Physiology of the Heart

Conduction System
Cardiac Cellular Electrophysiology
Electromechanic Coupling

Assoc. Prof. MUDr. Markéta Bébarová, PhD

Department of Physiology

Faculty of Medicine

Masaryk University

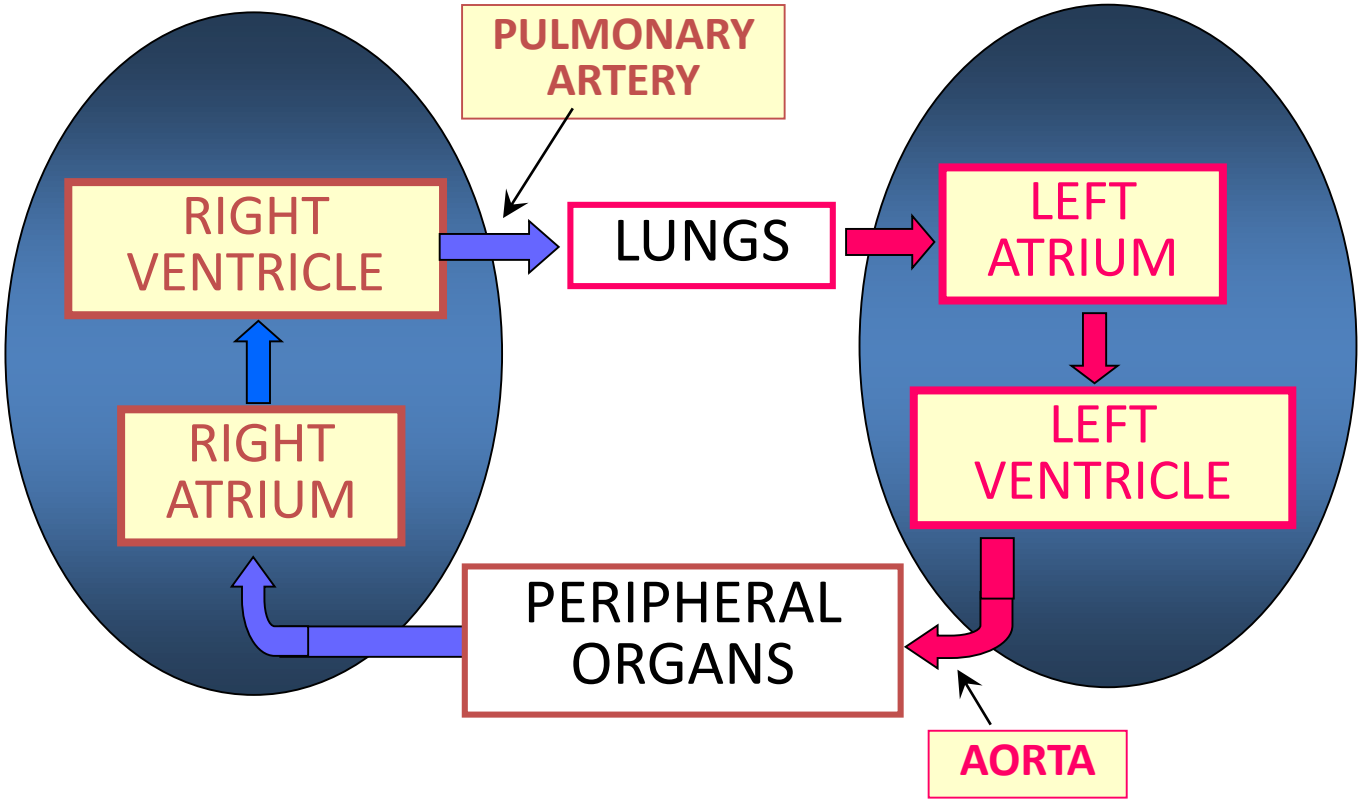
ORGANIZATION OF CARDIOVASCULAR SYSTEM

Roles of the Cardiovascular System

- **primary role** - distribution of dissolved gases and other nutrients
- **several secondary roles, for example:**
  - fast chemical signalling to the cells (circulating hormones and neurotransmitters)
  - thermoregulation (delivery of heat from the core to the surface of the body)
  - immune reaction
- **roles of the heart:**
  - primary role - pumping of blood
  - endocrinne organ (natriuretic peptides)

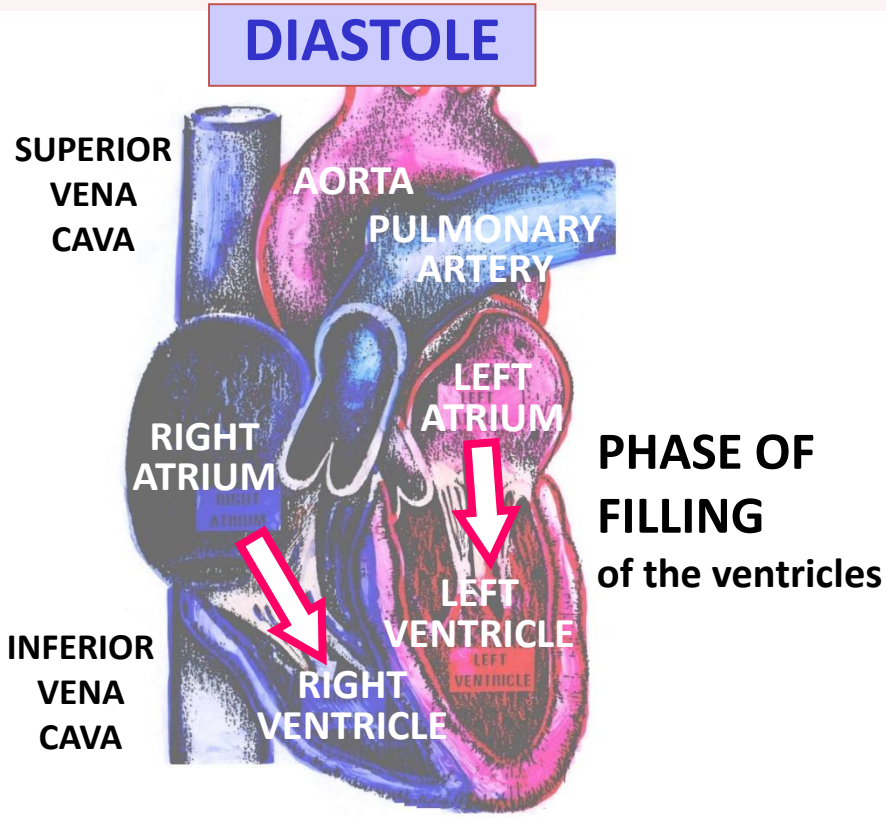
ORGANIZATION OF CARDIOVASCULAR SYSTEM

TWO PUMPS INTERCONNECTED IN SERIES

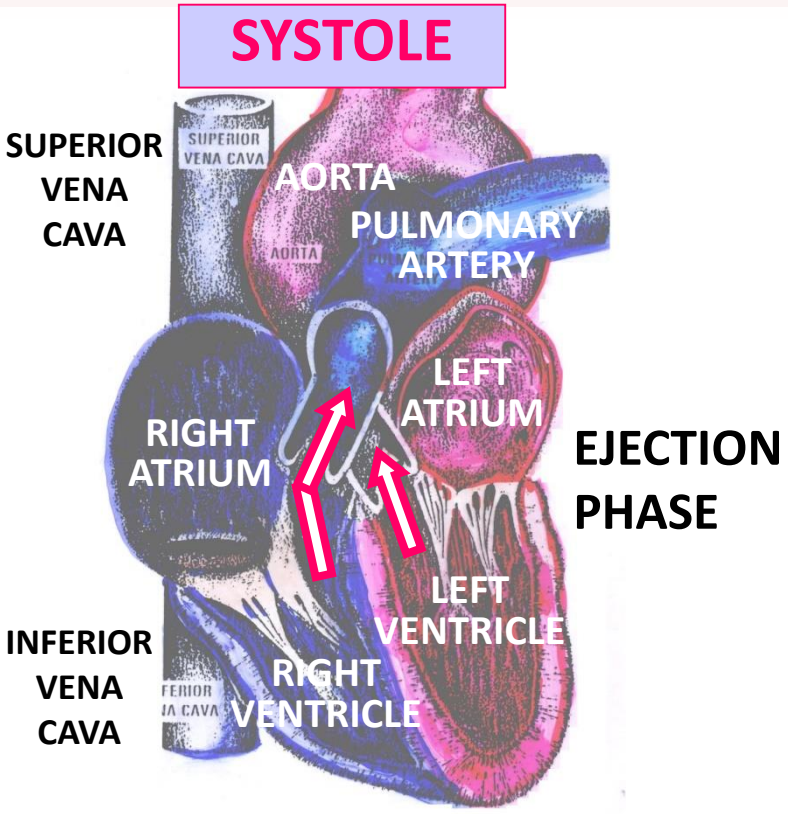


ORGANIZATION OF CARDIOVASCULAR SYSTEM

Two Main Phases of the Cardiac Cycle



PHASE OF FILLING
of the ventricles



EJECTION PHASE

ONE WAY VALVES	DIASTOLE	SYSTOLE
ATRIOVENTRICULAR (mitral and tricuspid)	open	closed
SEMILUNAR (aortal and pulmonary)	closed	open

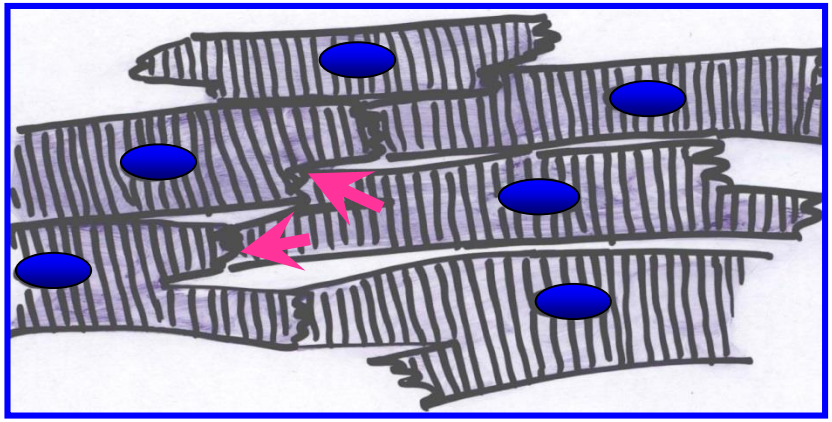
ORGANIZATION OF CARDIOVASCULAR SYSTEM

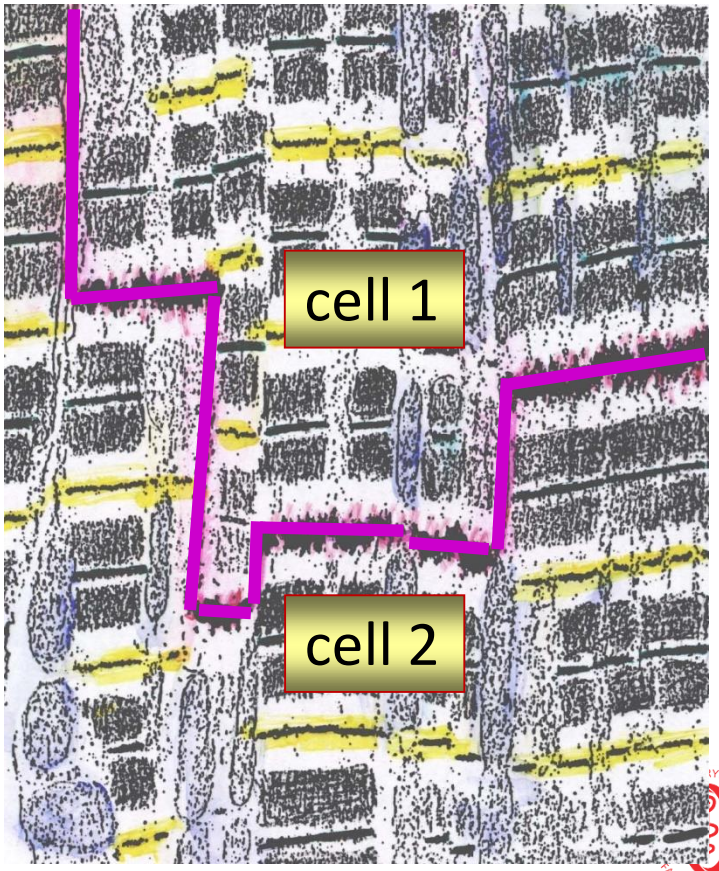
Two Major Types of Cardiac Cells

- **cardiomyocytes of the working myocardium** - specialized for contraction (atrial and ventricular myocytes)

FUNCTIONAL SYNCYTIUM

- mechanical connections
- electrical connections - **gap junctions**





ORGANIZATION OF CARDIOVASCULAR SYSTEM

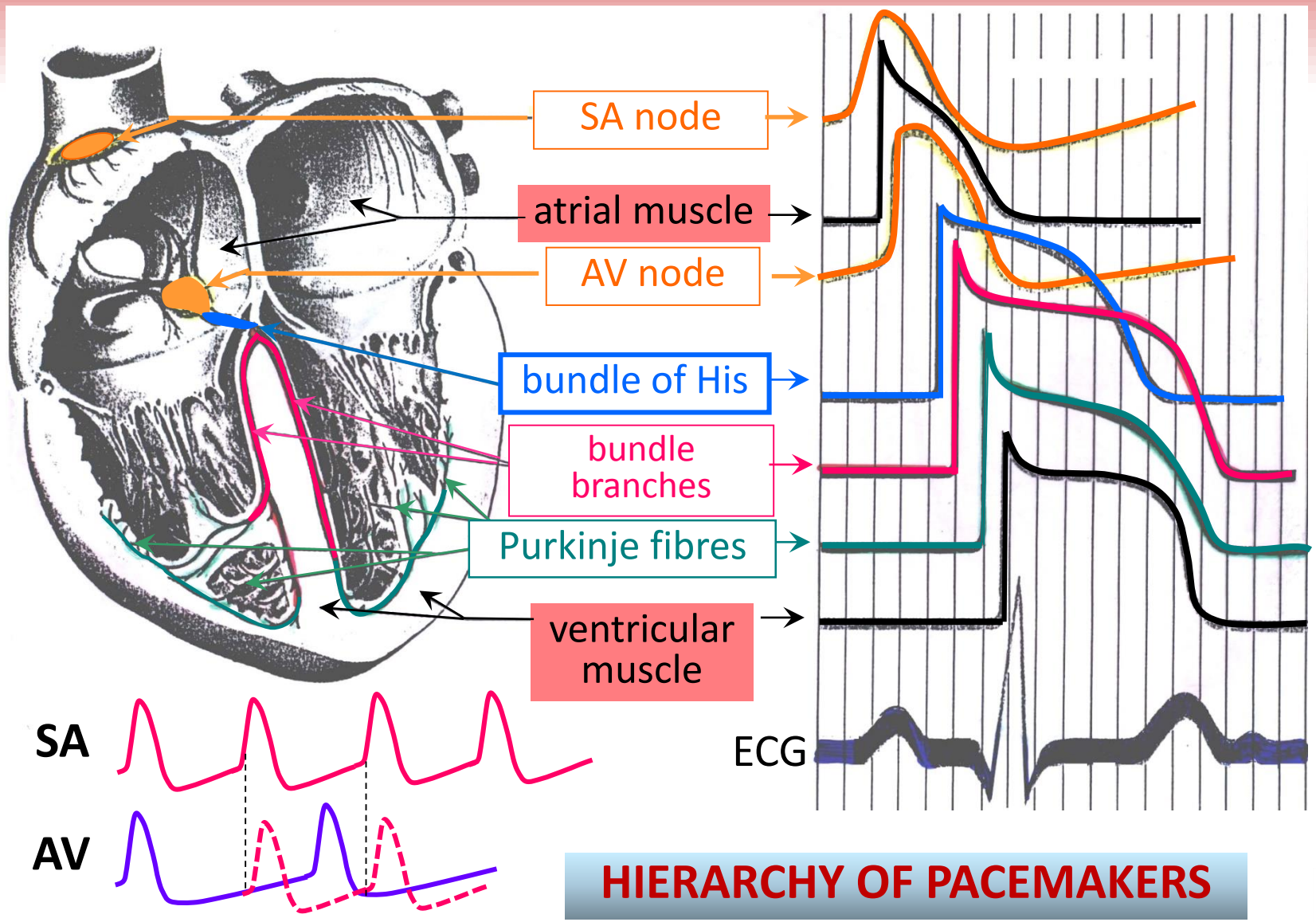
Two Major Types of Cardiac Cells

- **cardiomyocytes of the working myocardium** - specialized for contraction (atrial and ventricular myocytes)
- **cardiomyocytes of the cardiac conduction system** - specialized for:
  - automatic excitation (pacemaker activity)
  - conduction of excitation

The cardiac conduction system ensures:

1) generation of automatic electrical activity of the heart (pacemaker activity) that initiates its mechanical activity
2) optimal timing of the mechanical activity of the heart as a pump

CARDIAC CONDUCTION SYSTEM



HIERARCHY OF PACEMAKERS

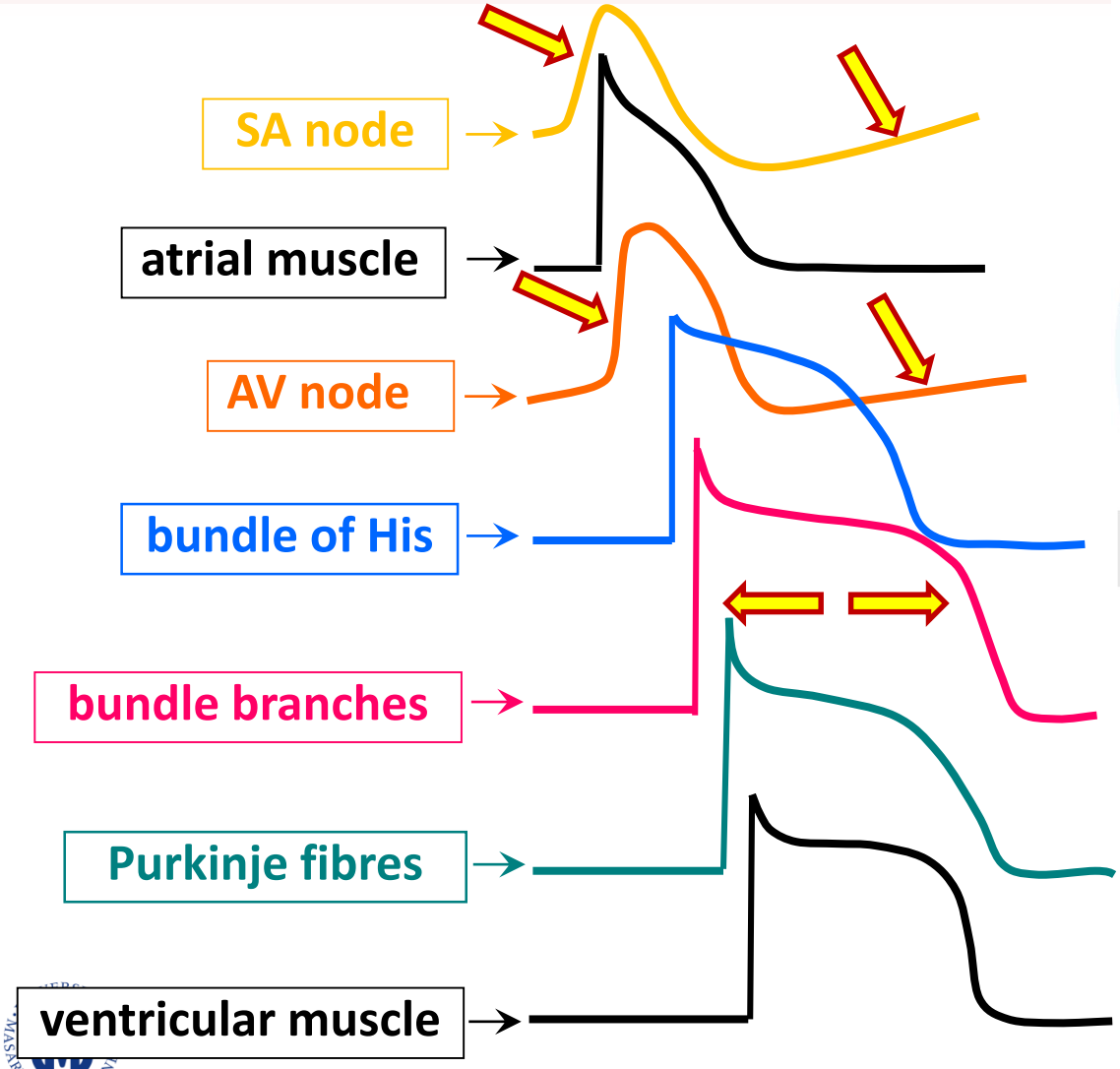
CARDIAC CONDUCTION SYSTEM

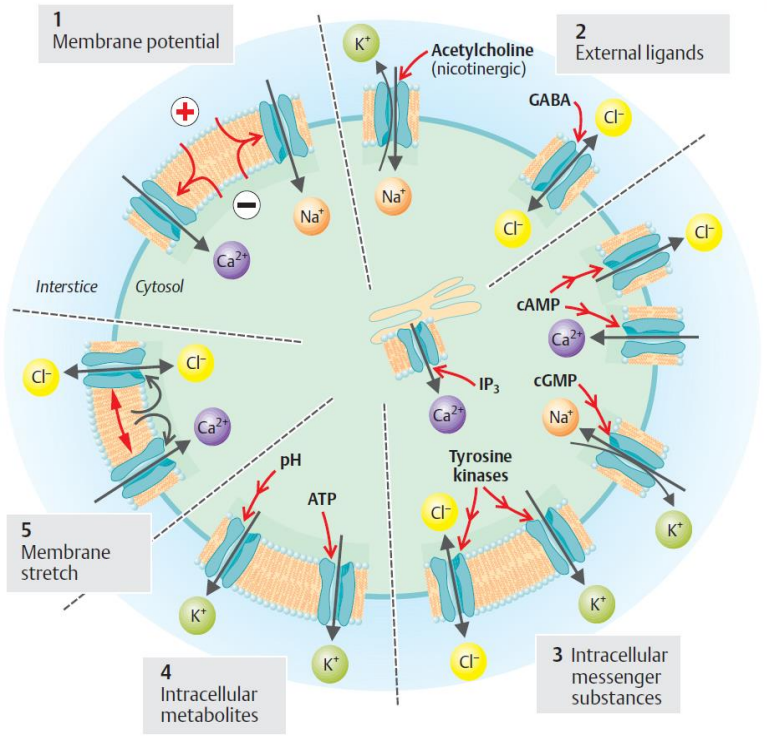
- **SINOATRIAL (SA) NODE**
  PRIMARY pacemaker (60-100 impulses/min) — **0.05 m/s**
- **INTERNODAL PREFERENTIAL PATHWAYS** — **1 m/s**
- **ATRIOVENTRICULAR (AV) NODE**
  SECONDARY pacemaker (40-55 impulses/min) — **0.05 m/s**
- **BUNDLE OF HIS** — **1 m/s**
- **BUNDLE BRANCHES** (LEFT AND RIGHT) — **1 m/s**
- **PURKINJE FIBRES**
  TERCIARY pacemaker (25-40 impulses/min) — **4 m/s**

Conduction velocity in atrial and ventricular muscle: 1 m/s

CARDIAC CELLULAR ELECTROPHYSIOLOGY

Ionic Currents Underlying Action Potential Configuration





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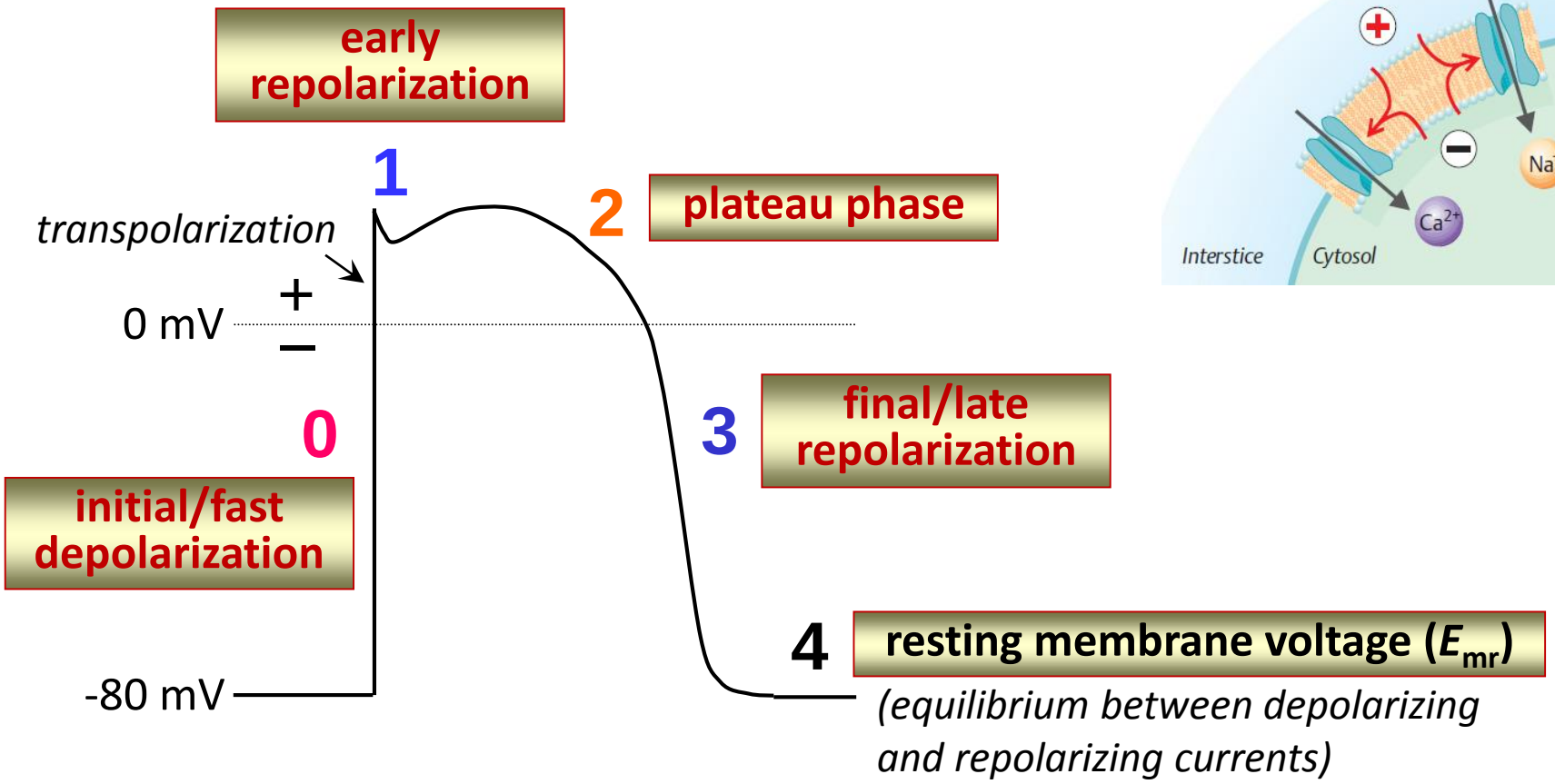
CARDIAC CELLULAR ELECTROPHYSIOLOGY

Ionic Currents Underlying Action Potential Configuration



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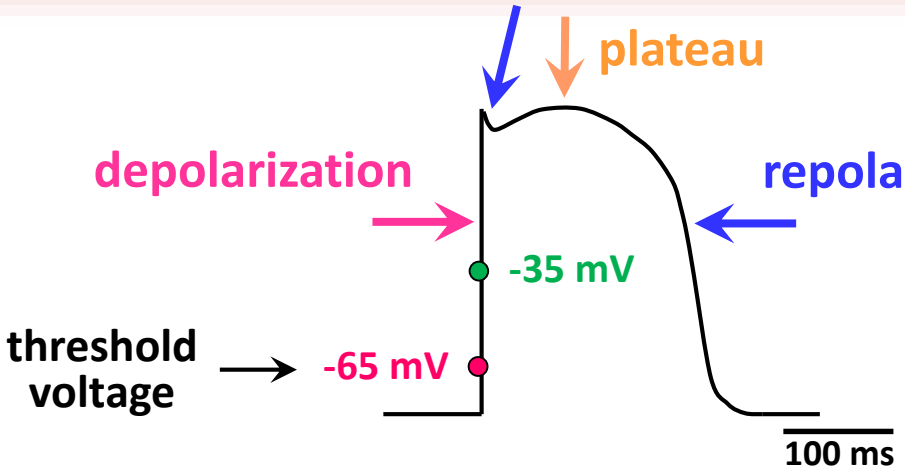
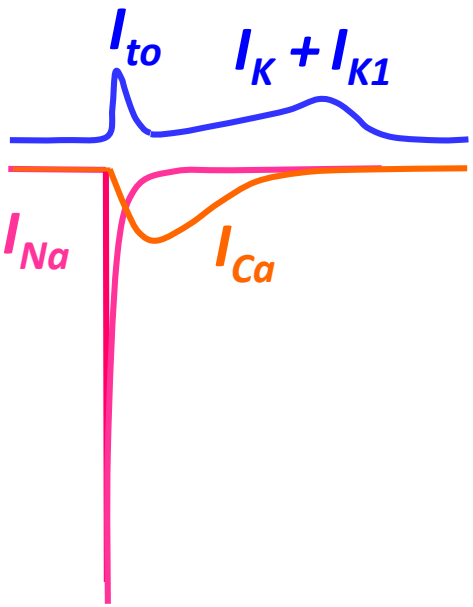
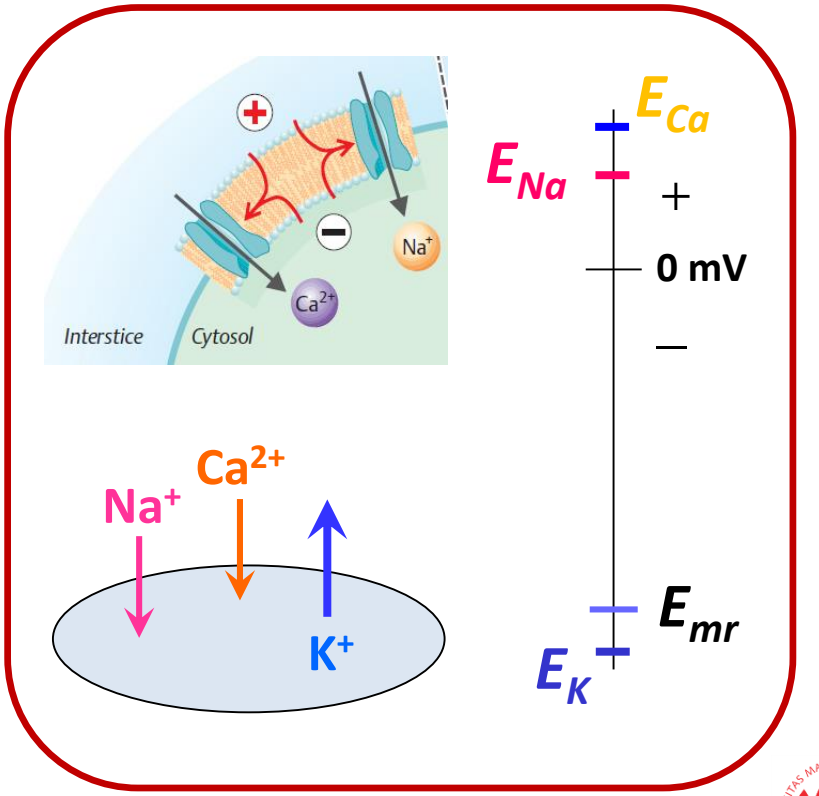
Ionic Currents Underlying Action Potential Configuration







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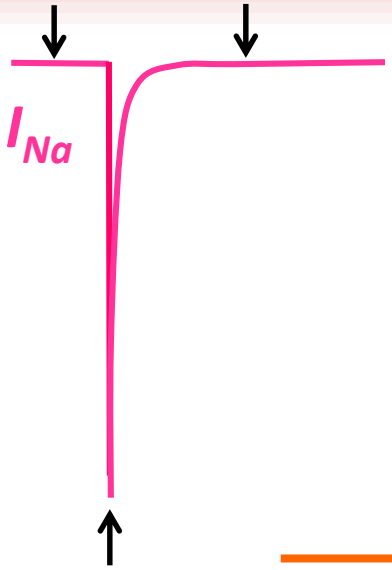
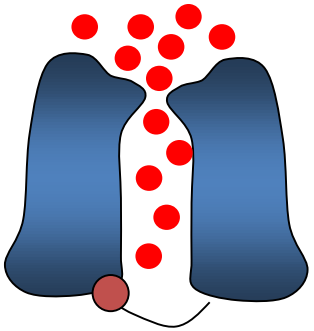
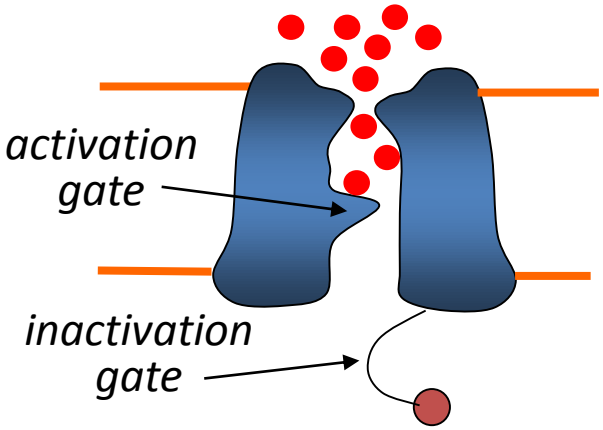
Ionic Currents Underlying Action Potential Configuration



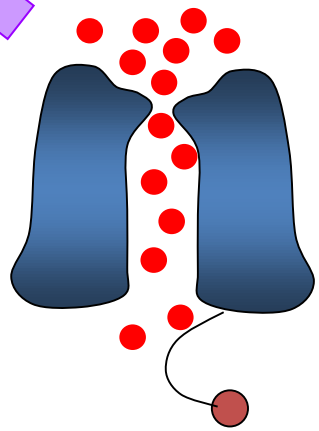
INACTIVATED STATE
(closed)



INACTIVATION
(at maintained membrane depolarization)



ACTIVATION
(depolarization over threshold voltage)

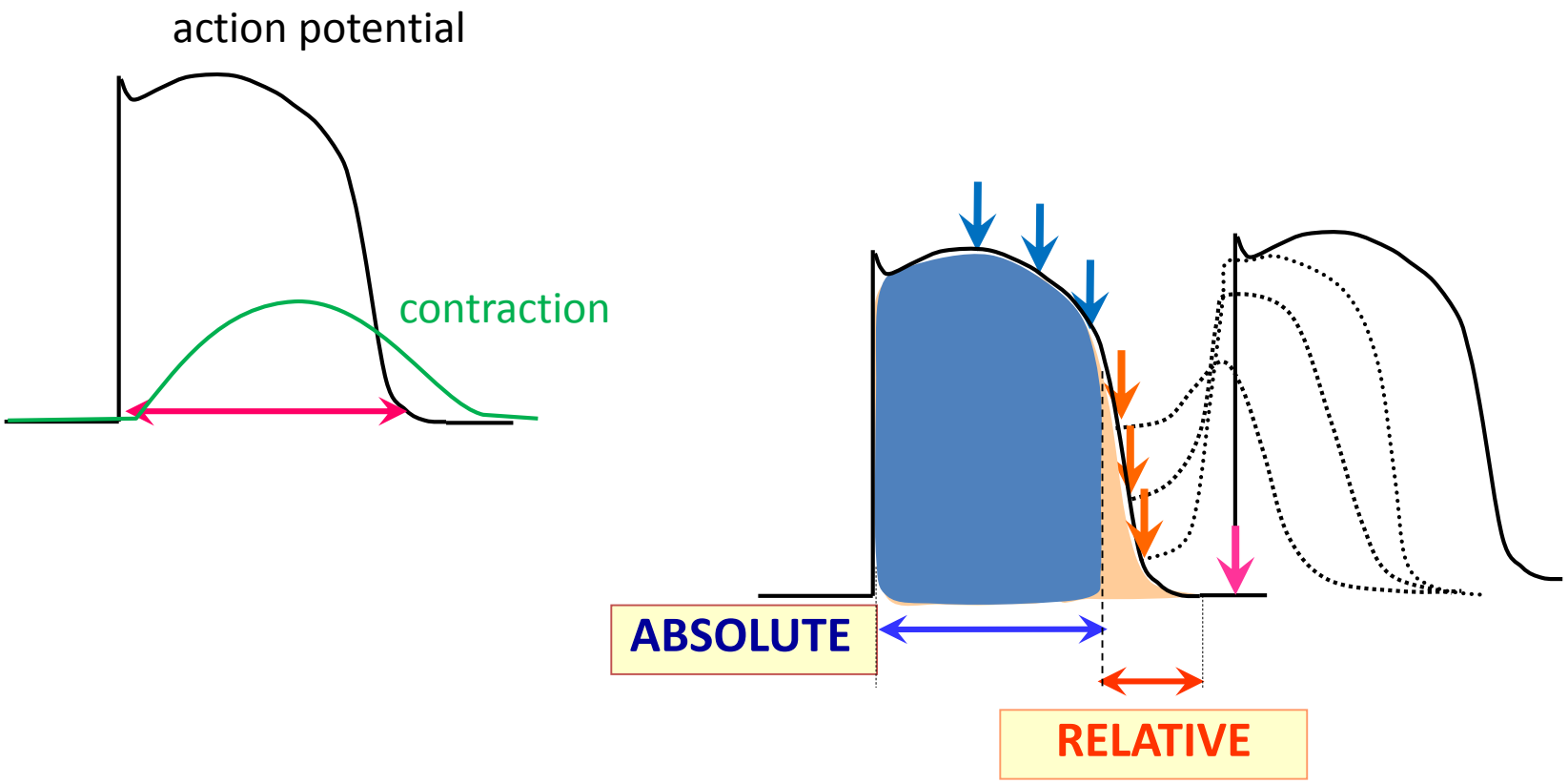


RESTING STATE
(closed)

OPEN STATE

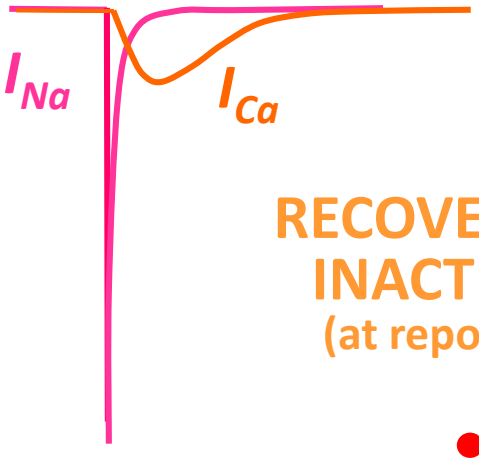
CARDIAC CELLULAR ELECTROPHYSIOLOGY

Refractory Period – Suppression of Excitability



CARDIAC CELLULAR ELECTROPHYSIOLOGY

Refractory Period - Mechanism



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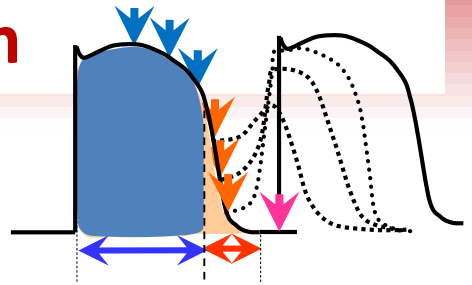
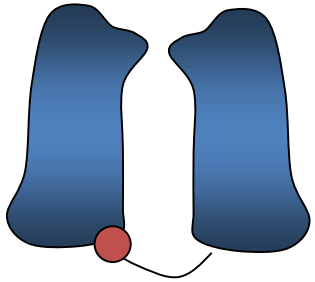
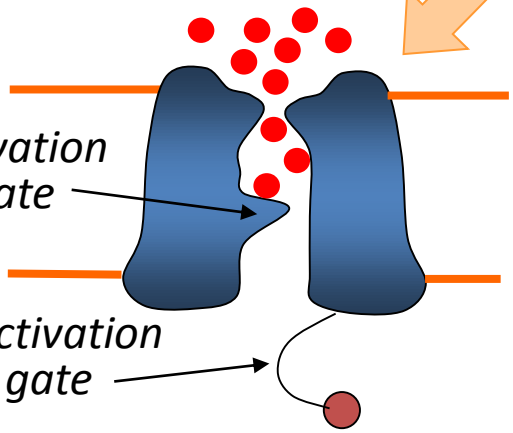


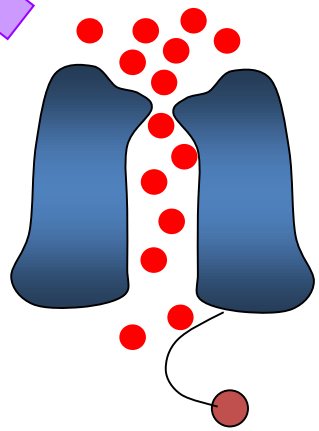
INACTIVATION
(at maintained membrane depolarization)

RECOVERY FROM INACTIVATION
(at repolarization)





ACTIVATION
(depolarization over threshold voltage)

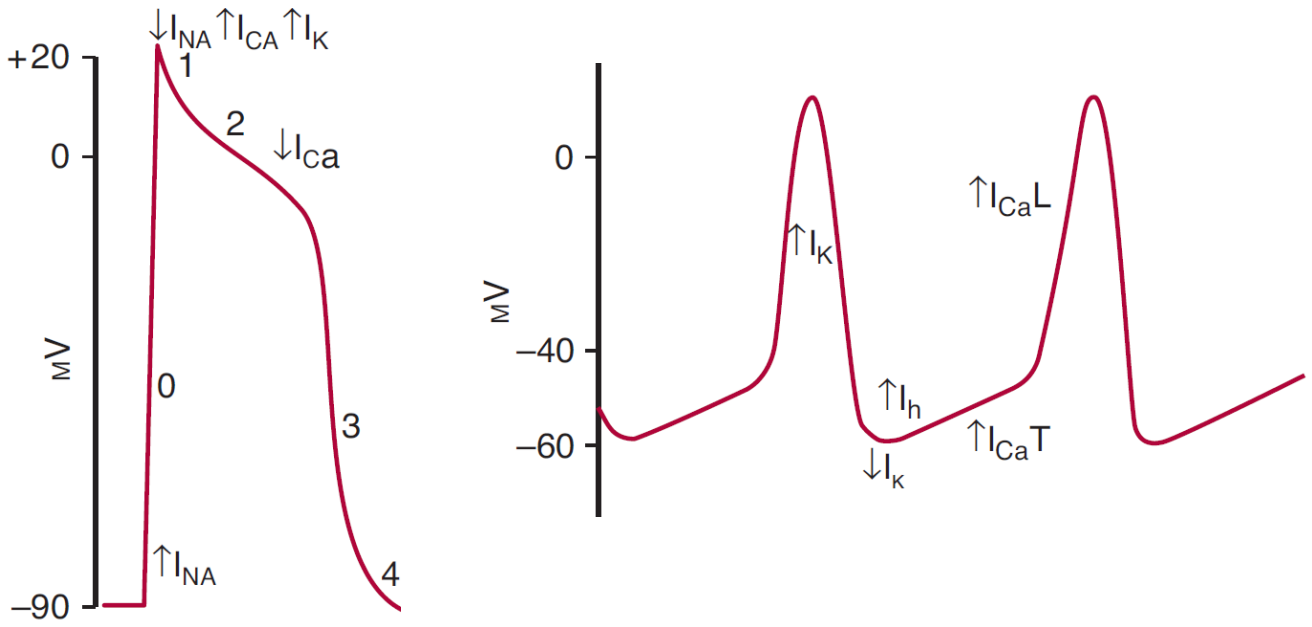


RESTING STATE
(closed)

OPEN STATE

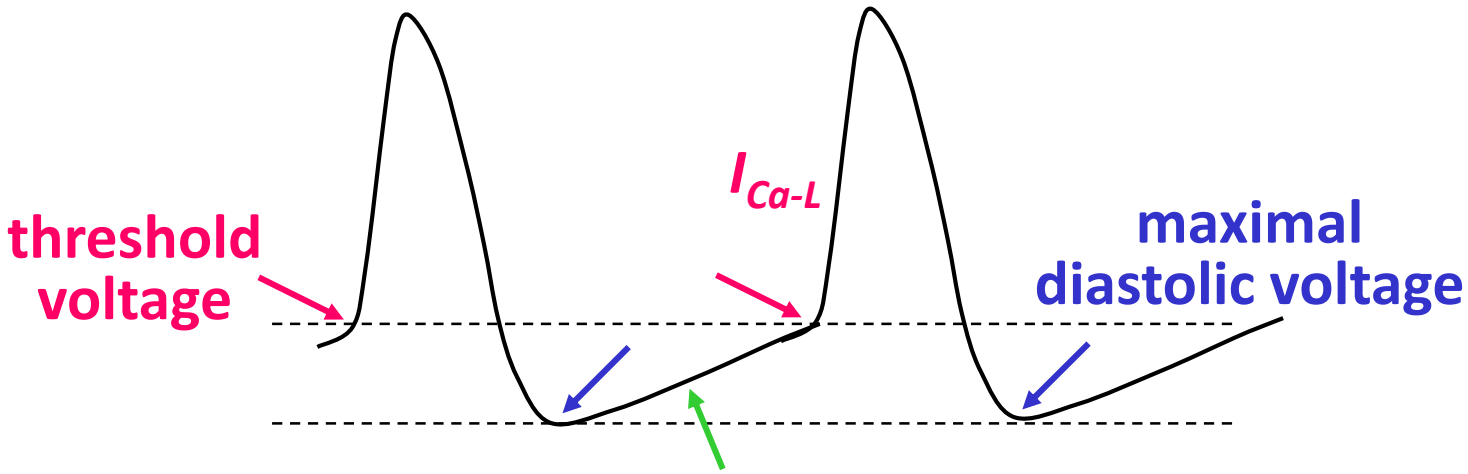
CARDIAC CELLULAR ELECTROPHYSIOLOGY

Pacemaker Activity - Mechanism



CARDIAC CELLULAR ELECTROPHYSIOLOGY

Pacemaker Activity - Mechanism

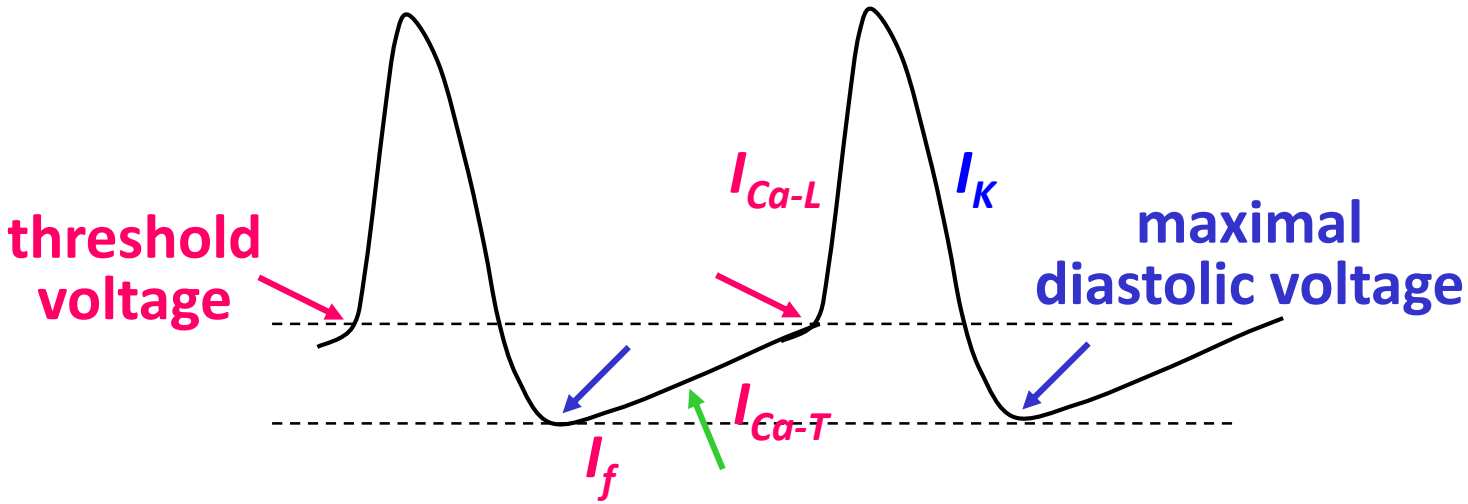


FACTORS DETERMINING THE HEART RATE:

1) maximal diastolic voltage
2) steepness of diastolic depolarization
3) threshold voltage for activation of $I_{Ca\text{-}L}$

CARDIAC CELLULAR ELECTROPHYSIOLOGY

Pacemaker Activity - Mechanism

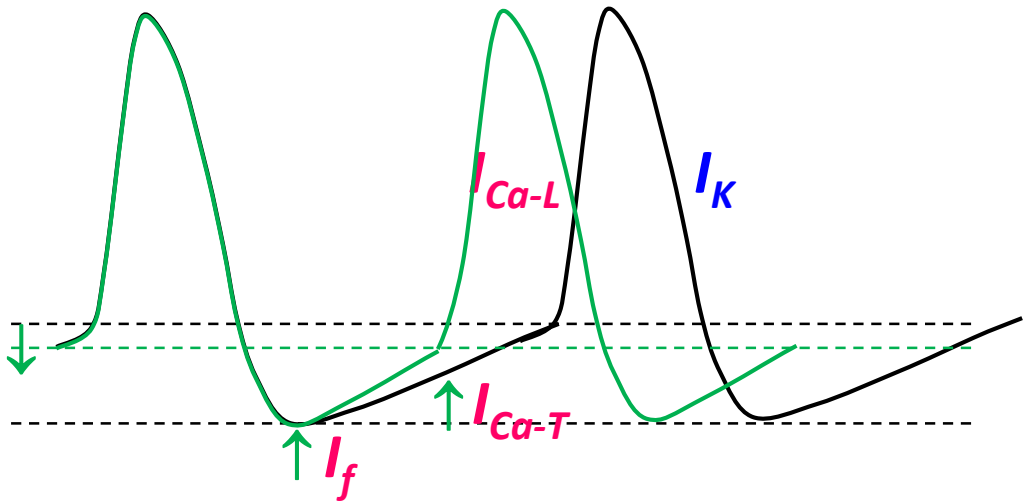


COMPLEX PROCESS resulting from an <u>INTERPLAY</u> between

- **REPOLARIZING CURRENTS, namely I_K (including $I_{K,Ach}$)**
- **DEPOLARIZING CURRENTS, namely I_f and $I_{Ca\text{-}T}$**

CARDIAC CELLULAR ELECTROPHYSIOLOGY

Pacemaker Activity - Mechanism

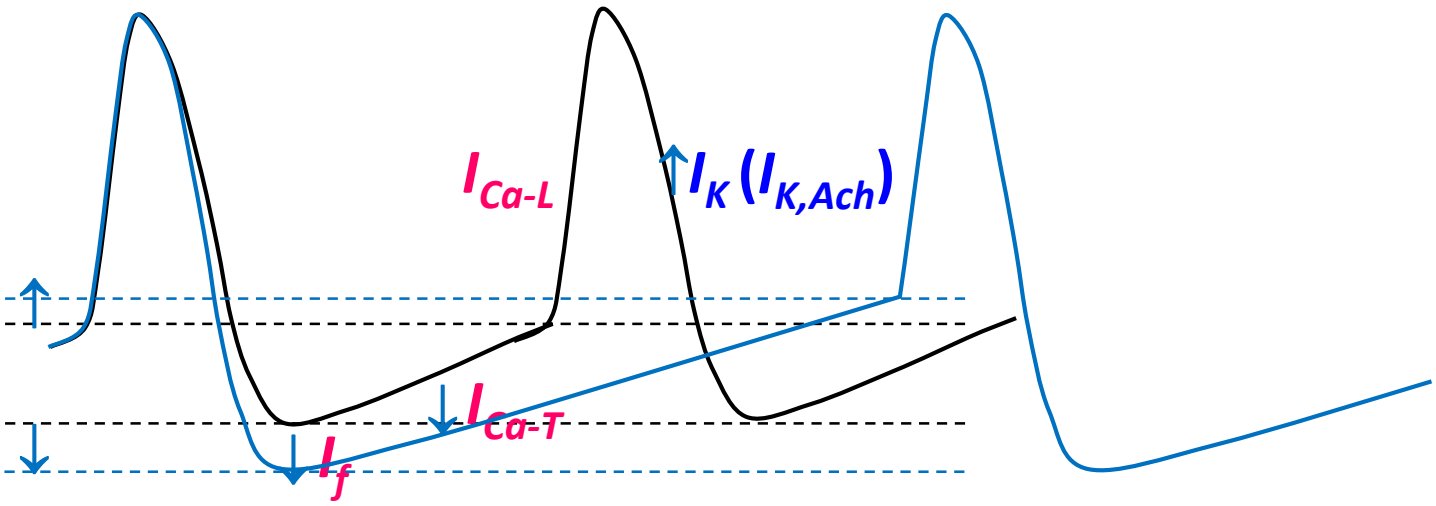


SYMPATHETIC STIMULATION

- ↑ cAMP ⟶ ↑ I_f and I_{Ca-T} ⟶ ↑ rate of diastolic depolarization
  ⟶ ↓ threshold voltage for activation of I_{Ca-L}
  (↑ excitability)

CARDIAC CELLULAR ELECTROPHYSIOLOGY

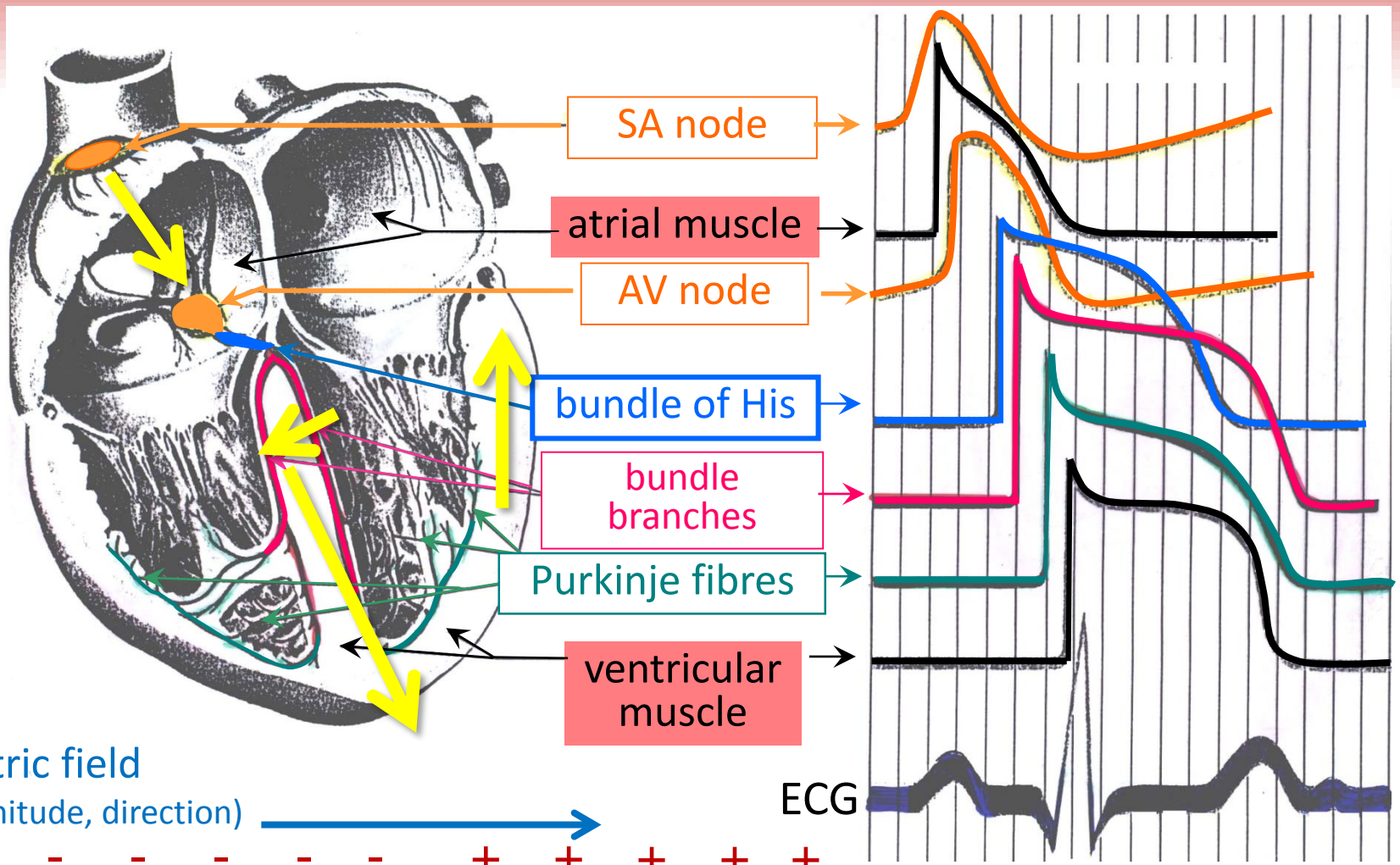
Pacemaker Activity - Mechanism



PARASYMPATHETIC STIMULATION

- ↓ cAMP ⟶ ↓ I_f and $I_{Ca\text{-}T}$ ⟶ ↓ rate of diastolic depolarization
  ⟶ ↑ threshold voltage for activation of $I_{Ca\text{-}L}$
  (↓ excitability)
- activation of $I_{K,Ach}$ ⟶ ↓ maximal diastolic voltage

SPREADING OF EXCITATION IN THE HEART

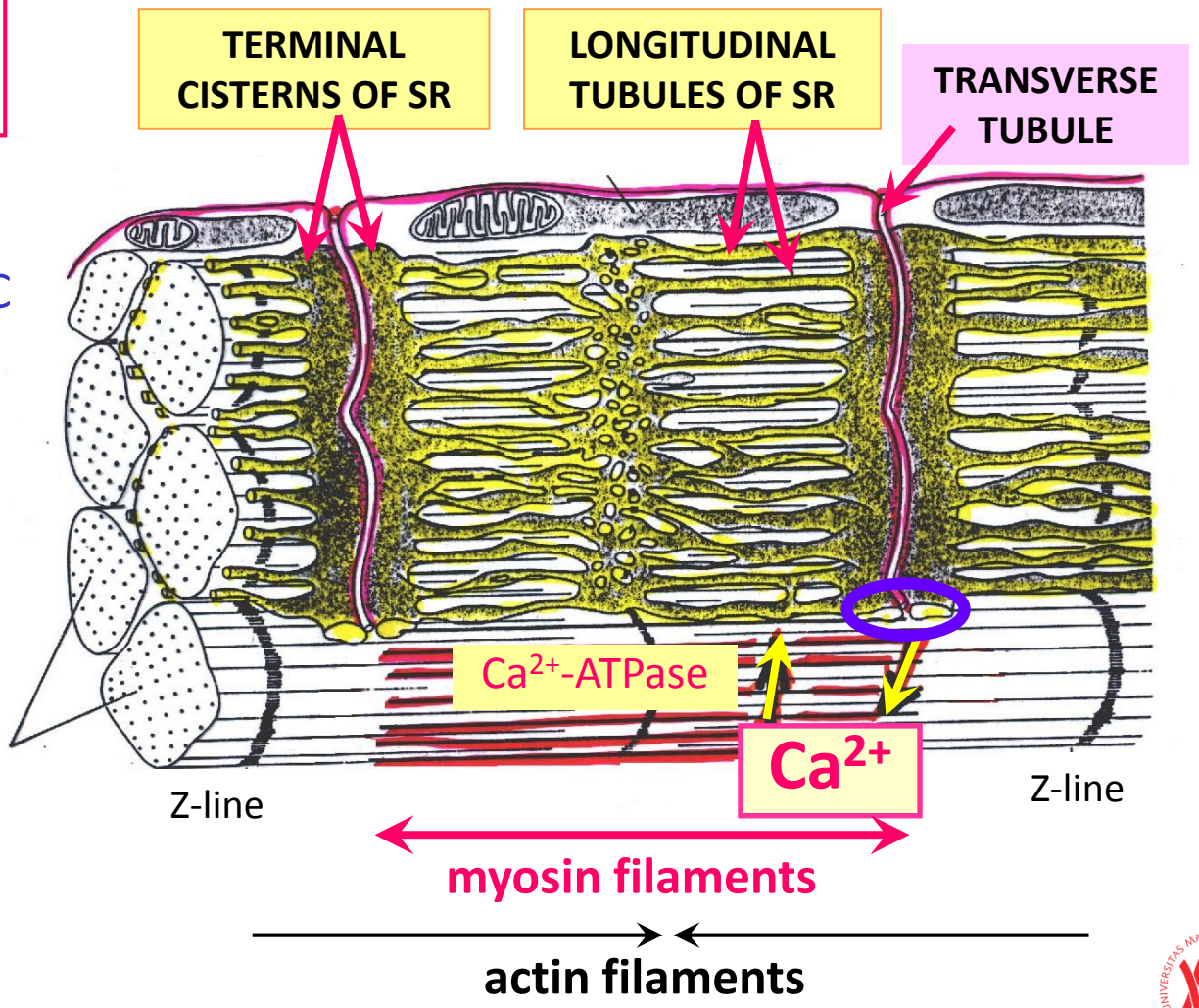


ELECTROMECHANICAL COUPLING

Excitation-Contraction Coupling

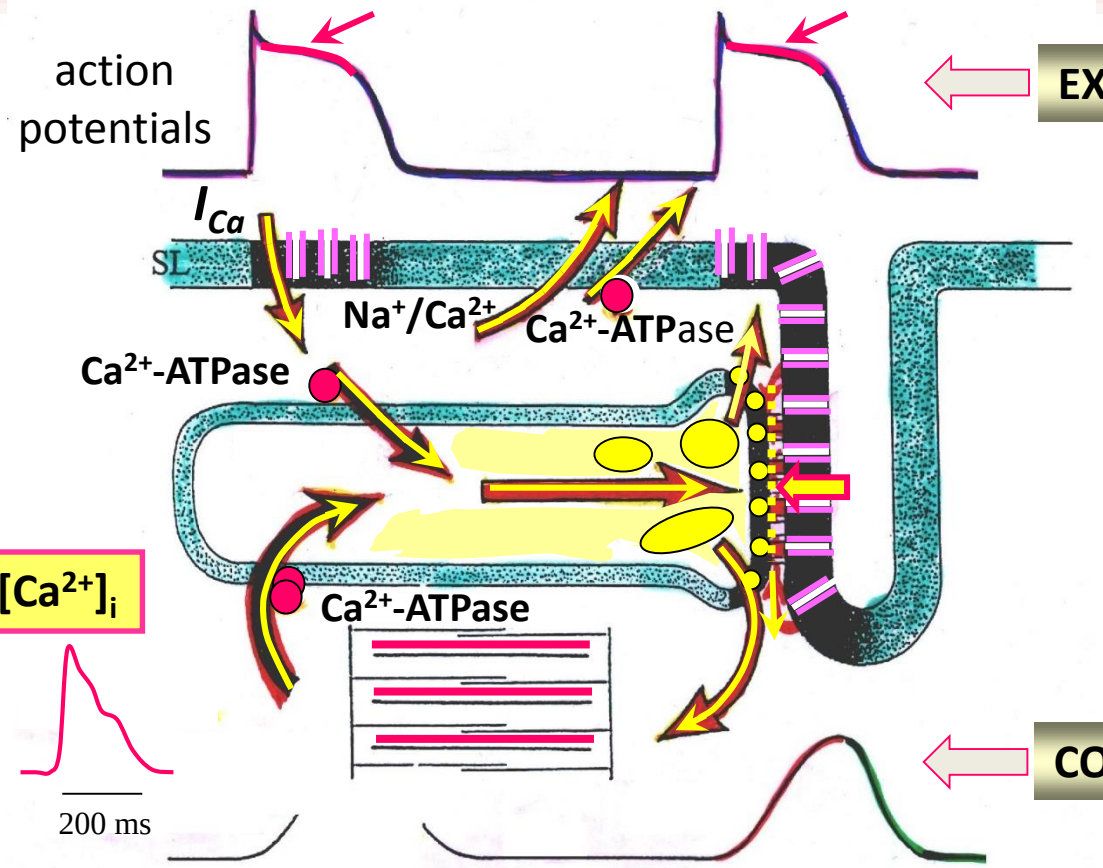
SARCOTUBULAR SYSTEM

SIMILAR ARRANGEMENT IN SKELETAL AND CARDIAC MUSCLE CELLS



ELECTROMECHANICAL COUPLING

Excitation-Contraction Coupling in Cardiomyocytes



voltage-dependent Ca^{2+} channels in the cell membrane (both the surface membrane and membrane of t-tubules)

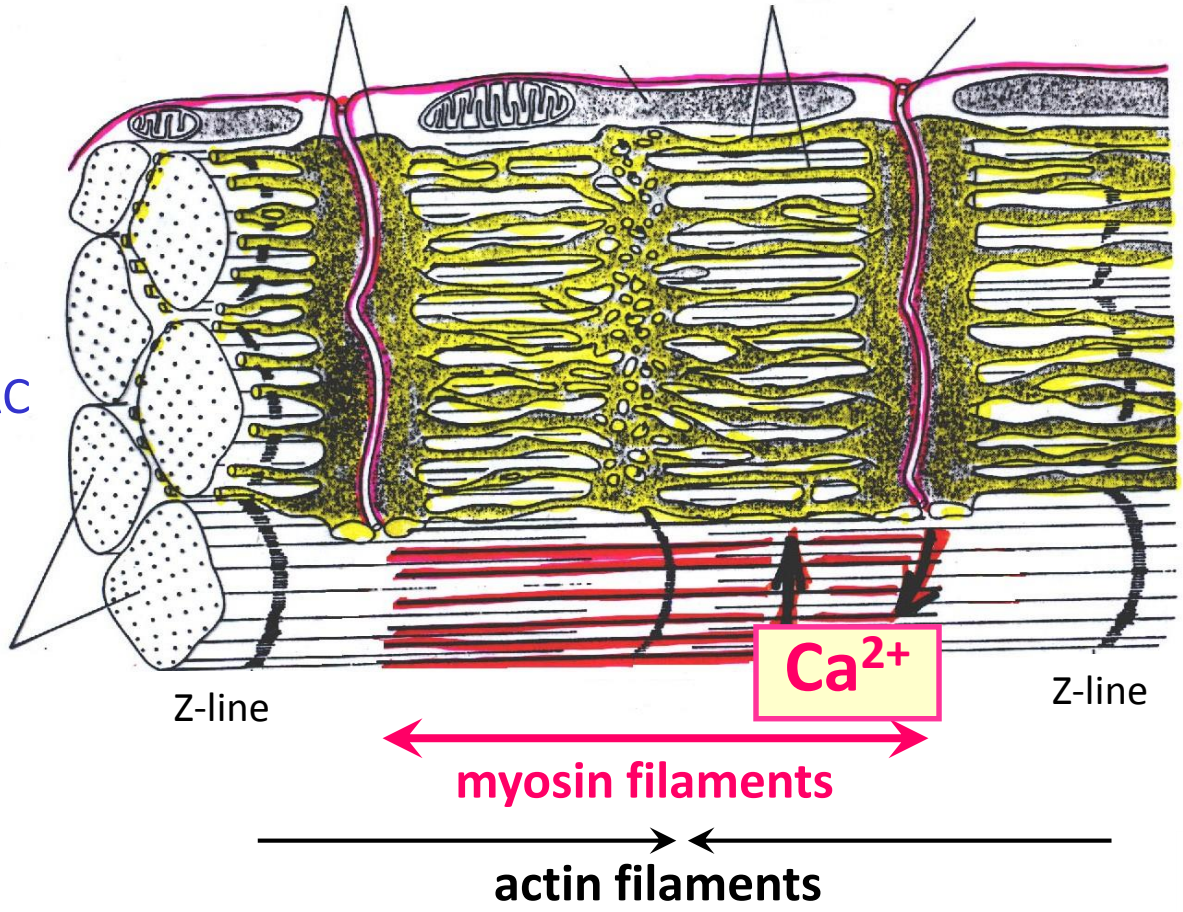
Ca^{2+}-RELEASE channels in SR (Ca^{2+}-sensitive)

ELECTROMECHANICAL COUPLING

Molecular Mechanism of Contraction

FORMATION OF CROSS BRIDGES BETWEEN ACTIN AND MYOSIN FILAMENTS

MECHANISM IDENTICAL
IN SKELETAL AND CARDIAC
MUSCLE CELLS

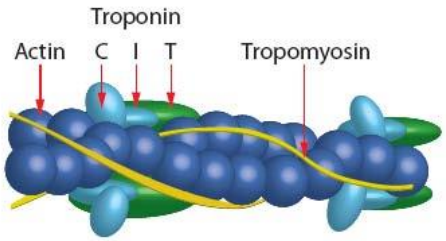


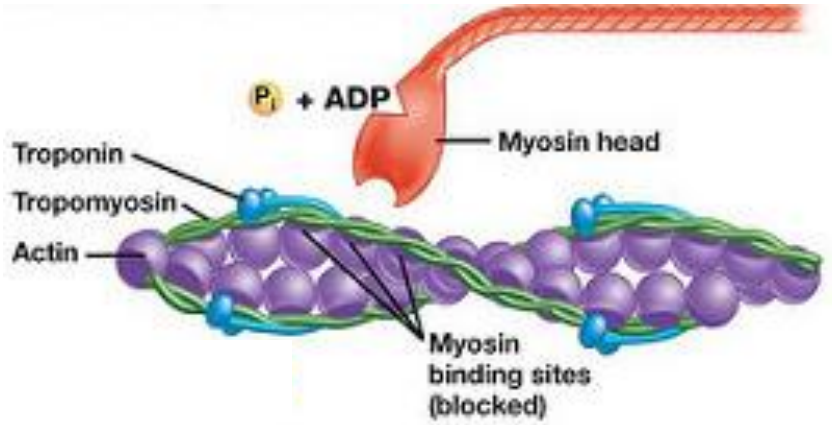
ELECTROMECHANICAL COUPLING

Molecular Mechanism of Contraction

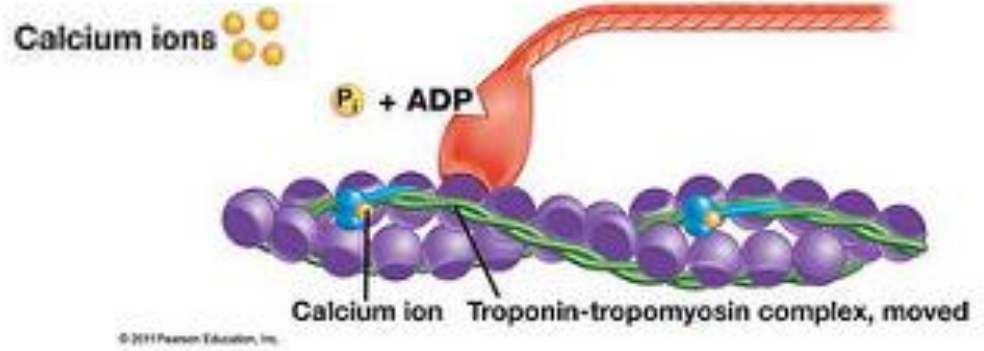
TROPONIN-TROPOMYOSIN COMPLEX

RESTING MUSCLE



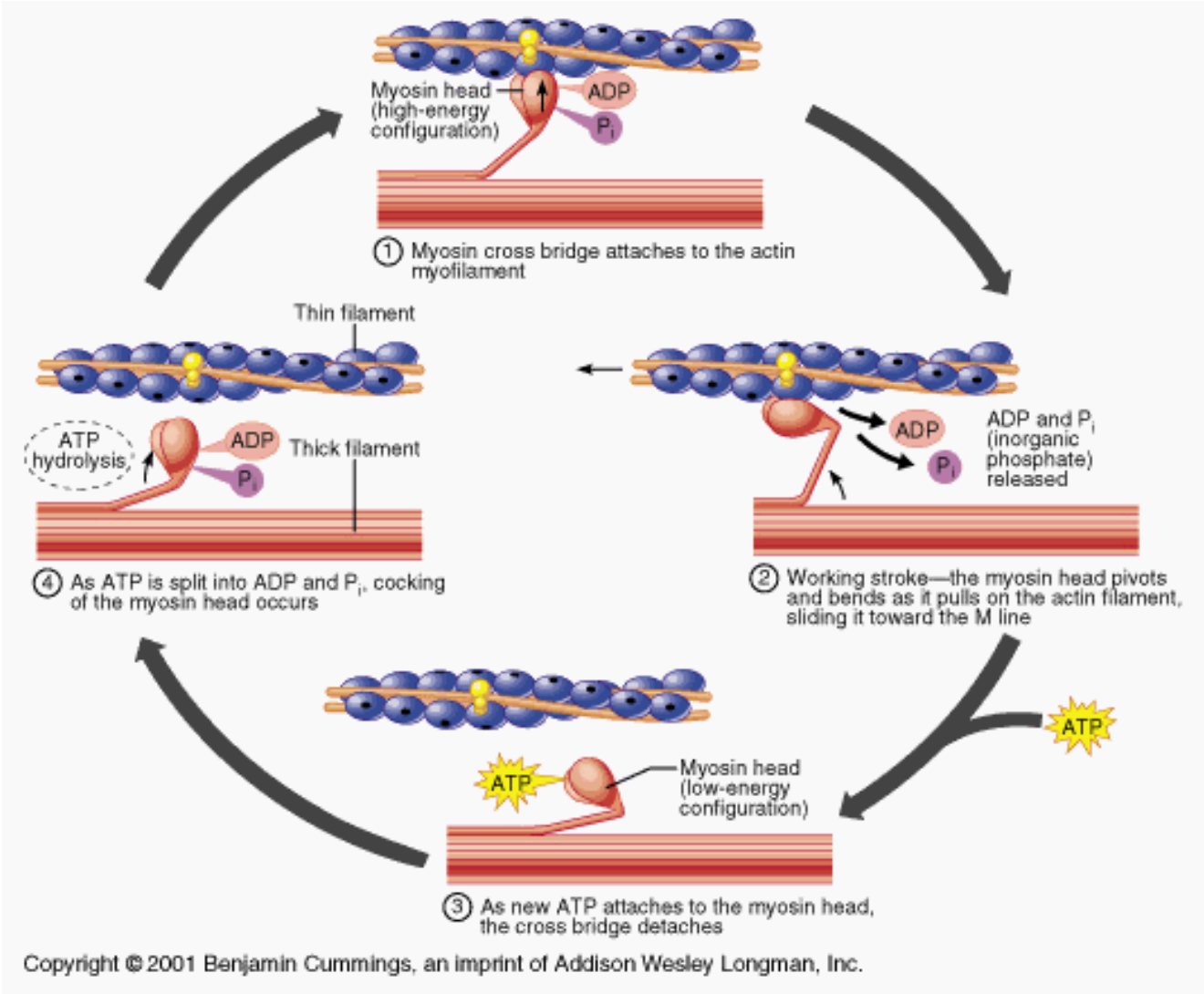


CONTRACTING MUSCLE



ELECTROMECHANICAL COUPLING

Molecular Mechanism of Contraction



ELECTROMECHANICAL COUPLING

Molecular Mechanism of Contraction