INTER-CELLULAR CONTACT

MECHANICAL COUPLING

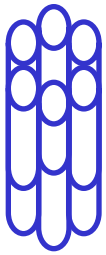
• desmosomes (macula adherens; cell adhesion and mechanical stability of tissues) – epidermis, liver, myocardium

ELECTRICAL COUPLING

• gap junction (nexus) (in intercalar disc; consists of conexons)

CONEXON

6 subunits
1-2 nm central channel



OPEN

CLOSED

HUMORAL COUPLING (REGULATION)

autocrine
paracrine
endocrine

NERVOUS COUPLING (REGULATION)

Integration of humoral and nervous regulations in organism.

Receptor, ligand, second messenger.
Neurotransmitters vs. tissue „hormones“ vs. hormones.

1. Number of receptors
2. Number of ligands
3. Subtypes of receptors
4. Competition on receptors
5. Endogenous ligands, exogenous ligands
6. Orphan receptors
7. Placement of receptors
8. Convergence and divergence of the effects
9. Transmission of information intracellularly

SECOND MESSENGER SYSTEMS

cAMP, cGMP, IP_3, DAG, Ca^{2+} - calmodulin

cAMP

H-R complex binds to G-protein – stimulatory or inhibitory
(α, β and γ subunits)
Mg^{2+}, HR β–γ
Activation or inhibition of adenylcyclase cAMP
Activation of proteinkinases protein phosphorylation

Direct regulation of ionic channels and pumps (K^+, Ca^{2+})

Gs: glucagon, oxytocin, histamine, dopamine, ADH, FSH, TSH, AD ($\beta_{1,2}$)
Gi: Ach, opioids, AGII, AD (α_2), dopamine

IP_3

H-R complex binds to G-protein – p

Activation phospholipase C ⟶ PIP_2 ⟶ IP_3 and DAG

DAG: activates proteinkinase C

Phosphorylation of Na+/H+ pump pHi

Effect of prostaglandines and prostacyclines

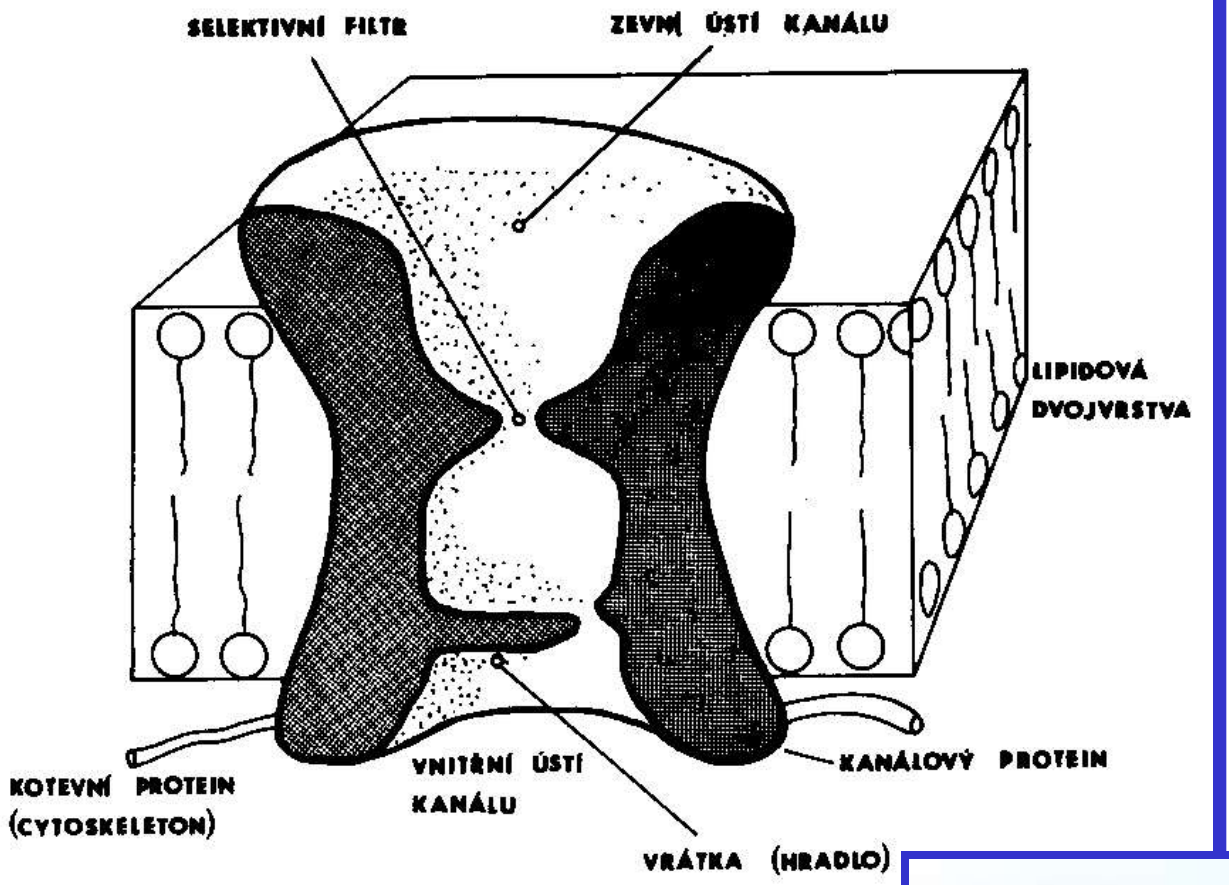
IP3: translocation to endoplasmic reticulum

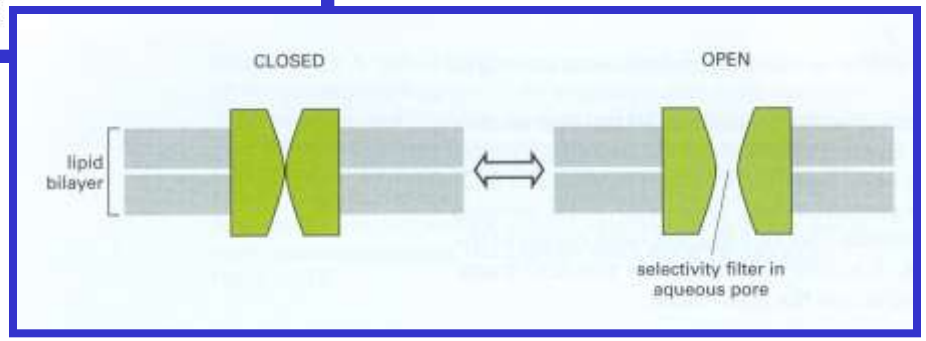
Increase in cytoplasmic availability of calcium

„third messenger“

AD (α_1), Ach, thyroliberin, ADH, tromboxans

IONIC CHANNELS





Membránová elektrofyziologie myokardu, P. Pučelík, Avicenum, 1990

Molecular biology of the cell. B. Alberts et al., Garland Science2002

CHANNELS WITHOUT GATES

GATED CHANNELS

1. LIGAND GATED CHANNELS (nicotinic cholinergic receptor; ATP-sensitive K^+ channel)
2. G-PROTEIN GATED CHANNELS (Ach-sensitive K^+ channel of SA node – muscarinic receptor)
3. MECHANICALLY GATED CHANNELS – „stretch“ receptors (K^+ , Ca^{2+})
4. VOLTAGE GATED CHANNELS

- One-gate channels (activation vs. deactivation)
- Two-gates channels (activation vs. inactivation vs. recovery from inactivation)

RESTING MEMBRANE POTENTIAL

= difference between electrical potential of intra- and extracellular solution (at rest). Different composition of IC and EC environment is kept by membrane transport membrane mechanisms.

DIFUSSION CURRENTS: ionic currents across the membrane (in both directions) through open ionic channels (specific channels) = simple diffusion according to concentration gradient

ELECTROCHEMICAL GRADIENT

- semipermeable membrane
- different conductivity for ions
- the force given by concentration gradient equals to the force given by electrical gradient

DONNAN EQUILIBRIUM (D. PHENOMENON)

Concentration of anions multiplied by concentration of cations on one side of membrane equals to concentration of anions multiplied by concentration of cations on the other side of membrane.

EQUILIBRIUM POTENTIAL

NERNST EQUATION

$$EP = (R \,.\, T / n \,.\, F) \,.\, \ln X_e / X_i$$

GOLDMAN (HODGKIN-KATZ) EQUATION

$$MP = g_K \,.\, E_K + g_{Na} \,.\, E_{Na} + g_{Cl} \,.\, E_{Cl} / g_K + g_{Na} + g_{Cl}$$

Respects the fact that even at rest there are membrane currents present – **background current (inward, outward).**

PHYSIOLOGICAL SIGNIFICANCE OF RESTING MEMBRANE POTENTIAL

Possibility to code and transmit information in living systems (excitable tissues) – in the way of action potential

Triggering muscle contraction

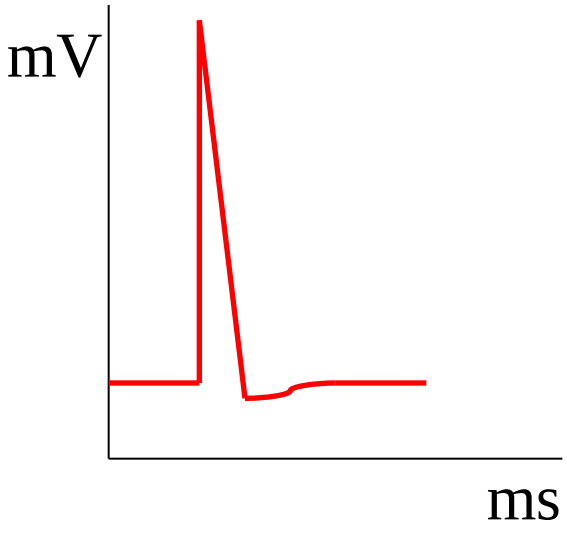
ACTION POTENTIAL

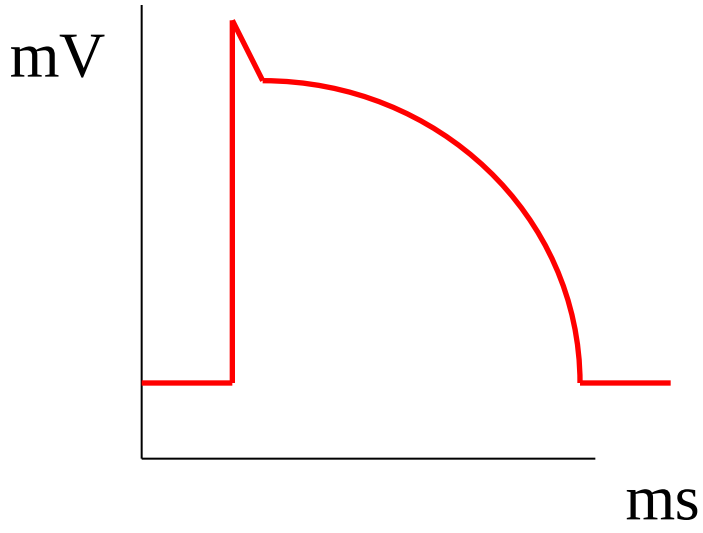
LOCAL RESPONSE

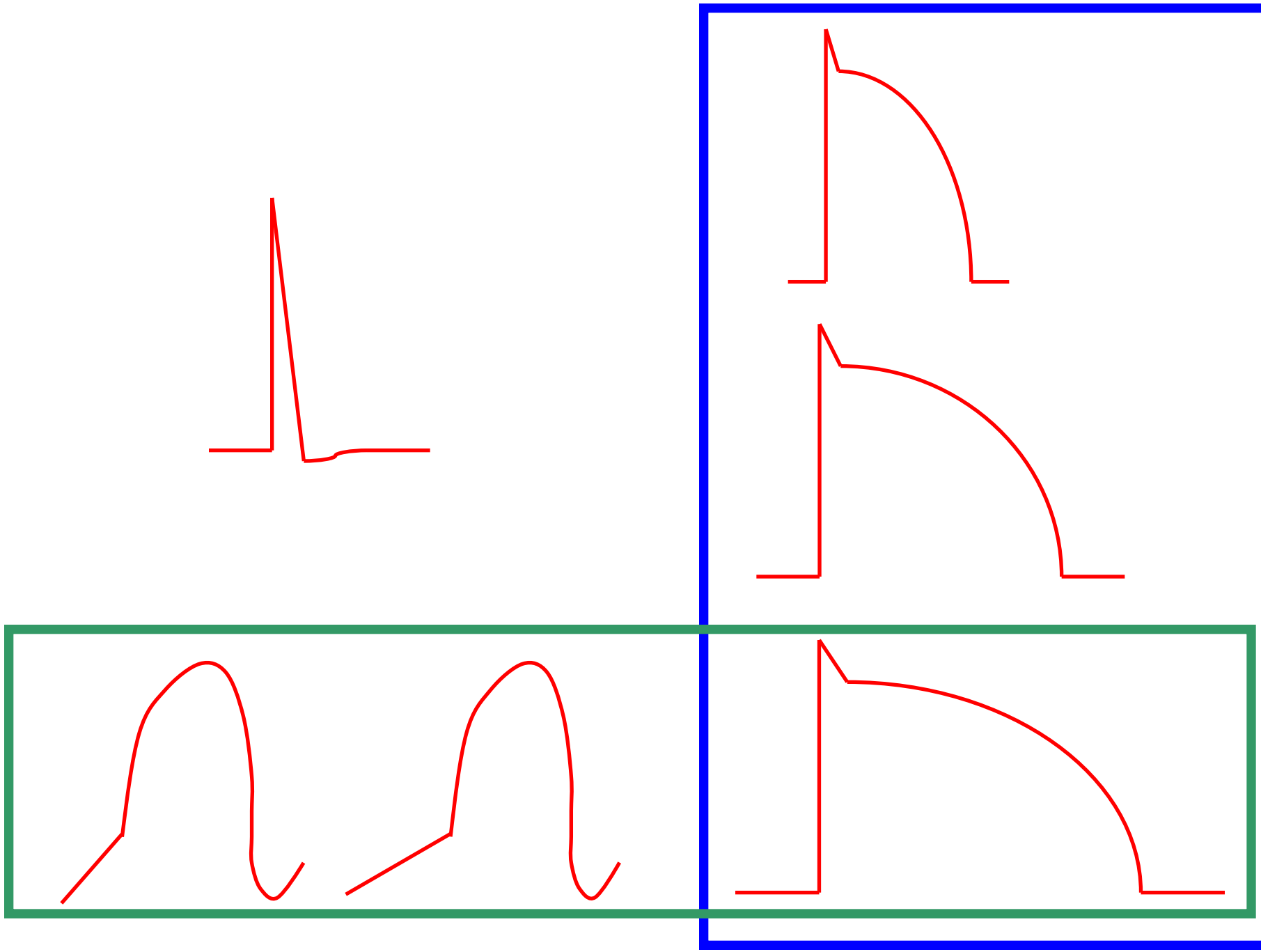
Changes of conductivity of the membrane for particular ions (opening the ion-specific channels)

Depolarization, transpolarization, repolarization.

Inward currents x outward currents.







MUSCLE CONTRACTION AND RELAXATION

CONTRACTILE PROTEINS

ACTIN – globular, 400 molecules = chain = F-actin; 2 chains in spiral = filament

MYOSIN – „thick“ filaments, head with ATP-ase activity, filament = 150 – 360 molecules of myosin
(head + neck = heavy meromyosin, light meromyosin)

MODULATORY PROTEINS

TROPONIN – C, I, T

TROPOMYOSIN

PHYSIOLOGICAL ROLE OF CALCIUM

PRINCIPLE OF MUSCLE RELAXATION

Removal of calcium from cytoplasm