

Cardiac Action Potential

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Page 1. Introduction

- The coordinated contractions of the heart result from electrical changes that take place in cardiac cells.

Page 2. Goals

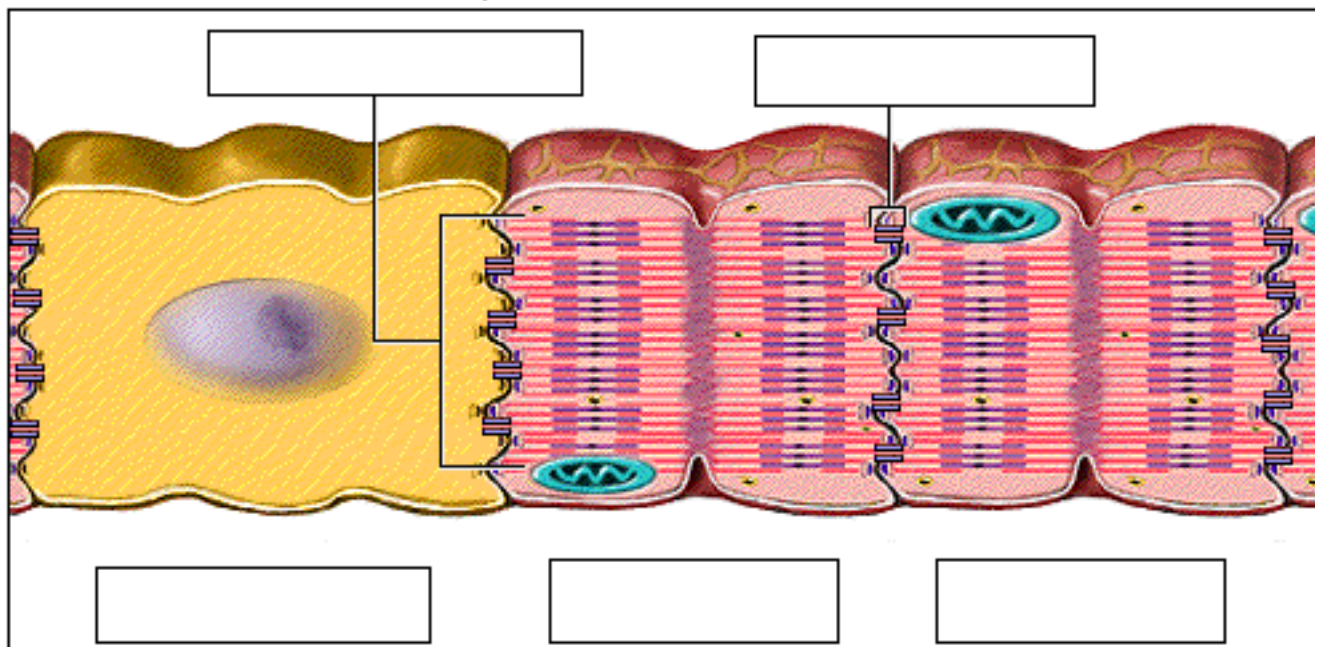
- To understand the ionic basis of the pacemaker potential and the action potential in a cardiac autorhythmic muscle cell.
- To understand the ionic basis of an action potential in a cardiac contractile (ventricular) cell.
- To understand that autorhythmic and contractile cells are electrically coupled by current that flows through gap junctions.

Page 3. Intrinsic Conduction System

- Cardiac autorhythmic cells in the intrinsic conduction system generate action potentials that spread in waves to all the cardiac contractile cells. This action causes a coordinated heart contraction. Of all the cells in the body, only heart cells are able to contract on their own without stimulation from the nervous system.

Page 4. Gap Junctions

- Action potentials generated by autorhythmic cells create waves of depolarization that spread to contractile cells via gap junctions.
- Label the parts of this diagram:



Page 5. Depolarization vs. Repolarization

- If depolarization reaches threshold, the contractile cells, in turn, generate action potentials, first depolarizing then repolarizing. After depolarization, the cardiac myofibrils in contractile cells slide over each other resulting in muscle contraction. After repolarization these cells relax.

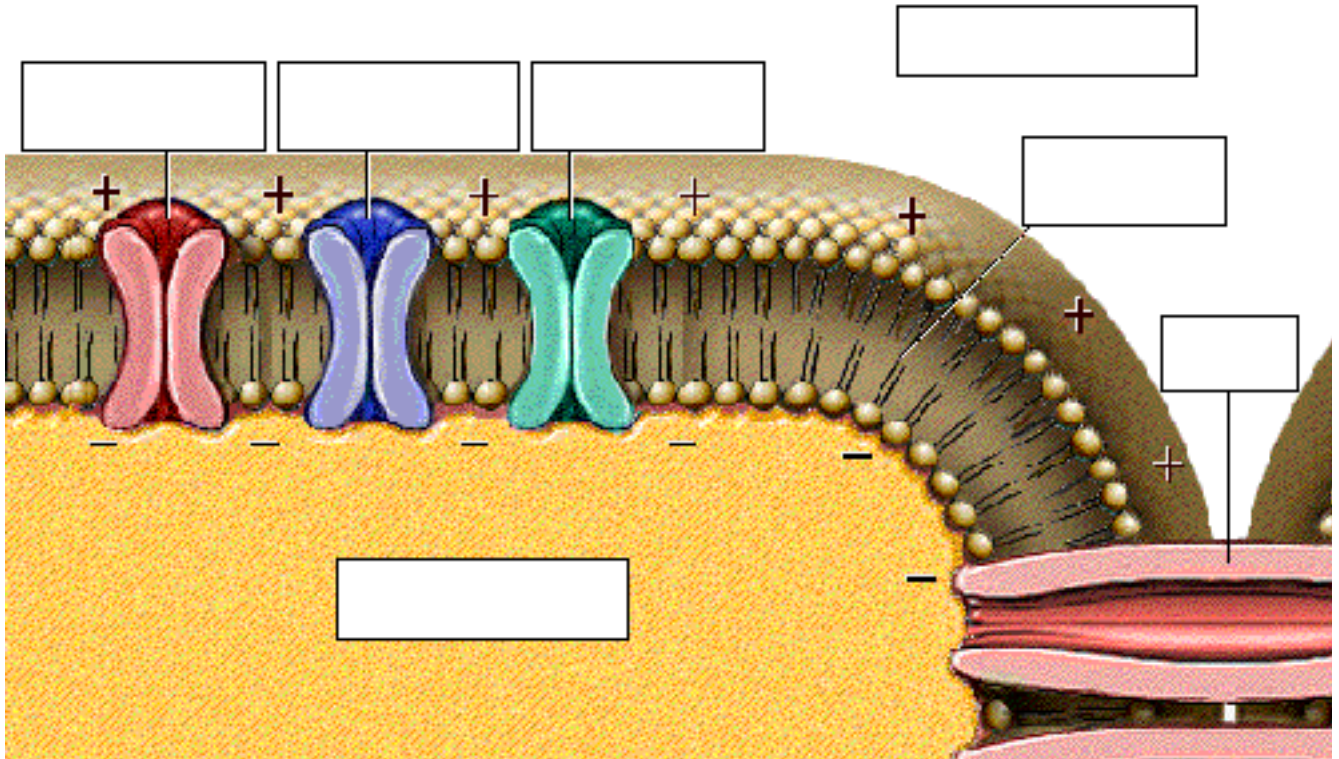
** You may repeat the animation again if you wish by clicking on the autorhythmic cell again.

** Now is a good time to go to quiz question 1:

- Click the Quiz button on the left side of the screen.
- After answering question 1, click the Back to Topic button on the left side of the screen.
- To get back to where you left off, click on the scrolling page list at the top of the screen and choose "6. Autorhythmic Cell Anatomy".

Page 6. Autorhythmic Cell Anatomy

- Embedded in the plasma membrane of an autorhythmic cell we see several protein channels that allow ions to move into or out of the cell. These are crucial for generating an action potential:
 1. Sodium Channels - allow sodium ions to enter the cell
 2. Fast Calcium Channels - allow calcium ions to enter the cell.
 3. Potassium Channels - allow potassium ions to leave the cell.
- The movement of ions affects the membrane potential (the voltage across the membrane).
- The membrane potential is a result of the relative concentrations of ions along the inside and outside of the plasma membrane.
- If there are more positive ions outside the cell, then the inside of the cell is relatively negative, as shown.
- If there are more positive ions inside the cell, then the inside of the cell is relatively more positive.
- Many transport channels are voltage-regulated. They open and close in response to specific voltage levels across the membrane.
- Gap Junction connects adjacent cardiac cells. This allows ions to pass between cells, allowing a ripple effect of initiating depolarization in one cell, and then another, and so on.
- Label the components of this autorhythmic cell:



Page 7. Action Potentials in Autorhythmic Cells

- Here is an overview of the initiation of action potentials in an autorhythmic cell.
- 1. Pacemaker Potential**
 - An autorhythmic cell has the unique ability to depolarize spontaneously, resulting in a pacemaker potential.
 - 2. Depolarization and Reversal of the Membrane Potential**
 - Once threshold is reached, an action potential is initiated, which begins with further depolarization and leads to reversal of the membrane potential.
 - 3. Repolarization**
 - Then repolarization occurs, returning the cell to its resting membrane potential.
 - The membrane potential slowly begins to slowly depolarize again and the sequence is repeated.

Page 8. Pacemaker Potential in Autorhythmic Cells

- Autorhythmic cells begin depolarizing due to a slow continuous influx of sodium, and a reduced efflux of potassium.
- As sodium ions enter the cell, the inner surface of the plasma membrane gradually becomes less negative, generating the pacemaker potential.
- Note that the cell starts out at resting membrane potential (~-60 mV), positive out, negative in.
 - There is a slow, continuous movement of sodium inside the cell. The inner membrane gradually becomes less negative, depolarizing slowly, generating the pacemaker potential.

Page 9. Depolarization in Autorhythmic Cells

- When the membrane potential gets to -40 millivolts, it has reached threshold for initiating an action potential. Fast calcium channels open and positively-charged calcium ions rush in.
- Calcium influx produces the rapidly rising phase of the action potential (depolarization), which results in the reversal of membrane potential from negative to positive inside the cell.
- Depolarization peaks at about +10 mV.

Page 10. Repolarization in Autorhythmic Cells

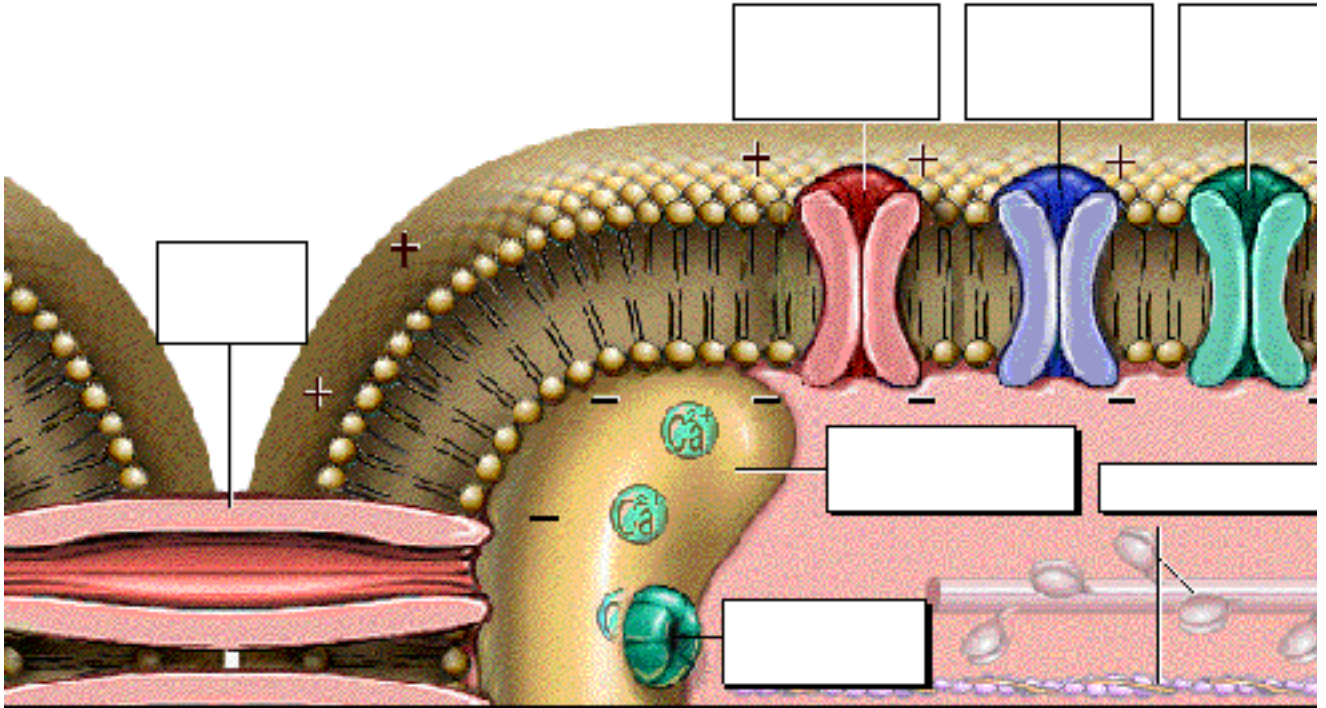
- This reversal of membrane potential triggers the opening of potassium channels, resulting in potassium rapidly leaving the cell.
- Potassium efflux produces repolarization, bringing the membrane potential back down to its resting level.
- Membrane potential goes from +10 mV to resting membrane potential (-60 mV).
- Ion pumps actively transport calcium back to the extracellular space during repolarization.
- Na⁺/K⁺ pumps also pump sodium out and potassium in.

** Now is a good time to go to quiz question 2:

- Click the Quiz button on the left side of the screen.
- Click on the scrolling page list at the top of the screen and choose "2a. Pacemaker Potential in Autorhythmic Cell".
- Work through questions 2a, 2b, and 2c.
- After answering question 2, click the Back to Topic button on the left side of the screen.
- To get back to where you left off, click on the scrolling page list at the top of the screen and choose "11. Contractile Cell Anatomy".

Page 11. Contractile Cell Anatomy

- The cardiac contractile cell relies on the autorhythmic cell to generate an action potential and pass the impulse down the line before the cell can contract.
- Like the autorhythmic cell, it has protein transport channels, but they are slightly different.
- Gap junctions link autorhythmic and contractile cells, and link contractile cells with each other.
- Notice the sarcoplasmic reticulum (SR), which is a storage site for calcium. Channels within the SR membrane allow calcium ions to be released within the cell.
- The myofibrils are the contractile units of the cardiac muscle cell.
- Label the parts of the cardiac contractile cell on the top of the next page.



Page 12. Action Potentials in Contractile Cells

- Overview of action potential generation in contractile cells:

1. Depolarization

- Once threshold is reached, the action potential starts with depolarization.

2. Plateau

- During the plateau period, ion movement balances out and the membrane potential does not change very much.

3. Repolarization

- Then repolarization begins and the membrane potential returns to its resting state.

Page 13. Ion Movement Through Gap Junction

1. Depolarization

- During depolarization in adjacent autorhythmic cells or contractile cells, positive ions move through gap junctions to adjacent contractile cells.
- This entry of positive ions creates a small voltage change, initiating depolarization.
- Note that neurotransmitters are not involved as they are with the innervation of skeletal muscles.

Page 14. Depolarization in Contractile Cells

1. Depolarization

- Voltage change stimulates opening of voltage-regulated fast sodium channels.
- Rapid influx of sodium results in depolarization and reversal of the membrane potential from negative inside the cell to positive.

Recall that for the autorhythmic cell its the rapid influx of calcium and not sodium that causes depolarization.

- Summary of Depolarization:
 - At rest, contractile cells have a resting membrane potential of about -90 mV
 - Neighboring cells (either autorhythmic or contractile cells) depolarize
 - Gap junctions open and positive ions (Ca^{+2} and Na^{+1}) move in to the contractile cells through gap junctions.
 - A small voltage change (of about 5 mV to about -85 mV) occurs which initiates depolarization.
 - Voltage gated sodium channels in the membrane of the contractile cells open allowing sodium to move into the cell.
 - This results in a reversal of charge (depolarization) (to about $+25$ mV) as sodium moves into the cell.

Page 15. Plateau Phase in Contractile Cells

2. Plateau

- Depolarization also causes opening of slow calcium channels allowing calcium entry from the extracellular space and SR.
- At the same time, potassium efflux begins.
- Slow calcium influx briefly balances the early potassium efflux, producing a plateau in the action potential tracing.
- Intracellular calcium initiates cell contraction.

Page 16. Repolarization in Contractile Cells

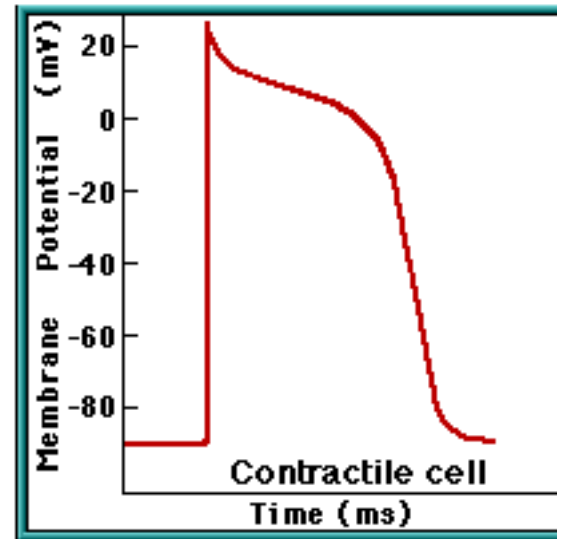
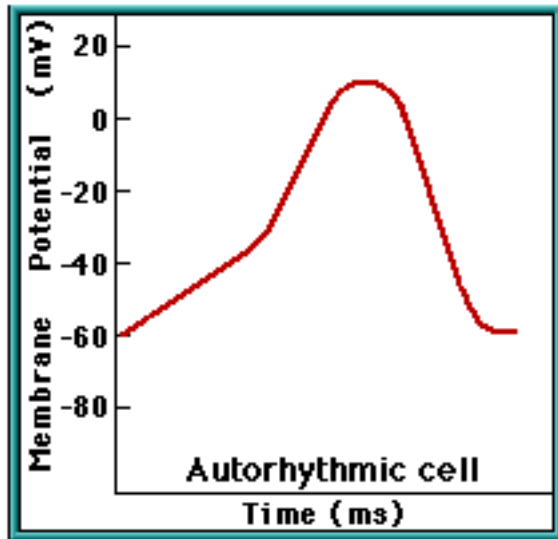
3. Repolarization

- The calcium channels close while more potassium channels open, allowing potassium to quickly leave the cell, resulting in repolarization
- The rapid potassium efflux results in repolarization bringing the membrane potential back down to its resting level. With the interior of the plasma membrane more negative than the exterior.
- Ionic pumps actively transport calcium ions are pumped back out of the cell and back into the sarcoplasmic reticulum.
- Ionic pumps also pump sodium out and potassium in.
- This pumping activity restores ion concentrations to their resting conditions
- As the calcium is pumped out of the cell and back into the SR, the contractile cell relaxes.

** Now is a good time to go to quiz questions 3 and 4:

- Click the Quiz button on the left side of the screen.
- Click on the scrolling page list at the top of the screen and choose "3. Gap Junction".
- Work through questions 3 and 4.
- After answering question 4, click the Back to Topic button on the left side of the screen.
- To get back to where you left off, click on the scrolling page list at the top of the screen and choose "17. Action Potential Wave and Graphs".

Page 17. Action Potential Waves and Graphs



** You may repeat the animation again if you wish by clicking on the autorhythmic cell again.

Page 18. Summary

- Initiation of action potential in autorhythmic cells:
 1. **Pacemaker Potential** due to influx of sodium and reduced efflux of potassium.
 2. **Depolarization** and reversal of the membrane potential due to increased influx of sodium.
 3. **Repolarization** due to efflux of potassium.
- Initiation of action potential in contractile cells:
 1. Opening of voltage-regulated fast sodium channels triggered by entry of positive ions from adjacent cell: **Depolarization** due to rapid influx of sodium.
 2. **Plateau** produced by calcium influx balancing potassium efflux.
 3. **Repolarization** due to efflux of potassium.

Notes on Quiz Questions:

Quiz Question #1. Membrane Potential

- This question asks you to drag the proper charge to the inside and outside of the cardiac contractile cells during both the repolarized and depolarized states.

Quiz Question #2a. Pacemaker Potential in Autorhythmic Cell

- This question asks you to identify the channel that brings about the pacemaker potential in a cardiac autorhythmic cell.

Quiz Question #2b. Depolarization in Autorhythmic Cell

- This question asks you to identify the channel that brings about depolarization and reversal of membrane potential in a cardiac autorhythmic cell.

Quiz Question #2c. Repolarization in Autorhythmic Cell

- This question asks you to identify the channel that brings about repolarization in a cardiac autorhythmic cell.

Quiz Question #3. Gap Junction

- This question allows you to identify the channel that allows positive ions to move from one cardiac cell to another.

Quiz Question #4a. Depolarization in Contractile Cell

- This question asks you to identify the channel that brings about depolarization in contractile cells.

Quiz Question #4b. Plateau in Contractile Cell

- This question asks you to identify the channels that brings about plateau in contractile cells.

Quiz Question #4c. Repolarization in Contractile Cell

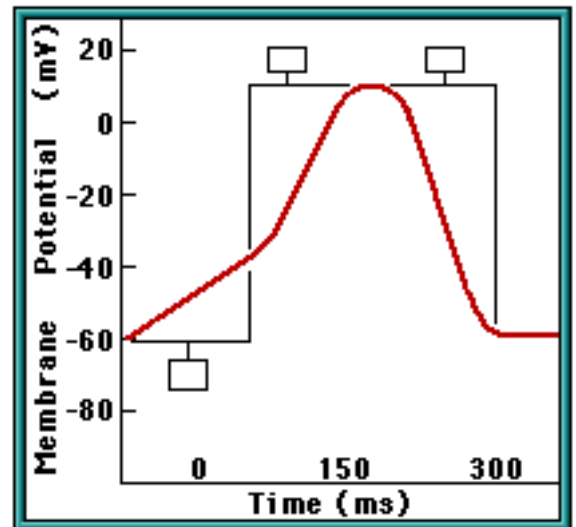
- This question asks you to identify the channel that brings about repolarization in contractile cells.

Study Questions on the Cardiac Action Potential:

1. (Page 3.) What two cell types are involved in producing a coordinated heart contraction?
2. (Page 4.) How do the cardiac autorhythmic cells and cardiac contractile cells work together to produce a coordinated heart contraction?
3. (Page 5.) Before cardiac autorhythmic and contractile cells depolarize, what is the charge inside and outside the cell.
4. (Page 5.) When cardiac autorhythmic and contractile cells depolarize, what happens to the charge inside and outside the cell.
5. (Page 5.) When cardiac autorhythmic and contractile cells repolarize, what happens to the charge inside and outside the cell.
6. (Page 5.) When do cardiac contractile cells contract and relax with respect to depolarization and repolarization of the cell.
7. (Page 6.) Embedded in the plasma membrane of an autorhythmic cell are protein channels that allow sodium, calcium, and potassium to move into or out of the cell. In which direction do the ions move through these channels?
8. (Page 6.) What is the function of gap junctions?
9. (Page 7.) What are the three steps in the initiation of action potential in an autorhythmic cell?
10. (Page 8.) What is responsible for the pacemaker potential?
11. (Pages 8-10.) What is the order of steps in an action potential within an autorhythmic cell.
 - a. Fast calcium channels open and positively-charged calcium ions rush
 - b. Depolarization peaks at about +10 mV.

- c. Autorhythmic cell starts out at resting membrane potential (~-60 mV), positive out, negative in.
 - d. When the membrane potential gets to -40 millivolts, it has reached threshold for initiating an action potential.
 - e. Potassium channels open, resulting in potassium rapidly leaving the cell.
 - f. Cell begins depolarizing due to a slow continuous influx of sodium.
 - g. Calcium influx produces the rapidly rising phase of the action potential (depolarization), which results in the reversal of membrane potential from negative to positive inside the cell.
 - h. Membrane potential goes from +10 mV to resting membrane potential (-60 mV).
12. (Page 10.) What is responsible for reestablishing ion levels in autorhythmic cells?
13. (Page 10.) Match the following events in autorhythmic cells:
- | | |
|--|-------------------------------|
| A. Repolarization | x. due to influx of sodium |
| B. Pacemaker Potential | y. due to efflux of potassium |
| C. Depolarization and reversal of the membrane potential | z. due to influx of calcium |

14. (Page 10.) Label the parts of this action potential tracing in autorhythmic cells:
- A. Repolarization
 - B. Pacemaker Potential
 - C. Depolarization and reversal of the membrane potential

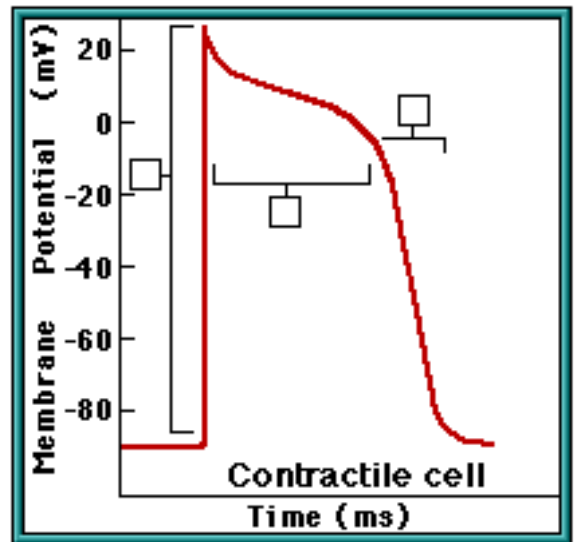


15. (Page 11.) What allows depolarization to move from autorhythmic cells to the contractile cells?
16. (Page 11.) What allows depolarization to move from one contractile cell to another contractile cells?
17. (Page 11.) Where is calcium stored within contractile cells?
18. (Page 12.) What are the three steps in the action potential in a contractile cell?
19. (Pages 14-16.) What is the order of steps in an action potential within an contractile cell? What calcium initiates cell contraction.

- b. Neighboring cells (either autorhythmic or contractile cells) depolarize.
- c. Rapid influx of sodium results in depolarization, resulting in a reversal of charge (depolarization) (to about +25 mV) as sodium moves into the cell.
- d. Ionic pumps actively transport calcium ions out of the cell and back into the sarcoplasmic reticulum. Ionic pumps also pump sodium out and potassium in, restoring ion concentrations to their resting conditions.
- e. The calcium channels close while more potassium channels open, allowing potassium to quickly leave the cell, resulting in repolarization.
- f. Gap junctions open and positive ions (Ca^{+2} and Na^{+1}) move in to the contractile cells through gap junctions.
- g. Depolarization also causes opening of slow calcium channels, allowing calcium entry from the extracellular space and SR. At the same time, potassium efflux begins producing a plateau in the action potential tracing.
- h. At rest, contractile cells have a resting membrane potential of about -90 mV.
- i. As the calcium is pumped out of the cell and back into the SR, the contractile cell relaxes.
- j. A small voltage change (of about 5 mV to about -85 mV) occurs, which initiates depolarization.

20. (Page 13.) Are neurotransmitters involved in the transmission of depolarization from one cardiac muscle cell to another?

21. (Page .) Label the parts of this action potential tracing in contractile cells.
- A. Repolarization
 - B. Depolarization
 - C. Plateau



22. (Page 16.) Match the position of the end of these action potential tracings to the corresponding appearance of the cells: (See next page.)

