Heart Valve Mechanics
The heart valve open and close because of pressure gradients. When pressure on one side is greater than the other, it pushes the valve open. For example, when pressure in the LV is higher than the aorta, then the valve opens, and blood rushes out. This lowers the pressure in the LV, and the pressure in the aorta is now higher so the semilunar valve closes. *To know if a valve is open or close, just need to know the pressure in each area.*

The one-way valves prevent backflow (regurgitation) and ensure efficient pumping. A valvular disorder such as Aortic Stenosis leads to hypertrophy due to the increased pressure required to push blood through the valve and cardiac failure.

Mechanics of LV vs RV
The LV and RV are structurally different because they have to produce different pressures. Recall that the right ventricle pumps to the pulmonary circuit and the left ventricle pumps to the systemic circuit.

- LV has to produce a lot more pressure than the RV
- RV produces about 5x less pressure than the LV
- LV is more muscular and is shaped like a true cylinder, with the RV a half cylinder next to it (like a bellows…it squeezes blood against the wall of the LV)
- RV squeezes against LV, not as much muscle b/c don’t need as much pressure
- LV has a wall thickness 3x greater than the RV. The 3x greater thickness produces 5x greater pressure due to the LV’s shape as a full cylinder, and the LV has a more efficient pump mechanism.

Histology of Cardiac Contractile Cells
Cardiomyocytes are the cells of the heart…there are two types…contractile cells and autorhythmic cells. We are talking here about the contractile cells.

How cardiac contractile cells are the same as skeletal muscle:
- They are striated
- They use the sliding filament mechanism
- Ca$^{++}$ is the key to contraction
How cardiac contractile cells are different from skeletal muscle:

- CMs are short and plump, SM is long and skinnier
- CMs branch and are interconnected by intercalated discs (desmosomes and gap junctions), SM do not branch and are independent
- CM has one (maybe two) nuclei, SM are multinucleate
- CM’s nuclei are in the center of the contractile proteins, SM’s nuclei are pushed off to the side by the contractile proteins
- CM have more mitochondria because they are highly aerobic and fatigue-resistant
- CM have fewer T-Tubules, no triads, and no neuromuscular junctions
- CM have two sources of Ca$^{++}$…from the SR and ECF
- CM has Ca$^{++}$ membrane channels

Physiologically they differ:

- CM contract/relax as a unit (via conduction system and gap junctions)
- CM depolarize via autorhythmic cells, SM use neuromuscular jxns
- CM have long refractory period (can’t summate, prevents tetanus), SM have short ARP and can summate
- CM are electrically connected, SM are not
- CM’s trigger for stimulus is AP of neighboring cell
- CM’s source for depolarization is the nodal cell, source for SM is motor neurons

**Intercalated Discs** = physical connection between contractile cells. They are desmosomes and gap junctions, which allow positive ions to pass from one cell to the next. The gap junction electrically connects each cell.

The tube is a connexon, and there are a lot of connexons in gap junctions.

**Review of Equilibrium Potentials ($E_{ion}$) and Electrochemical Gradients**

As a membrane’s permeability to a particular ion increases (relative to that of other ions), the $V_m$ (membrane potential) moves toward the equilibrium potential of that ion.

- $E_K = -94\text{mV}$
- $E_{Na} = +60 \text{mV}$
- $E_{Ca} = +130 \text{mV}$
The electrochemical gradient is the net driving force. It takes into account the concentration gradient AND the electrical gradient. The three ions we are concerned with in regards to contractile cells are Na\(^+\), K\(^+\) and Ca\(^{++}\).

**Excitation Contraction Coupling in Cardiac Contractile Cells**

This process is the pretty much the same as in skeletal muscle, but with a few differences. Both require an influx of Ca\(^{++}\), which pulls the troponin/tropomyosin off the attachment sites and allows for cross-bridge formation. However, there are two sources for Ca\(^{++}\) in the heart cell…sarcoplasmic reticulum stores and releases Ca\(^{++}\), AND there are Ca\(^{++}\) channels in the membrane (L-type because they stay open for a long time…~ 175 milliseconds). Some goes to the troponin/tropomyosin and some goes to the SR to open more membrane channels, bringing in more Ca\(^{++}\) (this is a calcium-induced calcium-release). The SR empties fast! Ca\(^{++}\) goes up up up! This is a positive feedback loop. Peak Ca\(^{++}\) levels result in peak tension!

**The Contractile Cell Action Potential**

- Phase 4: Resting membrane potential of the ventricle contractile cell is -90mV. It has a large permeability to K\(^-\)
  - All the K\(^+\) channels are open (permeability of K\(^+\) is going up), which is keeping the membrane potential close to the equilibrium potential for potassium (-94mV)
  - Voltage-gated Ca\(^{++}\) channels and Na\(^+\) channels are closed (decreasing the permeability for Ca\(^{++}\) and Na\(^+\))

- Phase 0: The cell has to receive an AP from a neighboring autorhythmic or contractile cell…the ions enter, and it depolarizes enough to lead to the opening of fast, voltage-gated Na\(^+\) channels. This increases the membrane’s permeability to Na\(^+\), there’s a Na\(^+\) influx, and the membrane potential becomes more positive.
  - Threshold potential is about -75mV. The Na\(^+\) causes a rapid depolarization that peaks at about +30mV. It doesn’t go any higher (because technically, it could go up to the equilibrium potential of sodium, which is 60mV) because the Na\(^+\) channels close. The closing of these channels in Phase 1 decreases the membrane’s permeability to Na\(^+\)

- Phase 1: Small repolarization due to the lowering of the membranes permeability to Na\(^+\) (closure of Na\(^+\) channels) plus a small amount of K\(^+\) leaving the cell.

- Phase 2: Plateau. At this stage we stop repolarizing and hold pretty steady. It’s actually a slight repolarization, but we say steady because AP is confusing! In this stage, depolarization triggers Ca\(^{++}\) channels open (L-Type), but they open so slowly so it doesn’t actually open until now. Also, the

<table>
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<tr>
<th>Contractile Cell</th>
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<tr>
<td><strong>Resting</strong></td>
<td>-90mV</td>
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<tr>
<td><strong>Threshold</strong></td>
<td>-75mV</td>
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<tr>
<td><strong>Positive peak</strong></td>
<td>+30mV</td>
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The autorythmic cell action potential

One of the main differences between contractile cells and autorthymic cells is that Ca^{++} causes the depolarization of autorythmic cells. Also, there is no resting membrane potential, and thus no rest! As soon as the cell repolarizes it right away starts depolarizing.

The negative peak of the action potential is about -65mV, and threshold is about -45mV. The positive peak of the AP is about +10mV.

**Drift Potential** is also called “pacemaker potential” and it is within the range of -65mV up to -45mV. During this phase, the permeability of potassium goes down due to the closure of the V-gated potassium channels. Note that these channels close as the membrane potential becomes more negative and open in response to depolarization. **However, in cardiac contractile cells depolarization triggers potassium channels to close and they open as the membrane potential becomes more negative.**

**In “Early Drift Potential”** the funny channels open. This increases the cell membrane’s permeability to sodium, causing a sodium influx, which is greater than the potassium efflux. This causes a slow depolarization up to -55mV. The funny channels close now!

**In “Late Drift Potential”** the fast V-gated calcium channels open. This increases the permeability of the membrane to calcium causing a calcium influx! This depolarizes the membrane potential to threshold (-45mV).

**At Threshold** the slow V-gated calcium channels open, still increasing the membrane’s permeability to calcium, causing an even greater calcium influx to result in a rapid depolarization. Note that the long-lasting, slow calcium channels allow more calcium influx than the fast ones (the Type Ts)…plus they also allow a slight influx of sodium, which enhances the depolarization.

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membrane is still leaking a little bit of K^+, but the **voltage-gated K^+ channels are closed.**

- This influx of Ca^{++} results in contraction of the ventricle!
- Plateau ends as slow, V-gated K^+ channels open and the slow, V-gated Ca^{++} channels finally close.

- Phase 3: Repolarization. This is due to the **opening of slow, V-gated K^+ channels**, which raise the membrane’s permeability to K^+, causing a K^+ efflux. The membrane potential becomes more negative. The V-gated Ca^{++} channels are closed, so the membrane is less permeable to Ca^{++}. The V-gated Na^+ channels are also closed. Once it gets to -90mV, then it is at rest. Whew!

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**Type T Ca^{++} channel = transient, fast**

**Tyle L Ca^{++} channel = long-lasting, slow, allow more Ca^{++} in**
**Rapid Depolarization** occurs next due to the increased permeability of the membrane to potassium, combined with the decreased permeability to calcium (Type-L channels closed). In this stage the membrane potential goes from +10mV down to -65mV. The initial depolarization stimulated the opening of the slow V-gated potassium channels which caused an efflux of potassium and dropping the membrane potential.

**The Cycle Repeats**…as the membrane potential approaches -65mV, the V-gated potassium channels close again, which decreases the membrane’s permeability to potassium…this allows the sodium influx to dominate as the funny channels open. We begin depolarizing once again!

**Conduction System**

![Conduction System Diagram](image)

**The SA node** is the normal pacemaker of the heart at 80 APs/minute (=80bpm). Note that the node that has the first action potential sets the pace for the heart…it is usually the SA node…but others can initiate as well…not as effective.

**The AV node** provides a 100ms delay so that the atria contract before the ventricles. The slower transmission of the AP is due to the small cells (increased resistance to current flow) and few gap junctions. The AV’s rhythm is about 50 APs/minute

**The AV Bundle** is the electrical connection between the atria and the ventricles. Rhythm is about 30-40 APs/min.

**The L/R Bundle Branches** conduct APs into the left and right ventricles. (30-40 APs/min)

**Purkinje Fibers** spread APs throughout the myocardium of ventricles. The papillary muscles are excited prior to the rest of the myocardium to anchor the valves prior to ventricular contraction. Rhythm is about 30-40 Aps/min

The direction of the APs (the wave of depolarization) and the spiraling fibers of the myocardium contribute to the “wringing effect” of the ventricular contraction.

**Q.** What ensures the atria and ventricles do not contract at the same time?

**A.** Pause at the AV node
Contractile cells are electrically separated

I think the moderator band gets the stimulus to the papillary muscles right before ventricular contraction in order to anchor the chordée tendineae.

**Autonomic Nervous System Control of Heart Rate**
So, if you want to change the heart rate, what do you do? You have options...you can change the shape of the drift potential, causing it to take longer to reach threshold or enabling it to reach threshold faster. You can also change the peak negative potential...if it doesn't go down as far, it doesn't have as far to travel to once again depolarize. In general the PANS slows down the heart rate, and the SANS speeds it up!

**The medulla oblongata** in the CNS contains two distinct nuclei that exert reflexive control over heart rate and mediate changes in heart rate as instructed by higher brain centers such as the hypothalamus...the hypothalamus is the “boss” of the ANS. The heart has dual innervation...the PANS goes through Vagus nerve to innervate the autorhythmic cells and the SANS goes through the sympathetic cardiac nerve to innervate both types.

**Q.** How do you change drift potential?

**A.** Change the levels of ions moving across the membrane. The catecholamines bind, opening a 2nd messenger pathway to allow more sodium and calcium to come in.

**The Cardioacceleratory Center (SANS)** sends action potentials down the sympathetic cardiac nerve. It releases E/NE that binds to Beta-1 receptors, stimulating a 2nd messenger pathway! The pathway causes T-type calcium channels and funny channels to open, so more calcium and sodium can come in to the cell (causing depolarization to initiate!) This leads to a reduced repolarization (doesn’t have to go down as far during repolarization), and to an increase in the drift potential...it has a steeper slope!

- This results in MORE action potentials per minute, so heart rate goes up!
- It also speeds the propagation along the conducting cells, resulting in less time between atrial and ventricular contraction.

**The Cardioinhibitory Center (PANS)** sends action potentials down the Vagus Nerve. It releases acetylcholine which binds to muscarinic Ach receptors, opening potassium channels and inhibiting the opening of T-type calcium channels and funny channels. This increases the membrane permeability to potassium (K^+ goes up), and reduces the permeability to
calcium and sodium (funny and t-type closed). This results in hyperpolarization and decreased slope of the drift potential, so it takes longer to depolarize.
  - This results in fewer action potentials per minute, so heart rate slows down!
  - In addition, the speed of propagation is decreased along the conducting cells, resulting in more time between atrial and ventricular contraction.

The Cardiac Cycle
Graphical representations of the electrical, pressure and volume changes in the left ventricle. For the LV and RV, equal volumes are ejected, but against different pressures.
  - Systemic pressure = 120/80
  - Pulmonary pressure = 24/8 (5x less work for the right ventricle!)

Some misc. things to know:
  - The volume of blood ejected from each ventricle is the stroke volume.
  - While the heart is relaxed it is filling passively. The “active filling” comes from the atrial contraction. 80% is passive.
  - 1 Cardiac Cycle = 1 Systole + 1 Diastole
  - Pressure in the aorta peaks at 120
  - Aortic semilunar valve opens at 80
  - One cycle takes about 800 ms
  - AS, AD, VS, VD, repeat…
  - P-wave = atrial depolarization, which is followed by atrial contraction
  - QRS = ventricular depolarization, which is followed by ventricular contraction
  - T-wave = ventricular repolarization, ventrical relaxing
  - Volume goes up during diastole (passive filling)
  - Contraction is during systole
  - The atria spend much more time in diastole than the ventricles do
  - Cardiac output is 5ml/min
  - Common stroke volume is 70
  - Common resting heart rate is 75
  - You can increase volume return (ESV) by moving! It squeezes the vessels causing blood pressure to go up and return more blood to the heart.
  - You can increase EDV by upping the preload (SANS)
  - You can lower ESV by increasing contractility ??

\[
SV = EDV - ESV
\]

End diastolic volume minus end systolic volume

\[
Ejection Fraction = \frac{Stroke V}{EDV}
\]
**Isovolumetric contraction**

The pressure in the ventricle gradually increases because of the accumulation of blood in the ventricle. The pressure in the atria begins to lower as the atria relaxes. At this time, the ventricle begins to contract. This further increases the pressure in the ventricle so that the pressure in the ventricle now is greater than that in the atria. This results in the closing of the AV valves (due to the blood trying to move back into the atria). The closing of the AV valves is so forceful that it makes a sound (the 'lub' or first heart sound). The pressure in the ventricle during this stage is still lower than that in the artery so the semi-lunar valves are still closed. Therefore, there is no movement of blood into or out of the ventricle as both sets of valves are closed thus the term **isovolumetric**.

So in the isovolumetric contraction stage, the $P_{\text{vent}} > P_{\text{atria}}$ so the AV valves are closed and the $P_{\text{vent}} < P_{\text{artery}}$ so the semi-lunar valves are closed.

**Isovolumetric relaxation**

As the ventricle begins to relax, the pressure in the ventricle begins to decline. The pressure in the artery (which now has all the ejected blood) is now greater than that in the ventricle. The blood now closes the semi-lunar valve as it tries to go from the artery into the ventricle preventing any backflow. Although the pressure in the ventricle is declining, it is still greater than that in the atria so the AV valves are still closed. Thus as the ventricle is relaxing, the volume of blood in the ventricle is not changing. This stage will continue until the ventricular pressure becomes lower than the atrial pressure and the filling stage starts again.

So in the isovolumetric relaxation stage, the $P_{\text{vent}} > P_{\text{atria}}$ so the AV valves are closed and the $P_{\text{vent}} < P_{\text{artery}}$ so the semi-lunar valves are closed.

**The sounds of the heart**

- The “lubb” is when the AV valves close = louder, stronger sound
- The “dupp” is when the SL valves close = shorter, sharper sound
- Murmer is an abnormal heart sound usually due to a defective valve resulting in some degree of regurgitation

If HR is equal to 75 bpm, then it takes about 0.8 seconds for one cardiac cycle.