Excitation-Contraction Coupling

- Excitation-contraction:
  - Excitation: events that transmit AP along sarcolemma
  - Contraction: sliding of myofilaments
- AP is propagated along sarcolemma and down into T-tubules where voltage-sensitive proteins in tubules stimulate Ca\(^{2+}\) release from SR.
- Ca\(^{2+}\) released leads to contraction.
- AP is briefly and ends before contraction is seen.
- At low intracellular Ca\(^{2+}\) concentration:
  - Tropomyosin: blocks active site on actin
  - Myosin: head can’t attach to actin
  - Muscle fiber: relaxed
- Voltage-sensitive proteins in T tubules change shape, causing SR to release Ca\(^{2+}\) to the cytosol.
- At higher intracellular Ca\(^{2+}\) concentration Ca\(^{2+}\) binds to troponin.
  - Troponin: changes shape and makes tropomyosin away from binding site
  - Myosin: allowed to bind to actin forming a cross bridge
  - Cycling is initiated, causing sarcomere shortening and muscle contraction.
When nervous stimulation ceases, Ca$^{2+}$ pumped back into SR and contraction ends.

**Cross Bridge Cycling**

- **4 Steps:**
  1. Cross bridge formation
  2. Power stroke
  3. Cross bridge detachment
  4. Cocking of myosin head

- **Cross Bridge Formation:**
  high energy myosin $\rightarrow$ actin active site

- **Working (power) stroke:**
  myosin head pivots & pulls thin fila toward M line

- **Cross bridge detachment:**
  ATP attaches to myosin head
  Cross bridge detach

- **Cocking of myosin head:**
  hydrolysis of ATP "cocks" head to high energy (myosin)
  Will now be used for power stroke

- This process is repeated as long as:
  - Cat$^{2+}$ ions present
  - ATP present

- When a neural impulse stops:
  - The calcium ions are no longer released from the SR
  - ATP is used actively to: transport Cat$^{2+}$ back to SR binding sites exposed
  - Without calcium ions the crossbridge cannot reattach because: binding sites exposed
  - The thin actin myofilaments will slide back into the relaxed position
  - The membrane potential is re-established by ion pumps along the T-tubules and the sarcolemma.

**REVIEW:**

- 1. Neural impulse - SMN
- 2. Motor neuron axon
- 3. Chemical released - Ach messenger
4. Sarcolemma depolarized (AP generated)
5. AP $\rightarrow$ T-tubules
6. SR releases Ca$^{2+}$
7. Sarcoplasm
8. Sarcomele
9. Actin myofilament (exposes myosin binding sites)

Clinical - Homeostatic Imbalance
- Rigor mortis
  - When: 3-4 post mortem
    - 12 hr $\rightarrow$ peak
  - Why: Ca$^{2+}$ can't be pumped back into SR

- Results: (2)
  - Cross bridge formation
  - Myosin & actin stay bound
- ATP's roles:
  - Detachment of bridge

Whole Muscle Contraction
- Same principles apply to contraction of both single fibers and whole muscles
- Contraction produces muscle tension, the force exerted on load or object to be moved
- Contraction may or may not shorten muscle
  - Isometric: no shortening, ten T doesn't exceed load
  - Isotonic: muscle shortens, tension $\geq$ load
- Force and duration of contraction varies in response to: stimuli & intensities
- Each muscle is served by:
  - Motor Nerves
    - Contains axons of up to hundreds of motor neurons
  - Axon branch into terminals, each of which forms NMS with a single muscle fiber
  - Motor Unit: motor neuron & all muscle fibers it supplies
    - Smaller the fiber number the greater the fine control hands! eyes!
Muscle fibers from a motor unit are spread throughout the whole number, so stimulation of a single motor unit causes only weak contraction of entire muscle.

**Muscle Twitch**

- **Muscle Twitch:** simplest contraction resulting from a muscle fiber's response to a single AP from a motor neuron.
- **3 Phases:**
  
  - **Latent Phase:**
    - Events of excitation-contraction coupling
    - Muscle tension: none
  
  - **Period of Contraction:**
    - Tension increases
    - What is formed: cross bridge
  
  - **Period of Relaxation:**
    - Ca+2 reentry into SR
    - Tension declines to zero

- Muscle **contracts** faster than it **relaxes**

**All or None Principle**

- Once stimulated muscle **fibers** contract completely
- There are no: partial contractions
- We are talking about: muscle cell/motor unit X whole muscle
- Whole muscle does have graded or varying degrees of contraction, the amount of force (tension) produced varies according to the number of motor units called into ACTION!

**Graded Muscle Response**

- Normal muscle contractions are: smooth, strength varies
- Responses are graded by:
  - A **frequency** of stimulation
  - A **strength** of stimulation

- Muscle response to changes due to: **stimulus** frequency
- Single stimulus results in single contractile response, **muscle twitch**

- Temporal summation:
  2 stimuli received in rapid succession
  - Muscle fibers do not have time to completely relax between stimuli, so twitches increase in **force** with each stimulus
  - Additional Ca+2 that is released with second stimulus stimulates more shortening
  - Producing smooth, continuous contractions that add up, **summation**
    - Further increase in stimulus frequency causes muscle progress to sustained **quivering** contraction referred to as **unfused tetanus (incomplete)**

[Diagram showing tension over time with different stimulus types: twitch, wave summation, unfused and fused tetanus]

- Stimuli frequency increases, muscle tension reaches **maximum** referred to as **fused (complete) tetanus**
  - Why is it called “fuse”: one smooth sustained contracrt plateau
  - Muscle fatigue results from: **prolonged contraction strength**

- Muscle response to changes in stimulus
  - Recruitment: multiple motor unit summation, sent to many fibers ⇒ precise

- Types of Stimulus:
  - **Subthreshold stimulus**
    - Contraction: **NONE**
    - Strength: **NOT STRONG**
  - **Threshold stimuli**
    - Strength: **STRONG ENOUGH**
    - Contraction: **YES, FIRST**
- **Max stimulus**
  - Strength: **strongest**
  - Contraction: **max force**
  - Recruitment works on **size principle**
    - Which fibers are recruited first: **smallest**
    - When are larger fibers recruited: **intensity ↑, most powerful**
    - Some fibers contraction while others rest because: **prevent fatigue**

**Muscle Tone**
- Describe: **constant, slightly contracted of all muscles**
- Due to: **spinal reflexes**
  - Groups of motor units are alternately activated in response to input from **stretch receptors** in muscles
- Keeps muscles firm, healthy and ready to respond