BIOEN 3202 Lecture #2
3/6/06

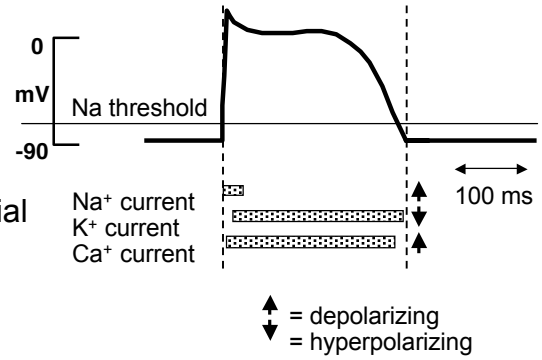
Joel Welch and Rob MacLeod

Important Vocabulary

- Myocyte
- Voltage Clamp
- Inward/outward Currents
- Driving Force
- T-tubule
- Frank-Starling Mechanism

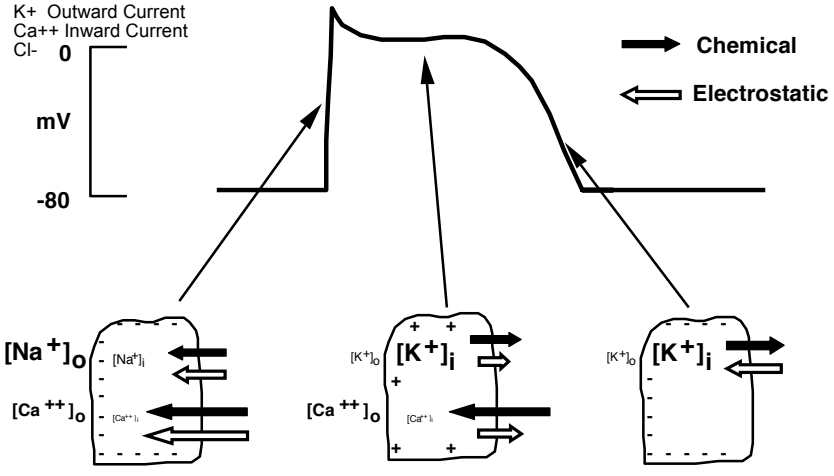
Cardiac Action Potentials:

- How does Cardiac AP differ from Neural AP?
  - Cardiac AP enormously long compared to neural.
    - Cardiac AP duration: 200-300 ms
  - Stable resting potential (usually).



Cardiac AP Features

- Stimulus
  - Electrical
- Ionic Currents
  - Channels
    - Na+ Inward Current
    - K+ Outward Current
    - Ca++ Inward Current
    - Cl-



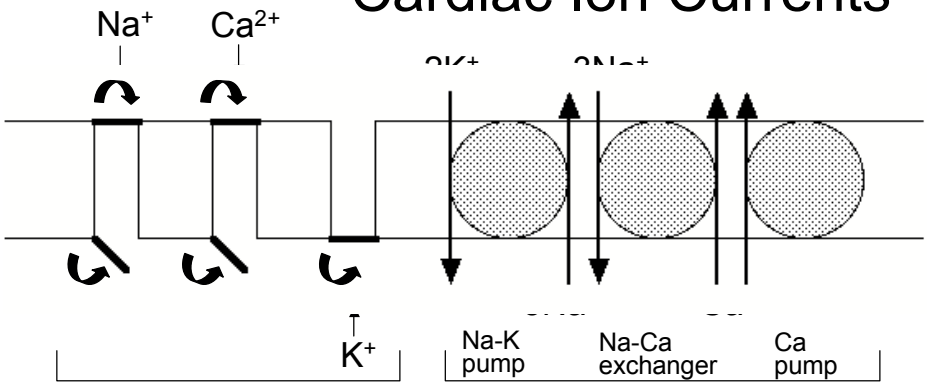
Why is Cardiac AP so Long?

- Where is [Ca++] largest? **Outside**
  - Outer [Ca++] ~ mM
  - Inner [Ca++] ~ μM
- Ca++ Electrochemical Gradient Produced
  - Driving Force
- Cardiac AP Plateau
  - Balance between outward current of K+ and inward current of Ca++.
  - K+ eventually “wins”.
- Ca++ channels are similar to Na+ channels
  - Different time course

Myocyte Membrane

- Na+/K+ pump
  - ATP required
  - electrogenic
- Ca++ pump
  - ATP required
- Na+/Ca++ **Exchanger**
  - No ATP required
- T-tubules
  - Next slide

Cardiac Ion Currents



Ion channels

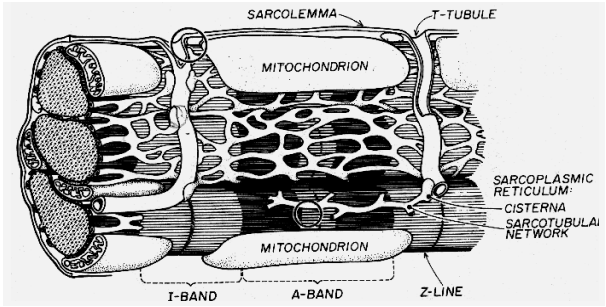
- Passive ion movement
- Driven by concentration and electrostatic gradients
- Channels are selective
- Gates control opening

Carrier mediated ion transport

- Na-K and Ca pumps require ATP
- Capable of driving against concentration gradient
- Na-Ca exchange does not require ATP

T-tubules

- "Fingers in balloon/bubble gum"
- Why? Purpose?
  - Decrease intracellular diffusion distance
  - Increase Surface Area
- Concentration of L-type Ca++ channels high in T-tubules
  - Membrane AP cause inward Ca++ flow through L-type channels



Important Features of Cardiac Ionic Currents

- Resting potential depends almost entirely on [K].
- Na channels require time at potentials more negative than -65 mV in order to recovery. Without it, they will remain inactive.
- Slow (Ca) channels have a threshold of -35 mV
- The plateau represents balance between Ca and K currents.
- Some cardiac cells depolarize spontaneously; most do not.

Sarcoplasmic Reticulum

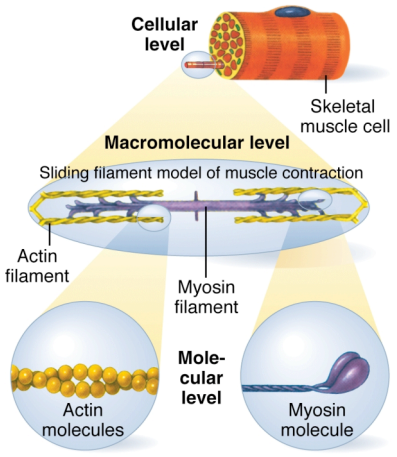
- [Ca++] high in SR
- SR “foot” associated with T-tubule
- Ryanodine Receptor in SR foot
  - Ca++ ions (from inflow through L-type channel) interact with ryanodine receptor to cause “huge” SR Ca++ release
- Ca++ pump in SR membrane
  - Pumps Ca++ back into SR after “huge” release
    - Ca++ pump in myocyte membrane also pumps Ca++ out of cell to restore original intracelluar [Ca++].

Excitation/Contraction Coupling

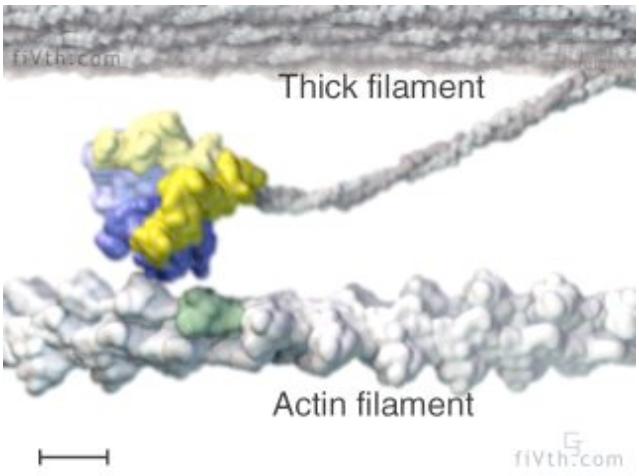
- Membrane Action Potential
- L-type channels open
  - Ca++ ions in
- Ca++ ions reacts with Ryanodine Receptors
- Large SR release of Ca++
  - **Contraction**
    - Occurs after AP
- Pumps work to restore original intracellular [Ca++]

EC Coupling

- Action potential causes influx of Ca^{2+}
- In mammals and birds, this causes release of more Ca^{2+}
- Ca^{2+} interacts with actin/myosin to cause contraction
- Pumps gather up Ca^{2+} or remove it from cell

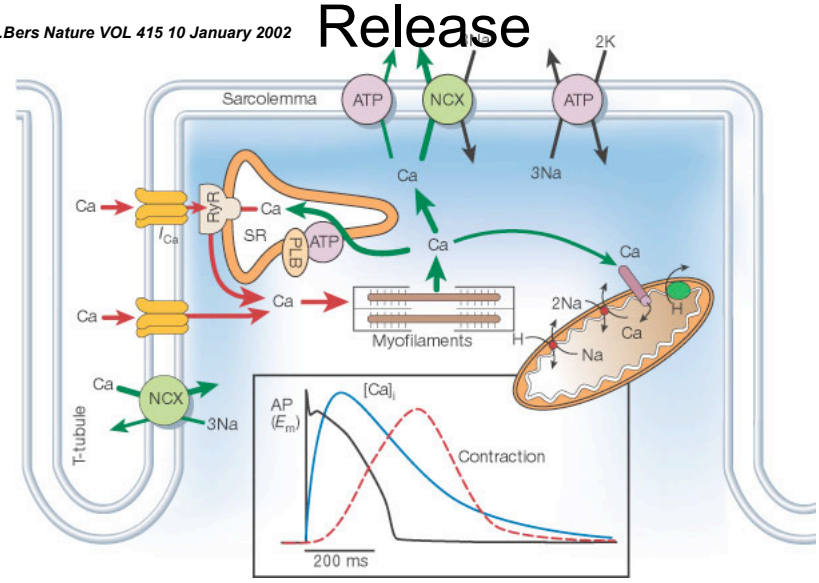


Actin-Myosin Interaction



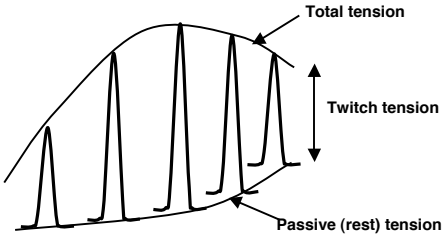
Calcium-induce Calcium Release

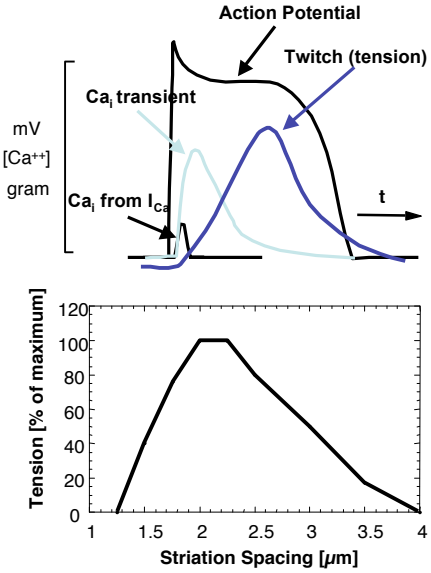
D.M.Bers Nature VOL 415 10 January 2002



Intrinsic Regulation of Cellular Contraction

- Adjust pretension to improve spacing in contractile elements
  - Optimal spacing





Striation Spacing

- Myocyte prestretch and contractile force related to heart blood volume
  - Cellular level graph and Heart level graph
- Cardiac Output
  - Cardiac Output=(stroke volume) x (heart rate)
  - Rest: 4 l/m
  - Exercise: 25-30 l/m
- In Lab:
  - Prestretch heart
  - Measure Strength of Contraction