because it's a conservative field

VOLTAGE

WATCH VIDEO
LECTURE (EXTRA)

vector, angular magnitud
dirección
nos ubicamos en
gradiente
$E = -\Delta V$

Voltage = Δ electrical potencial (A - O) → E

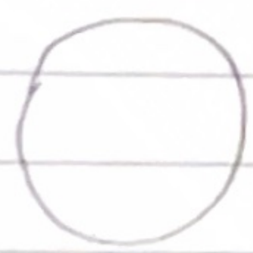
(A - O) = points

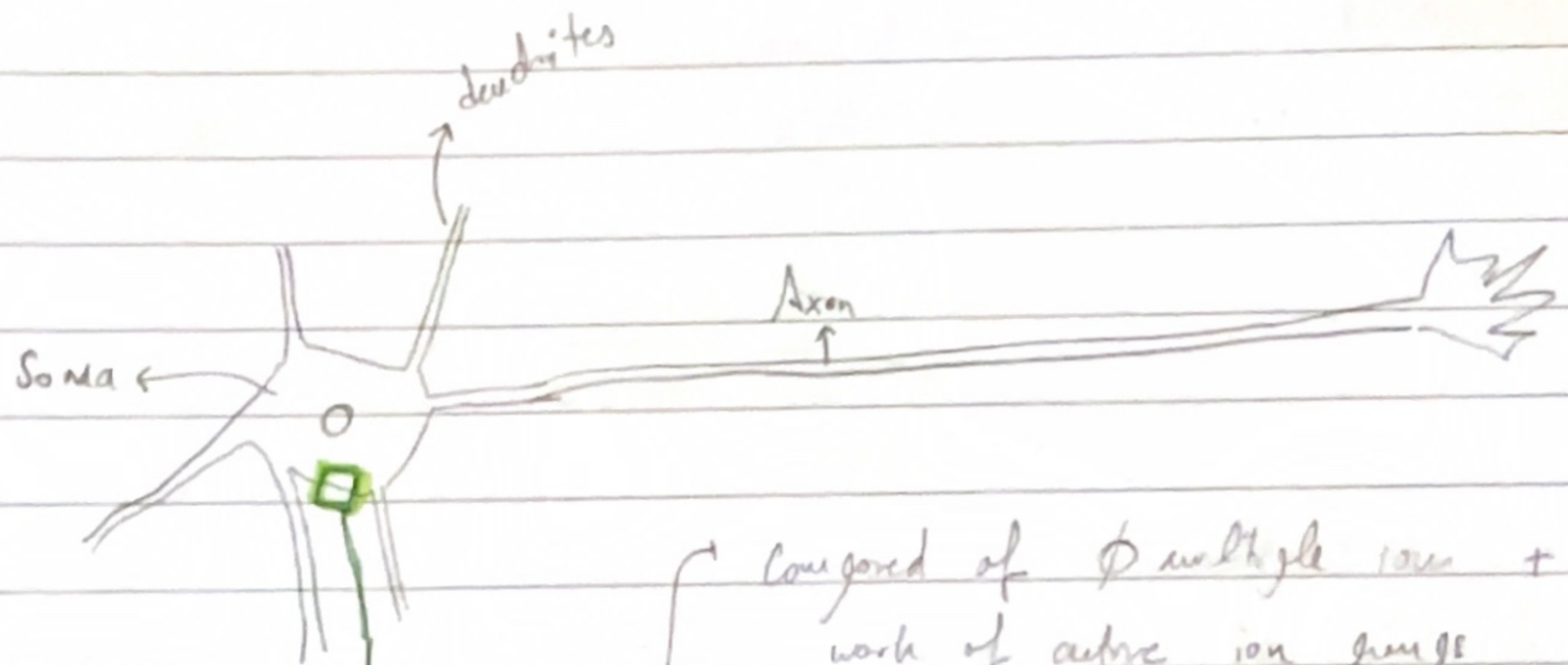
↳ measured = Volts

Electrostatic force = $\vec{F}$ (atraction / repulsion) between ions (+ / −)

↓ outside = Ground es 0 →

Cell





Composed of ∅ multiple ions + work of active ion pumps

Membrane potencial = Voltage at any time → from −90mV to +60mV

Resting potencial → "at rest" → NOT sending / receiving signals

↓

−60mV to −75mV

at rest inside more negative

there have ↑[]

↓

important in resting potencial

Baterías
↓
partes electrofísicas
movendo e⁻

Proteins

Ions Na^+ K^+ K^+ Cl^-

Sugar

- → membrane potencial is measured from inside of cell relative to the outside.

Ej → if a measure of 60mV is taken outside → Δ es 60

Voltage = $EP_{inside} - EP_{outside} = -(EP_i + EP_o) = -60mV$

0 − 60 (?)

(?)

DIFFUSSION / ELECTROSTATICS

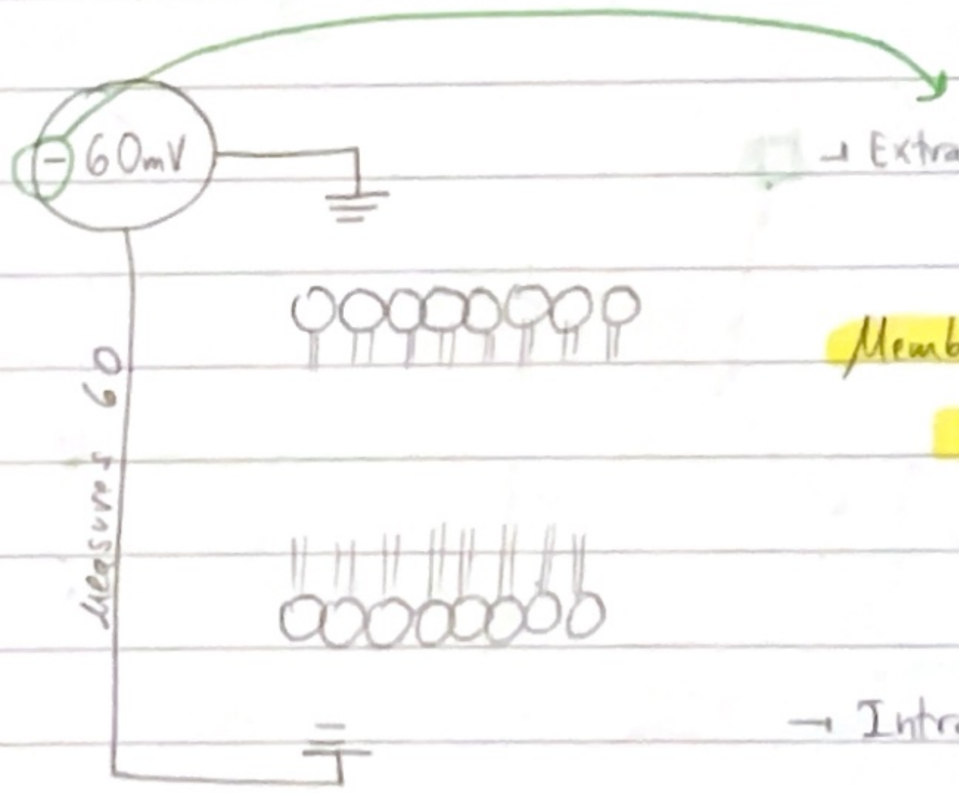
Resting potential

balance between

diffussion (die in water) → ↑[ ] to ↓[ ]

$\vec{F}$ to move molecules according to [ ] gradient

electrostatics



→ Extra Cel → taken as ground ~ "0"

Membrane potential = ΔEP

$EP_e - EP_i = 60$

$0 - 60 = 60$

→ Intra Cel

→ Most cells in body → resting potential −5 to −100mV

→ NEURONS → −40 to −90 mV

→ Each side of membrane = electroneutral

↓

→ Membrane potential → imbalance close to the membrane → CAPACITOR

↓

creates electric field

→ Bilay membrane

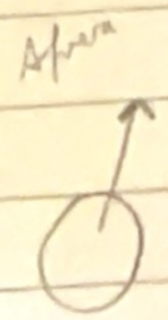
Corriente + de adentro hacia afuera ⇒ membrane potential is ⊖

⇓

Corriente ⊖ adentro - afuera

MP → ⊕

$E_{inside} - E_o = 100 - 5$



$MP = \overset{+}{\overset{\frown}{E_{fe}}} - \overset{-}{\overset{\frown}{E_{fl}}}$

Si sale K^+ de adentro afuera → adentro ↓ carga + afuera ↑ carga +

↓

el potencial de membrana se vuelve más negativo

↓

Como sabemos de que el resting potential es −60, en este caso el membrane potential va a ser por ej −80

& el K^+ sale, la membrana se europa.

→ Moving 1 ion in 100 000 across the membrane is enough to create a −80mV membrane potential

$\vec{F}$ electrostática >>> $\vec{F}$ difusión → gradiente

$[K]_e$ 5mM

$[K]_i$ 140mM

if for example I wanted a more negative resting potential, I should

↑ $[K]_i$

↓ $[K]_e$

140 → ϕ and eq → $[\,]_i$

Cl^- → [ ] inside neuron 15mV
[ ] outside " 140mV

} if channels open and ions flow, what are the new [ ] ?

↓

~ The same as only a few ions moving generates equilibrium

⇒ [ ] gradient is like an engine driving electrical potential

↓

NERST equation

NER

universal gas constant

$E_{ion} = \frac{RT}{zF} \ln$

equilibrium potential

valence

~

Nerst potential →

~

Reversal potential

⇒ For a neuron potential

Iang → doesn't cha
z N net charge

DRIVING $\vec{F}$

Iang

1. diffusion
2. electrostatic balance
3. Nerst potential
single ion

NERST POTENTIAL

universal gas constant

abs temp below

$$E_{ion} = \frac{RT}{zF} \ln \frac{[\text{ion outside cell}]}{[\text{ion inside cell}]}$$

Equilibrium potential

Faraday constant

valence of ion

Equilibrium of single ion.

~

Nerst Potential → point where electrostatic force balances out diffusional $\vec{F}$ (for a given ion, given [ ])

~

Reversal Potential → point at which the net flow of ions switches direction

|

talking about ion channel

⇒ For a neuron, the resting potential is close to the Nerst potential of K^+ → because K^+'s permeability is ↑

temp → doesn't change much

z ~ net charge

Nerst

Cl ~ -70mV

DRIVING $\vec{F}$ = how hard an ion is getting pushed across the membrane

$$\text{driving force} = V_{membrane} - E_{ion}$$

current membrane potential

Nerst potential for an ion

Na+ ~ 80mV

K+ ~ -60mV

close to resting potential

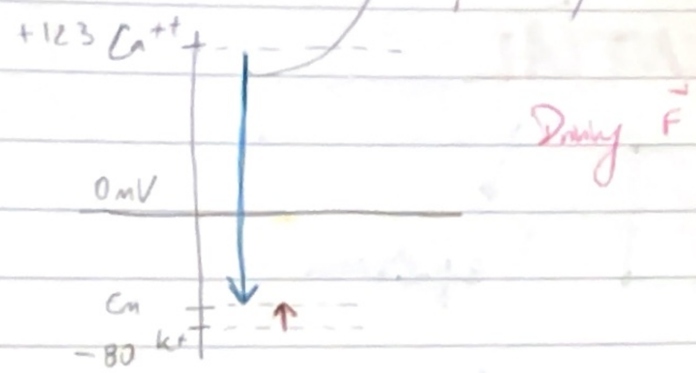
this is why Na^+ opens in fast

eager to equilibrate

they really want to go inside if they can

↓

so they take the membrane potential close to theirs → (+120) (as they are ⊕)



Em = resting potential = -70mV

Ca^{++} Nerst Potential = +123mV

K^+ " " = -80mV

eg Cl^- out 140 → ↑[]o so goes inside (diffusion)

in 15

↓

electrostatic $\vec{F}$ sends them out to balance

↓

at this point, Cl will have moved inside neuron → membrane potential ↑ negative

→ Nerst - el sign

Depolarization =

Hyperpolarization =

Nerst → concentration & difference

↓ ↙

sign

Scenario 1 →

1° dif

2° ele

→ Nerst po

de

gra

Scenario 2 [K]o = 1

[A]o = 1

→ Ions will

move

they can
↓
so they take the membrane potential closer to them → (+120)
(as they are ⊕)

side (diffusion)

F search them out

ce

+, cl will have
cations → membrane
↑ negative

→ Nerst - el signo es genero a la ↑ electrostática excitando -

Depolarization = positive change in membrane potential
(to ↓ negative)

Hyperpolarization = negative change in membrane p.t
(to ↑ negative)

Nerst → compute of
differences
↓
sign

Scenario 1 → $[k]_{intracell}$ = 100 mM } ~ fisiológico
$[k]_{ex}$ = 10 mM
↓
1° difusión → k^+ sale
2° electrostática → k^+ entra cel

→ Nerst potential is negative because ↑[] de carga negativa dentro de la célula (y + afuera) creó la $\vec{F}$ electrostática para balancear -

Scenario 2 $[k]_i$ = 10 mM } 1) k^+ entra por difusión
$[k]_e$ = 100 mV } 2) electrostática fuerza salir k^+
↓
Nerst es ⊕

→ Ions will always flow in a direction that brings the current membrane potential closer to that ion's own Nerst potential

→ 0.0267

a1) $E_{ion} = \frac{R\,T}{z\,F} \cdot \ln \frac{[out]}{[in]} = -0{,}087\ V \rightarrow -87\,mV$

(R: const, F: const)

$R = 8.314\ J/K \cdot mol$

$F = 96{,}485\ C/mol$

$T = Celsius + 273.15$

ln → base e

1) $K_i = 140$ $\quad -87\,mV$

$K_e = 5.3$

2) $Cl_i = 12$ $\quad 0{,}0612\ V \rightarrow 61\,mV$

$Cl_e = 119$

$Na_i = 10$ $\quad 0{,}0730 \rightarrow 73\,mV$

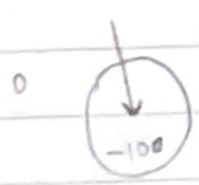
$Na_e = 154$

→ When asked what is the Nerst potential for "ion x" in "x glace" then "x glace" is the inside

$Ca^{2+}_i = 0{,}0001$ $\quad 0{,}1308 \rightarrow 130\,mV$

$Ca_e = 1.8$

4) −100mV across membrane → charges move to reach this potential



GHK equation

In resting neuron

(≠ D

Permeability → "conc

≠ ions

$V_m = \frac{R\,T}{F}$

0,0267

equilibrium → net a

Steady state → C

−55mV = thresh

7 V →

- 87 mV

- 87 mV

0,0612 V → 61 mV

0,0730 → 73 mV

0,1308 → 130 mV

ach this potential

GHK equation → resting potential → 2 most important factors in its determination are ∠ ions [ ] (int, ext) ; permeability

In resting neuron → **Steady State** → net ϕ of charges is equal and opposite

(≠ Vrest)

No one is at equilibrium → [ ] gradient = electrical gradient

Permeability → "ease" by which ion flow across membrane (K^+)

≠ ions ≠ permeability → "pX"

coefficients for permeability to weight their relative effect

$$V_m = \frac{R \cdot T}{F} \ln \left(\frac{P_K [K]_o + P_{Na} [Na]_o + P_{Cl} [Cl]_i}{P_K [K]_i + P_{Na} [Na]_i + P_{Cl} [Cl]_o} \right)$$

0,0267

P		
100	K^+	
4	Na^+	
10	Cl^-	

$$\ln \left(\frac{530 + 616 + 120}{14000 + 40 + 1190} \right) = \frac{1266}{15230}$$

$= -0.0664 \rightarrow$ **-66 mV**

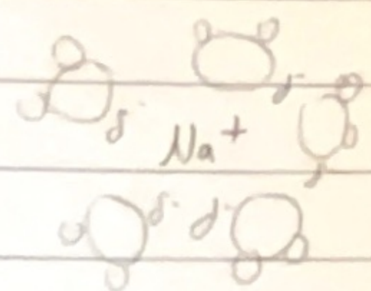
equilibrium → net action of 2 gradients cancel out (eq for 1 ion)

Steady state → [ ] are stable and steady → even if lots of energy is invested to reach this

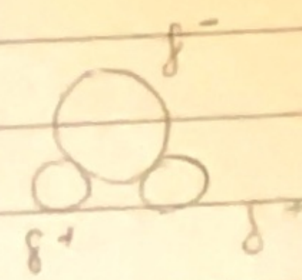
-55 mV = threshold Voltage

ION FILTERS

Ion travels with water → shell of water molecules surrounding the ion → SOLVATION SHELL



H_2O →



lowest energy configuration when (for Cation) interactions between negative ends of oxygen and the Cation and the interference and electrostatic interactions between water molecules just balance out

→ Selective ion channels → made of protein

have a special mechanism in front = selectivity filter

the protein places the AA in order to reproduce a spacing and charge of the neutrally owning solvation shell ← This simulates the spacing of the solvation shell for the desired ion

each ion has a "particular spacing" ← depends on size

LESSON 2: PASSIVE MEMBRANE PROPERTIES

Neurons → change in membrane potential

Electrical signals

Action potential

properties ← resistance, capacitance } determined by factors such as n° of ion channels on a neuron's membrane.

→ each ion has a characteristic Nernst potential (based on [] inside and outside) → is an example of an equilibrium

→ All of ions' movements balance at the Resting potential, which is an example of a steady state

→ Resistance = quantity that describes how much a conductor opposes the ∅ of charge
↳ Ω | Ω/mm² → membrane resistance

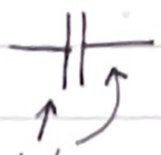
→ I = ∅ - current through conductor

Conductance = $\frac{1}{R}$ Copper ↓ Resistance than salt water
↓
siemens

if Saltier = ↓ Resistance
↑ diameter

Capacitor - element that can store charges

insulating region = dielectric

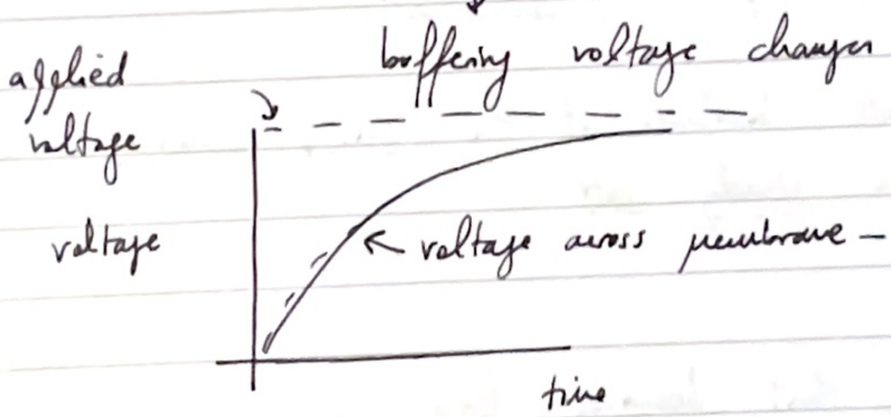


conductor

Capacitance = ability to store charge
↓
↑ with larger surface area
↓ thickness
↓ if Axon diameter ↓

voltage applied across → charge accumulates
↓
plates saturate
↓
voltage across capacitor = to applied voltage

→ By storing the charges, the speed in which voltages changes is ↓
↓
buffering voltage changes



→ GHK → Calculated according to relative permeabilities of several ions.

Relative ratio of permeabilities K^+, Na^+, Cl^- at rest
↓
if individual permeabilities change (eg. opening channels)
↓
ratio changes
↓
charges move → create a current
↓
described by Ohm's law

I -

RC Resistor → low

Current → f

λ → length

depen

V

36%

100 mV

10mm

150mV

A

e =
o store charge
↓
with larger surface
thickness areas
f Axon diameter ↑

to applied
voltage

changes is ↓

es of several

sening channels)

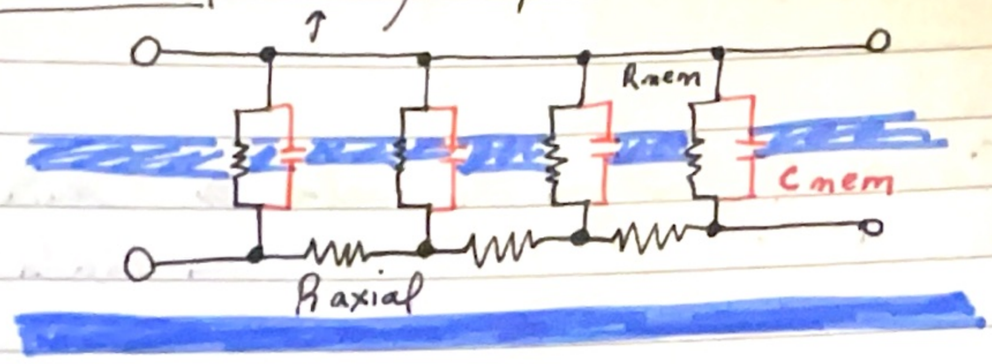
ohm's law

Resistance = $\frac{1}{\text{permeability}}$

$$I = \frac{V}{R}$$

$\boxed{\text{RC Resitor}}$ → low pass filter → allows slow < frequencies variations, blocking < ↑ frequencies fast changes

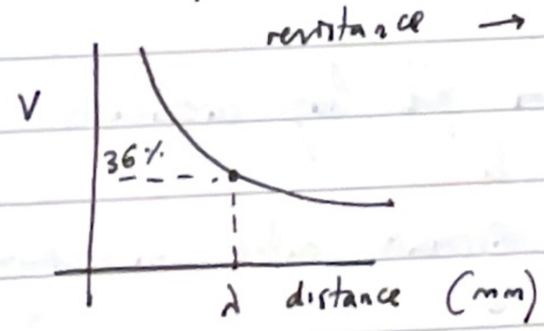
membrane → capacitor
channel → resistors
↓
alter conductance and permeability



Current → flow of charge through a conductor per unit of time

λ → length constance → distance it takes for a potential change to fall off about 37% of its initial value

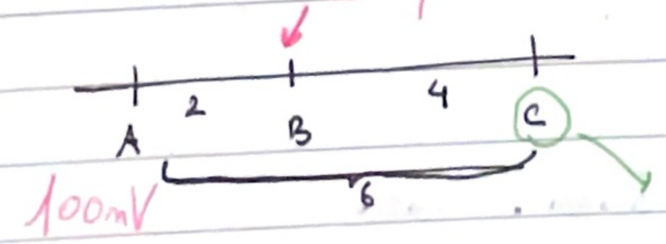
depends on resistance → $\lambda = \sqrt{\frac{R_{membrane}}{R_{axial}}}$ → $\frac{ohm \cdot m}{ohm \cdot m / m}$



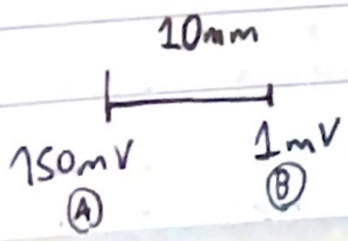
100 mV A
B 2mm away from A
C 6 mm away from A

Voltage decreased to 37mV as 1 lenght constant away

λ = 2



3 length constant away so 100mV · (0.37mV)³ ≈ 5mV



Volt A · (0.37)^x = Volt B

0.37^x = Volt B / Volt A

$\frac{10mm}{5} = 2mm$

→ estaba bien!!
x ≈ 5.04

LESSON 2: PASSIVE MEMBRANE PROPERTIES

Neurons → change in membrane potential

Electrical signals

Action potential

properties ← resistance, capacitance } determined by factors such as n° of ion channels on a neuron's membrane.

→ each ion has a characteristic Nernst potential (based on [] inside and outside) → is an example of an equilibrium

→ All of ions' movements balance at the Resting potential, which is an example of a steady state

→ Resistance = quantity that describes how much a conductor opposes the ∅ of charge
↳ Ω | Ω/mm² → membrane resistance

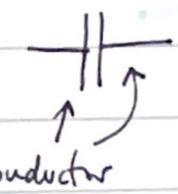
→ I = ∅ - current through conductor

Conductance = $\frac{1}{R}$ Copper ↓ Resistance than salt water
↓
siemens

If Saltier = ↓ Resistance
↑ diameter

Capacitor = element that can store charges

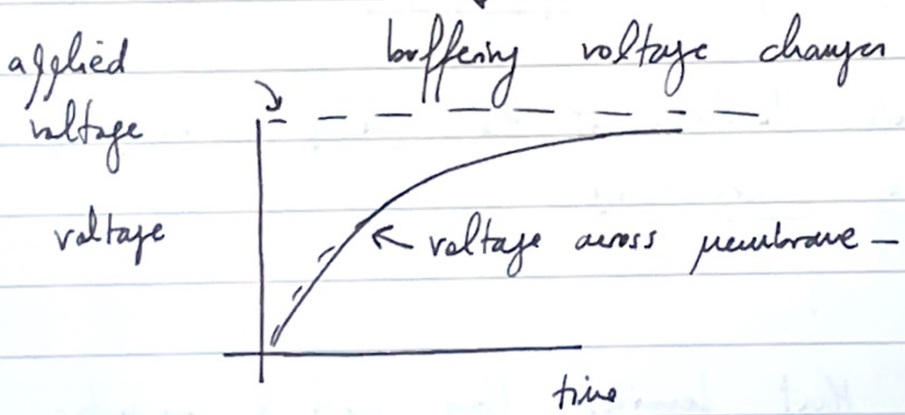
insulating region = dielectric



Capacitance = ability to store charge
↓
↑ with larger surface area
↓ thickness
↓ if Axon diameter ↓

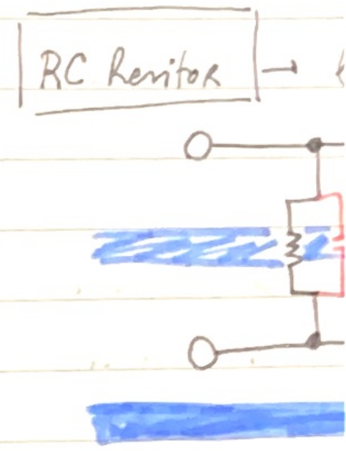
voltage applied across → charge accumulates
↓
plates saturate
↓
voltage across capacitor = to applied voltage

→ By storing the charges, the speed in which voltages changes is ↓
↓
buffering voltage changes



→ GHK → Calculated according to relative permeabilities of several ions.

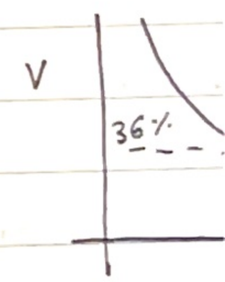
Relative ratio of permeabilities K^+, Na^+, Cl^- at rest
↓
if individual permeabilities change (eg. opening channels)
↓
ratio changes
↓
charges move → create a current
↓
described by Ohm's law



Current →

λ → length

depe



100 mV

10mm

150mV

(A)

=

store charge

↓

with larger surface area

thickness

of Axon diameter ↓

to applied voltage

charges is ↓

es of reversal

gening channels)

Ohm's law

Resistance = $\frac{1}{\text{permeability}}$

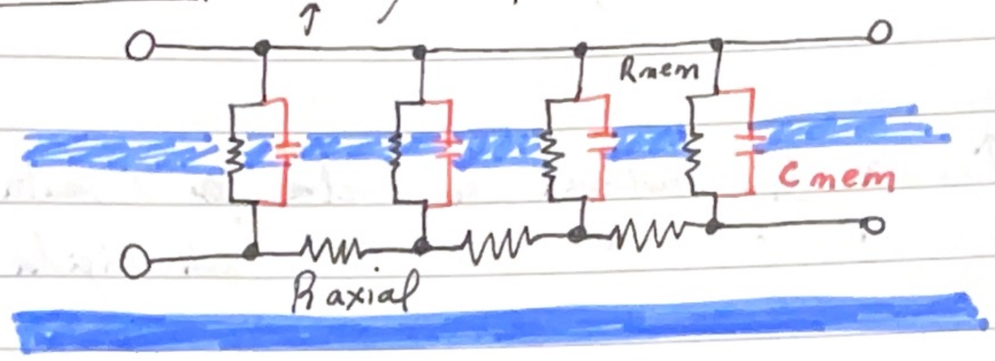
$$I = \frac{V}{R}$$

RC Resitor → low pass filter → allows slow frequencies variations, blocking ↑ frequencies fast changes

membrane → capacitor

channel → resistors

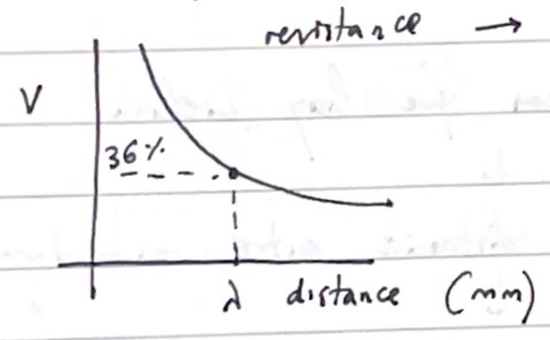
alter conductance and permeability



Current → flow of charge through a conductor per unit of time

λ → length constance → distance it takes for a potential change to fall off about 37% of its initial value

depends on resistance → $\lambda = \sqrt{\frac{R\ membrane}{R\ axial}}$ → $\frac{ohm \cdot cm}{ohm/cm}$

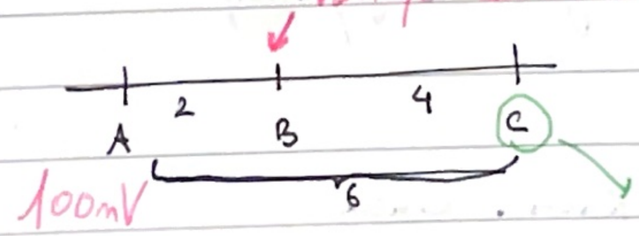


100 mV A

B 2mm away from A

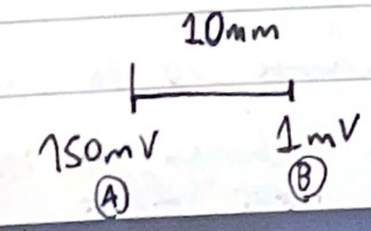
C 6 mm away from A

Voltage decreased to 37mV as 1 lenght constant away



λ = 2

3 length constant away so 100mV · (0.37mV)³ ≈ 5mV



$\cancel{Volt\ A \cdot (0.37)^x = Volt\ B}$

$0.37^x = \frac{Volt\ B}{Volt\ A}$

$\frac{10mm}{5} = 2mm$

→ estaba bien!

x ≈ 5.04

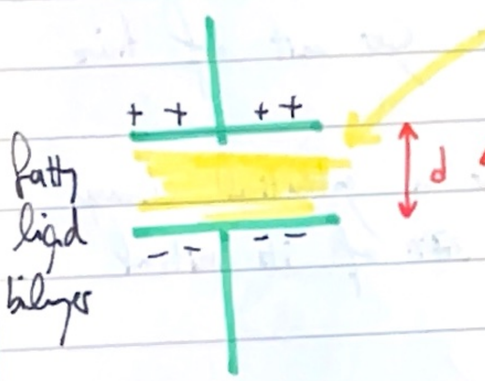
CAPACITANCE (Farads)

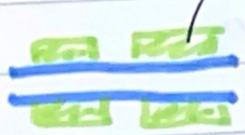
→ Si no hay cambios de Voltaje, no importa si se modifica la capacitancia.

→ Si la capacitancia ↑ → la membrana se vuelve ↑ lenta
↓ → " " " " más rígida

Determinants of capacitance → material inside capacitor → if ↑ dielectric constant
↓
capacitance ↓
(and viceversa)

↑ distance between conductors → ↓ capacitancia





EJ 1 → en las neuronas que hay mielina
↓
↑ distancia entre conductores
↓
↓ capacitancia
↓
↑ velocidad señal

EJ 2
A veces necesitamos que baje la $\vec{v}$
(↑ capacitancia)
por ej. en temporal integration (synapses)

Time Constant = Rmem . Cmem
↓
how long it takes a piece of membrane to charge up to 63% of its final value in response to a step change in its input voltage

(E) λ, τ + ion
→ τ_m

↑ open ch

(E) if we ↓ diam
(n° ion channels

$V(x) = V_m$

(E) 10mm
A B
Voltage change
" "

$I = \frac{V}{R} =$

modifica la

e ↑ lenta
más rígida

→ if ↑ dielectric
constant
↓
capacitance ↓
(and viceversa)

mielina

tre conductores

hd señal

harge up to 63%
charge in its
input voltage

(E) λ, τ + ion channels and R_m =
→ τ_m and λ describe temporal and spatial decay
in cable theory

$\tau_m = R_m \cdot C_m$ speed of voltage changes (reaching 63%)
$\lambda = \sqrt{\frac{r_m}{r_i}}$ defining distance for voltage to decay 37%

↑ open channels ↓ resistance membrane → shortening λ and τ

(E) if we ↓ diameter of axon → λ ↓ as (R_{axial} ↓)
(nº ion channels the same) τ_m ↓ as smaller axon diameter
means ↓ surface area
(therefore ↓ C_m)

$V(x) = V_{max} \cdot e^{-x/\lambda}$ V_{max} is voltage at $x=0$

(E) 10mm
A B τ 4msec

Voltage change A = 120mV
" " B = 10.35 after 4msec

(?) λ? → A is $120 \cdot 0{,}63 = 75.6$ mV
constant d even for entire λ

$75.6 \cdot 0{,}37^{x} = 10.35$

$x = \frac{\ln}{\ln}\left(\frac{0.1369}{0.37}\right) = 2$

$\frac{10\,mm}{2} = 5\,mm = \lambda$

$I = \frac{V}{R} = \frac{V}{\frac{A}{C}} = V \cdot C$ ↑

ACTION POTENTIAL

Passive movement of ions → leakage channels → as they follow [] gradients
Resting potential's driver is that the membrane is semi-permeable
↓
can avoid developing charge separation as + exchange positive charge for positive charge

Passive leakage channels:

have — constant permeability
constant resistance

Voltage gated-channels
they open or close depending on what happens around them:
depending on membrane potential
↓
can have ≠ conductances.

Complex molecular machines" → made from proteins
↓
as the voltage across the membrane changes, the pushes and pulls of the charged part of their structure shifts the conformation of the protein, opening or closing the channels

Na^+

"mechanism 1"

→ open / close quickly

→ likely to open if membrane potential is positive

→ usually closed at -70mV (resting potential)

↓

membrane potential ↑

open gate

"GATES"

positive feedback loop

Na^+ channels open

Na^+ rushes in

looking for its own Nernst potential

→ very few Na^+ ions needed to change potential

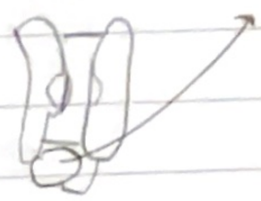
inactivation gate

"mechanism 2"

→ Voltage-gated

→ closes channel when voltage trends positive

like a ball not allowing Na^+ to pass through → even when channel is open



→ this is ≠ from original resting (closed) state → it's <u>INACTIVE</u>

→ this mechanism inactivates the channel soon after they open

→ slower than mechanism 1

K^+

→ mechanism

"delayed rectifier channels"

→ voltage-gated mechanism that "resets" the membrane potential to be able to send many signals

→ open when membrane potential is +

→ slower than Na^+ channels

Resting → Stimulation → Rise ①

②

Na^+ front

reaches threshold

oscillomeg

instantaneous voltage

-25

③

①

②

-60

→ Probab

→ Malewi

→ Reaction

VOLTA

y potential)

ing for its own
Nerst potential

+ Ions needed
potential

→ even

it's INACTIVE
after they

membrane potential

Resting phase ① → Stimulation ② → Rising phase ③ → Falling phase ④ → Undershoot ⑤ → recovery ⑥

reaches threshold

Na^+ fast → Na^+ slow (inactivation) → K^+ → leakage and voltage-gated channels open → they close

↓

this is the absolute refractory period

↓

membrane potential starts going back to resting potential

↓

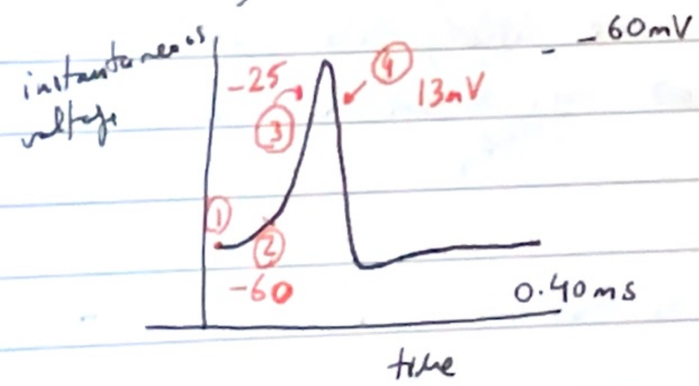
when voltage gated Na^+ are deactivated but K^+ channels still open → relative refractory period

↓

membrane potential goes more ⊖ than resting potential

cell goes back to resting potential

oscillonage



← this shape is the average of the action of many probabilistic channels in a patch of membrane

→ Probability and kinetics → channels open / close when random fluctuation of energy allow it to shift from one state to the other

→ Molecular reaction and conformational changes are usually more stable in one state or the other

↓

→ Reaction tends to drive towards lowest energy state

VOLTAGE-GATED → the probability of channels being opened or closed is a function of VOLTAGE

Na^+ and K^+ channels are more likely to be open when membrane is ⊕ → yet they don't open at the same time due to

↓

KINETICS:

Probabilistic temporal dynamics of a reaction or movement from one state to another

faster eg Na^+ — slower eg K^+ "stickier"

all of this movement is given by thermal jostling at molecular level

↘ parts that fit together more tightly take more energy to be shaken loose by random thermal movements.

Refractory period — Absolute → driven by inactivation kinetics of Na^+

relative → at tail end of action potential Na^+ are opened but voltage gated K^+ also opened

Tetrodoxin (TTX): toxin that blocks voltage gated Na^+

↳ puffer fish

↓

if applied → action potential doesn't start

→ Na^+/K^+ pump

membrane

movement

ore
ents.

of Na^+

→ Na^+/K^+ pump restores the ion gradients

4. understanding action potential propagation

copper → lower R ⇒ lower distances

↓

Conductivity of cytoplasma is ↓↓↓

in axon → loses over ⌈ leakage of current
capacitive effects across membrane

options → ↑ amplitude → would reach breakdown voltage

↓

lipid bilayer stops acting as insulator

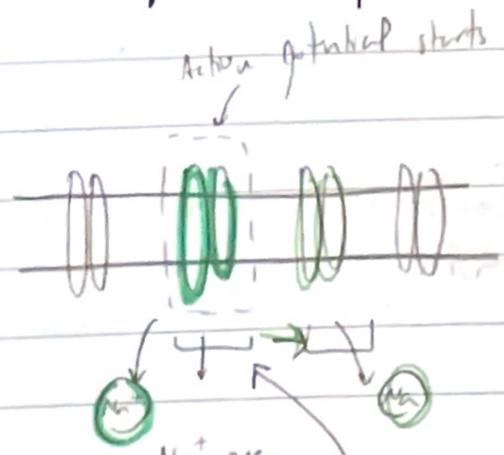
repeatedly regenerate signal to get it down the axon

↓

what moves is the state of depolarization down the axon

↓

cf 'state of wave from water'



if branch in → direction then axon soma ||

Na^+ opens

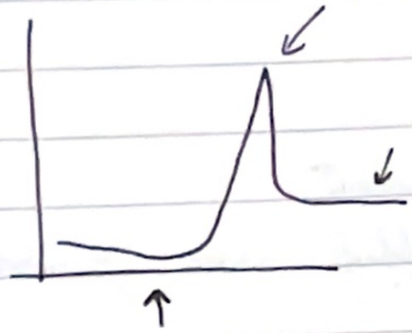
Na^+ enters

Depolarizes this area and adjacents

Action potential propagate

When we measure w/ oscilloscope there's a delay in the action potential ← properties of membrane
it is propagating

If we measure V(distance)



regions to the left are in later stages of action potential (PAST)

→ Axion potentials can travel in both directions

(opposite direction) ANTIDROMIC Stimulation

If 2 action potentials collide, they stop as they sum and then they'd need to stimulate a part of the axon that is in their absolute refractory period
↓
they cancel out
↓
used by researches

To ↑ speed we need:
↓ R axial
↓ C membrane

propagation $\vec{v}$ of action potential down the membrane depends on:
λ, time constant, n° of voltage-gated channels in membrane, axial resistance in axoplasm

Squid giant
1mm =

Downsides of
- sp
- ha
- lo
- ↑

every
comming

Myelin
→ pr
→ l
→ m
water +

Myelin → ↑
↓ Cm
↓
↓ τ

n the action

)

otentials collide,
s they sum
they'd need to
part of the
is in their
refractory period

ced out

, researches

ch depends on:
els in membrane,

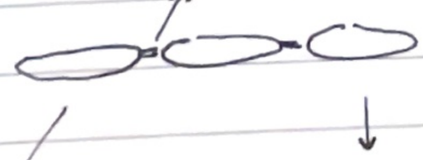
Squid giant axon → Hodkin + Huxley
1 mm = diameter

Downsides of large axon:
- space
- harder to maintain resting potential
- larger axons require more voltage-gated Na+ channels
- ↑ mitocondria needed to allow cellular process to occur

↑ energy consuming

Myelin
→ produced by glia ↗ oligodendrocites → CNS
↘ Schwann cells → peripheral NS
→ physical barrier that prevents ion leakage → ↑ membrane resistance
→ larger, better insulator → ↓ membrane capacitance

→ made of:
water + lipids
white colour ↗ axon
white matter



Ranvier nodes: ↑ density of Na+ voltage gated channels
↓
SALTATORY CONDUCTION

Myelin → ↑ the λ in the internode region (as ↑ Rm) just so the signal can reach the next node and regenerate
↓
where Na+ voltage gated channels are

↓ Cm
↓
↓ τ

demyelinating diseases → lose ability to transmit signals through axons

↓

gradual, debilitating paralysis

Hi g