# Muscle Contraction

## A BIOCHEMICAL PERSPECTIVE

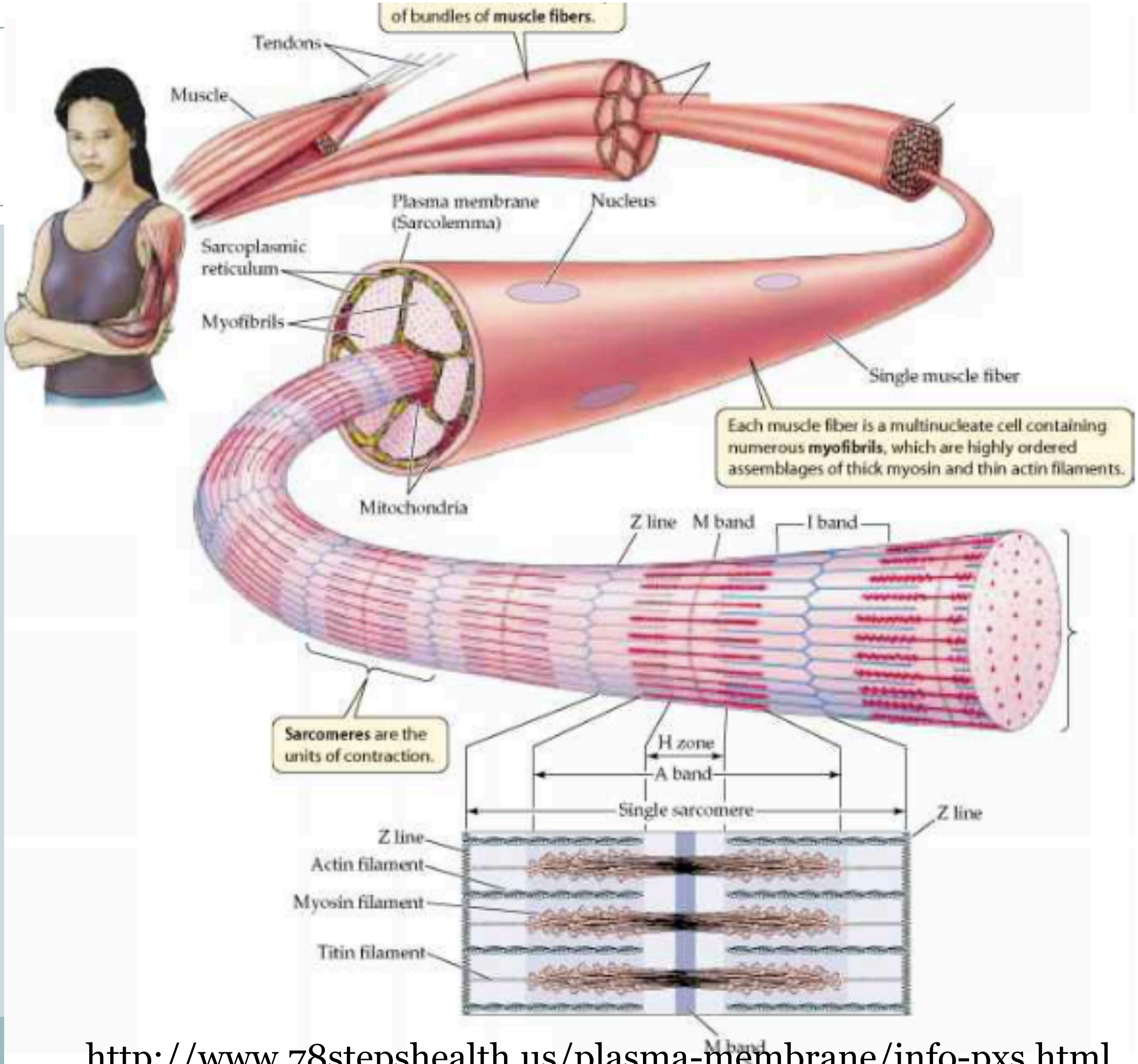
This presentation was last edited Oct 2016, by Koni Stone, Professor of Chemistry
California State University, Stanislaus

# Muscle cells

- Myoblasts are large fused cells in muscle tissue.
  - They have many nuclei and mitochondria
  - There is one plasma membrane (sarcolemma)
    - Invaginations in the sarcolemma create a network of tubules that increase the surface area for oxygen exchange.
- Myofibrils are the machinery that make the muscles contract and do work. (Like moving your eyes as you read this.)
- Each myofibril contains myofilaments and is surrounded by a sarcoplasmic reticulum.
  - This membrane bound organelle stores $Ca^{+2}$
  - A specialized pump (SERCA) is used to move $Ca^{+2}$ into the sarcoplasmic reticulum (sign up for CHEM 4420 to learn more!)

# Proteins in the Muscle fiber

- Sarcomeres are the core building block of a muscle cell. They contain myofilaments.
- Each myofilament has thick and thin filaments that are in hexagonal arrays and anchored to the proteins in a Z disk.
- Thick filaments: myosin, connected to the Z disk proteins by titan. Myosin is a heterohexamer. There are two heavy chains that consist of a long alpha helix connected to a head group. The head groups bind actin and hydrolyze ATP to cause muscle contraction. The two heavy chain alpha helices form a coiled coil. There are two light chains bound to the region between the head group and the coiled coil. There are a total of four light chains: two regulatory and two "essential" light chains.
- Thin filaments: polymers of actin that are bound to troponin(three subunits TnC, TnT, TnI) and wrapped in tropomyosin (a coiled coil of two α-helices).
- Z disk proteins: vimentin, desmin, α-actinin

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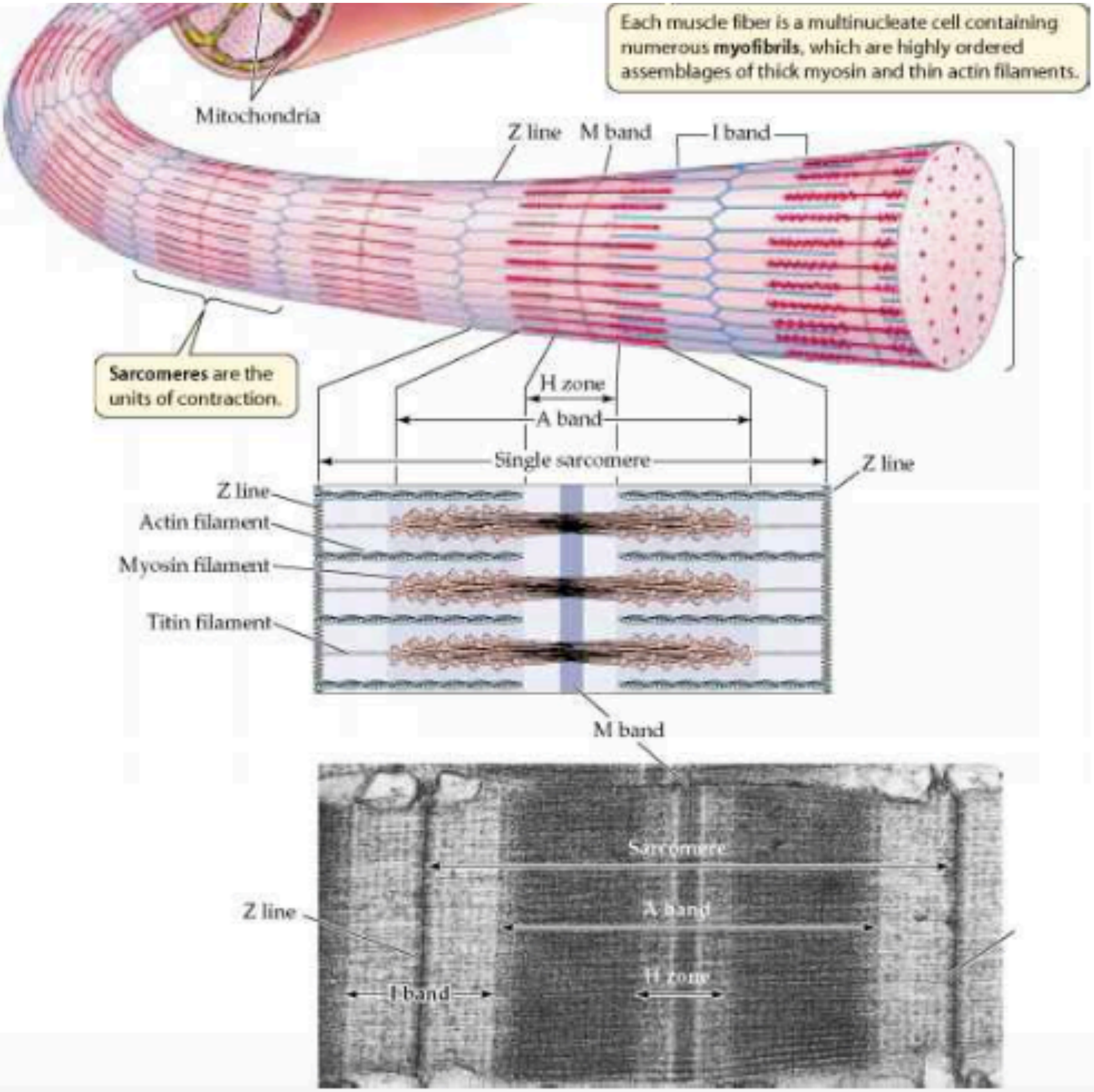


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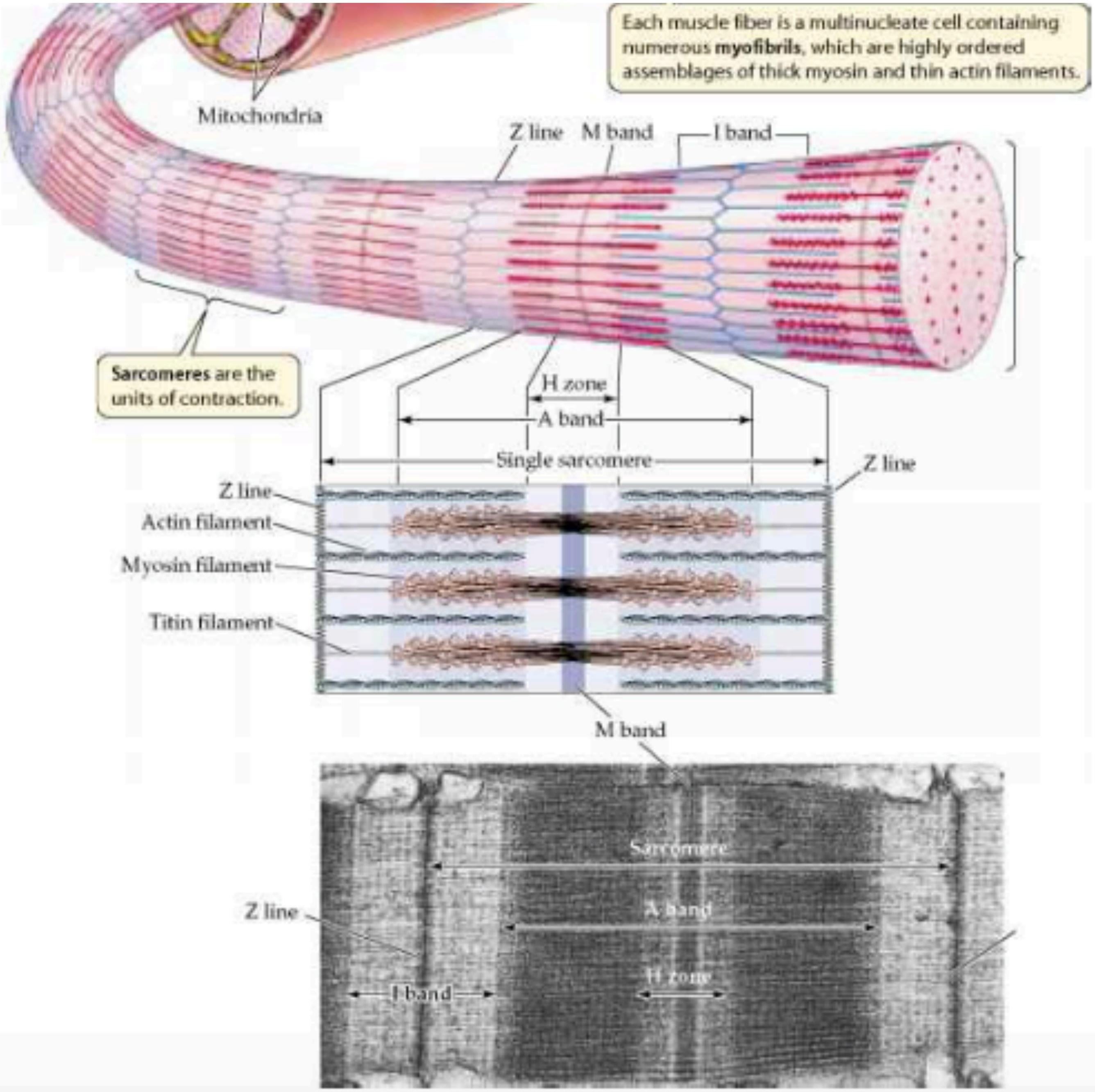
# The Power Stroke

- Myosin filaments slide past the actin filaments, using a racheting movement
- There are five steps to the power stroke
- Each power stroke moves the myosin filament 70 Angtroms ($70 \times 10^{-10}$ m)
- Myosin is attached to the Z line proteins, so as it moves, it brings the Z lines closer together.
- The A band remains the same size
- The I band becomes smaller

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# Five Steps to a Power Stroke

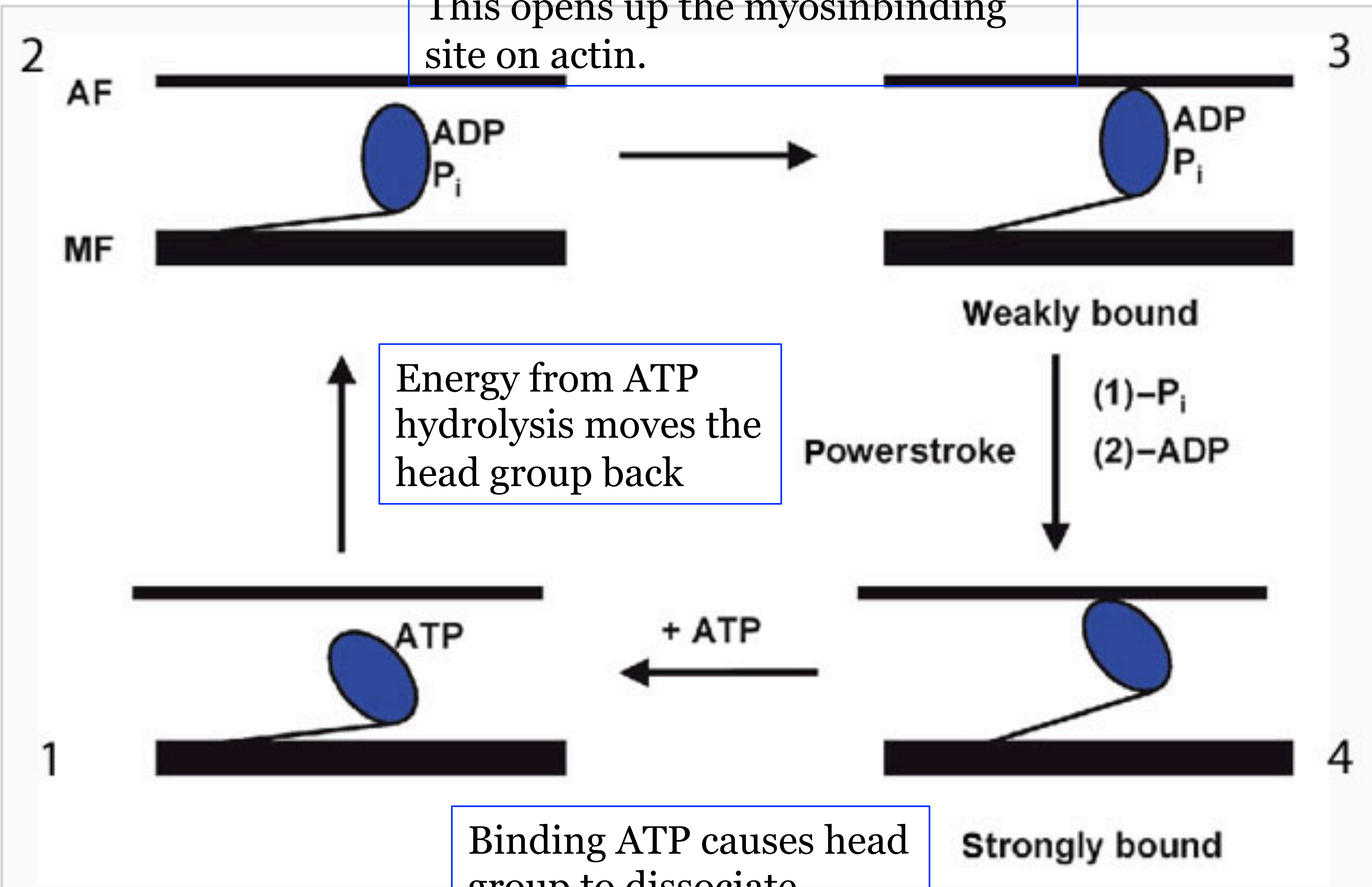
- In the relaxed state, tropomyosin is wrapped around the actin filament and troponin is bound to both.
- This complex blocks the binding of myosin to the actin filament.

1. Nerves send a signal to the muscle ("hey, that pencil needs to be picked up"). The signal releases $Ca^{+2}$ from the sarcoplasmic reticulum and it binds to TnC. This causes a shape change in the troponin/tropomyosin/actin filament that opens up the site on actin that binds myosin.

# More steps…

2. Myosin binds to actin, this binding causes a shape change in the myosin head group that releases Pi (inorganic phosphate ion).
3. The departure of Pi causes the myosin head group to move forward (towards its tail). This drags the actin to the center of the sarcomere, compresses the titan protein and moves the Z disk proteins closer together.
4. ADP departs, making room for an ATP to bind. Once ATP is bound, the myosin dissociates from the actin. If no $Ca^{+2}$ is present, the troponin and tropomyosin revert back to covering up the binding site, titan is no longer compressed and the Z disks move further apart.
5. ATP is hydrolyzed and the energy is used to move the head group back, ADP and Pi remain bound to the myosin head group. The head group is cocked and ready to bind actin. If $Ca^{+2}$ is present, the cycle repeats and the muscle is contracted further, moving the Z disks closer together.

Ca$^{+2}$ ions bind troponin C.
This opens up the myosinbinding site on actin.




Energy from ATP hydrolysis moves the head group back

Binding ATP causes head group to dissociate

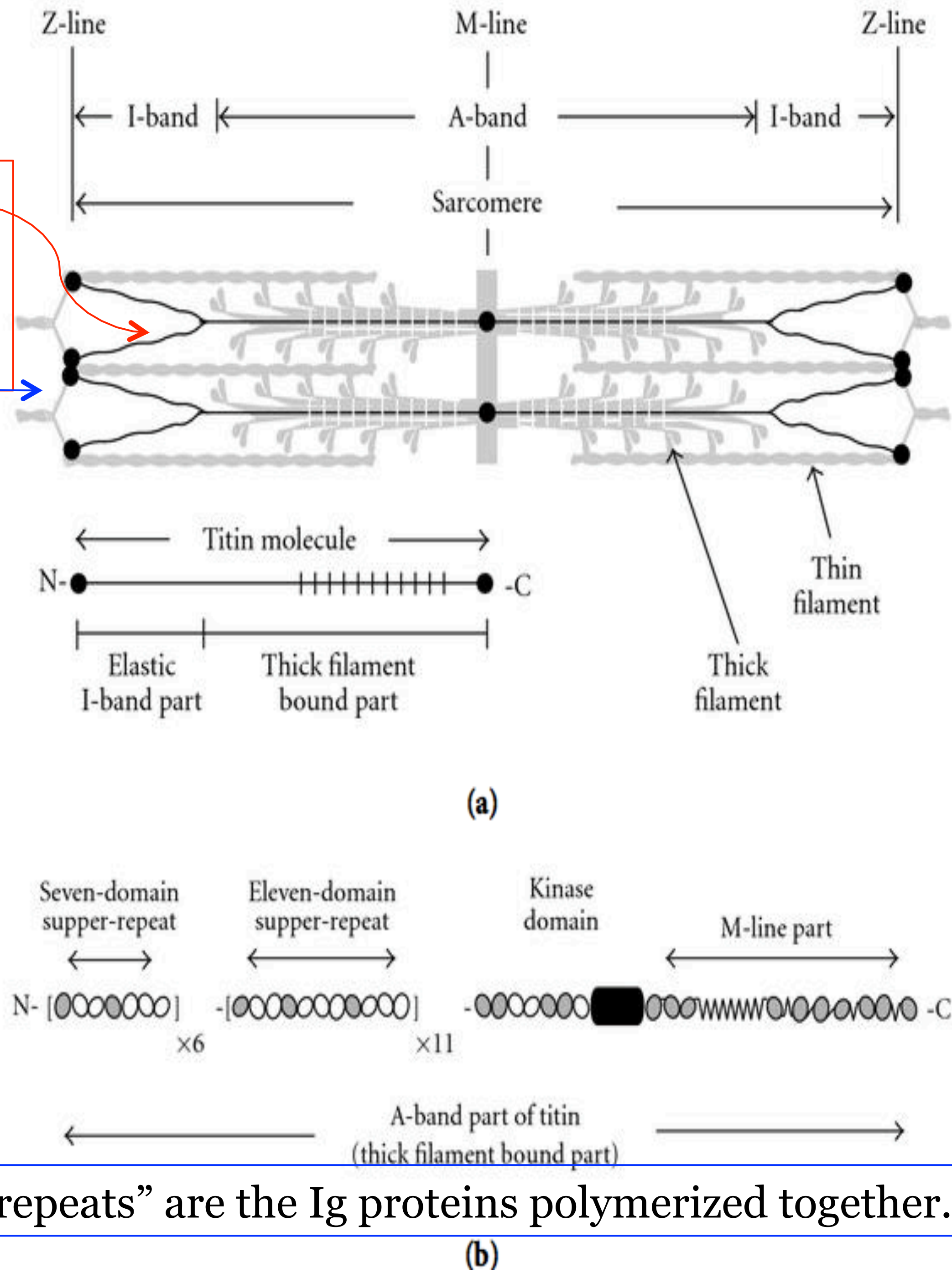
**Figure 4: Illustration of the cycle of changes in myosin shape during cross-bridge cycling (1, 2, 3, and 4)**

ATP hydrolysis releases the energy required for myosin to do its job. AF: actin filament; MF myosin filament. Modified from Goody (2003).

# Titan

- It's a  big protein, 36,000 amino acids!
- It anchors the myosin filaments to the Z disk, some papers have it attached to actin as well.
- It is stretchy (it can be compressed)
- It is involved in repair of damaged muscle
  - Damaged muscle proteins need to be degraded
  - New muscle proteins need to be synthesized
  - Somehow, Titan is involved in the signalling this repair
- It has many repeating Ig subunits (as in immunoglobin) proteins,

Titan may anchor both actin and myosin to the Z band proteins




The super "repeats" are the Ig proteins polymerized together.

# Possible Exam Questions

1. Describe the role of ATP in muscle contraction.
2. What protein binds to myosin and the Z disk proteins?
3. Which bands compress during contraction?
4. A common theme in biochemistry is "shape change leads to function change" describe one step in the Power cycle that is an example of this theme.
5. When an animal stops breathing (dies), its muscles slowly become rigid. If you watch CSI, you know that time of death can be determined by this phenomena if death has occurred with hours of analysis. Oxygen is required to make ATP in skeletal muscle (unless the animal is in fight/flight mode—sign up for CHEM 4420 to learn more). Explain how a deficiency of ATP leads to rigor mortis.

# Because you asked…

- How does the Tetnus toxin cause paralysis?
  - The tetnus toxin is produced by soil bacteria (that can also live on rusty nails). If the bacteria enter a person's blood via a deep wound, they are at risk of "Lock Jaw".
  - Tetnus toxin blocks the cell signalling that turns off a nerve signal. (Sign up for CHEM 4420 to learn more!) The muscles are constantly contracting and this leads to painful spasms. It is not clear why the jaw muscles are often affected first. The effect can spread to the lungs. This is a problem because in order to exhale, a person's diaphragm and intercostal (rib) muscles must relax. The tetnus toxin prevents this relaxation and this prevents normal breathing.
  - A vaccine to the bacteria is available and is highly recommended.

# References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