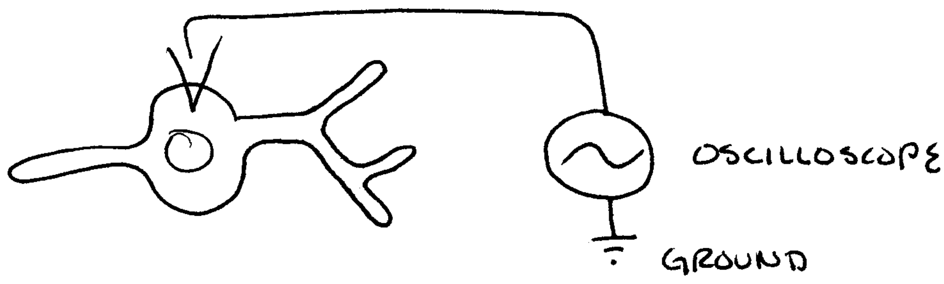
ELECTRICAL PROPERTIES

HANDOUT



MEASURE Vm ⟷ Vm = Voltage across membrane

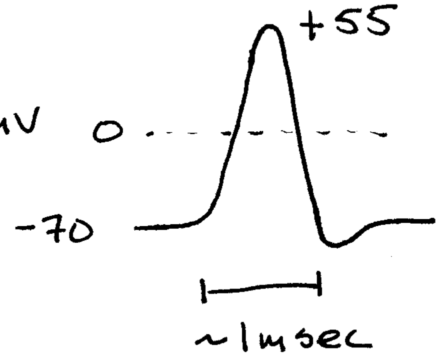
observe: ~ -70mV → millivolts

RESTING POTENTIAL

ACTION POTENTIAL

MEASURE Vm in axon

shock → OBSERVE:



→ milli-second

WHAT? HOW?

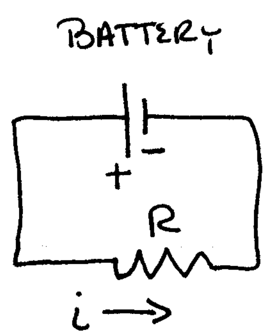
VOLTS - POTENTIAL (e)

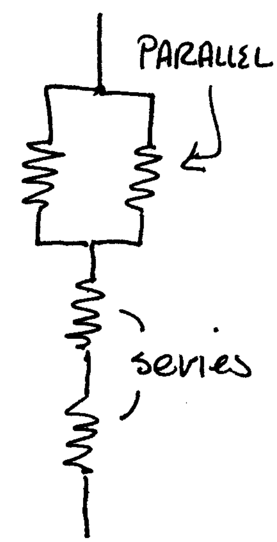
CURRENT - (i) AMPS

RESISTANCE - R OHMS (Ω)

CONDUCTANCE - g $\left(\frac{1}{R}\right)$

CAPACITANCE





Ohm's LAW: $e = iR$

BIOLOGICAL COMPONENTS → ELECTRICAL PROPERTIES

1. MEMBRANE - LIPID / SEMIPERMEABLE
2. CHARGED IONS - Na^+ K^+ Ca^{++} Cl^- Mg^{++}
3. PROTEINS - cytosolic vs. transmembrane
   - aminoacids - hydrophobic vs hydrophilic
   - charged (-)
4. DIFFUSION GRADIENTS

Nernst Equation / Goldman Equation

Physiologists modeled the behavior of nerve cells using electrical theory. For example, Katz and Keynes used the Nernst Equation to predict what voltage (Vm) the membrane would go to if a particular ion was suddenly allowed to become freely permeable across the membrane. They used the Nernst Equation to determine the Nernst Potential for K^+ and for Na^+, in order to understand the driving forces at work during an action potential in the squid giant axon.

$$\text{Nernst Potential of a cation}(V_{ION}) = \frac{RT}{F}\ln\frac{[ION^+]_{out}}{[ION^+]_{in}} \qquad \frac{RT}{F} = 25.2\,\text{mvolts}$$

This equation gives V_{cation} of the inside of the cell relative to the outside. Also, for an anion, the in and out concentrations are reversed. (If divalent ion, divide RT/F by 2.)

$$\text{Nernst Potential of a anion}(V_{ION}) = \frac{RT}{F}\ln\frac{[ION^-]_{in}}{[ION^-]_{out}}$$

	IN	OUT	
$[K^+]$	400mM	20mM	
$[Na^+]$	50mM	440mM	SQUID GIANT AXON
$[Cl^-]$	26mM	560mM	

Solving this equation for K+, for example, gives us a value of -76mV, which is amazingly near the resting potential of the cell (but this should be no surprise to you):

$$(V_K) = 25.2\,\text{mV}(\ln\frac{20\,\text{mM}}{400\,\text{mM}}) = 25.2\,\text{mV}(-3.00) = -75.5\,\text{mV}$$

BUT, we know that multiple ions are involved during both the resting potential and the action potential AND the membrane is not equally permeable to each ion (some ions can move across the membrane more freely than others).

Goldman modified the Nernst Equation to (1) examine the contributions of all ions AND (2) account for differences in their permeabilities (**p**).

$$Vm = \frac{RT}{F}\ln\frac{pION^+_{out1}[ION^+]_{out1} + pION^+_{out2}[ion^+]_{out2} + \ldots pION^-_{in1}[ION^-]_{in1} + pION^-_{in2}[ION^-]_{in2}\ldots +}{pION^+_{in1}[ION^+]_{in1} + pION^+_{in2}[ION^+]_{in2} + \ldots pION^-_{out1}[ION^-]_{out1} + pION^-_{out2}[ION^-]_{out2} + \ldots}$$

Because this is an algebraic formula, relative values for "p" are sufficient to solve the equation. In the case of the squid giant axon, the relative permeabilities are K^+:Na^+:Cl^- 1:0.04:0.45

Solving this equation, for squid giant axon AT REST:

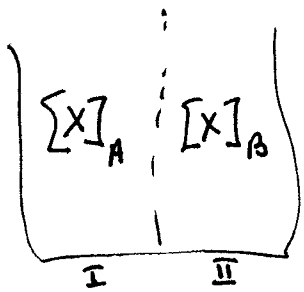
$$V_m = (26\,\text{mV})\ln\frac{p_K[K^+]_{OUT} + p_{Na}[Na^+]_{OUT} + p_{Cl}[Cl^-]_{IN}}{p_K[K^+]_{IN} + p_{Na}[Na^+]_{IN} + p_{Cl}[Cl^-]_{OUT}}$$

$$V_m = (25.2\,\text{mV})\ln\frac{1(20) + 0.04(440) + 0.45(60)}{1(400) + 0.04(50) + 0.45(540)} = (25.2\,\text{mV})(-2.31) = -58\,\text{mV}$$

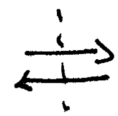
which again is a very close prediction of the resting potential across the axon membrane.

NERNST - EQUATION

WHAT VOLTAGE IS REQUIRED TO MAINTAIN CONCENTRATIONS AT EQUILIBRIUM ?



AT EQUILIBRIUM
SAME # IONS MOVING RIGHT & LEFT



OSMOTIC WORK

$$W = RT \ln \frac{[X]_{I}}{[X]_{II}}$$

WORK AS FUNCTION OF IONIC CONC.

$$W = E \cdot F \cdot z$$

WORK AS FUNCTION OF E (ELEC. POTENTIAL)

- W = WORK
- R = GAS CONSTANT
- T = °K
  - 273°K = 0°C
- F = FARADAY CONSTANT
- z = VALANCE
- E = voltage

$$E = \frac{RT}{Fz} \ln \frac{[X]_{I}}{[x]_{II}}$$

= NERNST EQUATION

UNITS = MV

UNITS CANCEL

GOLDMAN EQUATION - 1943

CONSTANT FIELD THEORY

PREDICT V_m → membrane voltage

- Na^+, K^+, Cl^- relevant ions
- factor in permeabilities
- Permeabilities different for each ion (measured)

$E = V_m$

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

Keynes measured relative permeabilities in frog muscle using isotopes

P_{K^+} :	P_{Na^+} :	P_{Cl^-}	
1	0.04	0.45	Resting Potential
1	20	0.45	Peak of Action Potential

$\log 10 = 2.3 \cdot \ln 10$

$\frac{RT}{F} \approx$ **25 mV**

$V_m = 25 \cdot \ln \frac{X}{X}$

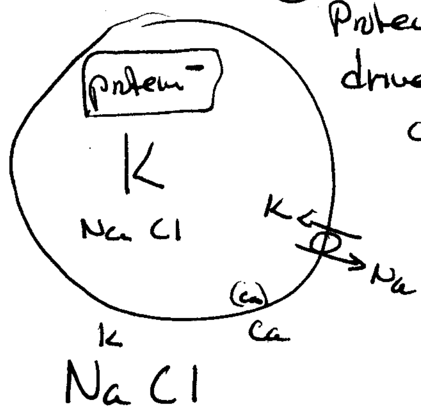
$V_m = 58 \cdot \log \frac{X}{X}$

UNITS = mV

Ca^{++} permeability is VERY LOW so CONTRIBUTION can be ignored

(I) Thermodynamic Model

$$V_m = \frac{RT}{F} \ln \frac{pK^+[K^+]_o + pNa^+[Na^+]_o + pCl^-[Cl^-]_i + pCa^{++}[Ca^{++}]_o}{pK^+[K^+]_i + pNa[Na^+]_i + pCl^-[Cl^-]_o + 2 \cdot pCa^{++}[Ca^{++}]_i}$$



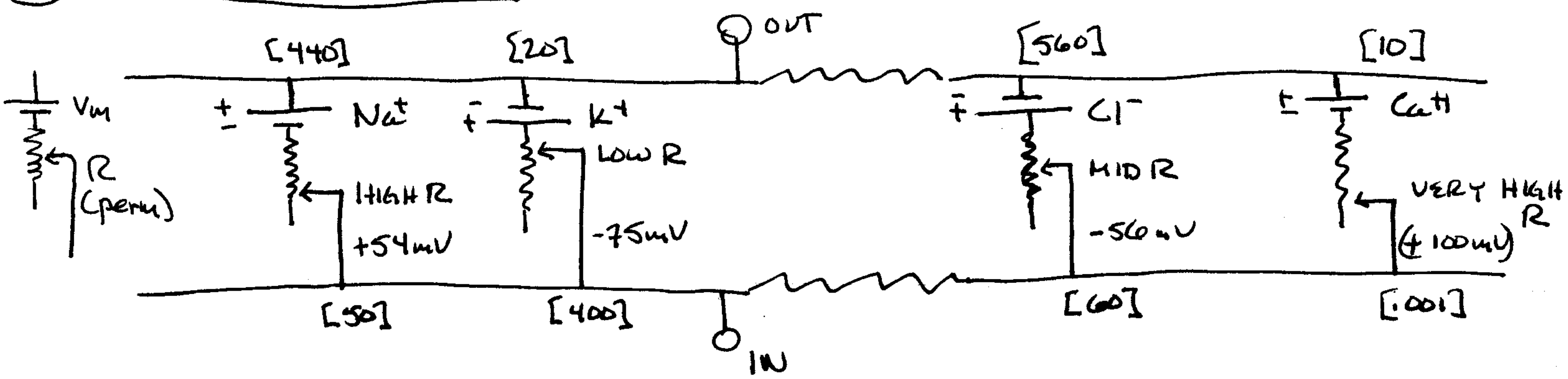
① Protein drives dist of charge

② NaK Pump sorts K^+ & Na^+

electrochemical equilibrium

DURING AP - permeabilities change

(II) ELECTRIC CIRCUIT MODEL

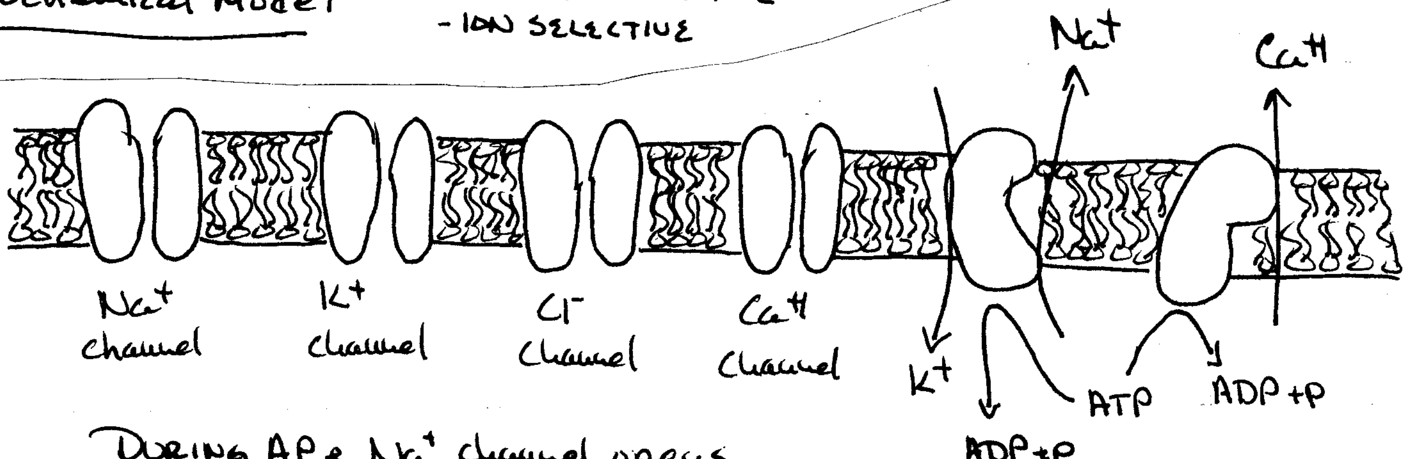


DURING AP: RESISTANCES CHANGE

(III) Biochemical Model

Protein Ion Channels
- VOLTAGE SENSITIVE
- ION SELECTIVE

ION PUMPS: Na/K ATPase
Ca ATPase

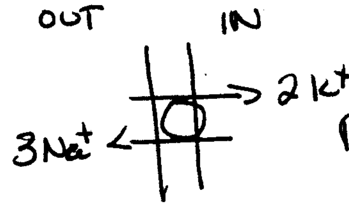


DURING AP: Na^+ channel opens
K^+ channel opens

["Background" leakage currents account for RP permeabilities]

ION PUMPS

Na^+ | K^+ ATPase



per ATP

tetramer $(\alpha\beta)_2$
α: 100KD, β: 38KD

subunits cloned & sequenced: Kawakami 1985 Nature 316:733
Noguchi 1986 FEBS LETTERS 196:315

identified when Keynes did ^{15}Na perm. studies –
^{15}Na extrusion required K^+ suggesting presence of a pump

Ca^{++} ATPase

1 Ca^{++} out per ATP   requires Mg^{++} for ATP binding

$[Ca^{++}]$ squid – 10mM out (1×10^{-2} M)
10-100nM in (1×10^{-8} - 1×10^{-7} M)

$[Ca^{++}]$ is highly regulated, Ca^{++} is 2nd messenger

Exchanges

Cl^- / bicarbonate exchange driven by Na^+ gradient

Ca^{++} / Na^+ exchange / direction Vm dependent

Ca^{++} current is outward above -70mV

PROBLEM SET

- Calculate Nernst Potential for each ion
- USE GOLDMAN EQUATION TO CALCULATE V_m at REST & DURING ACTION POTENTIAL (USE Keynes' P values)

① COCKROACH LEG MUSCLE

	OUT	IN
K^+	27mM	110mM
Na^+	111mM	27mM
Cl^-	150mM	44mM

② SQUID GIANT AXON

	OUT	IN
K^+	20mM	400mM
Na^+	440mM	50mM
Cl^-	560mM	51mM

③ CAT MOTOR NEURON

	OUT	IN
K^+	5.5mM	150mM
Na^+	150mM	15mM
Cl^-	125mM	9mM