Cardiovascular System: Heart

- **Heart**: Roughly size of human fist (~ 250 – 350 grams)
- Located in the mediastinum (medial cavity of thorax)
- "Double pump" composed of cardiac muscle

- **Base**: Point of maximum intensity
- **Coronary sulcus**: Anterior intraventricular sulcus
- **Apex**: 2/3 of heart mass lies left of mid-sternal line

- **Pericardial cavity**: Contains serous fluid (friction-free environment)
- **Fibrous pericardium**: Protects heart, anchors heart, prevents overfilling
- **Parietal pericardium**: Double-walled sac enclosing the heart

- **Pericarditis**: Inflammation of the pericardial sac

- **Cardiac tamponade**: Compression of heart due to fluid / blood build-up in pericardial cavity
Heart layers:
- Epicardium: anchors cardiac fibers, reinforces heart structures, directs electrical signals
- Myocardium: contains fibrous skeleton
- Endocardium: anchors cardiac fibers

Heart:
- Atria: receiving chambers, small, thin-walled
- Ventricles: discharging chambers, large, thick-walled

Cardiovascular System – Heart

Heart – Chambers, Vessels & Valves

Pulmonary circulation:
- Pulmonary veins: returns blood from lungs to left atrium
- Pulmonary trunk: carries blood to lungs

Systemic circulation:
- Superior vena cava: returns blood above diaphragm to right atrium
- Inferior vena cava: returns blood below diaphragm to right atrium
- Aorta: carries blood to body

Marieb & Hoehn (Human Anatomy and Physiology, 8th ed.) – Figures 18.2, 18.3, 18.4
Side-by-side pumps of the heart serve separate circuits.

Pulmonary circuit (short, low pressure loop)
- Oxygenated: high pressure
- Venous return to right atrium

Systemic circuit (long, high pressure loop)
- Deoxygenated: low pressure
- Venous return to left atrium

In steady state, cardiac output from each ventricle must be equal as well as the venous return to each atrium.

Blood in the atria / ventricles provides little nourishment to heart tissue.

How does the heart itself get nourishment?

Answer: Coronary circulation

Coronary circulation delivery limited to when heart is relaxed...

Answer: Coronary circulation

Angina pectoris:
- Thoracic pain caused by fleeting deficiency in blood delivery

Myocardial infarction:
- Myocardial cell death resulting from prolonged coronary blockage
- Heart attack

Great cardiac vein (empties blood back into right atrium)

Middle cardiac vein

Small cardiac vein

Great cardiac vein

Anastomosis (junction of vessels)

Circumflex artery (feeds left atrium and posterior wall of left ventricle)

Anterior interventricular artery (feeds interventricular septum and anterior ventricular walls)

Posterior interventricular artery (feeds right lateral ventricular wall)

Right marginal artery (feeds right interventricular wall)

Right coronary artery

Left coronary artery

Answer: Coronary circulation

Blood in the atria / ventricles provides little nourishment to heart tissue.
Blood flows through the heart in a single direction due to the presence of valves.

Right atrioventricular valve (tricuspid valve) and Left atrioventricular valve (bicuspid valve) (mitral valve)

Pulmonary semilunar valve and Aortic semilunar valve

Atrioventricular valves (prevent backflow into atria) and Semilunar valves (prevent backflow into ventricles)

Valves open / close based on pressure differences

Papillary muscle and Chordae tendineae

Papillary muscles tighten

Valvular Regurgitation:
- Valve does not close properly;
- Blood regurgitated

Causes:
- Congenitally deformed valve
- Post-infectious endocarditis
- Infective endocarditis
- Rupture of cord / muscle

Valvular stenosis:
- Valve flaps become stiff;
- Opening constricted

Causes:
- Congenitally deformed valve
- Post-infectious scarring
- Calcification of valve

Pathophysiology:

Aortic semilunar valve (pig)

Causes:

Treatment = Valve replacement
Heart – Chambers, Vessels & Valves

Heart designed to create complex flow patterns (direct / maintain blood momentum)

1) Chambers arranged in loop pattern
2) Delivery vessels curved
3) Grooves / ridges within chambers

Muscle Fiber Anatomy

- Striated, branched cells (~ 85 – 100 μm)
- Single nucleus (sometimes two...)
- Large [mitochondria] (~ 15x skeletal muscle)
- High fatigue resistance
- Electrical synapses (intercalated discs)

Cardiac Electrophysiology

System allows for orderly, sequential depolarization and contraction of heart

Intrinsic Conduction System:

Sinusoidal node: (SA node)
- Located in right atrial wall
- Initiates action potentials (APs)
- Pacer (60-100 beats / min)

Atrial internodal tracts

Atrioventricular node: (AV Node)
- Conduction from atria to ventricles
- Slowed conduction velocity
- Ventricular filling

Bundle of His

Conducting cells:
Cardiac cells specialized to quickly spread action potentials across myocardium
- Weak force generators

Functional syncytium:
The entire myocardium behaves as a single coordinated unit

Gap junction

Less elaborate T-tubule system and sarcoplasmic reticulum compared to skeletal muscle

Normal sinus rhythm:
1) AP originates at SA node
2) SA node fires at 60 – 100 beats / min
3) Correct myocardial activation sequence

Intrinsic Conduction System: Normal sinus rhythm:
1) AP originates at SA node
2) SA node fires at 60 – 100 beats / min
3) Correct myocardial activation sequence
Cardiovascular System

The concepts applied to cardiac APs are the same concepts as applied to APs in nerves / skeletal muscle

Review:

- Membrane potential determined by relative conductances / concentrations of permeable ions
- Ions flow down electrochemical gradient toward equilibrium potential (Nernst equation)
- Membrane potential expressed in mV;
  - inside cell expressed relative to outside
- Resting membrane potential determined primarily by $K^+$ ions (leaky $K^+$ gates at rest)
- $Na^+/K^+$ pumps maintain gradients across membranes
- Changes in membrane potential caused by flow of ions in / out of cell
- Threshold potential represents the point at which a depolarization even becomes self-sustaining (voltage-gated channels)

Cardiac Electrophysiology

APs of Atria, Ventricles & Purkinje System:

- Long duration AP (150 – 300 ms)
  - Maximum heart rate: ~ 240 beats / min
- Plateau: Sustained period of depolarization
  - $Ca^{2+}$ entry initiates release of more $Ca^{2+}$ from intracellular stores (excitation-contraction coupling)
  - Brief period of repolarization
  - $Na^+$ channels close ($g_{Na}$)
  - $K^+$ exits via VG channels ($g_{K}$)
  - Steep electrochemical gradient

Phases of the Action Potential:

Phase 0 – Upstroke
  - Period of rapid depolarization
    - $Na^+$ enters via VG channels ($\beta_{Na}$)

Phase 1 – Initial repolarization
  - Brief period of repolarization
  - $Na^+$ channels close ($\alpha_{Na}$)
  - $K^+$ exits via VG channels ($\beta_{K}$)
  - $Ca^{2+}$ enters via VG channels ($\alpha_{Ca}$)

Phase 2 – Plateau
  - Stable, depolarized membrane potential
  - $K^+$ exits via VG channels ($\beta_{K}$)
  - $Ca^{2+}$ entry initiates release of more $Ca^{2+}$ from intracellular stores (excitation-contraction coupling)
Cardiovascular System

APs of Atria, Ventricles & Purkinje System

Costanzo (Physiology, 4th ed.) – Figure 4.13

Phases of the Action Potential:

Phase 3 – Repolarization
- Period of rapid repolarization
  - Ca²⁺ channels close (↓gCa)
  - K⁺ exits via VG channels (↑gK)

Phase 4 – Resting membrane potential
- Membrane potential stabilizes
- All VG channels closed
- K⁺ exits via “leaky” channels
- Na⁺ / K⁺ pumps restore gradients

Changes in RMP (due to gradient issues) directly affect responsiveness of heart

# of VG Na⁺ channels available to respond decreases as RMP becomes more (+)

Cardiac dysrhythmia = irregular heartbeat

Cardiac Electrophysiology

Refractory Periods:

Absolute refractory period (ARP)
- Na⁺ channels closed (reset at ~ -50 mV)

Relative refractory period (RRP)
- Greater than normal stimulus required to generate AP (some Na⁺ channels recovered)

Supranormal period (SNP)
- Cell is more excitable than normal due
  - Full Na⁺ channel recovery
  - Potential closer to threshold than at rest

Effective refractory period (ERP)
- Not enough Na⁺ channels have recovered

Cardiac Electrophysiology

Pacemaker of the Heart:

Marieb & Hoehn (Human Anatomy and Physiology, 8th ed.) – Figure 18.13

1) Exhibits automaticity (spontaneous AP generation)
2) Unstable resting membrane potential
3) No sustained plateau

Phase 0 – Upstroke
- Slower than other cardiac tissue (T-type Ca⁺ enters via VG channels (↑gCa))

Phase 1 / Phase 2
- Absent

Phase 3 – Repolarization
- Similar to other cardiac cells

Phase 4 – Spontaneous depolarization
- Accounts for automaticity of SA node
  - Na⁺ enters via VG channels (↑gNa)
  - Open via repolarization event
  - Once threshold reached, VG Ca²⁺ channels open (pump in Phase 5)

Rate of depolarization sets heart rate
Cardiovascular System – Heart

Other myocardial cells also have the capacity for spontaneous phase 4 depolarization; these are called latent pacemakers.

<table>
<thead>
<tr>
<th>Location</th>
<th>Intrinsic firing rate (impulses / min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sinoatrial node</td>
<td>70 – 80</td>
</tr>
<tr>
<td>Atrioventricular node</td>
<td>40 – 60</td>
</tr>
<tr>
<td>Bundle of His</td>
<td>40</td>
</tr>
<tr>
<td>Purkinje fibers</td>
<td>15 – 20</td>
</tr>
</tbody>
</table>

The pacemaker with the fastest rate controls the heart rate.

Overdrive suppression:
Latent pacemakers own capacity to spontaneously depolarize is suppressed by the SA node.

Ectopic pacemaker: Latent pacemaker takes over and becomes the pacemaker
1) SA node firing rate decreases (e.g., damage / drug suppression)
2) Intrinsic rate of latent pacemakers increases
3) Blockage in normal conduction pathway (e.g., disease)

Cardiac Electrophysiology

Conduction velocity (speed at which APs propagate in tissues) differs among myocardial tissues.

- Atria: 1 m/sec
- AV node: 0.01–0.35 m/sec
- His/Purkinje: 2–4 m/sec
- Ventricle: 1 m/sec

Permits proper timing of heart events.

Repolarization of atria (hidden) correlates with conduction time through AV node.

Duration corresponds to atrial conduction rate.

Electrocardiogram (ECG or EKG):
Graphical recording of electrical currents generated and transmitted through heart.

- P wave: Depolarization of the atria
- QRS wave: Depolarization of the ventricles
- T wave: Repolarization of the ventricles
Cardiac Electrophysiology

Contents:

- Cycle length
  - Time between one R wave and the next
  - Heart rate = 60 / cycle length (beats / min)

- Junctional Rhythm
  - SA node nonfunctional

- Heart block
  - Poor conduction at AV node

- Fibrillation
  - Out of phase contractions

- The autonomic nervous system can directly affect the heart rate; these effects are called **chronotropic effects**

  **Positive chronotropic effects:**
  - Increase heart rate
  - Under sympathetic control
  
  ![Image of positive chronotropic effects](image1.png)

  **Negative chronotropic effects:**
  - Decrease heart rate
  - Under parasympathetic control
  
  ![Image of negative chronotropic effects](image2.png)

- The autonomic nervous system can also directly affect conduction velocity at the AV node; these effects are called **dromotropic effects**

  **Positive dromotropic effects:**
  - Increase conduction velocity
  - Under sympathetic control
  
  ![Image of positive dromotropic effects](image3.png)

  **Negative dromotropic effects:**
  - Decrease conduction velocity
  - Under parasympathetic control
  
  ![Image of negative dromotropic effects](image4.png)
Cardiac Muscle Contraction

The basic contractile machinery between cardiac and smooth muscle is similar

Contraction occurs according to sliding filament model

Excitation-contraction coupling translates the action potential into the production of tension

Cardiac AP initiated in membrane

1) Ca\(^{2+}\) reaccumulated in SR
   - + Ca\(^{2+}\) ATPase
2) Ca\(^{2+}\) released from cell
   - + Ca\(^{2+}\) ATPase
   - + Ca\(^{2+}\) / Na\(^{+}\) exchanger

Ca\(^{2+}\) enters cell (plateau phase)

- + Triggers L-type Ca\(^{2+}\) channels in membrane
- + Triggers Ca\(^{2+}\)-induced Ca\(^{2+}\) release from SR

Ca\(^{2+}\) floods cytoplasm

Mechanisms for changing tension production:
1) + Ca\(^{2+}\) in SR = + Ca\(^{2+}\) release to cytoplasm
2) + Ca\(^{2+}\) inward current = + Ca\(^{2+}\) in cytoplasm

Cross-bridging cycling initiated

- + Ca\(^{2+}\) binds to troponin C; cross-bridging occurs

The magnitude of the tension developed is proportional to the intracellular [Ca\(^{2+}\)]

Relaxation

1) Ca\(^{2+}\) reaccumulated in SR
   - + Ca\(^{2+}\) ATPase

2) Ca\(^{2+}\) extruded from cell
   - + Ca\(^{2+}\) ATPase
   - + Ca\(^{2+}\) / Na\(^{+}\) exchanger

Mechanisms for changing tension production:
1) Phosphorylation of Ca\(^{2+}\) channels in sarcolemma
   - + T Ca\(^{2+}\) enters during plateau / released from SR
2) Phosphorylation of phospholamban (regulates Ca\(^{2+}\) ATPase activity)
   - + T uptake / storage of Ca\(^{2+}\) in SR
   - + Faster relaxation time
   - + Increased peak tension during subsequent ‘beats’

Positive inotropic effects:
- 1) Faster tension development
2) 1) Peak tension

Mechanisms of action:
- + Under sympathetic control
- + Also triggered by circulating catecholamines

Cardiovascular System – Heart

The autonomic nervous system can directly affect heart contractility; these effects are called inotropic effects

Inotropism:
- Intrinsic ability of myocardial cells to develop force at a given length

Cardiac Muscle Contraction

Cardiovascular System – Heart

Marieb & Hoehn (Human Anatomy and Physiology, 8th ed.) – Figure 18.12

Mechanisms of action:
1) Phosphorylation of Ca\(^{2+}\) channels in sarcolemma
   - + T Ca\(^{2+}\) enters during plateau / released from SR
2) Phosphorylation of phospholamban (regulates Ca\(^{2+}\) ATPase activity)
   - + T uptake / storage of Ca\(^{2+}\) in SR
   - + Faster relaxation time
   - + Increased peak tension during subsequent ‘beats’

Marieb & Hoehn (Human Anatomy and Physiology, 8th ed.) – Figure 18.12

• + Shorter twitch time allows for more time for ventricle to fill
• + Increased tension generation equals stronger contraction
Cardiac Muscle Contraction

The autonomic nervous system can directly affect heart contractility; these effects are called inotropic effects.

Positive inotropic effects:
- Increase contractility

1. Cardiac glycosides inhibit Na⁺-K⁺-ATPase
2. Intracellular [Na⁺] increases
3. Change in Na⁺ gradient slows down Ca²⁺-Na⁺ exchanger
4. Intracellular [Ca²⁺] increases
5. [Ca²⁺]↑ → tension development

Cardiac glycosides are a class of drugs that act as positive inotropic agents.

Cardiac tissue (atria)
ACh → Muscarinic receptors
- ACh decreases inward Ca²⁺ current during plateau
- ACh increases outward K⁺ current (shortens plateau phase)

Costanzo (Physiology, 4th ed.) – Figure 4.20

Negative inotropic effects:
- Decrease contractility

- Under parasympathetic control
  - ACh decreases inward Ca²⁺ current during plateau
  - ACh increases outward K⁺ current (shortens plateau phase)
  - Both ↓ Ca²⁺ entering cell and thus the amount of Ca²⁺ available for tension development

Costanzo (Physiology, 4th ed.) – Figure 4.19

Costanzo (Physiology, 4th ed.) – Figure 4.18

Changes in heart rate also produce changes in cardiac contractility

Example:
- Increase in heart rate = Increase in cardiac contractility

1) ↑ heart rate = ↑ APs per unit time = ↑ total amount of Ca²⁺ entering cell per unit time
AND
2) ↑ Ca²⁺ entering cell per unit time = ↑ accumulation of Ca²⁺ in SR for future release

Positive staircase effect
- As heart rate increases, the tension developed on each beat increases disproportionately to a maximal value

Costanzo (Physiology, 4th ed.) – Figure 4.19
Cardiovascular System – Heart

The maximum tension that can be developed by a myocardial cell depends on its resting length (similar to skeletal muscle).

Sarcomere length of ~ 2.2 µm = L_{max} for cardiac muscle.

Cardiac Muscle Contraction

Additional Length-dependent Mechanisms:
1) Increasing muscle length increases Ca^{2+}-sensitivity of troponin C
2) Increasing muscle length increases Ca^{2+} release from SR

Cardiovascular System – Heart

Cardiac Muscle Contraction

Cardiac Output: Total volume of blood ejected by each ventricle per unit time (usually one minute)

Cardiac output = Heart rate x Stroke volume (ml / min) (beats / min) (ml / beat)

Stroke volume = End diastolic volume - End systolic volume (ml)

Ejection Fraction: Fraction of the end diastolic volume ejected in each stroke volume

Ejection fraction = Stroke volume (ml) / End diastolic volume (ml)

Heart rate = 75 beats / min
End diastolic volume = 140 ml
End systolic volume = 70 ml

Calculate:
Stroke volume: 70 ml
Ejection fraction: 0.50
Cardiac output: 5250 ml / min

Frank-Starling Law of the Heart:
The volume of blood ejected by the ventricle depends on the volume present in the ventricle at the end of diastole.

Preload: The resting length from which cardiac muscle contracts.
Frank-Starling Law of the Heart:
The volume of blood ejected by the ventricle depends on the volume present in the ventricle at the end of diastole.

This relationship ensures that the volume the heart ejects in systole equals the volume it receives in venous return.

Positive inotropic effect = ↑ ejection fraction
Negative inotropic effect = ↓ ejection fraction

Cardiovascular System – Heart

Cardiac Muscle Contraction

Physiologic range

Sarcomere length = ~1.9 μm
Sarcomere length = ~2.2 μm

Optimal overlap = optimal tension

Optimal overlap = 1.9 µm
Optimal tension = 90 g

Cardiovascular System – Heart

Cardiac Muscle Contraction

A ventricular pressure-volume loop allows for the function of a ventricle to be observed for a single heart beat.

Isovolumetric contraction (1 → 2):
• Ventricle activates (systole)
• Space: no change
• Pressure: ↑ volume
• Aortic / mitral valves closed
• P_{ventricle} > P_{aorta} > P_{atrium}

Ventricular ejection (2 → 3):
• Aortic valve opens
• Blood rapidly ejected (4 volume)

Aortic valve opens

Isovolumetric relaxation (3 → 4):
• Ventricle releases (early diastole)
• Space: no change
• Pressure: ↓ volume
• Aortic / mitral valves closed
• P_{ventricle} > P_{aorta} > P_{atrium}

Ventricular filling (4 → 1):
• Mitral valve opens
• P_{ventricle} < P_{aorta} < P_{atrium}
• Blood refills

Slight pressure increases due to passive filling of compliant ventricle.
Cardiovascular System – Heart

A ventricular pressure-volume loop allows for the function of a ventricle to be observed for a single heart beat

- Increased preload
  - Increased end diastolic volume
  - Increased stroke volume (Frank-Starling Law)

- Afterload:
  - Pressure in the vessel leaving the heart (e.g., aorta) that must be overcome to eject blood
  - Increased internal pressure
  - Decreased stroke volume

- Increased contractility
  - Increased tension / pressure
  - Decreased end systolic volume
  - Increased stroke volume

The stroke work is defined as the work the heart performs on each beat

\[ \text{Work} = \text{force} \times \text{distance} \]

Cardiac minute work:
Work performed by the heart during a unit time (e.g., minute)

- Force = aortic pressure
- Distance = cardiac output

Increases in cardiac output or increases in aortic pressure will increase work of the heart

The myocardial O₂ consumption rate correlates directly with the cardiac minute work

\[ \uparrow \text{cardiac minute work} = \uparrow \text{O}_2 \text{ consumption} \]

HOWEVER

The largest percentage of O₂ consumption is for pressure work.

THUS

Mean aortic pressure = 100 mm Hg
Mean pulmonary pressure = 15 mm Hg

Law of Laplace:
In a sphere (e.g., heart), pressure correlates directly with tension and wall thickness and correlates inversely with radius

\[ P = \frac{2HT}{r} \]

What are the ramifications if a person exhibits systemic hypertension?
Cardiac Output equals the total volume of blood ejected by a ventricle per unit time.

The cardiac output can also be measured using the Fick principle (conservation of mass).

In the steady state, the rate of O₂ consumed by the body must equal the amount of O₂ leaving the lungs (pulmonary veins) minus the amount of O₂ returning to the lungs (pulmonary artery).

\[ \text{O₂ consumption} = \text{CO (left ventricle)} \times [\text{O₂ (pulmonary veins)}] - \text{CO (right ventricle)} \times [\text{O₂ (pulmonary arteries)}] \]

Solve for cardiac output:

\[ \text{Cardiac Output} = \frac{\text{O₂ consumption}}{[\text{O₂ (pulmonary veins)}] - [\text{O₂ (pulmonary arteries)}]} \]

A man has a resting O₂ consumption of 250 mL O₂ / min, a femoral arterial O₂ content of 0.20 mL O₂ / mL blood, and a pulmonary arterial O₂ content of 0.15 mL O₂ / mL blood.

What is his cardiac output?

\[ \text{Cardiac Output} = \frac{250 \text{ mL O₂ / min}}{0.20 \text{ mL O₂ / mL blood} - 0.15 \text{ mL O₂ / mL blood}} = 5000 \text{ mL / min} \]
Cardiovascular System – Heart

Mechanical / Electrical Overview:

Cardiac Cycle: Mechanical and electrical events during single heart beat

Phases of the cardiac cycle:

A. Reduced Ventricular Ejection:
- Ventricles begin to repolarize (start of T wave)
- Ventricular / atrial pressure falls (blood still moving out)
- Atrial continues to fill (pressure rising)

B. Isovolumic Ventricular Relaxation:
- Pressure falls rapidly (diastole)
- Mitral valve closely

C. Aortic valve closes

D. Reduced Ventricular filling:
- Mitral valve opens
- Atrium continues to fill (pressure rising)
- Ventricular volume increases rapidly
- Little change in ventricular pressure (compliance)
- Aortic pressure decreases (blood carried away)

E. Mitral valve opens (
P_atrium > P_ventricle)

F. Aortic valve opens

• Longest phase of cardiac cycle
• Final portion of ventricular filling
• Increase in heart rate reduces G phase interval; if heart rate too high, ventricular filling compromised

G. NO VOLUME CHANGE

http://www.youtube.com/watch?feature=endscreen&NR=1&v=xS5twGT-epo