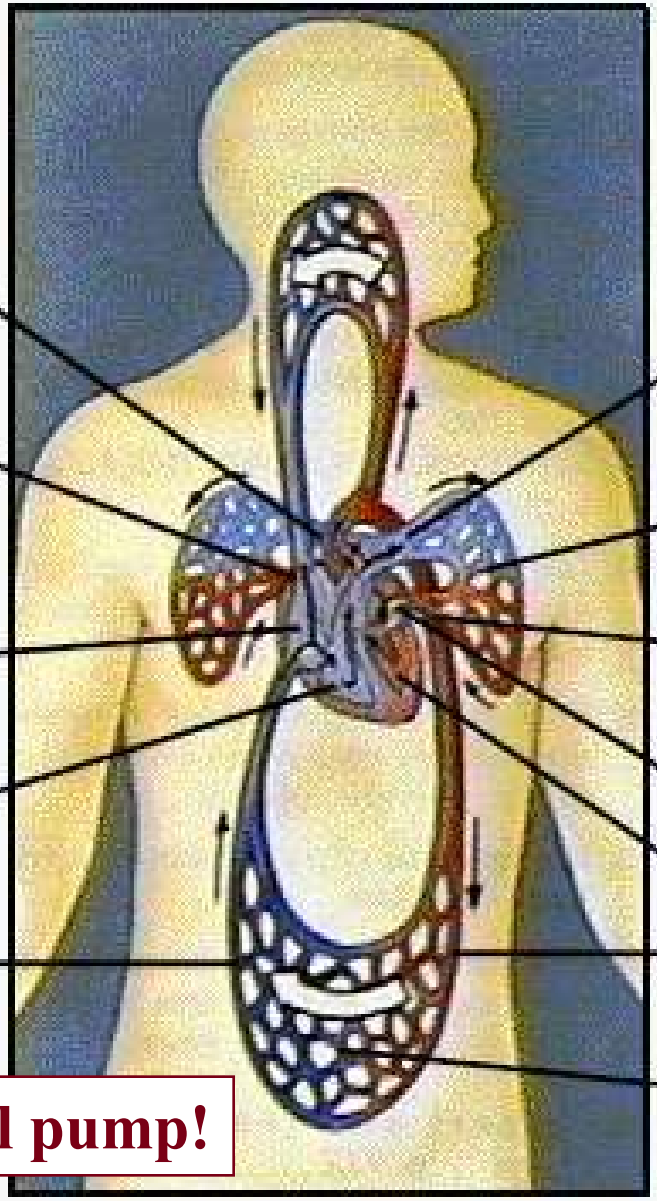
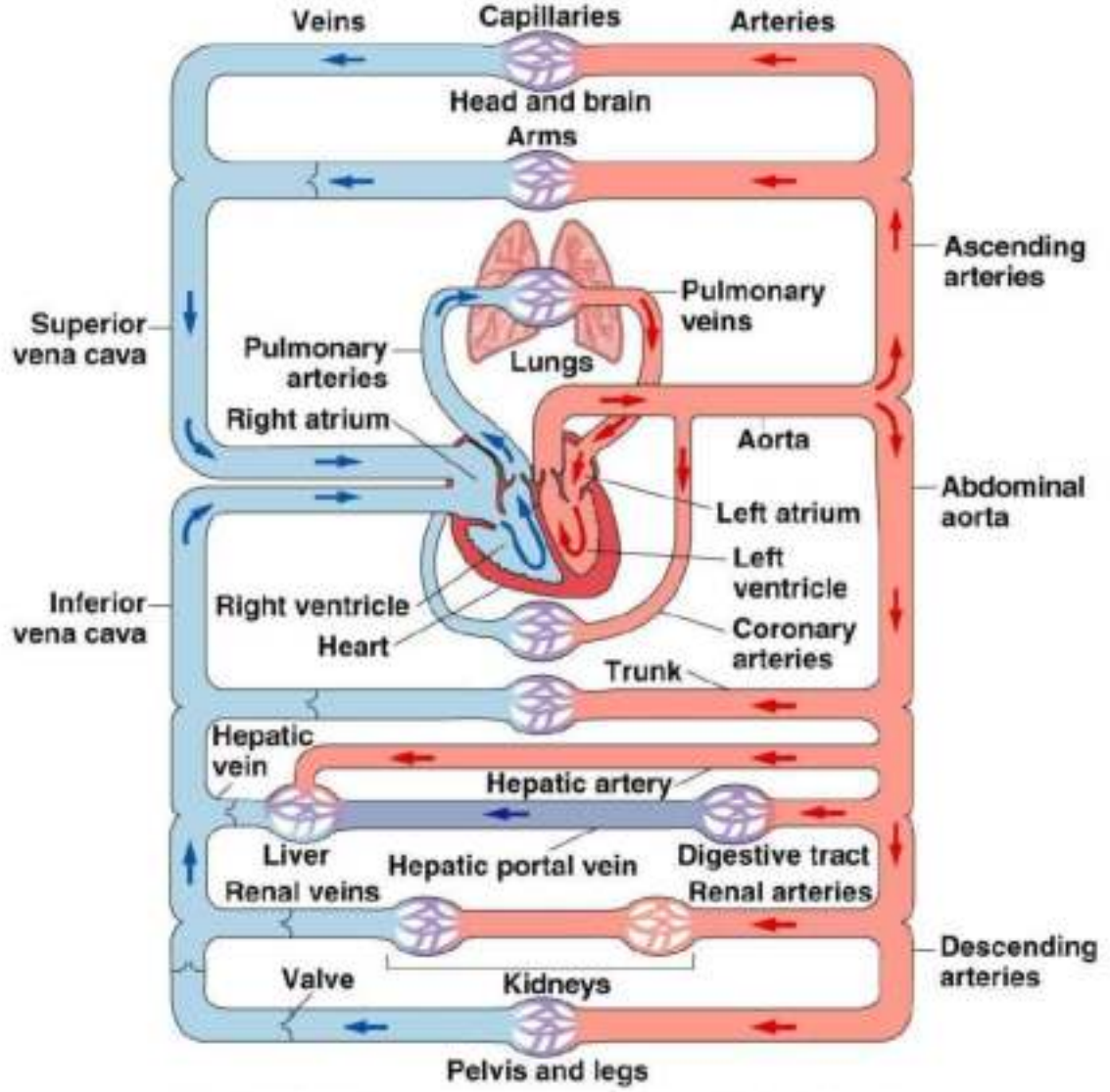
Overview of Cardiovascular System



3 basic components: ?

The heart is a dual pump!

Circulation Review

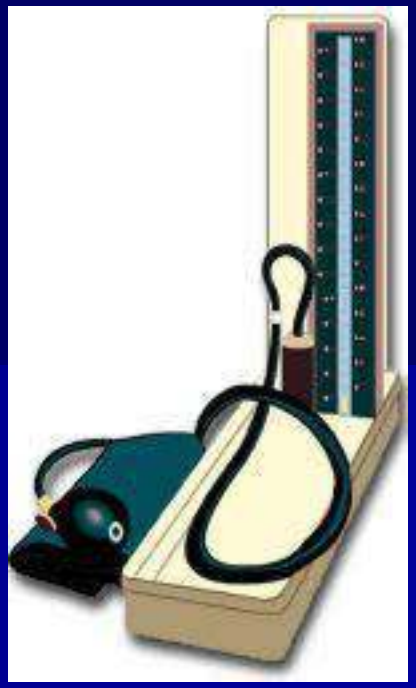


Blood Flow

- Why does blood flow through cardiovascular system? (teleological vs. mechanistic answers)
- *Teleological:* Because diffusion is too slow to support a large and complex organism
- *Mechanistic:* Because the contractions of the heart produce a hydrostatic pressure gradient and the blood wants to flow to the region of lesser pressure. Therefore, the Pressure gradient (ΔP) is main driving force for flow through the vessels

Blood Flow Rate $\propto \Delta P / R$

Pressure



- Hydrostatic pressure is in all directions
  - Measured in mmHg: The pressure to raise a 1 cm column of Hg 1 mm
  - Sphygmomanometer
- Flow is produce by Driving Pressure
- Pressure of fluid in motion decreases over distance because of energy loss due to friction

Blood Flow Rate $\propto \Delta P / R$

Plumbing 101: Resistance Opposes Flow

3 parameters determine resistance (R):

1. **Tube length (L)**
    1. ***Constant in body***
2. **<u>Tube radius</u> (r)**
    1. **Can radius change?**
3. **Fluid viscosity (η (eta))**
    1. **Can blood viscosity change??**

Poiseuille's law

$$R = \frac{8L\eta}{\pi r^4}$$

$$\Rightarrow \quad R \propto 1 / r^4$$

Blood Flow Rate $\propto \Delta P / R$

Velocity (v) of Flow

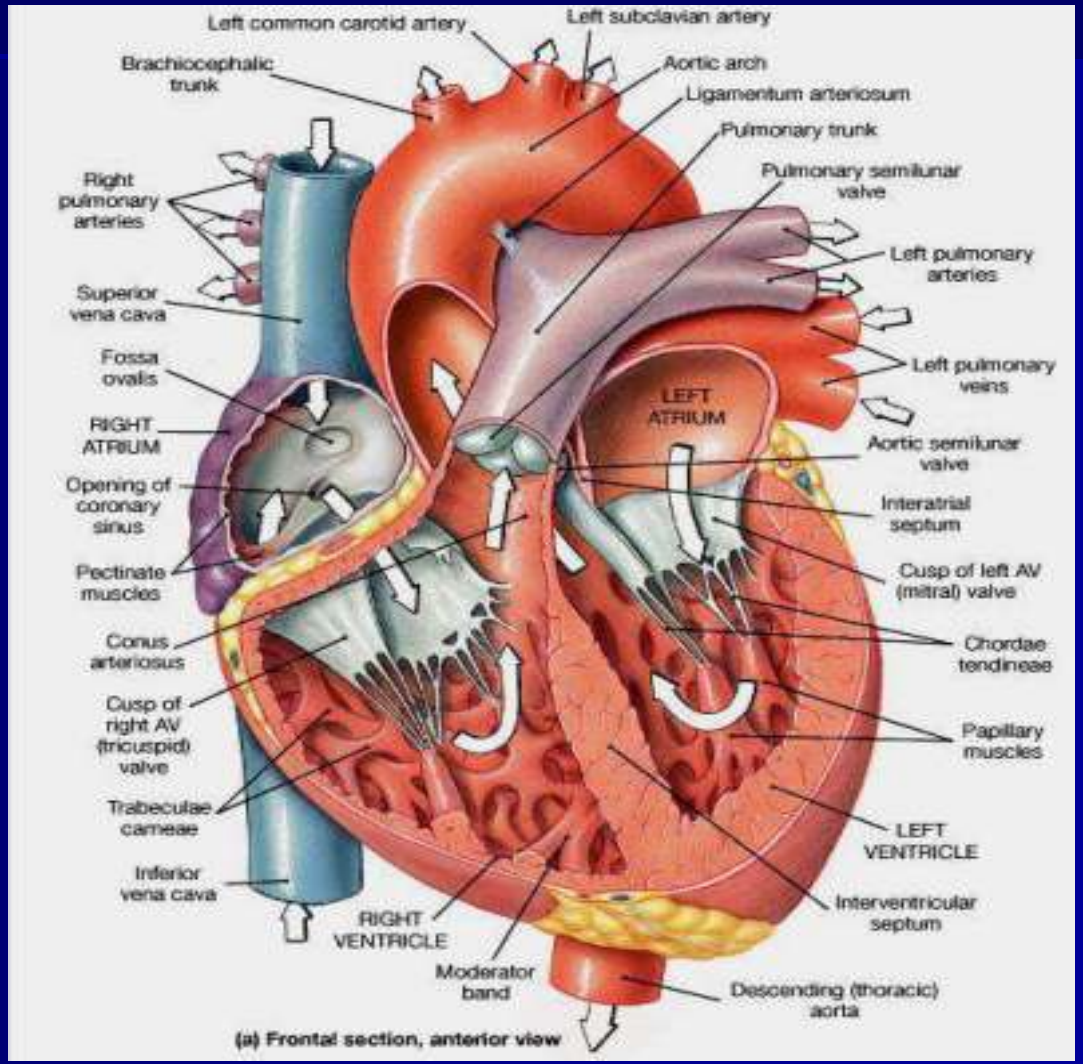
Depends on Flow Rate and Cross-Sectional Area:

- **Flow rate (Q) = volume of blood passing one point in the system per unit of time (e.g., ml/min)**
  - **If flow rate ↑ ⇒ velocity ↑**
- **Cross-Sectional area (A)** (or tube diameter)
  - **If cross sectional area ↑ ⇒ velocity ↓**

$$v = Q / A$$

Cardiac Anatomy

The pathway of a blood cell should be well known to you!



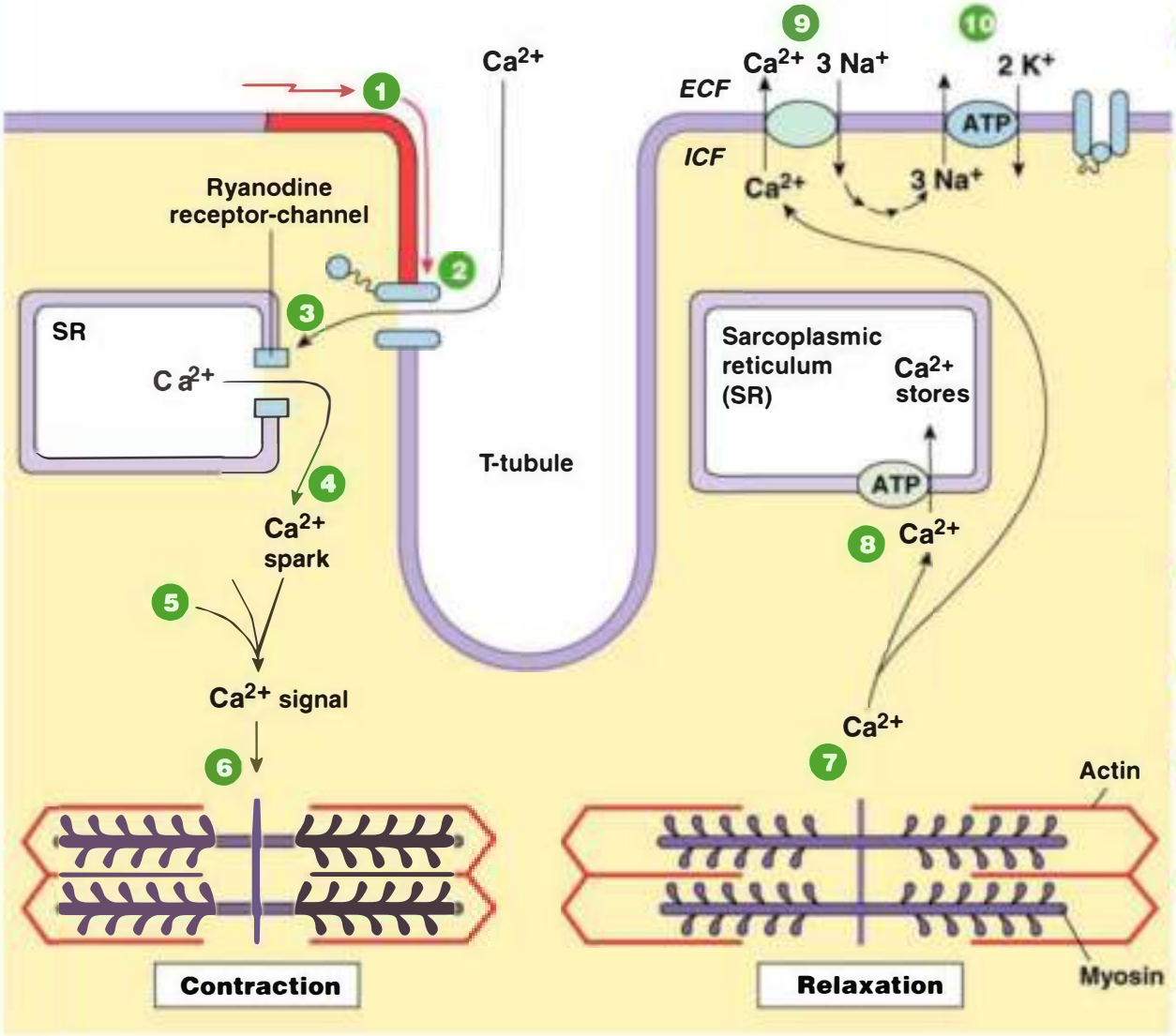
Unique Microanatomy of Cardiac Muscle Cells

- 1% of cardiac cells are autorhythmic
  - Signal to contract is myogenic
- Intercalated discs with gap junctions and desmosomes
  - Electrical link and strength
- SR smaller than in skeletal muscle
  - Extracelllar Ca^{2+} initiates contraction (like smooth muscle)
- Abundant mitochondria extract about 80% of O_2

Excitation-Contraction (EC) Coupling in Cardiac Muscle

- Contraction occurs by same sliding filament activity as in skeletal muscle
- Relaxation similar to skeletal muscle
  - Ca^{2+} removal requires Ca^{2} -ATPase (into SR) & Na^{+}/Ca^{2+} antiport (into ECF)

  [Na^{+}] restored via
- AP is from pacemaker cells (SA node), not neurons
- AP opens voltage-gated Ca^{2+} channels in cell membrane
- Ca^{2+} induces Ca^{2+} release from SR stores



1. Action potential enters from adjacent cell.
2. Voltage-gated Ca^{2+} channels open. Ca^{2+} enters cell.
3. Ca^{2+} induces Ca^{2+} release through ryanodine receptor-channels (RyR).
4. Local release causes Ca^{2+} spark.
5. Summed Ca^{2+} sparks create a Ca^{2+} signal.
6. Ca^{2+} ions bind to troponin to initiate contraction.
7. Relaxation occurs when Ca^{2+} unbinds from troponin.
8. Ca^{2+} is pumped back into the sarcoplasmic reticulum for storage.
9. Ca^{2+} is exchanged with Na^{+}.
10. Na^{+} gradient is maintained by the Na^{+}-K^{+}-ATPase.

Cardiac Muscle Cell Contraction is Graded

- **Skeletal muscle cell:** all-or-none contraction in any single fiber for a given fiber length.
  Graded contraction in skeletal muscle occurs through?

- **Cardiac muscle:**
  - **force ∝ to sarcomere length** (up to a maximum)
  - **force ∝ to # of Ca^{2+} activated crossbridges** (Function of intracellular Ca^{2+}: if $[Ca^{2+}]_{in}$ low → not all crossbridges activated)

Foxglove for a Failing Heart

See cardiac glycosides p. 492

- **Cardiac glycosides from *Digitalis purpurea***

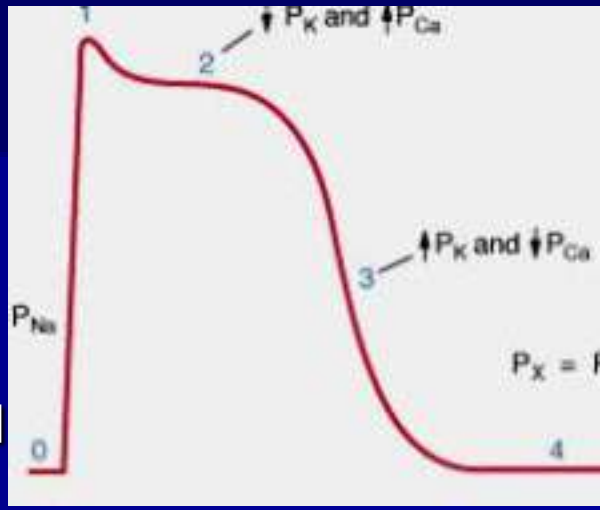
  ⇓

  digoxin

- **Highly toxic in large dosage: destroys all Na^+/K^+ pumps**
- **In low dosage: partial block of Na^+ removal from myocardial cells**
- **The Na^+ - Ca^{2+} pump is less effective and there will be more Ca^+ for coupling**

Explain mechanism of action !

APs in Contractile Myocardial Cells

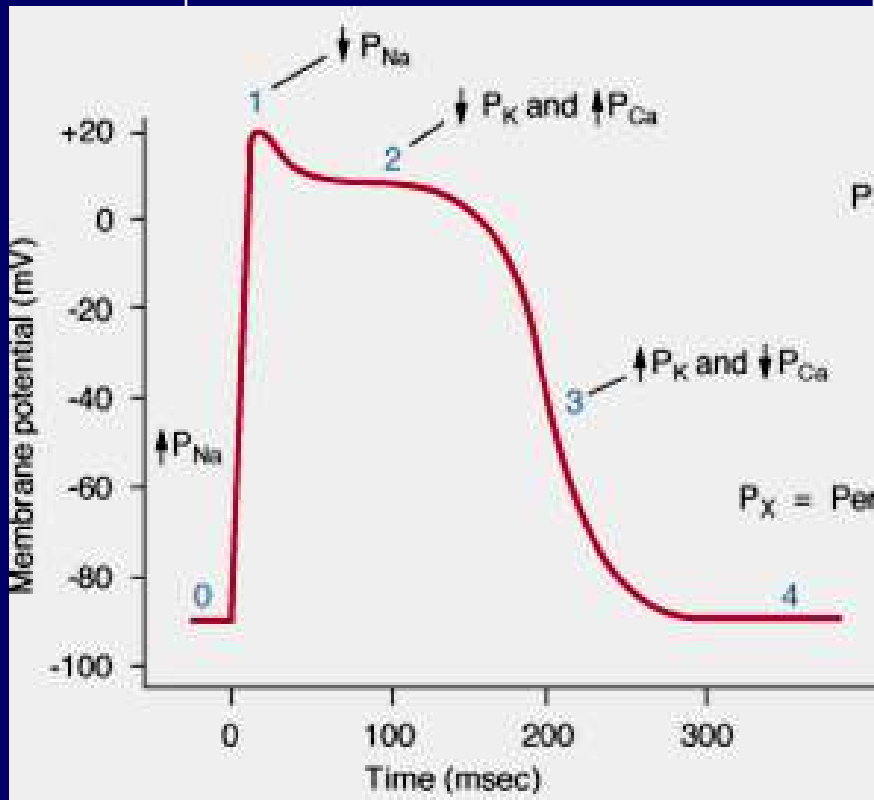


- Similar to skeletal muscle
- Phase 4: Stable resting pot. ~ -90 mV
- Phase 0: Depolarization due to voltage-gated Na^+ channels *(Na^+ movement?)*
- Phase 1: Partial Repolarization as Na^+ channels close and voltage-gated K^+ channels open *(K^+ movement?)*
- Phase 2: Plateau: ↑ K^+ permeability and ↓ Ca^{2+} permeability
- Phase 3: Repolarization: Back to resting potential

APs in Contractile Myocardial Cells

- Much longer AP
- Refractory period and contraction end simultaneously - Why important?

AP in skeletal muscle : 1-5 msec
AP in cardiac muscle :200 msec



Myocardial Autorhythmic Cells

- Anatomically distinct from contractile cells – Also called pacemaker cells
- Membrane Potential = – 60 mV
- Spontaneous AP generation as gradual depolarization reaches threshold
  - Unstable resting membrane potential (= pacemaker potential)
  - The cell membranes are “leaky”
  - Unique membrane channels that are permeable to both Na^+ and K^+

Myocardial Autorhythmic Cells, cont'd.

I_f-channel Causes Mem. Pot. Instability

- Autorhythmic cells have different membrane channel: I_f - channel

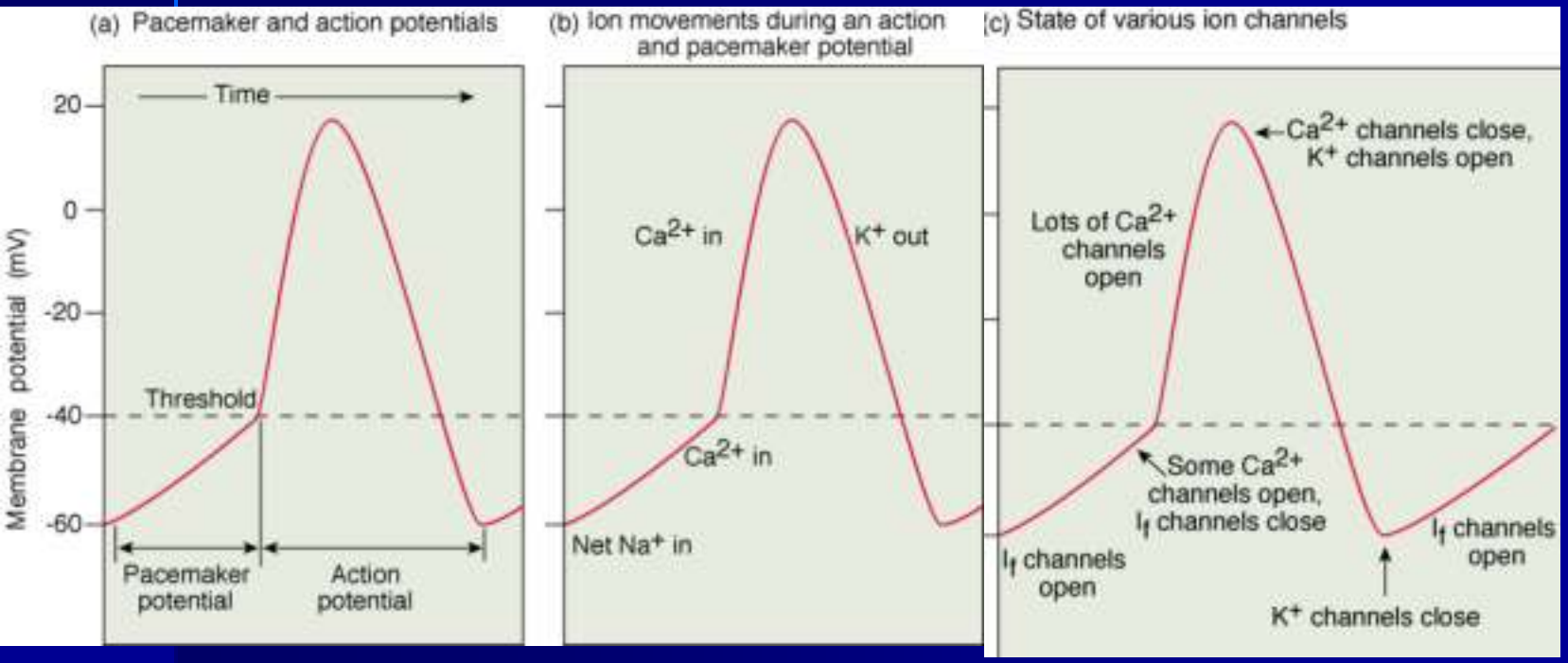
allow current (= I) to flow

f = "funny": researchers didn't understand initially

- I_f channels let K^+ & Na^+ through at -60mV
- Na^+ influx > K^+ efflux
- slow depolarization to threshold

Myocardial Autorhythmic Cells, cont'd.

"Pacemaker potential" starts at ~ -60mV, slowly drifts to threshold



AP

Heart Rate = Myogenic
Skeletal Muscle contraction = ?