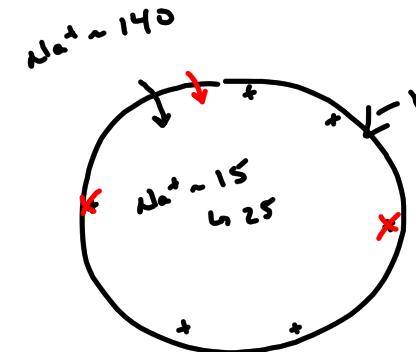
↳ less ion channels



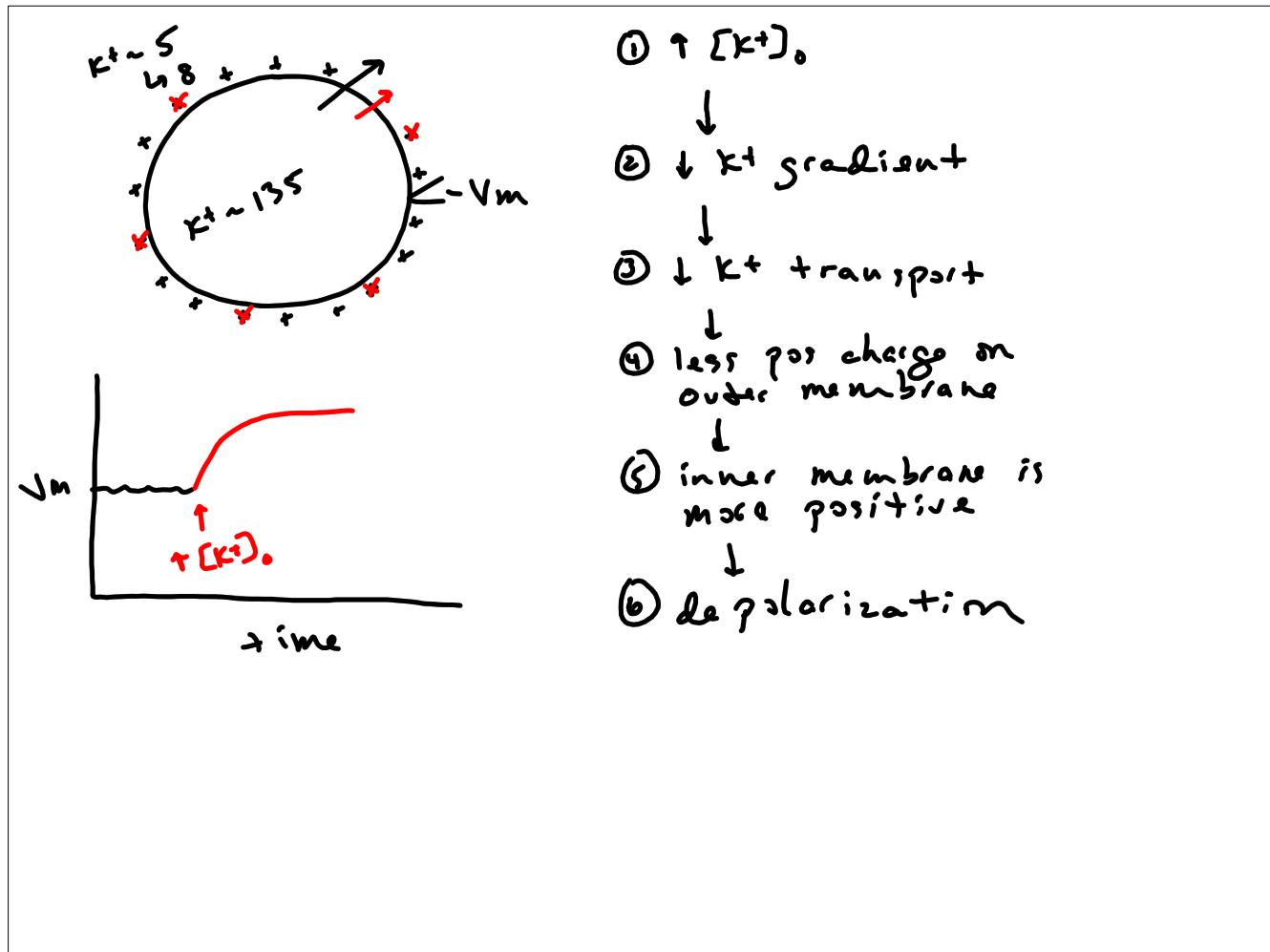
- * If $\uparrow \text{Na}^+$ transport
 - \hookrightarrow more pos charge on inner membrane
 - \hookrightarrow depolarization
- * If $\downarrow \text{Na}^+$ transport
 - \hookrightarrow less pos charge on inner membrane
 - \hookrightarrow hyperpolarization

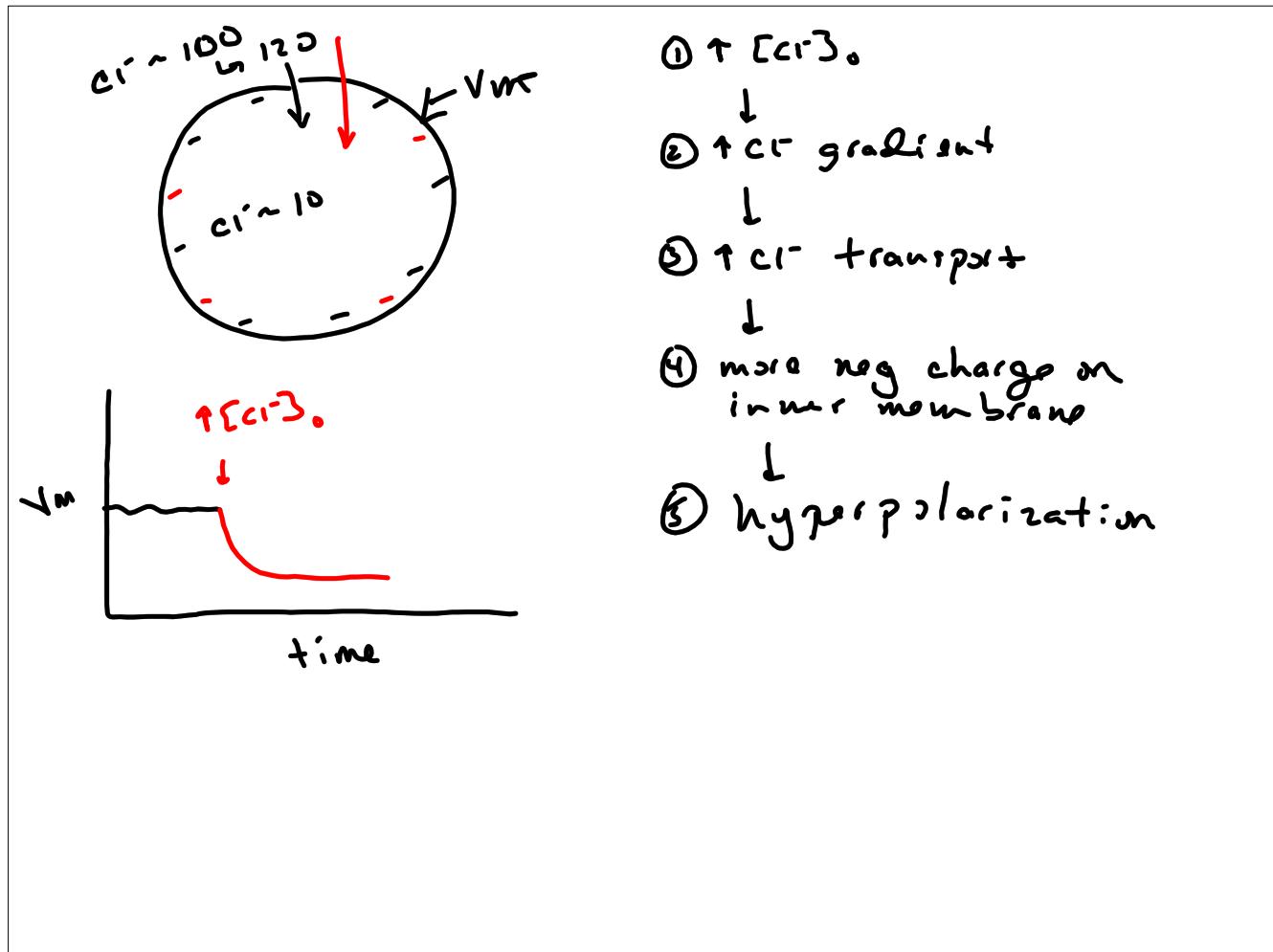
- * If $\uparrow \text{Cl}^-$ transport
 - \hookrightarrow more neg charge on inner membrane
 - \hookrightarrow hyperpolarization
- * If $\downarrow \text{Cl}^-$ transport
 - \hookrightarrow less neg charge on inner membrane
 - \hookrightarrow depolarization

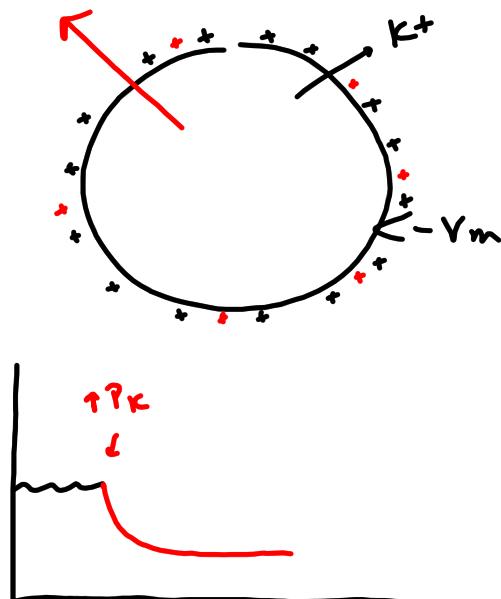
- * If ↑ K^+ transport
 - ↳ more pos charge on outer membrane
 - ↳ outer membrane is more pos
 - ∴ inner membrane is more neg
 - ↑ hyperpolarization
- * If ↓ K^+ transport
 - ↳ less pos charge on outer membrane
 - ↳ outer membrane is less positive
 - ∴ inner membrane is more pos
 - ↑ depolarization



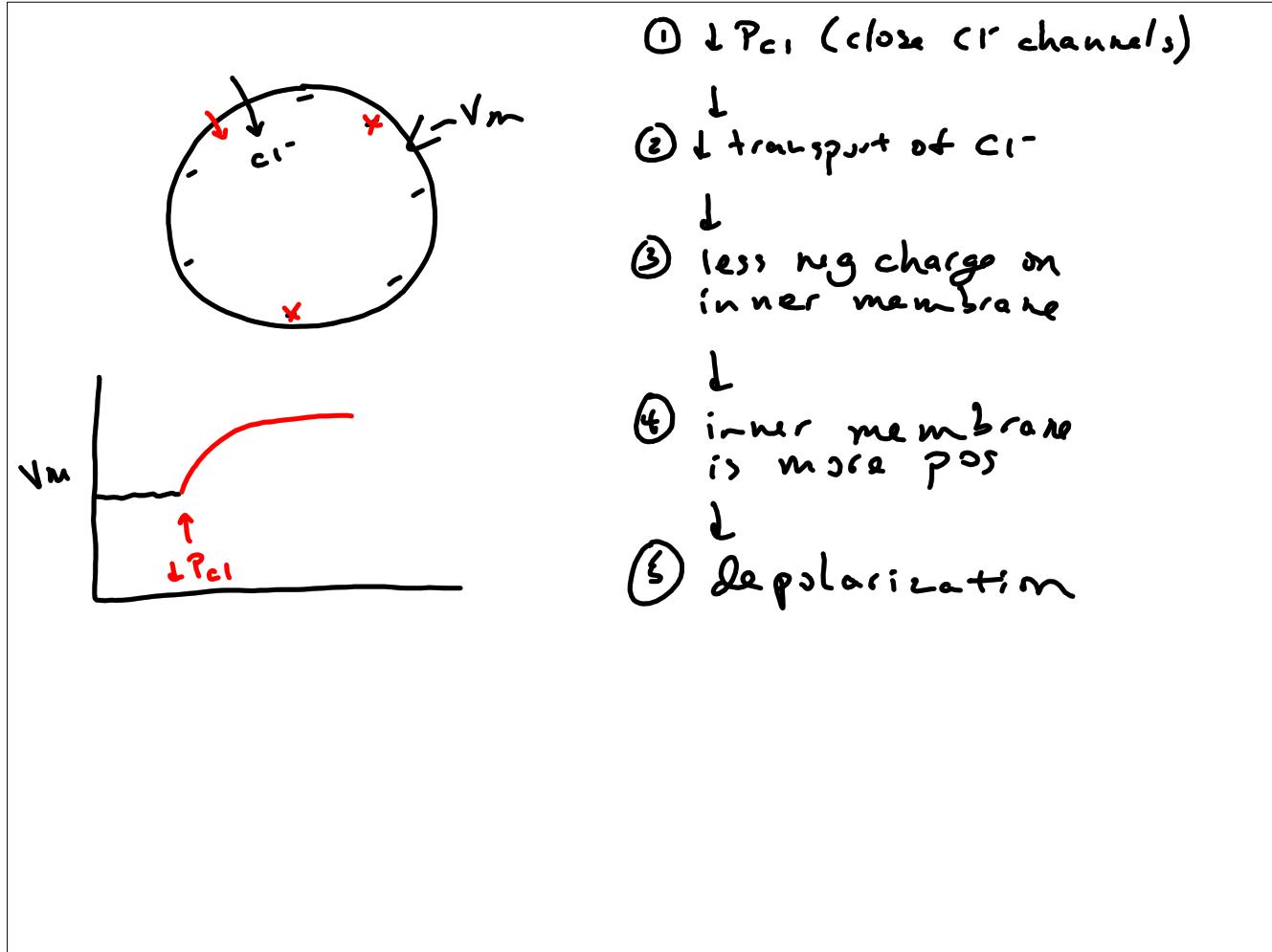
- ① $\uparrow [\text{Na}^+]_i$
↓
- ② ↓ Net gradient
↓
- ③ ↓ Na^+ transport
↓
- ④ less pos charge on
the inner membrane
↓
- ⑤ hyperpolarization

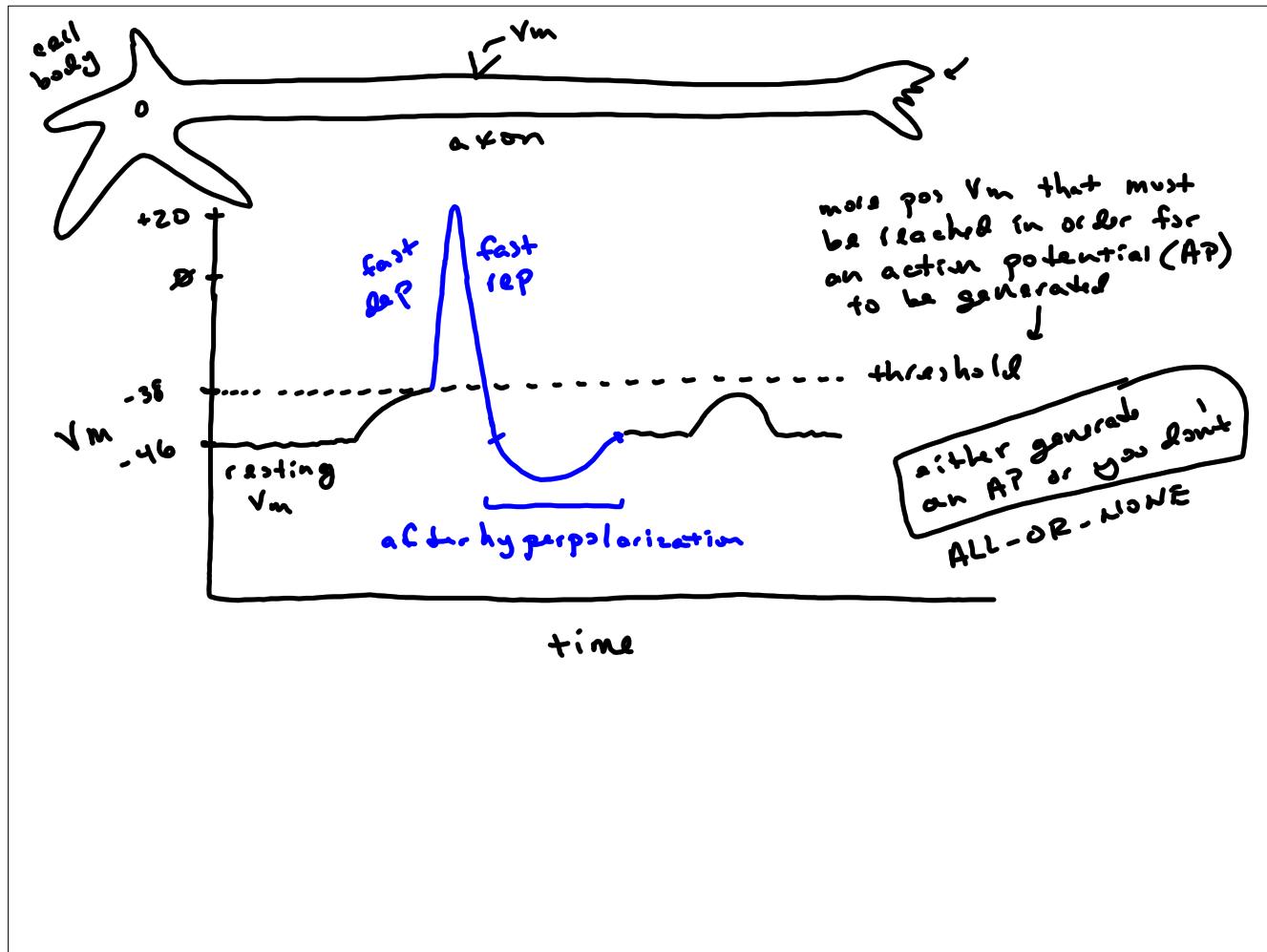


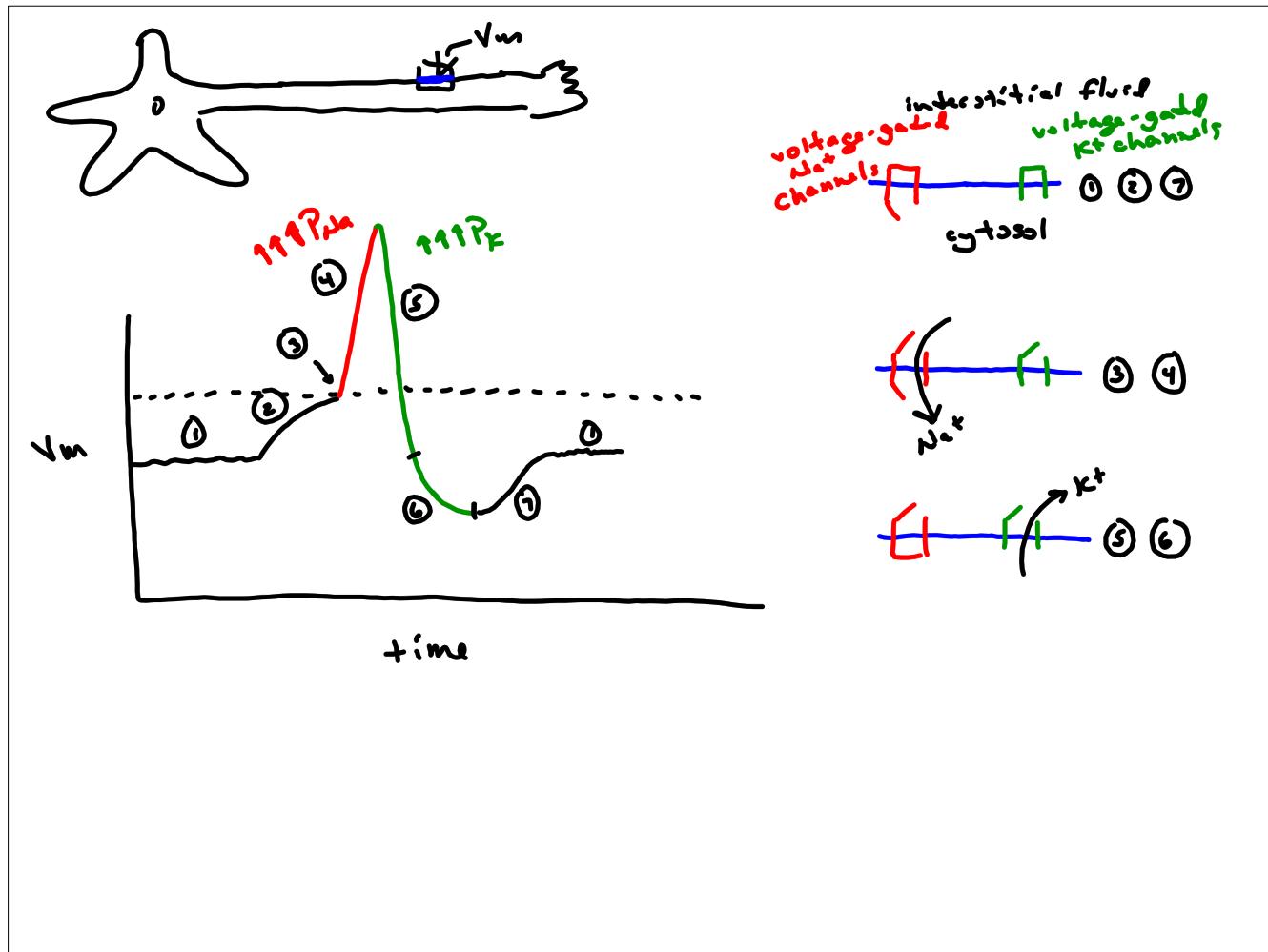


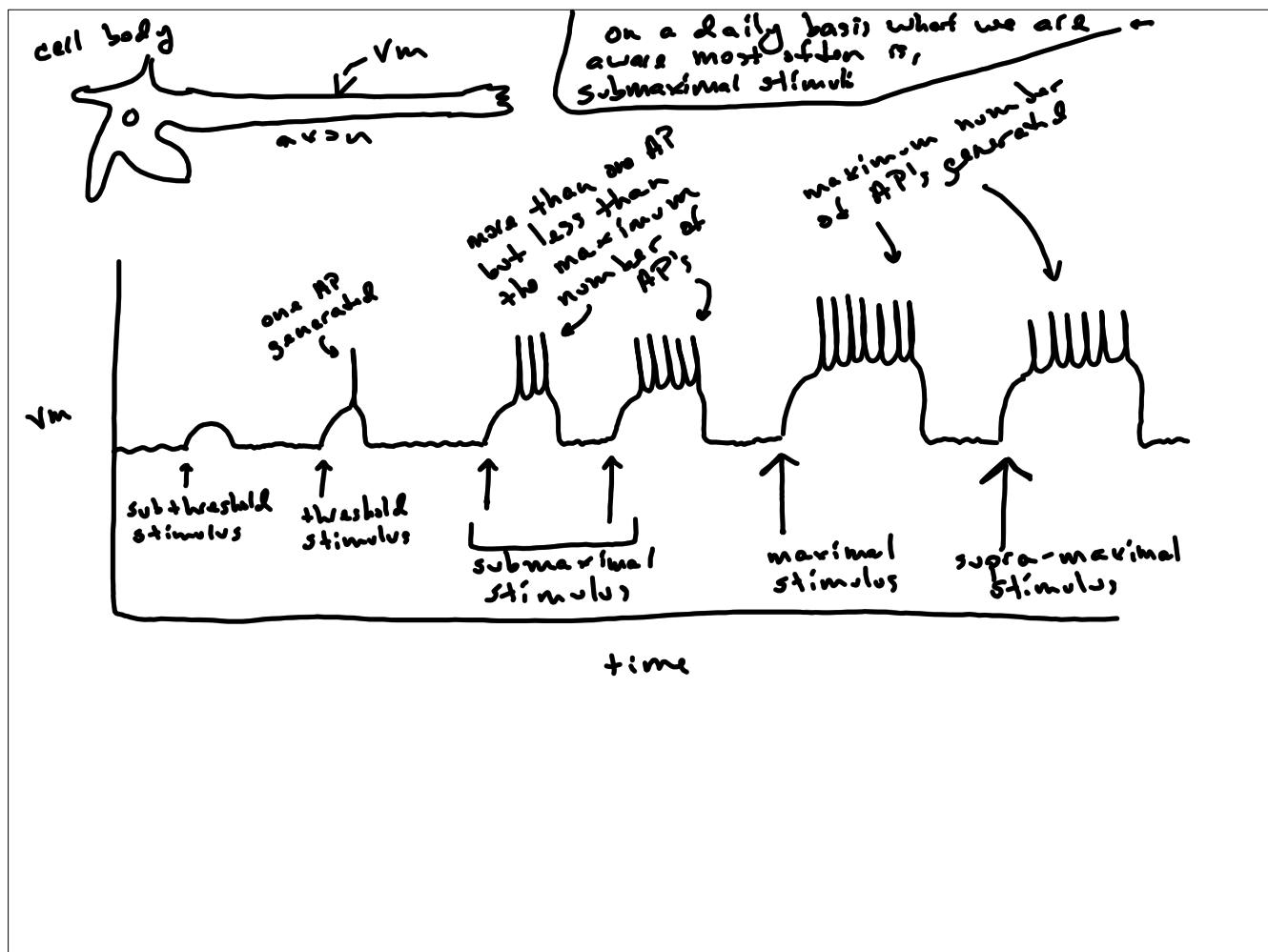


- ① $\uparrow P_K$ (open more K^+ channels)
- ↓
- ② \uparrow transport of K^+
- ↓
- ③ more pos charge on outer membrane
- ↓
- ④ inner membrane more neg
- ↓
- ⑤ hyperpolarization



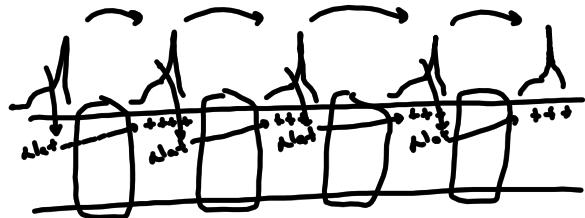








- * continuous conduction
 - ↳ unmyelinated axons
 - ↳ muscle cells
- * conduction velocity
 - < 2 meters/sec

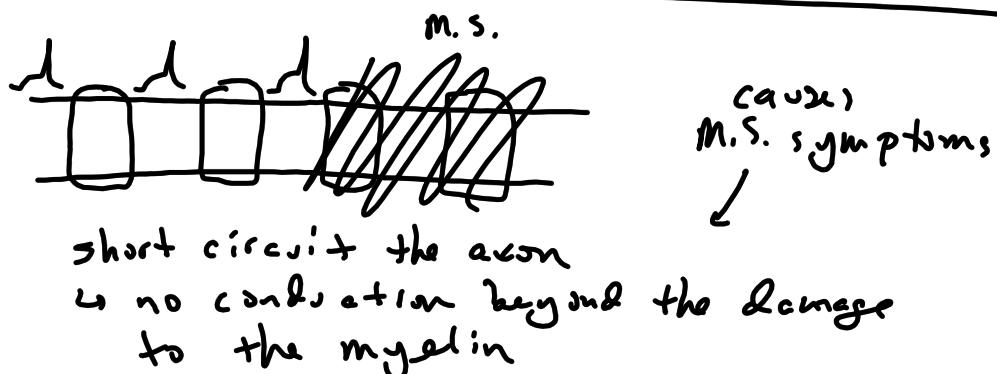


no voltage-gated channels where the myelin is
+ voltage-gated channels solely at nodes of Ranvier

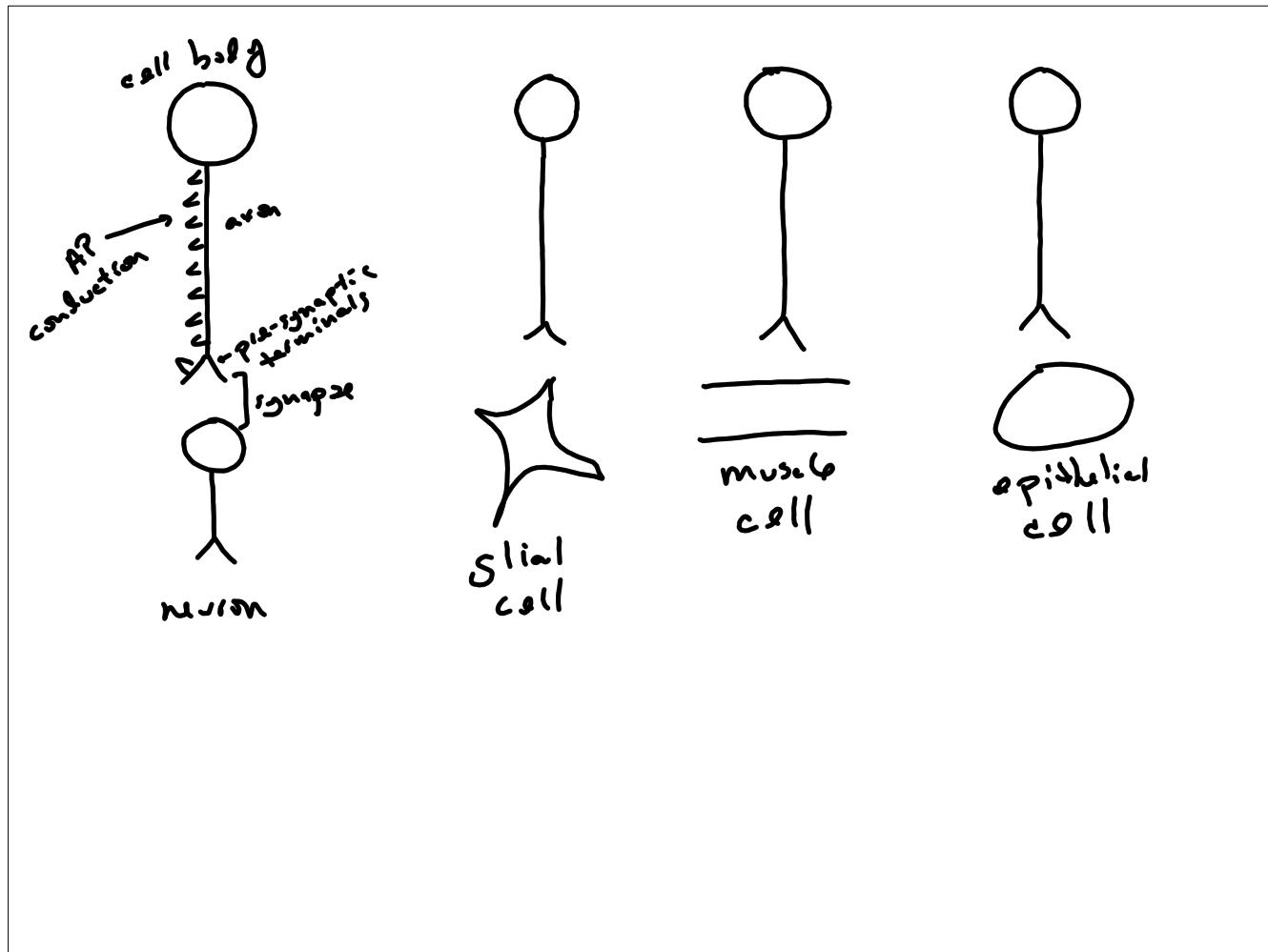
- * Saltatory conduction
 - solely in myelinated axons
 - 3 to 120 meters/sec

* Why is saltatory faster than continuous?

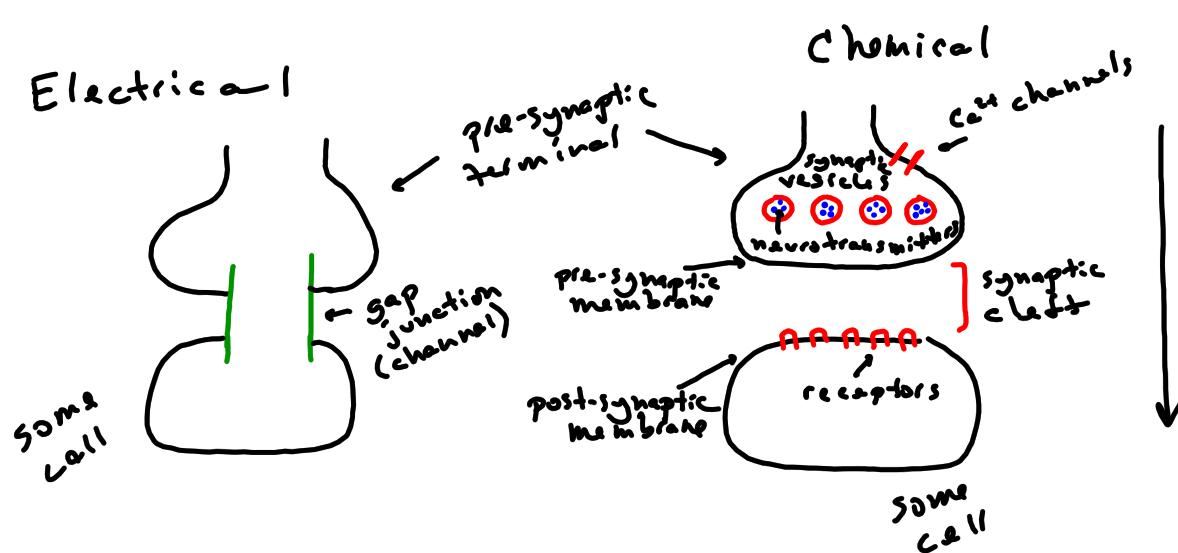
↳ less AP's need to be generated
over the same distance

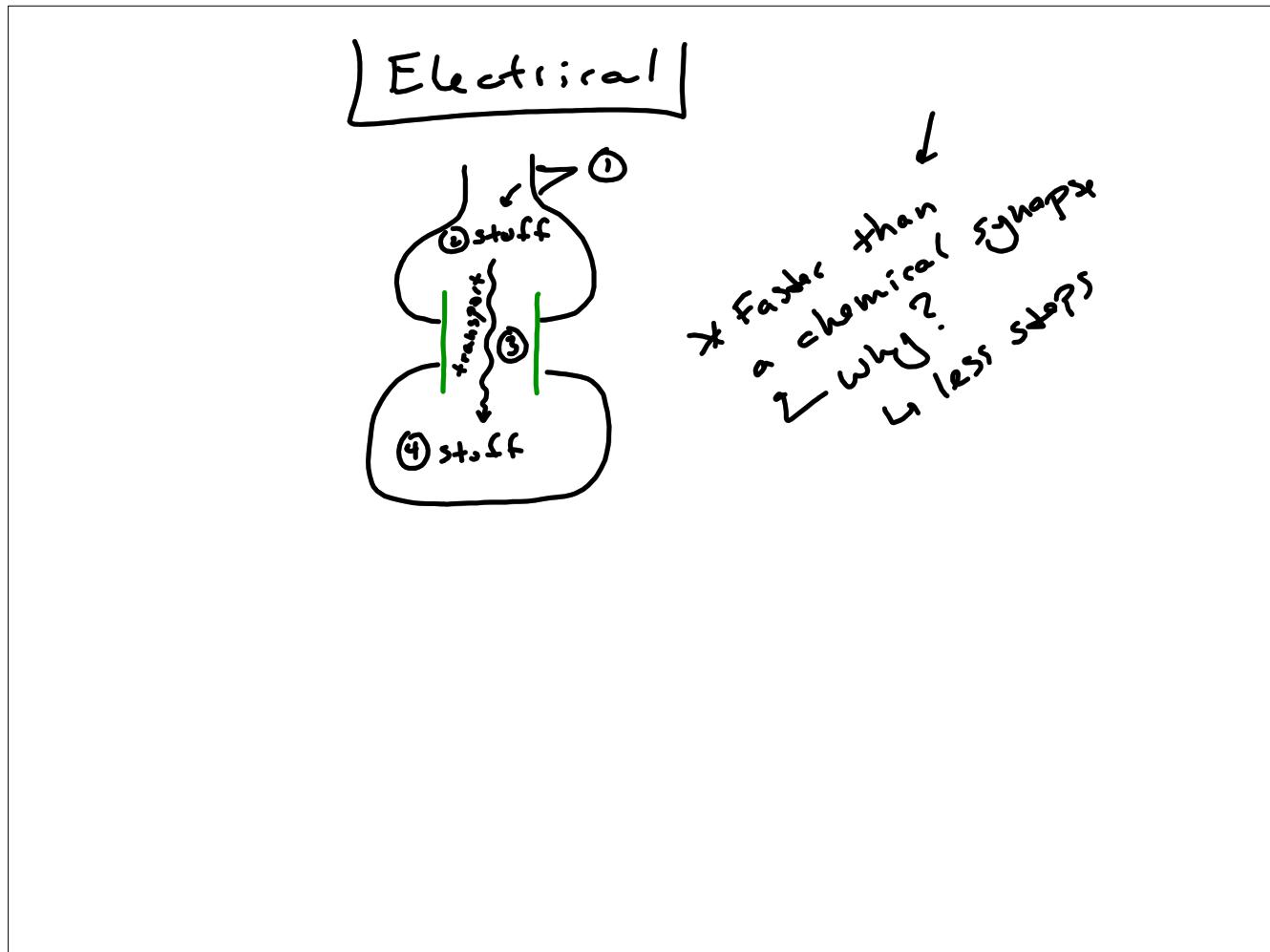


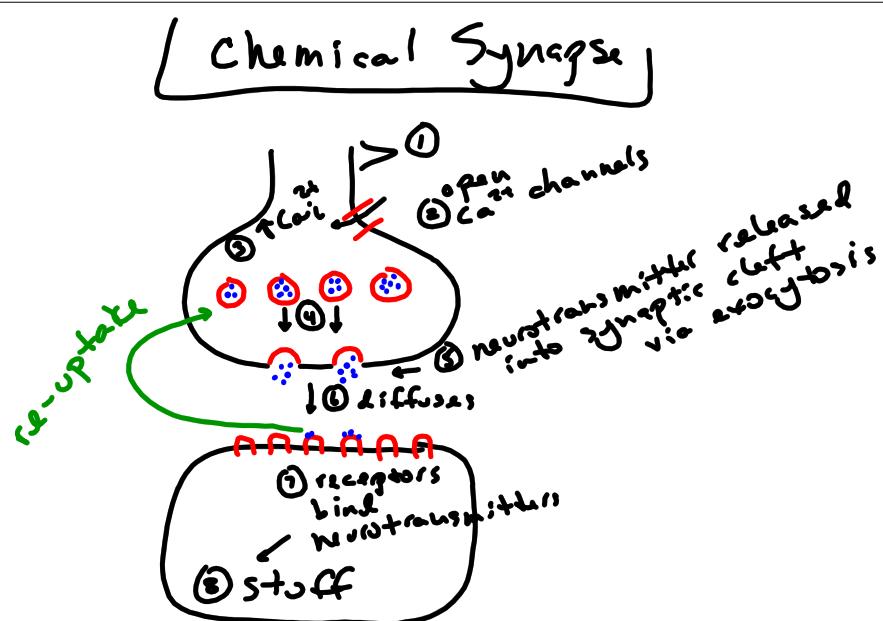
causes
M.S. symptoms

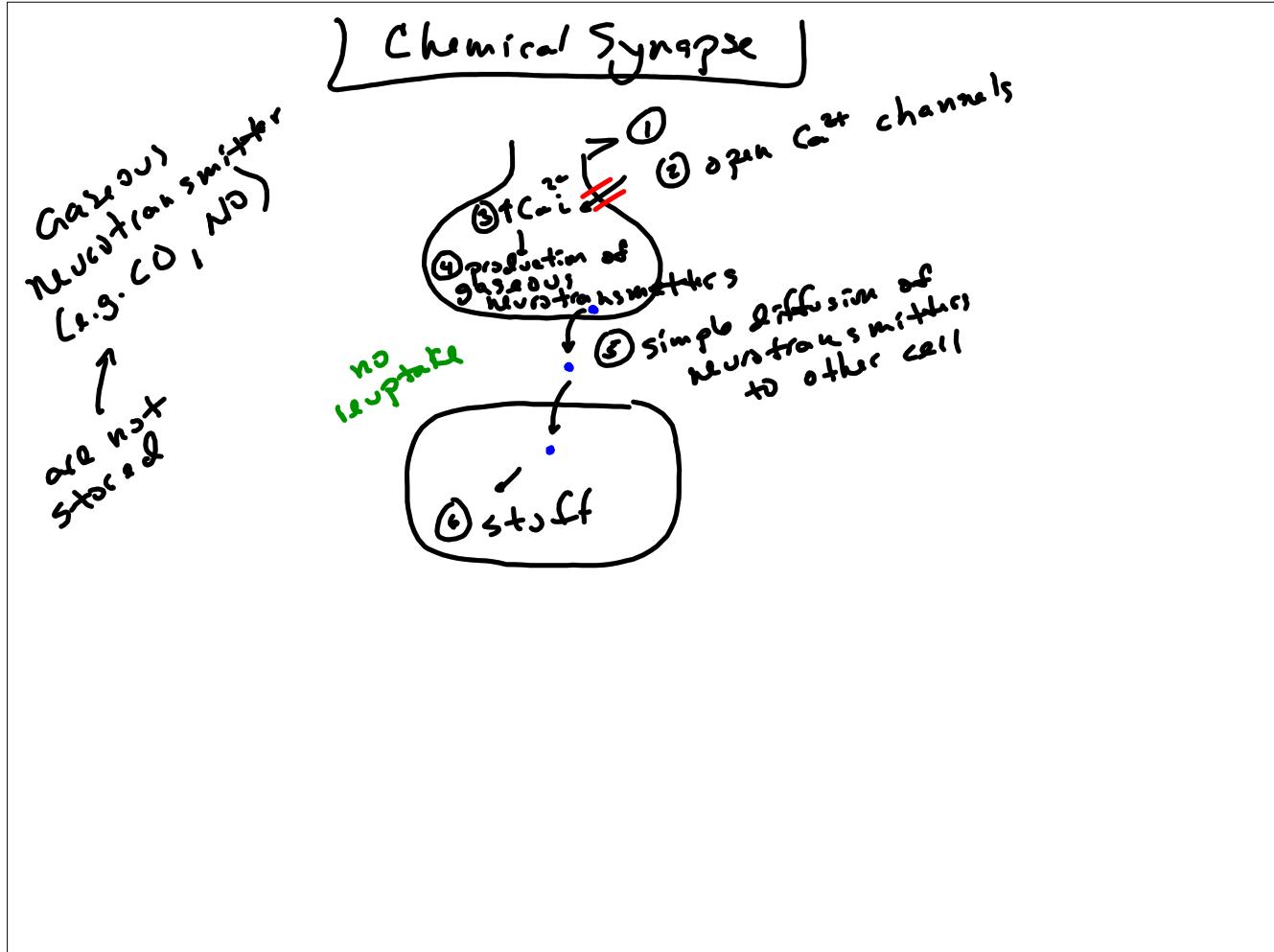


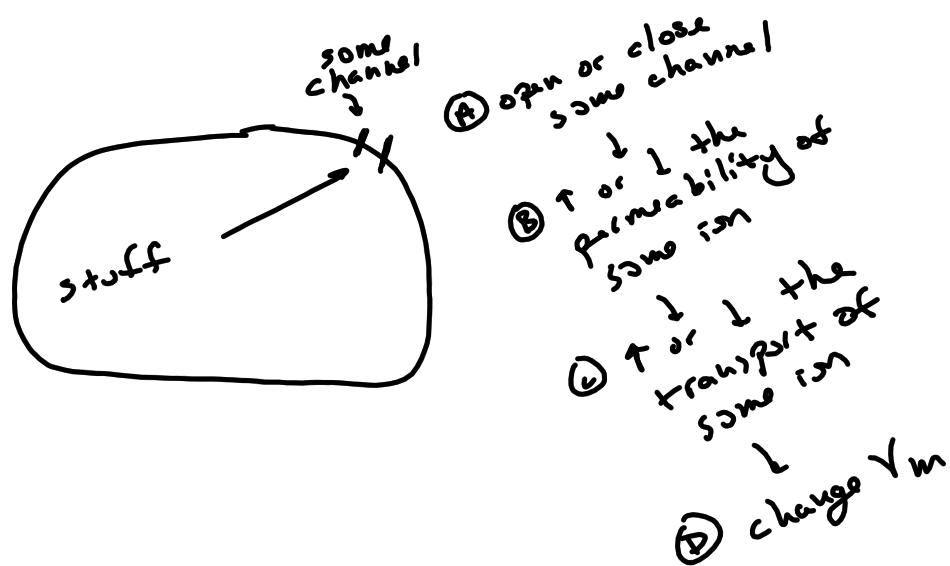
2-types of synapses









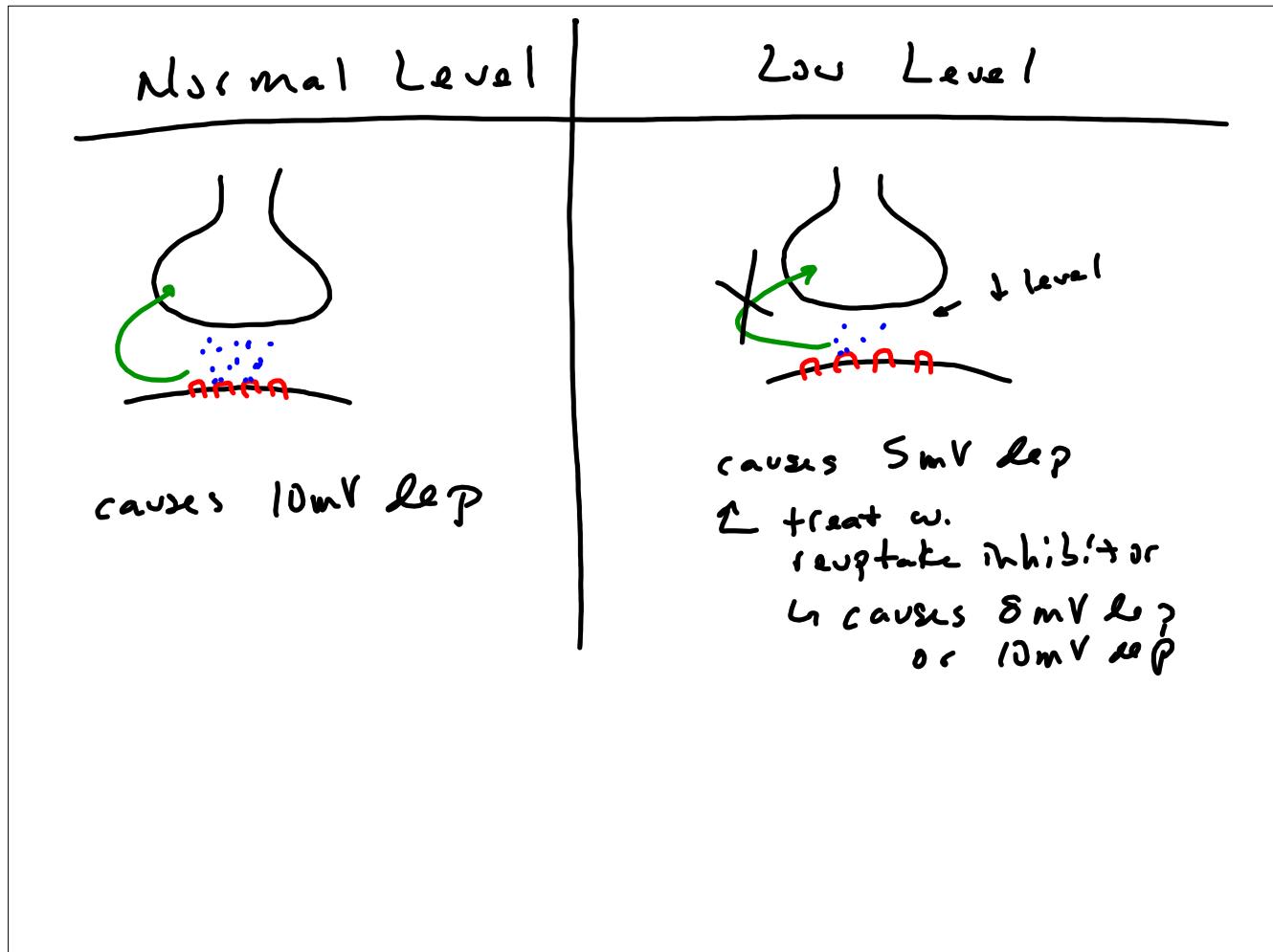


* Reuptake Inhibitor

↳ inhibits the transport (re-uptake) of neurotransmitter into pre-synaptic terminal

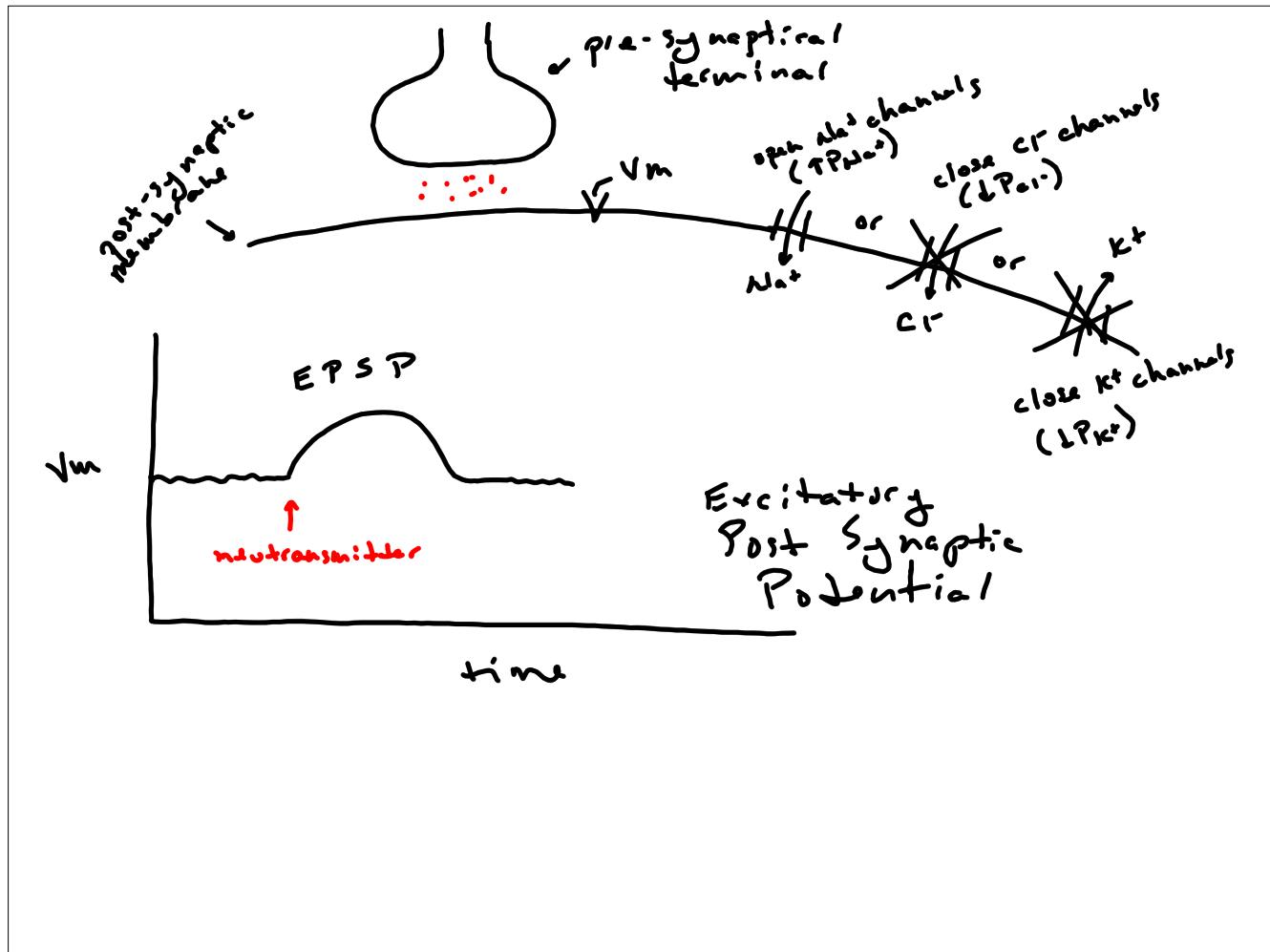
↳ why prescribed?

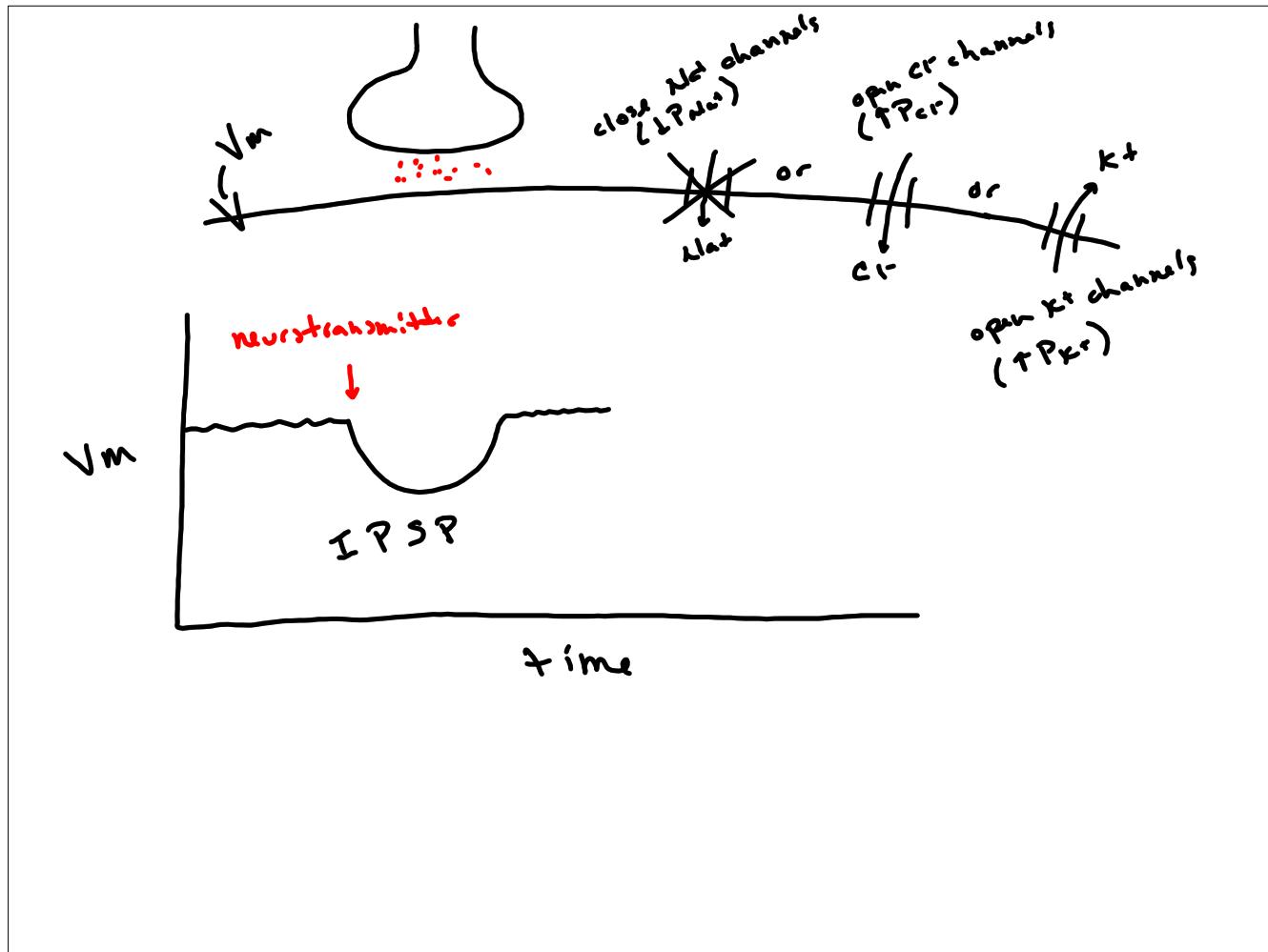
↳ when the level of neurotransmitter is too low



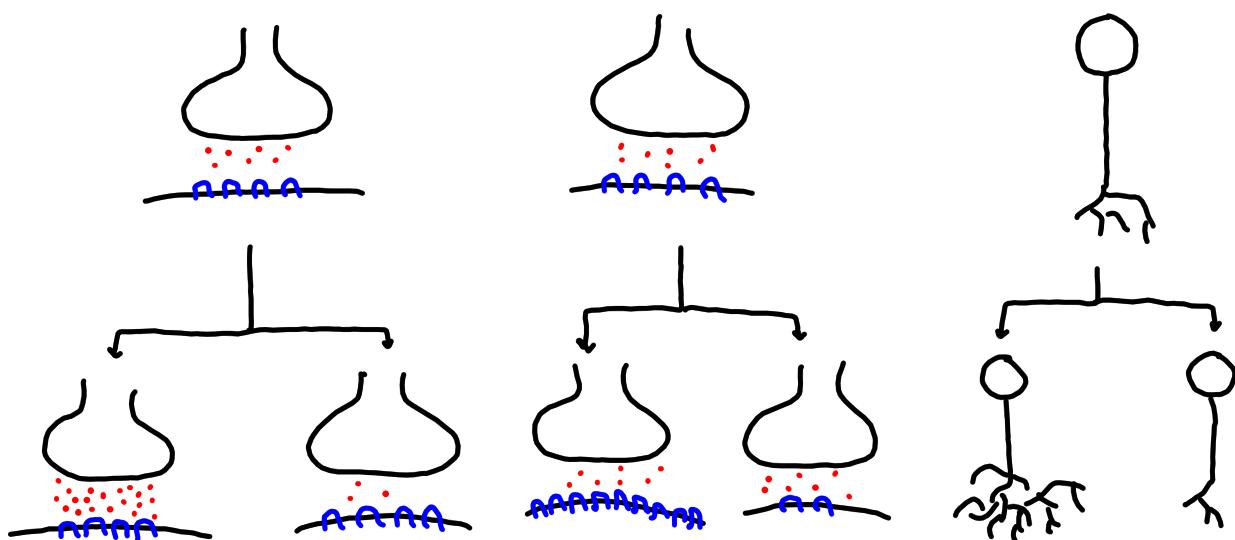
* Reuptake inhibitor

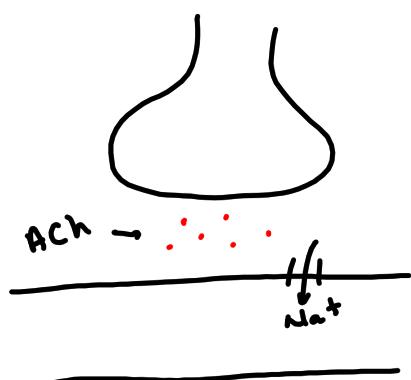
- ↳ cause neurotransmitter to stay in synaptic cleft longer
- ↳ receptors are activated longer
 - ↳ change in permeability occurs for a longer period of time
 - ↳ bigger change in ion transport
 - ↳ bigger change in V_m





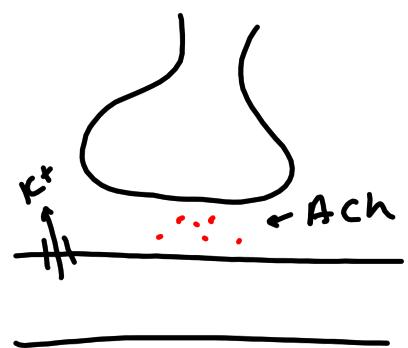
Synaptic Plasticity





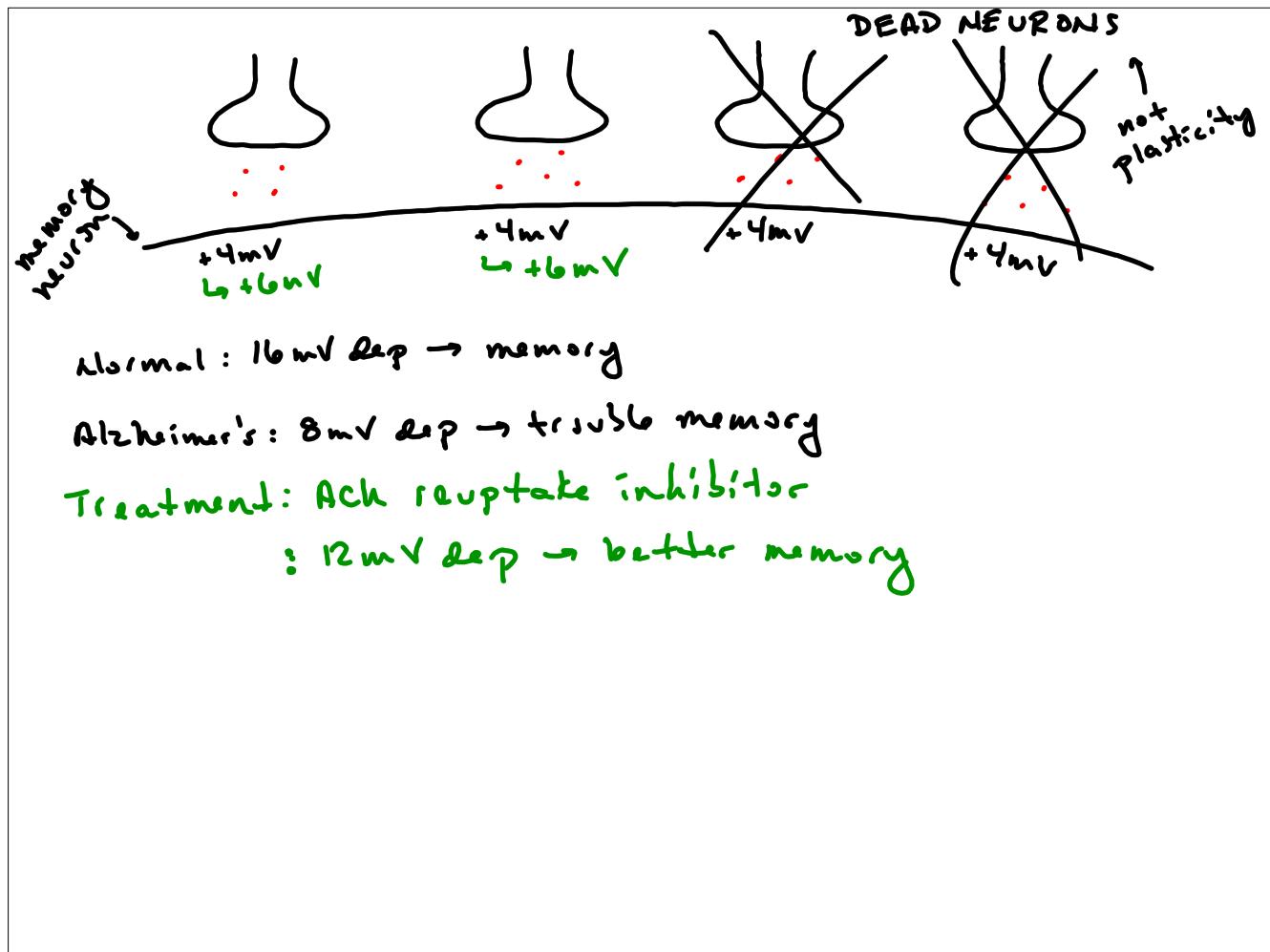
skeletal muscle cell

Excitatory



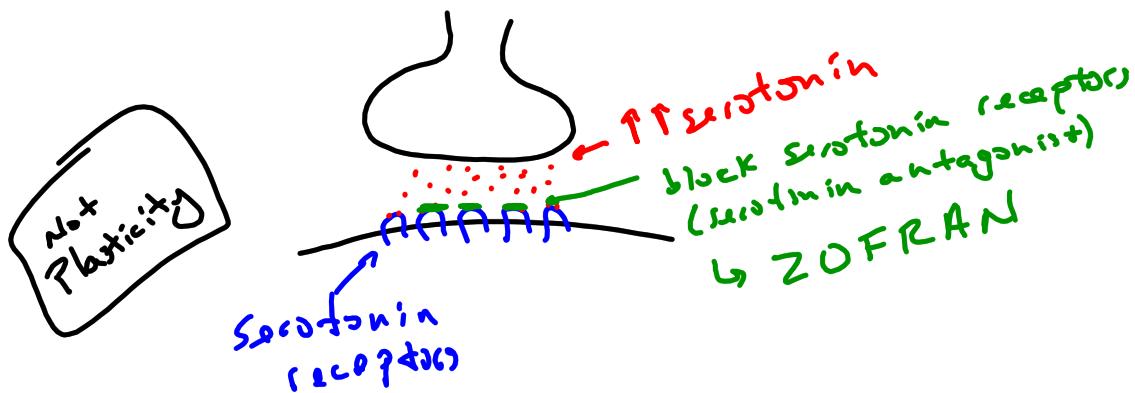
cardiac muscle cell

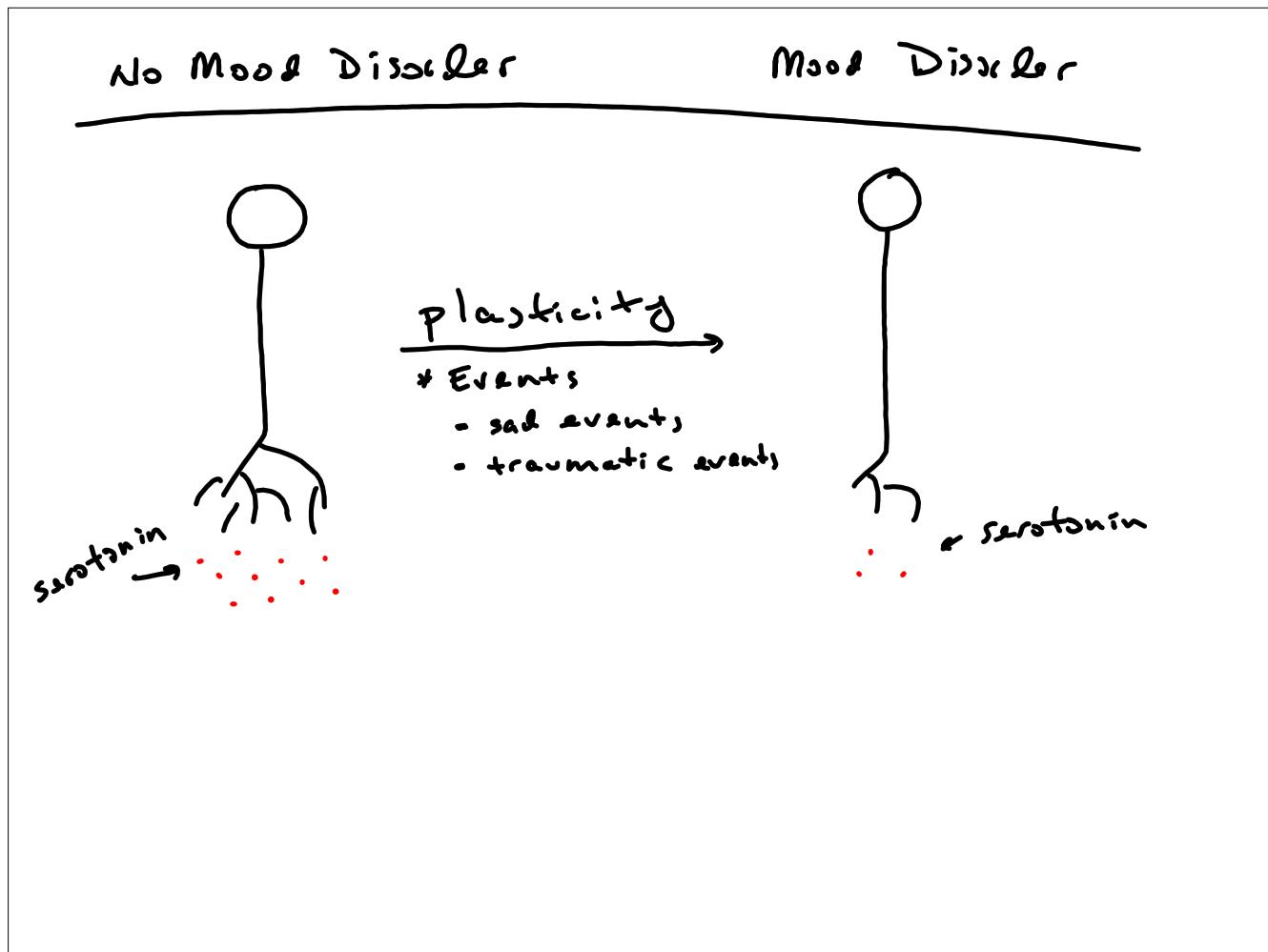
Inhibitory



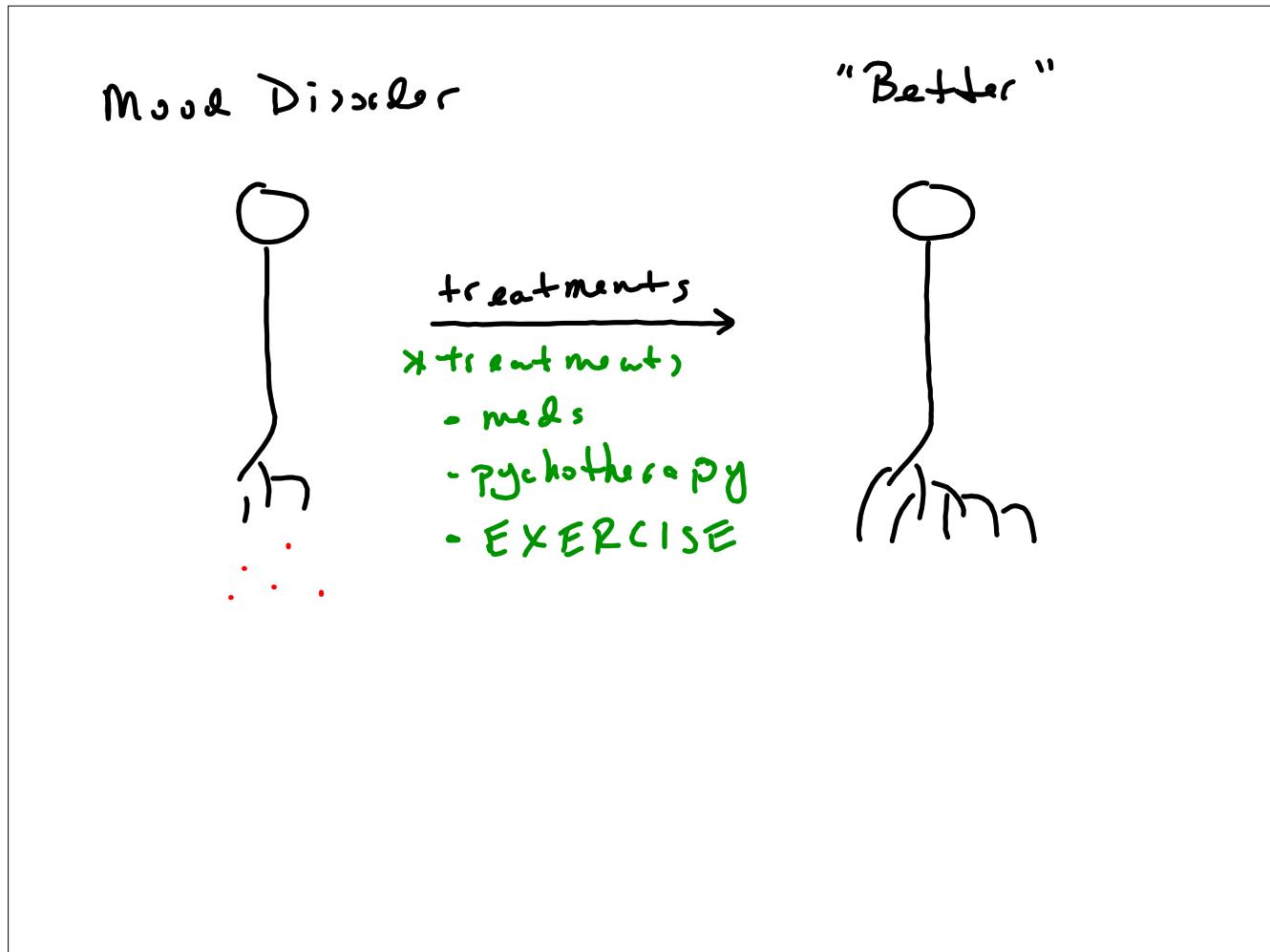
* when one feels nauseated

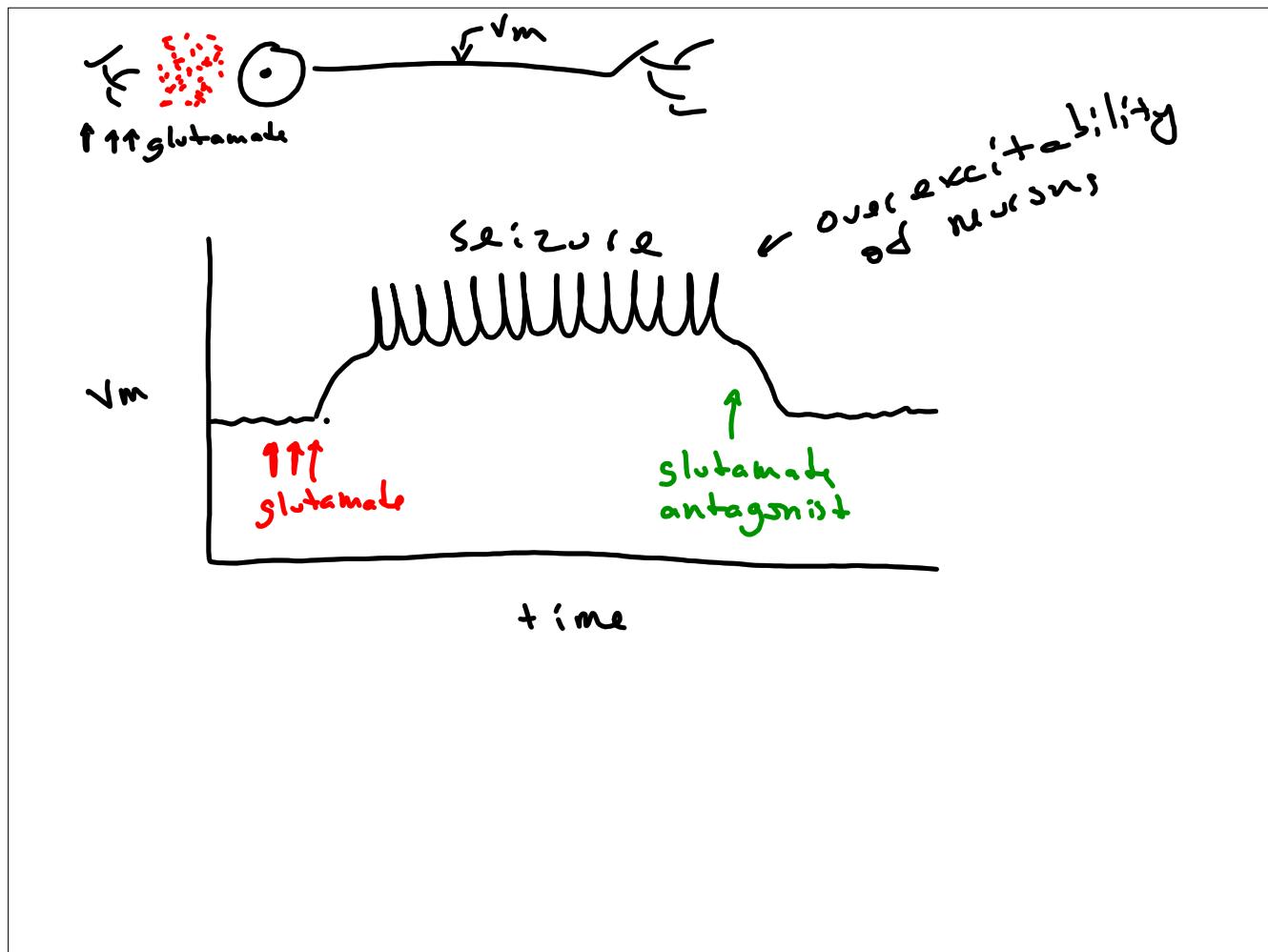
↳ due to ↑ serotonin in
the vomiting center of brain





- ✗ Sadness → hyperpolarize neurons
 - ↳ ↓ AP's
 - ↳ ↓ serotonin release
- ✗ Happy → depolarize neurons
 - ↳ ↑ AP's
 - ↳ ↑ serotonin release

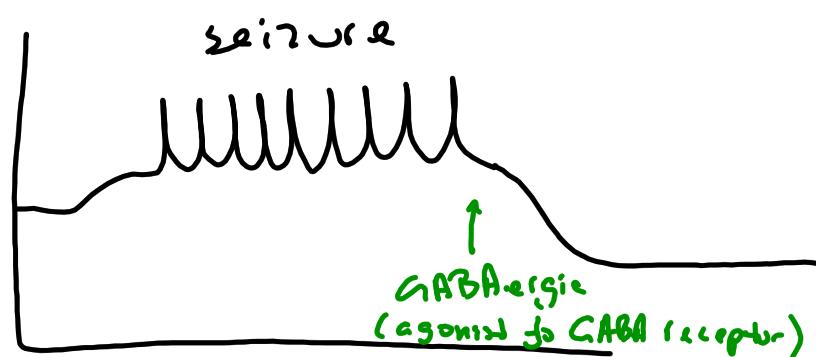


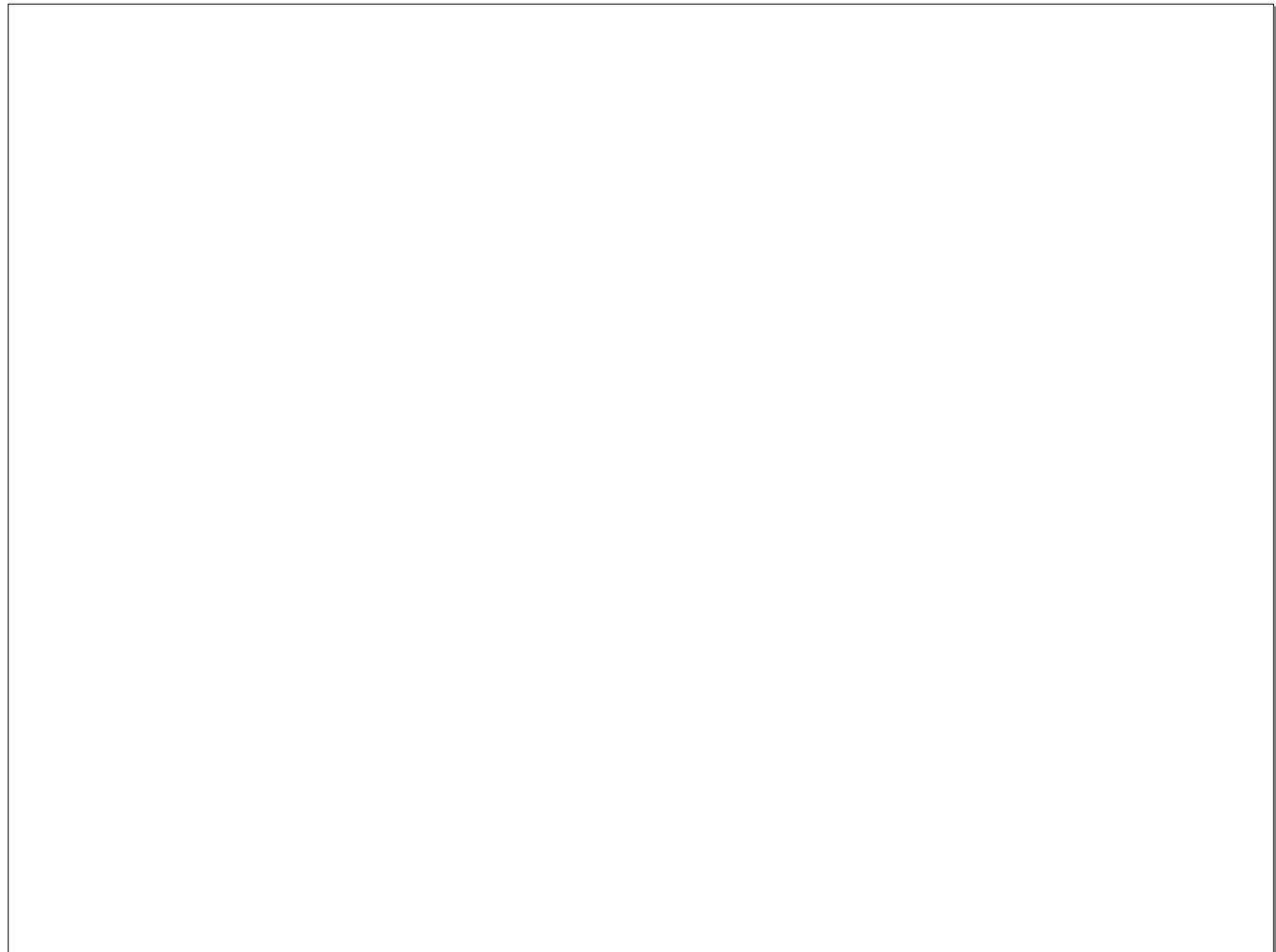


when neurons are over-excited
that can cause them to die

Neuronal degeneration

ALS (Lou Gehrig's Disease)



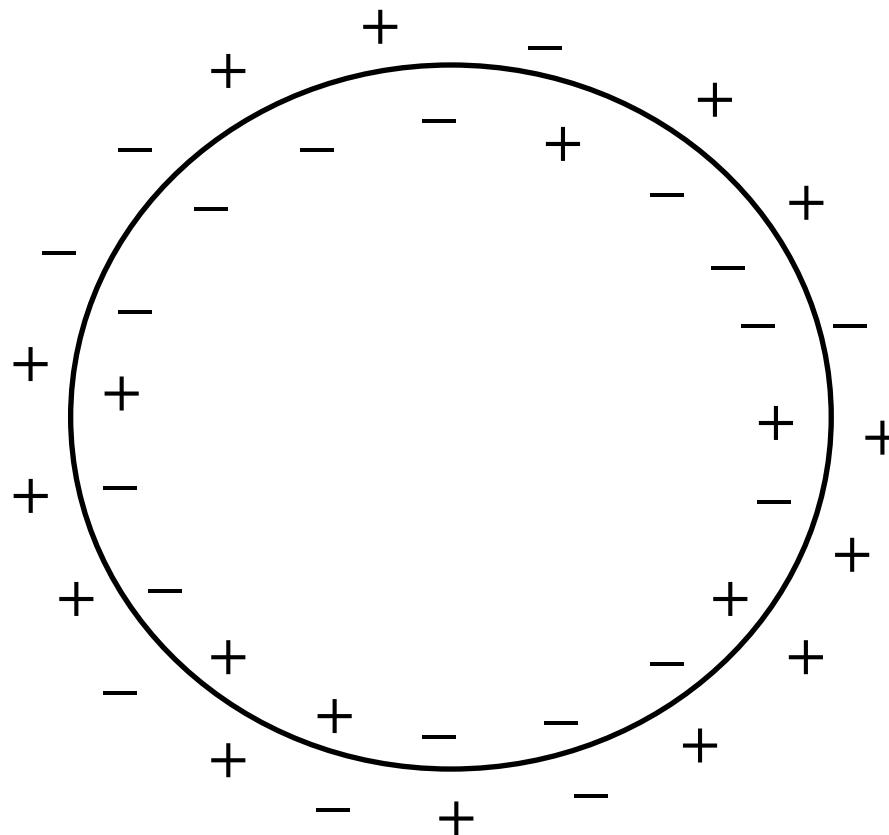


Membrane Potential (V_m)

Voltage (i.e. potential) generated via the difference between negative and positive charges lining the inner membrane and lining the outer membrane of cells
Measured value based on inner membrane charges relative to outer membrane charges

Measured in **millivolts (mV)**

All cells have a V_m



Resting Membrane Potential

V_m of a cell when it is not being stimulated or inhibited

Influenced mainly by the distribution of potassium

Small influence by the distribution of other ions (such as sodium and chloride)

Small influence by proteins (which have negative charge) lining inner membrane

Potassium (K^+)

$[K]_i$ (intracellular potassium concentration): ~135 mEq / L

$[K]_o$ (extracellular potassium concentration): ~ 5 mEq / L

P_K (permeability of potassium): 1.0 (value at rest)

Reason K^+ plays the biggest role in determining resting V_m

Sodium (Na^+)

$[Na]_i$ (intracellular sodium concentration): ~ 15 mEq / L

$[Na]_o$ (extracellular sodium concentration): ~ 140 mEq / L

P_{Na} (permeability of sodium): 0.05 (value at rest)

Chloride (Cl^-)

$[Cl]_i$ (intracellular chloride concentration): ~ 10 mEq / L

$[Cl]_o$ (extracellular chloride concentration): ~ 100 mEq / L

P_{Cl} (permeability of chloride): 0.45 (value at rest)

Na^+ and K^+ concentration gradients maintained by the Na^+/K^+ pump

The Na^+/K^+ pump IS NOT RESPONSIBLE FOR RESTING V_m

Many books, websites, teachers, profs etc. will tell you it is

They are ALL WRONG (tell them I said that)

Cl^- concentration gradient maintained as well

V_m is Dictated by Two Main Factors

- 1) Magnitude of the concentration gradients of ions*
- 2) Permeabilities of the membrane to ions*

The concentration gradients and permeabilities create an environment that dictates the relative movements of ions, which ultimately establishes V_m

Establishing Resting V_m

Passive transport of ions primarily establishes resting V_m

K^+ is transported out of the cell during resting conditions

At resting V_m , permeability of K^+ is the largest

Very large amount of positive charge on outer membrane

Therefore, K^+ has the greatest influence on resting V_m

Na^+ is transported into the cell during resting conditions

At resting V_m , permeability of Na^+ is small

Small amount of positive charge on inner membrane

Cl^- is transported into the cell during resting conditions

At resting V_m , permeability of Cl^- is large

Large amount of negative charge on inner membrane

Predicting V_m with Goldman-Hodgkin-Katz (GHK) equation

$$V_m = \frac{RT}{F} \ln \frac{P_K [K]_o + P_{Na} [Na]_o + P_{Cl} [Cl]_i}{P_K [K]_i + P_{Na} [Na]_i + P_{Cl} [Cl]_o}$$



Using the average values for Na^+ , K^+ and Cl^- at rest

Resting V_m would be approximately -65mV

However, V_m can vary wildly

This is due to varying concentrations permeabilities

$[Na]_i$ (intracellular sodium concentration): ~15 mEq / L

$[Na]_o$ (extracellular sodium concentration): ~ 145 mEq / L

P_{Na} (relative permeability of sodium): 0.05

$[K]_i$ (intracellular potassium concentration): ~135 mEq / L

$[K]_o$ (extracellular potassium concentration): ~ 5 mEq / L

P_K (relative permeability of potassium): 1.0

$[Cl]_i$ (intracellular chloride concentration): ~ 8 mEq / L

$[Cl]_o$ (extracellular chloride concentration): ~ 110 mEq / L

P_{Cl} (relative permeability of chloride): 0.45

Equilibrium Potential (E_x) of an Ion

Membrane potential in which there is no net movement of an ion

Electrical driving force balances chemical driving force

Electrical driving force on an ion

Positively charged ions attracted to negative charge

Positively charged ions repulsed by positive charge

Negatively charged ions attracted to positive charge

Negatively charged ions repulsed by negative charge

Chemical driving force on an ion

Passive movement of ions down a concentration gradient

Nernst Equation

Calculates the equilibrium potential (i.e. Nernst potential) of an ion

$$E_x = \frac{RT}{zF} \ln \frac{[X]_o}{[X]_i}$$

X is the ion of interest

$$E_{Na} \approx +60 \text{ mV}$$

∴ no net movement of Na^+ at a V_m of +60mV

$$E_K \approx -90 \text{ mV}$$

∴ no net movement of K^+ at a V_m of -90mV

$$E_{Cl} \approx -70 \text{ mV}$$

∴ no net movement of Cl^- at a V_m of -70mV

Ions move passively towards their equilibrium potential

The more permeable an ion the closer the V_m will be to the E_x of that ion

If a cell is permeable to only one ion, V_m will be equal to the E_x of that ion

How does V_m change (i.e. how does V_m get more positive or get more negative)?



Change the transport of ions

How does ion transport change?



Two ways:

- 1) Change the concentration gradient of ions
- 2) Change the permeability of ions

Depolarize: V_m becomes more positive

Hyperpolarize: V_m becomes more negative

Repolarize: V_m returns towards resting V_m after a change in V_m

Membrane Potential Changes

Depolarize: V_m becomes more positive

Inner membrane becomes either more positive or less negative

Outer membrane becomes either less positive or more negative

Hyperpolarize: V_m becomes more negative

Inner membrane becomes either more negative or less positive

Outer membrane becomes either more positive or less negative

Repolarize: V_m returns towards resting V_m after a change in V_m

Effect of Changing the Concentration Gradients of Na^+ , K^+ or Cl^- on V_m

Increase extracellular Na^+ : causes a depolarization

Predicted by GHK equation

Increases the gradient for Na^+ to leak into the cell

More Na^+ leaks into cell (more positive charge on inner membrane)

Increase extracellular K^+ : causes a depolarization

Predicted by GHK equation

Decreases the gradient for K^+ to leak out of the cell

Less K^+ leaks out of cell (less positive charge on outer membrane)

Increase extracellular Cl^- : causes a hyperpolarization

Predicted by GHK equation

Increases the gradient for Cl^- to leak into the cell

More Cl^- leaks into cell (more negative charge on inner membrane)

Decrease extracellular Na^+ : causes a hyperpolarization

Predicted by GHK equation

Decreases the gradient for Na^+ to leak into the cell

Less Na^+ leaks into cell (less positive charge on inner membrane)

Decrease extracellular K^+ : causes a hyperpolarization

Predicted by GHK equation

Increases the gradient for K^+ to leak out of the cell

More K^+ leaks out of cell (more positive charge on outer membrane)

Decrease extracellular Cl^- : causes a depolarization

Predicted by GHK equation

Decreases the gradient for Cl^- to leak into the cell

Less Cl^- leaks into cell (less negative charge on inner membrane)

Increase intracellular Na^+ : causes a hyperpolarization

Predicted by GHK equation

Decreases the gradient for Na^+ to leak into the cell

Less Na^+ leaks into cell (less positive charge on inner membrane)

Increase intracellular K^+ : causes a hyperpolarization

Predicted by GHK equation

Increases the gradient for K^+ to leak out of the cell

More K^+ leaks out of cell (more positive charge on outer membrane)

Increase intracellular Cl^- : causes a depolarization

Predicted by GHK equation

Decreases the gradient for Cl^- to leak into the cell

Less Cl^- leaks into the cell (less negative charge on inner membrane)

Decrease intracellular Na^+ : causes a depolarization

Predicted by GHK equation

Increases the gradient for Na^+ to leak into the cell

More Na^+ leaks into cell (more positive charge on inner membrane)

Decrease intracellular K^+ : causes a depolarization

Predicted by GHK equation

Decreases the gradient for K^+ to leak out of the cell

Less K^+ leaks out of cell (less positive charge on outer membrane)

Decrease intracellular Cl^- : causes a hyperpolarization

Predicted by GHK equation

Increases the gradient for Cl^- to leak into the cell

More Cl^- leaks into cell (more negative charge on inner membrane)

Effect of changing the permeability of Na^+ , K^+ or Cl^- on V_m

Increase the permeability of Na^+ : causes a depolarization

 Increase the transport of Na^+ into the cell

 More positive charge on inner membrane

Decrease the permeability of Na^+ : causes a hyperpolarization

 Decrease the transport of Na^+ into the cell

 Less positive charge on inner membrane

Increase the permeability of K^+ : causes a hyperpolarization

 Increase the transport of K^+ out of the cell

 More positive charge on outer membrane

Decrease the permeability of K^+ : causes a depolarization

 Decrease the transport of K^+ out of the cell

 Less positive charge on outer membrane

Increase the permeability of Cl^- : causes a hyperpolarization

 Increase the transport of Cl^- into the cell

 More negative charge on inner membrane

Decrease the permeability of Cl^- : causes a depolarization

 Decrease the transport of Cl^- into the cell

 Less negative charge on inner membrane

Action Potential

Local, very large and very rapid depolarization followed by repolarization

Only a handful of cells generate action potentials

e.g. neurons and muscle cells

Threshold

Depolarized V_m that must be reached to generate an action potential

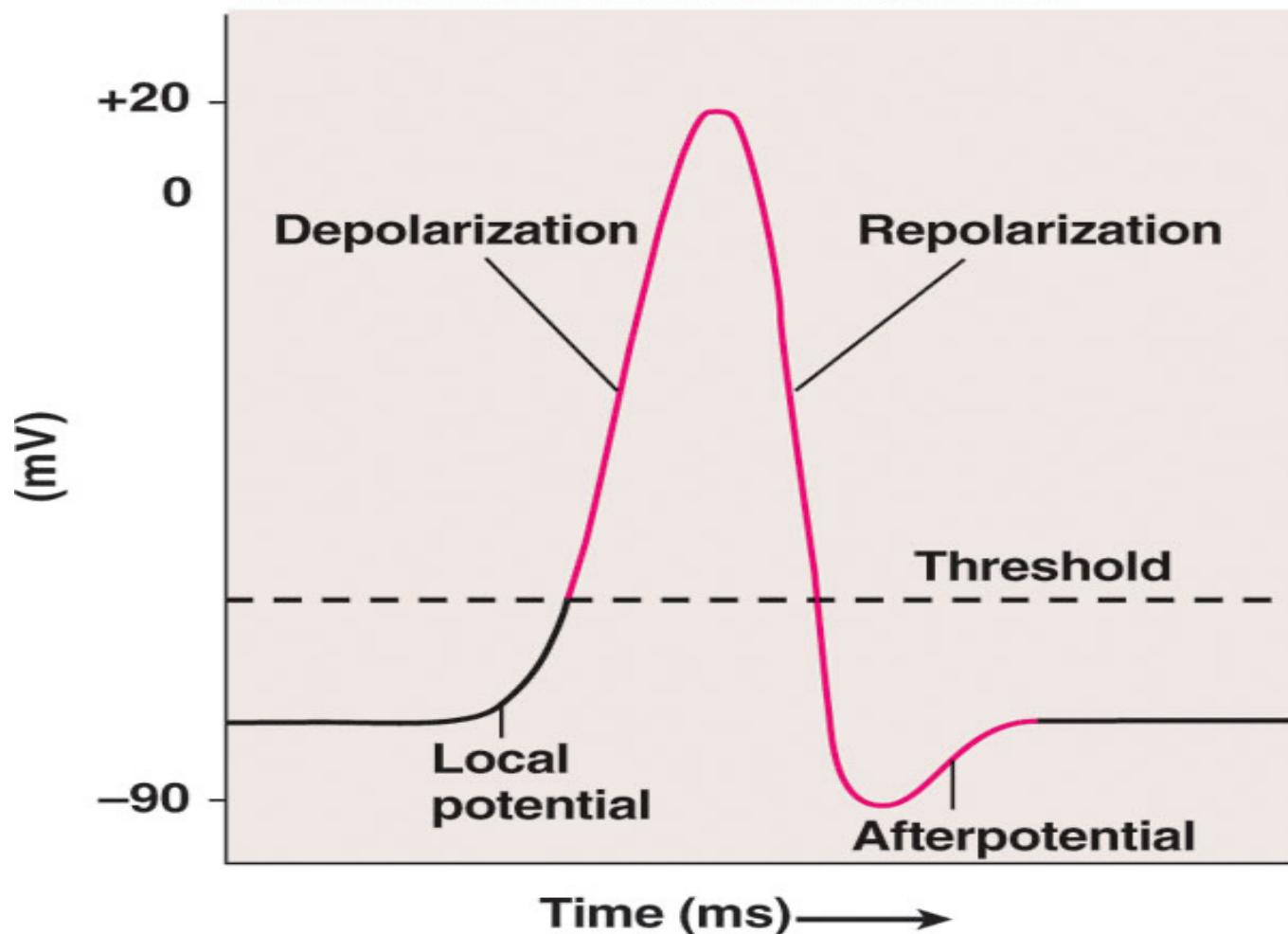
All-or-none response of an action potential

If threshold is met an action potential will be generated

If threshold is not met an action potential will not be generated

Action Potential

Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display.



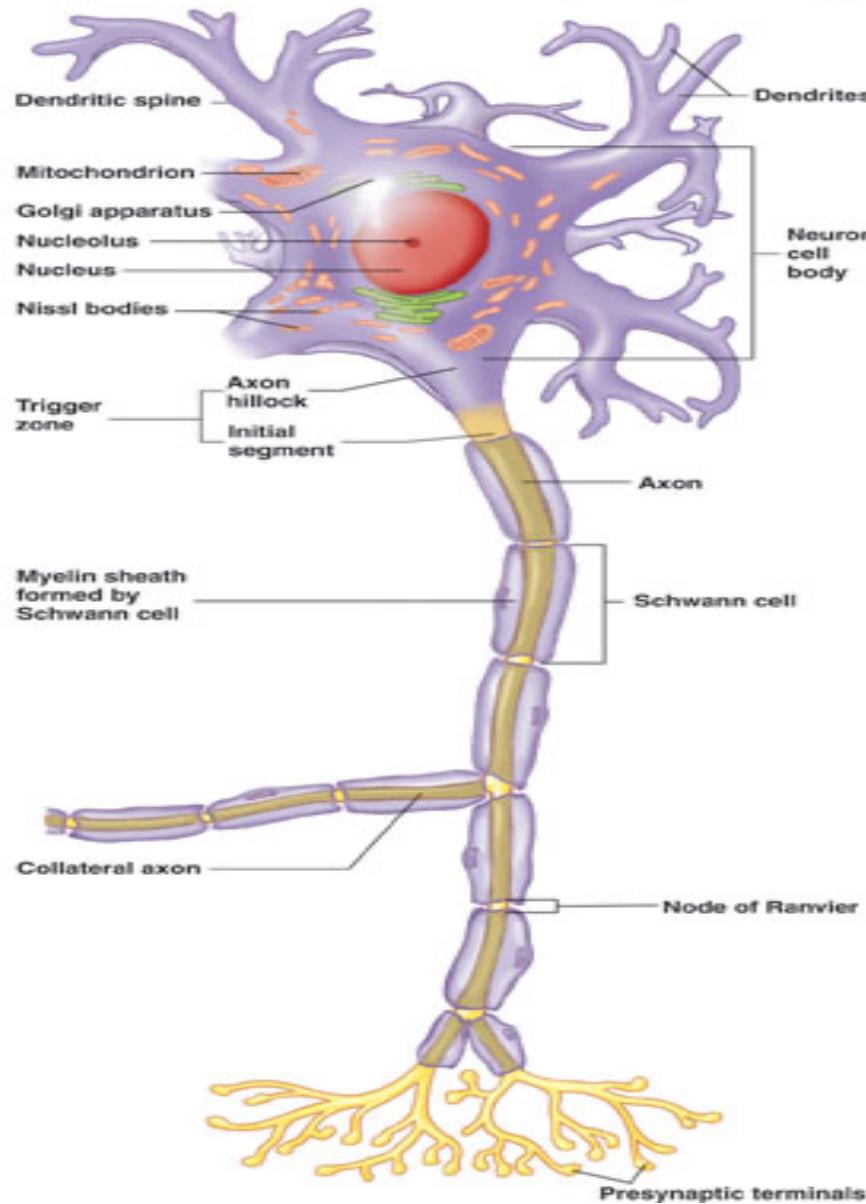
Action Potential

Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display.

cell body

axon

presynaptic terminal



Generation and Dynamics

of an

Action Potential

Generation and dynamics of an action potential in a neuron

Neuron is stimulated to cause the V_m to depolarize

Threshold is reached

Voltage-gated Na^+ channels activate rapidly (Na^+ permeability increases)

Rapid movement of Na^+ into the cell

Causes a very large and very rapid depolarization of V_m (fast depolarization)

~~Action potential passes through zero and toward E_{Na}~~

Large depolarization causes voltage-gated Na^+ channels to inactivate

Na^+ movement into cell stops (~~thus, E_{Na} is never reached~~)

Action potential reaches its peak

Voltage-gated K^+ channels open but less rapidly (K^+ permeability increases)

Rapid movement of K^+ (but not as rapid as Na^+) out of the cell

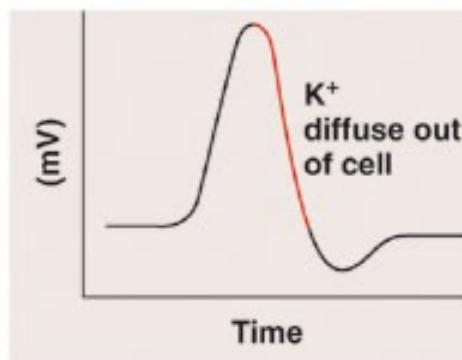
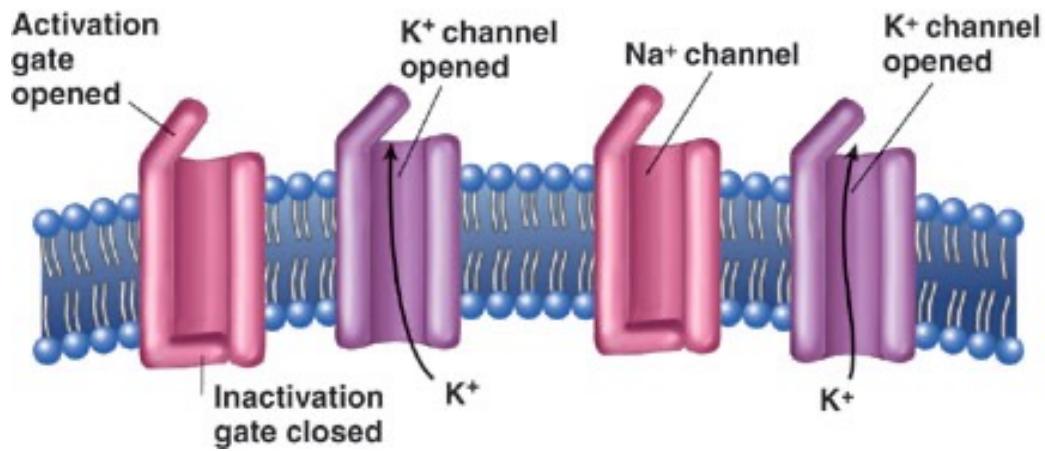
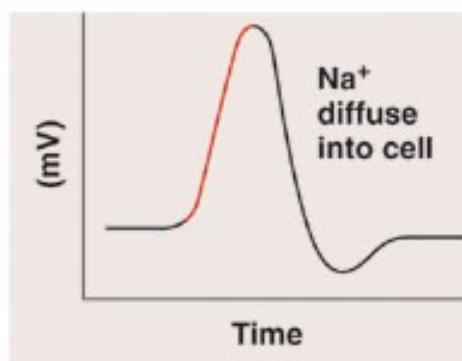
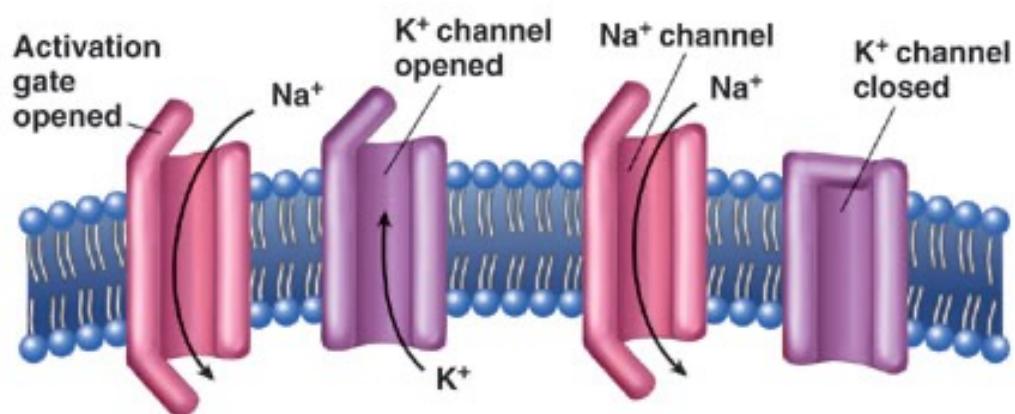
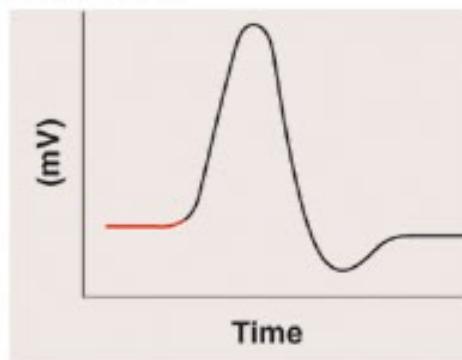
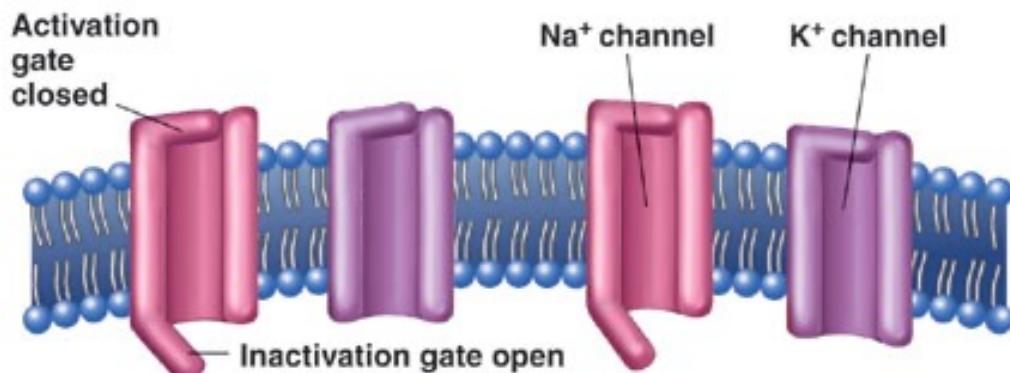
Causes a very large and very fast repolarization towards resting V_m starting at the peak of action potential

~~V_m continues towards E_K (voltage-gated K^+ channels close slowly)~~

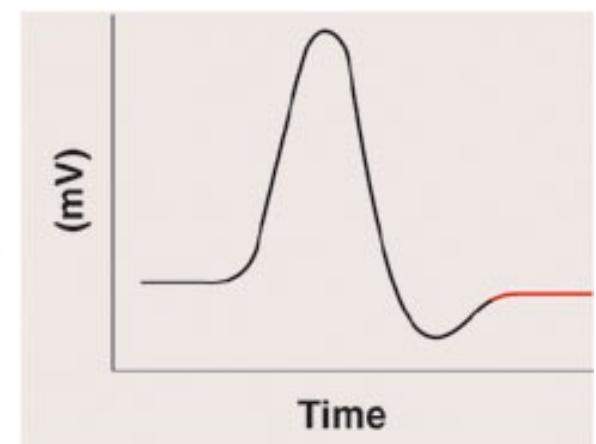
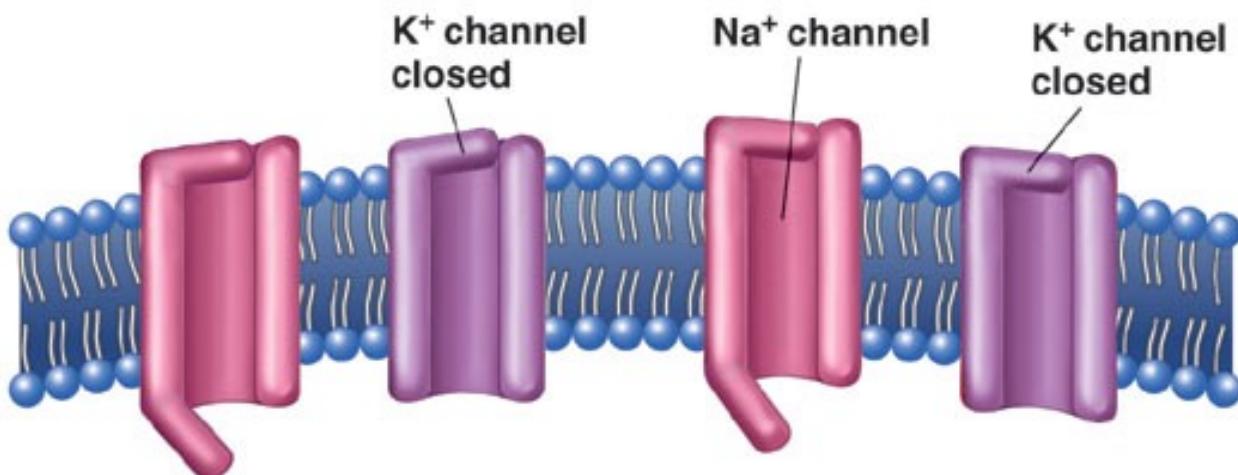
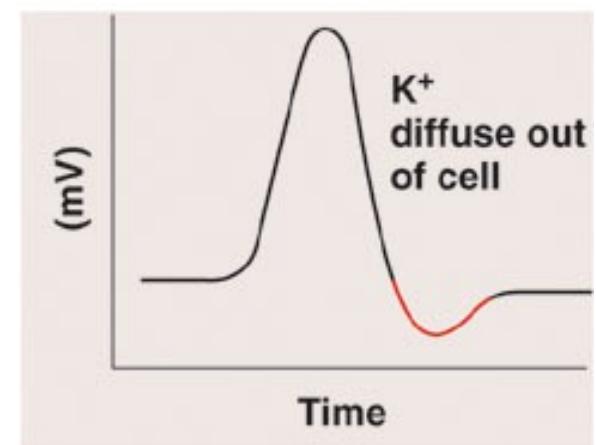
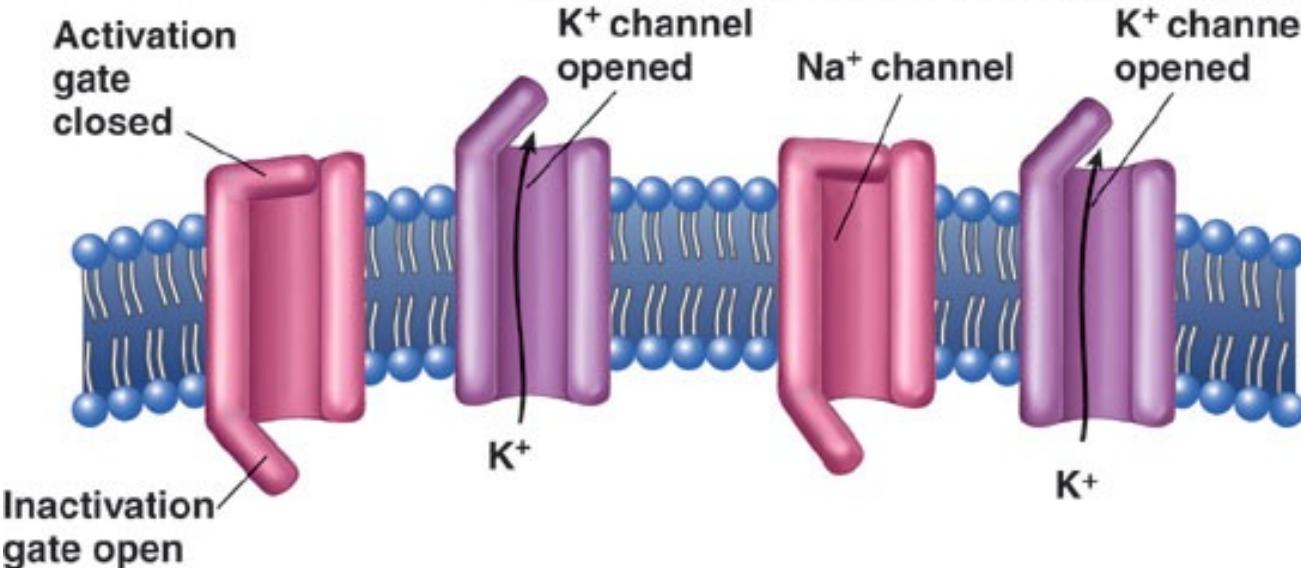
Produces an **afterhyperpolarization** of V_m

V_m is actually more negative (hyperpolarized) than resting V_m

Resting V_m re-established by channels responsible for establishing resting V_m



Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display.



Refractory Period

Period of time when a cell fails to respond to a stimulus of threshold intensity

Absolute refractory period

Occurs from the peak of the action potential and repolarization phase

Due to *inactivation* of Na^+ channels

Period of time when no action potential can be generated

This is regardless of the stimulus intensity

Relative refractory period

Occurs during the after-hyperpolarization phase

Most Na^+ channels begin to activate

Most K^+ channels can be opened or are still opened

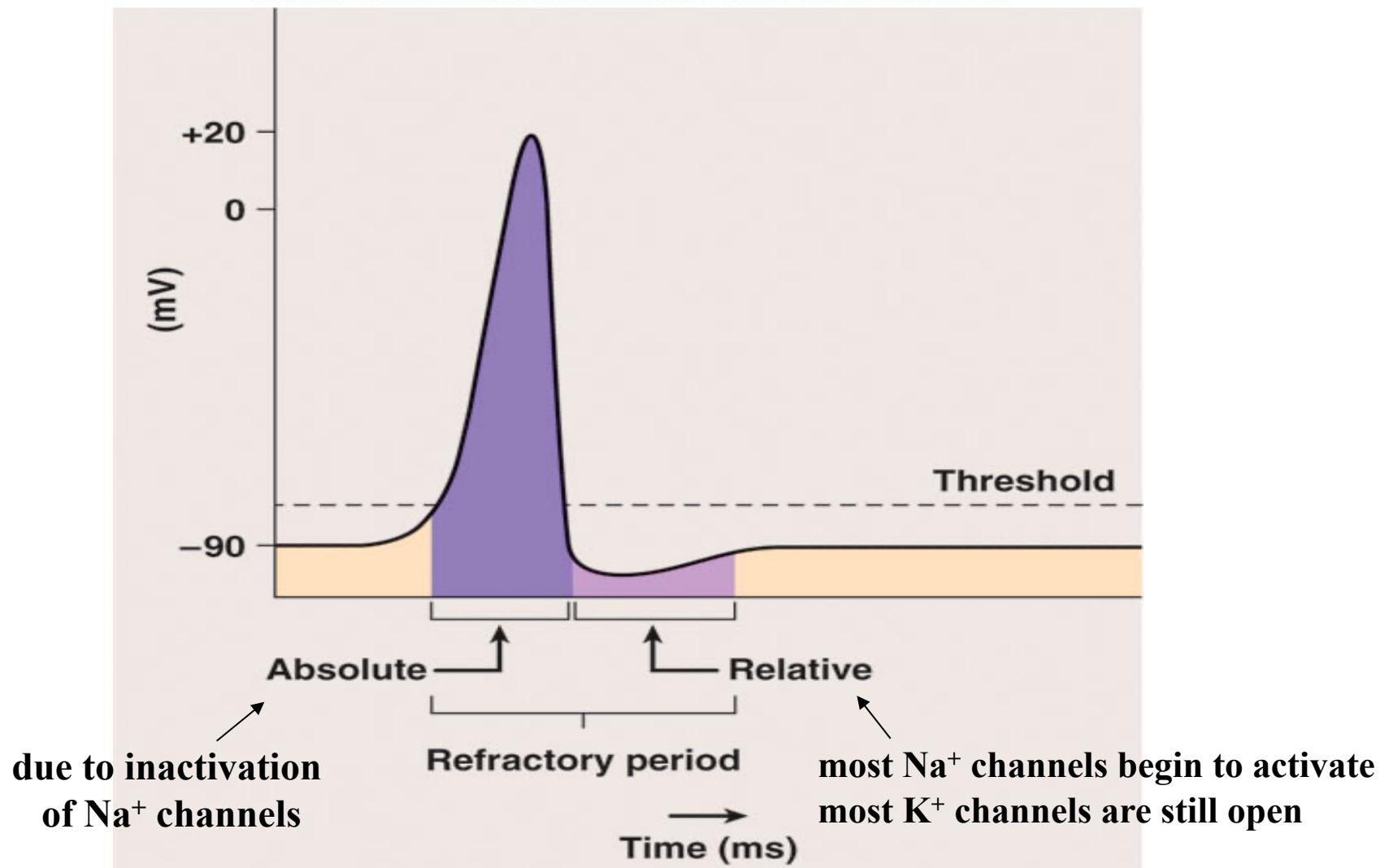
Possible to generate an action potential during this period of time

However, a bigger stimulus (i.e. bigger depolarization) needed

Cell is further away from threshold during this time

Refractory Period

Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display.



Action Potential Frequency

~~Maximum frequency dictated by the absolute refractory period~~

~~Shorter absolute refractory period = greater number of action potentials~~

Directly proportional to the stimulus strength

The greater the stimulus, the greater the action potential frequency

Action Potential Frequency

Directly proportional to the stimulus strength

The greater the stimulus, the greater the action potential frequency

Sub-threshold stimulus

Very small stimulus that does not cause a cell to reach threshold

No action potential elicited

Threshold stimulus

Stimulus that causes a cell to just reach threshold

One action potential elicited

Submaximal stimulus

Greater than threshold stimulus but less than maximal stimulus

Greater than one action potential but less than the number of action potentials generated with a maximal stimulus

Maximal stimulus

Stimulus that causes the maximum action potential frequency

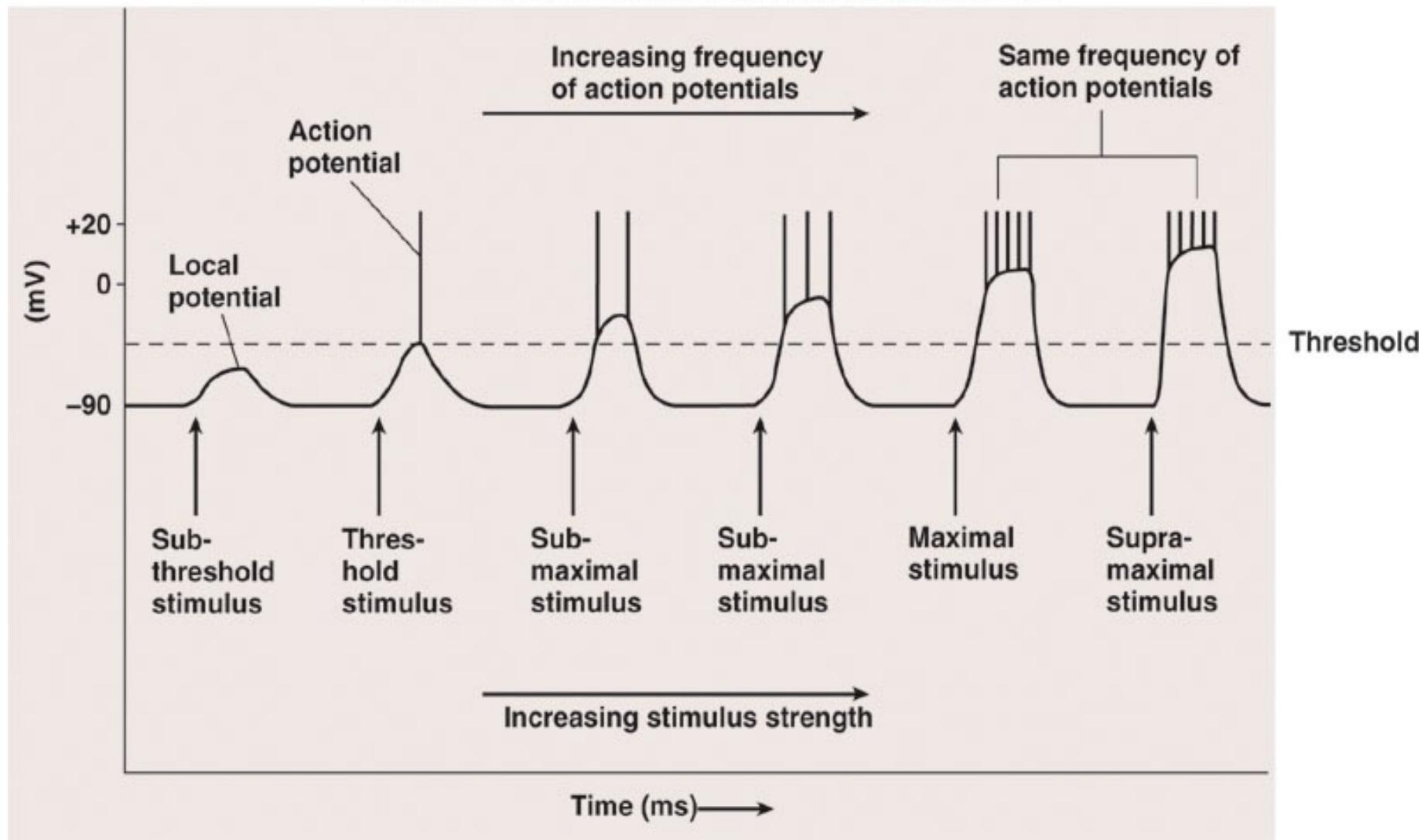
Supra-maximal stimulus (greater than maximal stimulus)

Action potential frequency does not increase despite larger stimulus

Cannot go beyond a maximum action potential frequency

Action Potential Frequency

Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display.



Action Potential Conduction

Propagation / spread of action potentials along a membrane

Action potential does not move across a membrane

Action potential causes generation of another in an adjacent region

Analogous to dominos toppling, one after another

Velocity of conduction in axons depends on fiber diameter and myelin

Larger axons conduct action potentials faster

Greater surface area with more voltage-gated ion channels

Myelinated axons conduct action potentials faster

More myelin = faster conduction

Action Potential Conduction

Two Types

Continuous Conduction (unmyelinated axons)

“one foot in front of the other”

Saltatory Conduction (myelinated axons)

“hopping”

Continuous Conduction

Occurs unmyelinated axons and membranes of excitable cells

Action potential in one region stimulates another in an adjacent region

Conduction velocity is less than 2 meters / sec

Dynamics

Sodium ions from action potential diffuses to adjacent regions

Causes depolarization of membrane

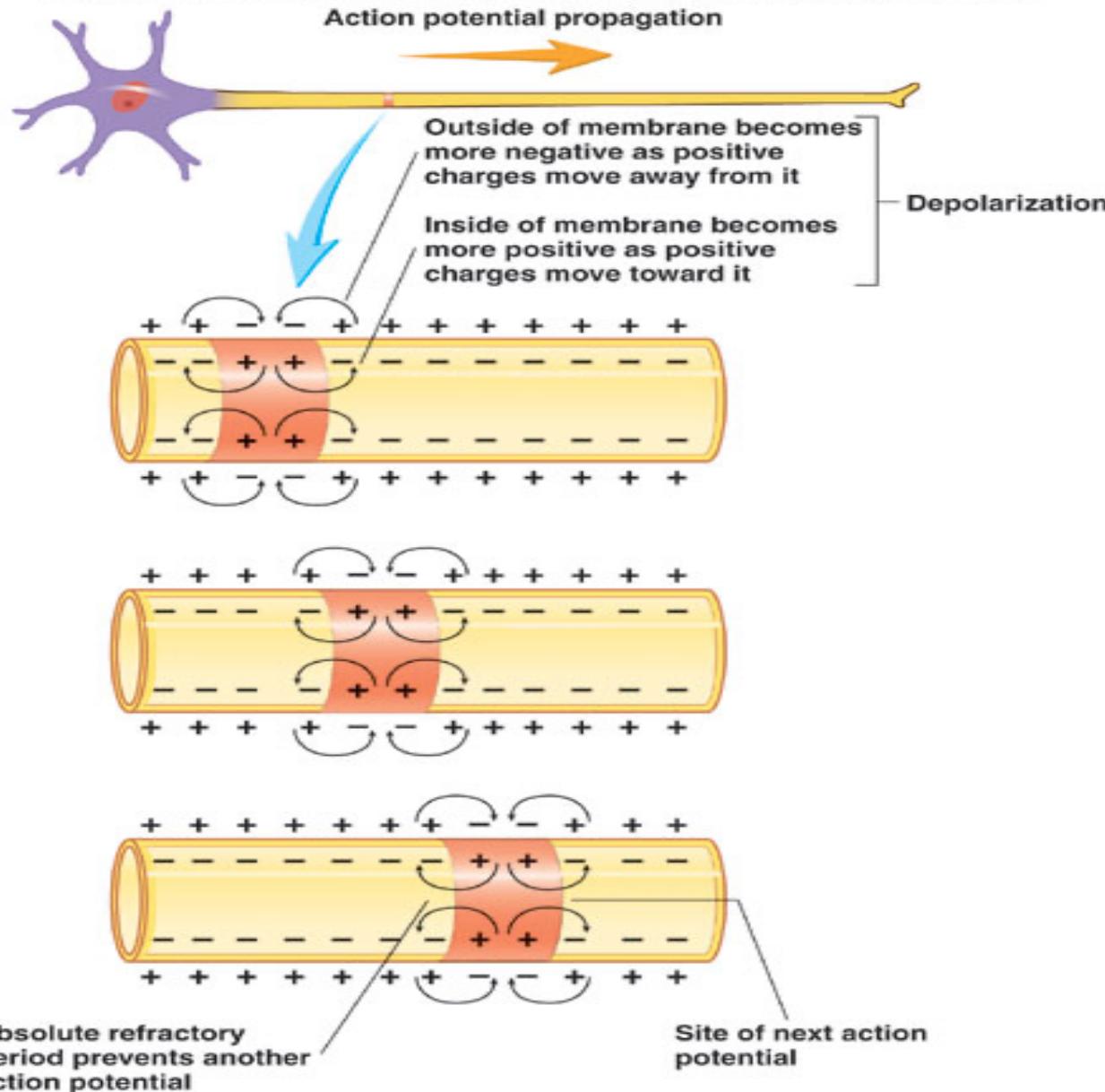
When threshold is reached, another action potential is generated

Conduction of action potentials continues in one direction

Ensured by the refractory period

Continuous Conduction

Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display.



Saltatory Conduction

Occurs solely in myelinated axons

Action potentials elicited at nodes of Ranvier

High concentration of voltage-gated Na^+ and K^+ channels at nodes

Conduction velocity is anywhere from 3 to 120 meters / sec

Dynamics

Sodium ions from action potential diffuses to adjacent node

Causes depolarization of membrane

Myelin sheath allows the diffusion of sodium to be rapid

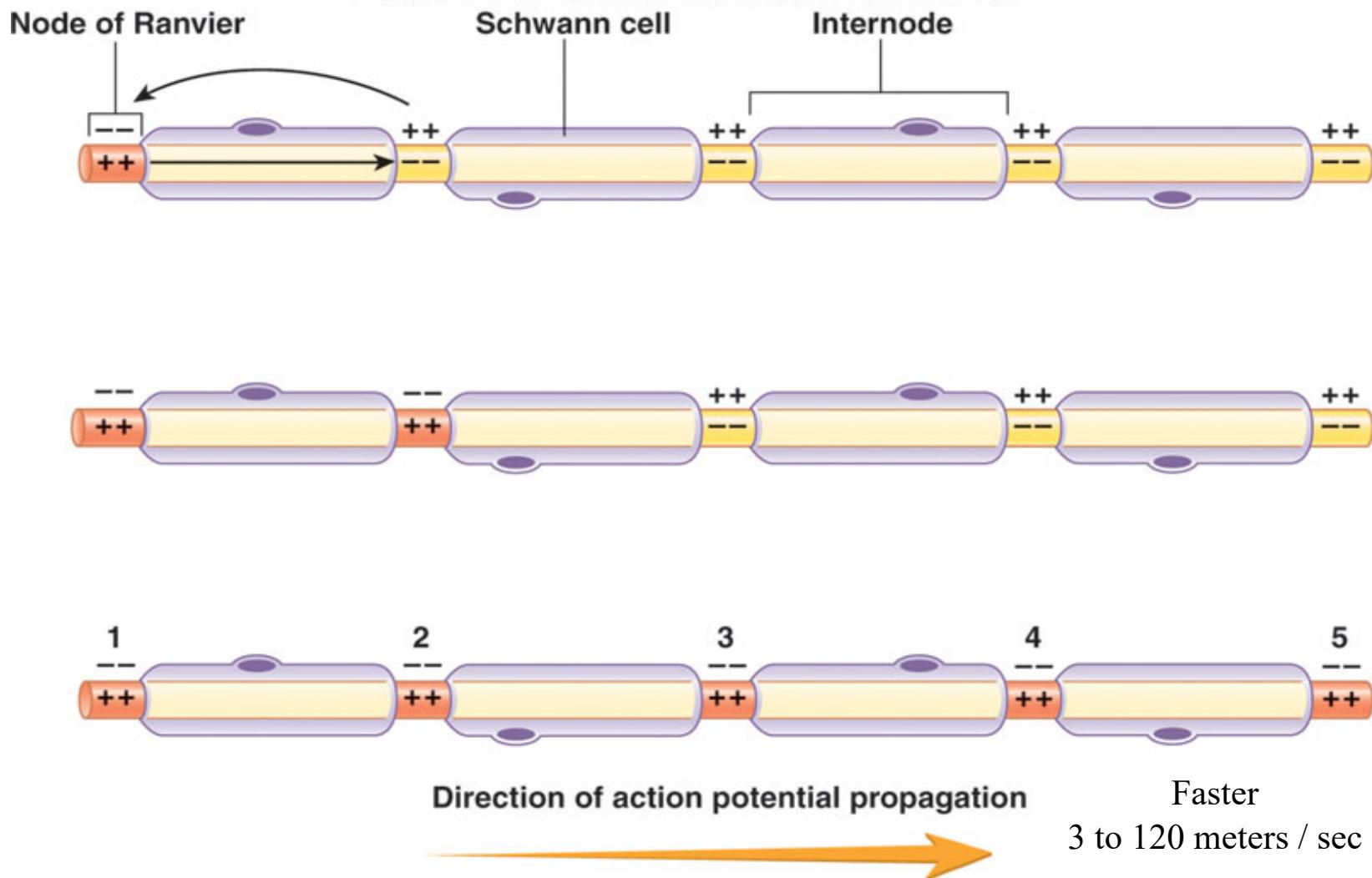
When threshold is reached, another action potential is generated

Conduction of action potential continues in one direction

Ensured by the refractory period

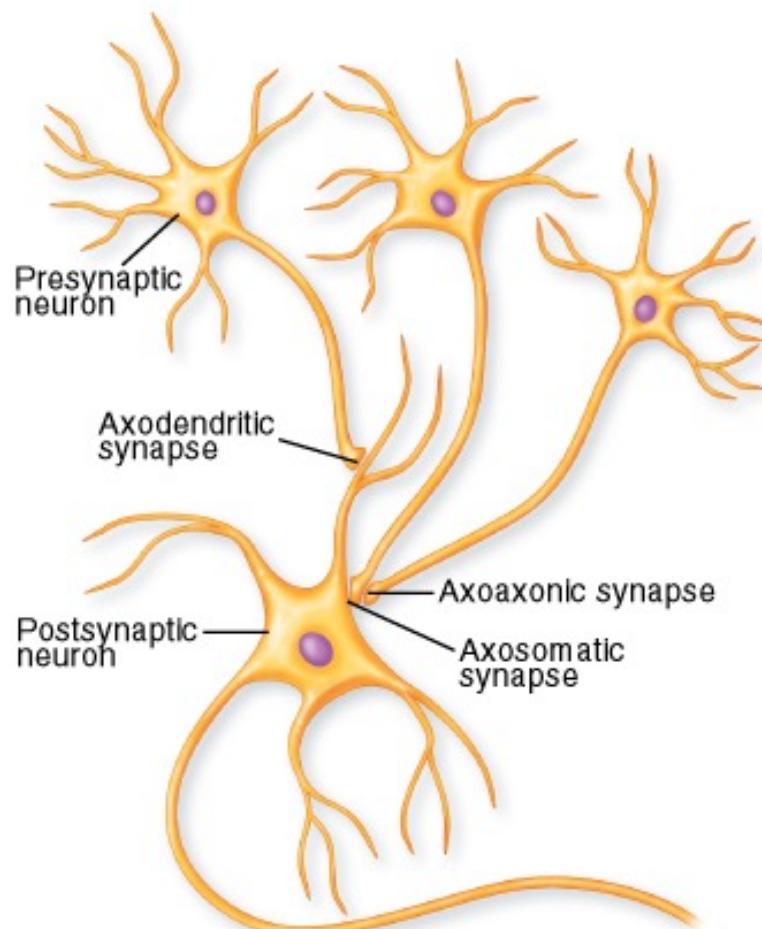
Saltatory Conduction

Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display.

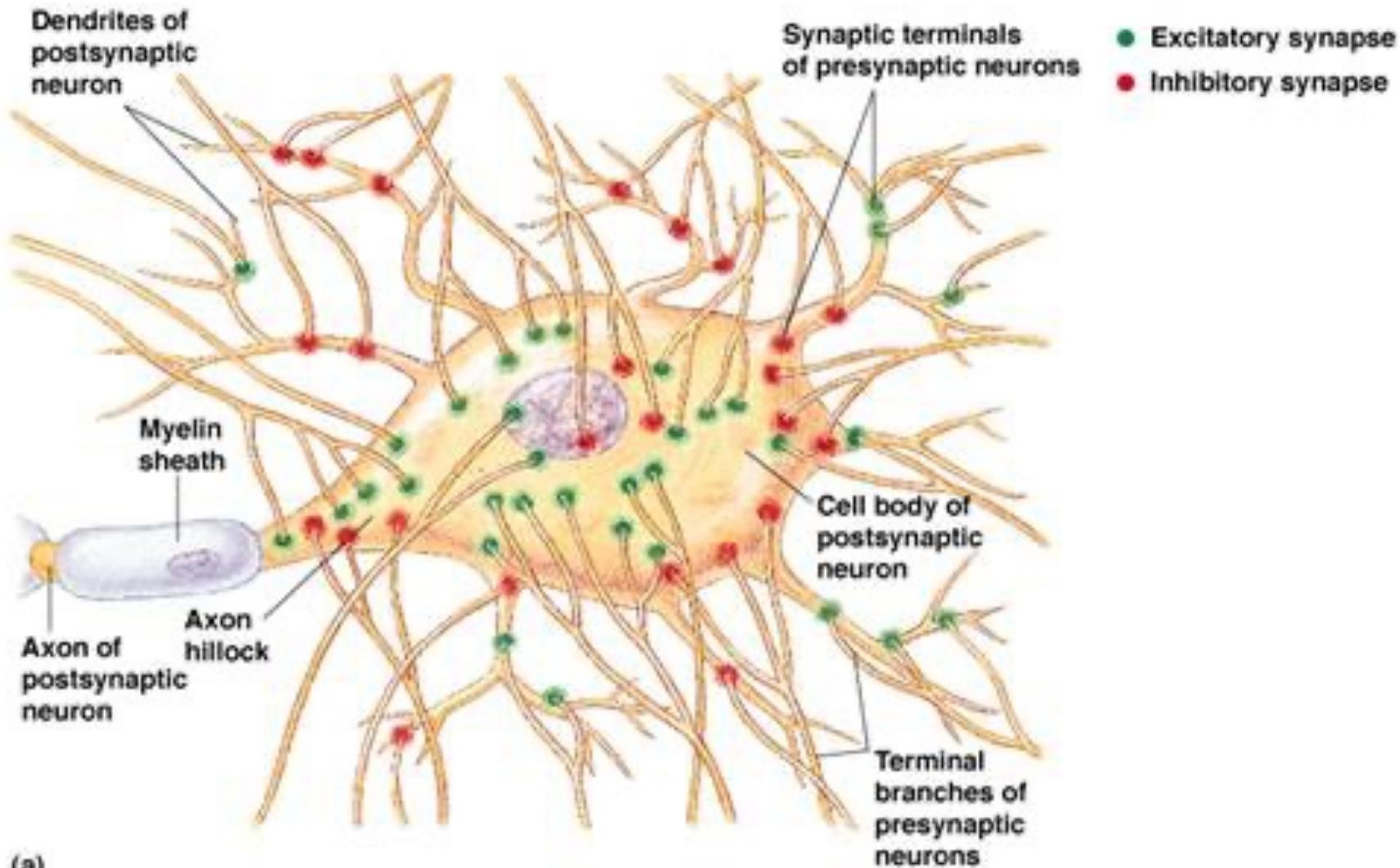


Synapse

Junction between two cells that allows communication between those two cells



Synapse



Two Types of Synapses

Electrical

Chemical

Electrical Synapse

Communication between two cells via **gap junctions**

Formed via two **connexons** (one from each adjoining cell)

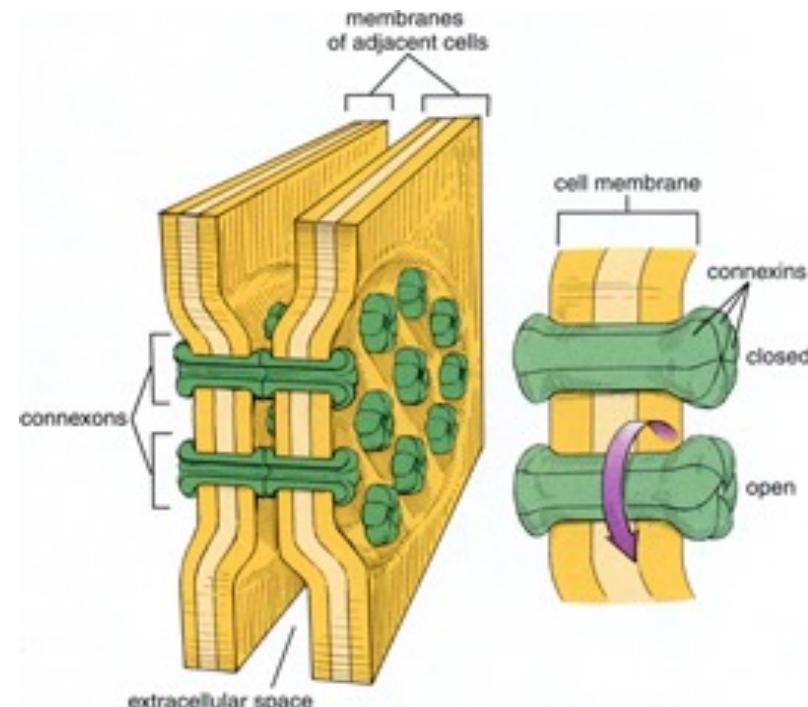
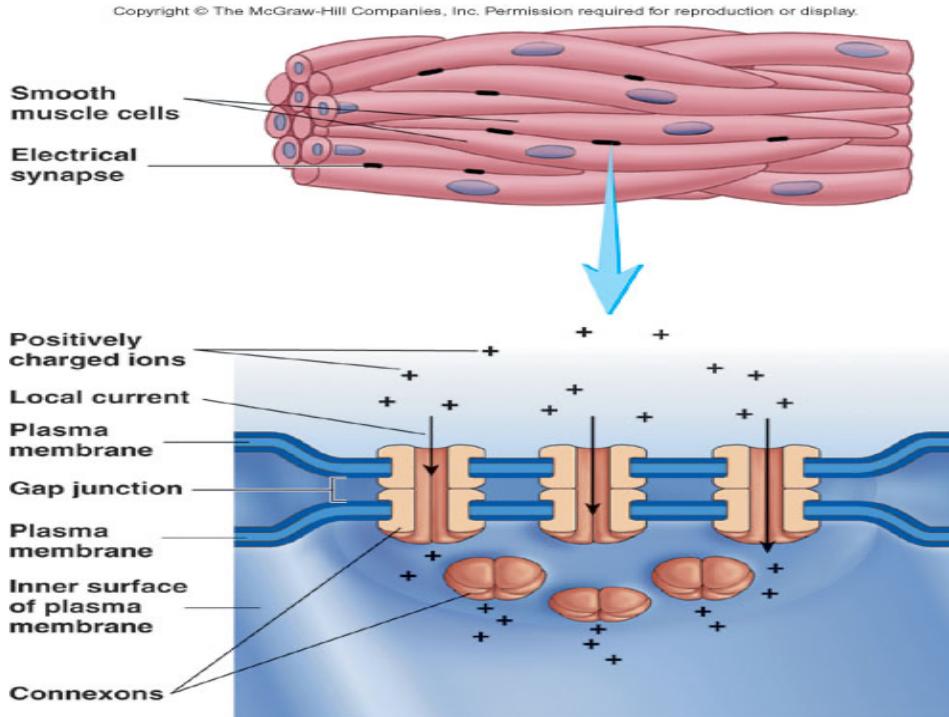
Connexon formed from proteins called **connexins**

Six connexins form a single connexon

Molecules flow freely through gap junctions when open

Allows for rapid passage of information between adjoining cells

Allows for coordination between electrically coupled cells



Chemical Synapse

Communication between two cells via release of chemicals

Presynaptic membrane

Membrane at the synapse that is carrying the information

Postsynaptic membrane

Membrane at the synapse that is receiving the information

Synaptic cleft

Small space between presynaptic and postsynaptic membranes

Neurotransmitters

Chemicals released from presynaptic cell to postsynaptic cell

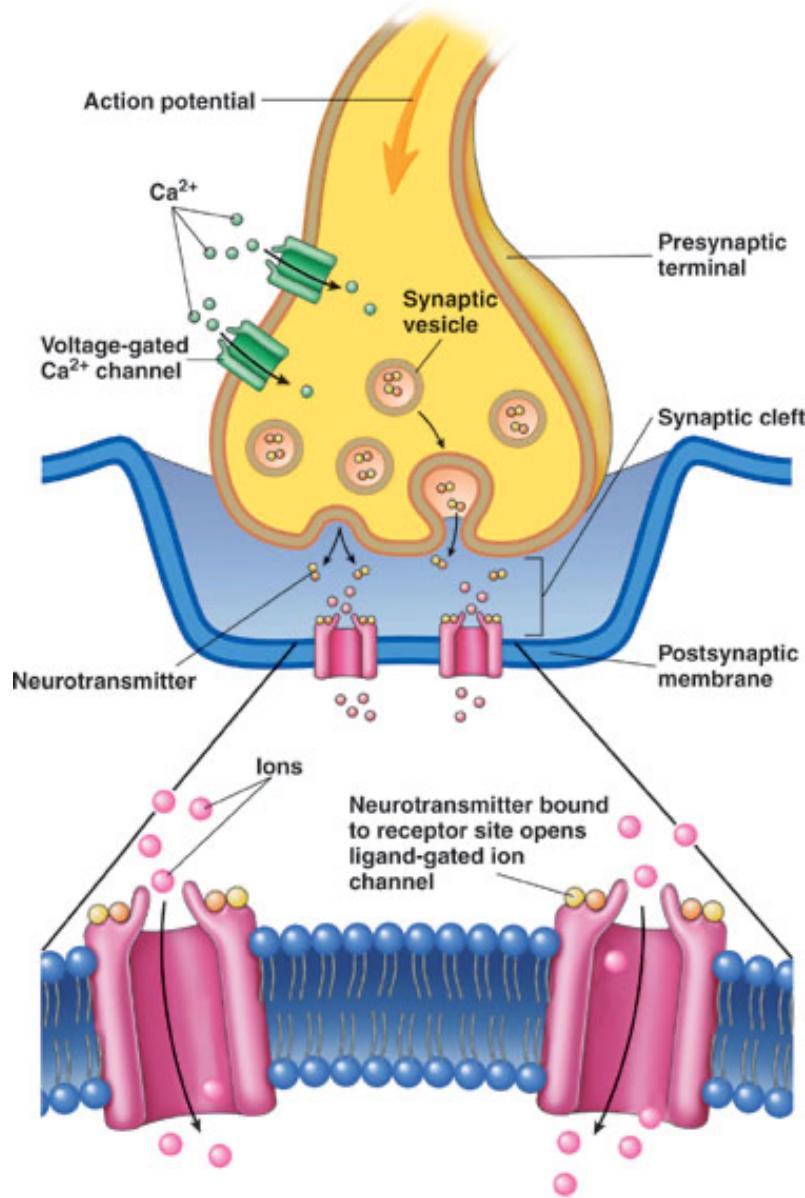
Produced by presynaptic cell and most stored in **synaptic vesicles**

Gaseous neurotransmitters produced and released when needed

Therefore, gaseous neurotransmitters are not stored

Chemical Synapse

Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display.



Synaptic Transmission

Action potential conducts to synaptic terminal of presynaptic membrane

Causes voltage-gated calcium channels to open

Intracellular calcium concentration increases

Causes synaptic vesicles to fuse with presynaptic membrane

Neurotransmitter is released into synaptic cleft via exocytosis

Diffuses across synaptic cleft

Binds to specific receptors of the postsynaptic membrane

Modulates ion channels in the postsynaptic membrane

OR

Causes production of *gaseous neurotransmitter*

Neurotransmitter released from presynaptic cell via diffusion

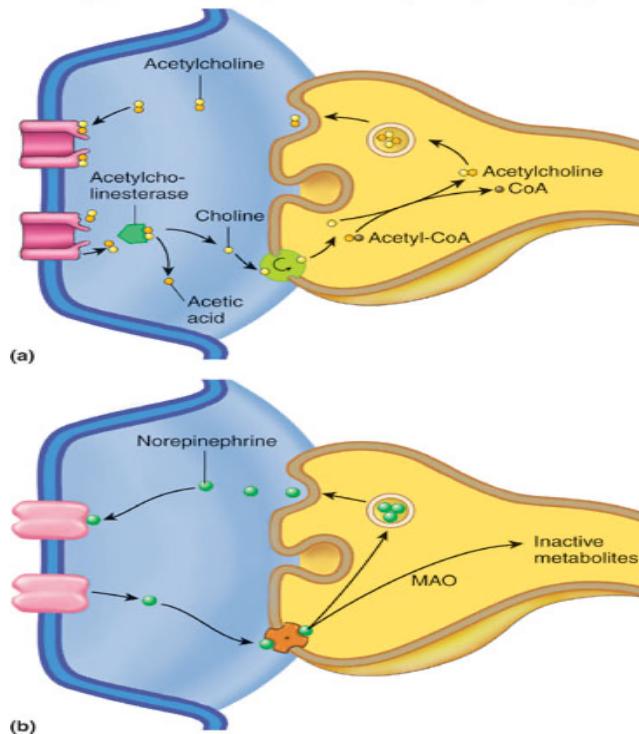
Diffuses across synaptic cleft

Diffuses into postsynaptic cell

Modulates ion channels in the postsynaptic membrane

Fate of Neurotransmitter

Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display.



Reuptake of chemical neurotransmitter by presynaptic membrane

Gaseous neurotransmitters are metabolized by postsynaptic cell

Reuptake inhibitor

Drug that inhibits the reuptake of neurotransmitters

Neurotransmitter remains in synaptic cleft longer

Effect of the neurotransmitter is enhanced

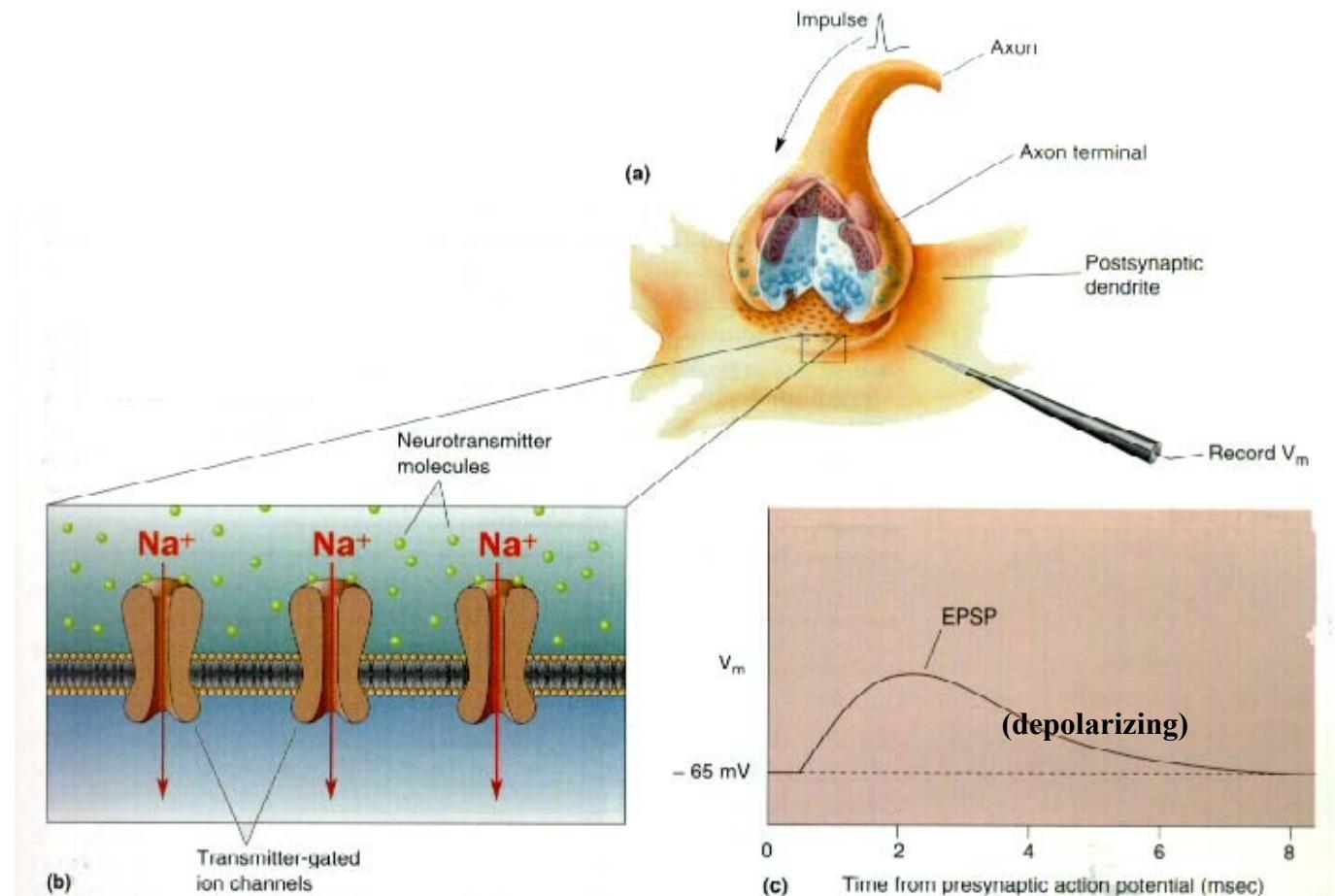
Administered when natural neurotransmitter level is low

Postsynaptic Potential

Transient V_m change of postsynaptic membrane

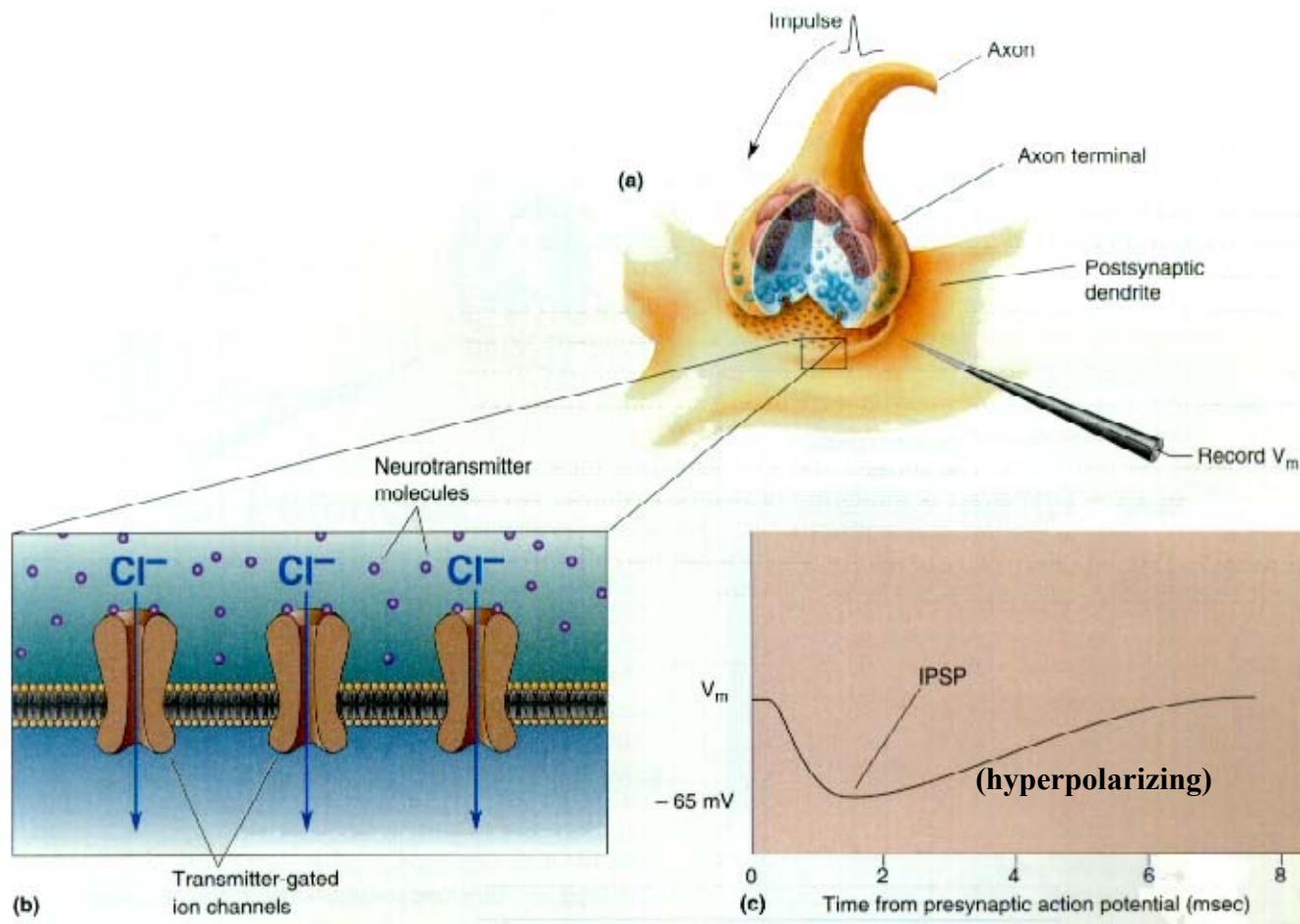
Due to neurotransmitter release on postsynaptic membrane

Excitatory Postsynaptic Potential (EPSP)



Depolarization followed by repolarization
Influx of cations (e.g. Na^+) or efflux of anions (e.g. Cl^-)

Inhibitory Postsynaptic Potential (IPSP)



Hyperpolarization followed by repolarization
Influx of anions (e.g. Cl^-) or efflux of cations (e.g. K^+)

Summation of Postsynaptic Potentials

Integrated sum of EPSPs and IPSPs

Determines V_m change (if any)

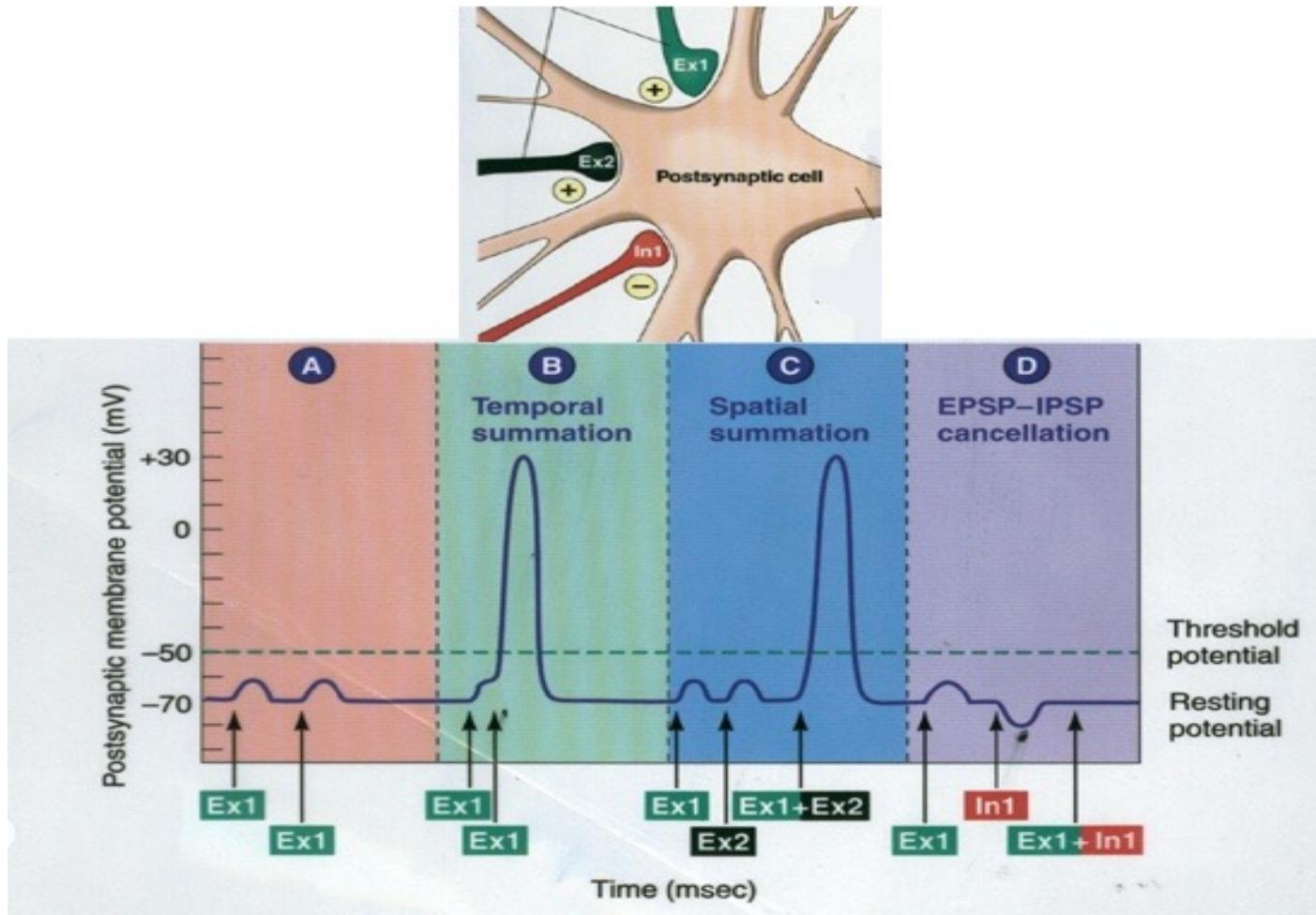
Spatial summation

When multiple postsynaptic potentials from different synapses occur at about the same time

Temporal summation

When multiple postsynaptic potentials from the same synapse occur at about the same time

Summation



Ex = Excitatory (produces an EPSP)

In = Inhibitory (produces an IPSP)

Synaptic Plasticity

Ability of some structure of a synapse to change

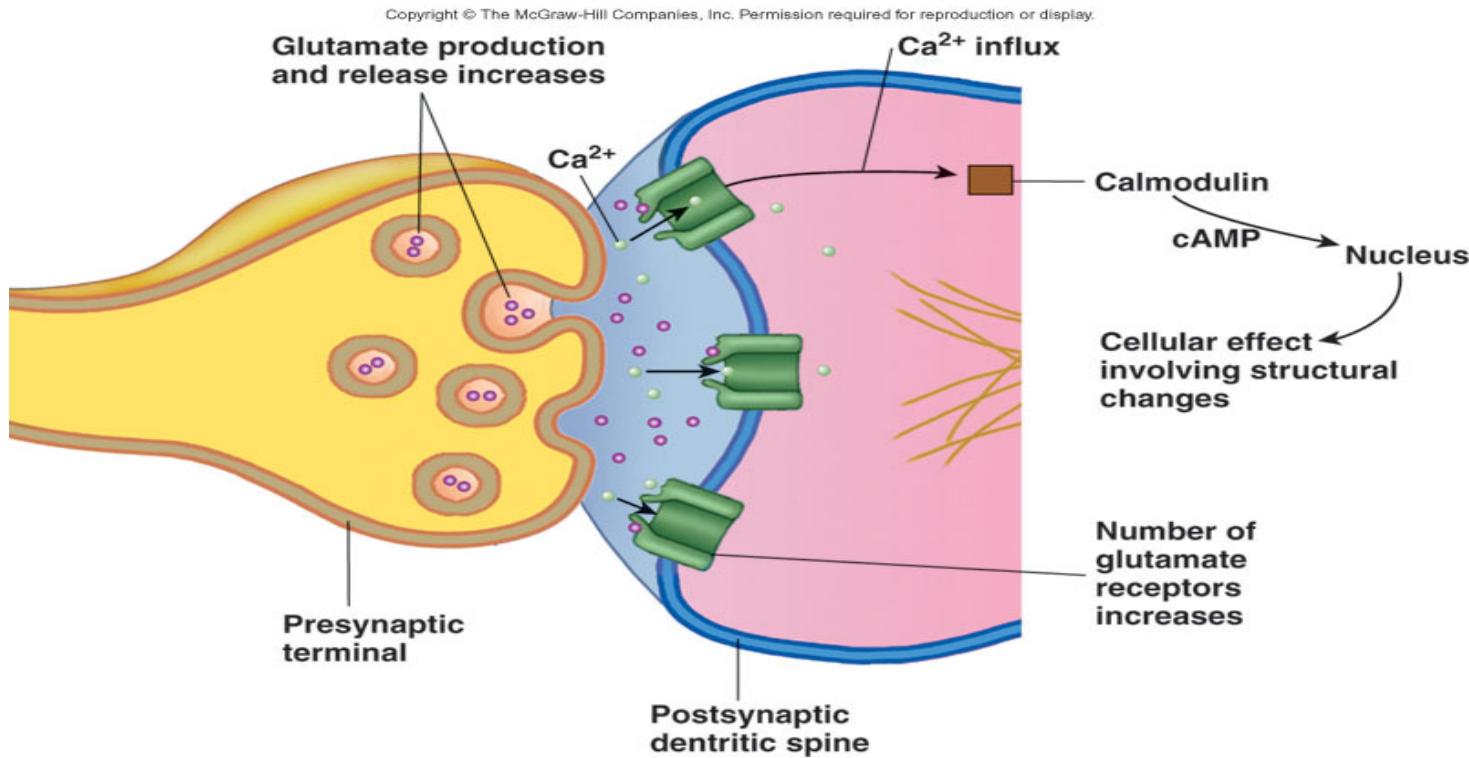
e.g. decrease or increase in neurotransmitter release

e.g. decrease or increase in the number of receptors

Formation of new synapses

Loss of synapses

Large “events” must take place to cause plasticity



Types of Neurotransmitters

Acetylcholine

Monoamines

Amino Acids

Neuropeptides

Gaseous Neurotransmitters

Acetylcholine (ACh)

Found in the CNS and PNS

Excitatory or inhibitory

Important in arousal, sleep, attention, memory

Neurotransmitter of the somatic nervous system

Neurotransmitter of the autonomic nervous system

Loss of ACh-producing neurons implicated in memory loss w. Alzheimer's

Treatment option is ACh reuptake inhibitors

Monoamines

Serotonin

Norepinephrine

Dopamine

Serotonin / 5-HT

Found in the CNS and PNS (most found in the gut)

Excitatory or inhibitory

Important in temperature regulation, sleep, mood, nausea, vomiting

Stimulates the gut

Low levels linked to:

Depression, Anxiety, Obsessive compulsive disorder, PTSD

Treat with **selective serotonin reuptake inhibitors (SSRIs)**

e.g. Prozac, Paxil, Zoloft, Celexa, Lexapro

Treat with **psychotherapy**

Talk therapy

Cognitive behavioral therapy

Exposure therapy

MDMA / Ecstasy / Extasy / E / X / Molly / etc.

Serotonin reuptake inhibitor

Norepinephrine

Found in the CNS and PNS

Excitatory or inhibitory

Important in decision making, attention and mood

Neurotransmitter of the sympathetic nervous system

Low levels linked to

Depression, Attention deficit disorder

Treat with norepinephrine reuptake inhibitors

e.g. Wellbutrin, Ritalin

Treat with psychotherapy

Dopamine

Primarily found in the CNS

Excitatory or inhibitory

Important in movement, attention, motivation and pleasure

High levels linked to Tourette's and psychosis

Treat with dopamine receptor antagonist

Low levels linked to:

Depression, Attention deficit disorder, Addictive behavior

Treat with dopamine reuptake inhibitors

e.g. Wellbutrin, Ritalin, Chantix

Treat with psychotherapy

Loss of dopamine-producing neurons leads to Parkinson's disease

Amino Acids

Glutamate

Found primarily in the CNS

Major excitatory neurotransmitter in the CNS

Has many functions including learning and memory

High levels cause seizures and neural degeneration

Treat with drugs that block glutamate release and receptors

GABA

Found primarily in the CNS

Major inhibitory neurotransmitter in the CNS

Drugs that increase GABA used to treat epileptic activity

GABAergic drugs

~~Death of GABA producing cells leads to Huntington's disease~~

~~Treat with GABAergic drugs~~

Glycine

Found primarily in the CNS

Inhibitory neurotransmitter in the CNS

Neuropeptides

Endorphins and Enkephalins

Found in the CNS and PNS

Opioid compounds

Inhibitory

Important in regulation of pain and gut motility

Diminishes pain and slows the gut

Morphine, Oxycontin, Heroin are agonists of opioid receptors

Narcan is an antagonist of opioid receptors

Therefore, narcan blocks the effect of heroin

Substance P

Found in the CNS and PNS

Excitatory

Important in the regulation of pain, anxiety, nausea and breathing

Inhibiting Substance P receptors reduces pain and prevents nausea

Gaseous Neurotransmitters

Cannot be stored

Produced as they are needed

Nitric oxide

Found in the CNS and PNS

Excitatory and inhibitory

Involved in many processes

e.g. erection, blood vessel tone, memory

Carbon monoxide

Found in the CNS and PNS

Excitatory and inhibitory

Thought to be a co-neurotransmitter with nitric oxide

Similar functions to nitric oxide

Memory

Sensory

Short-term

Long-term

Memory

Sensory memory

Very short-term retention of sensory input

Sensory information from the external environment that is scanned, evaluated

One does not realize this is happening

Lasts less than a second

Electrical in nature

Solely a change in V_m

Gone if it is ignored

If perceived (not a conscious act) it is stored in short-term memory

Short-term memory

Lasts seconds to approximately a minute

Electrical in nature

Solely a change in V_m

Forgotten if an effort is not made to retain it or an “impression” is not made

Memory

Long-term memory

Lasts minutes to hours and as long as a lifetime

Information stored when an effort is made or an impression is made

Synaptic in nature

Synaptic plasticity

e.g. increased neurotransmitter release

e.g. increased receptor sensitivity

e.g. increased number of receptors

e.g. new synapses formed

Memory

Long-term memory

Two types

Declarative / Explicit

Retention of events, people, places, dates, facts, etc.

Procedural / Implicit

Development of skills

e.g. walking, eating a spoon, driving a car

Conditioned reflexes

e.g. associate an event / person with a smell



Memory

Main areas of the brain involved in memory

Hippocampus

Prefrontal cortex

Amygdala

Striatum

Mammillary bodies

01 - Neuro - 18OCT2021

Fri, 10/29 4:30PM • 31:51

SUMMARY KEYWORDS

membrane potential, cell, potassium, permeability, interstitial fluid, ions, charges, membrane, sodium, sodium potassium pump, chloride, resting, transported, draw, battery, concentration, negative charges, inner membrane, gradient, outer membrane

00:01

I think we're all here. Why don't we get started.

00:05

So we are going to talk about membrane potential. Before we do that, we're actually going to talk about batteries. You'll see why. So I'm going to draw a couple of batteries here, before I do that,

00:18

write down the word voltage here, voltage and potential are the same thing, I can use both of those words interchangeably, I'm going to assume you guys have heard the term voltage, I'm going to explain to you what voltage is. Now,

00:34

I'm going to draw a couple of different batteries here, batteries that we should be familiar with.

00:39

So that is a triple A battery,

00:44

the kind of batteries that you would put in a remote control, and I'm going to assume that we know that a battery has a positive end.

00:51

And it has a negative and actually, I'm gonna draw that just a little bit bigger. So we have two ends of this battery, and it's placed in a device in a specific way.

01:02

So there's our triple A battery, there's a positive end, and that's the negative end.

01:08

This battery has 1.2 volts of energy, if that was a double A battery would be 1.5 volts. If we drew

01:19

a nine volt battery, the one that you put, for example, in a smoke detector, which also has a negative and a positive end that has nine volts of potential energy. Now how is that energy or how are those volts in part? We're separating charge. On the positive end, there's a bunch of positive charges and on the negative end, all there's a bunch of negative charges, the same holds true over here. Negative,

01:49

positive and those charges are separated. That's what that line indicates. That's what this line

01:56

indicates.

01:58

And the amount of charges that we separate is going to dictate

02:03

the volts. So when we separate charge, so separation of charge,

02:12

generates voltage.

02:18

Now why am I talking about this, because your cells do something very similar to this. Actually, I should say batteries do something very similar to cells, because cells came before batteries.

02:30

So now I'm going to draw a hard line here, and I'm going to draw a cell.

02:35

And so here we have a cell.

02:39

And I'll label it as such.

02:41

Then on either side of that membrane, we have charges.

02:47

Now it's not put together exactly the same way that a battery is with the battery, you have all positive charge on one end and all negative charges on another. Although you do get the flow of the negative charges to create current that makes the things work that you plug him into. That's not important. What's important to realize is that

03:06

it's going to be a little bit different with the cell because we have both positive and negative charge on the outer membrane and on the inner membrane of a cell.

03:17

Now I want you to think of these charges as being stuck

03:22

to the membrane, as if they're velcroed onto the membrane glued onto the membrane. But they're stuck to that outer membrane, we also have charges on the inner membrane, and I'm going to draw those charges as well.

03:34

And so what this membrane is doing,

03:38

it's separating these charges.

03:41

And in so doing is going to generate voltage, a potential.

03:48

So the cell membrane

03:53

separates charge.

04:00

And like a battery

04:03

generates voltage, but we call it instead. membrane potential.

04:12

membrane potential is abbreviated by the way, capital V,

04:17

little m.

04:20

This is something that we can measure, just like we can measure the voltage of a battery we can measure the voltage of a cell the potential of a cell. Now when it comes to the measurement of a cell in its membrane, it's not in volts. That's humongous compared to what the value is for a cell.

04:39

The units

04:42

is in what is called millivolts. 1000s of volts 1000 millivolts would be one volt. And when it comes to the value for a cell,

04:56

it's anywhere from negative 40 to about negative nine

05:01

Although in many books, many websites, it's going to tell you that membrane potential in the cell is negative 70 millivolts. I'm going to tell you what the negative means just a little bit. Is that false? That's not false. But it's not the full story, it depends on the cell. Depends on where it's located, depends on ion concentration depends on permeability depends on a whole bunch of different things. But there's a wide range when it comes to membrane potential in a cell, whereas with the battery will the AAA battery is that a nine volt battery is that the battery in your car is 12 volts. It is what it is. But with a salary of 220 different kinds of cells and the cells are in all different kinds of places in the body, membrane potential is going to vary, do you have to know what the values are? Yes.

05:45

potential varies. Does that mean that the question

05:48

doesn't mean that what

05:51

the threshold varies to yes, if we're talking about a cell that has a threshold, yes. And we'll get to that kind of thing, not in this lecture. But in the next obviously, this lecture tonight, it's only going to be about a half an hour long.

06:02

So we're separating these charges in the cell. So what we have here. So far, all we've talked about, is we've just defined what voltage generated via the difference between negative and positive charges lining the inner membrane, and aligning the outer membrane. And that's something that's very important to understand, too. And so what I'm also going to do here is I'm going to write the word cytosol. Here, because Well, we certainly know that that's the cytosol. That is the intra cellular compartment.

06:31

And then we have an extracellular compartment, the interstitial compartment,

06:37

which is made up of interstitial fluid. And so that's what this is out here. Now, I have all of these positive and negative charges lining the inner membrane and lining the outer membrane,

06:50

there's way more charges in the fluid of the cytosol, there's way more charge in the fluid of the earth in the interstitial fluid, way, way, way, way more, this is just a little drop in the bucket when it comes to these charges. But it's those charges on either side of that membrane, that are going to dictate what membrane potential is, that is incredibly important to understand. And so much so that I'm actually going to write that down. So it's just

07:22

the charges

07:25

on either side

07:30

of the membrane

07:34

that

07:36

generate

07:39

membrane potential.

07:42

That's why it's called membrane potential. We don't call it side assault potential. We don't call it interstitial fluid potential, we call it membrane potential. Because it is the membrane that is separating these charges, just like we have something in a battery, it's called a capacitor that separates the charges in a battery. So you can think of the fuse take physics class, the membrane is capacitor here separating charge. That is it the membranes intact.

08:10

Now, when it comes to these charges, and how they're separated, they're separated in a very specific way. It is not random. And it might look like I drew these positive and negative charges randomly. It's not random at all. Cells have very specific membrane potentials, it allows them to do the kind of work that they need to do based on that membrane potential. And it's something that I'll explain later, when we get further into membrane potential. I'm just giving you the basics right now. Now, let me ask you this. What do you think is carrying these positive and negative charges?

08:43

What kind of molecule says with an eye

08:46

glance, positive ions and negative ions, sodium, potassium, and chloride are going to be the three that we concentrate on. Now also involved in this are proteins, because proteins also have charges on them. And that's actually in the notes. And let me show you that.

09:05

Oh, by the way, every single cell in your body has a membrane potential, everyone why? Because every cell has a membrane.

09:13

Every cell is surrounded by a social fluid. Every cell has a cytosol. Every cell has charged on I decided as membrane. So every cell has a membrane potential. And so that's another important point to realize. So all 40 trillion that your cells in your body, they have a membrane potential under normal conditions, of course.

09:32

Now, when it comes to once again, what is going to generate this membrane potential, we have these ions but as I have in the notes as well, there's a small influenced by proteins. We're not going to worry about we're going to keep this simple. But we do have proteins lining this inner membrane that will contribute to membrane potential, but it's not a big contributor, which is why I'm really not going to talk about it. I just mentioned it in the notes. It's the

10:00

ions that we have in the notes here, these three main ions, although others are involved, but these are the three that we're going to be discussing. And of these three, potassium is going to have the biggest influence on something called resting membrane potential. So there's different kinds of membrane potential.

10:18

The first one we're going to discuss is resting membrane potential. What does that mean? It's a cell that's not being stimulated, it's a cell that's not being inhibited, is just sitting there chilling out, that's what resting membrane potential is. And that's what we're going to concentrate on first. And that's what we need to understand first, in order for us to understand other things in this chapter. So now what we're going to do is we're going to draw a cell again. And now we're going to put this stuff in it right there. So that's what we're about to draw this. And we'll also include the sodium potassium pump as well, that's going to be important to this discussion. So let's draw cell now. And what I'll put up here at the top, is resting membrane potential so that we understand that this is what the topic is at this point.

11:11

Okay, so let's draw cell.

11:13

So here's our cell.

11:17

And now we're going to put these sodium potassium and chloride concentrations outside and inside the cell. So earlier on this semester, I talked about how sodium concentration is high outside of the cell, and low inside of the cell, and potassium is the opposite. And we discussed why so you're going to actually tell me that just a little bit. So the osmolarity of sodium in the interstitial fluid is about 140. Now there's a range to it, it's between 135 and 145, I pick the sweet spot, the sodium concentration inside the cell

11:55

is about 15.

11:57

Give or take. Potassium is going to be the complete opposite potassium concentration is high on the inside of the cell, it's about 135. And a slow outside the cell

12:11

is roughly about five. And again, this is something that we had already discussed, we talked about how sodium concentrations high outside low inside potassium concentration is low inside or high inside and low outside, we did that in the transport chapter, when we were talking about active transport, we want to remind you, and then chloride fluoride concentration, like sodium concentration is high on the outside of the cell and the interstitial fluid in a slow on the inside of the cell. It's roughly about 10.

12:43

Now something else I want to add,

12:46

this is interstitial fluid out here. We know that that is an extracellular fluid, right? What are the other two extracellular fluids that we talked most about, there's actually three more

12:59

plasma, right and left, that's the other one, then to transfer the fluid was the other, we really didn't talk much about that. But the other two we did plasma in limp, which are also extracellular fluids like an interstitial fluid. So what that means is, is that these concentrations for sodium in the interstitial fluid, and chloride in the interstitial fluid and potassium in the interstitial fluid are the same in the plasma in the lip. And I'm going to write that down. That's how important this is. So interstitial fluid

13:37

I ion concentration

13:43

is the same

13:47

in the plasma, and the limp.

13:52

Now, why is that so important for me to state? Well, clinically, is going to be important.

13:58

Because when you take the blood of a patient, you're looking at a whole bunch of things, including the concentration of sodium, the concentration of potassium, and chloride, and calcium and a whole mess of other things. And the normal values for those, the normal value for sodium in your blood is 140, plus or minus about five, the normal concentration of chloride in your plasma is 100, plus or minus about five. Same thing with potassium. It's not plus or minus five, it's plus or minus about one, one and a half. So there's not as big a leeway with potassium. So what does that mean? That means on an exam, if I talked about the concentration of sodium in the plasma,

14:40

talking about this too,

14:42

same thing here, if I talk about the concentration of chloride in the plasma, you know that this is a normal value, and then if I have it higher or lower than 100, that is significantly higher or lower, you know that that's not normal. So that's why I mentioning this. So if I talk about blood work

15:00

I talk about the concentrations in these ions, you know, that 140 for sodium 100, for chloride five for potassium, those are the normal values. And if I deviate from those normal values,

15:12

well, then you're gonna have to do some type of,

15:15

you're gonna have to answer a question that revolves around it, you'll see how not till the next lecture though. All right.

15:21

Something else we got to talk about here, too, is

15:25

channels. So we're going to do an awful lot of transport in this chapter. So we're going back to something that we did back in chapter three. And the first transport process that we're going to bring up is facilitated diffusion. Now when you hear the word facilitated diffusion, what transporter should you think of immediately

15:46

starts with a C

15:49

channels. So we're going to talk about channels again.

15:53

So we have sodium channels, chloride channels, potassium channels, and I'm going to label them as such. So that sodium channels and I'm making it plural, because there's a whole mess of them in the membrane of that cell. And it's going to be a chloride channel,

16:09

it's going to be plural, because there's tons of them. Same thing over here, potassium,

16:15

potassium channels. And because we have these channels, these ions are permeable. So now we're going to talk about permeability, what's the word you should think about when you hear permeability

16:28

ability, right. So permeability means that the ion in this particular case is an ion unnecessarily have to be an ion is permeable to the membrane. Why? Because these channels are going to facilitate their transport facilitated diffusion. Now, facilitated diffusion is what kind of transport passive or active

16:50

passive, when we talk about passive transport, are we going down a gradient or up a gradient, we're going down a gradient. So tell me in which direction sodium is going to be transported into the cell or out into the cell from a high concentration to low concentration. And so what we'll do is, we'll just draw a little arrow indicating that sodium is going to be transported into the cell chloride, same direction, yes, absolutely high concentration outside the cell concentration inside the cell.

17:24

And then potassium clearly is going to be going in the opposite direction from high concentration to low concentration out again, this is passive transport.

17:34

And so our potassium is going to be transported out of the cell passively.

17:39

Now,

17:41

permeability, if you recall, is a measured value, we talked about this, let me remind you, by the way,

17:48

remember this picture,

17:50

page 12, in your notes, and so we drew a picture, and we were talking about the size of gradients and the size of the permeability, and how permeability can change based on a number of different things. So the value for permeability can be different. And it can change and milliseconds, which we'll be talking about later. But permeability can vary from one ion, one molecule to the next, and it's going to at rest. And so now what we're going to do is, again, that's a picture that's already on pilot, you saw it back in chapter three of the first section this semester. So so far, what have we done, we've taken potassium, sodium and chloride concentrations, and we stuck them in that picture. And that's these values here. Now, one thing I want to point out as well, you see that little subscript i, that just simply means intracellular, those are the concentrations inside the cell. And then there's a subscript Oh, that's outside the cell,

18:45

plasma lamp interstitial fluid. And those values are going to correspond to what we see in the picture that we just drew. Now we have our permeability values, and permeability is going to be abbreviated with a capital P. And the permeability of each ion is going to be indicated in subscript by the abbreviation of each IAM. And so let's add these values to the picture. That value there, that value here and this value will be here. And the value for permeability is going to indicate how much of this molecule or of a molecule is going to be transported across the membrane, such that the smaller the value, so the permeability of sodium is about 0.05. That is an itty bitty number. Compared to potassium, potassium is permeability

19:34

is about one. So potassium is permeability is 20 times as much as sodium. What does that mean? What that means is, is that 20 times as much potassium is going to be transported out of that cell as sodium is going to be transported into the cell. Now why is that? Well, we go back to the picture that we drew one of the main reasons is

19:58

has to do with numbers.

20:00

There's 20 times as many potassium channels. That's the reason that's the reason we're going to talk about are there other reasons? Yeah, but that's the main reason. It's a numbers game. More channels for transport.

20:14

Chloride somewhere in between permeability of chloride, spot 0.45.

20:23

So now we've set the table here, we've set the table for transport.

20:29

We have gradients, right, what's the word you should think of when you hear gradient, what's the one word you should think of this starts with the D,

20:37

a difference. So we have gradients here, a difference in concentration for all three of these ions, which is going to dictate the direction in which these ions are transported, which you guys told me, that's what these arrows are indicating their direction. And we have these different permeabilities. And again, these are values at rest,

20:58

the concentrations are going to be the same almost regardless, so they can change a little bit. The permeability is can change vastly, and they will, and I'll show you in the next lecture, but at rest, the permeability is of sodium chloride and potassium are those,

21:14

the bigger the number, the more the transport. And that's going to be a vital component of what the membrane potential is going to be. And we'll see that in just a little bit. So now that we've set the table, now we can move forward and talk about membrane potential itself. Now one of the things I want to point out, and actually I'm going to add it to this picture as well.

21:39

We had the sodium potassium pump, which I'm going to assume you guys remember, that uses ATP, this is primary active transport, to pump molecules up there green. And if it's the sodium potassium pump, well, it's going to be pumping sodium out of the cell of its gradient in potassium into the cell, up its gradient. And as we learned back in chapter three, I told you and we learned that the sodium potassium pumps job is to create the sodium gradient, and the potassium gradient, and to maintain those gradients that as far as you're concerned, is the job of this pump. That's its job. Now, I have something written in the notes, it's very important to state that the sodium potassium pump is not responsible for resting membrane potential. Even though almost every book out there, every website, very, very reputable websites, most people will teach you 99% of people will teach you that the sodium potassium pump is responsible for resting membrane potential. And they're all wrong.

22:47

Khan Academy, I bet you guys have probably at least heard that that's how they teach it. And that's a very reputable website, most of the stuff that they have on there is right. But that is something that is absolutely untrue. Yeah, how this started in y and still talk the way that it is. I have no idea. But it is what it is. So you're one of the few people literally in the world that know that that's not the truth. What is responsible for resting membrane potential? It's mainly potassium channels. Moving potassium, why is that?

23:21

Well, the status over here to the right,

23:24

the ion

23:28

with

23:31

the largest

23:33

permeability.

23:37

Hair has

23:39

the biggest

23:42

influence

23:45

on

23:47

membrane potential.

23:50

And because potassium at rest has the biggest permeability, it is going to have the biggest influence on resting membrane potential.

24:02

Now one of the things, and I've heard this in the past, well, Dr. Are Why are you the only person on the planet that while I'm not the only person on the planet? That's right. But why is my wire are most people wrong? And again, I don't know. But I promise you I know what I'm talking about. I don't know if you guys know this, but I was a scientist for 10 years. And that's one of the things I used to do. I used to study the brain. I used to measure membrane potential in cells. I know how membrane potential works.

24:30

It is what it is, I promise you that I'm right. And I promise you that most everybody else is wrong. That's and again, I don't know why. I just I guess I got lucky and I was taught by smart people. Not that the other people aren't smart. That's just one thing that they don't understand. All right. So anyway,

24:47

by the way, I hated my job, which is why I'm teaching now.

24:51

I was miserable being a scientist. But anyway, so please understand that this is the case and you'll probably see that on the exams. Just put the

25:00

Even

25:01

now, the chloride concentration gradient, why is it what is I'm not getting into it, just understand that we have a chloride gradient, and that it has been obtained by something, actually a number of things, but we're not going to get into it. The sodium potassium gradients, however, I do want you to understand and know, because we've already learned it, that this pump is responsible for it again, not for resting membrane potential.

25:28

So now what,

25:29

so what have we taken care of so far, took care of all this right here,

25:34

took care of all these words right here. And so once again, we've set the table, we've set the table for me to show you how membrane potential is actually generated, how these charges are separated, just the perfect way. So that all of these cells have once again, a normal membrane potential. And it's going to be dictated by two main factors. And that is how big the concentration gradient is. And the permeability of the individual ions, those two things are going to dictate number one, the direction in which the ions are going to be transported. And again, number two, how much of the ion is going to be transported.

26:15

And so if we can understand that, I hope we do, because we already learned it, in chapter three, you guys were tested on it on the first exam, that that lays the foundation for us to understand how membrane potential works.

26:29

So now what, these are the words

26:33

that explain to you how resting membrane potential is generated. And so what I'm going to do now is I'm going to take those words, and I'm going to draw a picture. And by the time that picture is done, it's going to look an awful lot like this picture.

26:49

So let's do that. So we're going to combine this picture right here, with this picture right here.

26:56

By writing, or drawing everything that's sitting there. So let's draw our cell again. So once again, this is going to be resting membrane potential.

27:06

resting membrane potential. So now we have a cell.

27:13

And we're gonna put our sodium potassium and chloride concentrations, there's nothing wrong with that repetition is a good way to learn. So we're sitting at 140,

27:22

and 15, inside the cell potassium, by the way, you should know these values like the back of your hand, at some point, it's very important that you do especially if you are going to be a physician or a PA or something in the medical field someday, because these values are going to be the same values. Once again, as we see in your blood work. Or in a patient's blood work. Oops, I should say 10. And then we have our channels here.

27:46

Our chloride channel, our sodium channel, our potassium channel, we know what they are, they've been defined in the previous picture.

27:52

Now,

27:53

we are going to now have these molecules, these ions get transported into and out of the cell, we're going to start with potassium, because that's the one with the biggest permeability. And so we're going to give ourselves a visual, a nice big, huge arrow, indicating that an awful lot of potassium is going to be transported out of the cell. Now, the vast, vast, vast, vast majority of potassium is going to end up in the interstitial fluid.

28:23

But as these potassium ions are transported out of the cell, some of them a small, small percentage, are going to get stuck to the outer membrane.

28:38

So I'm going to put a lot of potassium ions on this outer membrane. Now the other thing that I'm going to do as well is I'm going going to put just a smattering of other little positive charges here and there that aren't potassium and some negative charges as well. So do understand that we have some negative charges on that outer membrane, some positive charges on that outer membrane that aren't potassium, but there's a lot of potassium on that outer membrane. Again, the vast majority of potassium is going to end up in the interstitial fluid. But some are going to get stuck to that outer wall.

29:16

Let's do sodium. Now, because this has the least amount of permeability again, at rest, I'm going to make this arrow

29:23

really small.

29:26

The vast majority of these sodium ions are going to end up in the cytosol. But a small percentage are going to end up on the inner membrane, but nowhere near as many

29:38

potassium ions on the outer membrane.

29:42

Why is that because the permeability is so small,

29:47

and chloride,

29:49

so somewhere in between, so the arrow is going to be somewhere in between the size of the sodium and the potassium arrow. And so now I'm going to put

29:59

a D

30:00

Setting number of chloride ions on this inner membrane.

30:09

So now we have separation of charge.

30:13

And these charges that are on the inner and the outer membrane are just the right number of charges. Why? Because these permeability values that we have here are not by accident,

30:26

they are what they are because they're supposed to be what they are, the concentrations of these ions are exactly what they are, because that's what they're supposed to be. So the concentrations of these ions are going to dictate how much or the ions will move into the cellar of the cell. And so to have the permeability, so we're going to have the exact amount of sodium moving in the exact amount of chloride moving in and the exact amount of potassium moving in so that these ions are distributed perfectly on the outer membrane, and the inner membrane. And so we have a separation of charge

here. And the separation of charge is going to generate a certain membrane potential. membrane potential is negative.

31:09

I'm going to leave you with that because I think I only have one minute left, I'm going to explain what that means. It doesn't mean that the charge the potential, the membrane potential,

31:20

is something bad because it's negative. It's dictated by how its measured.

31:26

A battery doesn't have a negative potential. But it could if we measured that potential in a different way, if we reverse the electrodes when we measured it, it would read negative.

31:37

A negative membrane potential simply means well, you know what? I'm going to explain it. I'm not going to rush right now. I'll explain it to you on Wednesday, but this is a good foundation, I think for the next lecture. Alright guys, I'll see you Wednesday.

02 - Neuro - 20OCT2021

Fri, 10/29 4:30PM • 1:11:32

SUMMARY KEYWORDS

membrane potential, inner membrane, cell, sodium, membrane, channels, potential, potassium, transport, permeability, resting, depolarization, ions, chloride, resting membrane potential, neuron, potassium channels, negative, called, action potentials

00:02

Let's get started, folks.

00:06

So at the end of lecture on Monday, we had talked about resting membrane potential, and how it's established. It is established via these channels and the main channel that is going to give us a resting membrane potential, the one that has the biggest influence, that's going to be the potassium channels. Why is that?

00:27

Because that's the one that has the highest permeability. That's the reason. So whatever ion has the highest permeability, that's going to have the biggest influence on membrane potential and it rests, it just happens to be potassium channels, I actually wrote this in at the very end of lecture, if you don't have this in your notes right here. That might be the reason you missed it is because I wrote it, right, the very, very, very, very end.

00:53

It's on pilots. So it's, so it's the pictures there, the way that it's up here up on the screen, but in case it's not your notes.

01:00

There it is. Now,

01:04

when it comes to membrane potential, and this is something that I mentioned at the end of class, it's negative, it has a negative value resting membrane potential that is, now it all has to do with how we make the measurement, the reference for membrane potential is going to be the inner membrane versus the outer membrane. And if we look at the distribution of charge, and the distribution of charges, such because of how these ions are being transported, as sodium is transported into the cell, a small small percentage will get stuck to the inner membrane, same thing with chloride, and then as Pat potassium is being transported out of the cell, there's going to be a small percentage that are going to get stuck to the outer membrane. Because we're moving so many potassium ions, once again, because

its permeability is so large, we're going to have an awful lot of positive charge on the outer membrane, much more so than we do on the inner membrane. And that's the reason that membrane potential is negative. Now, I'm going to explain to you what that means. So I'm going to draw a theoretical cell here with only positive charge. And I'm going to show you that with just positive charge, we can still have a negative membrane potential.

02:17

So VM, resting VM.

02:22

And that's all we're talking about right now is resting membrane potential resting membrane potential is negative, the actual measured value is negative. So I'm going to draw a cell.

02:35

And I'm just going to put positive charges in this picture a whole bunch of positive charges on the outer membrane, and they very small number of positive charges on the inner membrane.

02:48

The membrane potential of that cell is negative. So I'm going to ask you a question, I'm going to make a statement,

02:55

the outer membrane,

02:59

as compared to the inner membrane, so the outer membrane is more positive

03:07

than

03:09

the inner membrane nearby that,

03:13

yeah, there's more positive charges on the outer membrane is posted the inner membrane that's easy to see.

03:19

If that's the case, therefore, therefore, three little dots, therefore, the inner membrane

03:30

is more negative

03:37

than the outer membrane has to be.

03:41

If the outer membrane is more positive, the inner membrane must be more negative, even if there's not a negative charge there, because what we're doing is, is that we're comparing the outer membrane and the inner membranes, that's how membrane potential, that's how it is, that's how it is with a battery. That's how it is with itself.

04:01

And so because our reference is the inner membrane, membrane potential is negative. Now, if we measured membrane potential in a different way, if the reference was the outer membrane, then it would be positive is just a measurement. That's all. And when it comes to the actual value, I'm not going to have you know the actual value for membrane potential. I think I mentioned it in the last lecture, I'm just going to throw it down here. So resting VM

04:29

is anywhere from depending on the cell, depending on the location,

04:35

anywhere from negative 40 millivolts to negative 90 millivolts. You don't have to know that. The reason I throw that out there is because you'll hear you'll see books you'll hear all the time, membrane potentials, net resting membrane potentials, negative 70, millivolts. Is that wrong? No, it's not wrong at all. But it could also be negative 40, negative 41 or 42 or 88, or 89, or whatever.

05:00

If you can say people are five foot tall as I know, people are five foot tall. But then there are people who are four foot six, and six foot two and seven foot tall, there's a range. Now, why is the membrane potential has such a big huge wide range? It depends on go back to this picture, it depends on the specific permeability of potassium. So potassium might not have a permeability of one, it might be point nine, six, the permeability of sodium might not be point 05, it might be point 04. So these are average values. If I actually took all these average values, for sodium concentration in and out and chloride concentration in and out potassium concentration in and out, and all of those particular values for permeability, the membrane potential, if I did the calculation, and I've done it is negative 65 millivolts, given these values, which is kind of right there in that sweet spot. And how do I do that calculation? Well, I use that equation that you're not going to have to know, they already tell you, you don't have to know this material? I don't think I did. So some good news is the material that you don't have to know. So there won't be any calculations on this exam.

06:08

So why don't we just talk about what you don't have to know. And I'm not really sure what page this is. But at the top there, you should see the golden Hosking cast equation into the equation that can predict membrane potential based on those three ions or concentrations inside and outside of the cell. And their permeabilities, you're not going to have to know how to do it.

06:28

You also don't have to know equilibrium potential, or nursed potentials nerds equation, if you want to talk about this stuff in my office, I'd be more than happy to do that. But I think you probably already have enough on your plate when it comes to this particular exam and the material. But if you're curious, I'll talk to you about it, but it will not be on the exam, I promise. What will be on the exam, though, is how membrane potential changes. And so what we're going to do now is we're going to talk about how membrane potential deviates from resting membrane potential. And so the next thing we're going to do, next picture we're going to draw is a cell. So here's a cell

07:10

that doesn't matter what cell and we're going to measure membrane potential. Remember that little drawing there is indicative indicative of us measuring membrane potential

07:22

of some cell.

07:25

And silver Tucci is in his lab, completely miserable, measuring the membrane potential of cells.

07:34

And what might he see? Well, he might see this initially.

07:42

Tell me what that is.

07:44

Nice and steady. That's the resting membrane potential, right there. So we're measuring the resting membrane potential of that cell nice and steady is not being stimulated, it's not being inhibited. So we're going to put resting membrane potential. So on the computer screen on the oscilloscope, that's what it would look like.

08:04

Now what can happen

08:08

is this

08:10

membrane potential, all of a sudden changes membrane potential, all of a sudden is getting more positive. Let's put some values in here, I'll make that negative.

08:20

I don't know, negative 58 picked it up just right out of the year. And now I'm going to say that we have a membrane potential now of

08:30

No, no, negative 51.

08:34

That's more positive than negative 58. Not positive.

08:38

But it's more positive than negative 58. And we're going to talk about how this happens. By the way, this is some terms that I want to define right now. And it's just a nice segue into what we're going to be talking about for quite a bit of the lecture today. There's a term for that, when membrane potential gets more positive, we say that it is depolarized. So we depolarize the membrane potential, which by definition means it gets more positive. And again, I'm going to show you how that happens.

09:07

Then,

09:08

membrane potential, we're going to say is going to return to resting membrane potential. And when it does that, we say that the membrane re polarized. So this is repolarize. That is membrane potential returning back to resting membrane potential after some change. And the change in this particular case is a depolarization. And then we're back to arresting.

09:36

And then we're going to change it again, except this time, it's going to get more negative. So I'm just going to once again pick a number right out of the air. I don't know negative 62, which is more negative than negative 58. That also is called something that's called hyperpolarize.

09:54

So now we know what all these terms mean. And then we'll return membrane potential back to resting

10:00

that two is going to be repolarize.

10:09

I'm going to write it on the other side.

10:13

So now we know what these terms are. So that right there is repolarize.

10:19

And then we are once again, that resting

10:24

cell membrane potential changes changing out. Yes.

10:28

So when you say the most part, it's the majority of the time it's in resting.

10:36

Depends on the cell. Yeah, there are some cells that that are at resting membrane potential for milliseconds, like split split split. split seconds is like a type of heart cell that that happens with other cells that can just be kind of chilling, like maybe an epithelial cell that's releasing a hormone, for example, until it's told to release a hormone. Alright, something else that's important to know is this is that when you depolarize,

11:04

you're stimulating

11:07

the cell Asterion. Now there's an exception to this rule, we're not going to talk about the exception. So this is going to be our rule. If you make a cell more positive, you are stimulating that cell and then the opposite is going to hold true when you make it more negative when you hyperpolarize it,

11:23

you're inhibiting the cell. Now, what does that what does that mean? Well, let's say it is an epithelial cell that releases a hormone. And that cell is controlled by the nervous system, or something else that's causing its membrane potential to get more positive, then maybe hormone is released.

11:41

Let's say that this is a neuron, and we hyperpolarize it. Well, now it's going to get more negative, we'll see exactly what that means. And it's further away from something called threshold. And we'll talk about threshold today. So changing the membrane potential of cells controls the actions of the cells. And again, this is going to be our rule for this course. Okay, that is pretty much the rule. Again, there's only like one or two exceptions. So far, so good.

12:14

How does this happen? Now we're going to talk about how it happens. How do we change membrane potential? Well, given how we establish our membrane potential, that is the transport of ions, and then therefore, a certain distribution of ions on either side of the membrane.

12:32

That's how we're going to change membrane potential, we are going to change the distribution of ions across the membrane by changing the transport of the ions into and out of the cell. So that's going to be our question that we're going to start to answer. How

12:51

is membrane potential? changed?

12:56

That's our question. Here's our answer.

13:00

You change the transport

13:04

of ions.

13:07

That's how you do it. Because if you do that, you're going to change the distribution of charge across the membrane.

13:15

Now, how do you do that?

13:20

How do you change the transport of ions? That's our next question. So how is ion

13:28

transport changed? Which is going to obviously, ultimately, change membrane potential? I'm not going to answer that question yet. Let me come back to

13:40

let's stick with this. And let's talk about our three ions. So what I'm going to do here is slowly

13:48

now I'm going to do it on another page here. And I'm just going to draw say, I'm going to remind ourselves here, of the direction in which these ions are being transported, we're talking about passive transport here, facilitated diffusion through channels.

14:01

Sodium is transported into the cell, chloride is transported into the cell. And again, this is passive transport. Potassium is transported out.

14:11

Just as a reminder,

14:14

now, we're going to change the transport of these ions, and then we're going to talk about what's going to happen.

14:20

Let's start with sodium.

14:23

So if

14:25

we increase sodium transport,

14:31

what does that mean? Well, more sodium is now going to come into the cell.

14:36

How do we do that? I'm going to answer that question in just a little bit, which is this question right here. We'll get to it. So if we increase sodium transport, more of it's going to go into the cell, that's going to cause more positive charge

14:52

on the inner membrane, right, of course, because a certain percentage of those sodium ions are going to get stuck to the inner

15:00

membrane, if the inner membrane is more positive,

15:04

that's a depolarization. Because once again, the reference is the inner membrane.

15:11

If

15:14

we decrease sodium transport,

15:19

well, now we're not going to have as many positive charges on the inner membrane.

15:24

And so we're going to have less positive charge

15:29

on the inner membrane.

15:31

And so now that embrace that inner membrane is going to be less positive, which means it's going to be more negative.

15:38

And so that's going to cause a hyperpolarization.

15:43

hyperpolarization, by the way, is the noun hyperpolarized depolarize. Those are verbs. All right, which is why the word is different than what I used here. When I define depolarize, hyperpolarize, so more sodium being transported into the cell, this was going to happen,

16:02

we're going to depolarize less sodium being transported into the cell, this is what's going to happen. And we're assuming that we're sitting at rest first, that's going to be our assumption, not that it would matter. Okay, but because we talked about resting membrane potential, let's just imagine that the cell is doing this, all of a sudden, more sodium is transported, boom, we're gonna stimulate the cell, less sodium, boom, we're gonna inhibit the cell, because we're making them more negative. Moving on, let's go to chloride.

16:33

If

16:34

we increase chloride transport, which is now a negatively charged ion, so the story is going to be different, now it's going in the same direction as sodium is going into the cell.

16:45

So now we're going to have more negative charge

16:49

on the inner membrane.

16:52

And so of course, now, because the inner membrane is our reference, well, we're going to have a hyperpolarization

17:01

with more sodium coming into the cell, and then the complete opposite is going to hold true. If we decrease chloride transport,

17:12

well, now we're going to have less negative charge.

17:17

If we have less negative charge on the inner membrane,

17:21

well, now the inner membrane is going to be less negative, which means it's more positive, so we get a depolarization.

17:33

Now potassium is going to take a little bit more wording to define what's going to occur. And so now let's talk about potassium, which is a positively charged ion that's being transported out of the cell. And so let's now do potassium. So if we increase potassium transport,

17:54

well, now, can we do the same type of wording? Yep. Now we're going to have more positive charge on the outer membrane, not inner membrane, more positive charge on the outer membrane?

18:08

Well, if that's the case, the outer membrane

18:13

is more negative, I'm sorry, more positive?

18:18

Well, let's go back to something that we already did. This here,

18:23

outer membrane is more positive, that means the inner membranes more negative, because again, we're comparing the two that's how we get our membrane potential value. So outer membrane is more positive. And so what that means is, therefore I'll even do the little three dots again, there for the inner membrane

18:43

is more negative.

18:49

We get a hyperpolarization.

18:51

more potassium ions on the outer membrane causes membrane potential to get more nade. And let's be thorough.

19:00

If we decrease potassium transport, well, not not as many potassium ions are going to be on that outer membranes, now we have less positive charge

19:11

on the outer membrane.

19:15

And so what does that mean? Well, it means the outer membrane

19:22

is less positive.

19:27

Therefore, the inner membrane compared to it because that's what we're doing. And your membrane

19:36

is more

19:39

positive

19:42

depolarization

19:47

by changing the transport of these charged molecules, so what we've done here on this page, what we've done here on this page

20:00

addresses this I was VM changed, change the transport of ions. I've shown you how. But how is the transport of the ions done? That's our next question. So we're increasing and decreasing the transport of these ions. Well, how the hell do we do that? Well, we already know. How do we already know that? Well, because we already learned it.

20:21

We learned it. In chapter three. We learned it on page 12 of your notes, when we were talking about concentration gradients, which is all about ion concentration,

20:34

and permeability. So now I'm going to state it. So we're just going to repeat what we already know. But we're applying it to something very specific now. membrane potential. So how is ion transport changed? Answer, we change

20:53

ion concentration gradient, what's the word you think of when you hear gradient direct with a D,

21:01

difference in concentration between two compartments. In this particular case, it would be interstitial fluid, and the cytosol, the intracellular compartment, such that remind you of this, as you increase the gradient,

21:17

as you increase the ion concentration gradient.

21:24

You increase transport.

21:28

Right, we learned that this is nothing new.

21:32

If you decrease the ion concentration gradient,

21:37

well, then you decrease transport.

21:42

So that's one way to change transport, you change the concentration of the ions. What's the other way you change the permeability.

21:52

So you change

21:55

ion permeability.

21:58

Now, at resting conditions, the permeability of potassium is one, sodium is point 05. Chloride is point four or five. Does that mean that that's the way it's always going to be? No, it's not the way is it all the time. And most times, they are changing, they're changing in you and me right now.

22:18

And so, permeability go up permeability and go down, the permeability goes up more transport permeability goes down less transport, such that if we increase permeability

22:32

not put ion permeability just to be thorough.

22:36

If we increase ion permeability,

22:41

we increase transport.

22:44

Again, we already learned this. Now how do we do that?

22:48

So for example,

22:51

we open more channels.

22:58

channels aren't always open, sometimes they're closed, maybe half of them are closed, and then we open 20 More percent of them, we just increase permeability. Or you can have more channels.

23:12

You can make more channels and stick more channels in the membrane. So a greater number of channels in the membrane. That would be another way to increase permeability.

23:21

What's the word you think of with permeability, by the way?

23:26

Ability, right, the ability to move across the membrane. Well, these ions that we're discussing here,

23:33

have permeability well, because of the channels, the channels are giving them, their permeability, otherwise they're not getting through. They're charged. It's not simple diffusion, it's facilitated diffusion. So the channels are facilitating their movement across the membrane. And if you have more of these channels, or if more of them are open, you're going to get more movement, more movement, you're going to change the distribution of the charge across the membrane. And we'll be thorough, of course, we always are.

24:04

Where the hell am I? Here we are.

24:08

So

24:10

decrease ion permeability.

24:13

And you therefore will get a decrease in transport.

24:19

And how does this happen? Well, you close

24:23

ion channels

24:28

or you have less

24:32

ion channels.

24:35

Let me put the word ions over here open more ion channels.

24:42

So that's how it's going to be done. And now we're going to demonstrate this.

24:48

So we've introduced everything now we're going to actually see it open more ion channels

24:54

or have more ion channels.

25:00

So now we're going to do this. And this is going to be material. So we're going to start with changing the grading, that's the first thing that we're going to do. And then we'll do permeability. Now, if you look on page, hell, I don't know what page it is 27, maybe

25:16

this 27 had a whole bunch of Sudan, like 12 of them, I think that's the page, right? We're going to do maybe two or three of those,

25:24

what I'm doing on that page is either increasing or decreasing an ions concentration, either inside the cell or outside the cell. Given, there's three ions that we're talking about, there's going to be 12 Total scenarios for each.

25:41

And so let us move forward. And let's talk about this.

25:45

So the first one we'll do is I'm going to do Sony. And this is the one that I always do first, because it's actually a tougher one to understand initially, but then once you really see it, it's easy from this point forward. So we're going to have a cell. And all we're going to do is change sodium concentration inside the cell, I'm going to actually draw just a little bigger.

26:09

And we're going to put our normal sodium concentrations here, 140 on the outside good for us we're repeating that's a good way to learn repetition. sodium concentration on the inside the cell, as we know, or we'll know eventually is about 15 values, you have to know

26:25

what I'm going to do is I'm going to change intracellular sodium concentration. And by the way, we're assuming everything else is going on the way that it's supposed to go on. And that is, potassium is being transported out of the cell chlorides being transported out of the cell, sodium is being transported into the cell, we're at resting conditions, that's our assumption. So we have the distribution of ions across the membrane, I'm just not going to draw him in here, I'm just going to concentrate on one thing, and that is sodium. And so the way that we have this drawn right now, that's the amount of sodium

26:59

that is being transported into the cell at rest, that's where we're sitting.

27:05

First thing we're going to do is, we're going to change sodium concentration, I'm going to pick a number 25, I picked it right out of the air. So I just increased intracellular sodium concentration, that's going to be number one. So number one, I'm going to increase intracellular sodium concentration, that's what that little eye is.

27:31

Now you tell me,

27:33

what does that do to the sodium gradient does the sodium gradient go up does the sodium gradient go down the gradient

27:43

goes down, right gradient is difference, the difference initially was 140 versus 15. But now it's 140 versus 25. That's a smaller gradient. Now, certainly, you could probably already see that if we add a whole bunch of positive charge in the cytosol, membrane potential should get more positive, right?

28:05

Wrong. membrane potential is going to get more negative, we're going to add positive charge to the cytosol. And membrane potential is going to get more negative.

28:16

And this is how we actually just talked about it a second ago. So we have a decrease in the sodium gradient. You guys just told me that. And you told me that correctly. So is the decrease in the sodium gradient.

28:30

If there's a decrease in the sodium gradient, are we going to get more or less sodium getting transported into the cell more or less,

28:39

less. So this is going to cause a decrease in sodium transport. And so what we'll do is we'll give ourselves a visual, the red arrow is going to indicate the change that's occurred, that is less sodium being transported into the cell. And the other thing that we'll do is we'll put the positive charges from sodium

29:03

on the inner membrane and black, that's what we had initially. And now because of this change, because we're not transporting as many sodium ions into the cell, well, now we got to get rid of some

29:14

because it just not gonna be as many because we're not transporting as many positive charges into the cell. So not as many of them Oh gets stuck to the inner membrane. So with the decrease in sodium transport,

29:27

whenever we're going to have less positive charge

29:31

on the inner membrane.

29:34

And if there's less positive charge on the inner membrane, well, what does that cause?

29:40

A hyperpolarization. So we added positive charge to the cytosol. And yet we got a hyperpolarization. Because it's about the membrane right? Is this cytosol potential? No, it is not. It is membrane potential. And that's why I made that a point. To say that on Monday, it's membrane

30:00

Potential now, does the cytosol influence membrane potential? Of course it does. I just showed you that it does. But it's not what the actual measured value is. And so if we go back to what we just did a little bit ago,

30:13

if you decrease the transport of sodium, what do we get?

30:17

We get hyperpolarization.

30:20

I don't know which one it is on that list, it might be the sixth or seventh one down, I don't know. But if you look, increase intracellular sodium concentration, I promise you, we'll see hyperpolarization on page 27.

30:35

So far, so good.

30:37

Let's do another one. Let's do potassium. Oh, you know what we'll do also, let's do this, let us measure the membrane potential of that cell during this little scenario.

30:49

So initially, we were resting.

30:52

And then all of a sudden, at this particular point in time, we actually even do it in red.

30:59

We got to hyperpolarization. Why, because over here at this point,

31:04

well, we increased

31:09

intracellular sodium and we get hyperpolarization.

31:15

Now what, let's do potassium.

31:18

So once again, we're just going to take one variable at a time.

31:22

And we know that potassium concentration is high on the outside of the cell or low on the outside of the cell, it's around five ish.

31:29

And it's high on the inside of the cell.

31:34

And so what I'm going to do here, and we have this much potassium being transported out of the cell, that's what that arrow is going to indicate. What I'm going to do is I'm going to change that to eight,

31:45

which is really ridiculously high. By the way, if you have a patient and you find that their potassium concentration in their plasma is eight,

31:53

that's really a bad thing. Doesn't sound like a bad thing, because five to eight is only three, but proportionately wise, it's a bad thing. Why did I say plasma? By the way?

32:04

The hell does the plasma have to do with anything, I don't have a blood vessel in this picture.

32:10

Because it's the same right? Let me remind you. So when it comes to the interstitial fluid values,

32:18

it's the same as what it is in the plasma, as it is an Olympic. Please remember that. These are all extracellular concentrator extracellular fluids, plasma, lamp, interstitial fluid,

32:30

right?

32:32

We learned that the first day of class. So getting back to this.

32:37

So I just increase that. So number one,

32:41

I am going to increase extracellular, that's what the O stands for outside potassium concentration, well, you tell me did the gradient get bigger did the gradient gets smaller,

32:54

they got smaller, the difference now between concentration of potassium inside and outside the cell has now shrunk by three. Again, doesn't seem like a lot, but it is a lot. And so because of that, we are going to decrease the potassium gradient.

33:13

And when you decrease potassium gradient, well, you're obviously going to decrease potassium transport. So we're going to decrease potassium transport.

33:23

And so let's do this right here. So now we're going to have less potassium being transported out of the cell, let's put our positive charges that were there initially,

33:34

there's going to be a whole bunch of them because potassium is permeability is so high.

33:39

By the way, changing the gradient isn't going to change the permeability, let me make sure that we understand that there are two completely independent variables, if one changes doesn't mean the other one's going to change at all. They can change independent of each other. So now, because of this, we're not going to have as many potassium ions

33:58

on the outer membrane, because not as many potassium ions are being transported out of the cell. And so what this is going to do and result in is not there going to be less positive charge

34:11

on the outer membrane.

34:16

And so what that means is, is that the outer membrane is less positive, which means the inner membrane is more positive. So the inner membrane is therefore

34:31

is more positive. And what do we call that?

34:38

A depolarization.

34:42

So if you draw it out,

34:46

that's time. Here's our membrane potential. We were sitting at rest and now all of a sudden

34:53

that happens. Why? Because we increased extracellular the

35:00

Testing concentrates. Now, you might be asking yourself why the hell we learn in this doctor? Or could this be that important? It's, it's a wildly important

35:07

this could be. So if you have a patient and they have a heart arrhythmia, we'll learn about arrhythmias next semester, where their heart just not being properly and you take their blood work, and that's something that you've got to do. And you see that their potassium concentration is high, that's probably the answer.

35:23

Or if you have a patient who's having seizures, which is when the activity of neurons in your brain is too high,

35:32

that could that could absolutely 100% Cause that depolarization what are we doing? We are

35:40

stimulating, so we're overstimulating when our potassium concentration is high.

35:48

So I can't even begin to tell you how important this is clinically. And I think almost everybody in here, at some point wants to go into medicine of some kind. This is a really important, that's why we take blood from patients, by the way,

36:03

because we're trying to diagnose their condition. And a lot of times bloodwork will tell us what's going on. Now, that's just going to be one part of the puzzle, then you have to figure out what why the hell's potassium concentration on they have kidney disease, for example? Are they on some medication that's causing the potassium concentration to be high?

36:24

So important to understand what happens to membrane potential when you change the concentrations of these ions? It's incredibly relevant when it comes to clinical scenarios. All right, let's do one more. Let's do chloride.

36:39

Let's do

36:41

what are we going to do here?

36:44

So fluoride, as we know, but 100 out here, and about 10 inside the cell. And so we know that chloride goes in this direction. And because of that, we're going to have these negative charges on the inner membrane, because a small percentage of those chloride ions will get stuck to that inner membrane. And so what I'm going to do is, is that I'm going to, we want to do to chloride.

37:07

Let's make chloride, what have I done so far?

37:11

I've made the gradients small, I'm going to make the gradient big. Let's go 120.

37:18

So the gradient just got bigger clearly. So number one, we have increased extracellular chloride concentration. And when that concentration goes up, well, we have just increased the chloride gradient.

37:34

And when we do that, well, of course, we have increased chloride transport.

37:40

And so let's draw that in the picture. Now we have a bigger arrow.

37:44

So because of that, now, we're going to have more negative charge on the inner membrane.

37:51

So number four more negative charge

37:57

on the inner membrane.

38:00

And if that's the case, well,

38:03

we have ourselves a hyperpolarization, we are inhibiting the cell,

38:09

or use the verb or the noun, or use the noun.

38:13

So let's say that you have a patient who is in a coma,

38:18

and you take their blood work, and you see that their chloride concentration is 120.

38:24

That could be the reason that they're in a coma, the neurons in their brain have gone to sleep. Why? Because they have been

38:32

inhibited by the hyperpolarization.

38:37

Alright, what time do we have, let's take a break. When we come back, we'll do the top of the next page with permeability get through those two. And we'll continue our soil you don't want to while you're on break, I'm just going to draw our membrane potential graph here.

38:54

Resting

38:57

hyperpolarize. Why because we increased

39:03

extracellular chloride.

39:05

And of course, we did that by

39:07

measuring membrane potential.

39:14

If there's anything I need to put up on the screen, or you'd like me to put up on the screen, just let me know.

39:18

I know that there was one.

39:21

I'll keep that up there for just a sec.

39:27

Alright, folks moving on. Now let's start talking about permeability. And so

39:36

oops. So now let's talk about permeability here changing permeability making the go up or making it down. We'll do a couple of examples. There's only six total

39:46

permeability as it goes up or down. There's three ions that we're talking about. So that equals six. And so let's let me see let's do

39:56

let's do potassium again. And let's

40:00

So potassium does that. And we're going to cause the permeability of potassium to go up. So number one,

40:10

let's increase the permeability of potassium.

40:14

Well, what is that going to do? Well, number two, let's give ourselves a visual. Well, now we are going to transport more potassium, let's put our positive charges on the outer membrane.

40:29

And those are the positive charges that were there at resting membrane potential. And so because of that,

40:36

we're going to increase the transport

40:39

of potassium.

40:42

And if that's the case, well, now we have to add some more positive charge to the outer membrane. Of course we do because more is being transported out of the cell. So more, we're going to get stuck to the outer membrane.

40:54

And so number three, we're going to have more positive charge on the outer membrane.

41:03

And if that's the case,

41:08

well, then the inner membrane is going to be more negative than the outer membrane because the outer membrane is more positive. So inner membrane

41:21

is now more negative.

41:26

We have a hyperpolarization. Oops.

41:31

I actually wanted to, I wanted it to go down. Let's make it go down. I don't want it to do the same thing or depolarization. I don't want it to go down.

41:40

Do I?

41:42

What do we do for the other one that we make potassium? We made potassium high. So we did that we made it go down. Okay, yeah, let's make it go. Yeah, we're gonna make it go up, we're gonna do this. Okay, hyperpolarization, I thought we did something different before.

41:56

All right. So we get a hyperpolarization there. Let's track it.

42:02

So we're gonna measure membrane potential,

42:06

we're sitting at rest, we're going to increase again, the permeability of potassium, we're doing nothing to the concentration of potassium, nada, zero. We're simply increasing its permeability, we are opening more potassium channels, I'll even put that in parentheses.

42:25

So we opened more potassium channels. So we could have done that.

42:32

And so when we do that,

42:35

when we increase potassium permeability, that's the scenario we're going to have.

42:45

Alright, now what let's do, chloride. When we make chloride do the last time I made it go up, let's make it go down. So we're going to decrease the permeability here.

42:57

So we have a certain amount of chloride being transported into the cell. And so because of that,

43:05

we'll have a number of negative ions or negative charges, I should say, on the inner membrane. And so what we're going to do to chloride is that we're going to make its permeability go down. So number one,

43:18

we're going to have a decrease in chloride permeability.

43:22

And so let's give ourselves a visual. So there's our visual, and let's just cross off a couple of these negative charges, because we're certainly not going to have as many now. So as a result of this, we are going to decrease the transport

43:38

have chloride.

43:40

And as a result of that, well, we're going to have a decrease and we're going to have less, let's use the same wording we had before. So we'll have less negative charge

43:52

on the inner membrane.

43:57

If we have less negative charge on the inner membrane, what that means is that the inner membrane will be less negative, which means it's going to be more positive. So inner membrane

44:10

is now more positive.

44:19

And we know what that means.

44:22

We get a depolarization.

44:26

And so let's measure the membrane potential and let's track it.

44:31

Oh, and let's close chloride channels. That's how we would do that.

44:38

There's our membrane potential.

44:40

And so right there at that point,

44:43

that's gonna happen, how

44:46

we decreased the permeability of chloride.

44:51

Alright.

44:53

Yes.

44:56

The transport inner outs

44:59

are

45:00

membrane is always going to be a reference, regardless of which direction the ion is being transported. That's correct. So we always want to go back to the inner membrane and what it is compared to the outer membrane, that's going to dictate what our membrane potential is, again, it's just the way that is measured. If we measured it the complete opposite way, well, then these negatives would be positives and the positives would be negative. It's just the way that we measure it. And that inner membrane is always our reference. Yes. So that's a couple sites, on top of opening more channels, have more channels, that we can do that too.

45:38

Is more

45:40

the cell makes more. Okay, so it just happens like the cell, that cell can be given a signal make more channels

45:48

that you have so many channels?

45:52

Well, yes and no, but it can change. Yeah, it can check and change right now. And it can change at any time.

46:03

So are we good with the transport and how we change transport, how we change membrane potential and how we change transport by changing permeability and concentration gradients.

46:13

It's going to be something that we visit and visit and visit and visit. So we'll see more of this, I promise.

46:21

Now what?

46:23

Well, we're going to keep on talking about changing membrane potential, except now we're going to talk about an action potential, which is a change in membrane potential. But it's a very unique way of changing membrane potential, there's just a handful of cells in your body that have the ability to do this.

46:40

Every cell in the body has a membrane potential, every cell all 40 trillion cells do, there's 220 different kinds of cells in your body, and every single one of them has a membrane potential. But there's just a handful, that can generate what's called an action potential. And an action potential is a local, explain what that means very large, very rapid depolarization, we know what that means, followed by a repolarization. We know what that means. The cells that can do this are neurons, muscle cells, those are the two kinds of cells that we will discuss, there's a couple of others that we're not going to discuss. And actually, there's a certain type of glial cell that can do it as well recently discovered, and I say recently, like 1520 years ago,

47:24

but for us, neurons, muscle cells, those are going to be those action potentials and those cells that we're going to discuss, we're going to see now action potentials next semester, as well. So what we're going to do here is, given that this is the nervous system, we'll talk about the action potential of the neuron first, later on in the semester, we're going to deal with the action potential of a muscle cell in the next semester, more action potentials, so we're not done with them. So I'm going to draw a neuron.

47:58

So there's our neuron. So that's the cell body.

48:03

That's the axon. And those are the presynaptic terminals right there. And so what we're going to do is, we're going to measure membrane potential right there, at that spot.

48:17

So just that little itty bitty piece of membrane is what we're concerned about, and what's happening at that little itty bitty piece of membrane right there at the axon.

48:28

And so what we're going to do is, is that we're going to track it.

48:32

So once again, number two, he is miserable, doing his research measuring the membrane potential with neurons.

48:39

And what he sees initially on the computer screen

48:43

is that what's that, again,

48:46

its resting membrane potential

48:49

as a membrane, this is the interstitial fluid out here. This is the intracellular fluid here, that's where the cytosol is. We have our channels doing their thing that we talked about in the lecture on Monday, this is a cell. Whenever I draw cells, I draw a circle. Why? Because it's easy. I want to draw a stick in there and every time will take me forever. Plus, it looks like crap. But this is a cell like any other cell with a membrane like any other cell with the membrane potential, like any other cell, including a resting membrane potential. And so we have a resting VM

49:22

at that point in time. Now what's going to happen

49:26

is we're going to stimulate the cell tell me what's going to happen to the membrane potential more positive or more negative? We're going to stimulate it

49:34

for positive would we call that a depolarization. So we're going to depolarize this neuron.

49:42

So let's go do that. Now, how does that happen? Tell me. Give me one example of how that happens. Just one

49:54

we closed chloride channels.

49:57

We closed potassium channels.

50:00

We opened sodium channels,

50:03

we increase permeability of sodium, we decrease permeability chloride, we decrease permeability of potassium, where the hell am I getting this? Well, we just did. It's on the top of page, whatever the hell page that is 2728, I don't know. Or

50:18

maybe we increased extracellular sodium.

50:21

Maybe we increased extracellular potassium,

50:24

maybe we decreased intracellular sodium.

50:28

That's from the previous page,

50:31

we had to change the concentration of some ion that caused this depolarization, there was one example we did was another D polar, there's another one right there, increase there. So the potassium right there, causing look at that, a depolarization, looks exactly like that.

50:49

Until we reach this magical value called threshold, and I'm going to depict that with just this little dotted line.

50:58

And at the end of that dotted line, I'm going to write the word threshold, a very important point or on prayer, very important term to understand once we reach that point, is when the action potential is going to occur. And I'm going to draw it in a different color, I'm going to draw blue. So I haven't shown you the action potential yet, I shown you everything before it. Now this is going to happen.

51:26

In a draw that a little bit more broad on the bottom there.

51:34

Until we once again, reach resting membrane potential. So everything you see in blue, is an action potential. So we're getting very rapid changes in membrane potential. And these changes are humongous. Compared to what we've seen up into this point, up to this point, I've shown you membrane potential changes up what values do they have changes were like, what five or six milli volts somewhere in there.

52:01

Not anymore. So let's put some values here. So we might very well heavy resting membrane potential there, I'm just going to pick a number right out of the air.

52:10

Negative 46 millivolts picked it out right out of the air threshold, I'm going to make that

52:17

I don't know, negative 38 picked it right out of the air. It's something more positive than negative 46. We are actually going to go through zero.

52:27

We are actually going to be more positive I'm making it up 20. But could very well be positive 20 Look at how big that changes

52:35

66 millivolt change. And it's rapid, how rapid are we talking about how long does this take?

52:44

Less than 10 milliseconds. That means you can do this 100 times in one second. That's how fast these changes are occurring. And so what we have here is a rapid a fast

53:00

depolarization and a fast

53:06

repolarization repolarization. Is one membrane potential returning back to resting membrane potential after there has been a change well, what's the change? A big huge depolarization is the change that we see here.

53:21

And so again, only a handful of cells can do this and they cannot do that unless again they reach threshold. So what is threshold that is defined threshold threshold is

53:31

a more positive membrane potential that must be reached.

53:42

In order

53:44

for an action potential

53:49

to be generated.

53:52

I'm going to abbreviate as potential from now on AP, I don't want to draw I want to write out x potential because I have to write it a number of times and actually potential to be generated.

54:04

That is, by definition, what a threshold is.

54:07

If we don't reach threshold,

54:11

this is what it's going to look like you don't get an itty bitty action potential. You don't get an action potential. So it would look like this

54:23

you either reach threshold or you don't you either generate an action potential or you don't.

54:29

So you either

54:34

generate an ASHA potential

54:39

AP, or you don't

54:46

that's what's meant by all or none.

54:53

You either get all of an action potential or you don't get an action potential.

54:58

Now doesn't mean that this change

55:00

membrane potential doesn't mean something, it could mean something.

55:04

But it's not an action potential.

55:07

And when it comes to action potentials Well, what the hell is so special about an action potential action potentials and I'm pretty sure you guys talked about this with lecture receiver conduction, you guys did conduction, right? saltatory conduction that you guys do conduction, saltatory conduction, continuous

conduction. That's how neurons are going to communicate with other cells that neurons are synapse with. I'm gonna talk about synapses in a lot of detail next week, not tonight. That's how they communicate. That's how they talk.

55:36

Action potentials.

55:39

Run the show in your body. Right now you guys are having thoughts, good ones, bad ones, I don't know.

55:46

They're action potentials. Your thoughts are action potentials, you our fears, our action potentials your Likes are action potentials, I'm able to move my hands because of action potentials. I can speak because of it. I can do everything that your heart beats because of action potentials.

56:06

Action potentials, if they're absent in your body, you cease to exist.

56:13

That's the way that it is we are just simply a bunch of ions moving across membranes. That's what we are. And how do we know that? Because if we measure action potentials, and they're absent,

56:25

we no longer exist.

56:27

When they take about when they talk about brain activity and an individual, what do you think of measuring.

56:33

They're measuring action potentials. That's what an EEG is. EKG, ECG is measuring the X potentials of heart muscle EEG is measuring brain activity.

56:47

It's actually potentials in the for the EEG shows nothing,

56:52

then that person has to be put on life support. Why? Because the brain can control the damn thing. Why? Because that's how the brain controls things. Action potentials. So that's an That's how important these things are. Without them, literally, you are not a human being anymore. You see, so you're a vegetable is what they say people are without brain activity.

57:16

So let's talk about how that happens. How does an ash potential get generated? How do we get these big huge changes in membrane potential? Oh, by the way, I'm gonna define one more thing here.

57:27

You might notice that from there to there, that we are more negative than what we were at resting membrane potential, it actually got more negative, there's a reason for that.

57:39

It has a name is called after hyperpolarization.

57:45

Now, I don't think we're going to have time to talk about it, I typically don't.

57:51

But it is a phenomenon that occurs and not by accident. There's a reason for that. And I'm going to show you why it happens. So what we're going to do now is, is we're going to draw the same picture, except now we're going to go step by step. How did this happen?

58:08

Let's draw another neuron.

58:11

And we're going to measure membrane potential right at the axon. Again, I'm gonna shorten the neuron A little bit.

58:19

Right, so we're gonna measure it right there.

58:22

And so what we're going to do is, is that we're going to take this little itty bitty piece

58:28

of membrane that looks like crap, let me draw that a little bit bigger,

58:32

we are going to isolate that membrane.

58:37

Right

58:39

there.

58:43

We're measuring membrane potential right there.

58:47

And that little itty bitty piece of membrane is going to be

58:52

you know what, let me draw a different color.

58:55

That little piece of membrane right there is going to be this little piece of membrane.

59:01

Right here, we just took it out.

59:04

And I'm going to show you the channels that are responsible for these big huge changes. The reason that there are just a handful of cells in your body that have the ability to generate a Nash potentials, because they have special channels, that other cells don't have

59:19

that open and closed in such a way that allow these big huge changes in membrane potential. So what we're going to do too is is that we are going to track it of course, we are going to measure membrane potential.

59:31

So that's time

59:33

and that's membrane potential.

59:36

And so initially, what we're going to have is a nice steady resting membrane potential of course, we are now in this membrane

59:46

are going to be two channels.

59:50

And this is specifically for neuron by the way next semester when we see two other action potentials of the heart. The channels are going to be some of them are going to be the same. Some are going to be different

1:00:00

But this is specific for a neuron and a skeletal muscle cell by the way. So we're gonna have two different kinds of channels here, up to this point, I called a channel a channel. Now I'm going to tell you about a specific channel to specific channels I'm gonna draw on here. So one of them, I'm going to draw on red.

1:00:18

And I'm going to tell you what the channels are.

1:00:21

That channel has two doors, it has an outside door, and it has an inside door, the inside doors open, we're still at resting membrane potential. By the way, resting membrane potential is going to be number one. So chronologically, we're going to go through this.

1:00:37

By the way, this is the inter spatial fluid

1:00:42

out here,

1:00:44

and this is the cytosol. On this side. Again, it's this piece of membrane right here, out here, interstitial fluid in here, side of salt. And then we have another channel here to make it green. You don't he has one door.

1:01:00

But it too is closed. So not as late name these two channels, the one in red is called a voltage gated, I'm going to write it in red,

1:01:11

a voltage gated

1:01:16

sodium channel. So it's a sodium channel, but a special one. Now, what is voltage gated me gate if you gating means to open or close you open or close a gate. Now there's other terms called activation and inactivation. I'm not getting into that in this course. Okay, it opened or closed, that's what we're going to do, I thought, I do think I have the terms in activation and activation in my notes, we're just going to keep it simple.

1:01:42

So what this means is, is that membrane potential voltage is going to control whether this channel is open or closed. And that resting membrane potential, which is number one, which is what this is right here, the channel is closed. Same thing with this other channel, which is in green, it's also a voltage gated channel.

1:02:06

But it's a potassium channel,

1:02:09

I'm going to make it plural, because there's zillions of them.

1:02:13

So I'm going to call this time one, which is resting membrane potential. So a resting membrane potential. That's what those channels look like they're closed.

1:02:22

Now we're going to do this

1:02:26

slow depolarization, that's going to be number two.

1:02:30

And at number two, they're still closed.

1:02:35

But what are we going to reach?

1:02:38

We are going to reach threshold.

1:02:41

And when we reached threshold, this new magical membrane potential,

1:02:47

what do you think's going to happen to those channels,

1:02:50

they're going to pop up. That's when the action potential starts. And so now we have to draw the membrane again. Because now we have something different happening.

1:03:05

The inside doors already open, boom, the outside door just popped open in that voltage gated sodium channel. The membrane potential is what opened it. And so now what's going to happen is we're going to flood

1:03:22

sodium

1:03:24

into the cell, what happens when sodium transport goes up? What happens? The membrane potential?

1:03:29

It depolarizes we already looked at it, right?

1:03:34

And I'm going to make this red

1:03:37

beam. Big, huge depolarization. Fast depolarization? We're gonna call that three.

1:03:47

Do you think that sodium permeability is still point 05?

1:03:54

No, at rest it is. But no longer is it? Why? Why did the permeability go up? Because these channels open, we opened more channels, I told you, that's how we can increase permeability right? When I say that

1:04:09

center right here, increase, I operability. Open more channels, we just dealt with a ton more. So now instead of sodium kind of trickling in the cell, it's flooding into the cell. So I'm gonna get a ton of positive charge on the inner membrane. So what I'll also do here is I'm just gonna indicate

1:04:27

three arrows up. Sodium permeability is sky high at this point.

1:04:33

And so that's going to be time three.

1:04:37

Now, what's happening to the potassium channel, the potassium channels actually open up at the same time, but slower. Like if you had two people running a race. One person just started off really, really fast, and the other one is a slaw or something and they're just kind of slowly starting. That would be the potassium channel. The sodium channel would be

1:05:00

The rabbit, and the potassium channel would be the turtle in the race. They just open slower, but they're still opening at the same time. So I am actually going to open the potassium channel. But what I'm not going to do, because they opened so slowly, is having the potassium leaving the cell yet.

1:05:20

All right?

1:05:22

Now what? Well, we're going to reach a peak.

1:05:26

And at that peak, something is going to happen.

1:05:31

The sodium channel,

1:05:33

it's technically called inactivation, but we're going to call it just closed,

1:05:39

what's going to happen is, is that that sodium channels inside door closes, the outside door is still going to be open gunmen, like the suite of a hotel, one doors open, and the other ones closed, doesn't matter, you're not getting through from one room to another. So no longer is sodium going to come into the cell, which is why we reach a peak, it doesn't keep on getting depolarized.

1:06:07

And now, finally,

1:06:10

the turtle channel is going to start to allow lots of potassium to be transported.

1:06:19

But what happens when potassium is transported out of the cell membrane potential gets more negative. Right. So now the permeability of potassium

1:06:30

has gone up.

1:06:33

And that's going to be number four.

1:06:36

So now we have a really high

1:06:40

potassium permeability.

1:06:43

Well, sodium permeability has gone down tremendously, because those channels are no longer allowing sodium to come through. And so that's going to be for

1:06:54

now, those potassium channels, because they're kind of slow, stay open for just a little bit longer.

1:07:03

Which is why the membrane potential gets a little bit more negative than resting membrane potential. So why is it that we get more negative because the potassium channels stay open just a little longer, because it just takes them a little longer to close, they're slow to open, they're slow to close, it's not a bad thing, by the way, it's a necessary thing. It creates something called a refractory period. And that refractory period is necessary for a couple of things, I doubt we're going to have time to talk about it. But it is an important component of the action potential itself.

1:07:37

And so one resting to slow depolarization. Three, actually, you know what I'm going to do with three, I'm going to I'm going to make,

1:07:45

I'm going to do this, I want to add something here, I want this I want threshold to be three,

1:07:53

I want fastl polarization to be four. So this is three and four, I'm going to make this five

1:08:01

want, I just want to highlight threshold and how important it is. Gotta reach it.

1:08:08

Alright,

1:08:10

now,

1:08:12

I'm going to put a little imaginary line right there.

1:08:16

Because at that point, these potassium channels are actually going to close and are going to look like this again. So I'm going to call and I'm going to make another imaginary line right there, which marks we're resting membrane potential is. And I'm going to say that this is

1:08:35

six,

1:08:38

six, all right.

1:08:44

And I'm going to keep

1:08:48

that like that. Now, I know that that's not risky. I know up into this point, Black has indicated resting membrane potential. But the reason I made this blank and the reason I made it all blue here, although it is still hyperpolarization. But what I'm trying to highlight here

1:09:03

is what is responsible for bringing our membrane potential back to resting membrane potential conditions. And it doesn't have anything to do with these two channels, which is why not including the color in seven,

1:09:18

seven, we're back over here.

1:09:22

Those channels are going to take on this configuration again, at seven What do you think is responsible to bring us back?

1:09:32

The channels that we discussed on Monday that are responsible for resting membrane potential what kind of channels are those? By the way, I'm not gonna tell you because it can vary from cell to cell and it can cause some confusion because some of them have, it doesn't matter just those are channels.

1:09:48

These are the channels I need you to know the names of voltage gated potassium voltage gated sodium channels in neurons are responsible for the action potential. And how long does this take this entire process?

1:10:00

says all the red and all the green 10 milliseconds.

1:10:04

You don't have to know that number, but I'm just giving you an idea of how stinking fast this is.

1:10:09

It's mind bogglingly fast, how they're just, if you really had to think about what the hell the body is doing, it just doesn't even make sense, all the just marvelous things that your body is doing to make you work the way that you do.

1:10:24

So, all this right here, what we have here on this page.

1:10:30

And we'll go back to number one here. So that is our resting membrane potential. Once again, I'm going to show you the words that this figure corresponds to

1:10:40

all those words right there. Now there's a few things in those words are in this page in this these, this paragraph, that we don't have to know that line right there. That line right there had to do with equilibrium potentials, which we didn't cover. That's the stuff that we crossed out today. What I'm going to do is I'm going to send out I'm going to put on pilot slides where if I don't talk about something, I'll have it crossed out so that if you maybe missed it during lecture as to what's crossed out, you don't have to worry about it. So I will put it's going to be some it'll, it'll call it'll be called I don't know, omissions or something like that. I don't know what helmet to name it yet. All right.

1:11:21

Okay, folks,

1:11:23

that is that I will see you guys on Monday.

1:11:28

Take care

03 - Neuro - 25OCT2021

Fri, 10/29 4:31PM • 1:14:24

SUMMARY KEYWORDS

neurotransmitter, neuron, axon, conduction, synapse, action potentials, synapses, stimulus, membrane, presynaptic terminal, cell, draw, myelin, called, potential, generated, reuptake inhibitor, faster, chemical synapse, vesicles

00:01

Alright folks is 440 hots begin. So the last thing we discussed last week, the dynamics of the action potential, and we went over the detail that we need to know.

00:12

And I talked about the, what's so important about action potentials last week. And part of what I discussed, we're going to discuss again today.

00:23

Now, what we're not going to go over is refractory period, although beneficial to go over, it's not necessarily needed to understand everything else that we're going to be talking about from this point forward. So that will not be on the exam, I promise. Well, we'll be on the exam, however, is action potential frequency. So as I said last week, action potentials information. Now again, there are many other things about action potentials that are very, very important to understand. For right now, let's just talk about information.

00:58

The information that I'm talking about, is interpreted in part by the number of action potentials that are generated per second. And that's what we mean by frequency, how many action potentials are being generated in one seconds time.

01:14

And the number of those action potentials being generated is a way of interpreting that information. And I'm going to explain what that means. So what we're going to do in discussing this is measure membrane potential of a neuron. And looking at the number of action potentials that neuron is generating in one seconds time. And as we do that, we're going to be covering all this information, right here in all of those terms.

01:43

We're going to draw that right there. But we're going to do it ourselves on the screen so that we truly understand what's happening here. So what I'm going to do here,

01:54

like is find my bed, there it is, is draw a neuron.

02:00

And so here's our neuron. There's the cell body, that's going to be the axon. I'll label everything. Once again, there's a nucleus. So cell body,

02:14

axon, presynaptic terminals are on the end, and we're gonna measure membrane potential right there at that spot.

02:22

And as we do, we are going to track it.

02:27

So let's draw our little x&y axis here, actually, not little, it's going to be big.

02:34

So here's our x&y axis membrane potential versus time.

02:39

Now initially, what's going to happen is, there's going to be, of course, a resting membrane potential.

02:46

Now, what we're going to do is, is that we're going to stimulate this neuron. Now, that neuron can be responsible for a bunch of different things that might be the neuron in your brain that's responsible for you to hear my voice right now, that might be a neuron in another area of your brain is responsible for you to see that screen right now. That might be a neuron and another part of your brain that's responsible for you to have the ability to feel the pen or pencil in your hand right now. So you're able to write properly.

03:17

The neuron itself is going to be stimulated by those stimuli, light in the room sound of my voice,

03:26

pressure on your fingers because of the pencil or pen that you're holding.

03:30

And these neurons are located in different areas of the brain, right? If that's the neuron that's responsible for hearing tell me what lobe of the brain it is. Where is the

03:40

temporal lobe right? What about sight?

03:43

occipital lobe, right touch

03:47

the somatosensory area of the brain, right? X receiver went over all this stuff with you guys. Those areas of the brain had these neurons that are interpreting the stimuli. Now, it's not the only thing that that has to do with what we're going to discuss. But it's an easy way for me to explain it to you as we go over it. Or that might be a neuron that's responsible for pain.

04:10

Also in that somatosensory area of the brain. So what we're going to do is we're going to stimulate that neuron with some stimulus depends on what neuron it is. And I'm going to draw an arrow here.

04:22

I'm going to draw the arrow small, right there is where we're going to stimulate the neuron.

04:27

It's going to be really, really small, and we're going to stimulate the neuron and as we do, we're going to make the neuron what more positive or more negative stimulate

04:36

positive we're going to depolarize it, but it's going to be an itty bitty depolarization. It's going to do this. It's going to depolarize and it's going to repolarize

04:47

what are we not going to reach reaching threshold we know that because there's no action potential right?

04:54

If there is a stimulus that does not cause a neuron to reach threshold, we call

05:00

it a sub threshold stimulus.

05:07

And because that stimulus is so small, you won't even be aware of anything.

05:12

That won't be enough light to stimulate that neuron to generate an action potential or sound or touch or whatever. So you will be completely unaware of what's going on, depending on what neuron is, depending on what nerve the neurons job is to sense.

05:30

Later on,

05:32

we're going to increase the stimulus, which is why I'm making the arrow bigger now we're giving ourselves a visual. So we're going to stimulate a little bit more

05:43

such that we're going to reach threshold and we're going to generate one action potential that line is an action potential, not going to draw in the kind of detail that we drew it in the last lecture because well, there's no need to

05:57

if we just generate one action potential, so one AP action potential generated,

06:06

and only one

06:08

we call that a threshold stimulus. That too is a small stimulus, by the way.

06:17

And you will not be aware of this either, this stimulus simply will not be big enough. So threshold stimulus. So let's go with the pain receptor, for example.

06:29

pain receptors job the free nerve endings remember those from this. So the integumentary chapter, remember, the free nerve endings. Some free nerve endings are pain receptors, by the way, a free nerve ending is a dendrite. That's what free nerve endings are their dendrites. And so these dendrites are being stimulated these specific ones by pain, but the painful stimulus is not enough for you to feel pain.

06:55

So a sub threshold stimulus and a threshold stimulus once again, is just not a big enough stimulus. One action potential is not enough, zero action potentials is certainly not enough.

07:08

Now what we're going to do is

07:11

we're going to increase the stimulus strength even more, so the arrow gets bigger.

07:16

Now, what's going to happen is, we're going to generate more than 1x potential, I'm just going to say three.

07:22

Now, how many are there just defense could be three, it could be five, it could be 20. It could be whatever. But it's more than one.

07:32

And as we increase the stimulus strength even more, so now the arrow is going to get even bigger.

07:38

Well, now we're going to generate even more action potentials, I'm just going to draw five.

07:45

So the neuron is generating more action potentials, because there's a bigger stimulus, and that bigger stimulus is being interpreted. And if that's a pain neuron, you feel more pain. Why? Because I stuck you harder with the pin,

08:01

or I turn the lights on brighter,

08:04

or I talked louder. Why do you hear my voice now more clearly? Because I'm talking louder? Well, what's happening? Those neurons in your temporal lobe are being stimulated more by my voice, because I'm raising my voice. And the sound waves are creating that bigger stimulus. And now these action potentials increase. So my voice sounds louder. Why? Because there's more action potentials being generated.

08:32

That's how it works. Or if I press on my skin Harder, harder pressure, this is harder pressure than that is and you feel it as harder pressure, because that's how it's being interpreted.

08:45

Not going to give that a name yet those two stimuli. I wouldn't wait just a second though. Now what we're going to do is draw the arrow nice and big.

08:56

We're going to call this I'm going to draw 734567. Again, it could be whatever it could have been 27. I don't want to draw 27 action potentials seven is enough, because I'm running out of room.

09:11

That stimulus right there, we're going to call a maximal stimulus.

09:16

A maximal stimulus is a stimulus that will cause the maximum number of action potentials to be generated. And so I'm going to put that over here. So we have a maximum

09:30
number

09:33
of action potentials generated. Now when I say maximum number, well, what does that mean? Well, neurons can only generate so many action potentials in a second. Some neurons the maximum is 16. Some it's 23. Some it's less or more. It just depends on the neuron. But the bottom line is, is that a maximum stimulus is a stimulus that causes the neuron to generate the maximum amount

10:00
Number of action potentials. So what does that mean?

10:03
Well, that's the maximum amount of pain that you can feel. So I just stuck you really hard with that pin.

10:09
Or you were at a concert, and he got really loud at the concert. And so that was a maximum amount of sound that you can hear because well, that's the maximum number of action potentials that those particular neurons can generate. Same thing with light,

10:25
and smell a whole bunch of different things.

10:29
Now, could the stimulus get even bigger than that? It actually can. So I just said, well, a concert.

10:38
Well, I bet if you stood in front of a jet engine, that that jet engine is going to be louder than that concert.

10:45
And so we can have actually a stimulus that's bigger than a maximal stimulus.

10:50
And we call that a Supra maximal stimulus. Now, I just stated that a maximal stimulus causes the maximum number of action potentials.

11:05
And that is definitely the case. Which means that a supramaximal stimulus can cause more than seven in this particular neuron,

11:15
we've already reached

11:17

our maximum. So what does that mean?

11:21

It means that if you hear the loudest sound, that you can hear a louder sound, and that's not going to send them any louder to you.

11:28

Or if I cause a maximum amount of pain to you,

11:33

doesn't matter how much harder I push that pin in your skin, it's not going to hurt more. Why? Because that neuron that's responsible for you to feel pain can generate more than that many action potentials. So a supramaximal, and a maximal stimulus will cause the same exact number of action potentials.

11:53

And it will be no different. Even though the stimulus is bigger.

11:58

That leaves these two.

12:01

Those two are called submaximal less than maximum, but more than threshold. So these are sub

12:11

maximum.

12:13

So what are we going to say about the number of action potentials well, more than one action potential because well, a threshold stimulus generates one action potential, more than one action potential, but

12:27

less than the maximum number of action potentials.

12:35

That would be sub maximum.

12:39

And that would be that one. And that one.

12:45

Now, on a daily basis, this is pretty much where we are at sub maximal. So on a daily basis, for the most part.

12:56

So on a daily basis,

12:59

we experience for the most part,

13:03

sub,

13:06

I don't want to say experience, because we're experiencing sub threshold threshold. So I'm actually going to change the wording there we are aware of, that's what I'm going to put on a daily basis.

13:22

What we

13:25

are aware of most often

13:31

is submaximal stimuli.

13:38

As I said before, when I was talking about sub threshold and threshold, you don't even know that's going on.

13:46

It's too small. I mean, it's not happening. But you're simply not aware of it because the stimulus isn't big enough for you to be aware of any of it. And when I say on a daily basis, that we are most aware of these types of stimuli doesn't mean that if some maximal stimulus was brought to us, we're not going to be aware of it, we're going to be very aware of it, but it just doesn't often happen. That's my point there.

14:12

And pretty much everything we do is submaximal. If you pick up a feather, versus let's say you can, I don't know benchpress, a certain amount of 300 pounds, and you benchpress 250, and you pick up a feather they're both submaximal.

14:27

Or the light in this room right now is submaximal.

14:31

You go outside on a sunny day, it's still submaximal. Now if you look directly into the sun,

14:37

well now we're over here and you're blinding yourself.

14:42

Sound I gave an example of a jet engine if you stand in front of a jet engine. Well, yeah, we're supramaximal But if you go to a concert, let's say you're sitting in the middle of the crowd, probably sit submaximal. But if you sit in front of the speaker, maybe it gets the maximum but the max

15:00

type of things are not things that we are aware that we're exposed to on a daily basis.

15:06

Most often, we're talking about submaximal. Alright, are we understanding what this is all about?

15:14

Actually, potential frequency is information. And it's how we interpret the information. When I say we, I mean our neurons.

15:23

So please know all these terms understand what they mean.

15:26

Now, one,

15:28

so that's all this stuff. And again, we just defined all these terms. Now.

15:34

Last week, I talked about how action potentials allow us to communicate.

15:40

And so let's talk a little bit about that. Before we actually get to the communication part. Let's talk about how we're going to get to the communication part. And that is conduction. And this is something that you've already discussed with lecture Seaver. Seaver talked to you guys about saltatory conduction and continuous conduction, I'm actually going to show you how it happens. So when it comes to conduction, we're spreading action potentials across the membrane, the action potentials aren't moving. One action potential causes another causes another causes another causes another, I'm going to show you how that happens. So they're spreading across a membrane. And of course, the membranes that have the ability to generate action potentials, which are what the membranes have neurons in the membranes of muscle cells as far as we're concerned.

16:25

Now, a couple of things before we move forward, and that is the conduction velocity. What does that mean? I'll tell you in a little bit. But this is a general rule, bigger axons conduct action potentials, faster myelinated axons are also going to conduct action potentials faster. And that's something I'm going to

specifically address and I'm going to tell you what conduction velocity means in just a little bit. But I just wanted to kind of get these things out of the way.

16:51

And this analogy to Domino's toppling, I'm going to explain to you in just a sec. So again, two types of conduction, continue with conduction. And what we see when we see continuous conduction, we're talking about an axon that does not have myelin on it. And cells like muscle cells that have the ability to generate an action potential. Whereas with saltatory conduction myelinated axons End of story, you're not going to see it anywhere else, that's the only place you'll see saltatory conduction. So saltatory conduction myelinated axons, continuous conduction, everything else on myelinated, axons, muscle cells.

17:30

So the first one we're going to do is continuous conduction. And so what I'm going to do here to demonstrate it

17:36

is I'm going to draw, this will just be an axon, it could be a muscle cell, but I'm going to make it an x.

17:45

And so that's the axon of some neuron.

17:49

And there's no myelin on it.

17:53

So that's an axon.

17:56

Now we're going to generate our first action potential right here. And so I'm going to actually draw the action potential like we've seen, and we're going to hit threshold fast depolarization, followed by fast repolarization. There's our first action potential. And it's happening right there at that spot. And we know

18:17

that this fast depolarization that's occurring, is due to

18:24

those voltage gated sodium channels opening, right. And when they do a whole bunch of sodium is going to be transported into the cell. And that's why we have this fast depolarization because these sodium ions are going to stick to the membrane. We went over this on Wednesday. Now we have all of these sodium ions, and they are being transported into the cell, do you think they're all just going to sit right there?

18:48

Think that might spread. Like if I had a glass of water and I put a drop of dye in the water, the little drop of dye isn't going to sit in one spot. It's going to spread, let's say, red dye, that whole glass will look pink at some point. Well, the sodium ions are going to do the same thing. This is cytosol in here. And all of these ions are flooding into the cell, some of them

19:13

are going to end up right there. And they're positively charged ions. And at this point in time, which is slightly later than this point in time, what's going to happen to the membrane potential here or positive or more negative.

19:29

The inner membrane, it should get more positive. And so let's make it get more positive, slow depolarization. What are we going to reach

19:40

threshold and so we get our second action potential right there at that spot.

19:48

And the same exact thing is going to be happening right there in this little piece of membrane. Because we have a whole bunch of voltage gated sodium channels there. And all this sodium is going to be coming into the cell

20:01

diffuse over here to the adjacent membrane depolarize, that membrane to threshold,

20:09

and we get another action potential. So what's happening here is this, this action potential causes that action potential, the second action potential causes the third action potential, and so forth, and so forth. So that one's going to cause the next one.

20:31

And so we reach threshold,

20:33

another action potential, we reach threshold, another action potential, and it's continuous one after another in adjacent regions.

20:44

That's continuous conduction.

20:50

And if we look in the notes, and I'm going to show you in just a second,

20:55

what we're drawing here these words,

20:59

the dynamic sodium ions from x potential diffuses to adjacent regions, sodium ions, from an ash potential diffuses to an adjacent region

21:10

causes depolarization of the membrane causes depolarization of the membrane.

21:16

When threshold is reached, another action potential is generated when threshold is reached, and other action potential is generated over and over and over again,

21:26

conduction of action potential continues in one direction and has nothing to do with the refractory period we're not going to worry about.

21:32

So we have these x potentials, and they're conducting. And they're going to eventually make their way all the way to the presynaptic terminal, because that's the very end of the axon is we very well know. So if this was right here that we have our little axon edge potential potential exponential, eventually the action potentials will be generated till we get the very last one at the presynaptic terminal, which is going to allow us communication at a synapse, and we're going to talk about that just a little bit.

22:01

So here, again, we have continuous conduction.

22:06

You know, write that down.

22:10

And I'll repeat where we see continuous conduction on myelinated

22:16

axons.

22:18

And as far as we're concerned, muscle cells, there's a couple of other cells in the body that have the ability to generate as potentials we just not going to talk about

22:30

now, conduction velocity.

22:34

No, explain what that means. Now.

22:38

I'm going to give you a number less than two meters per second.

22:44

Okay, now, what does that mean? This is what conduction velocity is. So we have our first action potential here, let me draw these arrows to this to make sure that we understand one causes another causes another.

22:58

We have this first x potential and it's generated at a certain point in time times zero, then it takes time for this one to be generated next, and then this one takes time. And then this one takes time. And this one takes time, and so forth, and so forth, and so forth.

23:12

Conduction velocity is the time it takes the first action potential to be generated to the time, it takes the last action potential to be generated. So let's just say for sake of argument that this axon is two meters long, which is over six feet long, okay, six feet, six inches is what it is.

23:35

What that means is this is that if this was two meters long this axon, it would only take one second, for the first action potential DB generated until the last action potential is generated. That's how fast this is. That's a maximum rate. By the way, when it comes to anchor conduction velocity for continuous conduction, we're going to see something even more mind boggling when we get to saltatory conduction is ridiculously fast. This is ridiculously fast. But saltatory conduction is really, really, really, really fast compared to this. And I'm going to tell you why or how really.

24:15

So this will be here, all these words, right here. That's what we just did.

24:22

Now let's do saltatory conduction. And when it comes to saltatory conduction again, only myelinated axons. So now I'm going to draw an axon. I'm going to put myelin on I'm going to try and draw it the same length as this one.

24:37

And then I'm going to put myelin on it.

24:40

So myelin right there,

24:43

in right there.

24:47

Now if this was an axon from the peripheral nervous system, that myelin would be what

24:55

a Schwann cell, right. The Schwann cell wraps around an axis

25:00

The whole stinking cell does. If this was an axon from the central nervous system, the myelin would be what? An algo dendro site, but just the feet of the oligodendrocyte. Right, the whole article inside is not wrapped around the the axon, just the feet do. So there's a little bit of a difference between the two. But those are both what kind of cells,

25:21

glial cells. So anyway, just a little anatomy review there. So we're gonna have our first action potential here.

25:32

Same is going to hold true

25:34

sodium rushes in.

25:38

And now it's going to traverse a greater distance.

25:44

Why exactly it has the ability to do that, it's not going to be important for us to know what's important for us to know is it's made it to this next region here, which is called what, by the way.

25:54

And those of Ranvier correct notes around your nose around your nose around the year, that's where the action potentials are going to be generated at the notes, they're not going to be generated where the myelin is wrapping around the axon. And the reason is this. There are no voltage gated

26:14

channels

26:20

where the myelin is,

26:24

there's no reason for it to be there. So the neuron is not going to produce these voltage gated channels and stick them here in this membrane, because that's not where the action potentials are going to occur. That's a good thing. But then it can be a bad thing when it causes or can lead to, or be part of the reason that people have a certain condition that I'm going to be talking about that you guys have already read about.

26:48

So we've reached our threshold, we've generated our next action potential sodium diffuses. And just as we saw before makes its way to the next node, we bring it to threshold, and the same thing holds true. So it's exactly the same as continuous when it comes to the dynamics when it comes to what causes the next action potential in the adjacent region.

27:11

The difference is where it's happening exactly.

27:20

Now,

27:22

let's talk about some statistics. When it comes to Saltatory conduction,

27:28

myelin, no voltage gated channels where the myelin is located.

27:33

Let me also add to this then, just to be clear, voltage gated channels are only at the nodes

27:42

only at the nodes of Ranvier.

27:50

Now, this is saltatory conduction, of course.

27:56

Now let's look at the speed of saltatory conduction. So continuous was less than two meters per second. So let's make sure that we understand that this is only

28:09

solely in myelinated axons.

28:13

That's the only place we're going to see it. And when it comes to speed three to 120 meters per second. So it can be ridiculously fast. So let's just imagine that we have 120 meter axon which doesn't exist anywhere in nature, even in a blue whale.

28:37

What it means once again, is the time it takes the first action potential to be generated to the time it takes the next action potential to be generated.

28:46

If it's 120 meters long, which is about

28:50

well, football fields, we're looking at, you know, more than one and a half football fields.

28:56

One second, that's how faster this is. That's obviously much faster than continuous conduction.

29:04

Now why this is the main reason.

29:09

So why

29:12

is Saltatory

29:15

faster, and it's so much faster than continuous. This is the main reason is that the only reason it's not but it's the reason that you're going to know for the exam.

29:26

The reason is this. Less action potentials need to be generated

29:35

over the same distance.

29:38

What does that mean? Well, I'm going to show you

29:42

I'll go back to that.

29:44

So when we look at continuous conduction over the same length of axon,

29:50

you need to generate more action potentials. You're not generating just the nodes you have to generate in the entire axon itself each year

30:00

These takes time.

30:02

So it's going to take less time to generate this many action potentials versus this many action potentials. If I wanted to walk to that wall, and I wanted to do it quickly, I'm not just going to put one foot in front of the other, it's going to take me a long time, that's continuous conduction, what am I going to do instead? Nice big long strike. So I can make to that wall, I don't know in five strides. But if I put one foot in the front of the front of the other, I'm going to

30:29

have to do that about 20 times.

30:32

Now, I want you to understand that this action potential is not moving.

30:36

That's an action potential that's distinct from that one, which is distinct from that one, which is distinct from that one. That's what I mean by dominoes toppling by the way, that's my analogy that I like to use.

30:47

So what do I mean by that? So if I had a whole bunch of dominoes on that table right now, 20 of them lined up, and I hit the first one hits the second one, which is the third one, which is the fourth one, every time a domino gets hit. That's an action potential, and they're all distinct from each other. The last Domino is not the first domino, they're all distinct from each other. Just like all these action potentials, are distinct from each other.

31:13

So again, when we talk about conduction velocity is the number that are going to occur over a particular length of axon muscle cell that occurs in one second time.

31:26

Now, it doesn't mean that it has to take one second to get from point A to point B, well, it's probably not going to because the accents in our body are not this law. Even if you're Shaquille O'Neal, who's seven feet tall, he has long axons going from his lumbar region down to you know, his foot region. Still not six feet, maybe three, most axons are nowhere near this length. So these conduction

31:54

parameters here dynamics are happening really, really faster than this. How do I know it's faster than this? Because I can't do this, unless these action potentials happen in both the axons and the muscles in my hand, which we'll talk about later on in the semester.

32:12

Are we good with this? So understand the differences between continuous and Saltatory? No, the values? No, why no all that stuff. Before we move forward, I want to talk about one more thing.

32:24

This is a disease that lecture Siebert has you read about.

32:28

It's a disease of the central nervous system. Multiple Sclerosis, you guys read about that, right. So I'm going to show you what happens with multiple sclerosis.

32:39

So that is going to be a myelinated axon.

32:46

Now,

32:48

as we know, we're going to have action potentials generated at each of these nodes.

32:53

This is what happens with multiple sclerosis.

32:57

There you go. That's MS.

33:00

MS is a condition where myelin gets destroyed.

33:07

There's it's more complicated than that. But that's the way we're going to present it here. So I can demonstrate why it is that you get the symptoms of multiple sclerosis. Now, if we don't have any myelin, you might think to yourself, well, then it's going to go from saltatory conduction to continuous conduction. No, it's not. It goes from saltatory conduction, to no conduction, you short circuit, the axons. So you'll have one here, and then you'll have another here, and then you'll have another here, and then you're done. You're not going beyond the point where the damage has occurred. So with multiple sclerosis, what you're doing is you short circuit the axon.

33:55

Meaning

33:57

there's no conduction,

34:00

no conduction beyond

34:04

the damage

34:07

to

34:09

the myelin

34:12

in the reason that is we're going to go back to this.

34:16

There are no voltage gated channels, where the myelin is, there's nothing there. So you can't go beyond it. Whereas with continuous conduction, we have voltage gated sodium potassium channels, the entire length of these axons.

34:31

Now, not here, and so it stops right at that point because the myelin is gone. The sodium as it diffuses a document be enough to get to the next point.

34:41

And that's what causes the symptoms

34:46

causes the MS symptoms and there's you know,

34:49

Ms. There's like four different kinds of Ms. There's a bunch of different kinds. The symptoms of MS can vary from one person to the next. So there's motor deficits there

35:00

sensory deficits, there's all kinds of weird things that happen with Ms. And the reason is, is because communication is lost. When it comes to these action potentials no longer being able to conduct. We haven't talked about communication yet. We're about to.

35:18

So I said that these action potentials allow communication, it's in part because of conduction, and that it's in large part because of a synapse being formed. So now let's talk about synapses. That's the next thing. So it's a perfect segue from what we're discussing right here.

35:37

So what's a synapse? It's a junction between two cells that allows communication between two cells, yes.

35:48

The tingling will, because you have these

35:52

the sensory axons that are responsible for you to feel whole bunches of things.

35:57

When you have these axons that are leading to the brain, and then those areas of the brain can no longer conduct to the neurons that are responsible for you to have these sensations, the signal kind of gets screwed up. And you have these what are called Weird, they're called prestigious. The paraesthesia is a weird feeling that you get, and people with MS will often get pair of stages, because we're stopping the conduction of these particular action potentials within the brain itself, not allowing the neurons to interpret the information properly. And so weird things kind of happen. So that's the reason. Okay.

36:37

So now again, a synapse, junction between two cells, and the two cells communicate with each other. And in this particular picture, they show a bunch of different synapses between this neuron and this one, and this one in this one.

36:51

So let's talk about the Senate.

36:54

Here's just a fancy a picture of a synapse, this is one neuron with a ton of different synapses, each synapse having a red or a green little area right there, showing that you can have multiple, multiple, multiple, multiple synapses. And in certain areas of your brain, like your cerebellum, one neuron can have 1000 synapses.

37:13

And then that neuron that one neuron needs to interpret the information from that one synapse. So it can get wildly complicated depending on where you are. And when it comes to a synapse, we're going to concentrate on neuron synapses with some other cell. But I want you to understand that there could be synapses between two other cells that are not neurons at all, you can have two muscle cells that synapse with each other, for example, which I will talk about later on in the semester. But because this is the neuro information that we're discussing the stick with neurons. And so after I draw this picture, I'm going to give you a break. So when it comes to synapses, there's two kinds. But before I present that, I'm just going to draw some synapses between a neuron and some other cell. And I'm going to draw the neuron very, very simply,

38:00

the circle is going to be the cell body.

38:05

This line is going to be the axon, you know, label it.

38:12

And then that's going to be the presynaptic terminal.

38:17

So I draw that very simply.

38:21

And we know what all these things are, well, because you've gone over them with lecture Siebert, and we're certainly going to go over them now. I'm going to have this neuron right here synapse

38:33

with another neuron.

38:35

So there's a synapse, there's a junction between these two cells. So where's the synapse, that's the synapse.

38:43

So there can be a synapse between two nerves. There can be a synapse between a neuron. I'm not going to label everything on this one. Because while we already know what everything is

38:56

in a glial cell,

39:00

so again, there's our synapse right here. There can be a synapse. And this is something we're going to talk about detail later on this semester,

39:09

between a neuron

39:12

and a muscle cell.

39:15

And so that neuron is controlling the muscle cell. There can be a synapse between a neuron and an epithelial cell. So I've given you a few examples here.

39:25

And that epithelial cell could be the epithelial cell of a gland

39:31

that releases a hormone so that neuron can be telling this particular cell released the hormone this neuron is telling that muscle cell contract, this neuron is telling that glial cell to do something and telling her to do something.

39:44

So these are all these synapses here that allow again, communication Now one last thing before we take a break. The only way this is going to happen. The only way we're going to have communication between these two sets

39:57

is if we generate action potentials.

40:00

along that axon, so that's action potential.

40:05

So one of those is an action potential, I just didn't draw him in detail.

40:10

Conduction,

40:12

we need to get the last action potential generated at the presynaptic terminal in order for the communication to occur.

40:22

If it doesn't, then the communication is lost. And if we're talking about something like MS, for example, then weird things start to know I say weird things, because I'm talking about like the pair of the weird feelings that you can get, but a bunch of other bad things can happen. Like you lose motor skills with MS, there's a whole bunch of things that happen with MS, depending on what area of the brain is affected and a bunch of other things.

40:47

When we come back from break, we're going to go from here, I'm going to talk about the specific synapses that can be formed between cells, and then go into the dynamics of the synapse.

41:02

Continue.

41:04

So now the synapses there's two kinds. And so I'm going to draw both kinds.

41:11

There's some information that you're not gonna have to know it's crossed out here. I don't know if I mentioned it last week, but I will be putting a PowerPoint on pilot crossing out all the stuff that you don't have to know for this exam. So you don't have to fevers the cross anything, you certainly can if you want, but if you miss it, don't worry about it. It'll be on pilot very, very soon.

41:29

So now let's draw the two different types of synapses.

41:33

So two types of synapses.

41:39

One of them less complicated than the other,

41:43

they'll be here on the left hand side, we're going to draw what's called an electrical synapse.

41:49

So we're going to stick with our neuron.

41:53

So this right here, move it over just a teeny bit.

41:59

This right here is our presynaptic terminal.

42:09

So that right there is this.

42:15

So the very end of a neuron.

42:18

And what we're going to do here is that we're going to draw

42:23

a tube

42:25

right in that membrane. And you already know what the name of this tube is, because lecture receivers gone over it with you guys a couple of times this semester, that's a gap junction.

42:37

A gap junction allows communication between two cells, a gap junction is a channel.

42:44

That's what it is a channel that can open and close like any other channel that we've discussed up into a particular point in time.

42:52

And we're going to have some other cell now.

42:56

Now this can be a neuron, this can be a glial cell, it can be whatever the hell you want it to be.

43:02

So that is some cell

43:06

that the neuron is communicating with.

43:10

That's an electrical synapse. So as soon as you hear electrical synapse, gap junction boom, and to story

43:17

chemical synapses, the other type of synapse, this is a bit more complicated.

43:24

We have more structures here.

43:27

And so I'm once again going to draw our presynaptic terminal,

43:32

not going to put a hole in it draw a gap junction, well, because gap junctions are not involved with chemical synapses. But that too, is a presynaptic, terminal outpoint, the both of them and we're going to have some other cells, pick the cell that you want. And again, when I say that I'm talking about these cells can be another neuron, it could be a muscle cell, glial cell, epithelial cell, it doesn't matter.

43:56

Some cell

43:59

we have more structures to draw on this picture. And I'll put the structures in a different color, we'll go red.

44:07

There's going to be a channel here, we're going to name that channel. That is what we call a calcium channel. Now it's a special kind, and I'm not going to tell you what kind of a special channel it is. We're just going to call it a calcium channel that's important to this story.

44:22

We also have in this story vesicles.

44:30

And these vesicles are at the very ends of these presynaptic terminals, and they're called synaptic vesicles. Well, because they're part of the synapse.

44:43

And in those synaptic vesicles

44:47

Well, we have these chemicals, which is why it's called a chemical synapse. Now not all chemical synapses are put together like this, but the vast majority of them are I'm going to actually show you an exception in just a little bit.

45:00

Those little blue things, those little chemicals,

45:05

we're not going to call them chemicals, we're going to call it the big boy big girl name,

45:10

neurotransmitters.

45:15

So the job of those synaptic vesicles is to store the neurotransmitters to hold them until the time is right. For us.

45:27

Well, we'll just talk about what we need to talk about just a little bit right now just structures. Something else that we need to be aware of is also this space right here

45:38

is called the synaptic cleft.

45:41

And it's just literally a space between those two cells. There is no synaptic cleft when it comes to an electrical synapse, even though there can be space in between the two cells, because we have the gap junction that's connecting the two synaptic cleft does not come into play when it comes to the story of electrical synapses. But it certainly does here a

46:03

few other things that we need to be aware of. And that is,

46:08

we have on these on this membrane of the other cell receptors. And these receptors are going to be specific for the neurotransmitter in the presynaptic terminal.

46:21

So those are receptors and we know what receptors are and we know how they work, their job is to specifically bind a molecule in this particular case is going to be a neurotransmitter,

46:32

do more terms, one, that membrane right there of that presynaptic terminal is called

46:41

a presynaptic membrane.

46:51

The membrane of the other cell is called the post synaptic membrane.

47:04

And it's the presynaptic membrane that will be affecting the post synaptic membrane. So when it comes to communication, we're going in

47:14

that direction, from the neuron to the other cell, which is why this is called the pre synaptic membrane. This is the postsynaptic membrane. This is the synapse.

47:26

This is the beginning, this is the end of the synapses is before the synaptic cleft. This is after the synaptic cleft, that's where the names come from.

47:34

So these are the structures of each. So now let's see how each of them works. And the first one I'll do is electrical synapse, we're not going to get into this in any type of great detail here, this is just going to be a general overview of how these work. So electrical synapse, works like this.

47:52

So once again, we'll have our presynaptic terminal. You don't have to label anything in this picture, because well, we did it in the last picture. And there's our gap junction. And here's some other cells again, make it whatever the hell you want.

48:05

Step number one

48:09

is our action potential. Now, what x potential are we talking about here, we're talking about this very last action potential at the very end of the presynaptic terminal that must occur in order for this communication to occur. And that's our theme here, right communication. And I told you that action potentials allow communication,

48:29

this communication that we're about to see will not happen. Unless we get action potential conduction along that axon. It's not happening.

48:39

So that's step number one, the action potential. Now, I'm going to say that that action potential, this is a word that we visited in the past, causes stuff to occur in this cell, doesn't matter what that stuff is just know that it is stuck.

48:58

Then

49:00

whatever that stuff is,

49:03

is going to be transported through the gap junction, that's transport.

49:09

That's a channel we know what channels do channels transport things, and it's going to transport it to the other cell. And so all of that stuff that was going on in this cell.

49:21

Well, it's going to be going on in this cell now we have communication.

49:27

The neuron is telling that cell what to do, or it's giving an explicit instruction for something to do. So not too many steps occurring here.

49:38

And so because of that, we are going to learn that an electrical synapse is faster than

49:45

a chemical synapse.

49:51

Why

49:54

there's less steps

49:57

and the steps that are occurring are just simply faster.

50:01

We're going to talk about electrical synapses later on this semester, I'm going to give you one or two specific examples of them and show you the advantage of them

50:12

later. Now, let's go to the chemical synapse.

50:16

When it comes to a chemical synapse,

50:20

I'm going to show you two different mechanisms here, although they're pretty much the same, we just deviate a little bit.

50:27

So we're going to draw our structures. So here's our presynaptic terminal.

50:34

We're going to put our vesicles in here with code that I use read, I did.

50:39

So here are our vesicles.

50:43

We're going to put our neurotransmitters in those vesicles. By the way, the neurotransmitters in these vesicles, they were produced by the neuron, and then stored in these vesicles. So that's where they came from.

50:57

We have to put our calcium channel here,

51:01

we have to put our other cell, whatever the heck cell that is.

51:07

We need our receptors over here on the membrane.

51:12

And now the story can begin and the story is going to begin the exact same way that it began here, we need an action potential. And so here's our action potential that conducted all the way to the very end here. So that was that last ash potential that was generated, what that's going to do is going to open

51:33

the calcium channels, and that's what this is here labeled on the last picture.

51:38

So opening that calcium channel as to which is going to allow calcium to be transported into the cell, that's the direction at which calcium is going to go calcium concentrations high on the outside low on the inside.

51:52

And so as a result of that, number three, as that calcium comes in, it raises the calcium concentration at the presynaptic terminal.

52:02

What does that do?

52:05

The high calcium is going to cause these, these vesicles here

52:12

to literally move towards the very edge of the presynaptic terminal. So I'm going to draw that

52:23

like this.

52:26

So that's the vesicle.

52:28

And it fused

52:32

with the presynaptic terminals membrane, so both of those membranes fused together. And let us remember that as that is occurring, the neurotransmitters are still there.

52:45

But now there's a big hole in that membrane.

52:48

And the neurotransmitter is released, that's going to be step number five,

52:53

number five neurotransmitter

52:58

released

53:02

into the synaptic cleft.

53:05

Tell me what that process is called, please start with the knee

53:10

exocytosis via

53:14

exocytosis, something that we talked about back in chapter three. And the picture that I showed you was actually exocytosis of a neurotransmitter from a presynaptic terminal.

53:26

So we're going to release the neurotransmitter into the synaptic cleft. Well now what's going to happen? Is that the neurotransmitter

53:35

oops, I should be six

53:39

the neurotransmitter is going to diffuse across the synaptic cleft to the other cell.

53:50

And as it does, the specific

53:55

receptor is going to bind that neurotransmitter. So number seven

54:03

receptor

54:06

receptors bind the neurotransmitter.

54:13

Now not all the neurotransmitter is going to get released here, which is why I don't have all the vesicles moving just a certain number is going to depend on how high the calcium concentration goes. And that depends on some other things we're not going to get into.

54:25

Then what

54:28

will our good old friend stuff although we're going to talk about stuff in just a second. So if we're comparing what happens with the chemical synapse versus an electrical synapse, we can see why electrical synapse to hell lot faster. Just boom, channel opens. There we go. We're as we're talking about these vesicles moving exocytosis binding to a receptor that just that just takes time.

54:54

So that's why it's slower now when I say it takes time. It's still ridiculously fast. It's fast.

55:00

to the depths. And once again, how do I know that because I can't do this, unless this happened between a neuron and a muscle cell, and then the muscle cell needs to contract. And there's a whole bunch of stuff that happens that allows the muscle cell to contract. So it's faster than this. It's about 1000 times faster than this. So these things are happening quickly, even a chemical synapse. But even so, an electrical synapse is even faster than that, it's.

55:26

Now

55:28

one thing that I want to make sure that we understand too is, is that we have these vesicles storing the neurotransmitter.

55:36

We have another type of neurotransmitter that we're about to discuss neurotransmitters that are not stored by vesicles. But it's still a chemical synapse. So what we just drew here is

55:50

this, these words, this is what we just drew. Now we're going to do the order. And the order is the same story. See if you look here.

56:02

So these three lines right here, go all the way to causes synaptic vesicles to fuse, right? Do you see that? Right, so we're going to lose this line right here and replace it with this line.

56:15

And there's a few other things that are different down here.

56:18

So the very first parts of it are the same. What's different is once we get to this line right here, so let me show you.

56:26

So once again, this is going to be a chemical synapse.

56:30

But the neurotransmitters that I'm going to be discussing now are what are called gaseous neurotransmitters.

56:37

I'm going to put that over here to the side.

56:41

Now, what's a gaseous neurotransmitter, it is a neurotransmitter that is a gas, oxygens a gas, carbon dioxide gas, right? Well, they're not neurotransmitters, but there are other gases in the body that act as neurotransmitters. Carbon monoxide is one of them. I'm going to assume that as soon as I heard you heard carbon monoxide, you probably thought carbon monoxide poisoning.

57:03

We make carbon monoxide naturally in our body. And it is used as a neurotransmitter. Nitric oxide is the other one, we're going to actually talk about both of these neurotransmitters, hopefully on Wednesday.

57:17

So gaseous neurotransmitters,

57:21

the structures are going to be the same. But we're going to have the absence of a couple of things here. As you're going to see in just a second. In this story, we're still going to have our calcium channels. But in this story, we're not going to have our vesicles. And we're not going to have our receptors here. And the reason is this gaseous neurotransmitters, and I'll give you the two examples that I just spout it off. For example, carbon monoxide, dioxide has two oxygens, monoxide has one and nitric oxide.

57:56

Incredibly important. neurotransmitters in the body, by the way,

58:02
are not

58:05
stored. Why not? Because they're a gas, you put a gas inside these vesicles they're diffusing right out of it. They're not going to be held.

58:16
So then how are we going to store them? We're not, we're going to make them on demand. So let's the story begin, story begins the same

58:25
action potential

58:28
to

58:29
open calcium channels.

58:33
Three,

58:36
as calcium comes in,

58:38
we're gonna raise the level of calcium in that cell.

58:43
And then stuff will happen

58:47
that will cause the production

58:52
of the gaseous

58:56
neurotransmitter

59:04
and I'm going to put a little red dot here, actually, I'll make it blue.

59:10

So there's our gas star. Now, I'm just going to draw one but there's a hell of a lot more than one that's produced.

59:15

And so now what? Well, let's AGAS it'll simply diffuse into the synaptic cleft and then it will simply diffuse

59:25

into that cell.

59:27

So what Samson here the vesicles and the receptors on the postsynaptic membrane, we have simple diffusion here. So simple diffusion is going to be number five

59:41

simple diffusion

59:46

of neurotransmitter, and again, gaseous neurotransmitter

59:53

to again the other cell, whatever that other cell is.

59:59

And so then what

1:00:02

Six

1:00:04

stuff.

1:00:06

I think and we will talk about what stuff is.

1:00:08

So it's a little shorter. When it comes to the story, not much. But it is it's a little bit quicker, where book goes in, and then it just does its thing, whatever it's gonna do.

1:00:20

And these gases, neural transmitters have very, very important functions as we're going to see when we get to them.

1:00:27

So now what, let's talk about the stuff that happens. So the stuff that happens here, the stuff that happens here, the stuff that happens here, and we're really going to concentrate on the chemical stance when it comes to stuff.

1:00:39

So let's do that. So we're going to start the story at stuff. So we've gotten through all these steps to step six over here. And we've got to this all the way to step eight over here. So that's where the story is going to start stuff.

1:00:55

I'm going to put the word

1:00:58

stuff there.

1:01:00

And now we're going to chronologically go through what happens after stuff, what stuff is going to happen, or the stuff that happens causes what we're going to discuss. And there are many, many things that can happen after stuff, we're going to concentrate on one thing, channels. And so what I'm going to do here is that I'm going to put a channel in this membrane,

1:01:22

there's the channel that some channel

1:01:27

that's what that is.

1:01:29

sodium channels, potassium channel, chloride channel, calcium channel doesn't matter, it's some channel.

1:01:34

So what's going to happen is this, the stuff is going to affect that channel. And what it's going to do, and I'm going to use letters instead of 12345. Because I don't want to get mixed up with 123456 bla bla bla, bla here and go ABCD.

1:01:48

So stuff is going to cause a

1:01:52

we are going to open or close some channel.

1:02:00

In other words, we're going to increase or decrease the permeability of some ion.

1:02:06

And so open or closed some channel, which means B we are going to increase or decrease the permeability

1:02:17

of some ion,

1:02:20

which means c, we are going to increase or decrease the transport

1:02:30

of some ion.

1:02:33

Which means d, we are going to change

1:02:40

membrane potential. We learned this two lectures ago or in the last section don't even remember what lecture it was

1:02:47

when we were talking about opening and closing channels and what they did the membrane potential to depolarize or hyperpolarized. Remember that top of page 27.

1:02:55

So now I'm showing you how it actually happens,

1:02:58

it can happen because the releases some neurotransmitter, causing this particular cell to open or close some channel.

1:03:06

So that's the stuff that's happening.

1:03:10

Before we move forward and give you specific examples of what can happen. One more thing I need to talk about. And that's this, these neurotransmitters that bind to these receptors are not going to make their way into this cell. So what happens to them, after they bind to these receptors, their job is done.

1:03:33

And it's very, very quick. And so what's going to happen to these particular neurotransmitters

1:03:40

is going to be taken right back up into the presynaptic terminal that has a special name

1:03:46

is called reuptake.

1:03:49

That's the fate of these neurotransmitters. Now, there is no reuptake of gaseous neurotransmitters, they are going to make their way into this other cell. So there's no reuptake here. So what's their fate?

1:04:07

This cell is going to metabolize them after they're done doing that thing. That's what happens to those. So where's this information in your notes I'm gonna show you

1:04:17

right here reuptake of chemical neurotransmitters by the presynaptic membrane, that line right there

1:04:24

is this and then the next line, gaseous neurotransmitters are metab metabolized by the postsynaptic cell.

1:04:34

That would be this no reuptake here of these particular neurotransmitters.

1:04:40

And the concept and the phenomenon of reuptake is going to be very important to understand when we talk about a number of things. When we talk about specific neurotransmitters. When I talk about reuptake. I'm going to talk about reuptake inhibitors. There's a bunch of them out there you guys have probably heard of Prozac, right? That's a reuptake inhibitor so as Wellbutrin so

1:05:00

I was Paxil. So Zoloft. So are a lot of those things. There's one specific for Alzheimer's disease where we decrease the the uptake of acetylcholine. I'm going to show you examples of these kinds of things when we get to the specific neurotransmitters. So you guys have heard of reuptake inhibitors, you might have not known that they are reuptake inhibitors. So let's talk at the outlet. Let's talk about a reuptake inhibitor. So this is reuptake. But what we can do is inhibit reuptake. Now, why the hell would we want to do that? Well, I'm going to show you

1:05:37

so reuptake inhibitors.

1:05:41

This is how they work.

1:05:49

So it's an antagonist. It is an antagonist to this transport process. reuptake is transport for transporting the neurotransmitter back into the presynaptic terminal.

1:06:04

So a reuptake inhibitor.

1:06:08

What does it do? It inhibits

1:06:12

the transport the reuptake.

1:06:20

Of the neurotransmitter

1:06:26

into the presynaptic terminal.

1:06:30

That's what it does.

1:06:33

Now, why the hell would we prescribe this to somebody?

1:06:37

So why prescribe

1:06:41

or who gets this,

1:06:44

people who get this get this

1:06:49

when the level

1:06:52

of neurotransmitter

1:06:59

is too low,

1:07:04

I'm going to show you why.

1:07:06

So we're going to draw a picture and then I have normal level on the left hand side low level on the right hand side and how a reuptake inhibitor can help somebody with a low level of neurotransmitter.

1:07:18

So normal level,

1:07:23

low level in how we can treat it. And whoever discovered or whoever invented this. Absolutely genius who did it. I don't know who did it. But whoever it was, he or she, them, whoever they were very smart. So what we have here is this presynaptic terminal.

1:07:43

And

1:07:45

let's just say that that's some other neuron in the brain, and we're going to have our neurotransmitter getting released.

1:07:50

And the neurotransmitter binds to its receptors, and stuff happens. And then after the stuff happens, we're going to change the permeability of some ion we're going to get some change in membrane potential. Alright, so we're going to go all the way to step D here. And I'm going to say

1:08:09

that this is going to cause when the neurotransmitter is released at this synapse is going to cause

1:08:21

a 10 millivolt depolarization, the membrane potential of this neuron right here depolarize 10 milli volts, because this much neurotransmitter is released bound to a certain number of receptors.

1:08:36

This person will be here.

1:08:40

And again, all of these neurotransmitters will take him right back into the presynaptic terminal, all is good, everything's normal level on the right and the left hand side, this person over here, different story.

1:08:53

Now we only have

1:08:55
that much.

1:08:58
Let's put the receptors in here.

1:09:02
Okay, and they're going to bind.

1:09:04
Some of them we're going to bind a certain number of these neurotransmitters.

1:09:09
And we have our receptors over here.

1:09:13
But we don't have as much neurotransmitter.

1:09:16
So we have a decrease in the level.

1:09:20
And because of that, there's not going to be as many of these binding to as many receptors, which means not as much stuff is going to happen.

1:09:28
Which means we're not going to change the permeability as much, which means now instead of a 10 millivolt change, maybe it only causes

1:09:37
I don't know, I'm gonna make it up six milli volt depolarization where it should have caused 10.

1:09:43
Well, how can we treat this?

1:09:45
One of the ways to treat this is this

1:09:50
treat with

1:09:53
a reuptake

1:09:57

inhibitor

1:10:00

So what is that going to do?

1:10:02

It's going to do this number one, that reuptake inhibitor

1:10:15

is going to cause neurotransmitter.

1:10:22

To stay

1:10:24

in the synaptic cleft longer

1:10:32

can't be can't make its way to the presynaptic terminal, it's got to stay there, which means what?

1:10:39

Which means receptors

1:10:43

are activated

1:10:46

longer,

1:10:48

which means why,

1:10:51

which means the change in permeability

1:10:58

occurs

1:11:01

for a longer period of time

1:11:05

which means what?

1:11:08

You're going to get more transport

1:11:12

or less

1:11:15

bigger change

1:11:21

in ion transport,

1:11:24

which means what?

1:11:27

Bigger change

1:11:30

in membrane potential.

1:11:34

So,

1:11:35

let me make sure that we understand this.

1:11:38

So, let's say I'm just putting numbers out here. And these numbers are not real numbers. But let's say that these neurotransmitters sit here for one second under normal conditions, and a normal number of them do, let's say 100 of them do. Again, that's a ridiculously small number, but they're numbers that are easy to understand. So for one second 100 neurotransmitters are bound to two receptors, and it causes 100 ions to be transported. And it gives us this 10 millivolt change.

1:12:09

But now we have less neurotransmitter, let's say instead of 100. Now we only have 50 neurotransmitters, which now only binds to half the number of these receptors, which means half the amount of ions are going to be

1:12:22

being transported.

1:12:26

Half I'll just make it five, that's half a 10. We're not going to have as many

1:12:31

transported ions for one second. Each of these, let's say for one second, each of these receptors can move 50 ions in one second.

1:12:41

And so we have two receptors, and it'll cause 100 ions to be transported. But we don't have we only have one receptor. So that means we only have 50 in one set. But what if we could keep that on there for one and a half seconds? What does that mean? Instead of 50 ions, we would get 75 ions transported. If the channels are open for a longer period of time, you're going to get more transport of ions.

1:13:12

You might not be able to get it back up to 10.

1:13:17

But maybe you can get it back.

1:13:20

I don't know eight milli volts.

1:13:23

It's close to 10. Or maybe you can get it to 10. Who knows. It depends on the dose and you play with the dose.

1:13:35

People who get reuptake inhibitors get reuptake inhibitors to take advantage of this particular transport process and inhibiting it. So again, if these neurotransmitters are bound here longer, these are open longer, we can get more ions in here without having with if there's if there's less neurotransmitter here, you can't make more just seeing gonna happen.

1:14:00

So again, the person that figured this out, it seems simple, freakin genius, how this person put this together.

1:14:09

So that's how they work. All right.

1:14:13

Okay, folks, we're at 559. I was hoping to get a little bit further than this, but we didn't.

1:14:19

We will continue our story on Wednesday.

04 - Neuro - 27OCT2021

Fri, 10/29 4:30PM • 1:14:32

SUMMARY KEYWORDS

neurotransmitter, neurons, acetylcholine, serotonin, plasticity, excitatory, synapses, dopamine, released, people, called, brain, receptors, membrane potential, glutamate, treatment, reuptake inhibitor, gaba, synaptic plasticity, causing

00:03

Alrighty, folks, here we go.

00:07

So most of the lecture was spent on Monday, revolving around synapses.

00:14

And we went into detail about chemical synapses. Here's a picture that we drew. And we talked about when it comes to the neurotransmitter that's released, what's going to happen after stuff occurs.

00:28

And that would be here.

00:31

And so our angle is going to be we're going to change membrane potential in the postsynaptic membrane. And to remind you what the postsynaptic membrane is, that would be the membrane where we have our receptors that are finding the neurotransmitter.

00:46

So our story, once again, is going to be the membrane potential change in this cell, whatever that cell is, you can have it be whatever you want it to be a neuron, a muscle cell and epithelial cell, the glial cell, it doesn't matter.

00:59

That's what we're now going to begin our story, as we continue, our story is going to be

01:06

this more of this. And so what we're going to discuss now, are what we call post synaptic potentials.

01:17

So let's do that.

01:19

So what we're going to do here is that we're going to draw a synapse.

01:23

And we're not going to put the kind of detail that we had in the last lecture well, because we already did that. And so this is going to be our presynaptic terminal with neurotransmitter that's going to be released on the postsynaptic membrane. This is the post synaptic membrane, and I'll label it.

01:42

Again, I'm not putting all the detail that we had in the last lecture, there's no need to.

01:50

And obviously, this is the presynaptic terminal here of some neuron

01:57

that is going to be releasing

02:01

neurotransmitter, so let's release some neurotransmitter.

02:04

Now when that neurotransmitter binds to the receptor stuff is going to happen and then we're going to open and close chance.

02:12

And so what we're going to do here is I'm going to draw us a little bit longer here is we are going to measure the membrane potential right there, post synaptic potential, the membrane Panet potential of the postsynaptic membrane, and the membrane potential of this cell right here is going to change because the neurotransmitter is bound to the receptor.

02:35

So

02:37

just to make sure that we're understanding where we are, we're just doing this.

02:43

And so we're going to track it.

02:45

membrane potential versus time, membrane potential,

02:50

versus time.

02:52

And so we're going to have a nice resting membrane potential.

02:58

And then what's going to happen is, is that we are going to release neurotransmitter

03:03

right there. So that's where the neurotransmitter is released. And that's where it's going to bind to its receptor. And that's where we're going to open or close some channel. And when we do that, we're going to obviously change ion transport. Well, one of two things can happen here, we can either depolarize the membrane or hyperpolarize, a membrane, right? We've gone over this. And so in this particular instance, we're going to do that

03:33

we're going to depolarize followed by a repolarization. Now remind me when you depolarize the membrane of the cell, what are we doing to that cell? Are we inhibiting it? Or are we exciting it are stimulating it?

03:46

We're stimulating it. So what we would call this due to this neurotransmitter binding to the receptors causing again, a change in ion transport is an excitatory, post synaptic potential excitatory, we're depolarized excitatory, post synaptic on the postsynaptic membrane potential membrane potential. So what is it EPSP and EPSP is a depolarization followed by a repolarization. And it is excitatory to the cell. Now, how can this happen? Well, we're changing ion transport. And when it comes to these neurotransmitters are binding to these particular receptors causing stuff to happen and eventually the change in ion transport, what's gonna cause that is the opening or closing of some channel. And so let's talk about that. Now, let's put some channels here. So I'm going to put a channel there, then I'm going to put the word or put another channel there, put the word or stick another channel there and put the word or why because there are three channels that we are aware of. And I want you to tell me, if it's a sodium channel that's being affected by this neurotransmitter binding to its receptor.

04:58

Again, going back here

05:00

stuff is what's occurring once again, when stuff is occurring.

05:06

After the receptor is activated by the neurotransmitter stuff.

05:13

Stuff causes a channel to open or close. And when that happens, we change transport, we're going to change the membrane potential where I chose in this particular example, to make the membrane potential more positive. So tell me if that's a sodium channel, did we open or close the sodium channel?

05:30

We opened it. Which way does sodium get transported passively in?

05:40

And when those sodium channels open, more sodium gets transported into the cell more positive charge sticks to the inner membrane, and we get a depolarization. So we open

05:52

sodium channels, which means we did what to the permeability of sodium?

05:58

We increase the permeability of sodium.

06:02

How about a chloride channel? The next one will be a chloride channel, what are we going to do to the chloride channel open or close it?

06:09

Close it. So our chloride normally does this, right? Well, if we close the chloride channel,

06:18

now not as much negative charge will go into the cell, less negative charge on the inner membrane.

06:25

That means the inner membrane is more positive it depolarizes.

06:30

Next one is the potassium channel. So we're going to close

06:35

chloride channels.

06:37

And then obviously, we're going to be decreasing the permeability of chloride.

06:43

What are we going to do the potassium channel open or close?

06:47

Close it. Potassium is positively charged like sodium, but

06:53

to assay is going in this direction. That's its gradient.

06:57

And so here, we're going to close

07:00

potassium channels, when you close potassium channels,

07:05

less positive charges on the outer membrane, that means the outer membranes less positive, which means the inner membrane is more positive, the complete opposite. And so this would be a decrease in potassium permeability.

07:19

So those are three possibilities as to why

07:24

this occurred.

07:26

And what did we learn this, by the way, this is a talk page 27, we learned this on

07:31

I don't know what lecture was first, the second one might have been the second one, I think.

07:37

So that's an EPSP excitatory postsynaptic potential, I'll write it out excitatory postsynaptic, potential.

07:52

EPSP.

07:54

Now we're going to do the opposite, we're going to have the membrane potential hyperpolarize due to some neurotransmitter binding to some receptor.

08:04

And so here's our postsynaptic membrane. Once again, we're going to release some neurotransmitter.

08:11

We're going to talk about specific neurotransmitters today, by the way, we're going to measure the membrane potential of that cell,

08:17

we are going to have

08:20

three sodium share three channels here.

08:24

When you get to tell me what's happening to each of them, that's going to cause what we're about to see. So membrane potential versus time. Initially, we have a nice resting membrane potential. And then this is where the neurotransmitter gets released.

08:39

It does its thing. It binds to the receptor receptor causes stuff to happen. And we're going to open and close some channels. And as a result of that,

08:49

we're going to get an IPSP an inhibitory post synaptic potential, of course, because we are hyperpolarizing the membrane. Now here's another thing, I'm showing you these transient changes in membrane potential, can the membrane potential stay negative? Yeah. If we keep on releasing that neurotransmitter, well, just like this one, can this stay positive? Yes, if that neurotransmitter keeps getting released, but if the neurotransmitter is released, and then it's immediately sucked up, and then it doesn't get released again, then we're going to get an EPSP. So I want to make something clear here. When it comes to postsynaptic potentials. The definition is a transient change, transient mean short lived.

09:34

But Can these neurotransmitters cause a long term change in membrane potential? They absolutely can. But that would not be considered an EPSP or an IP SB. Want to make sure that that's understood, which is why I put the word transient there.

09:49

So going back to this, well, let's talk about what's happening with each of these particular channels.

09:56

I think you probably already know this, because it's going to be the complete opposite of what we had here.

10:01

So instead of opening the sodium channels, well, we're gonna close up.

10:08

And so close sodium channels.

10:12

And again, what's doing this the stuff that's happening inside the cell that we didn't even discuss. And so we're going to get a decrease in the permeability of sodium chloride,

10:26

we're going to open those more negative charge coming into the cell means more negative charge is going to be stuck to the inner membrane causing

10:35

an inhibitory postsynaptic potential again, if it's transient, and so open chloride channels, so we're going to be decreasing the permeability of chloride

10:48

or I'm sorry, increasing, decreasing that arrows going in the wrong direction.

10:54

And then potassium, we're going to open some potassium channels,

10:59

more positive charge on the outer membrane means that the inner membrane is less positive, or negative. And so we are going to open potassium channels.

11:12

And therefore we're going to increase the permeability of potassium.

11:17

And this is something that you need to know.

11:20

Right? Again, transient changes. And so this stuff right here, and this stuff right here, those words are here.

11:30

Okay, this stuff that's in your notes. And we just gave the examples that we know when it comes to the channels that we're aware of, and that we're familiar with.

11:40

Now, the next thing that's in the notes, a very short part of the notes underneath what I just discussed, some called summation, we're gonna skip it. If it takes too long, I don't think it's really that valuable to the knowledge that we are going to acquire that we need to understand what we need to understand again, as I said, I'm going to put on pilot, a PowerPoint that crosses off all the things that you don't have to know the reason I haven't done it yet is because well, I still don't know everything we're going to cross off. Although this might be the last thing.

12:08

Moving forward, then let's talk about plasticity. When you see or hear the word plasticity, I want you to think change. That's what plasticity means.

12:18

And so if we're talking about synaptic plasticity, well, that means that something at the synapse has changed. And so if we go back, and we look at the synapse, so we're talking about chemical synapses here, let's see the structures that we have at the synapse, and there are many. And I'm just going to give a few examples of the kinds of changes that we have. But we have a number of structures here we have neurotransmitter being released, we have receptors that are binding that particular neurotransmitter, we have a certain number of, of synapses that that are present. These are things that can change. And so let's draw synaptic plasticity now. So what I'm going to do here is, is that I'm going to draw two synapses that I'm going to draw on the right hand side and entire neuron, I'm going to show you what happens with synaptic plasticity. And then we're going to talk about synaptic plasticity, actually quite a bit today. And actually, I'm going to be here on Monday for just a little bit, it looks like I don't have to rush through this tonight, because well, I moved the test back to Wednesday or Thursday.

13:19

So let's look at synaptic plasticity.

13:24

And you're going to see where this is occurring. And it occurs all the time it's occurring, it never stops occurring, actually, it's occurring in you right now. That's how we learn by the way, synaptic plasticity is one of the ways that you have memories and learn, we'll talk about it when we get the memory. So what I'm going to do here is I'm going to draw a synapse,

13:43

very, very simply.

13:46

And all I'm going to put here

13:49

are some receptors, a certain number of receptors,

13:54

and a certain amount of neurotransmitter that's released. And I'm going to say that that's the amount that's going to be present, without plasticity having occurred yet. We do the same thing, I draw it again over here.

14:10

Same synapse.

14:15

Same number of receptors, same amount of neurotransmitter released

14:20

23456 and seven, right now let's see what plasticity is. So with plasticity, what can do, what can happen here is is a change. And that change can go in either direction, the change can be an increase in something or a decrease in something. And so I'm going to draw that same synapse over here.

14:43

And on the left hand side, what I'm going to do is is that I'm going to show that more neurotransmitter

14:50

is released because more is present within the presynaptic terminal.

14:55

And so this is I don't want to say a permanent change because it doesn't mean it's necessarily

15:00

I'm going to change but it is a long,

15:03

it's sustained over time, because there's been some change in the changes that this particular neuron is making more neurotransmitter and releasing more neurotransmitter, when it's stimulated to release the neurotransmitter, we're still going to have the same number of receptors, though. So that's a form of plasticity. They can go the other direction. And the other direction is, is that we just don't have as much neurotransmitter.

15:31

Now, why are these things occurring? Well, we'll talk about a few examples over the next lecture and a half. But that too, is plasticity.

15:42

So either an increase in the amount of neurotransmitter being produced or release, or the other way around to decrease that's a form of plasticity will be here on this side, what I'll do is, I'm going to affect the receptors.

15:57

And so we're going to have either more receptor or less receptors, that too is a form of plasticity.

16:06

So I will choose on this particular side to draw more receptors.

16:11

So this particular cell, whatever it is, has produced more receptors and has incorporated more receptors into the membrane. And we're just going to have the same amount of neurotransmitter being released, that doesn't change, although Can you have more neurotransmitter with more receptors,

yeah. But I'm just taking one thing at a time. And it can go the other direction, where we have less receptors

16:37

with the same amount of neurotransmitter 1234567, and instead of four, I don't know, I'm gonna put two, that's a form of plasticity as well.

16:47

And it'll be here on the far right hand side, what I'm going to do is I'm going to draw a neuron, very simply, there's a cell body, there's the axon, and we have some presynaptic terminals there.

17:00

Another form of plasticity is this,

17:04

we can grow more presynaptic terminals

17:08

are we can have less.

17:11

So that's a form of synaptic plasticity.

17:15

So we have many more presynaptic terminals, which then gives us the ability to release more neurotransmitter, or can go the other direction.

17:25

They can get pruned.

17:28

That's another form of synaptic plasticity. Now, when it comes to synaptic plasticity, I want you to read a very important line here. And I'll mention what this means in just a little bit. Large events that I have advancing quotes, must take place to cause plasticity. So these bless you these these things that are happening at the synapse are not randomly happening.

17:49

They're made to happen by these large events. And I'm going to explain what a large event actually a large event is happening right now, you listening to what I'm saying, when you walk to this classroom today, and you saw a tree and you remember the tree, that's a large event, if you remember the tree,

18:07

you hear a sound and you just remember the sound, and it's stuck in your head. That's plasticity. The reason that you can remember that sound is because you grew more synapses, and it caused a

memory. Those are just some examples. And I'll be talking about that in more detail. When we get to memory. There are other ways that plasticity occur. And I'll talk about them in the lecture today, but some event must make it happen. It's just not going to be random.

18:35

We're gonna come back to it. Now what? Let's talk about some neurotransmitters. There are tons of neurotransmitters that are being released in the body, we're going to discuss roughly a dozen of them.

18:48

There's over 100 How many actually I don't even know the number, but it's, it's, it's a hell of a lot more than a dozen, it's probably at least 100. But these are the main ones and these are the ones I'd like you to know. The first one we're going to discuss is acetylcholine. And the reason I picked that one first is because that was actually the very first neurotransmitter ever discovered. And so let's talk about acetylcholine. Now, acetylcholine acetyl.

19:14

Acetylcholine is either excitatory or inhibitory. What does that mean? Well, we already know what that means. It either will depolarize the membrane of some cell that is released on to or hyperpolarize the membrane of some cell that it is released on to it's the same exact acetylcholine.

19:34

So how can a neurotransmitter excite or not and but or

19:41

inhibit something? Well, I'm going to give you a specific example. And this is an example that we're going to explore later on this semester. And next, actually, but I'm going to give it to you right now. So this is going to be a synapse.

19:56

And this synapse is going to involve some neuron

20:00

synapses onto a skeletal muscle cell.

20:07

And these are the muscle cells that make up the muscles that you will be learning about very soon this semester, muscles that you typically think about when you think of a muscle, the ones that are attached to your bones, bicep muscle, quadricep muscle, pectoral muscle, that kind of muscle.

20:22

Over here, we're going to have a synapse between another neuron.

20:27

But this is going to be cardiac muscle. This is the muscle of your heart, which we'll be learning about a little bit this semester, but a lot next semester skeletal muscle, we're going to learn a lot about that this semester. And so we're going to be releasing acetylcholine onto these cells.

20:44

They're going to bind to their acetylcholine receptor. It's the exact same acetylcholine by the way, acetylcholine is abbreviated capital A capital ch. I'll label them both.

20:57

Something very different happens from one cell to the next. When it comes to skeletal muscle cells. When acetylcholine binds to acetylcholine receptor, it causes this to occur.

21:11

sodium channels to open

21:15

in heart muscle

21:19

causes that to occur. So you tell me which ones excitatory which ones inhibitory skeletal muscle excitatory or inhibitory excitatory. Acetylcholine is excitatory to skeletal muscle, while it is inhibitory to cardiac muscle.

21:38

Now, how does that happen? It has to do with the acetylcholine receptor, there are two there's two different kinds of acetylcholine receptors. I haven't told you that yet. I will later on this semester actually.

21:48

So the acetylcholine receptors of skeletal muscle caused this to happen and see the choline receptors of cardiac muscle cause this to happen.

21:58

That's how it works. So some of these neurotransmitters are going to be excitatory or inhibitory. Some will just be excitatory. And some will just be inhibitory. And you have to know that. Now do you have to know these two specific examples you actually don't. I presented this to help you understand, although you already did understand it. So I just want to do a sit solidify your understanding of how we excite cells and how we inhibit cells when it comes to opening and closing of channels. But you don't have to know this specifically. But you do have to know that once again, acetylcholine is either one or the other. And you have to understand what that means.

22:38

Now, when it comes to acetylcholine, what kind of functions does it have a ton. I've picked how many have I picked

22:47

four or five

22:50

helps you sleep when you release enough acetylcholine in the brain you sleep properly. When you have enough acetylcholine being released in your brain, you're able to keep your attention. When you have enough acetylcholine being released in your brain. You can keep memories you learn.

23:07

It keeps you alert. So it's there for arousal.

23:12

These are the functions that I'd like you to know. Acetylcholine is a neurotransmitter of the somatic nervous system, which is all about skeletal muscle.

23:23

And acetylcholine. If you don't know what somatic nervous system is, that's fine, you will in about two weeks because I'll be talking about it.

23:30

And then autonomic nervous system if you don't know what that is, you certainly will because I will be talking about it in a couple of weeks.

23:39

This is what I'm most concerned about is these particular functions right here and associating them with acetylcholine.

23:46

Now, let's talk about some pathophysiology. Right here, let's talk about Alzheimer's disease. For those of you that don't know what Alzheimer's disease is, is a condition where in your brain neurons are destroyed by these plaques that are formed. And we're getting at the heart of the issue as to why that happens. But we're not quite smart enough to know exactly what happens, which is why there's still yet a cure.

24:08

But we know enough about Alzheimer's that we can treat it. And one of the treatments of Alzheimer's is a reuptake inhibitor. So what I'm going to do here is I'm going to draw Alzheimer's disease for you in a simpler way that I possibly can.

24:22

I'm going to draw four different synapses. So that's going to be a neuron releasing acetylcholine, this is going to be a neuron releasing acetylcholine as this is. And as this is, so those are just the presynaptic terminals of these particular neurons. And these neurons are releasing all their acetylcholine onto this one neuron in the brain. And I'm going to call that a memory neuron. Now there are certain areas of

your brain that are responsible for learning in memory. We're actually going to talk about them on Monday when we talk about learning and memory. So that's the memory neuron.

25:00

job is to remember things, to learn things, etc, etc, etc. And it does that in part, not in total by releasing

25:11

acetylcholine here at these synapses and stimulating that neuron properly so that you do learn and keep memories, and form memories. And in this particular case, it's excitatory.

25:27

And I'm going to say that each of these particular synapses, that we are depolarizing, for milli volts, I just picked a number completely out of the air.

25:37

But it's a nice, even easy to work with number.

25:41

And I'm going to say at this particular point in time, this person doesn't have Alzheimer's. And I'm going to say that this one individual neuron, if all of these acetylcholine molecules are released at the same time, at these particular synapses, that the signal is going to be a plus 16 milli volt depolarization, I think we could probably see that when we do simple math, four plus four plus four plus four plus four is 16. So under normal conditions,

26:08

this particular individual neuron,

26:12

we have a 16, millivolt, depolarization.

26:17

Let me put the word depolarization. There 16, millivolt depolarization in the net allows us to form memory, because we're stimulating that memory cell, that memory neuron just the right way.

26:30

Here's Alzheimer's now. So what's gonna happen with Alzheimer's is this and again, I'm simplifying this to where it needs to be to have this discussion.

26:43

That's Alzheimer's,

26:46

we're killing neurons. Now, I don't want you to think that that's plasticity. Plasticity, is a change at a synapse, and is that a synapse and is that a change did it is, but not because something is changing at the synapse, but because something is being destroyed at the synapse, those neurons are dead.

27:07

So they're dead,

27:09

dead neurons.

27:12

Death is not plasticity, death is dead. There is no synapse, they're gone. So we can't say that they changed. They don't exist. And so I'm actually going to put that there. This is not plasticity.

27:31

So given that we've lost two of these neurons, and I picked two, I could have picked one or three or whatever.

27:36

But given that we've no longer have these neurons, now, what's the signal?

27:43

Take milli volts.

27:46

Now you have trouble with memory.

27:49

Because you're not stimulating the memory neuron properly.

27:54

Well, how can we treat this,

27:57

we can give a reuptake inhibitor right? When we talk about reuptake inhibitors, let's refresh our memory. Speaking of memory,

28:05

we give reuptake inhibitors

28:08

when the level of a neurotransmitter is too low.

28:12

And so we can give an acetylcholine reuptake inhibitor. And if we do that, the acetylcholine stays out here for a longer period of time, as it does out here, it'll bind to the channels for a longer period of time.

28:25

Or the receptors, I should say the channel stay open for a little bit longer, we're going to get a little bit more sodium into the cell. And we can depolarize a little bit more. So with treatment, you know, do it in a different color.

28:40

What's our treatment, an acetylcholine reuptake?

28:45

inhibitor.

28:48

And so if we do that, well,

28:53

maybe instead of plus four, we get at the plus six.

28:58

Now, what's our signal? Is it plus a now what is it?

29:02

Plus 12? Did we improve it from plus eight and proved a 50%? We might not get the plus 16 Like it was, but at least it's closer than what it was before that. And so with our treatment, well, now we have a 12 millivolt

29:20

depolarization.

29:23

So

29:25

a better memory not as good as it was.

29:28

And eventually with the particular disease itself, it progresses and we start to lose more and more neurons and the treatments aren't going to work as well and eventually well. The person is going to succumb to Alzheimer's and the complications of Alzheimer's unfortunately. Now I don't want you to think that acetylcholine reuptake inhibitors are the only way we treat Alzheimer's This is just one way to treat it because many other things are involved. But let's think about this for a second.

29:54

We have acetylcholine affecting memory course

30:00

So one of his jobs. And if you don't have enough of the acetylcholine Well, now you don't have the same number of memories or you can't form as many memories because of it or you have trouble doing it.

30:12

So this is a specific example of a reuptake inhibitor, and we're going to talk about more reuptake inhibitors in just a second. So I do want you to know this in the detail that we've discussed it right here and how it works.

30:27

Now what?

30:29

Let's talk about some other neurotransmitters, we're going to talk about the mono amines, serotonin, norepinephrine and dopamine, they're all monoamine. So they have very similar functions, but they also have some distinct functions. We're going to start with serotonin, otherwise known as five ht, although most often in clinical settings, it'll be called serotonin, and not five HD

30:49

excitatory or inhibitory depends on the cell.

30:53

What type of functions do I need you to know when it comes to serotonin, it's important temperature regulation, sleep mood moods, a big one, we're going to spend some time on

31:03

nausea, vomiting, temperature regulation, we've talked about temperature regulation, a cue occur at least a couple of times this semester. This is all about the regulator. Remember that receptor regulator effector. And we've talked about that a number of times with temperature regulation. I really didn't talk much about the regulator. I talked more about receptors and effectors. And we talked about temperature regulation. Let's talk about the regulator now, which is in your brain. And you know what that part of the brain is, by the way, because Seaver told you hypothalamus, remember that that little 1% of your brain

31:35

does a ton of things. Your hypothalamus is the thermostat. That's what sets the setpoint. That's why your body temperature is around 98.6 degrees. That's the thermostat. You put your thermostat is 70 degrees in your apartment or your house, that's what the temperature in your house is going to be.

31:53

Hypothalamus wants your setpoint to be 98.6 degrees. Why? Because that's just the way that the body works best.

31:59

It needs the right amount of serotonin to do that.

32:03

And so serotonin levels start to get screwed up. Well, then the thermostat gets screwed up and a thermostat gets screwed up

32:11

when you're not going to regulate your temperature properly, because it's going to be giving orders to effectors that well aren't the right orders.

32:19

Sleep you need enough serotonin to sleep properly. Just like acetylcholine mood.

32:28

Serotonin is known as the feel good neurotransmitter. Serotonin plays a huge role and what your mood is. And when the levels of serotonin aren't right? Well, then you could develop what are called mood disorders, which we are going to discuss in just a little bit. Nausea and vomiting. When you feel nauseated, that's a feeling that you might vomit you might throw up.

32:54

And then when you actually do vomit, there's a center in your brain is called the vomiting center. And the vomiting center in your brain is a part of your brain that controls the feeling of nausea, and the actual act of vomiting itself. Now, certainly when you have these feelings, something's going on in your gut, but then what's going on in your gut, because we have receptors send that signal to the brain.

33:21

And then we have this feeling.

33:24

And so one of the ways that you can combat nausea and vomiting is to give a drug that affects those neurons that are in your brain that are being affected by serotonin, I bet you most of you, not most of you, at least some of you have heard of this drug. So when you feel nauseous

33:43

when one feels nauseated

33:50

for example, I could put vomit there, but let's just do it. We'll just let's just do nausea.

33:57

Due to, again, stuff that's going on in the gut, we're talking about the brain right now due to high levels of serotonin

34:09

in

34:11

the vomiting center

34:14

of the brain.

34:18

So let's draw that. By the way, this is not plasticity either. This is just an area of the brain that's being stimulated.

34:28

Okay, so this is going to be that area of the brain.

34:32

And so here are serotonin receptors. And that's what those are, I'll even label them. Those are serotonin receptors.

34:42

And serotonin is going to be released onto those receptors. A lot now, because those neurons that release serotonin are being forced to release more serotonin. This is a defense mechanism. Why do you vomit? To get whatever the hell in your gut is causing you that discussion?

35:00

for it to get the hell out of your body. That's why you vomit to get rid of something from the body that doesn't belong in the body like

35:07

bacteria, virus of some kind that's in your gut. So that's serotonin.

35:14

And we have too much of it.

35:20

So high levels of serotonin.

35:24

Now, once you want to give a reuptake inhibitor,

35:28

that's the last thing you want to do to this person, you'd make it worse. What you want to do instead is diminish the effects of serotonin. Well, how can we do that? What we can do is

35:41

when by the way, serotonin is binding to these receptors, right? Well, if we can block that from happening,

35:52

you'll diminish the feeling of nausea.

35:55

Because obviously, as we went over the chemical synapse, you know that when the neurotransmitter binds to the receptor, that stuff happens. The stuff is what's causing you to feel nauseated. And so what we can do is

36:10

we can block

36:13

serotonin receptors.

36:16

Give me another name for block, please.

36:19

antagonists beautiful.

36:22

So a serotonin

36:25

antagonist, we're blocking the receptor.

36:29

And some of you might know the name of this drug or heard the name of this drug? Zofran. I

36:36

bet you there are many people in this room that might have taken Zofran or maybe even given it to a patient. That sounds so frameworks. So Fran blocks serotonin receptors. And it's very common drug. Finnegan used to be the one that was given before this. This one has been found to be better. I want you to know though Fran, even though it's not in your notes. All right.

36:58

Let's time are we at right here. We're still good.

37:03

So again, why am I talking about that? Well, because serotonin deals with this stuff right here.

37:11

Even though I just talked about serotonin in the brain with all this stuff over here, most of the serotonin in your body is actually in your gut. Most of it is but 80% of the serotonin in your body resides in your gut, it plays a role in your gut as well helps with gut motility. motility is the movement of your gut where it mixes things peristalsis. These are things we'll learn about next semester. So serotonin is located in a number of places in the body. Now, let's talk about some pathophysiology. Again, I want to remind you this is not plasticity. Let me let me put that down here as well. This is not plasticity.

37:47

This is going to be a short lived thing. The reason that we're releasing more serotonin is because well, these neurons are being stimulated to do that they haven't made more. And they're not releasing more because of plasticity, they're releasing more to make you vomit.

38:03

So going back here, so let's talk about this stuff over here.

38:08

Low levels of serotonin, linked to mood issues, depression, anxiety, OCD,

38:17

and PTSD, Post Traumatic Stress Disorder. Now, these are theories. By the way, these have not been 100% proven, but they are leading theories. And there's a lot of research out there. That certainly points to low levels of serotonin causing these particular what are called mood disorders.

38:36

So what I'm going to do here is I'm going to draw a mood disorder.

38:41

And so what I'll do here is I'm going to put no mood disorder, and what it would look like.

38:48

And over here, I'm going to put mood disorder.

38:52

And what we think it might look like

38:58

I'm just going to draw one neuron,

39:01

one neuron with some presynaptic terminals, releasing a certain amount of serotonin

39:10

and I'll label the Serotonin

39:16

Mood Disorder

39:23

There you go. Again, theory, not 100% proven.

39:31

That is plasticity.

39:34

We have some change at the synapse, where it now causes some type of an issue.

39:42

Now, why the hell would this happen?

39:44

Let me tell you after the break, because we're at 39 minutes and that's about break time. So after a break, we'll continue our story

39:57

Okay, folks, let us continue

40:01

All right, so we're talking about mood disorders.

40:04

And how plasticity is thought to be involved with them in this direction net, to where we have a decrease in the number of synapses. Now, is it this simple? It's not, but it's good enough for the discussion that we're going to have.

40:20

Now, you might be asking yourself, well, why the hell would this happen? Well, as I said, Before, in order to initiate plasticity, we have to have large events occurring. And so what kind of events can we occur or can occur that would cause something like this to happen? Well,

40:38

sad events in your life, the loss of loved ones, or just whatever traumatic events,

40:47

car accident,

40:50

sexual assault, getting bitten by a dog, just just just something traumatic, that's happening, that is this big, huge.

41:00

No event, again, for lack of a better word that's causing these particular neurons to kind of back off on the number of synapses that they have.

41:08

Now,

41:11

there are sad events that occur all the time in people's lives, there can be traumatic events that occur in people's lives. Not everybody develops these mood disorders like depression, and PTSD, and anxiety, those kinds of things. Why is that?

41:27

We don't know, if we knew the answer to that question, we might be able to cure these kinds of things and get the neurons back to where they're supposed to be, although the treatments that we have for them, which I'll talk about just a second, can actually reverse this. And we can have plasticity in the other direction. It could also be that somebody might be susceptible to mood disorders, because this might be somebody who has who was born with an awful lot of these, these terminals here, whereas somebody who's more susceptible might have neurons that look more like

41:59

that. And so they don't have to lose too many

42:04

to get here, whereas this person could lose half of them, and they still wouldn't be there. So that's the theory. But again, it's all theory. And

42:15

all of this is theory, none of this has actually been proven.

42:19

So you know, it's ongoing as to how all this occurs. And when it comes to, again, somebody getting afflicted by these kinds of things, and others, and so people can go through very, very traumatic events in their lives and not have something like I'll give you myself as an example. Back at the end of 2007, and beginning of 2008, in 2007, I lost my father in law, who I love like a dad. During that time, unfortunately, I was going through a divorce with his daughter,

42:46

I had a son, I was very worried about my two year old son at that, or three, or he was young at the time. I, my dad was dying, too, and died a couple of months later. And then I had an issue with some nerves in my body that were damaged that caused me

43:04

all kinds of problems that took me about a year to recover from. All of that happened in a matter of about three or four months.

43:12

I did not develop depression, I did not develop anxiety had not developed PTSD. I have a relative who got bit by this little yippee dog.

43:22

That's all that happened. Bitter. She developed OCD, PTSD from that, from that one little incident for this little puppy dog. It didn't even really disfigure her at all, she looks completely the same as she did before that.

43:38

But that one little incident took that and that was a relative. It's not like the single friend of mine who doesn't have the same genetic makeup. His idea was my sister, by the way.

43:47

But she developed those kinds of things. So why did she develop that with one little incident? And I didn't with all the things that were going on with me.

43:56

Nobody knows. In the end, I was lucky. And she wasn't. I mean, that's the way that I'm looking at it. I just got lucky that I just didn't develop any of those types of types of disorders because it's, it's very life altering. And that's the other thing too is is that to get diagnosed with these kinds of things. It has to alter your life in some way people use the word while I'm depressed. I'm depressed because well the Browns sucked for so long. Or I missed that sale at whatever or I'm having a bad hair day. Okay? You're not depressed? You're sad. Or by the way, why do you feel sad?

44:32

When you get sad when you have events that make you sad,

44:38

sadness,

44:40

the events themselves hyperpolarize your neurons?

44:46

What do you need to release the neurotransmitter? What's the Flip Step number one,

44:52

an action potential right?

44:54

Well, you're not going to fire as many action potentials if you're hyperpolarizing These neurons right?
So you have a decrease in

45:00

Action potentials, which means you're going to have a decrease in

45:04

serotonin release.

45:08

Now you're saying this the complete opposite, happy, you're depolarizing the neurons.

45:16

Now you're going to have more action potentials. Now you're going to release a little bit more serotonin.

45:24

Now you feel better, you feel good, you feel happy.

45:27

Goes again, there's

45:30

but this isn't this isn't depression over here when it comes to sadness because that can go away quickly. You missed a sale, you go back and get another city and a bad hair day. Well, tomorrow you have a better hair day.

45:41

So sadness depression are not the same thing. Can sadness again, if it's a big enough event in this person lead to depression? Of course it can. It does.

45:53

But again, it has to be life altering does it suck to have a bad hair day?

45:58

I have bad hair days almost every day. So I've gotten used to it, maybe some person is a bigger deal.

46:04

When I say life altering, what does that mean?

46:08

Means it affects your day to day life. It affects maybe the way that you sleep, your mood, those kinds of things. If it comes to OCD, for example, just give me as an example, again,

46:19

if you came to my house right now and you walked into my house, you think I had OCD. I'm a very neat person, everything's clean, my shoes are lined up in my closet, my shirts are hung up a certain way, you opened my dishwasher, I put my dishes in my dishwasher a certain way. If you looked at my lawn, I dare you to find one weed in my lawn. I very, you're not gonna find a weed in my lawn, my lawn looks like a carpet. I'm that guy.

46:45

I look like I have OCD. But I don't. Why? Well, this is a person with OCD, let's say the shoes are lined up in person that has OCD in a closet. But then they think that the shoes aren't lined up, or maybe that they're not.

47:01

They're completely obsessed about it the entire day and ruins your entire day, they got to get back home and fix the shoes. Because if they don't, they're convinced that something bad is going to happen. If my shoes are not straight in my closet, I don't give a crap, I like them straight. But if they're not, it's not going to ruin my day whatsoever. If there's a weed in my lawn, I'll go kill it.

47:21

If the dishwasher has dishes in it put in by somebody else that are not just the right way, I don't care.

47:28

None of that ruins my day, none of it alters my life. But for some people, it completely ruins their day. And

47:37

that's what I mean by affecting your life. Now, it doesn't mean that you can't function with these kinds of conditions because you can and people do it all the time.

47:48

It doesn't mean it's not life altering now, doesn't mean it doesn't affect them on a daily basis. And again, that's how you get the diagnosis. And there's mild, moderate and severe forms of these disorders.

48:03

So it's not just cut and dry when it comes to these disorders themselves. And so I just wanted to make sure that you understood something like that, in that, again, it has to alter your life in some way.

48:16

Now,

48:18

how do we treat these conditions, and they're very treatable?

48:22

Well, I have SSRIs here, so we have low levels of serotonin. So we take a reuptake inhibitor, specifically a serotonin reuptake inhibitor, otherwise known as SSRIs. And I have a few examples of SSRIs here, and you know, it's, so those are all SSRIs made by different companies. Some of these work for some people, some don't work for other people. And sometimes you have to play around with the dosages to get it right. And sometimes they'll work for a couple years, and then they don't work anymore, you got to change the dose or change the SSRI want to say a couple of years. Sometimes people have to take them for a year or two, and then they can come off of them. Whereas other people, they have to take them for a longer period of time. Why is that? We don't know.

49:07

And if somebody has to take them for a longer period of time, well, then they have to take them for a longer period of time. It's helping them

49:14

What else can you do to treat these particular conditions, something called psychotherapy. And psychotherapy can be something as simple as just talking to somebody doesn't have to be a professional. If you have somebody that you trust you confide in. Well, you can tell about whatever it is that is bothering you that's causing these particular conditions. That causes neurons to depolarize.

49:37

Release more serotonin, and then eventually you start to make more synapses, literally by talking to somebody.

49:45

How freaking cool is that?

49:47

Cognitive Behavioral Therapy is something that you're going to do with the professionals. For sure. Cognitive behavioral therapy is a therapy where it changes the way you think

49:58

that's what it is all about.

50:00

Don't get into the specifics of it, because I'm no expert on it at all. But it is a type of psychotherapy, where it's just more than just talking to somebody about your feelings and what's going on in your life. Okay, there's, there's much more to it than that. But if they can shape and change the way that you think, and the thoughts that are bothering, you might just kind of melt away. And then exposure therapy

is something that typically is done with somebody that might have anxiety, let's say somebody is too anxious to walk outside or going to crowds.

50:30

Exposure therapy is slowly but surely exposing them to those things that cause them. Anxiety.

50:36

This is something that should be done by a professional because it's not a good, absolutely backfire and didn't get way worse. So these are different kinds of psycho therapies. And so what's going to happen with these kinds of things is this. So now I'm going to draw treatments of these things. So here's our mood disorder.

50:56

Whatever one it is.

51:00

And again, I'm simplifying this.

51:03

One reason is because well, we don't have a ton of time to talk about this, too, is, is that, well, we don't have a ton of time to talk about it. And I'm not an expert on it. But I know enough about it, because I've been around enough people who have had mood disorders. And so I've done my best to learn as much as I possibly can about them, but I'm still not an expert.

51:26

There you go.

51:28

Treatment. Look what happens.

51:32

Plasticity, but in the other direction. And so what are the treatments? Again, meds

51:40

oops, I should have put that down here.

51:44

Treatments.

51:48

Medications like SSRIs. In psychotherapy,

51:54

you go the other direction, because those are large events.

51:59

And so these are the treatments.

52:02

Can this be permanent? Absolutely.

52:05

And I've seen people with severe, severe, severe, severe issues, friends, family members, to that come to mind.

52:13

Two years ago, when I'm trying to commit suicide, four years ago, when I'm trying to commit suicide, the one that tried to commit suicide two years ago, one month ago, so they've never been happier in their entire life. And they tried to commit suicide two years ago, the one from four years ago, she found this great guy. She couldn't be happier right now.

52:32

So do these treatments work? Absolutely, they do. And the best way to treat these things, studies have shown this to do both, especially if it's severe. Now mild forms of these particular conditions, one of the other has been shown to work pretty well. But if you had the luxury to do both, and you had the motivation to do both, and you know somebody that needs a little help, because sometimes it's very hard to get help when you're in these moods. And sometimes people will say, Well, just you know, what does that person have to be depressed about? It's got nothing to do with it. That person can be Hassett, handsome, pretty successful, have tons of money, and still be depressed. Why? Because this is happening. And it's completely out of their control.

53:15

Nobody wants to be depressed and anxious and have PTSD. And if they could get out of it, of course, they would get out of it.

53:23

But that's not the way that it works. And if we knew the way that it works, well, then we will be able to help those people a little bit better and sooner. So something that you don't want to do is judge somebody based on these kinds of things and look at them and say you don't have a damn thing to be depressed about, yeah, they do.

53:41

Something happened

53:43

and cause them to be depressed, anxious and those kinds of things. So, you know, don't want to judge and you want to try to help these the people with these particular disorders, because sometimes they

just can't help themselves. You don't want to be too pushy about it. If you want to gently guide them in the right direction, and let them know that they can get better and tell them the story that I just told you

54:06

till I have a professor. And he told me and I swear to God to you, I'm not lying. I wouldn't make something like that up. All right. So anyway,

54:17

now they're better.

54:20

And it can be a permanent thing, by the way. All right. So anyway, now

54:26

let's talk about the other all before we do. Ecstasy, MDMA, e x, Mali, whatever the hell you want to call it.

54:34

It's a serotonin reuptake inhibitor. That's what it is. And that's the original drug that was produced way back when was actually used what was supposed to be used for people with depression. And then somebody got a hold of it. And then they started to put some other things in it and they made ecstasy and well now people use it as a recreational drug. And when you do take this drug, you do feel very happy.

55:00

Not because I know but because I heard

55:03

but it does make you feel happy. Why? Well because you have more serotonin in the synaptic cleft for a longer period of time and so your moods going to be better. But people who are in ecstasy have trouble with temperature regulation and sometimes that kills them where their body gets so freakin hot they just fry their brain.

55:23

And here's the other thing when it comes to ecstasy is that if you take it enough over a long period of time you're going to fool the body into thinking that it has enough serotonin. What do you think the body's going to stop making?

55:34

Serotonin now where are you know you're here?

55:39

Okay, so careful out there guys.

55:43

How about the other two? Yeah. Is

55:47

one of the like a selective inhibitor?

55:50

So Fran Silfra is blocking the receptor.

55:55

Yeah, so we go back to the Zofran. Store. Yes. Just blocking the receptor.

55:59

Yeah, completely different mechanism. Yeah, completely different.

56:04

It's actually the complete it's going to have the complete opposite effect. Okay. Now let's go to the other two model means nor epinephrine, which is a monoamine. So it's dopamine, we're gonna see that they have very, very similar functions, but some unique functions as well.

56:18

Attention and mood with norepinephrine once again, just like serotonin. Also, decision making life is all about making good decisions or decisions. We can learn from our bad ones, of course, but norepinephrine levels in the brain can help us with proper decision making, so to speak. The sympathetic nervous system we'll talk about it later on this semester. So low levels linked to because again, attention and mood

56:45

depression, add Attention Deficit Disorder, not so much with serotonin and add but norepinephrine is more implicated with a DD? Because you just don't have enough of it.

56:56

And so how can you treat this well saying when you treat things when you have low levels of serotonin reuptake inhibitor, but not an SSRI, a norepinephrine reuptake inhibitor like Wellbutrin. And so sometimes if somebody is depressed, well, they might not have an SSRI that works for them. They might have to go through or go and take something like Wellbutrin instead,

57:19

it just depends.

57:21

Sometimes it's just a crapshoot. And, you know, you're prescribed something and you know, we, we hope that it works kind of a thing.

57:29

But psychotherapy, that's going to be consistent when it comes to all three of these, these particular model means well, because it's going to have the same types of effect, regardless of what the can what the disorder is, really, and by the way, is another norepinephrine reuptake inhibitor. It's also as well nutrient, a dopamine reuptake inhibitor, so it does both.

57:51

And so dopamine, again, it's a monoamine attention once again, motivation and pleasure, those kind of go along with mood. So again, very, very similar functions when it comes to these bottom amines. But dopamine also has a very distinct function. And that is important in movements. When I talk about movement, I'm talking about this right now you guys are writing down stuff. And I just picked this up, that's movement, I need the right amount of dopamine being released in certain areas of my brain in order for my movements to be nice and smooth. Now, if I don't have enough dopamine being released in my brain, my movements can get screwed up. And that's what happens with Parkinson's disease, you lose the neurons and a particular part of your brain called the substantia nigra that produces a lot of dopamine. And now you have this movement disorder, although about 10-15% of people with Parkinson's also has some cognitive issues. But most often it's attributed to a movement disorder. So right now I'm going to grab my water bottle.

58:49

Nice and smooth, you see how smooth retreated

58:52

nice and smooth. Now, if I had Parkinson's disease, this is how I would try to grab my water bottle.

58:58

I have trouble initiating movement. When I do I'm a little shaky. When I have the water bottle, I'm kind of shaken

59:03

a movement disorder because I'm not releasing enough dopamine in my brain. So I'd like you to know that

59:11

low levels linked to depression, add addictive behavior.

59:17

And so we're talking about motivation. And so a highly motivated

59:23

behavior would be addiction, alcoholism, gambling, addiction, those kinds of things could be attributed to high levels of dopamine. Now, high levels of dopamine, Parkinson's addicted behavior, what the hell are I'm sorry, let's go back to the high levels before we go to the low levels.

59:44

No, let's stick with the low levels then we'll go to the high level. So we have these low levels over here causing these particular things.

59:51

How do you treat it again with the reuptake inhibitor Wellbutrin or Ritalin are also dopamine reuptake inhibitors. Those two are also norepinephrine reuptake inhibitors, but then we have another one

1:00:00

chant tax chant tax is one that's really given for addictive behaviors. Typically, like people who smoke, you'll see commercials about Chantix, and I'll talk about it helped me stop smoking. But it can happen, it can help with other addictive behaviors as well.

1:00:14

Now, I want to go back to the movement and attention and motivation and pleasure blood cutting those, those couldn't be two more different things, movement, and then these kinds of things. Well, how can that be,

1:00:25

because they're being released in different parts of the brain. And you know about how we have these different parts of the brain that are responsible for different things. So that's how you can have a certain neurotransmitter cause of just completely different problems, because the problem is in different areas of the brain.

1:00:44

Now, high levels, Tourette's in psychosis, so if somebody has psychosis, if their diagnosis being psychotic, it could be high levels of dopamine in a certain area of the brain. They can also have a movement disorder known as Tourette Syndrome, because it's in a completely different area of the brain that's responsible for movement. Now, Tourette syndrome is a syndrome that most often is manifested by, people will call them nervous tics,

1:01:14

where somebody might have to blink, like every few minutes, and they do it kind of like in a pronounced way, or have to move their shoulder there, there might be people in this room right now that have Tourette's or might have had it when they were younger, a lot of times Tourette's, you kind of just outgrow it. That's the most common form of Tourette's. And the reason that people do these kinds of things is that they just have the urge to do it. And they have to move they have to blink. It gives them a sense of relief when they do because so much dopamine is being released out of dopamine, a lot of dopamine, a lot of doping full move. And they use that dopamine up and then it builds up, builds up, builds up, builds up, they move, boom, now it comes back down. Restless Leg Syndrome. You guys ever hear that? Where especially a night when you're trying to sleep, you just can't you just have this urge to move your legs, it's attributed to dopamine, not necessarily Tourette's, it's a completely different condition but attributed to the same neurotransmitter.

1:02:08

So anyway, Tourette's is a movement disorder, it's typically it's it's, it's not really life altering all unless, of course, you know, it's a little bit more severe. The most severe forms of Tourette's, by the way, are when people have the like they blurt out a certain sound,

1:02:24

or might blurt out something maybe inappropriate. They can't help it. They cannot help when they do that. And so when it comes to Tourette's and psychosis, if we have high levels of dopamine, we're not going to give a reuptake inhibitor we're going to give a blocker, we're going to block the dopamine receptor just the same way that we block the serotonin receptor, when we have the high levels of serotonin. So let's imagine that this is dopamine. We're going to block the dopamine receptors to help treat Tourette syndrome and certain psychosis.

1:02:57

What else do we need to know here?

1:03:00

Well, nothing. All right, so we took care of the model means

1:03:04

now what there are some amino acids

1:03:09

that are that are neurotransmitter glutamate is going to be the first one that we discuss.

1:03:15

Now, if you've noticed with dopamine, and norepinephrine and serotonin, acetylcholine, they've all either been excitatory or inhibitory. There are some neurotransmitters that are either excitatory. And that's it, or they're just inhibitory. And that's it. Glutamate is excitatory. So when it binds to the glutamate receptor, it's going to depolarize whatever it's binding to some other neuron in the brain. And that's known, that's pretty much where we're going to find glutamate, is in the central nervous system, which I'm going to assume that we know the central nervous system is a spinal cord in the brain,

1:03:49

major excitatory neurotransmitter in the CNS, so it is going to cause a PSPs it's going to cause depolarizations, it's going to cause action potentials to be generated because we're going to hit threshold with glutamate

1:04:04

has a ton of functions. The one that I've highlighted here is learning and memory. So I talked about acetylcholine, we need a normal amount of acetylcholine to learn to remember that for memory glutamates another one no talk about a couple more later as well.

1:04:20

Or tease out these these these, these neurotransmitters that kind of do the same thing. It's easy with a man means but there are a few of these neurotransmitters that aren't really related to each other that have similar functions, which is good. It's redundancy in the body in case something stops working, we have kind of a backup.

1:04:41

Anyway, so know the functions and again, glutamate excites pretty much everything. And learning and memory is another big one I'd like you to know. Now. patho Fitz, high levels cause seizures and neural degeneration. Let's draw a seizure.

1:04:56

So we're going to record some neuron in the brain

1:05:01

I'm going to start to draw neurons very simply like that. And we are going to measure the membrane potential of this neuron.

1:05:08

And we are going to track it. And it's a neuron in some area of the brain. And it's going to be overexcited

1:05:15

because we are releasing too much glutamate onto this particular neuron. And so what I'll do here is, is that I'm just draw another neuron here. So those are the presynaptic terminals of some other neuron releasing a lot of glutamate onto that neuron.

1:05:34

So we have high levels of glutamate.

1:05:39

And it's excitatory.

1:05:42

And if it's sustained, what that can do is this. So we were arresting and now all of a sudden, we're releasing a ton of glutamate.

1:05:53

And now

1:05:56

there, that's a seizure.

1:05:59

Those action potentials.

1:06:04

The seizure is just overactivity of some part of the brain. It's just gonna happen in many different parts of the brain.

1:06:12

And glutamate is attributed to some seizure activity. It's not the only way that you have seizures, but it is attributed to some seizure activities. Glutamate is high levels of glutamate that is, there are normal levels of glutamate that are not going to cause that glutamate being released, by the way is 100% normal, I want you to understand that. So this is an abnormal condition. Hell, I'll even put an extra arrow up just to make sure that we understand that well that a normal really, really high levels. Now, something else that can happen when you cause neurons to be overexcited is you can have a phenomenon called neuro degeneration.

1:06:48

So this can lead to so we are overexcited so a seizure is over excitability

1:06:58

of neurons is what causes a seizure. Now, when you over excite neurons,

1:07:05

over exciting neurons

1:07:11

can cause

1:07:13

neurons

1:07:16

to die.

1:07:19

That's neural degeneration. Now, it doesn't necessarily have to be attributed to seizures.

1:07:27

But it certainly can happen. It depends on how long the seizures lasted. Typically, seizures don't last that long.

1:07:34

But if we have a condition to where neurons are being overexcited, and not necessarily causing a seizure, we can have neurodegeneration.

1:07:44

I'll give you an example of a disease where we have neural degeneration because of too much glutamate being released, causing the neurons to die. ALS.

1:07:57

Anybody know what else ALS is called? More commonly,

1:08:01

Lou Gehrig's disease. Remember the ice bucket challenge I don't know how many years ago was you guys are probably in high school. And it happened that was all about ALS getting research money for ALS.

1:08:11

with ALS, what happens is your motor neurons both in the brain, the upper motor neurons and the lower motor neurons in the brainstem and spinal cord, they die.

1:08:20

And now you can't control your muscles anymore to the point to where you literally cannot even move your pinky, the only thing you can do is blink. Literally, that's all you can do. Those are the only muscles that are spared that in the external anal sphincter. Otherwise, every muscle in your body will eventually be paralyzed if you don't die yet.

1:08:36

And so if you're not put on a feeding tube, if you're not put on a ventilator, you're going to die. Because you need muscles to breathe you need muscles to swallow. devastating disease by the way, your mind is completely fine. Your mind doesn't go anywhere with ALS you just slowly but surely become paralyzed not because you have any spinal cord injury because you're damaging the neurons that control your muscles. completely devastating disease due to too much glutamate no cure for it. By the way, no treatment for it. By the way, you might think well, why don't you just block the glutamate receptors, which is what you can do here.

1:09:16

So in order to treat this condition, what can our treatment be?

1:09:20

I'm actually going to just I'm going to write that again. I promise. It's just kind of in the way of my treatment here.

1:09:27

So how can we treat it? Well, the treatment let's do that in green. So right there as they're having a seizure like activity or you can get the treatment before the seizure even happens. So preventive

1:09:39

is but I'm going to just put it here is that we block the glutamate receptors, so a glutamate

1:09:46
antagonist

1:09:49
and then when you do that,

1:09:52
come back

1:09:58
now

1:10:00
Put the neurodegeneration thing over here. Like you need to remember it doesn't matter I'll just put. So, when neurons are overexcited

1:10:13
that can cause them

1:10:18
to die.

1:10:21
NES known as neural degeneration

1:10:30
ALS, otherwise known as Lou Gehrig's disease.

1:10:36
The reason is called Lou Gehrig's disease because well Lou Gehrig was a baseball player back in the 20s. He got it. He was very famous. And so they named it after him from that point forward. It was it existed beforehand, they first discovered it way back in the late 1800s. Some people think he was the first person to get it. He wasn't he was the first famous person to get

1:10:59
Alright, so that's glutamate. What about GABA, the complete opposite of glutamate. GABA is the inhibitory neurotransmitter in the brain and spinal cord.

1:11:10
Now when it comes to GABA, it also does a bazillion different things, although I don't have any of the functions listed. But it has a lot of functions as well. What I wanted to choose to do with GABA is talk about drugs that increase GABA are used to treat or I'm sorry, drugs that increase GABA are used to treat epileptic activity, which is just seizures. So if we have seizures again,

1:11:36

and it's going to be inhibitory, so I'm going to draw a seizure again.

1:11:41

So here's our seizure. It could be due to too much glutamate, it could be due to other things.

1:11:49

But another treatment can be

1:11:52

something called a GABA ergic. Whenever you see ergic on the end of the word, it means it is a drug that mimics

1:12:01

whatever is to the left of the word urgent. So a GABA ergic drug is a drug that a pharmaceutical company made that looks like GABA. And so it will bind to the GABA receptor. So what do we call that starts with an A,

1:12:18

an agonist not an antagonist but an agonist very good. So that's a GABA agonist.

1:12:26

Or it will be an agonist. So GABA agonist to the GABA receptor is actually what I want to put.

1:12:35

And so what's going to happen here

1:12:42

is that because it's inhibitory,

1:12:46

it's going to work a little differently than GABA than the glutamate, the glutamate

1:12:51

will just stop the action potentials from occurring and bring us down to about resting membrane potential.

1:12:57

When it comes to a GABA ergic drug, what it will do is

1:13:04

it'll hyperpolarize so I told you before that when you hyperpolarize the membrane, you don't necessarily just have to have an IPSP

1:13:13

doesn't necessarily just have to do this.

1:13:16

It could be sustained, depends on how long whatever it is that's causing this to occur is binding to the receptor. And so if you give a GABAergic drug, well, this drug will stay around for some time you get a problem, you're gonna have to take the drug on a daily basis, it's going to be a certain half life to it. But it can do this and that was deemed more difficult to get to the seizure activity. Because you're further away from threshold, you're more hyperpolarized. So GABAergic drugs are another way to treat seizures, just like glutamate receptor blockers are a way to treat seizures.

1:13:53

Now, before we go, the last one on the list here that we'll talk about tonight is glycine. This is also inhibitory. So, you know, it'll do this kind of thing to the membrane potential, just like GABA does. We're not going to worry about Huntington's disease, by the way, so I crossed that out again, I'll put that on Pilate. Very, very soon. Hopefully tonight. I'll put it on Friday. So on Monday, I won't be here very long, probably about, I don't know 3035 minutes and see what will come in. And then your exams gonna be on Wednesday or Thursday. Right, you guys got that email. Alright, so you can enjoy your Halloween

1:14:27

a little bit more

3100 Practice Exam 3

1. Blocking solely Cl^- channels can alter V_m .
 - a. True
 - b. False
2. If a cell with a resting V_m of -60 mV was made more permeable to Na^+ , what would happen to V_m ?
 - a. Remain unchanged
 - b. Depolarize
 - c. Hyperpolarize
 - d. Repolarize
3. Given normal concentrations of Na^+ and K^+ if the permeabilities of K^+ and Na^+ are reversed (that is . . . P_K is 0.05 and P_{Na} is 1), what would resting V_m be?
 - a. Remain unchanged
 - b. Depolarize
 - c. Hyperpolarize
 - d. Repolarize
4. Increasing extracellular K^+ concentration would cause what to happen to the transport of K^+ ?
 - a. Increase the movement of K^+ into the cell
 - b. Decrease the movement of K^+ into the cell
 - c. Increase movement of K^+ out of the cell
 - d. Decrease the movement of K^+ out of the cell
5. If plasma $[\text{K}^+]$ was increased to 8 mEq / L and a cell had a resting V_m of -60 mV, which of these would be the only possible new resting V_m (no calculation needs to be done).
 - a. -90 mV
 - b. -75 mV
 - c. -65 mV
 - d. -60 mV
 - e. -52 mV
6. Inhibition of the Na^+/K^+ pump would cause an increase in $[\text{Na}^+]_i$.
 - a. True
 - b. False
7. Why does the rapid and large depolarization of an action potential stop?
 - a. Closing of K^+ channels
 - b. Threshold is not met
 - c. Na^+ stops moving into the cell
 - d. Lack of neurotransmitter

8. What would be absent from the action potential if voltage-gated K⁺ channels were inhibited?
- Afterhyperpolarization
 - Depolarization
 - Repolarization
 - Threshold
 - Two of the above
9. Increasing the permeability of which of the following channels can potentially cause an action potential to be generated?
- Chloride channels
 - Potassium channels
 - Sodium channels
 - All of the above
10. Destruction of myelin causes continuous conduction to slow.
- True
 - False
11. If the release of a certain neurotransmitter at a synapse is lower than normal, one treatment option is to increase the re-uptake of the neurotransmitter.
- True
 - False

Use the following to indicate which is greater than, less than or equal to the other.

- a. Greater than b. Less than c. Equal to
12. Speed of gap junctions ____ speed of chemical synapses
13. Level of dopamine with depression ____ level of dopamine with Tourette's
14. Number of action potentials with a maximal stimulus ____ number of action potentials with a supramaximal stimulus
15. With a chemical synapse, if the specific receptor for a neurotransmitter is absent from the postsynaptic membrane, the neurotransmitter can still have an effect on the postsynaptic membrane.
- True
 - False
16. Which of the following is not proportional to the stimulus intensity?
- Amount of neurotransmitter released
 - Action potential frequency
 - Action potential magnitude
 - EPSP magnitude

~~17. If an EPSP causes a +5mV change in V_m and an IPSP causes a -2mV change in V_m and they arrived at the same time, what would happen to the cell?~~

- a. ~~Hyperpolarize~~
- b. ~~Depolarize~~
- c. ~~Become inhibited~~
- d. ~~Become excited~~
- e. ~~Two of the above~~

~~Use the following information to answer:~~

~~Resting V_m of -60 mV; Threshold of -54 mV; Synapse A causes a +2 mV change in V_m ; Synapse B causes a +4 mV change in V_m ; Synapse C causes a +6 mV change in V_m~~

~~18. Which of the following would cause this cell to just reach threshold?~~

- a. ~~Temporal summation of Synapse A~~
- b. ~~Temporal summation of Synapse C~~
- c. ~~Spatial summation of Synapse A and Synapse B~~
- d. ~~Spatial summation of Synapse A and Synapse C~~
- e. ~~Two of the above~~

~~19. Increasing the number of postsynaptic receptors for a neurotransmitter is an example of synaptic plasticity.~~

- a. True
- b. False

~~20. What immediately precedes release of neurotransmitter during synaptic transmission?~~

- a. Action potential reaches presynaptic terminal
- b. Opening of calcium channels in presynaptic terminal
- c. Increase in calcium concentration in presynaptic terminal
- d. Exocytosis of calcium
- e. Opening of sodium channels in postsynaptic membrane

~~21. What occurs if a cell is transiently depolarized but does not reach threshold?~~

- a. IPSP
- b. Hyperpolarization
- c. EPSP
- d. After-hyperpolarization
- e. No change is seen

~~22. Solely a change in membrane permeability to ions is the mode of action in what process?~~

- a. Long-term memory
- b. Long-term potentiation
- c. Synaptic plasticity
- d. Procedural memory
- e. Sensory memory

23. Running to the dinner table when a bell rings is an example of what type of memory?
- a. Sensory
 - b. Declarative
 - c. Explicit
 - d. Procedural
24. Which of the following neurotransmitters can cause an EPSP?
- a. Glycine
 - b. Glutamate
 - c. Endorphins
 - d. GABA
 - e. Enkephalins
25. Cognitive behavioral therapy can be used for which of the following?
- a. Obsessive compulsive disorder
 - b. Decreased levels of serotonin
 - c. Decreased levels of norepinephrine
 - d. Alzheimer's disease
 - e. Three of the above

1. A
2. B
3. B
4. D
5. E
6. A
7. C
8. E (a and c)
9. C
10. B
11. B
12. A
13. B
14. C
15. B
16. C
17. E (b and d)
18. E (a and c)
19. A
20. C
21. C
22. E
23. D
24. B
25. E (a and b and c)

3100 Practice Exam 3

1. Blocking solely Cl^- channels can alter V_m .
 - a. True
 - b. False
2. If a cell with a resting V_m of -60 mV was made more permeable to Na^+ , what would happen to V_m ?
 - a. Remain unchanged
 - b. Depolarize
 - c. Hyperpolarize
 - d. Repolarize
3. Given normal concentrations of Na^+ and K^+ if the permeabilities of K^+ and Na^+ are reversed (that is . . . P_K is 0.05 and P_{Na} is 1), what would resting V_m be?
 - a. Remain unchanged
 - b. Depolarize
 - c. Hyperpolarize
 - d. Repolarize
4. Increasing extracellular K^+ concentration would cause what to happen to the transport of K^+ ?
 - a. Increase the movement of K^+ into the cell
 - b. Decrease the movement of K^+ into the cell
 - c. Increase movement of K^+ out of the cell
 - d. Decrease the movement of K^+ out of the cell
5. If plasma $[\text{K}^+]$ was increased to 8 mEq / L and a cell had a resting V_m of -60 mV, which of these would be the only possible new resting V_m (no calculation needs to be done).
 - a. -90 mV
 - b. -75 mV
 - c. -65 mV
 - d. -60 mV
 - e. -52 mV
6. Inhibition of the Na^+/K^+ pump would cause an increase in $[\text{Na}^+]_i$.
 - a. True
 - b. False
7. Why does the rapid and large depolarization of an action potential stop?
 - a. Closing of K^+ channels
 - b. Threshold is not met
 - c. Na^+ stops moving into the cell
 - d. Lack of neurotransmitter

8. What would be absent from the action potential if voltage-gated K⁺ channels were inhibited?
- Afterhyperpolarization
 - Depolarization
 - Repolarization
 - Threshold
 - Two of the above
9. Increasing the permeability of which of the following channels can potentially cause an action potential to be generated?
- Chloride channels
 - Potassium channels
 - Sodium channels
 - All of the above
10. Destruction of myelin causes continuous conduction to slow.
- True
 - False
11. If the release of a certain neurotransmitter at a synapse is lower than normal, one treatment option is to increase the re-uptake of the neurotransmitter.
- True
 - False

Use the following to indicate which is greater than, less than or equal to the other.

- a. Greater than b. Less than c. Equal to
12. Speed of gap junctions A speed of chemical synapses
13. Level of dopamine with depression B level of dopamine with Tourette's
14. Number of action potentials with a maximal stimulus C number of action potentials with a supramaximal stimulus
15. With a chemical synapse, if the specific receptor for a neurotransmitter is absent from the postsynaptic membrane, the neurotransmitter can still have an effect on the postsynaptic membrane.
- True
 - False
16. Which of the following is not proportional to the stimulus intensity?
- Amount of neurotransmitter released
 - Action potential frequency
 - Action potential magnitude
 - EPSP magnitude

17. If an EPSP causes a +5mV change in V_m and an IPSP causes a -2mV change in V_m and they arrived at the same time, what would happen to the cell?

- a. Hyperpolarize
- b. **Depolarize**
- c. Become inhibited
- d. Become excited
- e. Two of the above

Use the following information to answer:

Resting V_m of -60 mV; Threshold of -54 mV; Synapse A causes a +2 mV change in V_m ; Synapse B causes a +4 mV change in V_m ; Synapse C causes a +6 mV change in V_m

18. Which of the following would cause this cell to just reach threshold?

- a. Temporal summation of Synapse A
- b. Temporal summation of Synapse C
- c. **Spatial summation of Synapse A and Synapse B**
- d. Spatial summation of Synapse A and Synapse C
- e. Two of the above

19. Increasing the number of postsynaptic receptors for a neurotransmitter is an example of synaptic plasticity.

- a. True
- b. False

20. What immediately precedes release of neurotransmitter during synaptic transmission?

- a. Action potential reaches presynaptic terminal
- b. Opening of calcium channels in presynaptic terminal
- c. **Increase in calcium concentration in presynaptic terminal**
- d. Exocytosis of calcium
- e. Opening of sodium channels in postsynaptic membrane

21. What occurs if a cell is transiently depolarized but does not reach threshold?

- a. IPSP
- b. Hyperpolarization
- c. **EPSP**
- d. After-hyperpolarization
- e. No change is seen

22. Solely a change in membrane permeability to ions is the mode of action in what process?

- a. Long-term memory
- b. Long-term potentiation
- c. **Synaptic plasticity**
- d. Procedural memory
- e. Sensory memory

23. Running to the dinner table when a bell rings is an example of what type of memory?
- a. Sensory
 - b. Declarative
 - c. Explicit
 - d. Procedural
24. Which of the following neurotransmitters can cause an EPSP?
- a. Glycine
 - b. Glutamate
 - c. Endorphins
 - d. GABA
 - e. Enkephalins
25. Cognitive behavioral therapy can be used for which of the following?
- a. Obsessive compulsive disorder
 - b. Decreased levels of serotonin
 - c. Decreased levels of norepinephrine
 - d. Alzheimer's disease
 - e. Three of the above