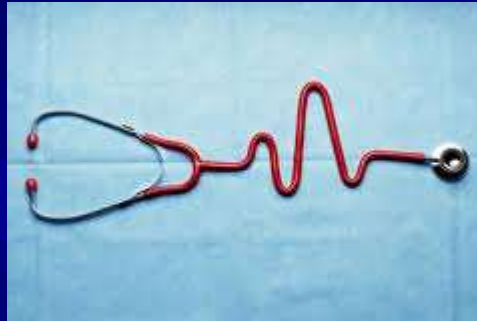
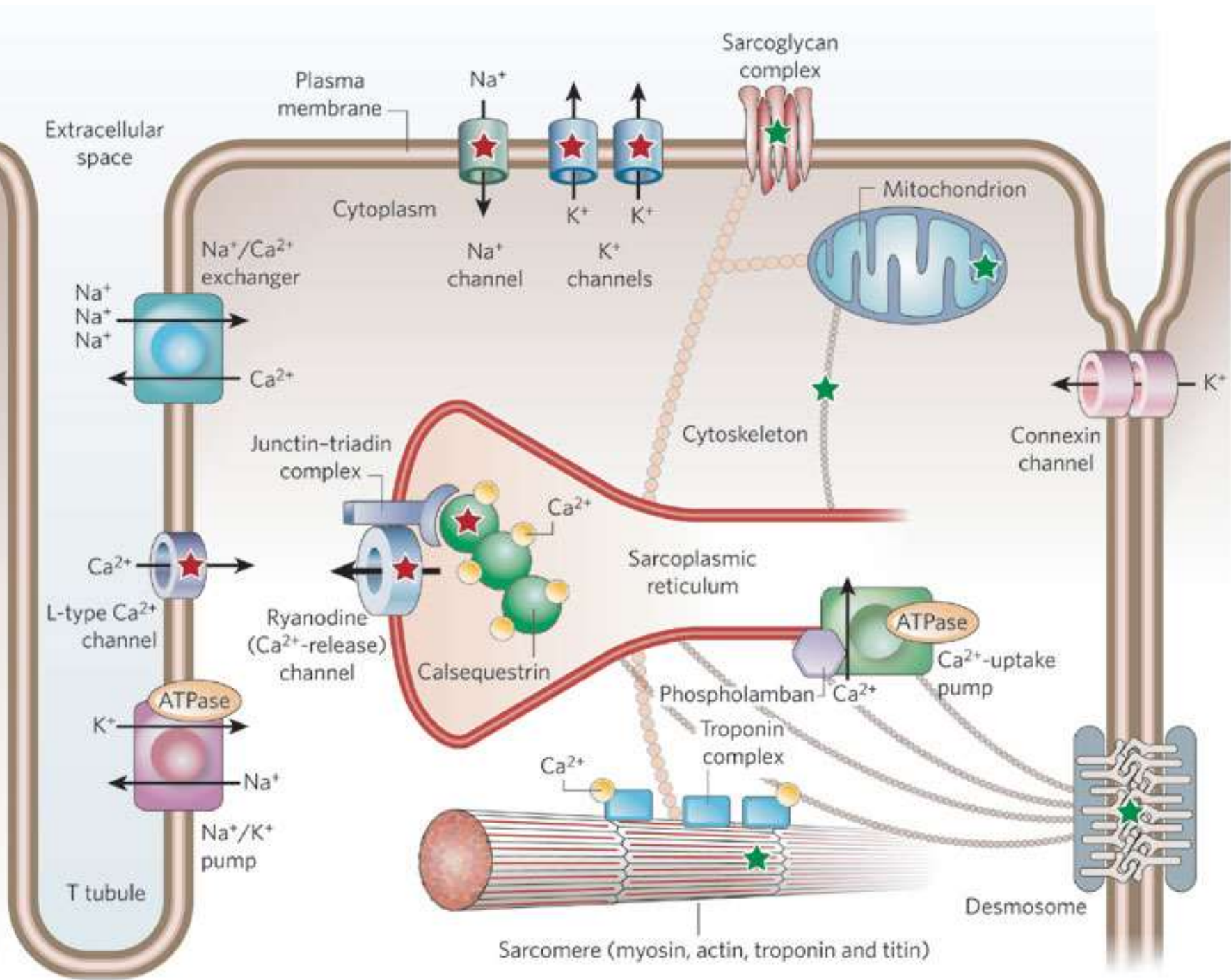
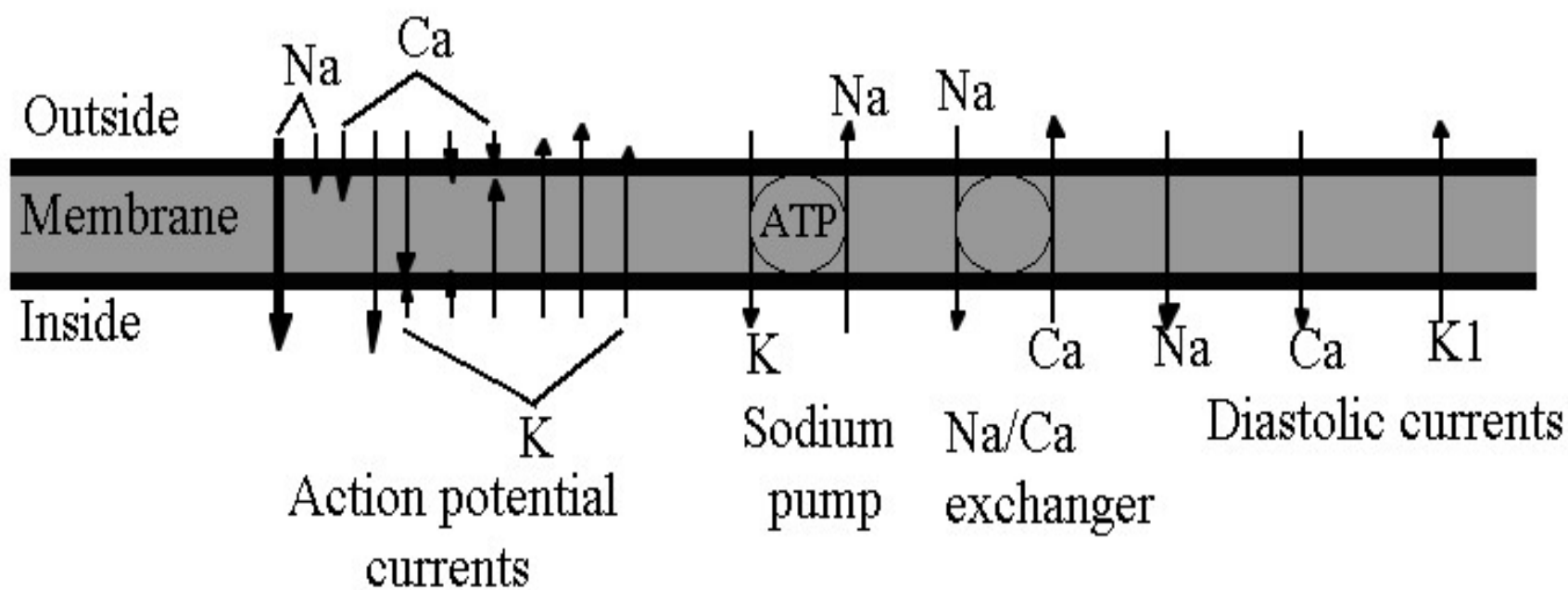
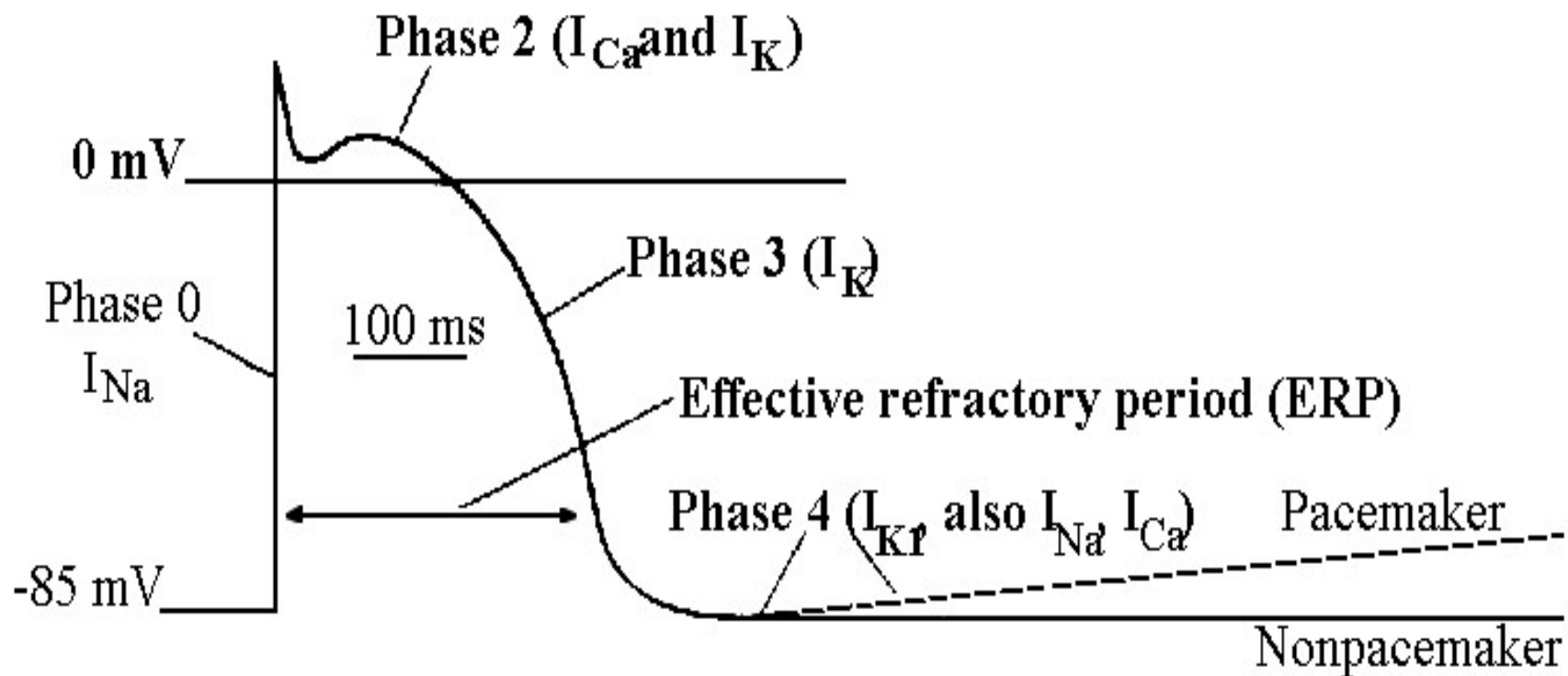


Experimentally induced arrhythmias in rat

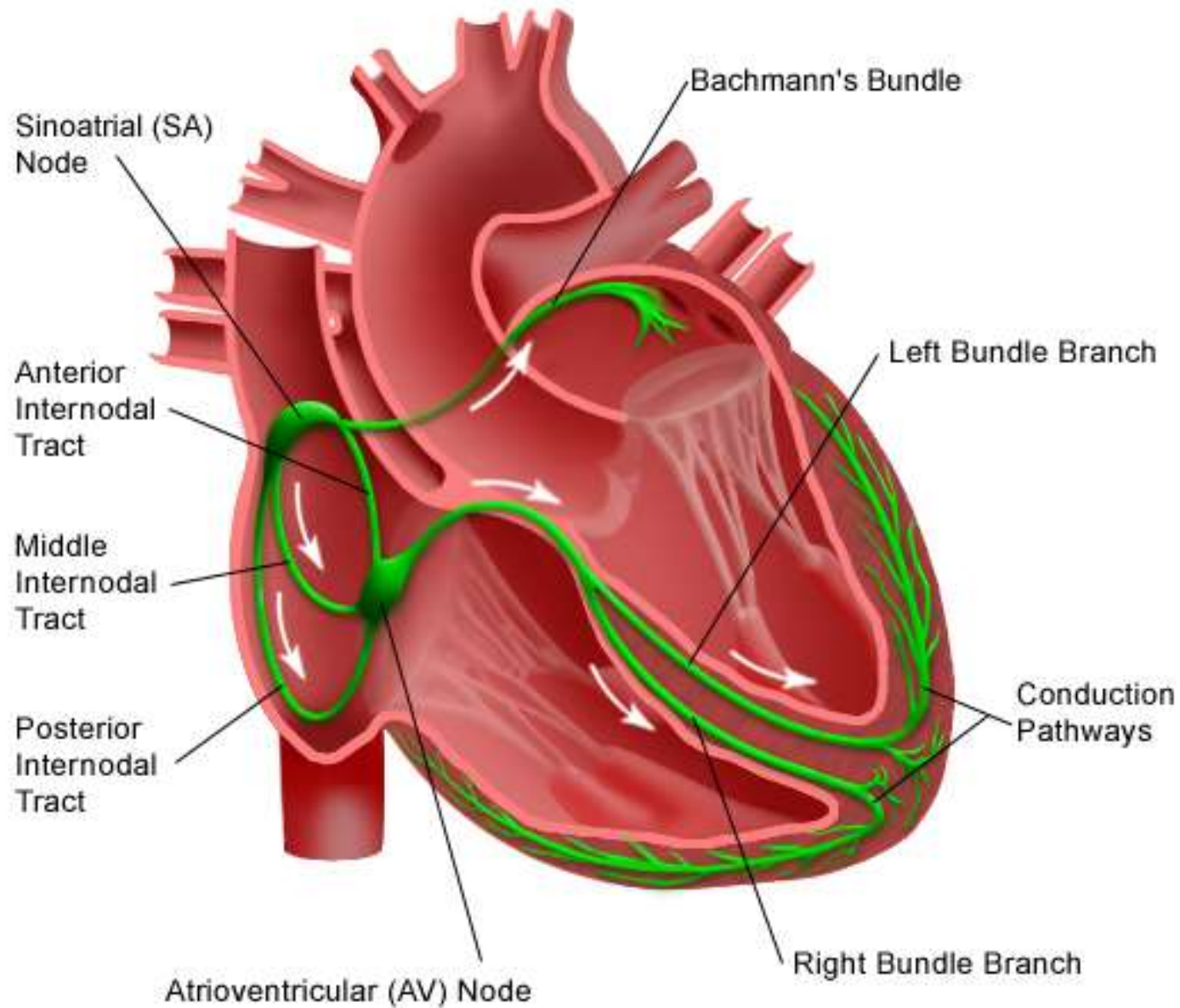


- Adrenergic hyperstimulation
- Hyperkalemia
- Block of cardiac calcium channels

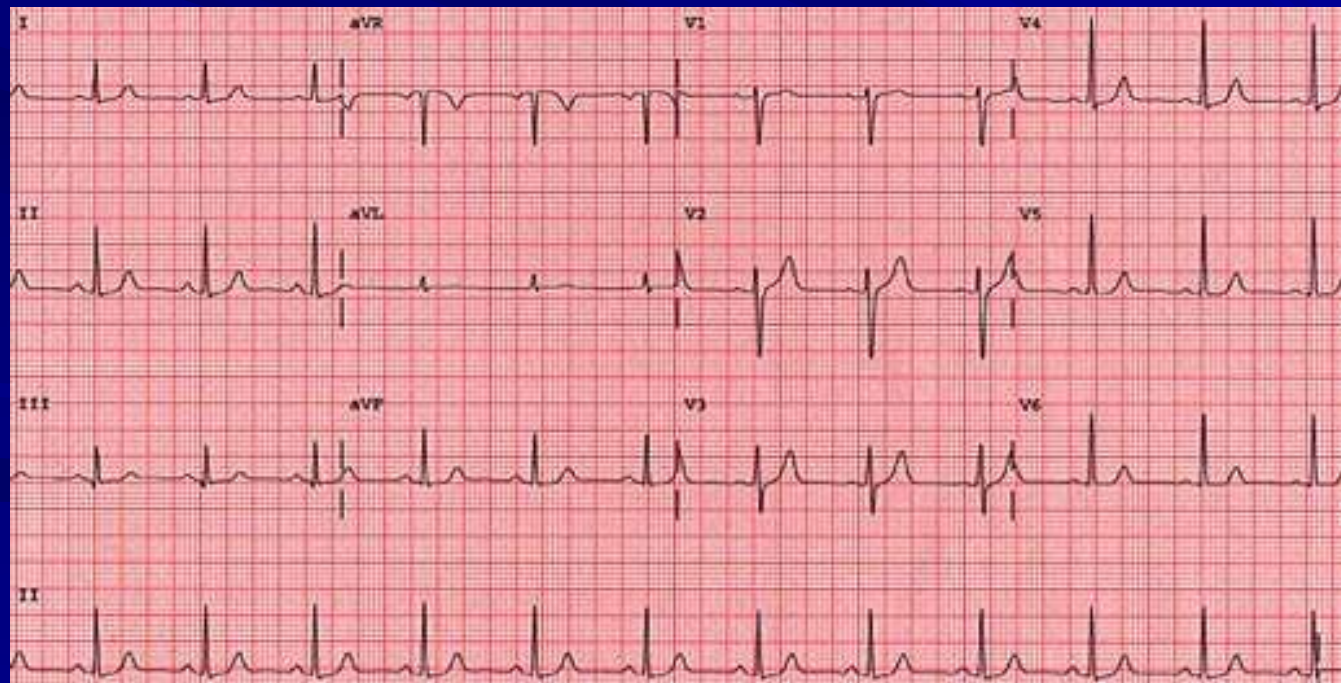
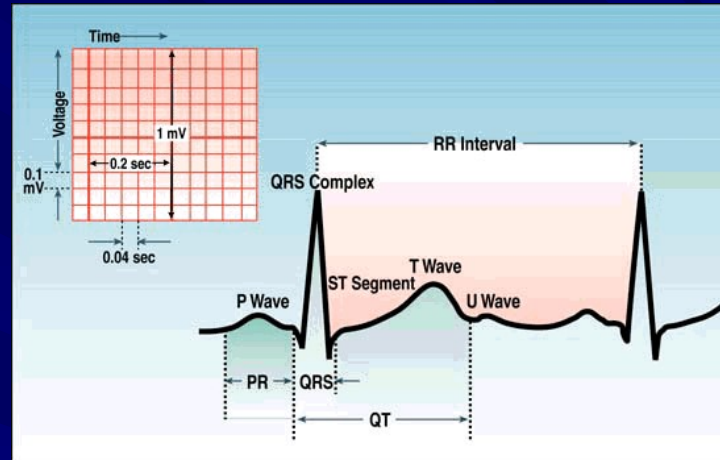




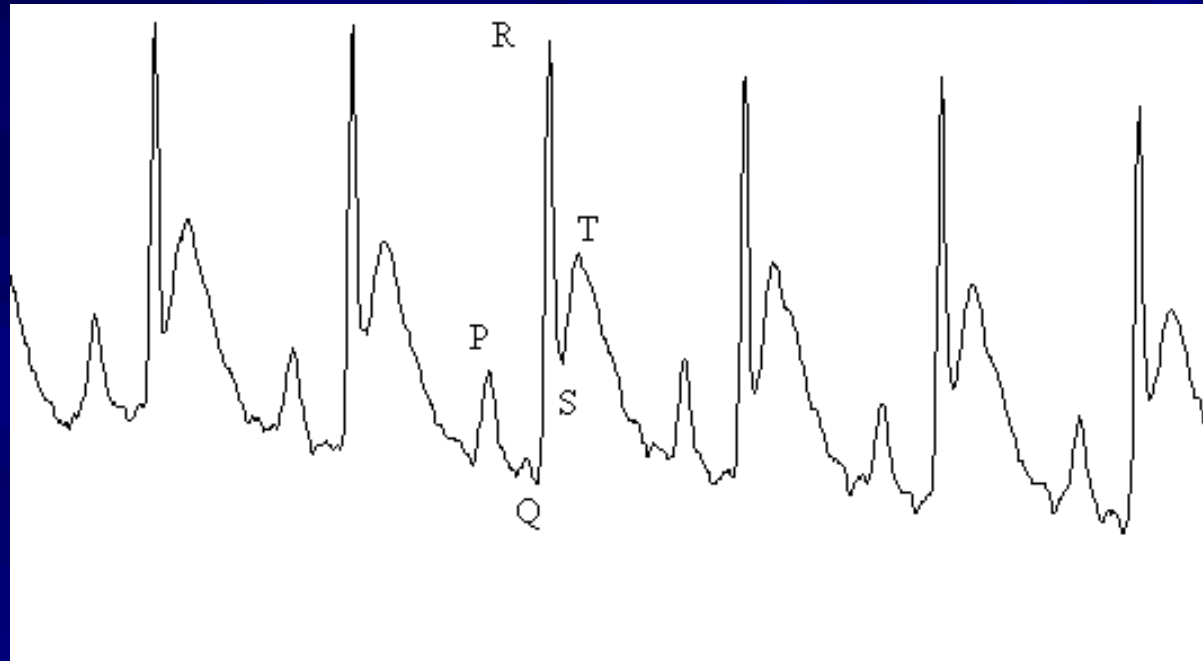
Electrical System of the Heart



Normal ECG curve in human...



...and in rat heart



Note the missing ST segment (phase 2 = plateau of the ventricles)
SA nodal rate about 300/min

Vegetative nervous system and the heart

Receptors:

■ Sympathetic nervous system:

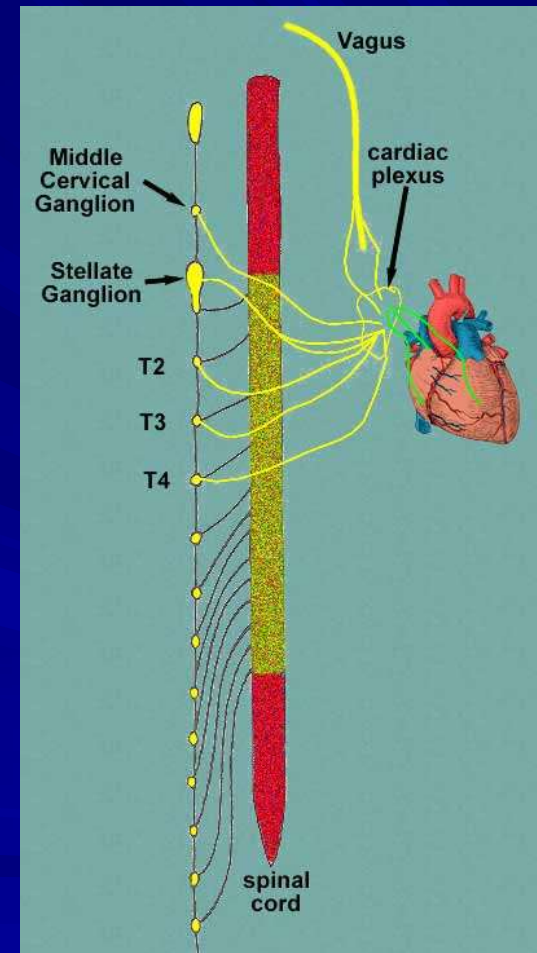
β_1 - positively inotropic, dromotropic and chronotropic (mainly through opening of pacemaker F-channels and Ca^{2+} channels in SA node, AV node and working myocardium)

β_2 – apical myocardium, vessels – vasodilatation

α_1, α_2 – vasoconstriction (lower effect in coronary vessels, norepinephrine effect)

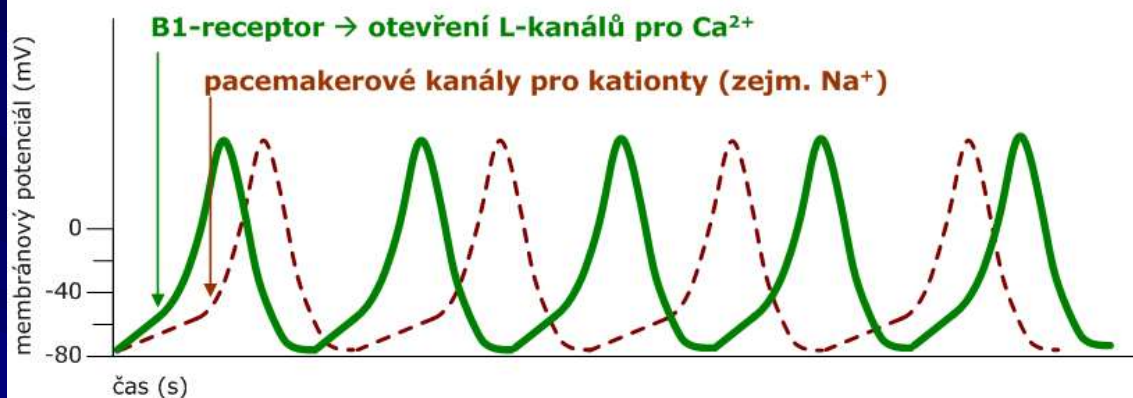
■ Parasympathetic:

M2 – negatively chronotropic (inhibits opening of Ca^{2+} channels, opens K_{Ach} channels)

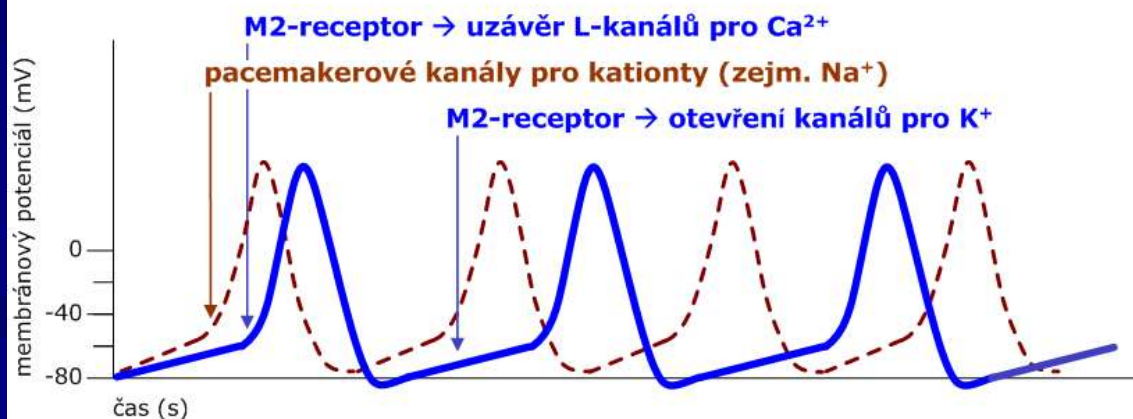


Effects of vegetative nervous system on pacemaker cells

A - adrenergní stimulace (SYMPATIKUS)

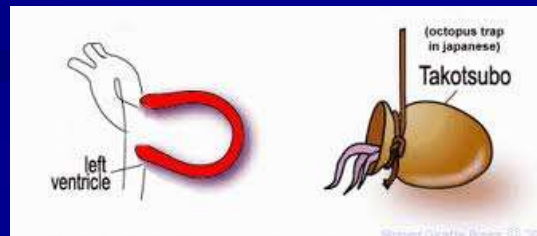


B - cholinergní stimulace (PARASYMPATIKUS)



Heart during catecholamine overload

- ↑ heart rate
- ↑ contractility
 - Increase systolic function at the expense of diastolic dysfunction
- Calcium overload of cardiomyocytes
 - DAD → premature beats
 - ↑ oxygen consumption → ischemia
- β_2 -receptor phosphorylation – transition from G_s to G_i signalization → decreased contractility in the apex
 - but it acts against Ca overload and necrosis
- Vasoconstriction?



Potassium

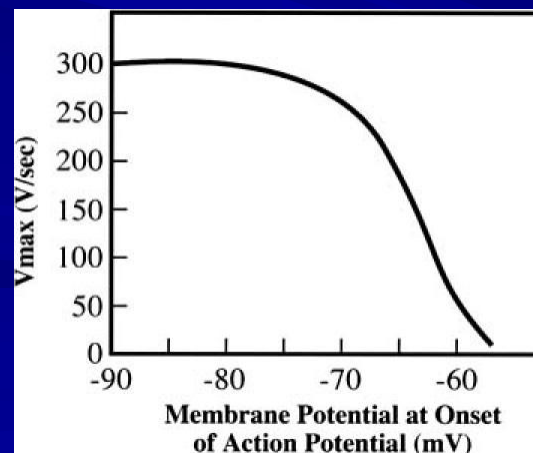
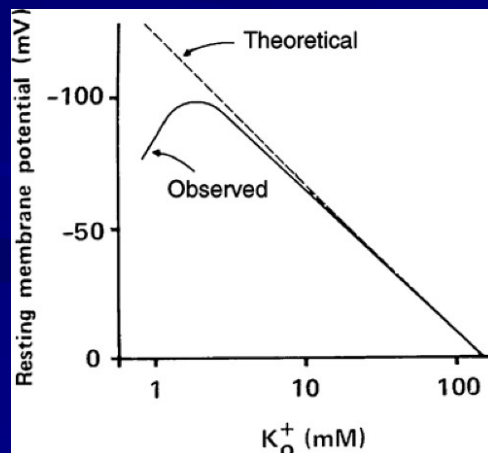
- The most abundant intracellular cation (98% intracellular)
- Most willingly passes cellular membrane
- Concentration gradient is maintained by Na^+/K^+ ATPase
- The extra/intracellular distribution is regulated by hormones (insulin, adrenaline, aldosterone) and pH
- Its total body content depends mainly on renal functions
- Both hyper- and hypokalemia are frequent conditions in clinical practice and both are proarrhythmogenic

Potassium and the membrane potential

- Positively charged, intracellular ion: ↑ concentration → lowering of membrane polarity (analogy of a small and a large basin connected by a hose)
- Various functionally different K^+ channels
- By various mechanisms, potassium increases the permeability of K^+ channels
 - direct binding
 - competition with Mg^{2+} that closes the K^+ channels
 - changes in expression and translocation

Effect on sodium channels

- Mild hyperkalemia – easier excitation
- Severe hyperkalemia – block of a portion of Na^+ channel
 - Slower conduction
 - Finally the threshold voltage „runs away“ from baseline voltage and the depolarization is no longer possible
- Mild hypokalemia – hyperpolarization
- Severe hypokalemia – lack of substrate for the Na/K ATP-ase → lower polarity, easier excitation



Potassium – main effects

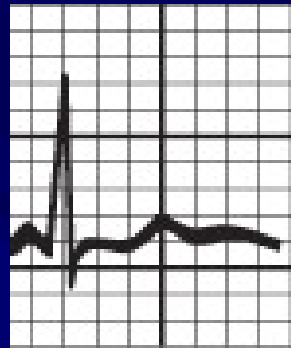
■ Hyperkalemia

- Peaked T wave (dif. dg. hyperacute phase of MI)
- Wide QRS (may merge into sinusoid wave with T)
- Widening, flattening and event. disappearing of the P wave (but sinus rhythm remains for a long time)
- Higher excitability at the beginning, then lower, diastolic arrest in the end (heart is depolarized compared to the normal state)
- ↑ risk of re-entry (↑ differences in conduction velocities)

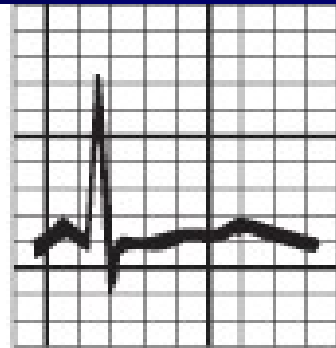
■ Hypokalemia

- Flat, wide T-wave
- Pathologic U wave (delayed repolarization), lengthening of QT (QU) interval
- EAD, torsades de pointes
- Sometimes, peaked P is present
- ↑ risk of re-entry (↑ differences in refractory periods)
- First lower excitability (hyperpolarization), then higher

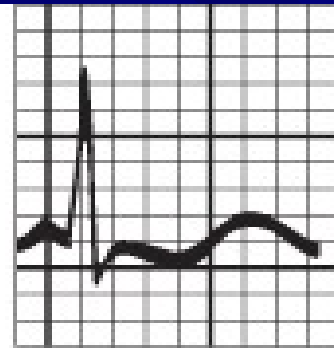
Changes of ECG in hyper- /hypokalemia



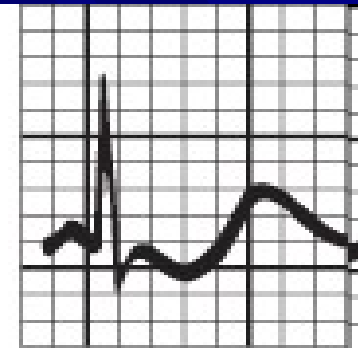
2.8



2.5

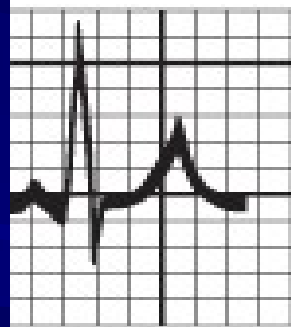


2.0

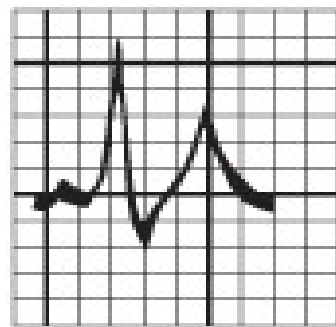


1.7

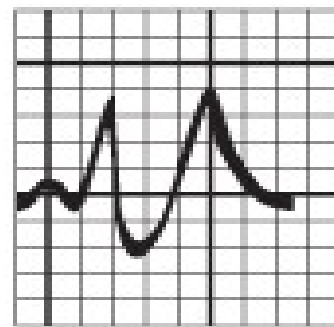
Hypokalemia



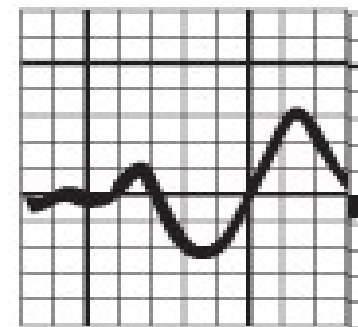
6.5



7.0



8.0



9.0

Hyperkalemia

Calcium

- Ion that is necessary for muscle contraction
- Intracellularly, it is present in very low concentration (making high gradient between cytoplasm and cell)
- In cardiomyocyte and skeletal muscle, it is also present in sarcoplasmic reticulum
- Cardiomyocyte (and smooth muscle cell) bears specific Ca^{2+} -channels, that are necessary for phase 2 (plateau), pacemaker function and conduction through slow cells
- They can be blocked by specific agents to slow the heart rate and enhance vasodilatation by smooth muscle relaxation

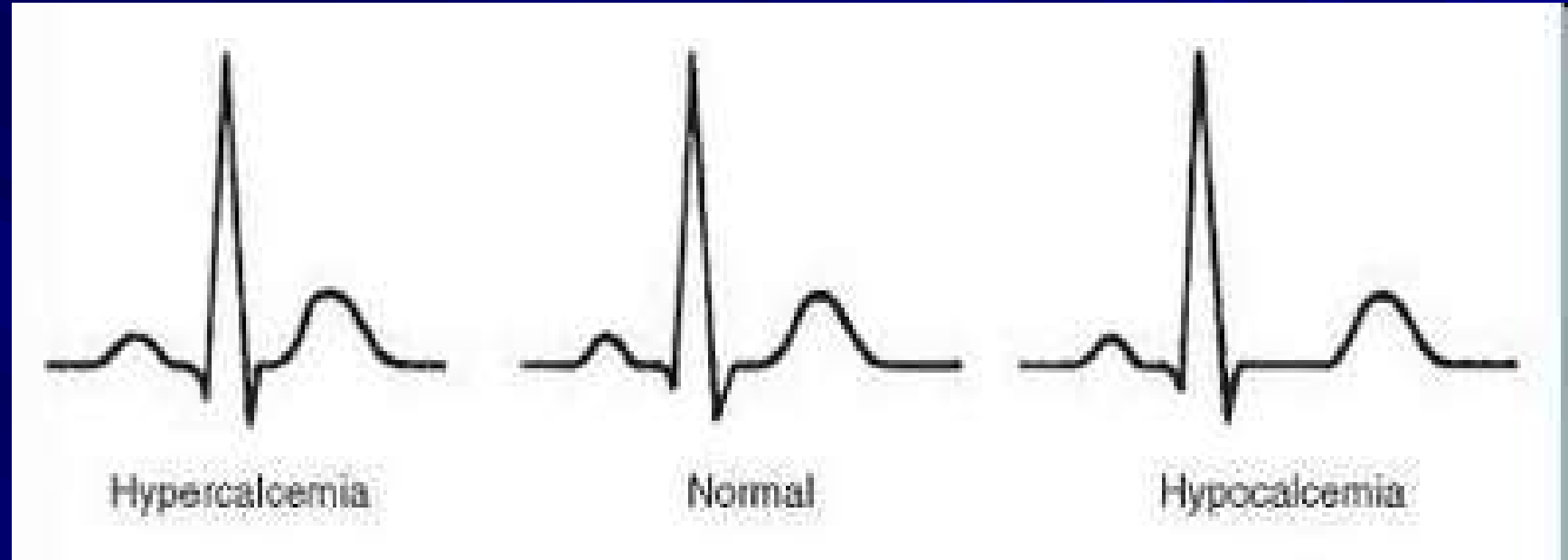
Calcium and the membrane potential

- Extracellular ion – Membrane potential gets into more negative values
- During the action potential, Ca^{2+} activate potassium (and chloride) channels, which shortens the phase 2 → repolarization leads into the closing of Ca^{2+} L-channels
 - the process is important for maintaining the calcium homeostasis in the cell
 - in extreme hypercalcemia, phase 2 may be missing
 - opposite effect may be present in hypocalcemia
- Mechanical effects
 - Extreme hypercalcemia: triggered activity (DAD), systolic arrest (very rare)
 - Extreme hypocalcemia: triggered activity (EAD), hypocalcemic cardiomyopathy, heart failure

Blocking the calcium channels

- Verapamil – class IV antiarrhythmic drug
- Tissue distribution roughly symmetrically in the heart and smooth muscle
- Indikace: antiarrhythmic, antihypertensive (rather rarely), local vasodilant
- Overdose – effect mainly on the slow cells
 - SA arrest and block
 - AV block
 - Low contractility
 - Long QT may sometimes be present

ECG in calcium levels changes



- The Ca^{2+} channels-blockers mainly induce the conduction (SA or AV) node blocks and slower pacemaker function

Practical

