Announcements

I'll give you written guidance on preparing your talk/paper.

Today: Ion Channels

Read Chpt 7 (membrane structure),
Chpt 48 (neurons), (49? Nervous system).

Lessons Learned Today

Ion Channels are membrane-bound proteins
Involved in communication
3 types, voltage, ligand and mechanically-sensitive
Heart of nerves--Fast, long-range
They rely on "batteries"—constant source of voltage
Voltage generated through K^+/Na^+ exchange.
On/Off is digital, not analog–have transistors in you.

Ion channels are used to communicate to a cell.
Are turned on/off by 3 types of signals.
Every cell in every organism has ion channels.

1. Voltage gated :
Nerves

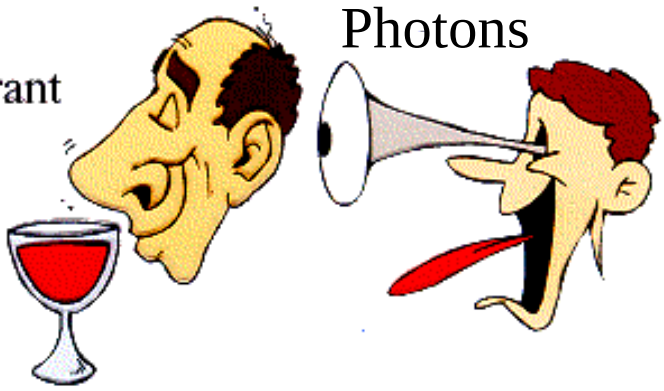
Ligand gated : hearing, seeing

2.

C.N.S.

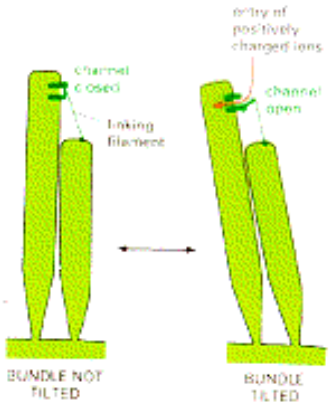
Odorant

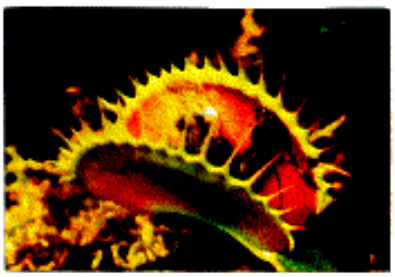
Photons



Mechanically gated: Motion/Pressure

3.

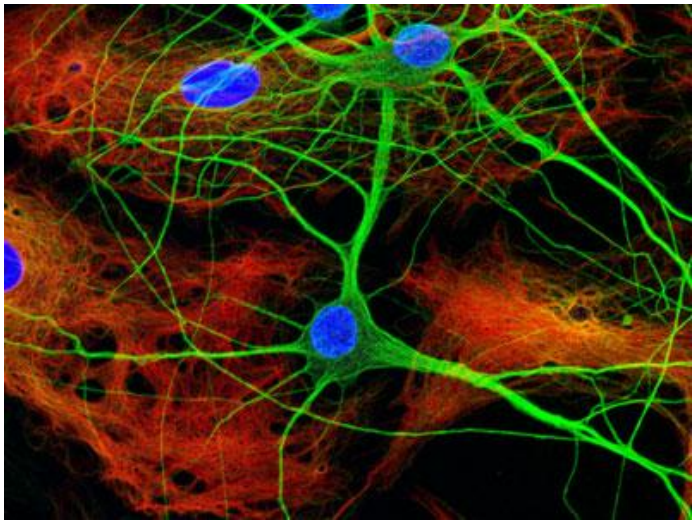




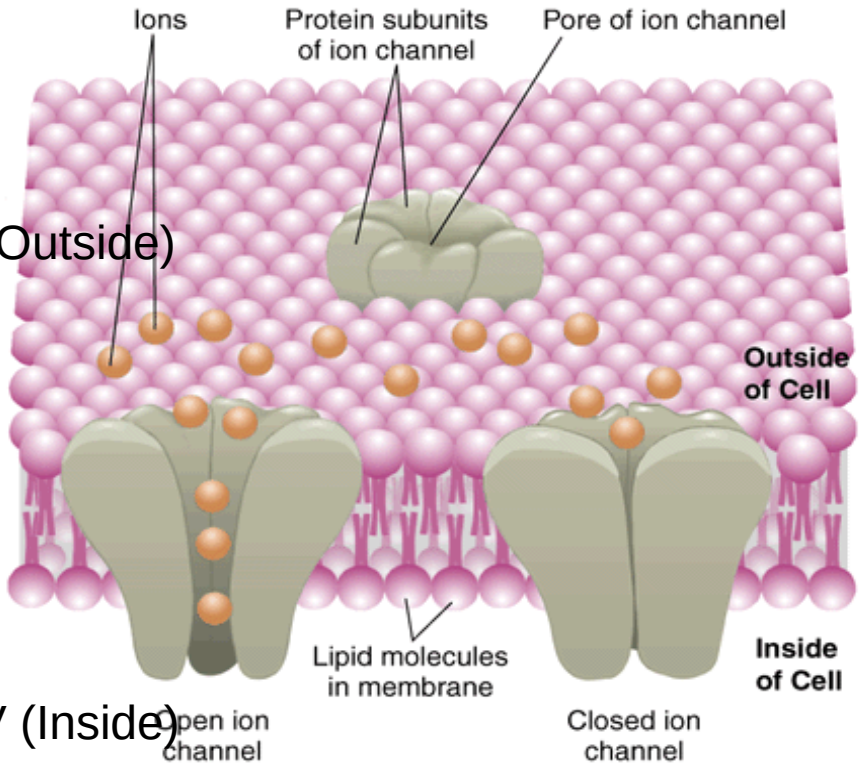
20% of genes in E.Coli are for ion channels.
If humans similar, how many different ion channels?

Ans: 25,000 genes: 5000 genes. One or more polypeptide/ion channel– could get less, or more, ion channels.

Ion Channels



www.nikonsmallworld.com/gallery/year/2005/36



0 mV (Outside)

0 mV (Inside)

open (depolarized)

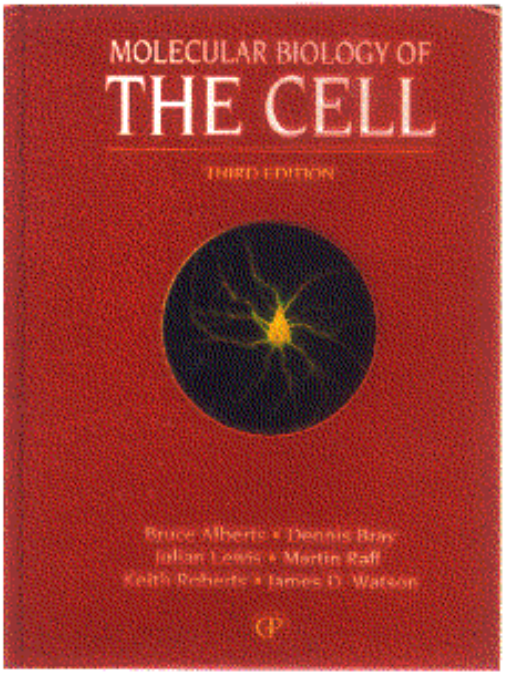
-60 to -100 mV (Inside)

closed (polarized)

In general, every cell is like battery.

"Ion channels
are major targets of psychoactive drugs"

Mol. Bio. of the Cell, Alberts et al.



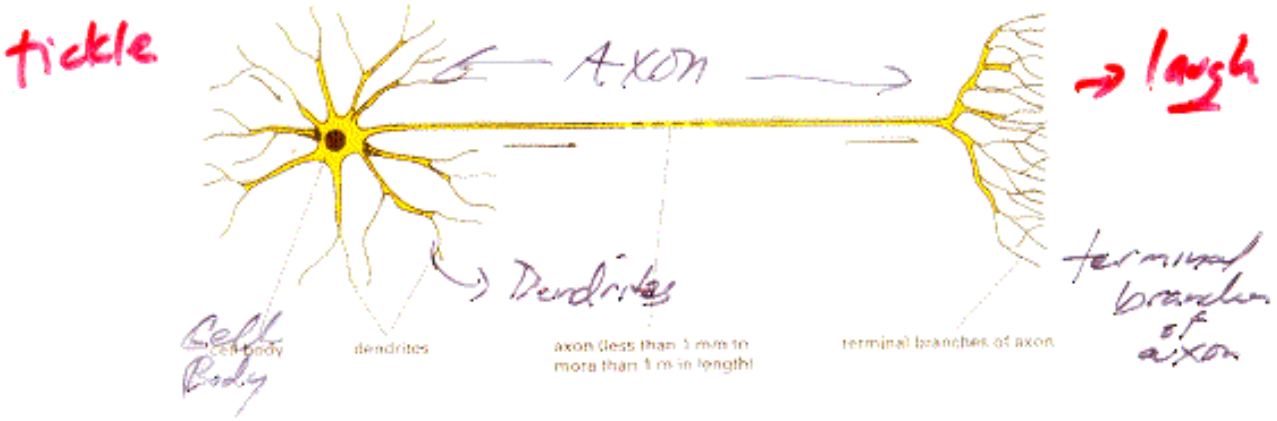
Major source of drug targets.

Valium binds to serotonin (ligand) receptor called GABA receptor– relaxes nerves.

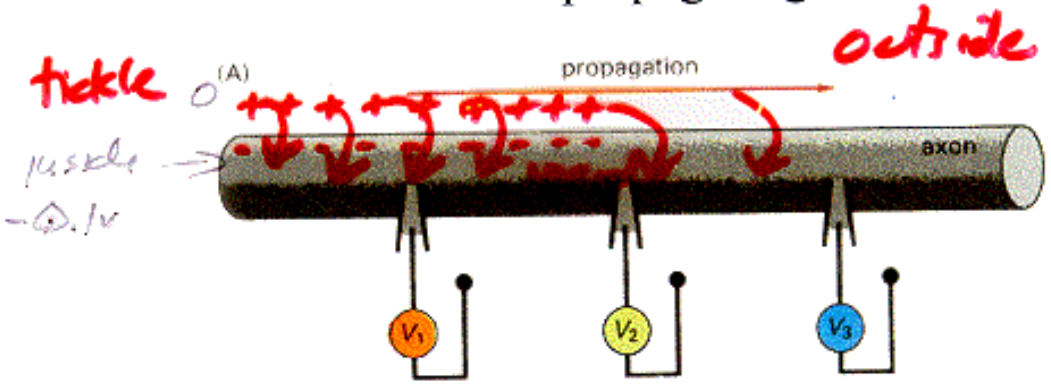
Nerves

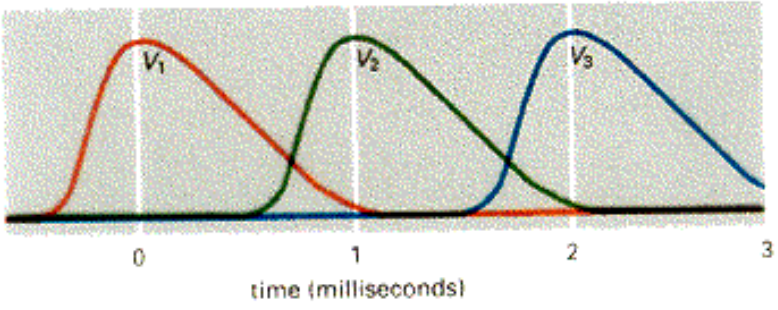
How (electrical) signal is transported along a nerve

At few hundred miles/hr.



Signal is wave of charges moving (current) from outside to inside of cell…propagating down nerve.





resting electrical potential

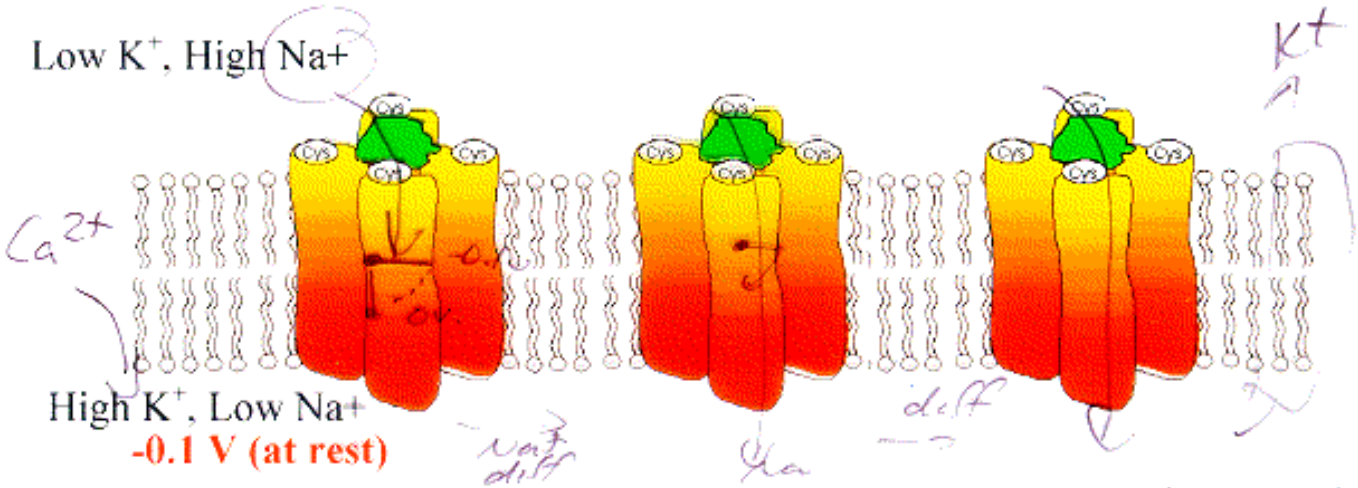
Yes, there is electricity in you!

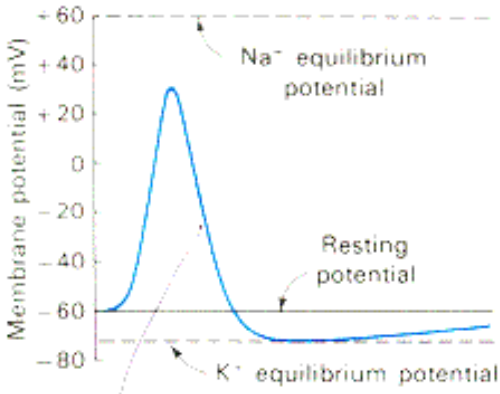
Action Potential

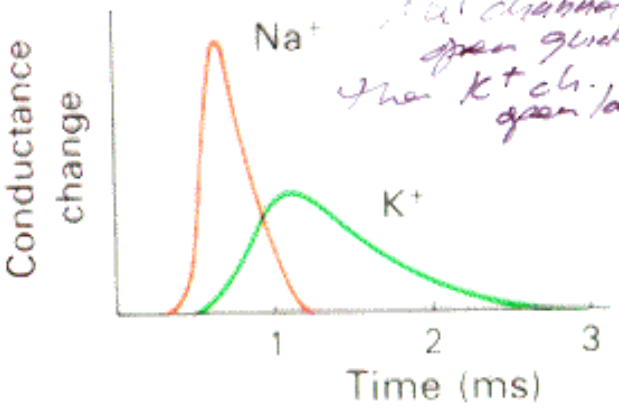
Rush of Na^+ in, followed by K^+ out.

At resting (negative) potential, channels closed.
At less negative potential (0mV), channels open.

At one end of neuron, some chemical released
→causes some charges (Ca^{2+}) injected/ depolarize membrane.



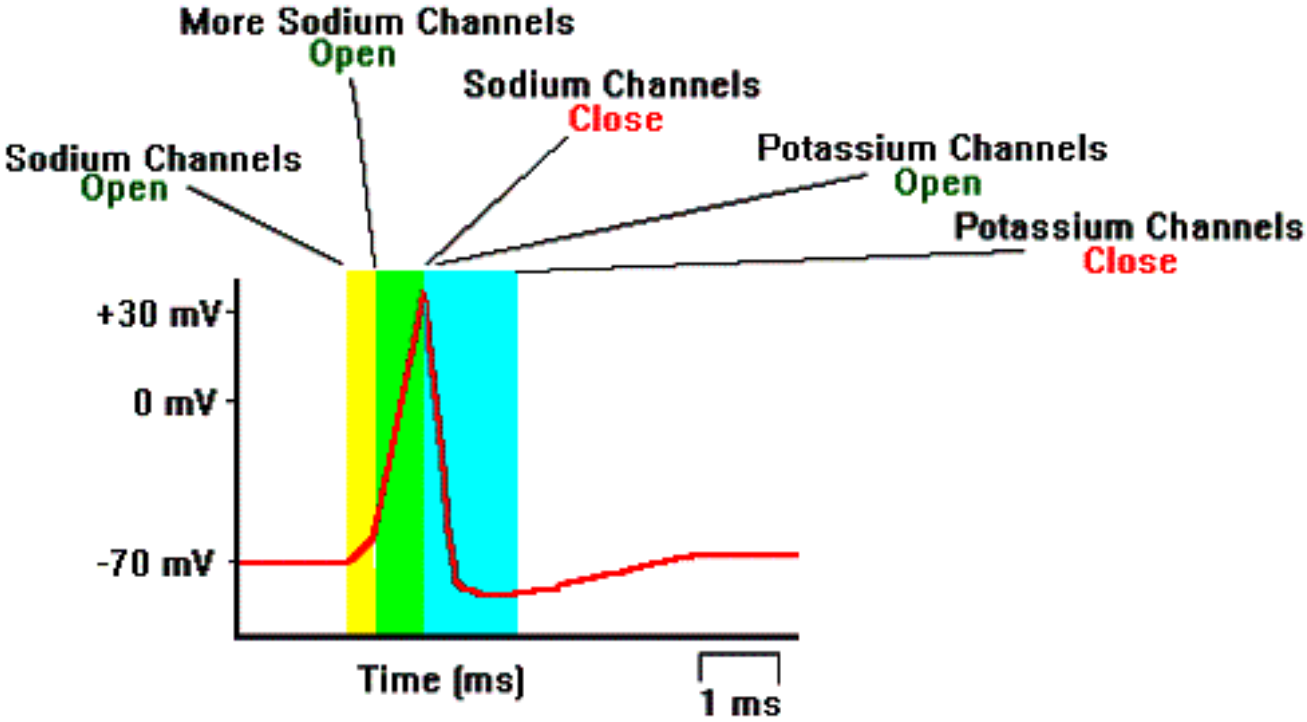


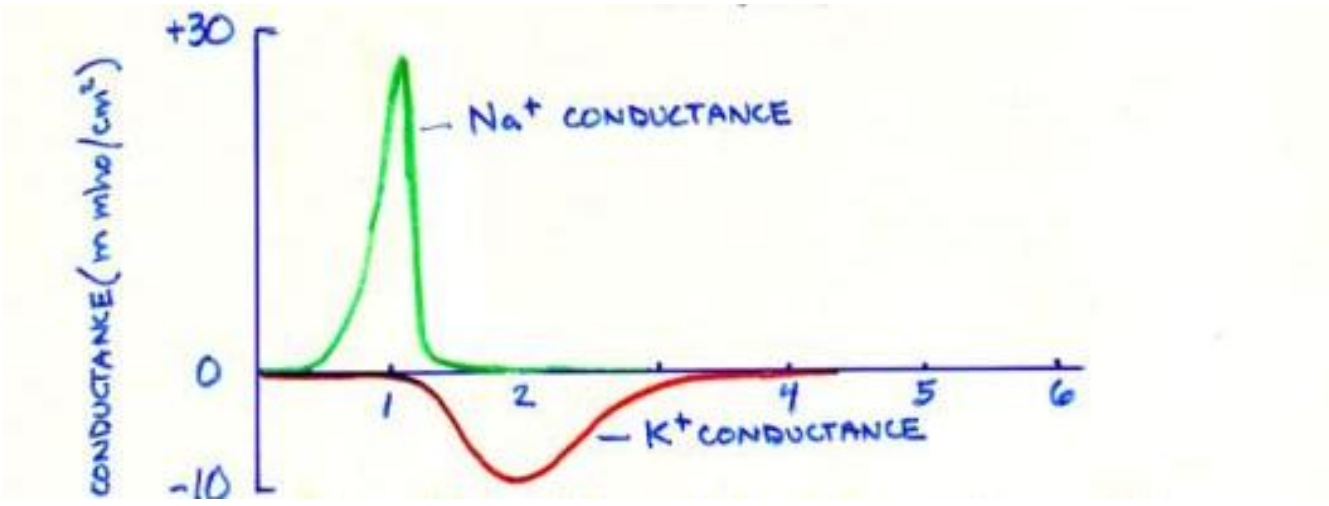


~10 million ions/sec go through single channel

Na^+ channels spontaneously close after being open for a while.

Action Potential– Nerves Firing





http://www.biologymad.com/NervousSystem/nerveimpulses.htm

Action potential

1. Some positive ions (Ca) injected at one side of nerve. Causes local depolarization.

2. Local Na channels open, Na^+ flows down electrochemical gradient
[Both conc. & voltage cause Na^+ to flow in.]

3. Causes further depolarization (even positive polarization). Na diffuse, opening neighboring Na, which allows more Na to enter, causing more depolarization….

Net: Wave of Na ions flowing from outside to inside, flowing along nerve.

To close ion channels, to stop wave:

4. Na^+ spontaneously close

5. K^+ open → brings membrane potential back down negative.

Why is there a non-zero electrical potential across our resting cells?

Why it's about – 60mV.

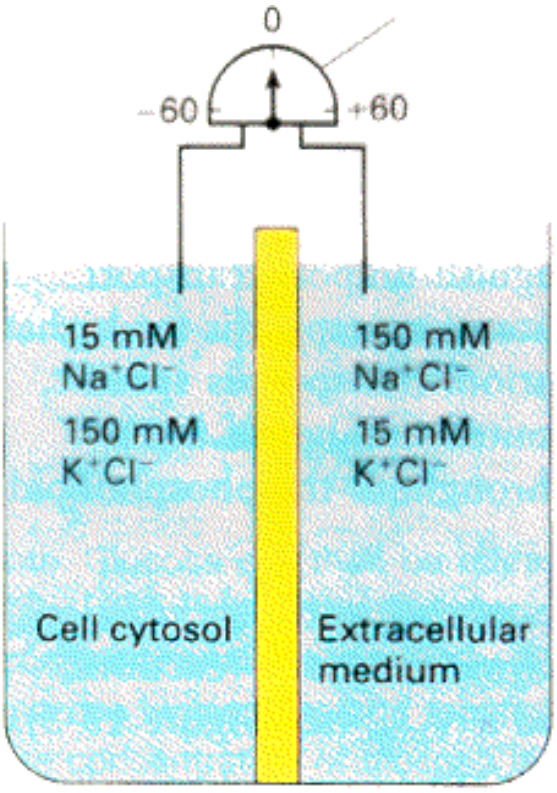
Answer: Concentration gradient & K^+ permeability largely determine resting potential

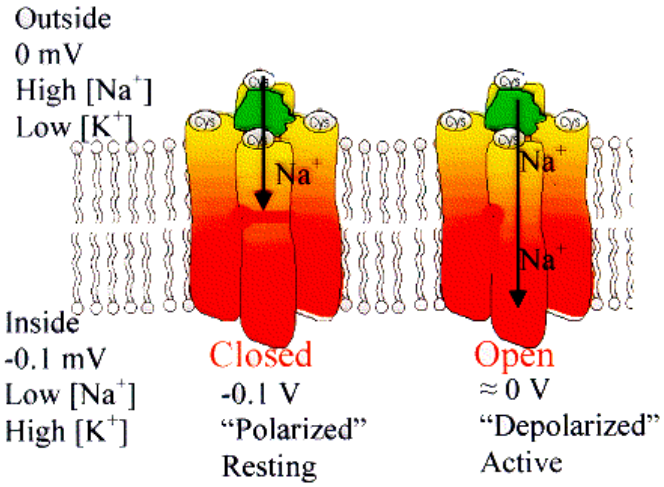
[Follows Lodish, Molecular Cell Biology]

What is potential in following case?
Concentration gradient, but impermeable membrane:

Gradient set-up by Na/K Transporters

[will go over]

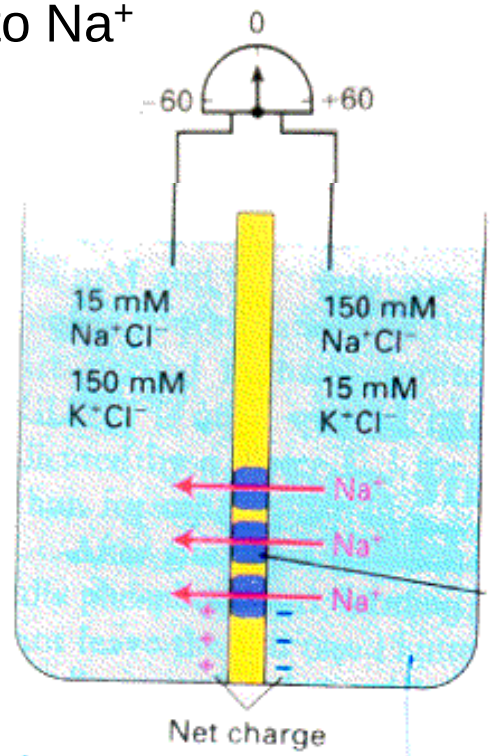




Membrane permeant to only one ion

What is voltage (electrical potential) in each case

Membrane permeant to Na^+

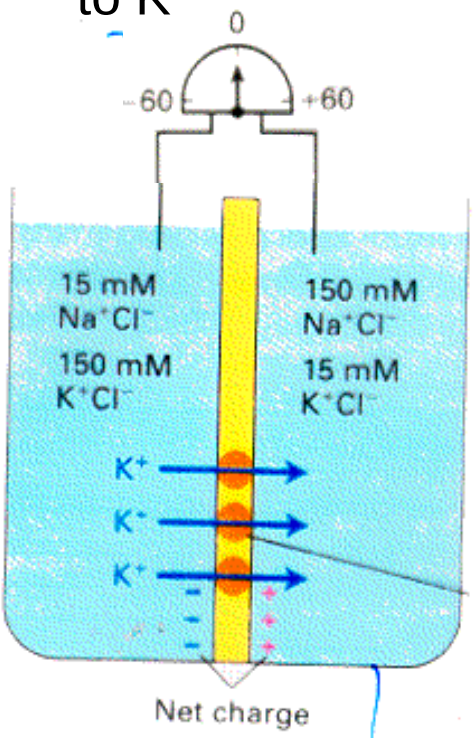


V>0 or <0?

Define $V_{out} = 0$

Permeant to Na^+

Membrane permeant to K^+



$V_{outside} = 0$

Just a tiny amount of charge causes potential, <u>much</u> less than 15 mM or 150 mM.

What causes charge to stop flowing?
A sufficiently large force (electrical potential) preventing more ions from going.

Given that V ~ -60mV and Na/K are two major ions, which is your membranes permeant to? **K^+**

What is magnitude of electric potential (voltage)? If permeant only to Na^+?

What is Boltzmann's Factor?: $Z\exp(-E_i/kT)$

Probability of being inside/outside? $\exp(E_{out}-E_{in}/kT)$

$$\frac{[Na^+]_{in}}{[Na^+]_{out}} = e^{(E_{out}-E_{in})/kT}$$

Let ϕ = voltage

Energy outside? $= q\,\phi_{out} = 0$

Energy inside? $= q\,\phi_{in}$

$$\frac{[Na^+]_{in}}{[Na]_{out}} = e^{-q\phi_{in}/kT}$$

$$\ln \frac{[Na^+]_{in}}{[Na^+]_{out}} = -q\phi_{in}/kT$$

$$\phi_{in} = \frac{kT}{q} \ln \frac{[Na^+]_{in}}{[Na^+]_{out}}$$

q = ? For Na^+?

$$\frac{kT}{|e|}$$

$\phi_{in} =$

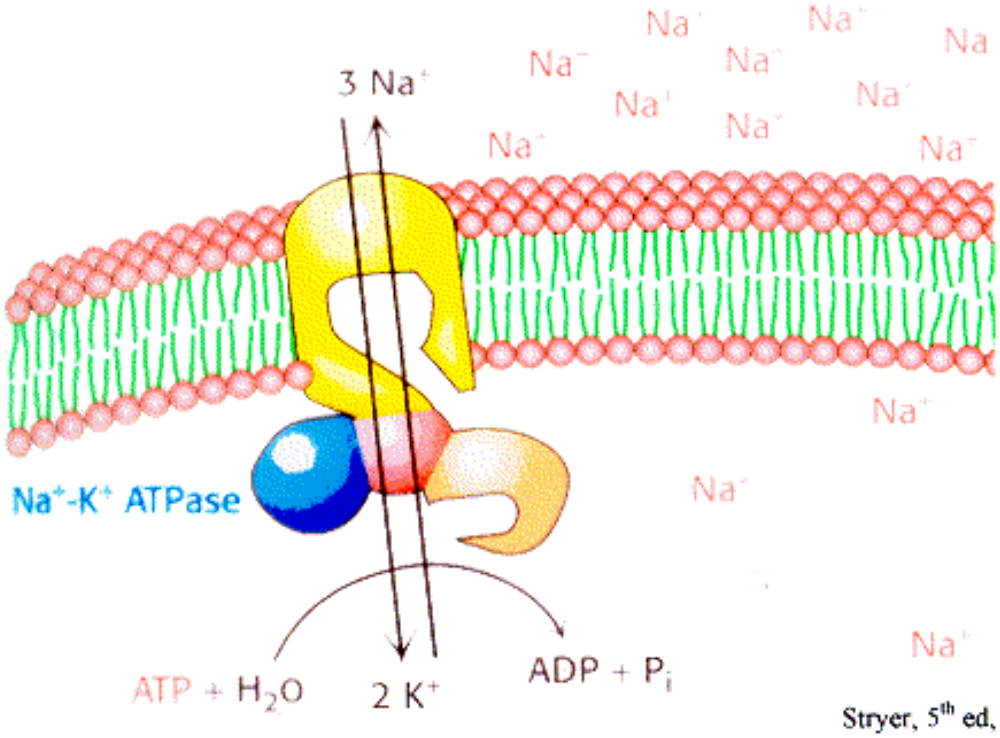
+59 mV if permeable only to Na^+

If permeant to only K^+,

resting potential = -59 mV

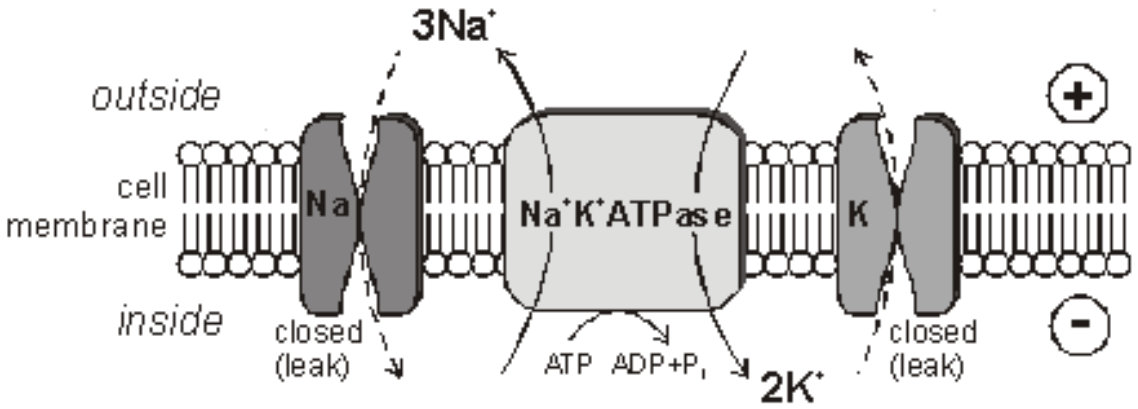
How is concentration gradient produced?

Na^+/K^+ Transporter = Exchanger = ATPase



Stryer, 5th ed, Fig. 13.12

Uses ATP to pump (exchange) Na^+ outside, K^+ inside.



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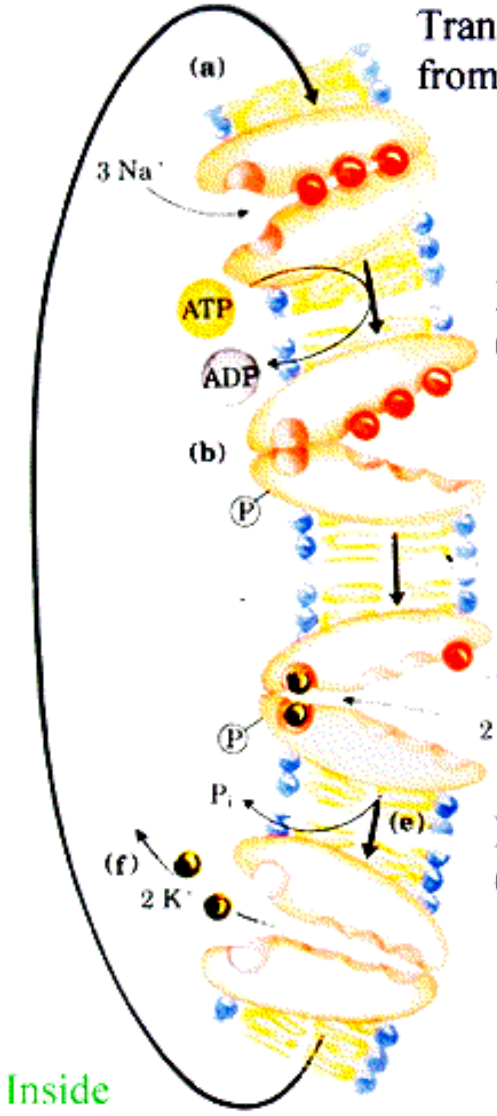
Na^+ K^+ ATPase Transporter

ATP Phosphorylation drives conformational changes



Transporter binds 3 Na^+ from inside of cell

Phosphorylation favors Conformation II.

Transporter releases 3 Na^+ to outside, & binds 2 K^+ from outside

Dephosphorylation favors Conformation I.

Inside

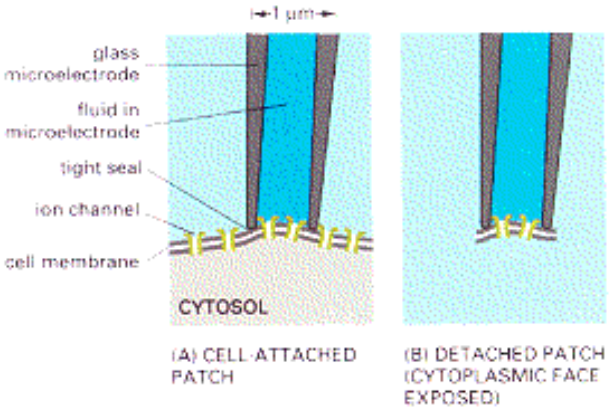
Outside

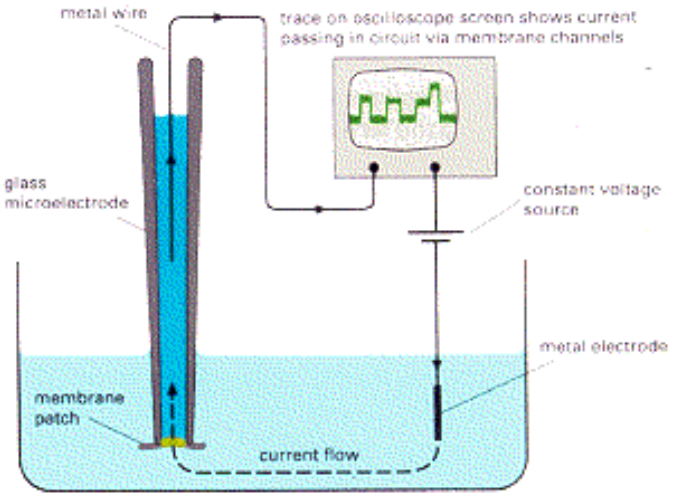
Lehninger, 2nd ed.

Is the Ion Channel Digital or Analog?

Current through a single channel can be recorded.

10 million charges/sec = 1pA/channel





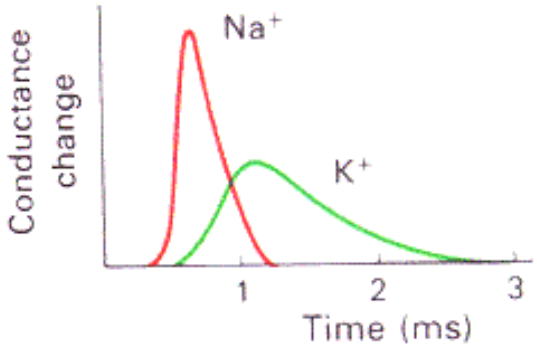
GΩ seal:
current only through channel

(microsecond resolution)

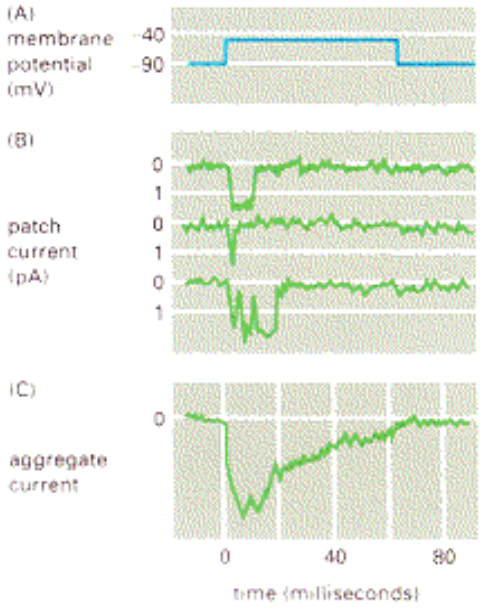
Patch-clamp technique: Nobel Prize, 1991
Erwin Neher and Bert Sakmann, invented 1976

Do ion channels open gradually or all or nothing?

Ensemble



Single Ion Channel



Patlack & Horn, 1982

Point mutation in Potassium Gene that affects Potassium Channel

Class evaluation

1. What was the most interesting thing you learned in class today?

2. What are you confused about?

3. Related to today's subject, what would you like to know more about?

4. Any helpful comments.

Answer, and turn in at the end of class.