

Sliding Filament Theory

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Page 1. Introduction

- When a muscle cell contracts, the thin filaments slide past the thick filaments, and the sarcomere shortens.

Page 2. Goals

- To explore the molecular structure and functional features of the thin and thick filaments.
- To understand the sequence of events in a single cross bridge cycle.
- To examine the sequence of events in multiple cross bridge cycling.

Page 3. Molecular Participants

- The chemical players in muscle contraction are:
 1. myosin (protein)
 2. actin (protein)
 3. tropomyosin (protein)
 4. troponin (protein)
 5. ATP (nucleotide)
 6. calcium ions

Page 4. Sarcomere

- The next several pages explain how each of these chemicals participate in the contraction of a sarcomere.

Page 5. Myosin

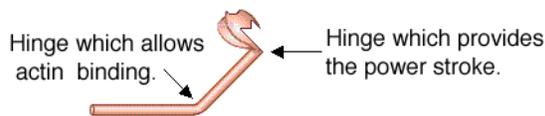
- Myosin is a protein molecule found in the thick filaments.

Page 6. Myosin Molecule with Hinged Head

- Myosin has a tail and two heads (called cross bridges) which will move back and forth, providing the power stroke for muscle contraction.

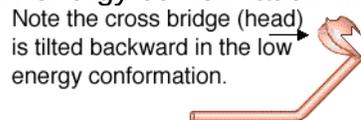
Page 7. Myosin Molecule with Hinged Head and Tail

- The tail of myosin has a hinge which allows vertical movement so that the cross-bridge can bind to actin.



Page 8. Myosin ATP Binding Site

- The cross bridge (head) of myosin has a binding site for ATP.
- Myosin is in its low energy conformation when the cross bridge is in this position:

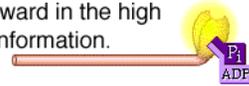


- ** Note: The term "conformation" is often used to indicate the shape of a protein. Proteins often change their shape or conformation as they function.

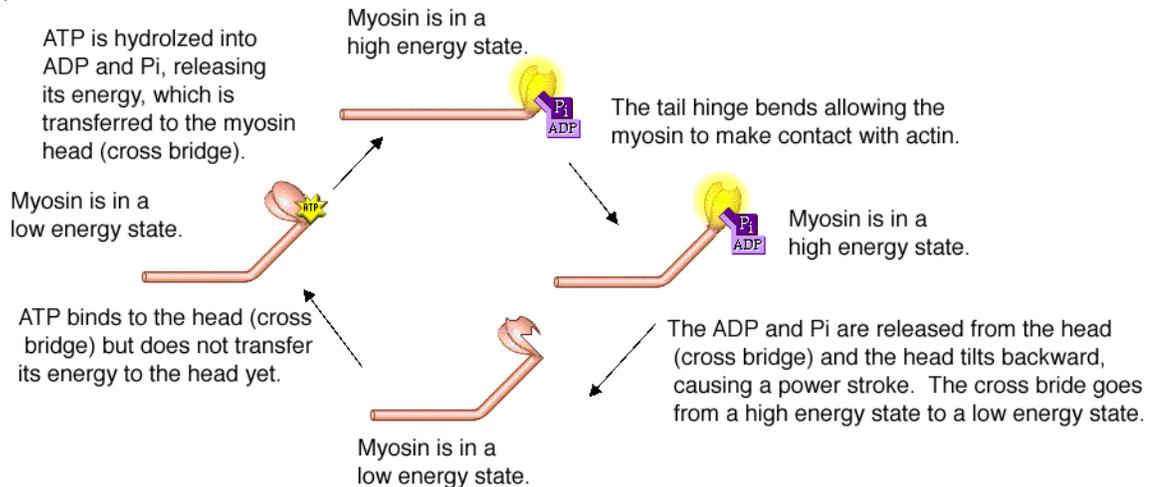
Page 9. Energized Cross Bridge

- ATP is a molecule with a high chemical energy. ATP binds to myosin heads when they are tilted back in their low energy position. When ATP is hydrolyzed into ADP and phosphate, the energy is released and transferred to the myosin head.
- Note that the ATP is glowing yellow indicating that it's in a high energy state. After the ATP has been hydrolyzed to ADP and phosphate, the energy is transferred to the myosin head. Now the head is glowing to show that it's high energy. When the myosin head is pointing up, it is in a high energy state.

Note the cross bridge (head) is tilted upward in the high energy conformation.



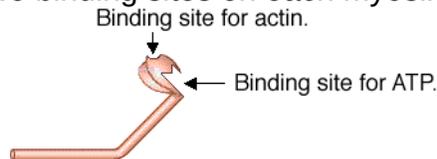
- As myosin functions within muscle cells, it undergoes the following four steps:



** This may seem like a lot of detail at this point, but later on this will be very important. At that time you may want to come back to this to review.

Page 10. Actin Binding Site on Myosin

- There are two binding sites on each myosin head, one for ATP and one for actin.



Page 11. Thin Filaments of the Sarcomere

- Thin filaments are made of these three protein molecules:
 1. actin
 2. tropomyosin
 3. troponin

Page 12. Actin

- The major component of the thin filament, actin is composed of a double strand of actin subunits each of which contain myosin binding sites.

Page 13. Tropomyosin

- The regulatory protein, tropomyosin, is also part of the thin filament. Tropomyosin twists around the actin. When the sarcomere is not shortening, the position of the tropomyosin covers the binding sites on the actin subunits and prevents myosin cross bridge binding.

Page 14. Troponin

- Troponin, which is found periodically along the tropomyosin strand, functions to move the tropomyosin aside, exposing the myosin binding sites.

Page 15. Calcium Ions

- Role of Calcium in Muscle Contraction:
Action Potential Occurs
↓
Calcium Ions are Released from the Terminal Cisternae
↓
Calcium Ions then Bind to Troponin
↓
Tropomyosin Moves Away from the Myosin Binding Sites on Actin

Page 16. Review of Molecular Participants

- Review of participants in the Cross Bridge Cycle:

<u>Participant</u>	<u>Will bind to:</u>
1. Myosin	ATP, Actin
2. Actin	Myosin, Troponin
3. Tropomyosin	Troponin
4. Troponin	Calcium, Tropomyosin, Actin
5. ATP	Myosin
6. Calcium ions	Troponin

- ** Now is a good time to go to quiz questions 1-6, 8, and 9:
- Click the Quiz button on the left side of the screen.
 - Answer questions 1-6, skip over question 7, then answer questions 8 and 9.
 - After answering question 9, 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. Overview: Single Cross Bridge Cycle".

Page 17. Overview: Single Cross Bridge Cycle

- This animation shows a single cross bridge cycle.
- ** There's a lot of important information in this animation, but don't worry about the details now, the animation will be explained over the next few pages, then you will be able to view it again.

Page 18. Six Steps of Cross Bridge Cycling

- Cross bridge cycling is broken down into six steps which will be explained in detail during the next six pages.

Page 19. Step 1: Exposure of Binding Sites on Actin

- Detail of steps required to expose the binding sites on actin:
 - Presence of an action potential in the muscle cell membrane.
↓
 - Release of calcium ions from the terminal cisternae.
↓
 - Calcium ions rush into the cytosol and bind to the troponin.
↓
 - There is a change in the conformation of the troponin-tropomyosin complex.
↓
 - This tropomyosin slides over, exposing the binding sites on actin.

Page 20. Step 2: Binding of Myosin to Actin

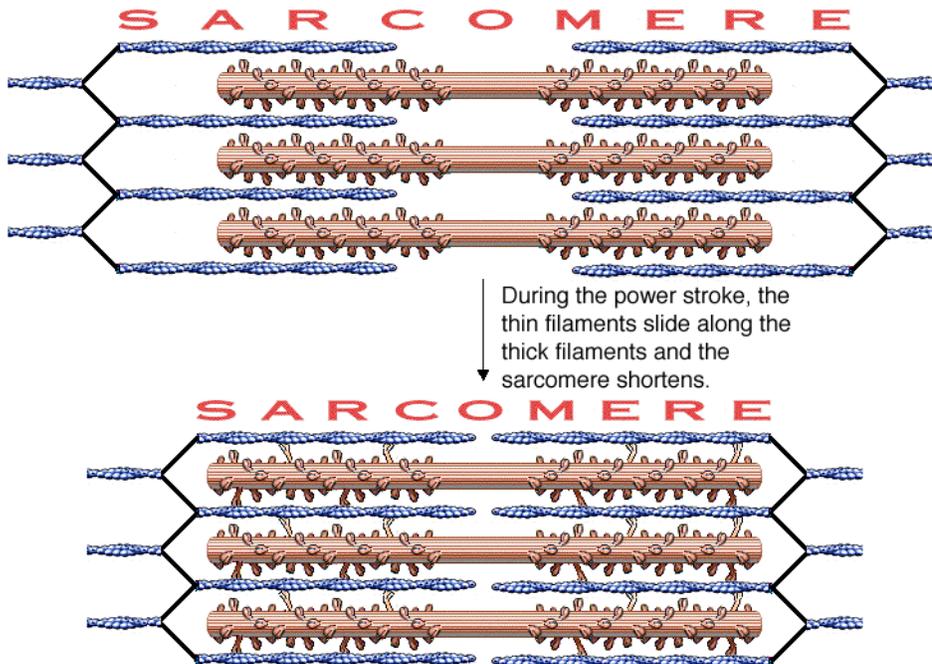
- The animation shows the hinge on the tail of the myosin bending and the energized myosin head binding into the actin.
- ** Note during this entire step, the myosin head is in its high energy, upright position. If it was tilted backward, in its low energy position, the actin binding site would not be in the proper position to bind the actin.

Page 21. Step 3: Power Stroke of the Cross Bridge

- Detail of steps shown in this animation:
 - The ADP and Pi are released from the actin.
↓
 - The myosin head (cross bridge) tilts backward.

↓

The power stroke occurs as the thin filament is pulled inward toward the center of the sarcomere.



- There has been a transfer of energy from the myosin head to the movement of the thin filament.

Page 22. Step 4: Disconnecting the Cross Bridge

- This animation shows ATP binding to the cross bridge, allowing the cross bridge to disconnect from the actin.
- ** Note that even though the ATP has bound, the energy has not yet been transferred from the ATP to the cross bridge since the head is still tilted backward.

Page 23. Step 5: Re-energizing the Cross Bridge

- In this animation, ATP is hydrolyzed into ADP and phosphate. The energy (yellow glow) is transferred from the ATP to the myosin cross bridge, which points upward.

Page 24. Step 6 Removal of Calcium Ions

- Detail of steps in this animation:
 - Calcium ions fall off the troponin.
 - ↓
 - Calcium is taken back up into the sarcoplasmic reticulum.
 - ↓
 - Tropomyosin covers the binding sites on actin.

- ** Note: Since the terminal cisternae and the sarcoplasmic reticulum are continuous, the pumping of calcium ions back into the sarcoplasmic reticulum causes an increase in calcium ions within the terminal cisternae as well. This animation shows the calcium ions being pumped back into the terminal cisternae, but they are really pumped back in along the length of the sarcoplasmic reticulum.

Page 25. Calcium Pumps

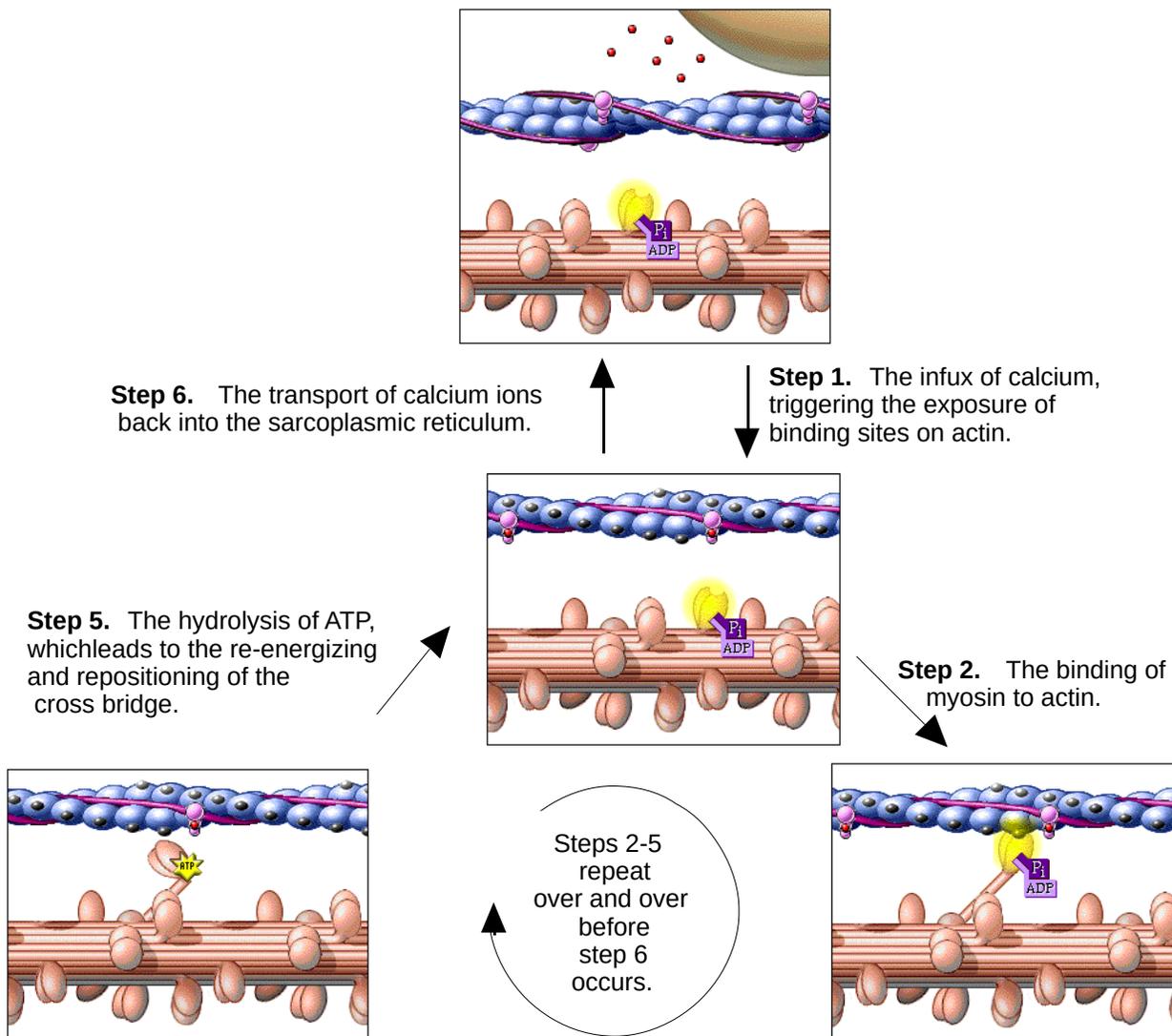
- This animation shows how calcium ions are pumped back into the sarcoplasmic reticulum. Two calcium ions enter the pump (transport protein embedded in the membrane of the SR). ATP binds to the pump and is hydrolyzed into ADP and Pi. The energy released from ATP hydrolysis is used to change the conformation of the pump, allowing the calcium ions to

move into the lumen of the SR. ADP and Pi fall off the pump, allowing it to return to its original conformation.

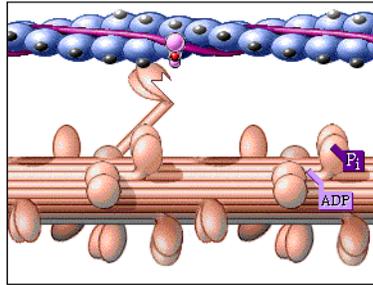
- In a relaxed muscle cell, the concentration of calcium ions about 10,000 lower in the cytosol than in the SR. During a muscle contraction, the concentration of calcium in the cytosol increases, but it is still higher inside the SR. To move the calcium against the gradient, from the lower concentration in the cytosol to the higher concentration inside the SR, Active transport is needed.

Page 26. Review: Single Cross Bridge Cycle

- This animation reviews the entire process of a cross bridge cycle.
- ** Note: If these six steps occurred exactly as shown in the animation, the sarcomere would not move very far - it would only shorten about 1%. In the contraction of a typical sarcomere, step 1 occurs then steps 2-5 repeat themselves over and over again, before step 6 occurs. This allows the thin filament to slide all the way inward. Steps 2-5 repeat themselves over and over as long as both ATP and calcium ions are present.
- Try to pick out these six steps:



Step 4. The binding of ATP to the cross bridge, which results in the cross bridge disconnecting from actin.



Step 3. The power stroke of the cross bridge that causes the sliding of the thin filaments.

** Now is a good time to go to quiz questions 10-13, and 15:

- 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 "10. What step just occurred?".
- Answer questions 10, 11, 12, 13, skip over question 14, then answer question 15.
- After answering question 13, 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 "27. Multiple Cross Bridge Cycles".

Page 27. Multiple Cross Bridge Cycles

- During the contraction of a sarcomere about half of the cross bridges are attached to actin and about half are bound at any given time. If all the cross bridges detached at the same time, then the thin filament would slide back on the thick filament.

** Note: Many myosins (about 200) make up each thick filament - so there are many myosin heads (cross bridges) available to bind the thin filament. In this animation you see only four of these cross bridges, but keep in mind there are many more on each thick filament.

Page 28. Multiple Myofilaments

- Many power strokes occur to bring the Z lines of the sarcomere closer together during the contraction of a muscle cell. During relaxation, the myosin heads detach from the actin and the thin filaments slide back to their resting position.
- The width of the H zone decreases during a contraction and increases during relaxation.
- The length of the sarcomere shortens during a contraction, but the thin and thick filaments do not shorten, they just slide by each other.

** This is an important animation. View it several times to make sure to understand the theory here. Remember as long as calcium ions and ATP are present, the thin filaments slide toward the center of the sarcomere. When the calcium is taken back up into the SR, then all the cross bridges let go and the thin filaments passively slide back to their resting position.

Page 29. Review of the Role of ATP

- Summary of the role that ATP plays in the contraction of muscle:
 1. ATP transfers its energy to the myosin cross bridge, which in turn energizes the power stroke.
 2. ATP disconnects the myosin cross bridge from the binding site on actin.
 3. ATP fuels the pump that actively transports calcium ions back into the sarcoplasmic reticulum.

Page 30. Summary

- The sequence of events in a single cross bridge cycle includes:
 1. Influx of calcium, triggering the exposure of binding sites on actin.
 2. The binding of myosin to actin.
 3. The power stroke of the cross bridge that causes the sliding of the thin filaments.
 4. The binding of ATP to the cross bridge, which results in the cross bridge disconnecting from actin.
 5. The hydrolysis of ATP, which leads to the re-energizing and repositioning of the cross bridge.
 6. The transport of calcium ions back into the sarcoplasmic reticulum.

- Multiple cross bridge cycling is coordinated sequentially to prevent all cross bridges from either being connected or disconnected at the same time.

** Now is a good time to go to quiz questions 7 and 14:

- 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 "7. Disconnects the Cross Bridge".
- Answer question 7 then click on the scrolling page list at the top of the screen and choose "14. Effect of ATP Depletion".

Notes on Quiz Questions:

Quiz Question #1. Participants in Sliding Filament Theory

- This question allows you to name the six chemicals which participate in the sliding filament theory of muscle contraction.

Quiz Question #2. Binding Site for Calcium Ions

- This question allows you to choose the participant that binds calcium.

Quiz Question #3. Connected to the Z Line

- This question allows you to choose the participant that is connected to the Z line.

** You may need to review: Anatomy Review: Skeletal Muscle Tissue p. 9.

Quiz Question #4. Composes the Thick Filament

- This question allows you to choose the participant that the thick filament is made of.

Quiz Question #5. Makes up the Thin Filament

- This question allows you to choose the participants that the thin filament is made of.

Quiz Question #6. Binding Site for ATP

- This question allows you to choose the participant that has a binding site for ATP.

Quiz Question #7. Disconnects the Cross Bridge

- This question allows you to choose the participant that is responsible for disconnecting the cross bridge.

Quiz Question #8. Covers Binding Sites on Actin

- This question allows you to choose the participant that covers the binding sites on actin.

Quiz Question #9. Stored in the Terminal Cisternae

- This question allows you to choose the participant that is stored in the terminal cisternae.

Quiz Question #10. What Step Just Occurred?

- In this question, you are shown a step of cross bridge cycle and asked what just occurred.

Quiz Question #11. What Step Will Come Next?

- In this question, you are shown a step of cross bridge cycle and asked what will happen next.

Quiz Question #12. What Has Just Occurred?

- In this question, you are shown a step of cross bridge cycle and asked what just occurred.

Quiz Question #13. What Step Will Come Next?

- In this question, you are shown a step of cross bridge cycle and asked what will happen next.

Quiz Question #14. Effect of ATP Depletion

- This question will ask you what will happen if ATP is depleted in the muscle.

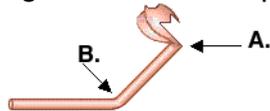
- An animation shows what happens in rigor mortis. Upon death, the body can't make more ATP, so ATP is unavailable to detach the cross bridges. The muscle contracts and can't relax.

Quiz Question #15. Events in a Single Cross Bridge Cycle

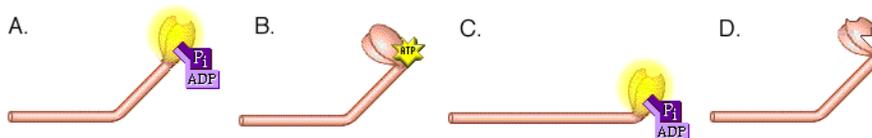
- This question asks you to list the steps in a single cross bridge cycle. Start at the top "gold bar". Hold down the mouse button and a list of options will appear. Drag the cursor to the first step in a single cross bridge cycle. Continue down the list - then check your answer.

Study Questions on the Sliding Filament Theory:

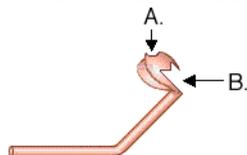
1. (Page 1.) According to the sliding filament theory, when a muscle cell contracts, the _____ filaments slide past the _____ filaments and the _____ shortens.
2. (Page 3.) List the six most important chemicals involved in muscle contraction.
3. (Page 5.) Where is myosin found in skeletal muscle cells?
 - a. in the thin filaments
 - b. in the thick filaments
 - c. in the sarcoplasmic reticulum
 - d. in the terminal cisternae
 - e. in the T tubules
4. (Page 6,7)
 - a. What are the two parts to a myosin molecule?
 - b. Which part moves providing the power stroke for muscle contraction?
 - c. Which part of the myosin molecule has a hinge which allows vertical movement so that the cross-bridge can bind to actin?
5. (Page 7.) In this diagram of actin, which hinge allows for vertical movement necessary for actin binding and which hinge allows for the power stroke cycle?



6. (Page 9.) Which of these are high energy conformations of myosin? Why?



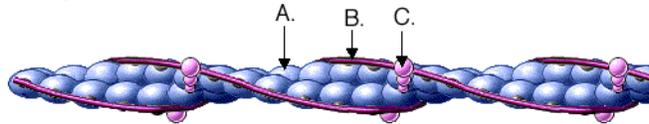
7. (Page 8,10.) What two important binding sites are found on the cross bridges (heads) of myosin?
8. (Page 10.) What binds at each of these sites on myosin?



9. (Page 11.) What three protein molecules are the thin filaments made of?
10. (Page 12.) Each subunit on actin contains binding sites for _____.
11. (Page 13.) What is the function of tropomyosin?

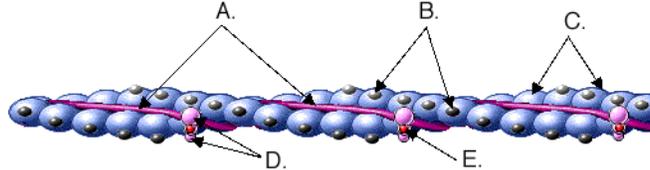
12. (Page 14.) What is the function of troponin?

13. (Page 14.) Identify the parts of the thin filament below.



14. (Page 15.) What causes the tropomyosin to move away from the myosin binding sites on the actin?

15. (Page 15.) Identify the parts of the thin filament below.



16. (Page 16). a. Which of the following will attach to myosin?
actin tropomyosin troponin ATP calcium ions

b. Which of the following will attach to actin?
actin tropomyosin troponin ATP calcium ions

c. Which of the following will attach to troponin?
myosin tropomyosin actin ATP calcium ions

17. (Page 19.) What causes the release of calcium ions into the cytosol from the terminal cisternae?

18. (Page 19.) What causes the myosin binding sites on actin to be exposed?

19. (Page 20.) What happens after the tropomyosin moves over, exposing the binding sites on the actin?

20. (Page 21.) What is it called when the cross bridge flexes, pulling the filament inward toward the center of the sarcomere?

21. (Page 21.) What happens to the myosin head (cross bridge) when the power stroke occurs?

22. (Page 22.) What causes the myosin heads (cross bridges) to disconnect from the actin?

23. (Page 23.) What causes the myosin cross bridges to go from their tilted state to their upright, high energy state?

24. (Page 24.) What causes the tropomyosin to cover back over the actin binding sites?

25. (Page 25.) What is required to move the calcium ions from the cytosol back into the sarcoplasmic reticulum?

26. (Page 26.) List the following steps in the order they would occur in a single cross bridge cycle.

- _____ a. ATP binds to the cross bridge and the cross bridge disconnecting from actin.
- _____ b. Myosin bind to actin.
- _____ c. Calcium ions are transported back into the sarcoplasmic reticulum.
- _____ d. Presence of calcium ions in the cytosol trigger the exposure of binding sites on actin.
- _____ e. The power stroke occurs.

_____ f. ATP is hydrolyzed, leading to the re-energizing and repositioning of the cross bridge.

27. (Page 27.) What would happen all the myosin cross bridges were synchronized (doing the same thing at the same time)?
28. (Page 28.) During the contraction of a muscle cell, what is happening to
- the length of the sarcomere?
 - the position of the Z lines with respect to one another?
 - the length of the thin filament?
 - the length of the thick filament?
 - the width of the H zone?
29. (Page 28.) After a sarcomere has contracted fully and the calcium ion concentration within the cytosol decreases, what happens within the sarcomere?
30. (Page 29.) Which of these is not a role of ATP in muscle contraction?
- Allows the tropomyosin to move over, exposing the myosin binding sites on actin.
 - Actively transports calcium ions into the sarcoplasmic reticulum.
 - Energizes the power stroke of the myosin cross bridge.
 - Disconnects the myosin cross bridge from the binding site on actin at the conclusion of a power stroke.