9.01 Introduction to Neuroscience
Fall 2007

9.01 Recitation
Section 1 (Mondays)

Chapter 3: Resting Membrane Potential

Molecules involved (p. 53-9): water (in cytosol and extracellular fluid; polar); ions (monovalent, divalent, cation, anion; Na^+, K^+, Ca^{2+}, Cl^-); phospholipid bilayer (phospholipids have polar, hydrophilic heads and nonpolar, hydrophobic tails); proteins (enzymes, cytoskeleton, receptors, channel proteins, ion pumps).

Ion channels
- membrane-spanning proteins (have hydrophobic bodies and hydrophilic tails); ion-specific
- no ATP needed; movement directed by diffusion along concentration gradients

Ion pumps
- membrane-spanning proteins
- ATP is needed; movement against concentration gradient
- Examples: sodium-potassium pump; calcium pump

Movement of ions (p. 59-61): diffusion (1. the membrane possesses channels permeable to the ions, 2. there is a concentration gradient across the membrane); electricity (1. the membrane possesses channels permeable to the ions, 2. there is an electrical potential difference across the membrane)

Current (I)
- movement of electrical charge
- flows in the direction of cations (i.e. sodium ions)

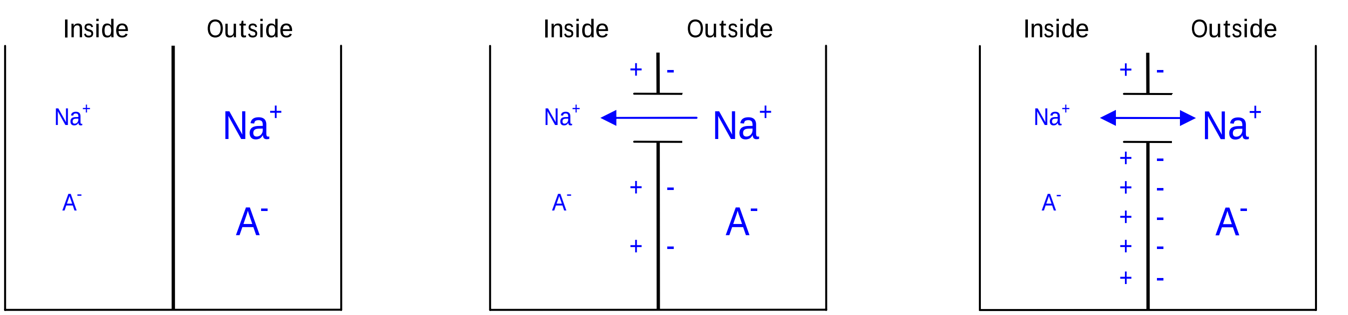
Potential (V)
- voltage, or the force exerted on charged particles
- the amount of force reflects difference in charge between anode and cathode; greater difference, greater force

Conductance (g)
- relative ability of charge to migrate; inverse of resistance
- depends on the no. of particles available to carry charge, no. of channels

Ohm's Law
- I = gV (or V = IR)
- Modified Ohm's: $\mathbf{I_{ion} = g_{ion} * (V_m - E_{ion})}$
- $(V_m - E_{ion})$ term is referred to as the driving force

Membrane potential, or V_m (p. 61): voltage (charge diff.) across the neuronal membrane; measured with microelectrode
For typical neurons, membrane potential with respect to the outside of the cell is -65 mV (open K+ channels; Na+ leakage).

Equilibrium potentials, or E_{ion} (p. 62-4): electrical potential difference that exactly balances an ionic concentration gradient; hypothetical/theoretical potential for one specific ion (see page 64, figure 3.14)



$g_{Na} = 0$; $V_m = 0$; $E_{Na} = 62$ mV
no potential difference
neutral charge on both sides

$g_{Na} > 0$; $V_m > 0$; $E_{Na} = 62$ mV
Na^+ channel added

$g_{Na} = >$; $V_m = E_{Na}$; $E_{Na} = 62$ mV
equilibrium reached

1. Large changes in membrane potential are caused by miniscule changes in ionic concentrations.
2. The net difference in electrical charge occurs at the inside and outside surfaces of the membrane.
3. Ions are drive across the membrane at a rate proportional to the difference between the membrane potential and equilibrium potential ($\mathbf{V_m - E_{ion}}$ is known as the driving force).
4. If the concentration difference across the membrane is known for an ion, an equilibrium potential can be calculated for that ion.

Nernst Equation (p. 65)

- see book for equation
- R = gas constant; T = absolute temperature, proportional to rate of diffusion; F = Faraday's constant; Z = valence
- calculates E_{ion}, a theoretical value for membrane potential of neuron with only one type of ion channel
- remember what log function looks like (log is negative when input is <1; less is positive when input is >1); if you know the valence and the log term (ratio of ions outside to inside), you can determine the sign of E_{ion}
- T, Z, and ion ratios needed to use Nernst Equation

Goldman Equation (p. 68)

- see book for equation
- P = permeabilities
- this equation gives "weighted average" of equilibrium potentials based on relative permeabilities of multiple ions
- calculates V_m, the real membrane potential (not theoretical like Nernst Equation)
- difference between Goldman and Nernst Equations: Goldman takes into account permeabilities

Distribution of ions (p. 65-7): K^+ more concentrated on the inside of the cell; Na^+ and Ca^{2+} more concentrated on the outside; concentration gradients arise via the **sodium-potassium pump** (Figure 3.16, exchanges internal sodium for external potassium, uses ATP).

Ion	[Ion] inside (mM)	[Ion] outside (mM)	E_{ion} (mV)
K^+	100	5	-80 mV
Na^+	15	150	62 mV
Ca^{2+}	0.0002	2	123 mV
Cl^-	13	150	-65 mV

Chapter 4: Action Potential

Depolarization: a change in membrane potential from normal resting value to less negative value; increasing extracellular potassium ions depolarizes cells

Threshold: critical level of depolarization that is needed to trigger action potential; membrane potential must depolarize beyond threshold to fire A.P.; action potentials are "all-or-none"; action potentials only have one size

Firing frequency: if more current is injected, size of action potentials do not change, firing rate increases; maximum firing frequency is 1000 Hz, because the absolute refractory period is 1 ms

Action potential conduction, propagation (p. 93-7):
1. Nerve impulse conduction is really the bumping of positive charge down the axon.
2. Action potentials initiated at one end of the axon only propagate in one direction. The action potential does not turn back — the membrane just behind it is refractory as a result of the inactivation of the voltage gated Na+ channels.
3. Action potentials can be generated (experimentally) by depolarization at either end of the axon and can propagate in either direction. Orthodromic — the normal direction of propagation (the reverse = antidromic)
4. To increase conduction velocity:
   A. increase axonal diameter
   B. myelination of the axon facilitates current flow down the inside of the axon. Breaks in the myelin wrapping occur at the Nodes of Ranvier, which have increased concentrations of voltage gated Na+ channels. Regeneration of the action potential occurs at the Nodes (known as **salutatory conduction**). See page 94 for garden hose analogy.

Tetrodotoxin (TTX)

- clogs sodium permeable pores (binds to outside of channel, which undergoes conformational change)
- blocks all sodium-dependent action potentials
- is found in puffer fish, a delicacy; is fatal if ingested

Review Questions for Ch. 3-4:

1) Which of the following values is unnecessary when finding the equilibrium potential of an ion using the Nernst equation?
   a) The temperature
   b) The ratio of external and internal ion concentrations
   c) The charge of the ion
   d) The permeability of the ion channel

2) Weaver mice have difficulty maintaining posture and moving normally. This defect has been attributed to a defect in some potassium channels that allows Na+ as well as K+ to pass through the channel. Increasing the sodium permeability will have what effect on the membrane potential of the neuron?
   a) The membrane potential will become more negative.
   b) The membrane potential will become less negative.
   c) There will be no change in membrane potential.
   d) There is not enough information to answer this question.

3) Assume that Cl-is more concentrated on the outside of the cell than on the inside of the cell, and that the membrane is selectively permeable to Cl-. Then we know that:
   a) The inside of the cell will have a positive voltage at equilibrium.
   b) The inside of the cell will have a negative voltage at equilibrium.
   c) The inside of the cell will have a voltage of 0 at equilibrium.
   d) There is not enough information to answer the question.

4) Which of the following gives the ordering of ions in terms of their ionic concentration inside the typical neuron, from highest to lowest?
   a) K+, Na+, Ca++
   b) Na+, K+, Ca++
   c) Ca++, Na+, K+
   d) Ca++, K+, Na+

5) The resting membrane potential is close in value to the Nernst equilibrium potential for ____ because ____.
   a) Na+ / there is a leakage of Na+ ions through the membrane channels
   b) K+ / there is a leakage of Ca++ ions through the membrane channels
   c) K+ / the membrane is very permeable to K+ ions at rest
   d) Na+ / due to its large driving force e) Cl- / because it's the only negatively charged ion

6) What effect does an intravenous injection of KCl have on behavior of neurons?
   a) Extracellular [K+] decreases and therefore the membrane potential gets closer to Na+ equilibrium potential.
   b) The membrane potential becomes more negative and it becomes more difficult to generate action potentials.
   c) Extracellular [K+] increases and therefore the membrane potential gets closer to Na+ equilibrium potential.
   d) None of the above is true

7) There is no movement of an ion when
   a) $V_m - E_{ion} = 0$
   b) When $g_{ion} = 0$
   c) $V_m = 0$
   d) More than one of the above but not all.
   e) All of the above.

8) Ion X is positively charged and in equal concentration on either side of the membrane of a typical neuron that has a resting membrane potential of -65mV. Opening up channels permeable to X+ would result in
   a) Ion X+ leaving the cell
   b) Ion X+ entering the cell
   c) No movement of ion X+
   d) No change in the cell's membrane potential

9) All of the following are necessary in order for there to be a net flux (movement) of sodium across the membrane EXCEPT
a) a membrane that is permeable to Na
b) (V_m – E_{ion}) does not equal zero
c) a membrane potential that is negative
d) there are no exceptions, all of the above are necessary in order to have a net movement of sodium

10) The equilibrium potential for anion Z- is +80 mV
a) opening a channel permeable to Z- would depolarize a cell
b) there is a higher concentration of Z- outside the cell than inside
c) Z- has the same concentration gradient as chloride (Cl-)
d) All of the above

11) The rising phase of the action potential is based on:
a) rapid depolarization resulting from the opening of Na+ channels
b) rapid depolarization resulting from the opening of K+ channels
c) rapid hyperpolarization resulting from the opening of Na+ channels
d) rapid hyperpolarization resulting from the opening of K+ channels

12) At the peak of the overshoot during an action potential, all of the following are true EXCEPT:
a) The driving force on Na+ is higher than the driving force on K+
b) The membrane potential is above threshold
c) The membrane is permeable to both Na+ and K+
d) The equilibrium potential for Na+ is about 62 mV

13) During the falling phase of the action potential:
a) Na+ channels activate and K+ channels open
b) Na+ channels inactivate and K+ channels open
c) Na+ channels deinactivate and K+ channels open
d) Na+ channels activate and K+ channels close
e) Na+ channels inactivate and K+ channels close
f) Na+ channels deinactivate and K+ channels close

14) During the absolute refractory period, it is impossible for a neuron to fire an action potential because:
a) The membrane potential is below threshold
b) Delayed rectifier K+ channels are closed
c) Chloride channels open, causing shunting inhibition
d) Voltage-gated sodium channels are inactivated

15) As a birthday treat, your friends bake you an amazing Fugu cake made with fresh puffer fish liver. You can't resist taking a bite and your lips rapidly develop an interesting numb feeling. This sensation results from the action of what TOXIN on what CHANNEL?
a) STX on Na+ channels
b) STX on K+ channels
c) TEA on K+ channels
d) TTX on K+ channels
e) TTX on Na+ channels

16) The following statements about propagation of action potentials (APS) are all true EXCEPT:
a) there is no limit to how far APs can propagate
b) propagation is initiated at the axon hillock
c) propagation is slower down fatter axons
d) propagation is faster in myelinated than unmyelinated axons
e) the refractory period prevents back propagation

17) Which of the following would be most likely to produce epileptic seizures:
a) Abnormally fast Na+ channel inactivation
b) Abnormally fast K+ channel rectification
c) Abnormally low Na+ conductance during the rising phase of the action potential
d) Abnormally low K+ conductance during the falling phase of the action potential

Notes

In class, there was some confusion over this statement:
Large changes in membrane potential are caused by miniscule changes in ionic concentrations.

The concentrations of the key ions can be thought of as constant when the neuron is at rest and even during an action potential. This is because membrane potential refers to the charge inside of the cell compared to the charge outside the cell. There can be a large change in charge even when there is a negligent change in ionic concentrations.

Think of it using this (made-up and very imperfect) example: there are 1,000,000 ions of valence +1 inside and outside the cell; the charge difference is currently 0. If 1,000 of those ions move into the cell, then the charge inside the cell is going to be +2,000 compared to the outside of the cell. And yet the concentration ratio is 1,001,000 to 999,000, which is still relatively close to 1.

Answers to Review Questions

1) D
2) B
3) B
4) A
5) C
6) C
7) D (A and B)
8) B
9) C
10) A
11) A
12) A
13) B
14) D
15) E
16) C
17) D

Explanations, Additional Info for Select Questions

<u>Question 6</u>

Remember that neurons have high potassium conductance at rest (a lot of potassium channels – not voltage-gated ones - are open at rest). Thus, when adding more KCl outside of the cell, the additional potassium will have an effect on membrane potential. The increase in chloride does not have as much of an effect, because chloride conductance is low at rest. When extracellular potassium increases, more potassium will enter the cell (because of concentration gradient and attraction to negative charge inside cell). The membrane potassium will become more positive. (There was some confusion re: the wording of the answer; increasing KCl has no effect on sodium channels. When the answer choice says that membrane potential "gets closer to Na+ equilibrium potential," it just means that the membrane potential is more positive.)

<u>Question 7</u>

Refer to the modified Ohm's Law.

<u>Question 8</u>

The question states that ion X is equal in concentration on both sides of the brain, thus diffusion does not play a part. Electricity and charge does. Opening up channels permeable to X+ will result in X+ flooding into the cell because it is attracted to the negative charge inside the cell.

<u>Question 17</u>

Epileptic seizures means there is an excess of electrical activity in the brain.