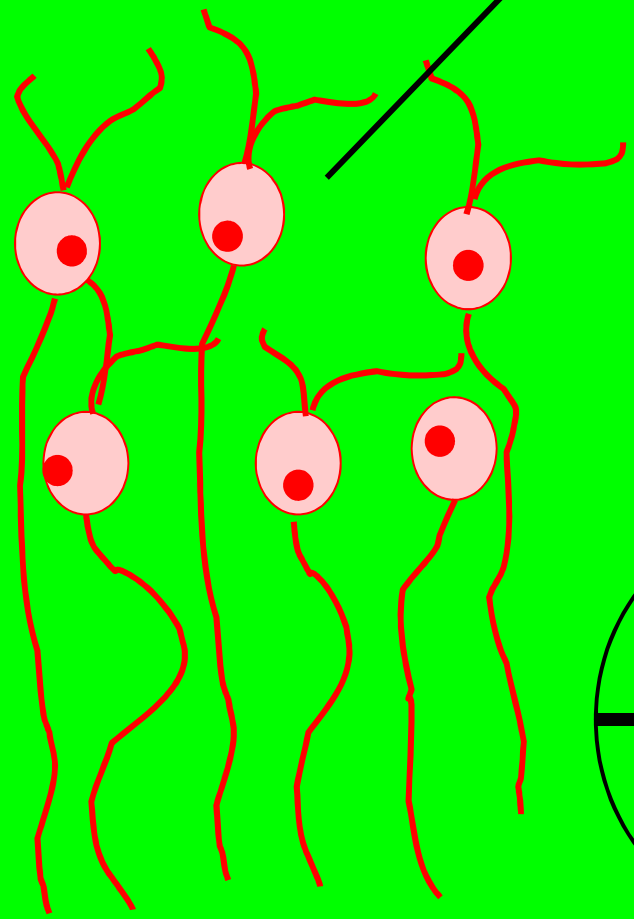
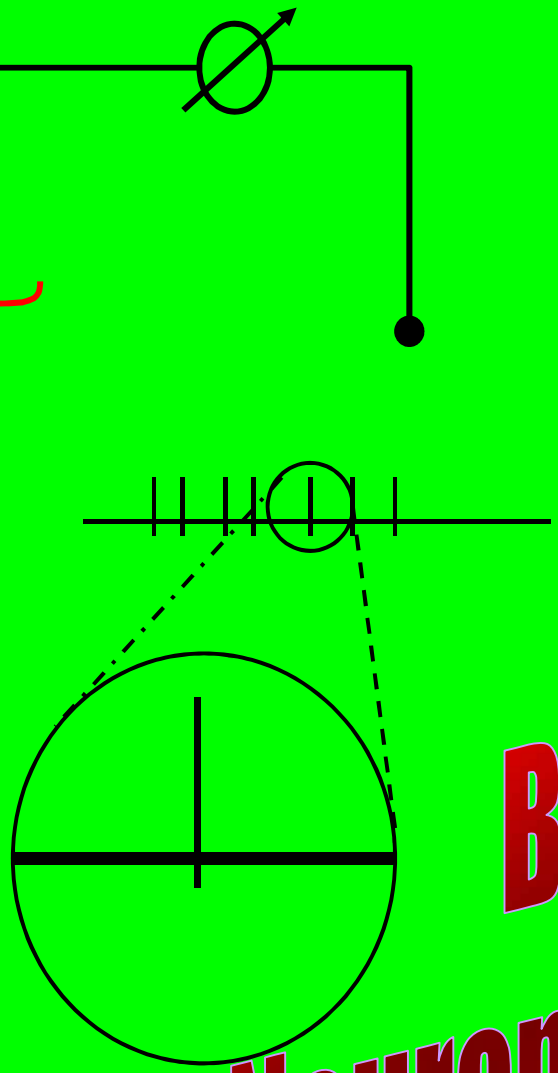




Basic Neurophysiology

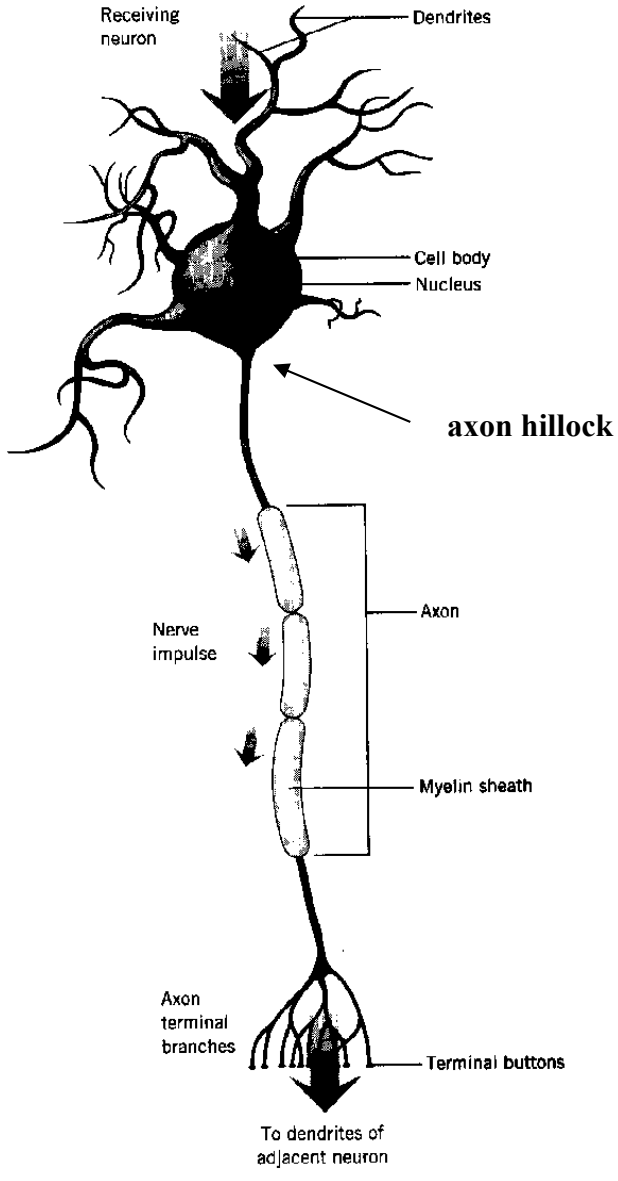
Membrane Potentials and Action Potentials

Although there are a great many neuron shapes...

...we discuss them as though they were functionally alike.

Most have: dendrites
cell body (soma)
axon hillock
axon
axon terminals

Some have myelin wrapping around the axon.



The signal of biological systems is partly based on the kind of electrical forces which are carried by wires, but there are some important differences.

To begin, we need to explain the concept of a

resting membrane potential

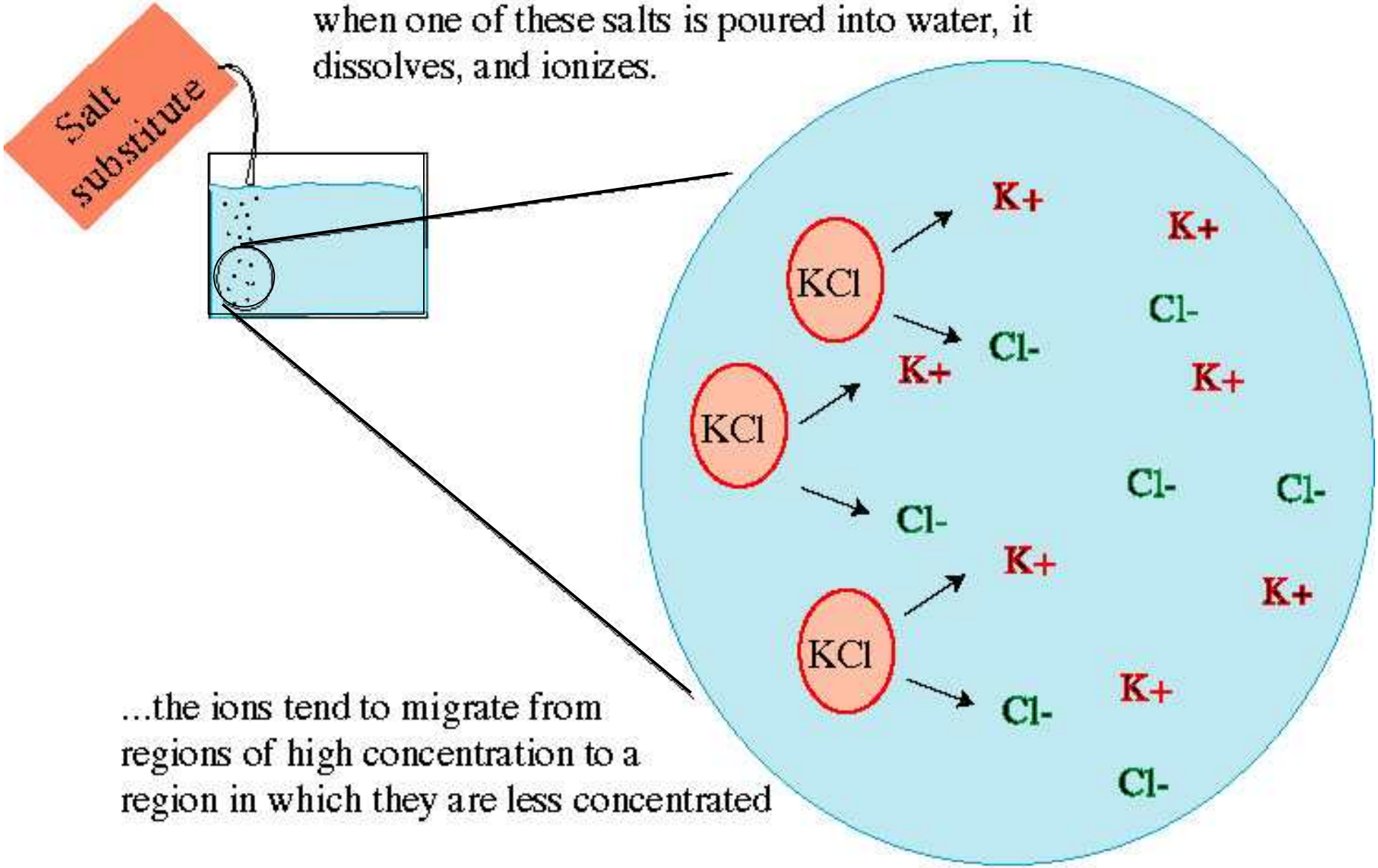
Check out membrane potentials caused by diffusion first

...the explanation begins with the salts which are dissolved into the fluids of the body, especially NaCl and KCl.

NaCl -- sodium chloride (table salt)

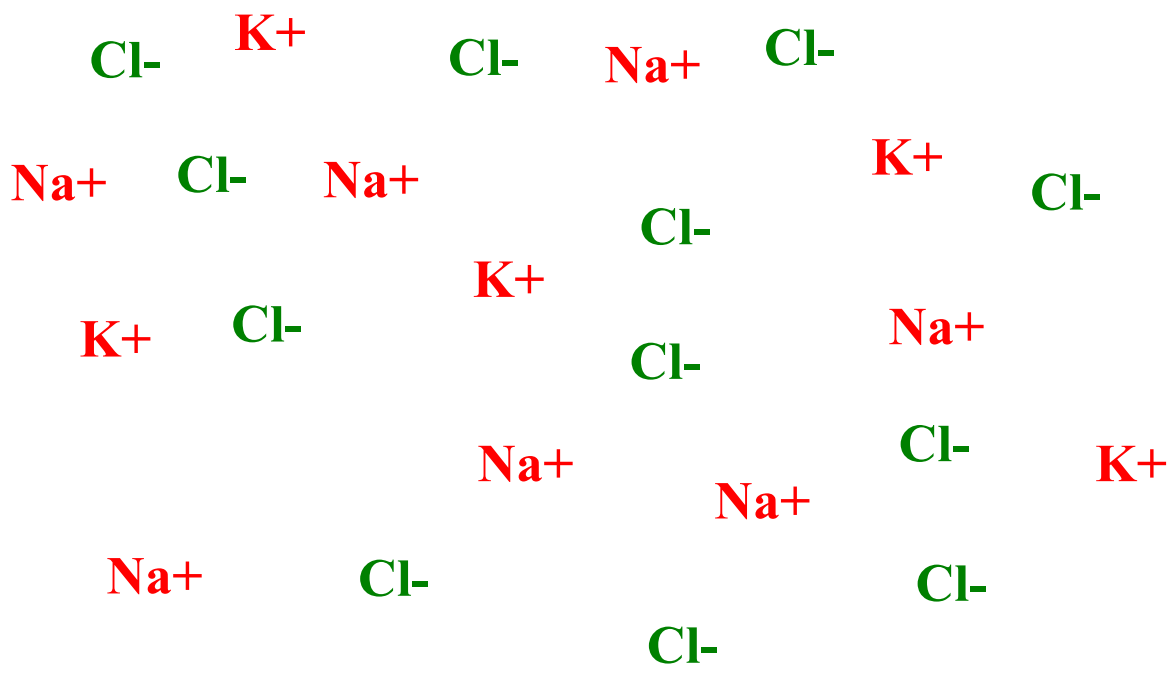
KCl -- potassium chloride (salt substitute)

when one of these salts is poured into water, it dissolves, and ionizes.

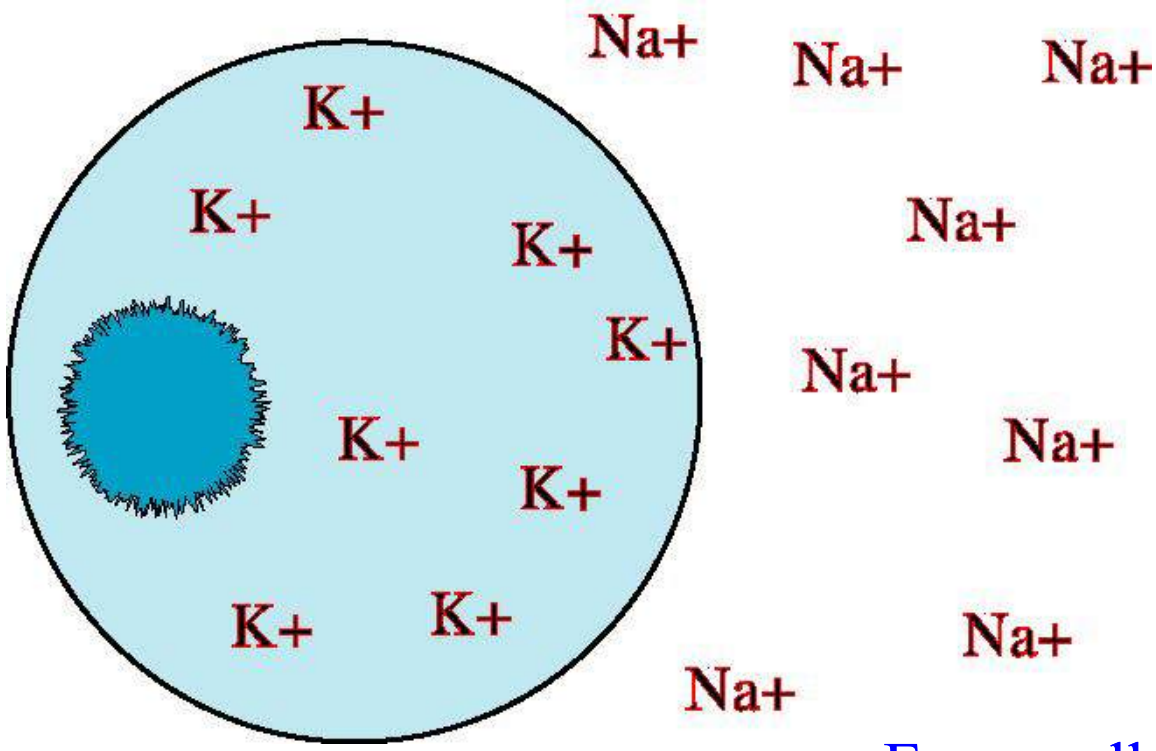


...the ions tend to migrate from regions of high concentration to a region in which they are less concentrated

--- this is know as moving down their concentration gradients.



Here is a mixture of sodium chloride and potassium chloride, wherein the molecules have ionized. All the sodium and potassium atoms carry a slight positive charge, and all the chloride atoms carry a slight negative charge.

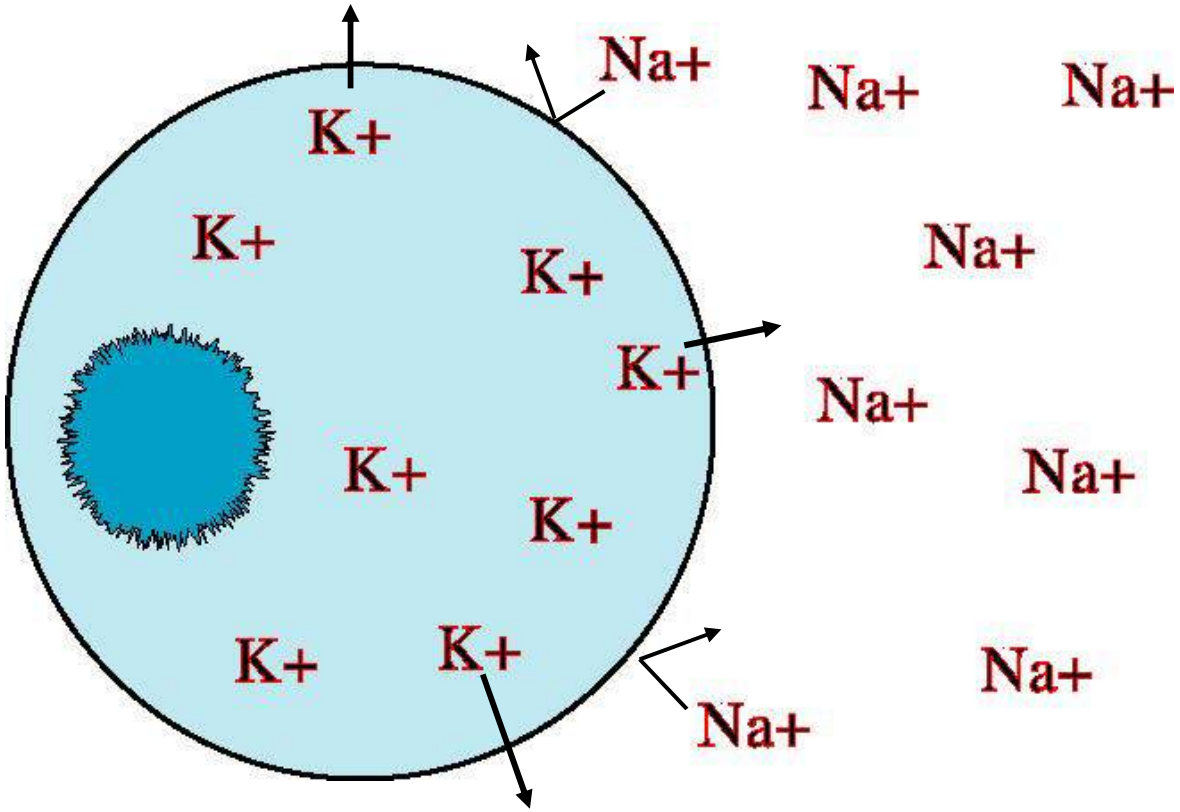


The role of the chloride ions can be ignored!

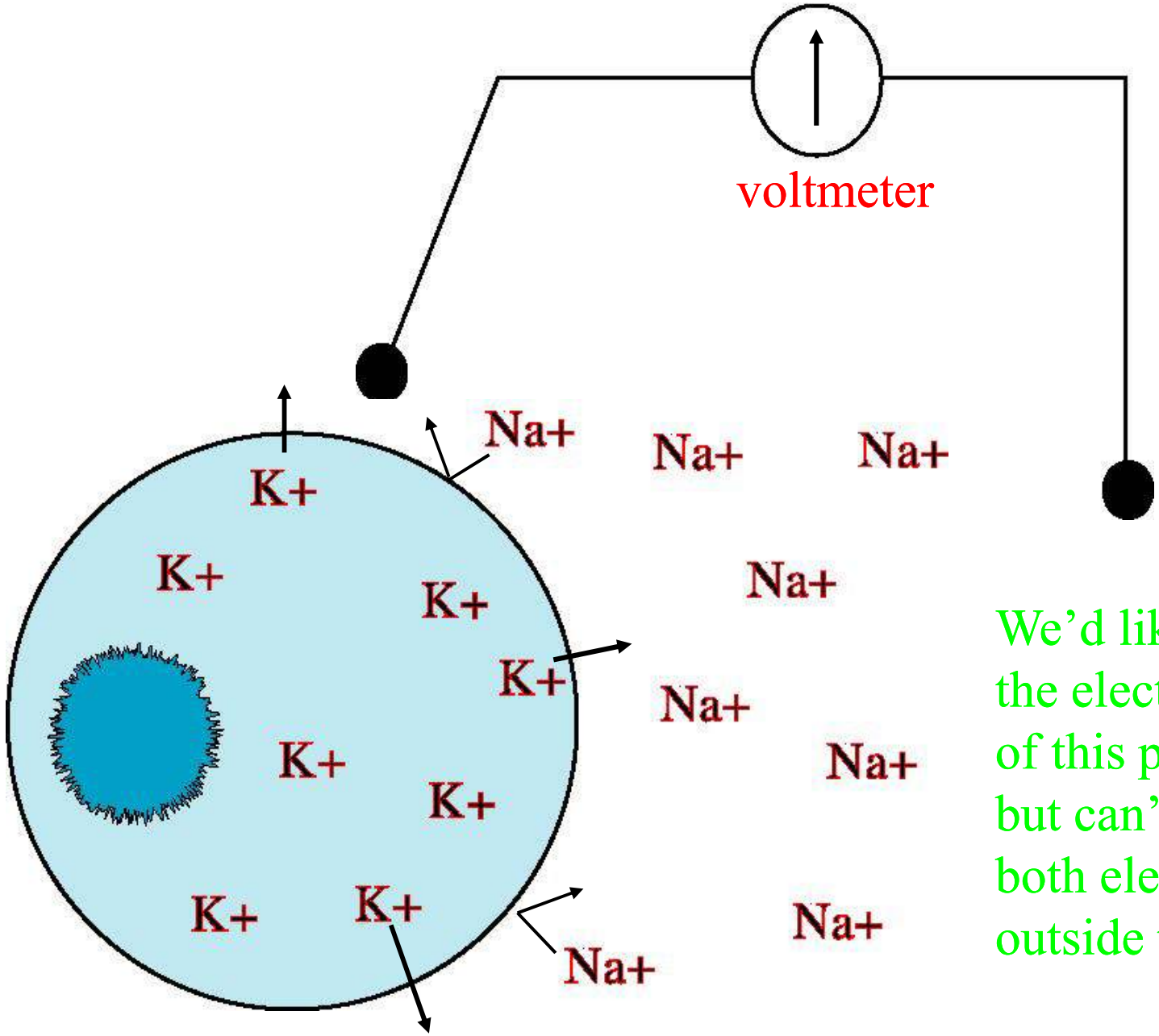
Every cell in the body has enzymes in the membrane which pump Na+ out of the cell, and pump K+ into the cell.

The Na/K pump thus produces concentration gradients for these ions!

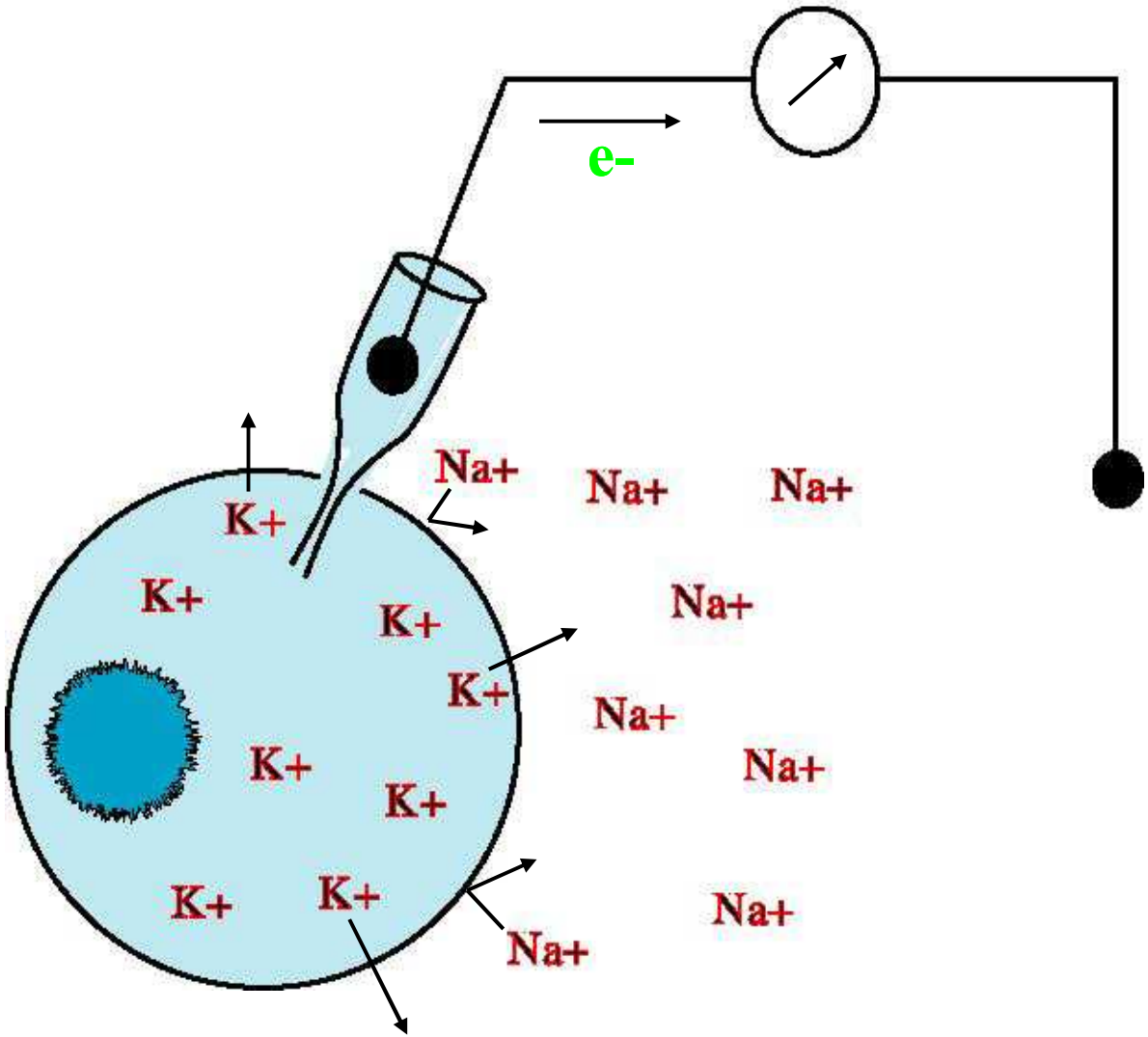
Additionally, the cell membrane is semipermeable to K+, but generally not to Na+.



So for most cells -- and for neurons at rest -- only the K+ is able to run down its concentration gradient!



We'd like to measure the electrical effects of this permeability, but can't do so if both electrodes are outside the cell.



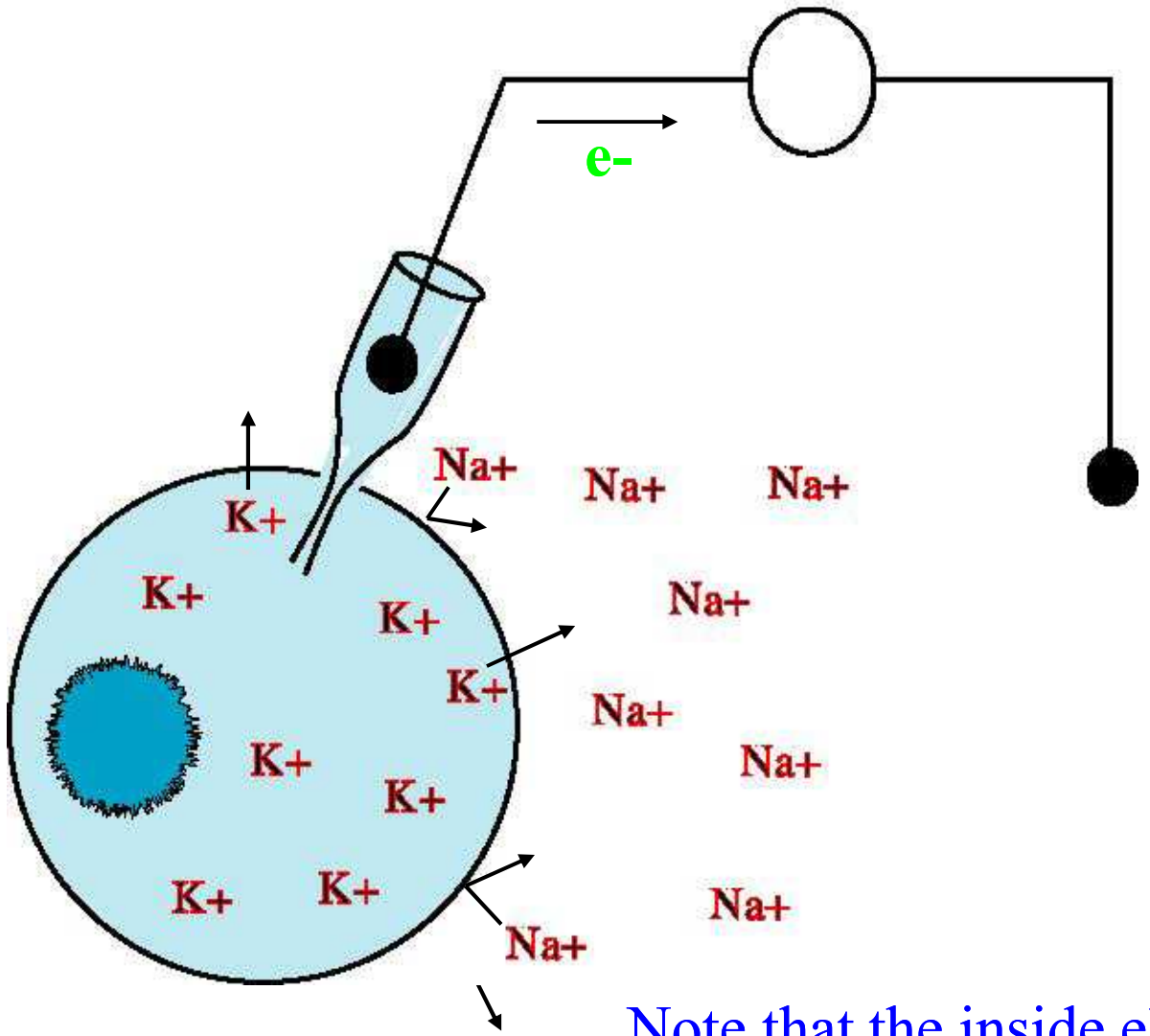
But we can see the resting membrane potential if we can get an electrode inside!!!

So the selective permeability of a potassium produces what is called a

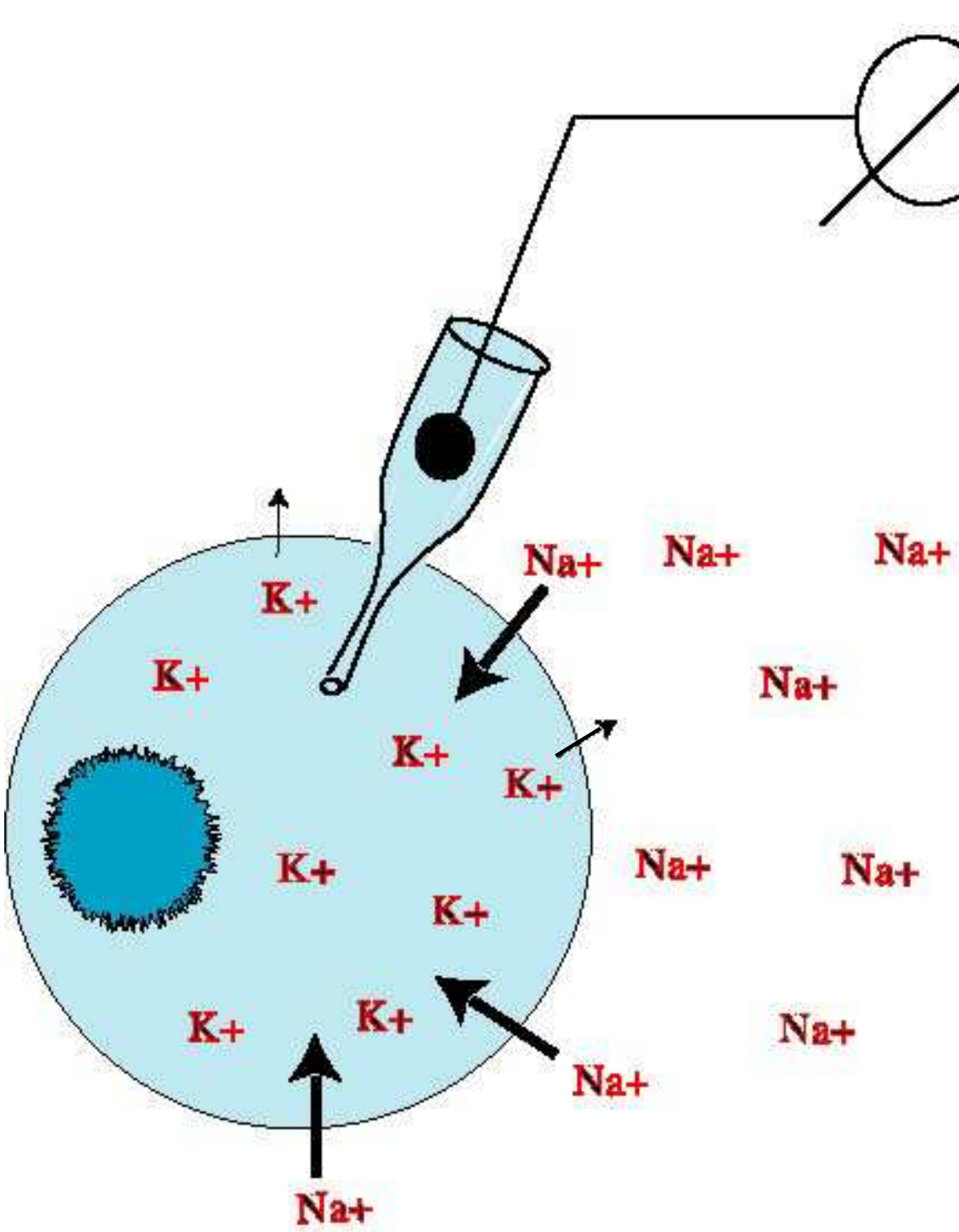
resting membrane potential

in that the flow of ions across the membrane will be registered by an electrode circuit.

The resting membrane potential of nerve fibers when they are not transmitting nerve signals is about -90mV.

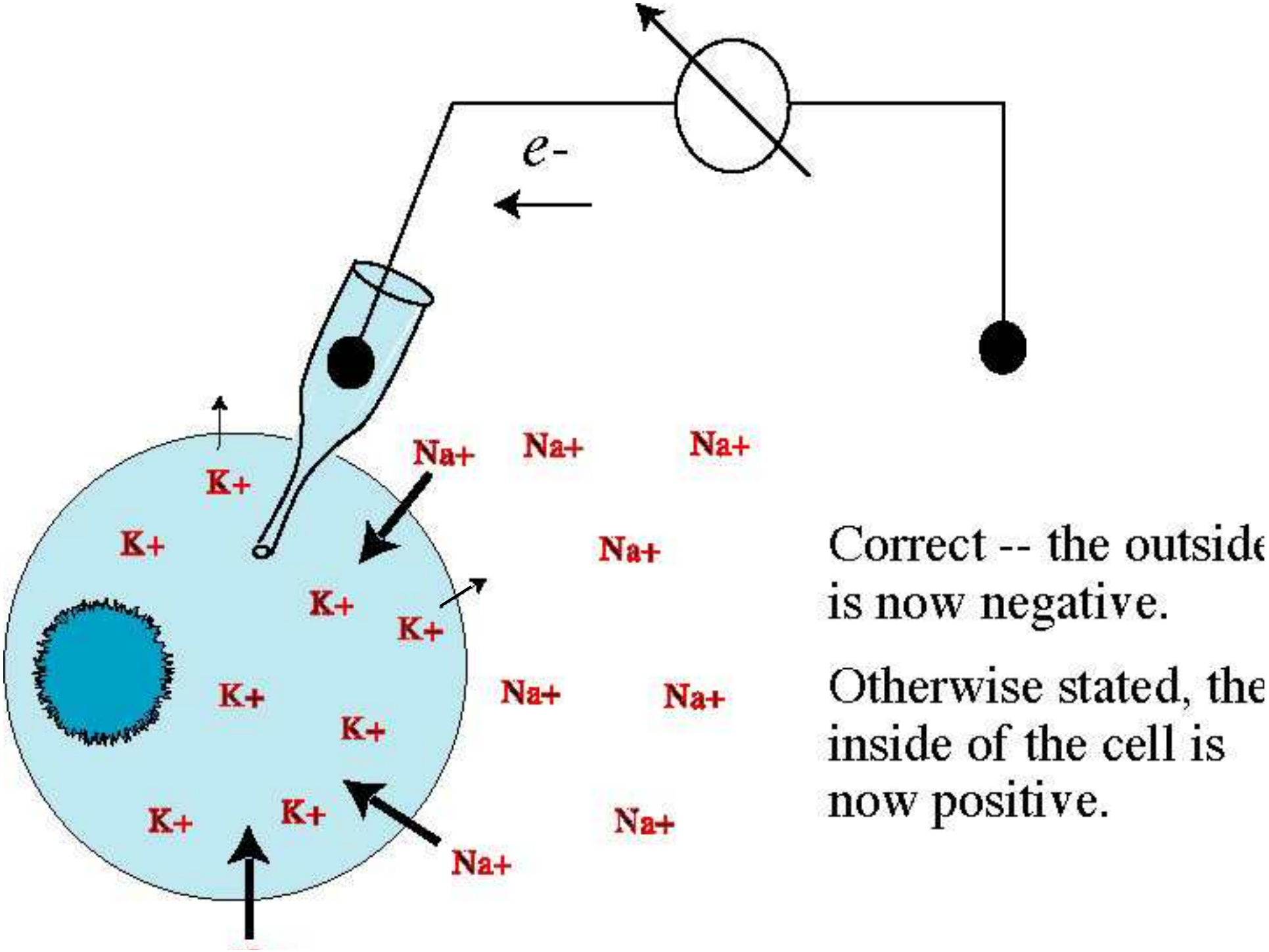


Note that the inside electrode is the source of electrons, i.e., is the negative electrode. But neurophysiologists like to say that the "inside of the cell" is negative.



But neurons and muscles have the ability to dramatically increase the permeability of Na+.

So which side is negative now?

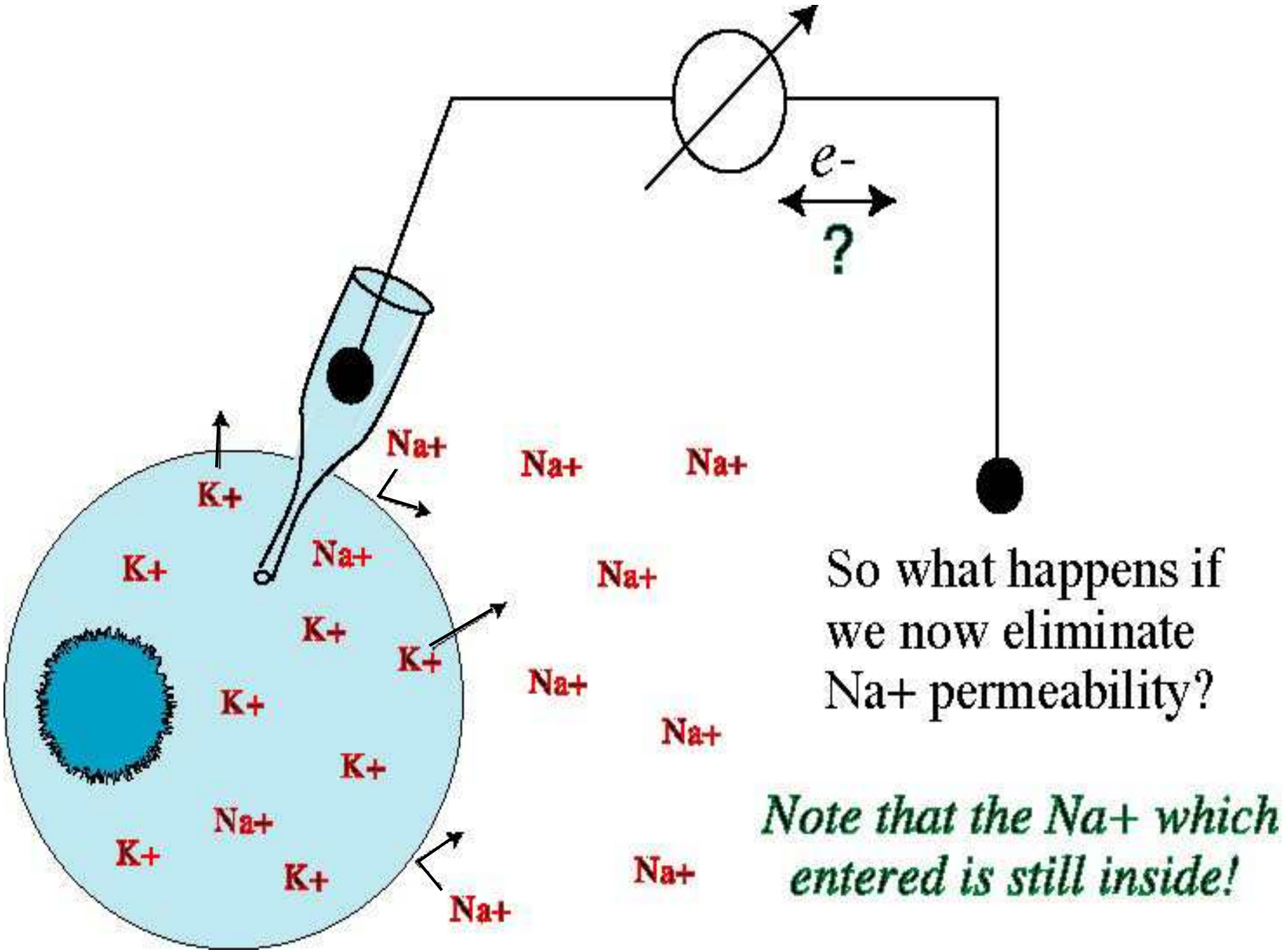


Correct -- the outside is now negative.

Otherwise stated, the inside of the cell is now positive.

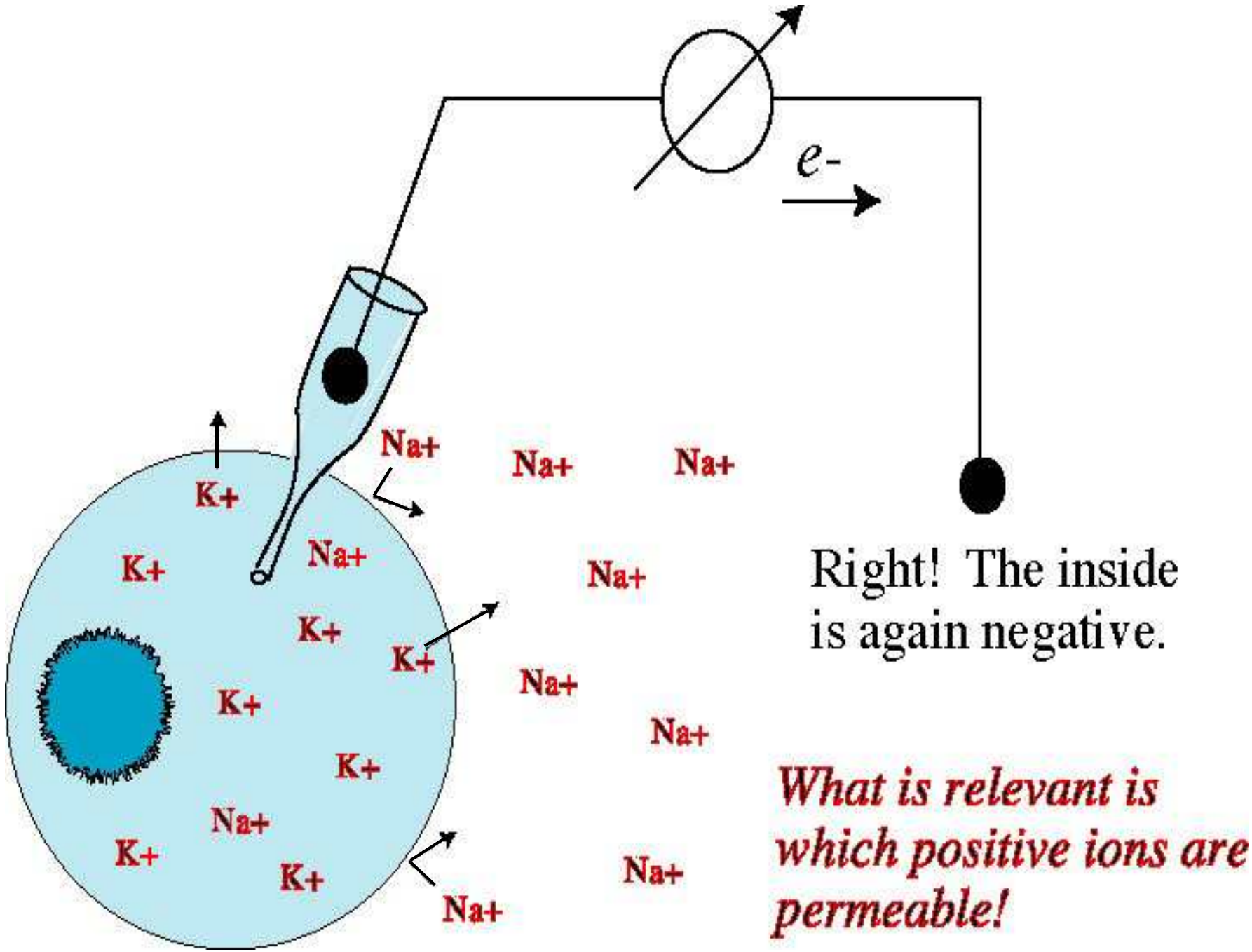
The result of increased sodium permeability is called

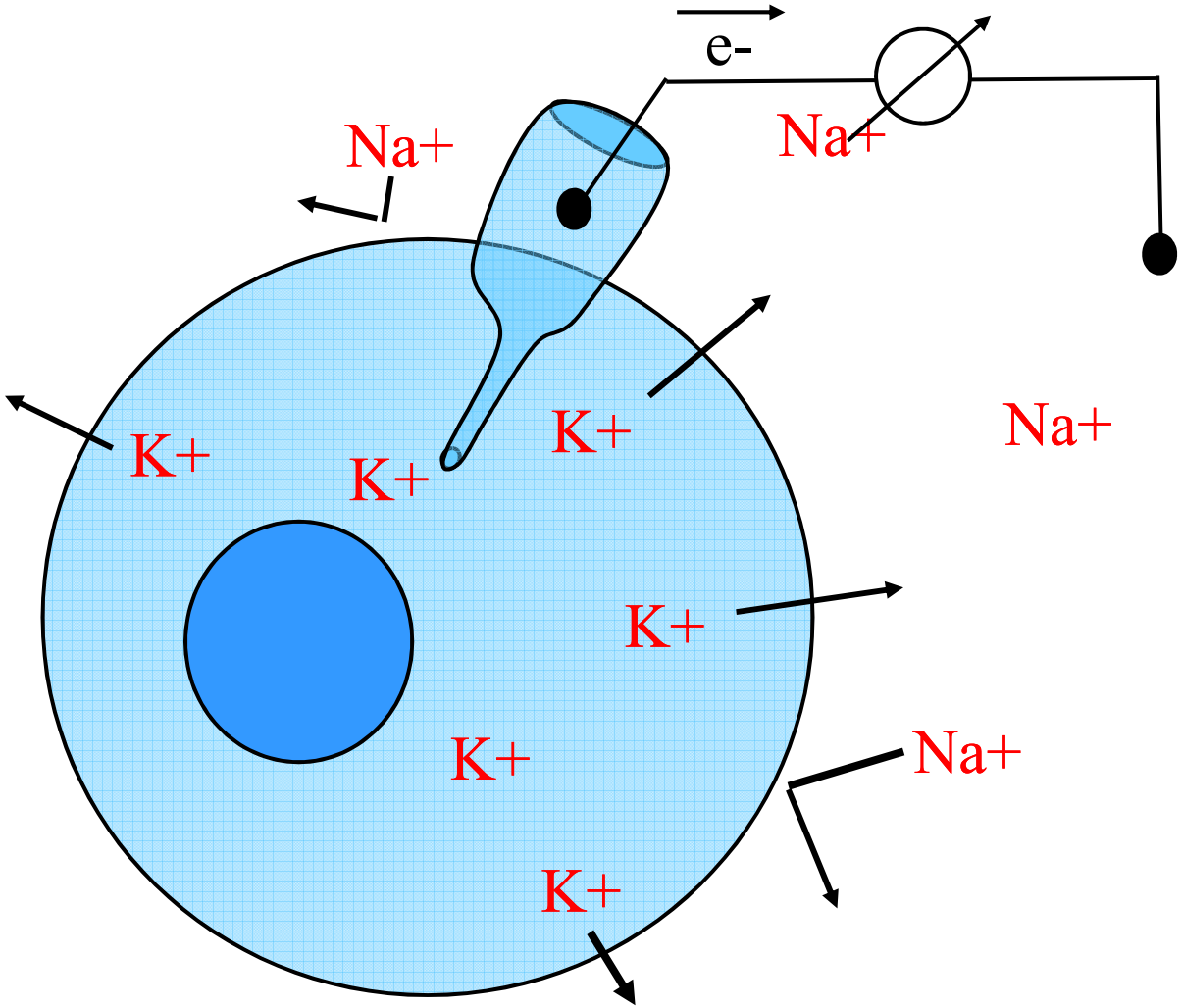
When sodium channels are temporarily opened, the external electrode is the source of electrons, and thus is the negative electrode. Thus the electrode inside the cell is positive.



So what happens if we now eliminate Na+ permeability?

Note that the Na+ which entered is still inside!


e-
Na+
Na+
Na+
K+
K+
Na+
Na+
K+
K+
Na+
K+
Na+
K+
Na+
K+
Na+
Na+
Right! The inside is again negative.
What is relevant is which positive ions are permeable!



It is possible, also for additional potassium channels to open. This results in the inside of the cell becoming more negative than at it is at rest, which is called **hyperpolarization**

We have been describing the electrical influence from flow of positive ions through the membrane.

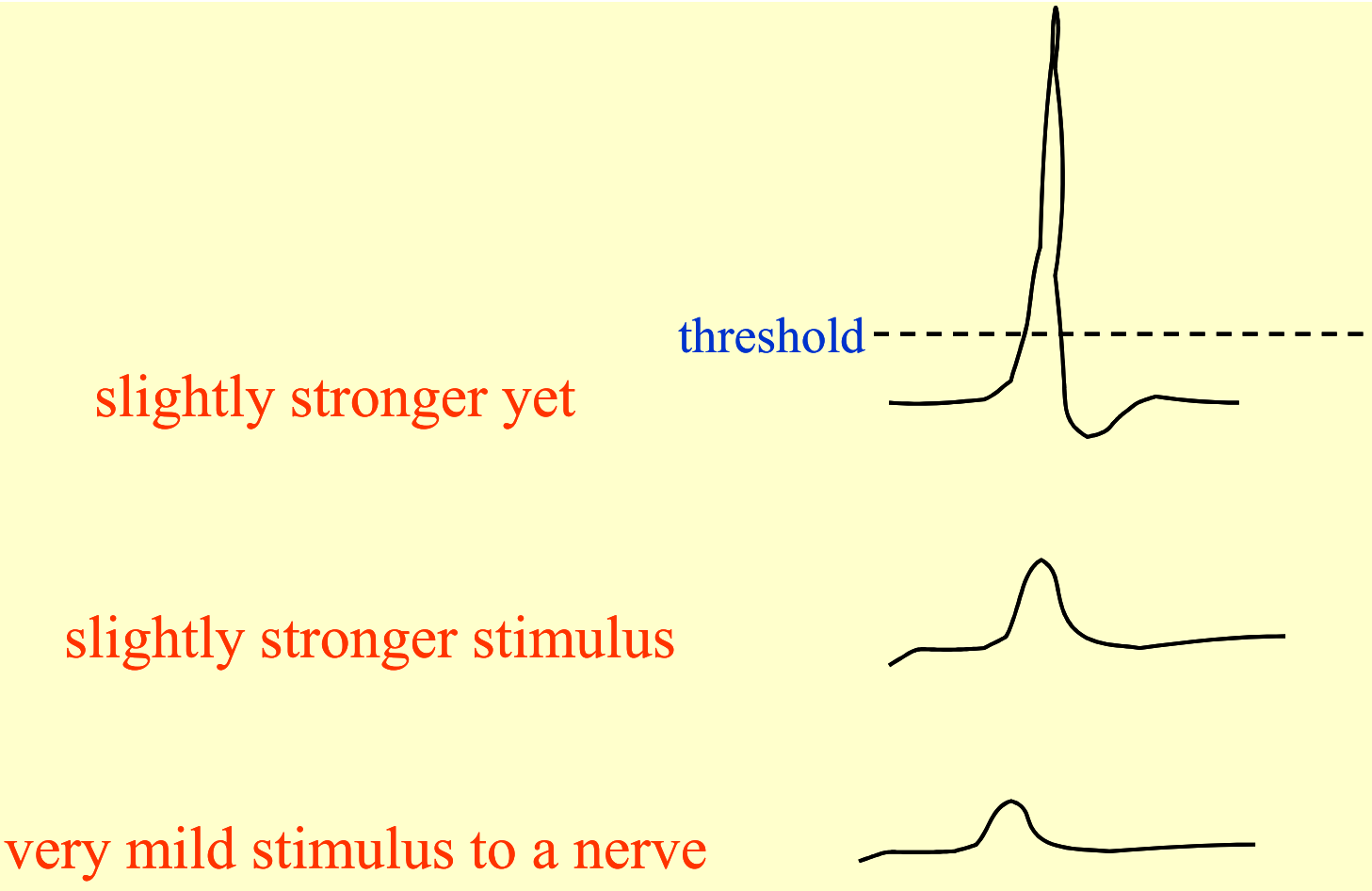
Physiologists prefer the term

electrotonic influences

The term “electrotonic” serves as a reminder that the electrical influences are being conducted by ions in a water medium -- and not by free electrons as would be the case in a metal wire.

Nonetheless, electrotonic influences are conducted through the medium almost instantaneously, so the pressure on electrodes reflects the relative permeability of the membrane at each moment in time.

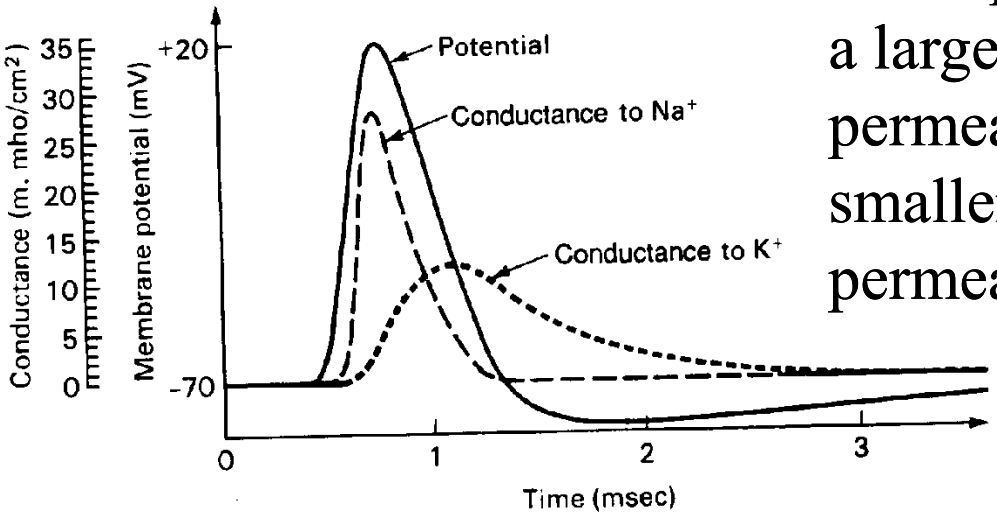
The changes in permeability themselves, however, are much slower, as we will see in the following slides.



When a neuron is stimulated, the increase in Na+ permeability produces depolarization.

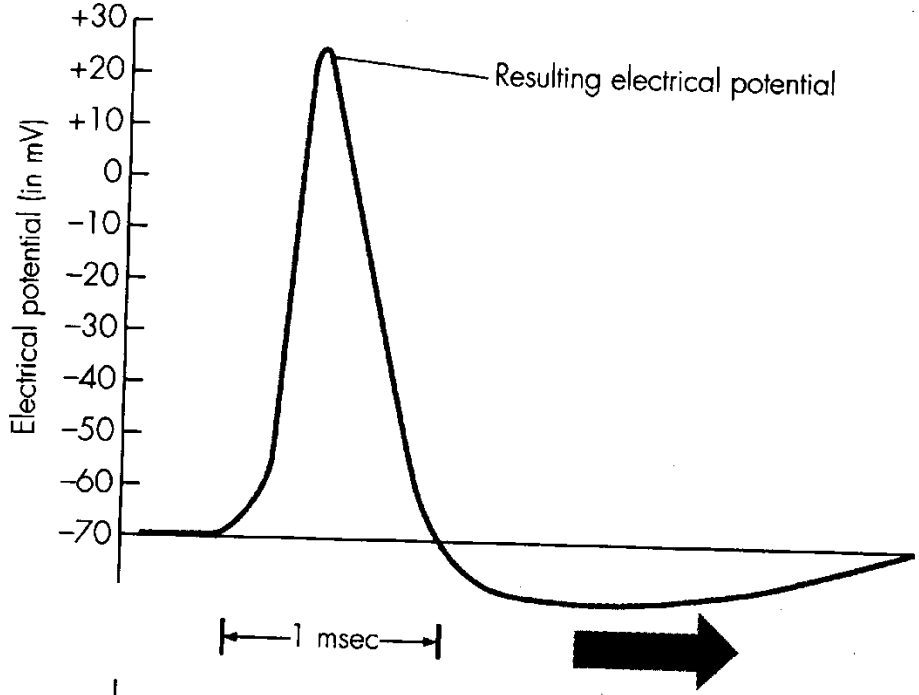
So nerve cells (and muscles) have an explosive change in their permeability to Na+ when the stimulated depolarization exceeds a threshold.

This is known as all or none responsiveness, which is to say, that if one exceeds threshold, there will be a depolarization of the same magnitude irrespective of the intensity of the stimulus which is applied.

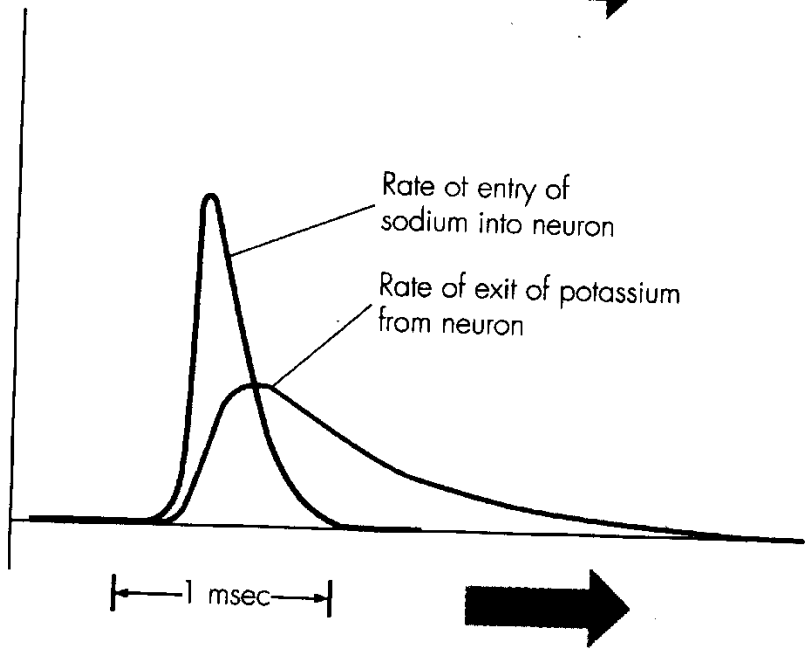


The action potential -- aka spike -- is produced by a large increase in Na+ permeability followed by a smaller increase in K+ permeability.

The rising phase is called depolarization, and the afterpotential (below the resting potential) is called hyperpolerization.

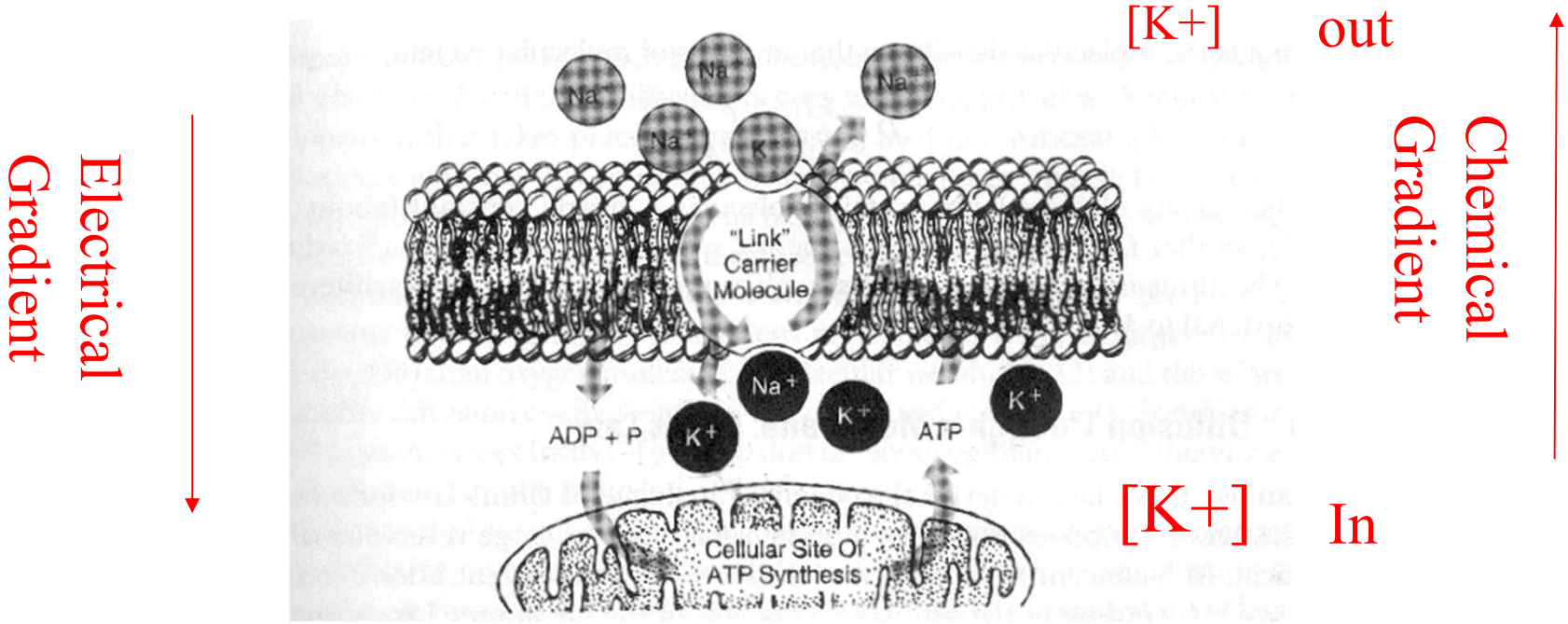


Here is another illustration of the same concept.



The permeability changes result in the large swings of membrane potential which are shown above.

- The resting membrane potential is generated by (1) differential distribution of ions (2) selective permeability
- Differential distribution of Na+ and K+ maintained by Na+-K+ pump
- 2 opposing forces for ion flux thru an open channel (1) chemical concentration (2) electrical gradient
- Equilibrium potential for K+: two forces acting on K+ ions exactly oppose each other

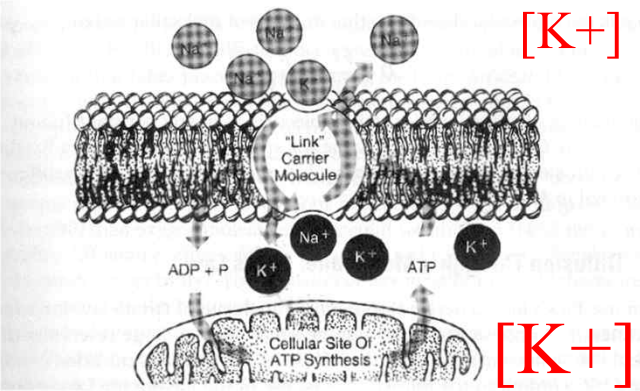


Nernst Equation

- In 1888, Walter Nernst, a German physical chemist derived an equation to calculate the equilibrium potential for an ionic battery
- Equilibrium potential = Nernst Potential
- For K+

$$E_{K+} = \frac{RT}{ZF} \ln \frac{[K+]_o}{[K+]_i}$$

  - R = Gas Constant
  - T = Temperature (degree Kelvin)
  - Z = Ionic Valence (원자가)
  - F = Faraday Constant
  - [K+]o = K+ Concentration outside cell
  - [K+]i = K+ Concentration inside cell



[K+] out

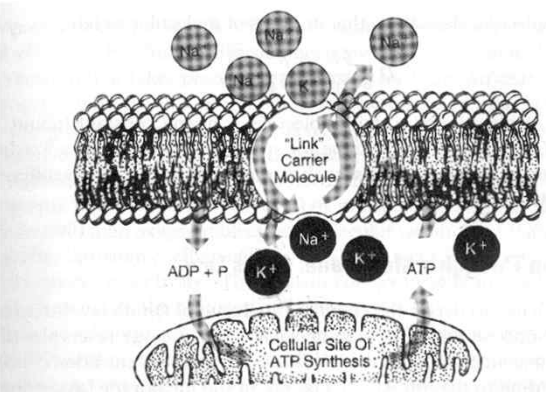
[K+] In

$E_{k+} \cong$ -75mV

- The membrane potential (Vm) may not be at the equilibrium potential (E) of an ion, Thus, a net driving force exists
- For K+: Vm – E_{k+}

- Cell membranes are permeable to a number of ions. The ionic battery of each permeable ion contributes to the resting membrane potential

[Na+] out



[Na+] In

$E_{Na+} \cong +55mV$

Goldman Equation

- The number of channels open for specific ions varies
- Thus, the permeability of the membrane for different ions varies
- P_{k+}:P_{Cl-}:P_{na+}=1.0:0.45:0.04
- The cell membrane is 25 times more permeable to K+ ions than Na+ ions
- The relative permeability of each ion determines its influence on the membrane potential
- Goldman equation is used to calculate Vm

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

- The number of open channels can be changed by voltage-dependent or ligand-dependent gating
- This changes the relative permeability of the membrane.
- This is the basis for electrical signaling

Cell Membrane

- Provides a boundary separating the internal structures from its external environment
- Selectively permeable, permitting the free passage of some materials, and restricting the passage of others
- Double layer (i.e., bilayer) of phospholipid molecules (Fig. 2.1)
- Lipid: water-insoluble, energy rich macromolecules, fats, waxes, oils
- Globular proteins in membrane: free to move within the layer
- Channels: protein-lined pores.
- Water-filled pores
- Intracellular and extracellular fluid: solution of dissolved salts (NaCl and KCl) which dissociate into Na+, K+, and Cl-
- Molecules transported across the cell membrane by passive and active processes

- Active process requires energy, ATP
- Passive process by inherent random movement of molecules
- Three passive processes
  - Osmosis: water transport
  - Diffusion: small molecules
  - Carrier-mediated diffusion (Fig. 2.2)
- Active process
  - Against concentration gradient
  - Thus require energy
  - Na+-K+ pump (Fig. 2.3)
  - The pump uses energy stored in ATP to pump Na+ out of the cell and K+ in
  - Let's look at the how membrane potential is caused by the movements of Na+ and K+

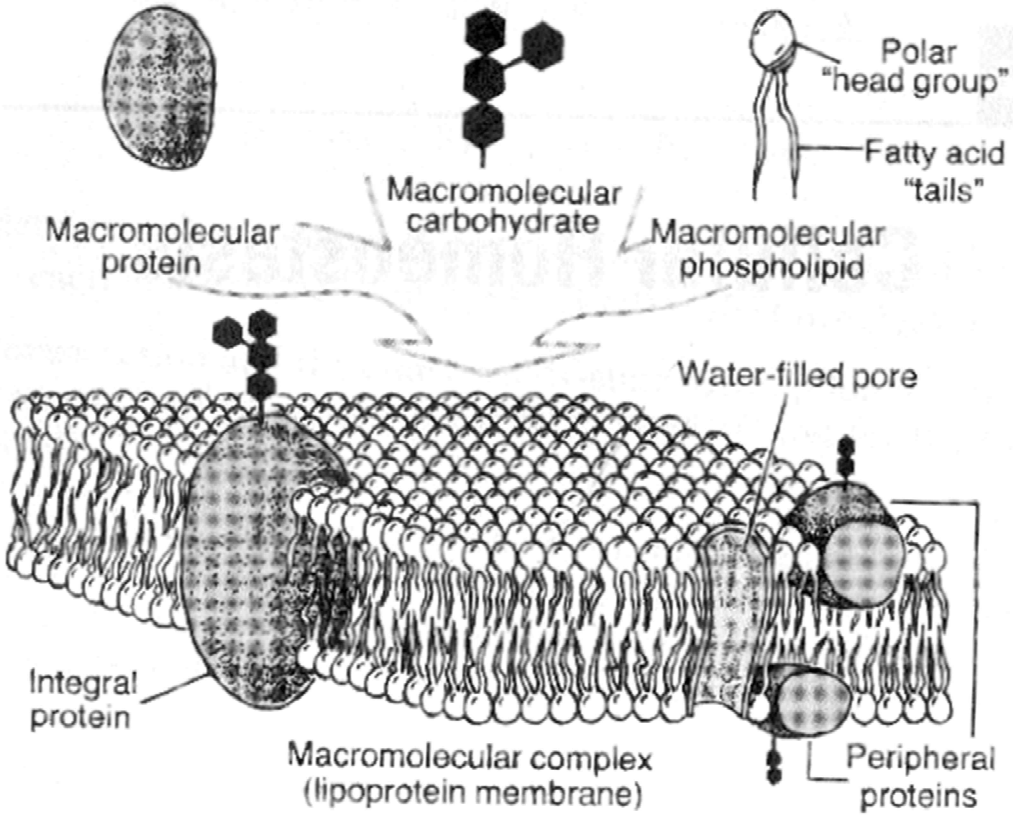


Figure 2.1 Schematic diagram of the cell membrane. (Davis et al., 1985, Fig. 3-1, p. 41.)

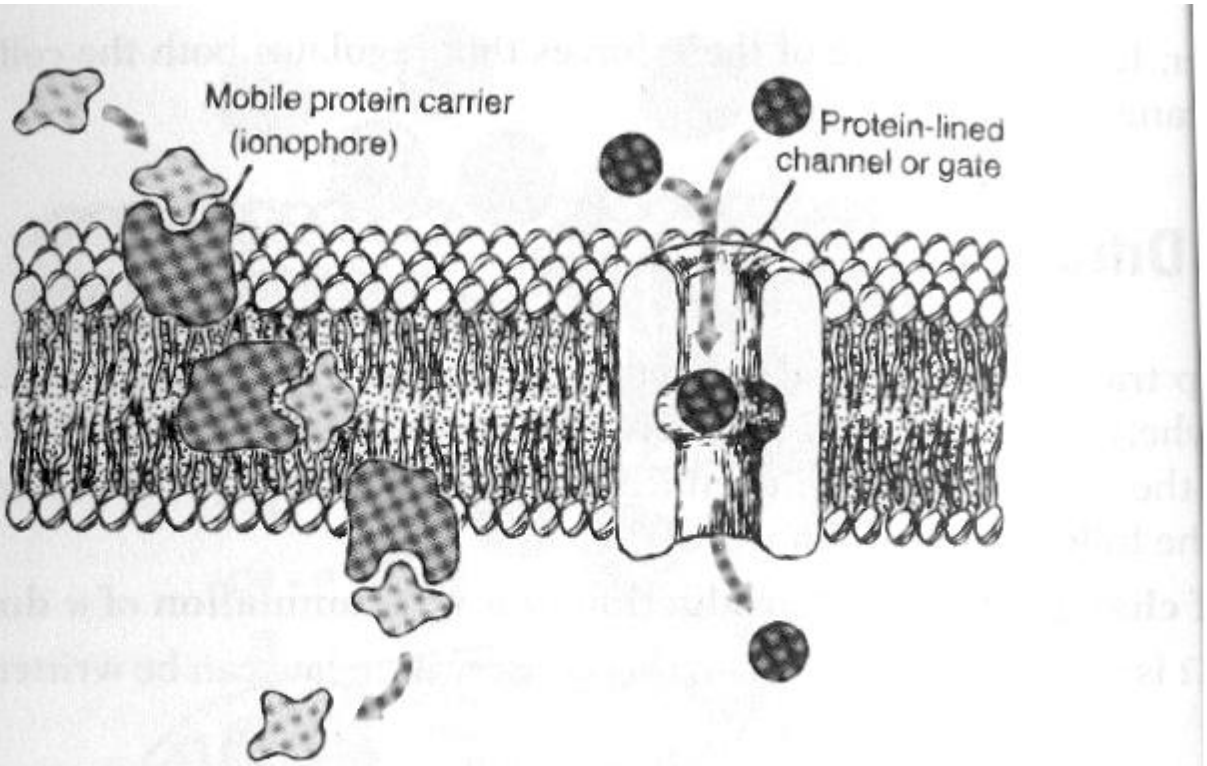


Figure 2.2 Schematic diagram of the cell membrane containing a protein carrier and a p
lined ionic channel. (Davis et al., 1985, Fig. 3-7, p. 45.)

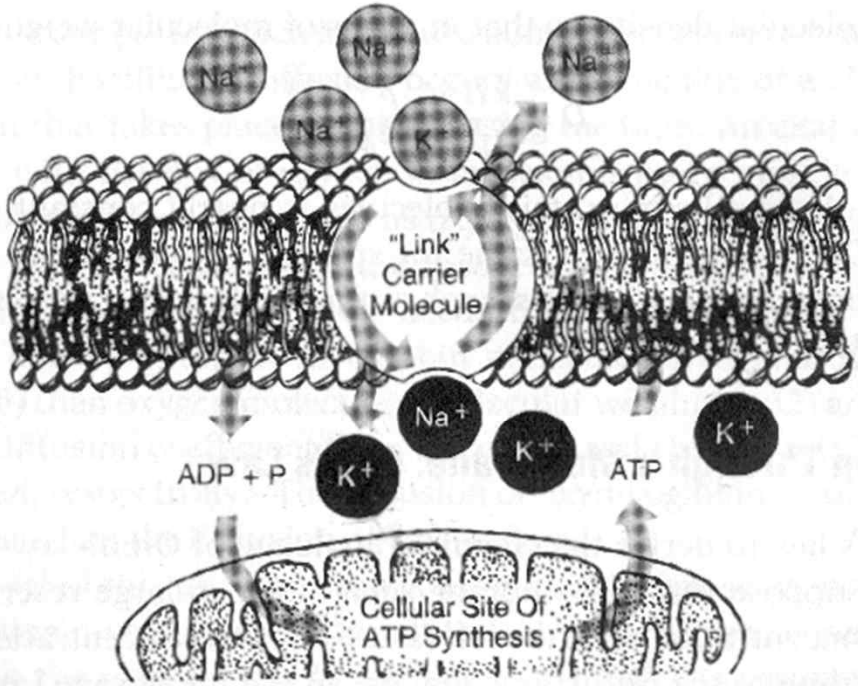


Figure 2.3 Schematic diagram of the cell membrane containing a $Na^+ - K^+$ pump. (Davis, et al., 1985, Fig. 3-11, p. 49.)