PRINCIPLES OF NEUROBIOLOGY
CHAPTER 2: SIGNALING WITHIN NEURONS

Cell Biological and Electrical Properties of Neurons

2–1 What is the transcription unit?
(a) The part of the gene that serves as a template for RNA synthesis
(b) The part of RNA that serves as a template for protein synthesis
(c) The part of the gene that serves as a template for protein synthesis
(d) The unit of RNA that is made from a particular gene

2–2 Proteins that function in the cytoplasm and nucleus are synthesized in/on which organelle?
(a) Free ribosomes
(b) Endoplasmic reticulum
(c) Golgi apparatus
(d) Nucleus

2–3 Proteins that are destined for export from the cell or that are inserted into the lipid bilayer are synthesized in/on which organelle?
(a) Free ribosomes
(b) Endoplasmic reticulum
(c) Golgi apparatus
(d) Nucleus

2–4 What is the function of exocytosis? Choose all that are correct.
(a) To take proteins to the plasma membrane
(b) To take proteins away from the plasma membrane
(c) Potential degradation of proteins
(d) To secrete proteins from the cell

2–5 What is the function of endocytosis? Choose all that are correct.
(a) To take proteins to the plasma membrane
(b) To take proteins away from the plasma membrane
(c) Potential degradation of proteins
(d) To secrete proteins from the cell

2–6 What does ‘local protein translation’ mean in neurons?
(a) Proteins are synthesized only in the nucleus.
(b) Proteins are synthesized only in the cell body.
(c) Proteins can be synthesized in dendrites.
(d) Proteins can be synthesized by a neighboring neuron.

2–7 What kinds of organelles have been localized to dendrites?
(a) Polyribosomes
(b) ER
(c) Golgi
(d) All of the above
(e) None of these are located in dendrites.

2–8 List in order of size: neurofilaments, microtubules, microfilaments.

2–9 The brains of patients with Alzheimer's disease show degradation of microtubule function, in part from over-phosphorylation of the microtubule-associated protein, tau. What might happen to neurons when microtubule function is disrupted?

2–10 **Figure Q2–10** shows an interpretive drawing of a microtubule moving rightward on a glass slide to which a substance purified from squid axoplasm had been immobilized, in the presence of ATP.

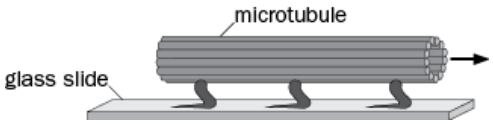

Figure Q2–10

A. What is the substance that was purified that allows movement of the microtubule?
B. What would happen if a non-hydrolyzable form of ATP was added to the solution?

2–11 In transportation within neurons, which direction is retrograde? Which direction is anterograde?

2–12 Which membrane proteins require ATP to move ions across the membrane? Choose all that apply.
(a) Symporters
(b) Pumps
(c) Antiporters
(d) Ion channels

2–13 Which membrane proteins use the electrochemical gradient to move ions across the membrane? Choose all that apply.
(a) Symporters
(b) Pumps
(c) Antiporters
(d) Ion channels

2–14 Label depolarization, repolarization, and hyperpolarization in **Figure Q2–14.**

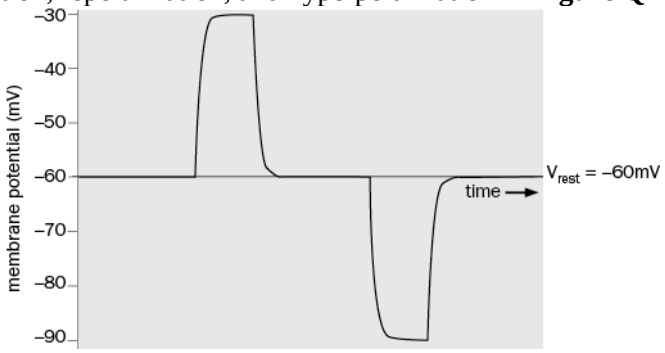

Figure Q2–14

2–15 What helps maintain the ion concentration across the membrane of neurons?
(a) The driving force for any ion
(b) Na^+/K^+ ATPase
(c) Leak K^+ channels

(d) Leak Na^+ channels

2–16 Which equation is used to determine the equilibrium potential of any ion?
(a) Ohm's law
(b) The driving force
(c) The Nernst potential
(d) The Goldman–Hodgkin–Katz equation

2–17 The equilibrium potential for any ion is the point at which two forces/gradients balance each other. What are the two forces/gradients?

2–18 In the cochlea of the ear sounds waves are turned into electrical signals through special cells called hair cells. When a wave travels through the cochlea it moves the 'hairs' and opens ion channels that are permeable to K^+ and Ca^{2+}. These 'hairs' are in a fluid that has a very high K^+ concentration compared to the inside of the cell.
A. When the ion channels open, in what direction do K^+ ions flow and why?
B. Based on this relative concentration difference of K^+, what do you predict the equilibrium potential for K^+ will be: positive, negative or zero?

2–19 According to the Goldman–Hodgkin–Katz equation, if the membrane were more permeable to Na^+ at rest, instead of K^+, what would the approximate resting membrane potential be?
(a) –70 mV
(b) +50mV
(c) –79 mV
(d) +100mV

2–20 Changes in ion conductance or ion concentration can alter the resting membrane potential of a cell. For each of the following, write in the letter indicating whether each condition would cause hyperpolarization (H), depolarization (D), or very little change (LC) in the resting membrane potential, and the reason for this change.

Condition	**Membrane potential change**	**Reason**
Increase in $[K^+]_O$	_____	_____
Increase in $[Na^+]_O$	_____	_____
Increase in K^+ permeability	_____	_____
Increase in Na^+ permeability	_____	_____

2–21
A. If there is a large voltage across a membrane and a low resistance, is the current going to be larger or small?
B. In order to have a large current, if there is a large resistance what should the voltage difference be?

2–22 What best describes current?
(a) Resistance
(b) Movement of charge
(c) Potential difference
(d) Storage of charge

2–23 What is the 'driving force'?

(a) The concentration gradient
(b) The conductance of an ion
(c) The equilibrium potential for an ion
(d) The difference between the membrane potential and equilibrium potential

2–24 Match each representative electrical component with its equivalent in a neuron.

A.	Resistor	____ membrane
B.	Capacitor	____ ion channel
C.	Battery	____ movement of ions
D.	Current	____ concentration gradient

2–25 What is the function of the 'capacitor' in a neuron? Choose all that apply.

(a) Storage of charge across the membrane
(b) To allow the movement of ions across the membrane
(c) To provide the ability to integrate signals
(d) To provide a delay in changes in voltage across the membrane

2–26 What is an RC circuit? Choose all that apply.

(a) A circuit with a resistor and capacitor
(b) An electronic representation of a biological membrane
(c) An electronic representation of voltage dependent ion channels
(d) A circuit with ions and voltage

2–27 Invertebrates and vertebrates have evolved different strategies to change the length/space constant (λ) of a neuron. For each strategy, say whether this increases or decreases the length constant and what property in the following equation it influences.

$$\lambda = \sqrt{dR_m/4R_i}$$

A. Invertebrates increased the diameter of the axon.
B. Vertebrates use myelination of the axon.

2–28 If myelin makes action conduction velocity faster, why are axons not completely covered with myelin? That is, what would happen to the electrical signal if the axon was completely covered in myelin and had no Nodes of Ranvier?

2–29

A. Label **Figure Q2–29** with the following terms: action potential threshold, action potential, subthreshold stimulus, suprathreshold stimulus.

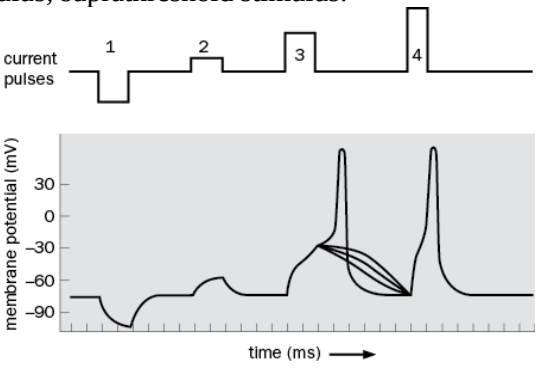

Figure Q2–29

B. In **Figure Q2–29**, stimulus 4 is of larger amplitude than stimulus 3. What happened to the action potential when a larger stimulus was provided and why?

C. In **Figure Q2–29**, what do you predict would happen if you increased the duration of stimulus 4?

How Do Electrical Signals Propagate from the Neuronal Cell Body to Its Axon Terminals?

2–30 In order to test the hypothesis that the rising phase of the action potential is caused by Na^+ influx, researchers recorded the magnitude of the action potential when in a normal solution (like sea water) and then again after increasing the extracellular Na^+ concentration. What do you predict will happen to the action potential with the increased extracellular Na^+ concentration and why? Draw the action potential on **Figure Q2–30**.

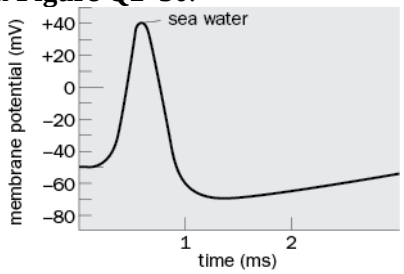

Figure Q2–30

2–31 In order to understand how currents move during an axon potential Hodgkin and Huxley used the voltage clamp technique. Why was this technique so important? Choose all that apply.

(a) It allowed the investigators to measure ions moving across single channels.

(b) It prevented the change in membrane potential associated with ions flowing across the membrane.

(c) It allowed them to calculate the conductance of the individual ions.

(d) It showed that currents vary with voltage and time.

2–32 Using the voltage clamp technique, Hodgkin and Huxley found an early inward current and a later outer current (**Figure Q2–32**, recorded current). What would happen to the current if you would apply tetrodotoxin to the bath before changing the voltage across the membrane? Please select between currents A and B and explain your answer.

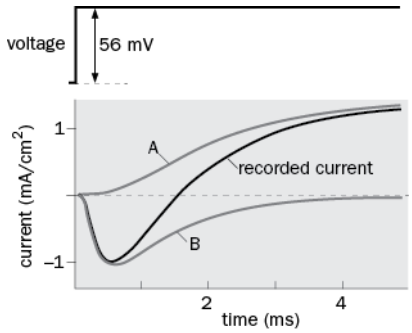

Figure Q2–32

2–33 Why does the Na^+ conductance decrease after a short time?

(a) The channels close.

(b) The cell reaches E_{Na}.

(c) The Na^+ channels inactivate.
(d) The K^+ channels start to open.

2–34 For each labeled point (A–D) on the action potential shown in **Figure Q2–34**, state whether the conductance through voltage-dependent Na^+ and K^+ channels is low, high, or no conductance. Explain. [Note: For this answer, ignore conductance through leak channels.]

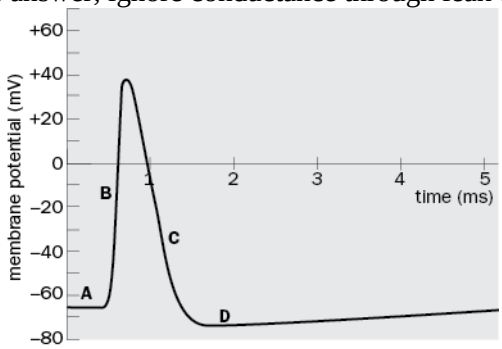

Figure Q2–34

2–35 Why are action potentials usually generated at the axon hillock in vertebrate neurons?
(a) There is a high concentration of Na^+ channels.
(b) There is a high concentration of K^+ channels.
(c) This is the point at which most synaptic contacts are made.
(d) It is located at the beginning of the axon.

2–36 Why do action potentials usually travel unidirectionally down an axon?
(a) Delayed activation of K^+ channels
(b) Inactivation of Na^+ channels
(c) Myelin prevents travel in the opposite direction.
(d) Action potentials are all-or-none.

2–37 **Figure Q2–37** shows a whole-cell sodium current (bottom trace) elicited by stepping the membrane potential from –70 mV to 0 mV (top trace). The dashed line is 0 nA. Upon depolarizing the membrane, there is an inward current. This whole-cell current is a reflection of the cumulative activity of many individual ion channels. What is the probable state of an individual sodium channel at each point (A, B, and C)?

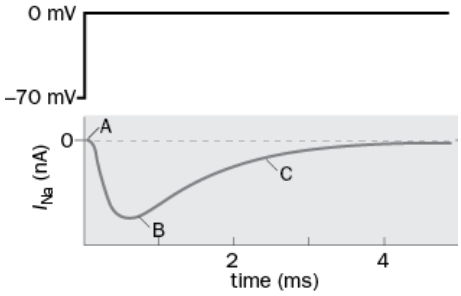

Figure Q2–37

2–38 **Figure Q2–38** shows the response of a single Na^+ channel patch clamp recording. Which individual ion channel state best describes the current in A, B, and C?

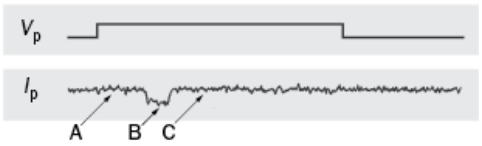

Figure Q2–38

2–39 You are in a lab and conduct a patch clamp experiment (**Figure Q2–39**) in which you change the voltage across the membrane by +20 mV (top trace). You record the resulting single channel current (lower three traces). Based on these single channel currents, what do you think the whole-cell current would look like?

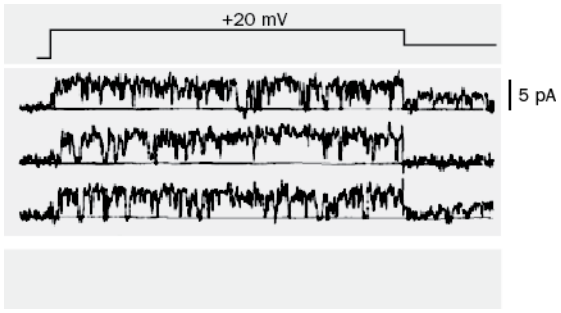

Figure Q2–39

2–40 What is the size of the primary structure of K^+ channels compared to Na^+ channels?

(a) It is twice the size.
(b) It is half the size.
(c) It is one quarter the size.
(d) It is four times the size.

2–41 How do Na^+ and K^+ ion channel structures allow them to detect changes in voltage across the membrane?

Note: Questions 2–42 and 2–43 refer to the data in Figure Q2–42. These questions may be used independently or as a group.

2–42 **Figure Q2–42** shows a patch clamp recording from the Shaker channel (ShB). What is the presumed molecular mechanism for inactivation of the channel?

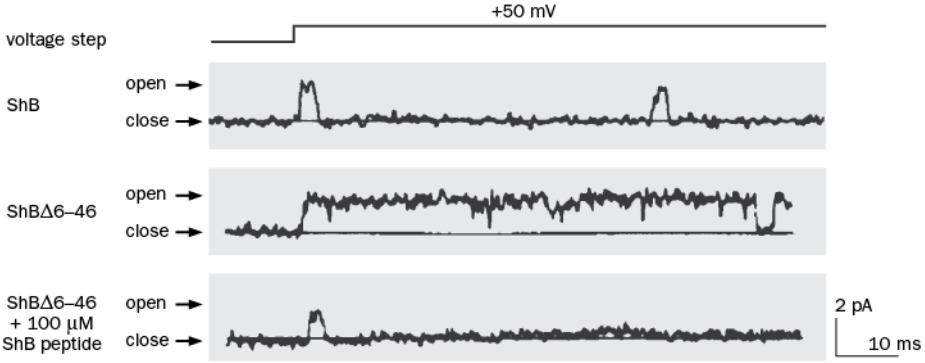

Figure Q2–42

(a) Several positively charged amino acids in S4
(b) Several negatively charge amino acids in S4
(c) The N-terminal ‘ball-and-chain’

(d) A block by Na^+ ions

2–43 In **Figure Q2–42**, amino acids 6–46 were removed from the ShB channel through mutagenesis.

A. What happened to the single channel response?

B. When the ShB peptide (the first 20 amino acids of the ShB protein) was added to the ShBΔ6–46 protein, what happened to the single channel response and what does that tell you about the function of the first 20 amino acids?

2–44 The structure of the selectivity filter is known.

A. Why are the electronegative carbonyl groups important for K^+ to move across the filter?

B. How do electrostatic forces of K^+ ions help move K^+ across the filter?

2–45 Reconstruct an action potential starting with the resting potential and ending with the voltage across the membrane coming back to rest after the action potential. Describe single channel behavior, whole cell current and/or conductance, and changes in voltage with respect to the equilibrium potential for each ion.

ANSWERS

2–1 (a)

2–2 (a)

2–3 (b)

2–4 (d) Exocytosis does not take proteins to the plasma membrane, as that is a form of transportation.

2–5 (b) Endocytosis takes proteins from the extracellular space and the membrane into the cell.

2–6 (c) In neurons proteins can be synthesized in dendrites because the molecular machinery to make proteins is located there.

2–7 (d)

2–8 Microfilaments < neurofilaments < microtubules

2–9 Axon transportation would cease, as proteins could not be transported down microtubules. After a short time, the neuron would not function and then would eventually die.

2–10

A. Kinesin (although dynein would not be a bad answer). This is from Box 2–1.
B. The microtubule would not move as you need ATP to provide energy for the kinesin.

2–11 Retrograde refers to movement toward the cell body. Anterograde refers to movement down an axon, away from the cell body.

2–12 (b) Pumps require ATP. The other choices use electrochemical gradients as the energy to move ions across the membrane.

2–13 (a), (c), and (d). All these types of transport use electrochemical gradients to move ions across the membrane. For symporters the electrochemical gradient of one ion is used to drive another ion in the same direction, up its electrochemical gradient. For antiporters, the electrochemical gradient of one ion is used to drive another ion in the opposite direction, up its electrochemical gradient.

2–14 See **Figure A2–14**. Hyperpolarization is more negative and depolarization is more positive. The first hyperpolarization and second depolarization could also be considered ‘repolarization’ as the voltage across the membrane is repolarizing back to rest.

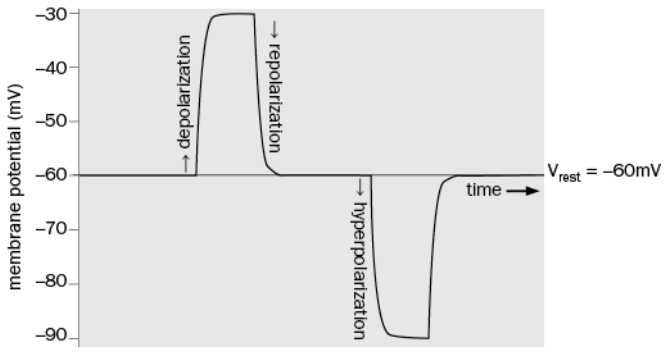

Figure A2-14

2–15 (b) Na^+ and K^+ leak into and out of the cell down their concentration gradient. This slow leak is countered, in part, by the Na^+/K^+ ATPase that uses ATP to move K^+ into the cell and Na^+ out of the cell, against their concentration gradient. Answer (a) is incorrect as the driving force is simply the difference in concentration gradient and equilibrium potential.

2–16 (b)

2–17 The chemical gradient and the electrical gradient. This comes from the Nernst equation in which the tendency of an ion to move down its concentration gradient is just offset by an equal and opposite electrical gradient.

2–18

A. The potassium will flow *into* the hair cell, down its concentration gradient.
B. Positive. Since there is more potassium outside than inside the cell, a positive potential is required to offset that concentration gradient; the log of a positive value is positive (from the Nernst potential).

2–19 (b) If we assume that the permeabilities to Na^+ and K^+ were reversed then the voltage across the membrane would be close to E_{Na} (which is about +50 to +55mV). In the Goldman–Hodgkin–Katz equation, the contributions of K^+ and Cl^- (and other ions) would be relatively small and there would be a large contribution from Na^+, so the voltage across the membrane would be close to E_{Na}.

2–20

Condition	**Membrane potential change**	**Reason**
Increase in $[K^+]_O$	D	Increasing $[K^+]_O$ results in a more depolarized E_K (closer to zero). As the cell is highly permeable to potassium at rest, a change in E_K will also depolarize the membrane potential
Increase in $[Na^+]_O$	LC	The membrane has a very low permeability to sodium at rest so there is little change on the membrane potential
Increase in K^+ permeability	LC	The permeability to K^+ is already relatively high, so there will be little change with a further increase in permeability

Increase in Na^+ permeability	D	E_{Na} is about +55 mV, increasing the permeability will increase the influence of Na^+ on the membrane potential and will drive the voltage across the membrane toward E_{Na}, which is more depolarized

2–21

A. Knowing the equation $I = V/R$, if ΔV is large and the resistance is small, the current will be large.

B. With the same equation, $I = V/R$, if the resistance is high and you want the current to be high, mathematically the voltage also has to be high.

2–22 (b) Current is produced when charged particles move.

2–23 (d) The difference between the membrane potential and equilibrium potential.

2–24 B, A, D, C

2–25 (a), (c), and (d). A capacitor gives a membrane the ability to store charge, this ability also slows down changes in voltage across the membrane. Slowing changes in voltage also allows the neuron to integrate inputs.

2–26 (a) and (b). The RC circuit is an electrical circuit with a resistor and a capacitor. It is used as a representation of a biological membrane where ion channels are resistors and the membrane acts as a capacitor. (c) is only partly correct as voltage dependent ion channels are represented by resistors, but this does not include capacitors.

2–27

A. This increases the length constant by decreasing the internal resistance (R_i) and increasing the diameter, d.

B. This increases the length constant by increasing the resistance across the membrane. Without myelin, it is like having a leaky hose; the flow of water decreases over distance due to leak out of the hose. However, if tape is put over the holes, increasing the resistance across the hose (like myelin) the water will travel further.

2–28 If axons were completely covered in myelin the current would slowly decrease down the distance of the axon to a point at which there would be no measurable current. Nodes of Ranvier contain a high density of sodium channels that regenerate the action potential to maintain the signal down the whole axon.

2–29

A. The threshold is the voltage at which an action potential is generated. In **Figure A2–29**, it is the point at which there are some ‘failures’ and a single action potential (2) The subthreshold stimulus refers to the current pulse stimulus that is given that does not generate an action potential. Either stimulus 1 or 2 are correct. The suprathreshold stimulus refers to any stimulus that generates an action potential. In this case, either of the last two stimuli is correct.

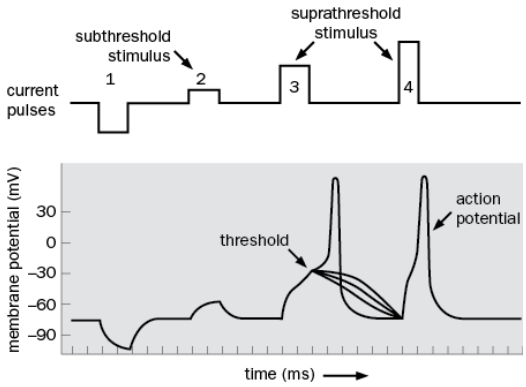

Figure A2-29

B. The rise time of the action potential is faster. This is because the larger current is able to activate more sodium channels, which brings the membrane potential to threshold faster by starting the regenerative process faster.

C. If you increase the duration of the stimulus, you will get more action potentials per unit time. If this is a neuron with different intrinsic membrane properties you may get different activity patterns, but the basic answer is an increase in frequency of action potentials.

2–30 The action potential amplitude increased. This is because E_{Na} is more positive and the membrane is very permeable to Na^+ during the rising phase of the action potential. E_{Na} is more positive because there now is a larger difference in concentration between $[Na^+]_{out}$ and $[Na^+]_{in}$ and so the electrical gradient needed to counterbalance the this difference is larger.

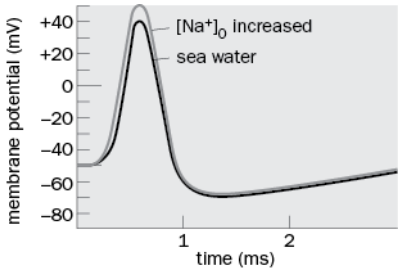

Figure A2–30

2–31 (b), (c), and (d). Ion movement across single channels was not measured until patch clamp methods were used. Voltage clamp allowed Hodgkin and Huxley to hold the voltage across the membrane constant by adding current that was equal and opposite of the current flowing across the membrane. Hodgkin and Huxley found that currents vary with voltage and with time. From measuring the currents Hodgkin and Huxley were able to calculate the membrane conductance.

2–32 Tetrodotoxin blocks voltage-dependent sodium channels. Applying tetrodotoxin would leave the potassium current, so would leave trace A. The potassium current is the outward current.

2–33 (c) Once sodium channels open they inactivate. This is a separate mechanism to closing as it involves a different change in the structure of the channel.

2–34

A. Low K^+ conductance and low Na^+ conductance. Both voltage-dependent channels are mostly closed (low probability of being open). The high K^+ conductance is through K^+ leak channels.

B. High Na^+ conductance as the sodium channels open. Low K^+ conductance as voltage-dependent K^+ channels are slower to open.
C. Low Na^+ conductance as sodium channels are inactivating. High K^+ conductance as potassium channels are open.
D. Low K^+ conductance as potassium channels are closing since the membrane is now hyperpolarized. The Na^+ conductance is basically zero since the channels are inactivated. This is why the membrane potential is near E_K.

2–35 (a) Action potentials are generated at the axon hillock because there is a high concentration of sodium channels. Opening of sodium channels is required to generate an axon potential and with a large concentration of these channels in one place the action potential threshold is decreased.

2–36 (b) Sodium channels inactivate very soon after they open. This leads to the inability of an action potential to travel in the direction the action potential was started.

2–37

A. The sodium channels have a high probability of being closed. (There is no current, therefore all sodium channels are closed.)
B. Individual sodium channels have a high probability of being open. (There is a current, which means that ions are moving across the membrane, so ion channels have to be open.)
C. Individual sodium channels have a high probability of being inactivated. (The current is quite small because large portions of sodium ion channels are inactivated.)

2–38

A. Closed
B. Open
C. Inactive

2–39 The whole cell current is a summation of the current through individual ion channels. In this case the individual channel opens almost immediately and stays open throughout the entire depolarization (on average), therefore the whole-cell current would increase almost immediately and would decrease after the voltage was returned to its starting value (**Figure A2–39**). This is an outward current similar to the delayed rectifier potassium current.

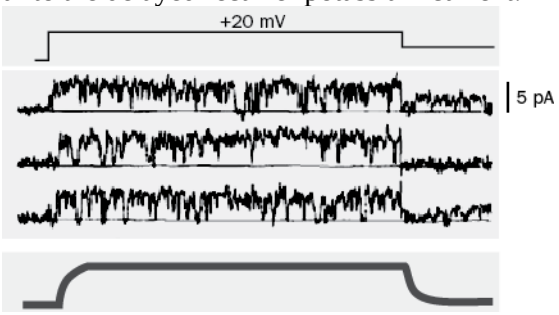

Figure A2–39

2–40 (c) A potassium channel requires four protein subunits to make up a single channel. The protein structure of a sodium channel is about four times larger than that for a single potassium channel.

2–41 There is a series of positively charged amino acids in the S4 region of the protein. When the voltage across the membrane becomes more positive inside this repels the positively charged amino acids, which changes the conformation of the protein.

2–42 (c) The ball-and-chain is a specific string of amino acids that blocks the open channel. The charges in the S4 region give the channel its voltage sensitivity. The K^+ channel is not blocked by Na^+ in normal circumstances.

2–43

A. The mean open duration of the channel increased.
B. The mean open duration decreased. This suggests that the first 20 amino acids of the protein are the 'ball' (of the ball-and-chain) that inactivates the channel. The amount of time the channel is open is greatly reduced. Since they added the first 20 amino acids back to the protein that lacked those amino acids (and amino acids that presumably make up the chain), the conclusion was that the first 20 amino acids form the ball, which physically blocks the channel.

2–44

A. They carbonyl groups mimic the stabilization of water for the potassium ion. This stabilizes the K^+ in the channel protein.
B. The electrostatic forces between the K^+ ions move potassium to the next set of carbonyl groups, down the chemical gradient of potassium. This helps K^+ to travel across the selectivity filter.

2–45 The resting potential is at about –70 mV inside the cell compared to the outside. At this point leak potassium channels are open so there is a high permeability to potassium. There is also a small Na^+ leak current so the voltage across the membrane to close to E_K, but a little more depolarized due to the influence of Na^+. Cl^- is also permeable at rest and contributes to the resting membrane potential.
Upon depolarization, at the start of an action potential, voltage-dependent sodium channels start to open and there is an increase in the sodium conductance. This increase in conductance drives the voltage across the membrane to E_{Na}. Towards the peak of the action potential the sodium channels begin to inactivate and the voltage-dependent potassium channels open. This decreases the conductance of sodium and increases the conductance of potassium, which drives the cell to E_K. At the undershoot of the action potential the sodium channels are inactivated and the sodium channels are open, so the voltage across the membrane is very close to E_K. Once the voltage-dependent sodium channels close the voltage across the membrane goes back to its resting potential.