

# **Биофизика возбуждения-сокращения кардиомиоцитов**

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Киев 2016



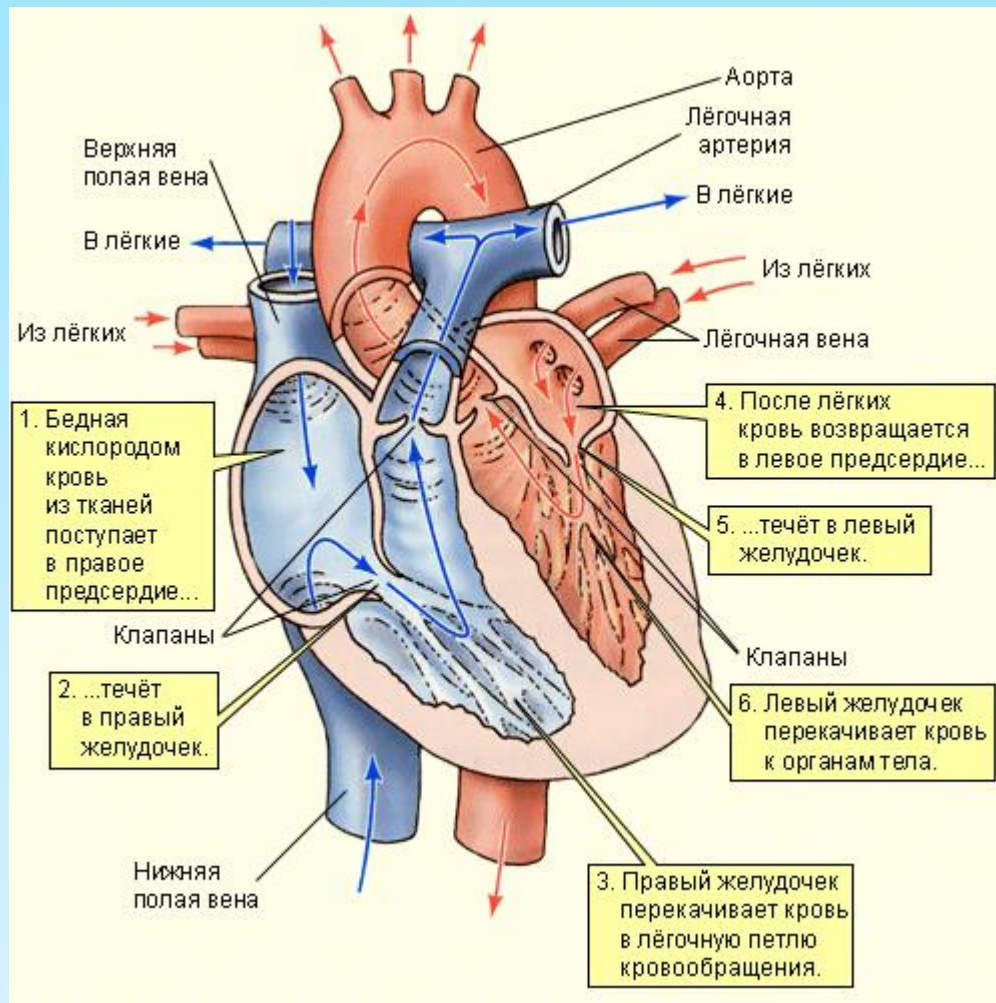
Cardiac muscle cell

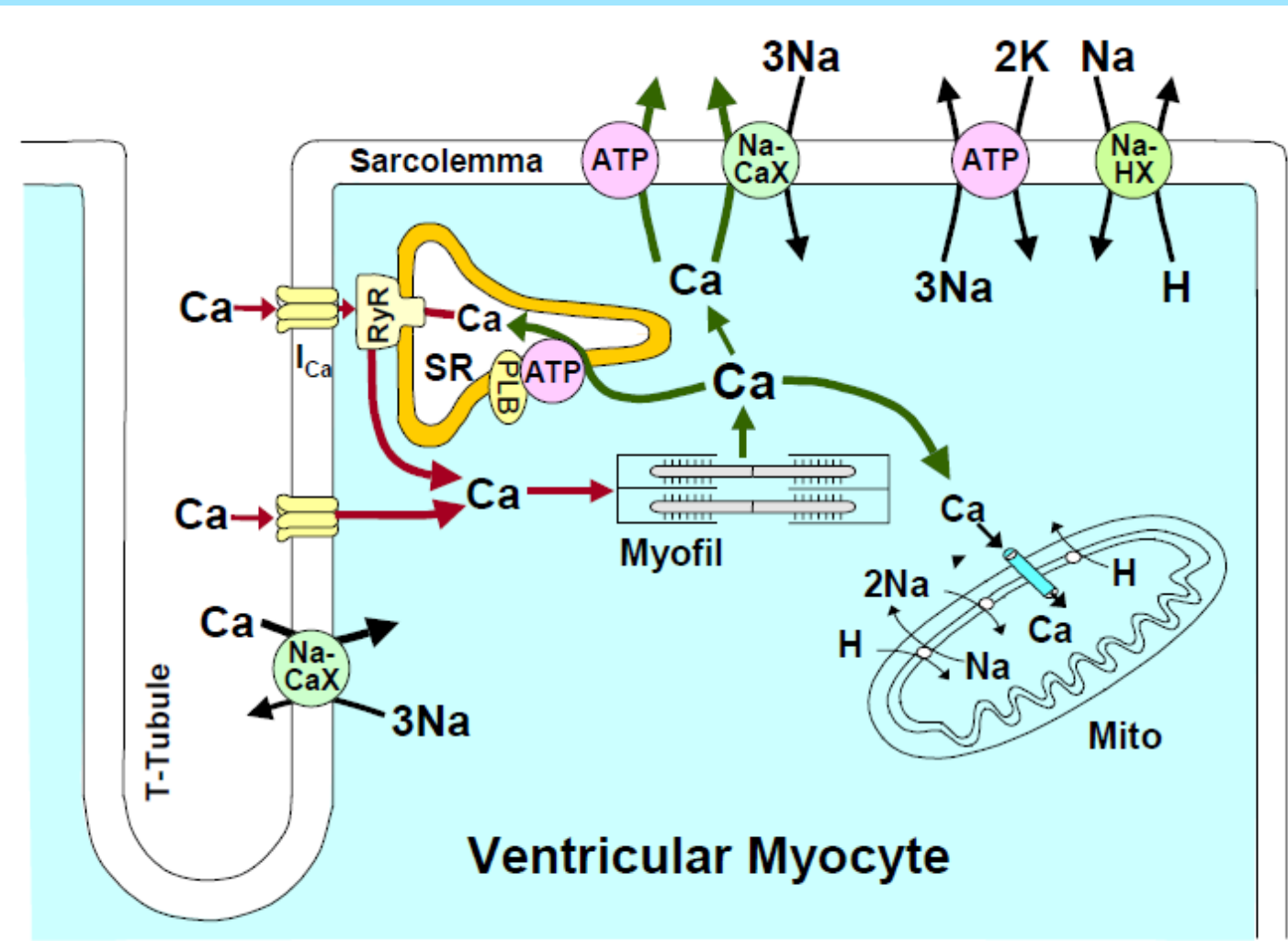


Skeletal muscle cell

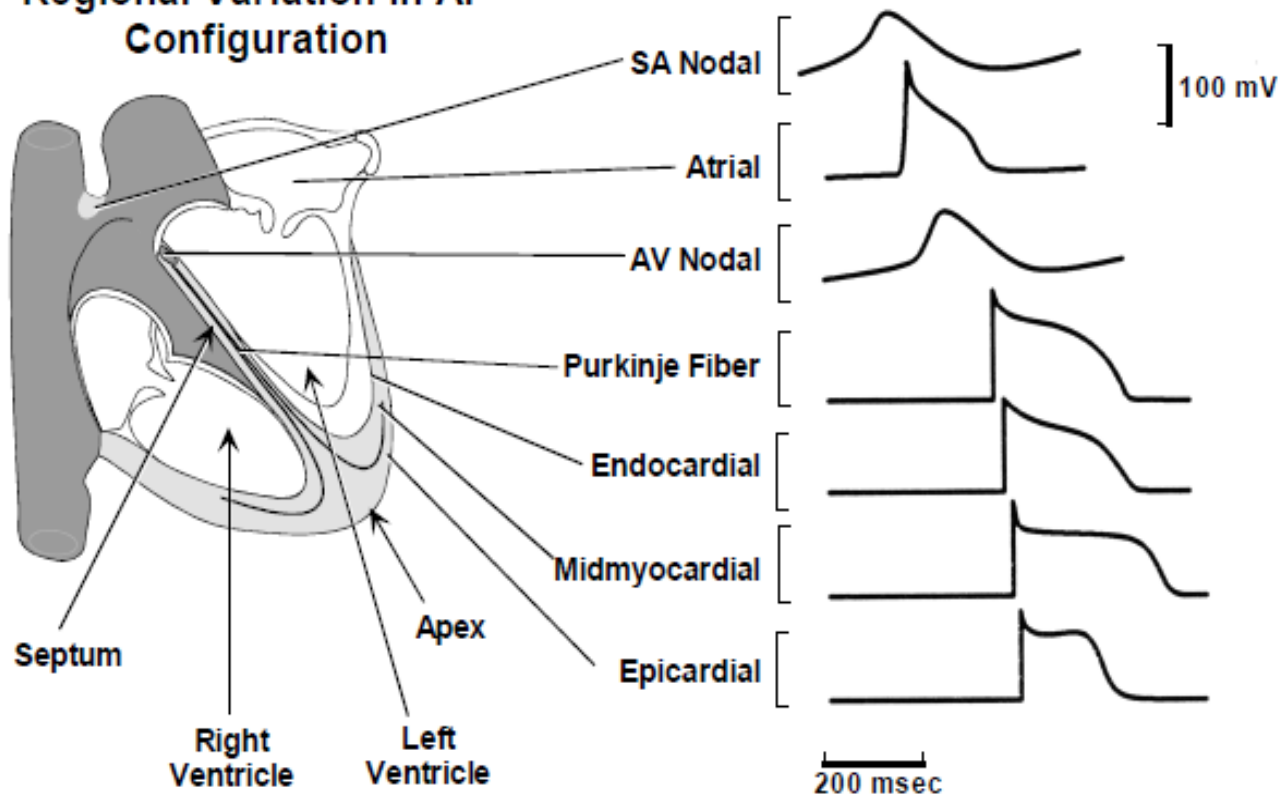


Smooth muscle cell

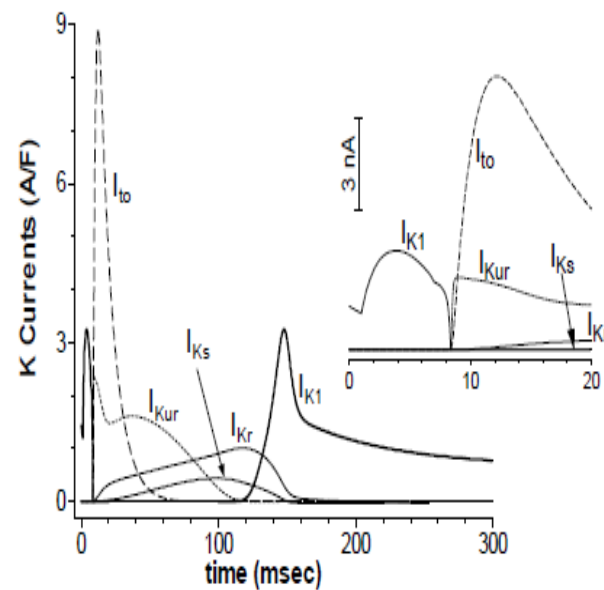
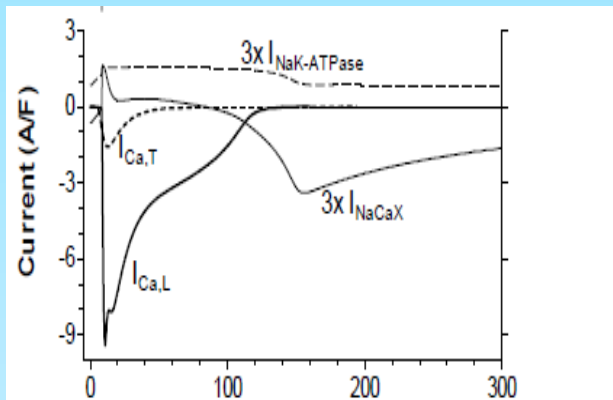
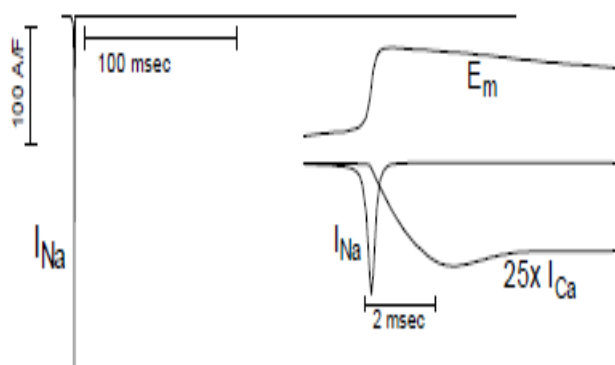
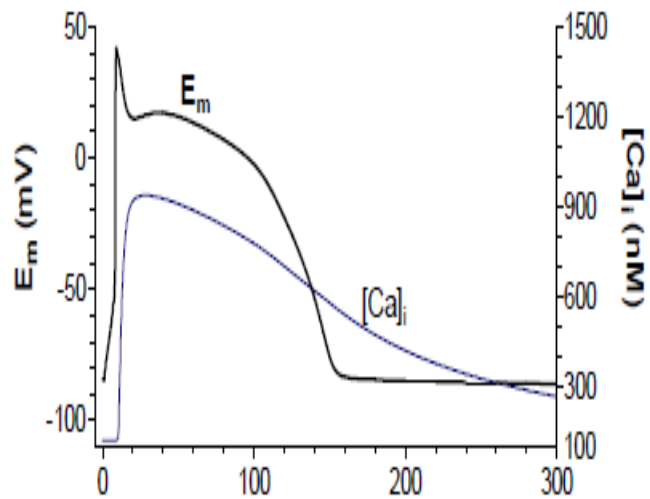




## Regional Variation in AP Configuration



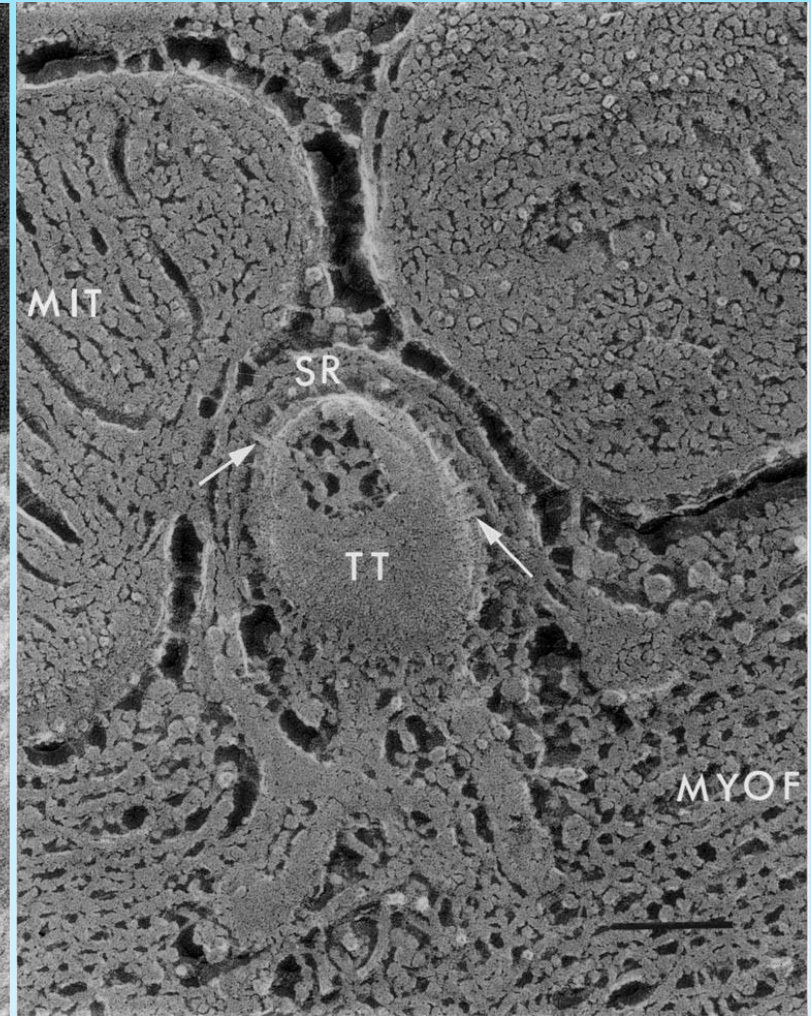
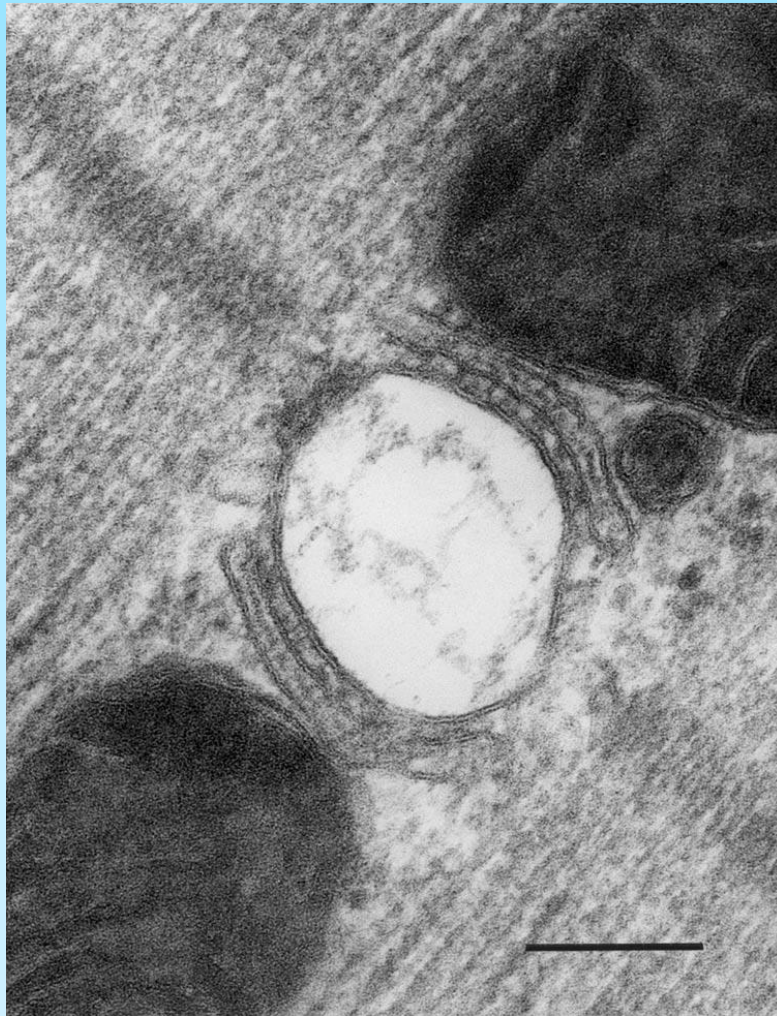
# Rabbit Ventricular AP



## Cardiac Ion Channels

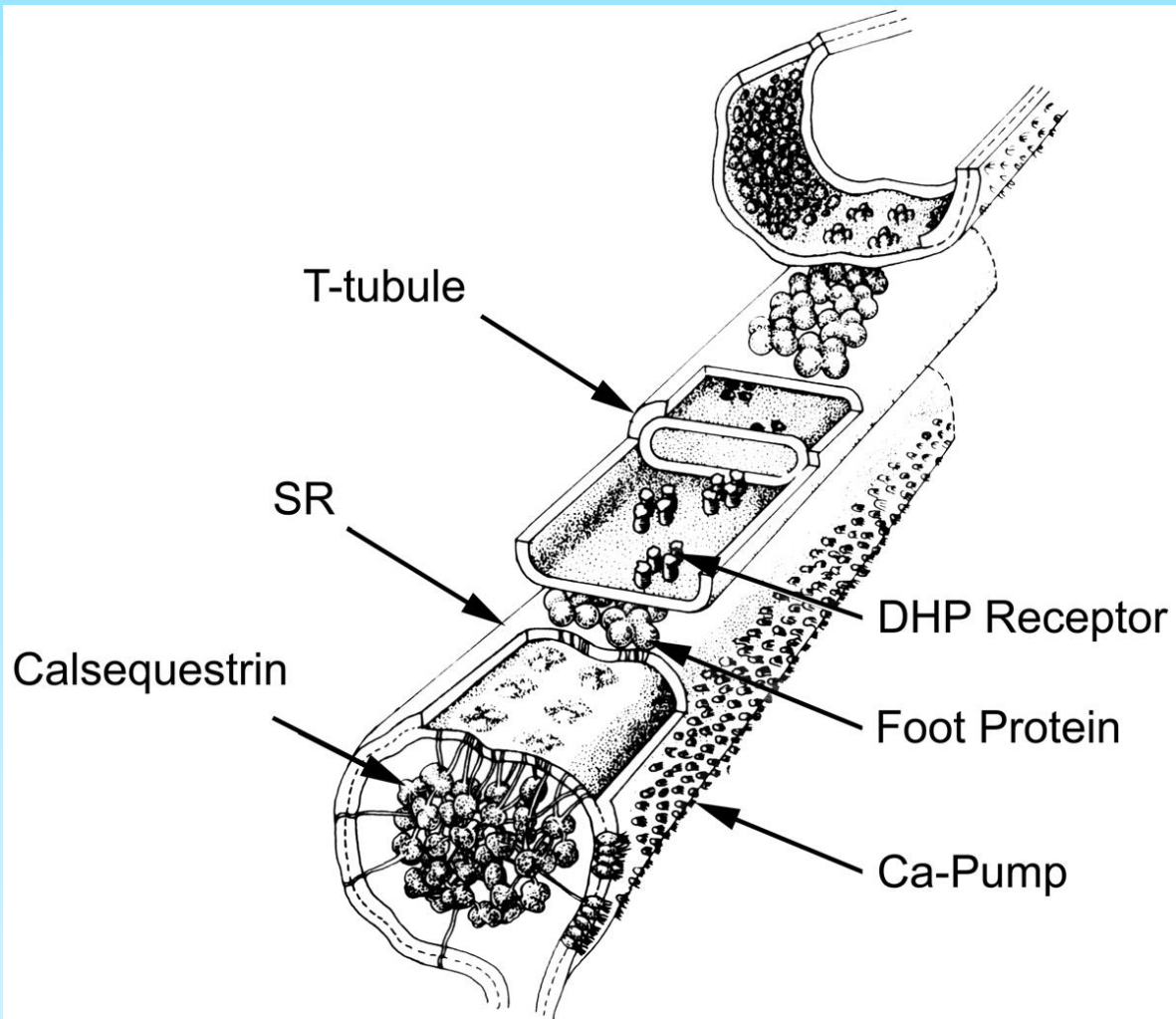
Current	Candidate Gene	Acti- vation	Inacti- vation	Role in AP	Subunits?	Blockers
<i>Voltage gated Channels</i>						
I <sub>Na</sub>	SCN5A	VVF	VF	Rapid Depol.	β	TTX,STX
I <sub>Ca,L</sub>	α <sub>1C</sub> , α <sub>1D</sub>	VF	M	Depol & Plat	α <sub>2δ</sub> , β	DHP, ΦAA
I <sub>Ca,T</sub>	α <sub>1G</sub> , α <sub>1H</sub>	VF	F	Depol-PMK	β	Mibefradil, Ni
I <sub>to,fast</sub>	Kv4.2, 4.3	VF	F	Early Repol	β	4-AP, 2,3-DAP
I <sub>to,slow</sub>	Kv1.4	VF	M	Early Repol	β	4-AP, 2,3-DAP
I <sub>Kr</sub>	HERG	M	VF	Plat-Repol	MirP1	Dofetilide, E-4031
I <sub>Ks</sub>	KvLQT1	VS	x	Plat-Repol	MinK	Chromanol 293
I <sub>Kur</sub>	Kv1.5	F	x	Plat-Repol		μM 4-AP
I <sub>Kp</sub>	Kv1.5?	F	x	Plat-Repol		Ba
I <sub>Ks,slow</sub>	Kv1.2	F	VS	Plat-Repol		TEA
I <sub>K1</sub>	Kir2.1 (IRK1)	VF	x	Rest E <sub>m</sub>		Ba
I <sub>f</sub>	HCN2, HCN4	MS	x	PMK		
<i>Ligand Gated Channels</i>						
I <sub>K(ACh)</sub>	Kir 3.1:3.4	ACh		↓ PMK		
I <sub>K(ATP)</sub>	Kir6.2	Pinacidil		↓APD & PMK	SUR	Glibenclamide
I <sub>Cl(Ca)</sub>	?	[Ca] <sub>i</sub>		Early Repol		DIDS,niflumate
I <sub>Cl(cAMP)</sub>	CFTR	cAMP		↑Repol.		9-AC, DNDS
<i>Mechanosensitive Channels</i>						
I <sub>Cl(Swell)</sub>	ClC-3	Swelling		↓APD?		Gd, DIDS
I <sub>NS(stretch)</sub>	?	Stretch		PMK?		Gd

Abbreviations: F=fast, S=slow, M=moderate, V=very and x=none. Depol=depolarization, Repol= repolarization, Plat= plateau, PMK= pacemaker, TTX = tetrodotoxin, STX= saxitoxin, DHP= dihydropyridine, ΦAA=phenylalkylamine, TEA= tetraethylammonium, 4-AP= 4-aminopyridine, 2,3-DAP = 2,3-diaminopyridine, DIDS= 4,4'-diisothiocyanatostilbene - 2,2'-disulphonic acid, DNDS= 4,4'-dinitrostilbene-2,2'-disulphonic acid, 9-AC= 9-aminoacridine, ACh= acetylcholine. The nomenclature for E<sub>m</sub>-dependent K channels (Kv) is based on homology to Drosophila gene families referred to as *Shaker*, *Shab*, *Shaw* and *Shal* for Kv1.x, Kv2.x, Kv3.x and Kv4.x (Jan & Jan, 1992; Pongs, 1992).



**Rat papillary muscle in a thin section electron micrograph (left) and freeze-etched electron microscopy after ultra-rapid freezing without fixation (right). Junctional "feet" between the SR and Ttubule (TT) can be seen to periodically span the gap. Bar=0.2  $\mu$ m. (From Frank, 1990 with permission).**





**Three-dimensional reconstruction of the relative positions of key proteins at the skeletal muscle triad. The SR is filled with calsequestrin and the non-junctional surface is covered with the Ca-pump protein.**

### A mRyR2 (wt)

a Control (before EGTA addition) + 20 mV  
 $P_o = 0.42$   $T_o = 2.03$  ms  $T_c = 2.74$  ms



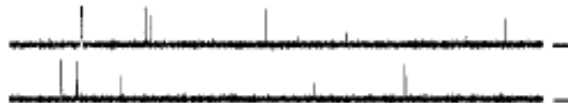
b + 0.1 mM EGTA

$P_o = 8.9 \times 10^{-6}$   $T_o = 0.58$  ms



### C R4496C

a 0.19  $\mu$ M  $\text{CaCl}_2$  + 20 mV  
 $P_o = 0.013$   $T_o = 2.12$  ms  $T_c = 138$  ms



b 0.26  $\mu$ M  $\text{CaCl}_2$

$P_o = 0.07$   $T_o = 2.40$  ms  $T_c = 27.6$  ms



c 0.35  $\mu$ M  $\text{CaCl}_2$

$P_o = 0.35$   $T_o = 2.84$  ms  $T_c = 5.23$  ms



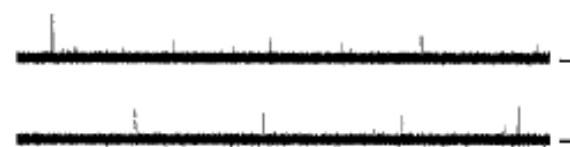
### B R4496C

a Control (before EGTA addition) + 20 mV  
 $P_o = 0.22$   $T_o = 1.60$  ms  $T_c = 4.44$  ms



b + 0.1 mM EGTA

$P_o = 1.3 \times 10^{-4}$   $T_o = 1.60$  ms

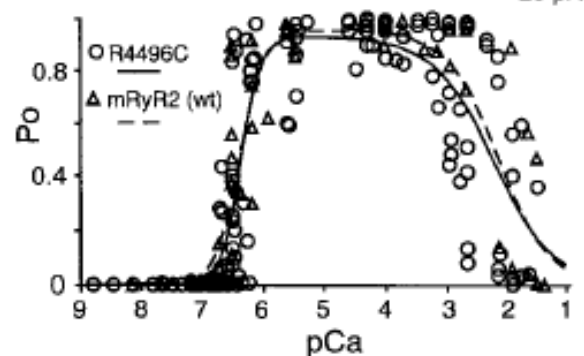


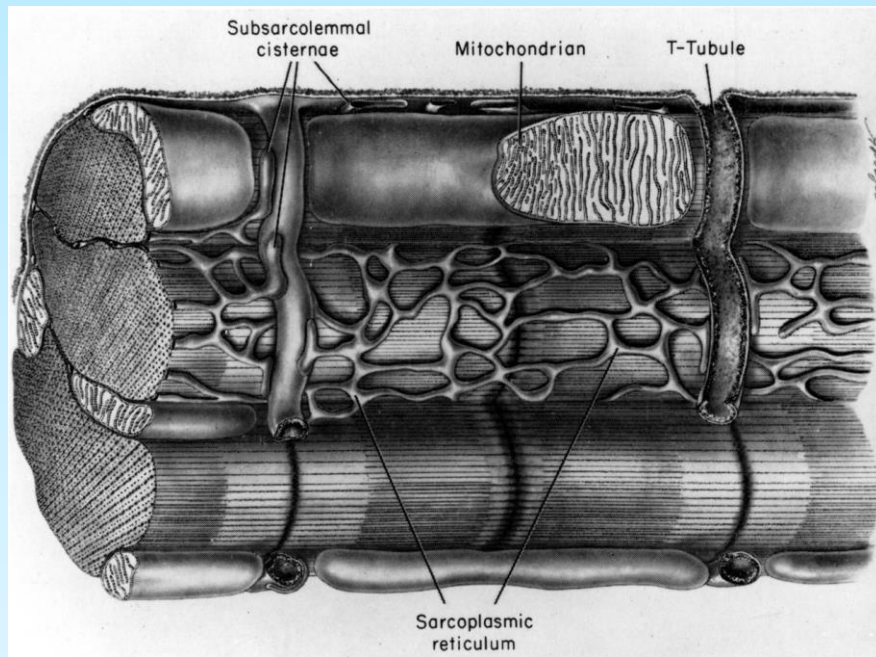
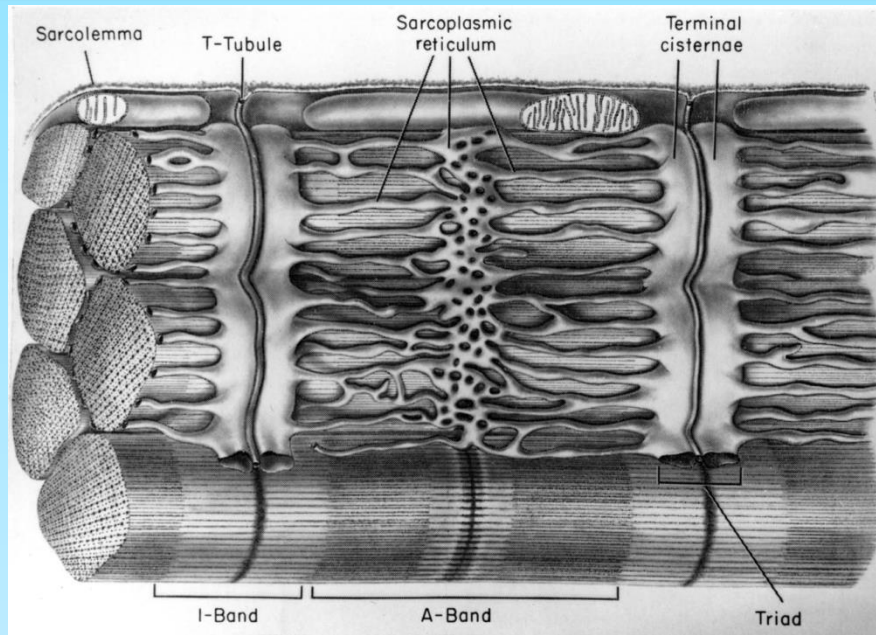
d 0.55  $\mu$ M  $\text{CaCl}_2$

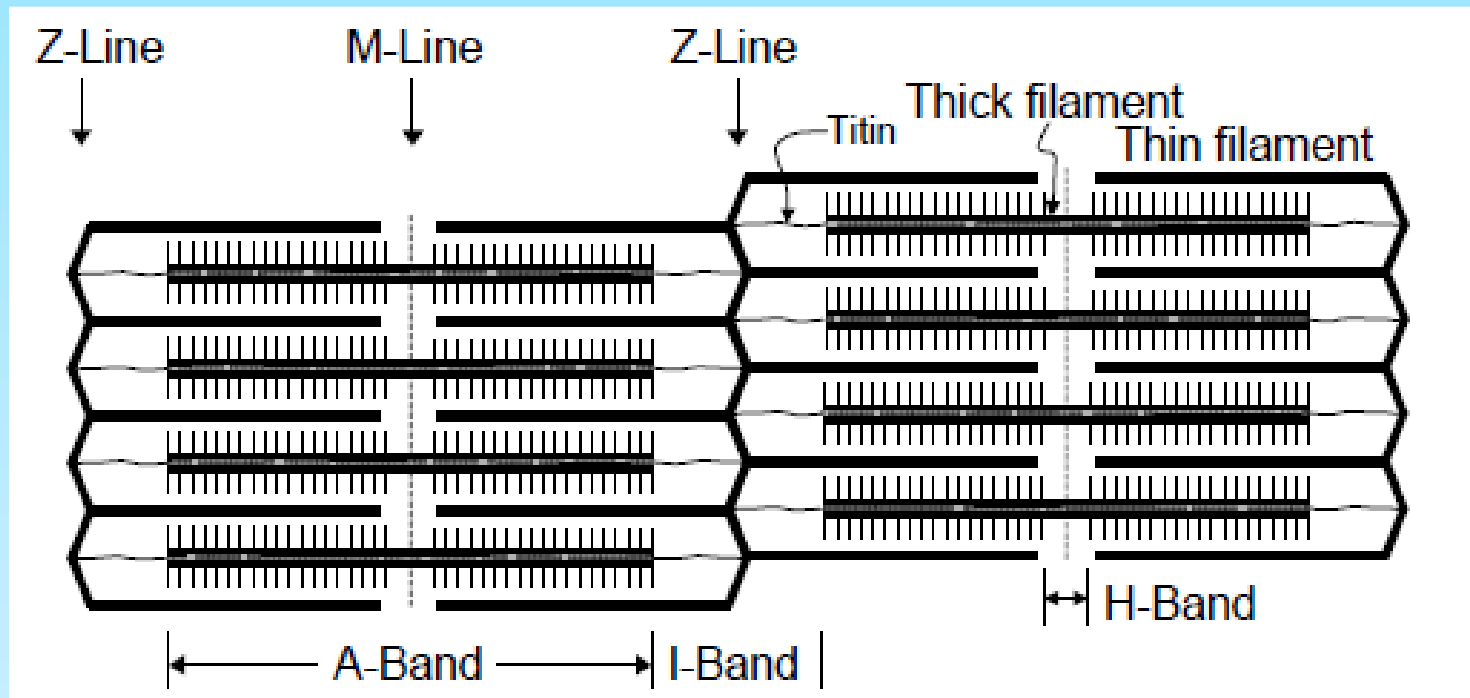
$P_o = 0.92$   $T_o = 6.87$  ms  $T_c = 0.79$  ms



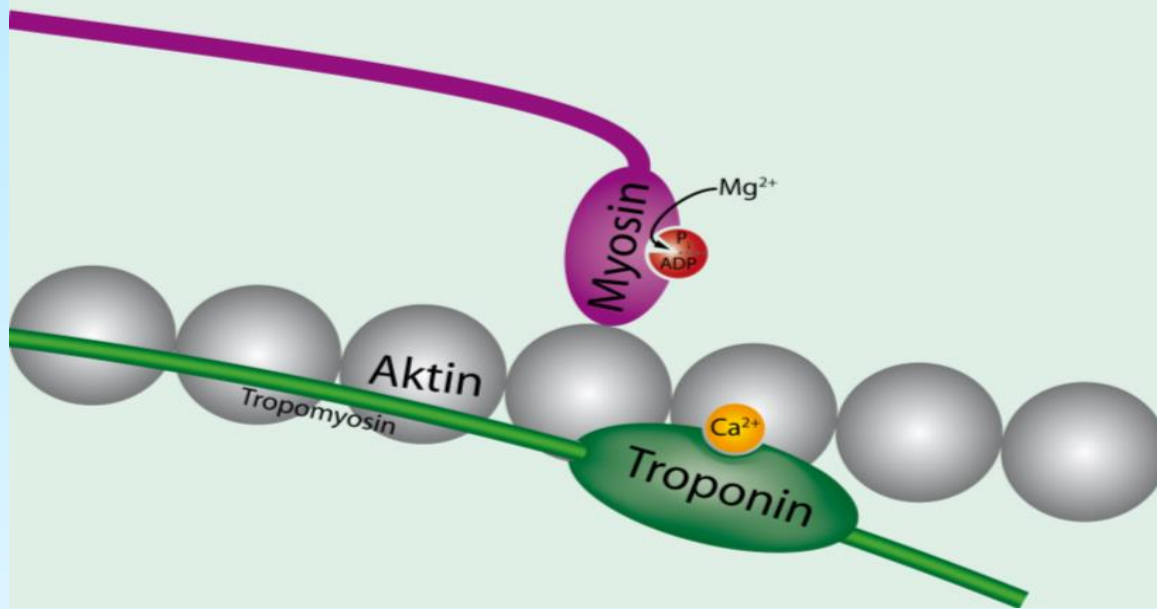
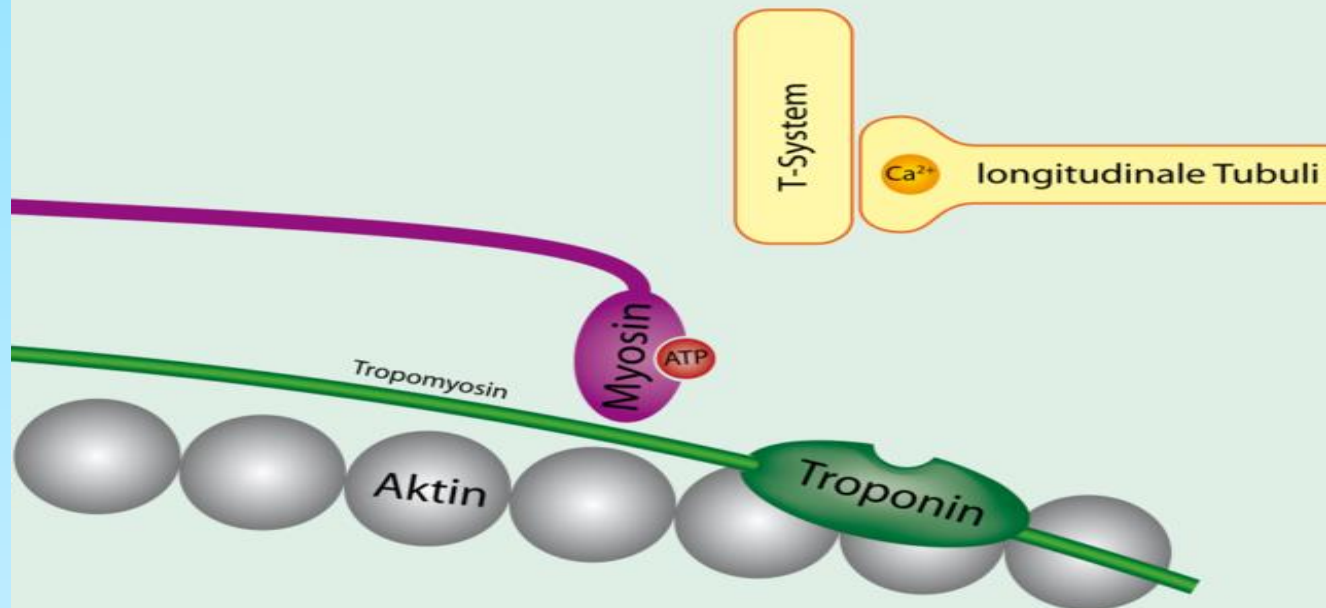
e  $\text{Ca}^{2+}$  response



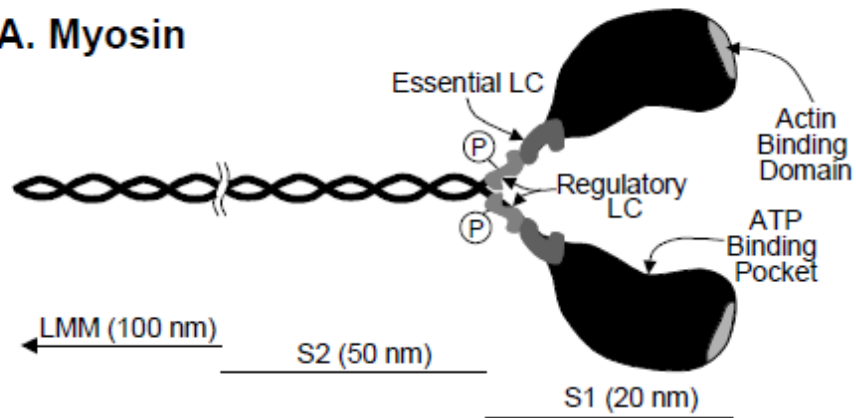




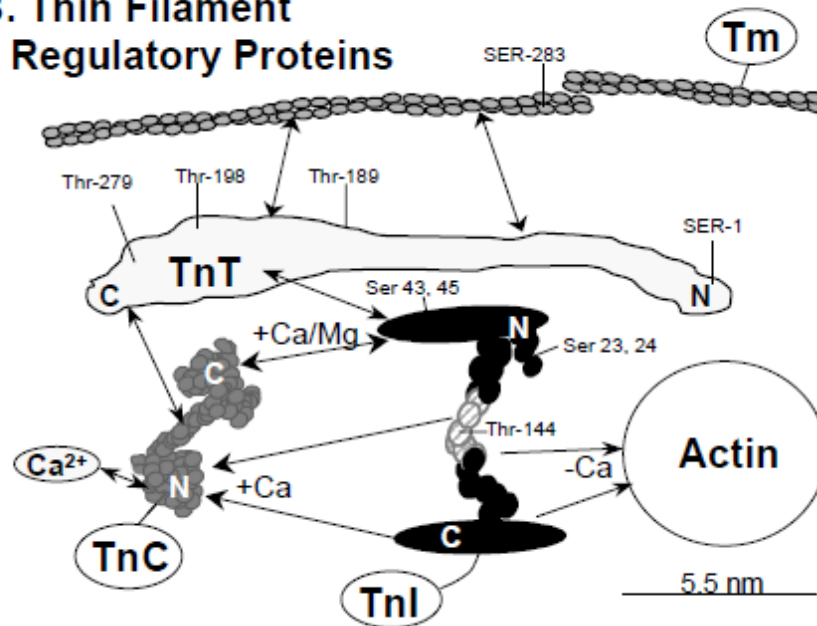
The organization of the sarcomere. The thin filaments meet at the Z-lines and the center of the thick filaments is known as the M-line. The I-band (or isotropic band) is the area where there are only thin filaments and the A-band (or anisotropic band) is the length of the thick filaments. The region of the thick filament where there is no overlap with thin filaments is known as the H-band (or H-zone).



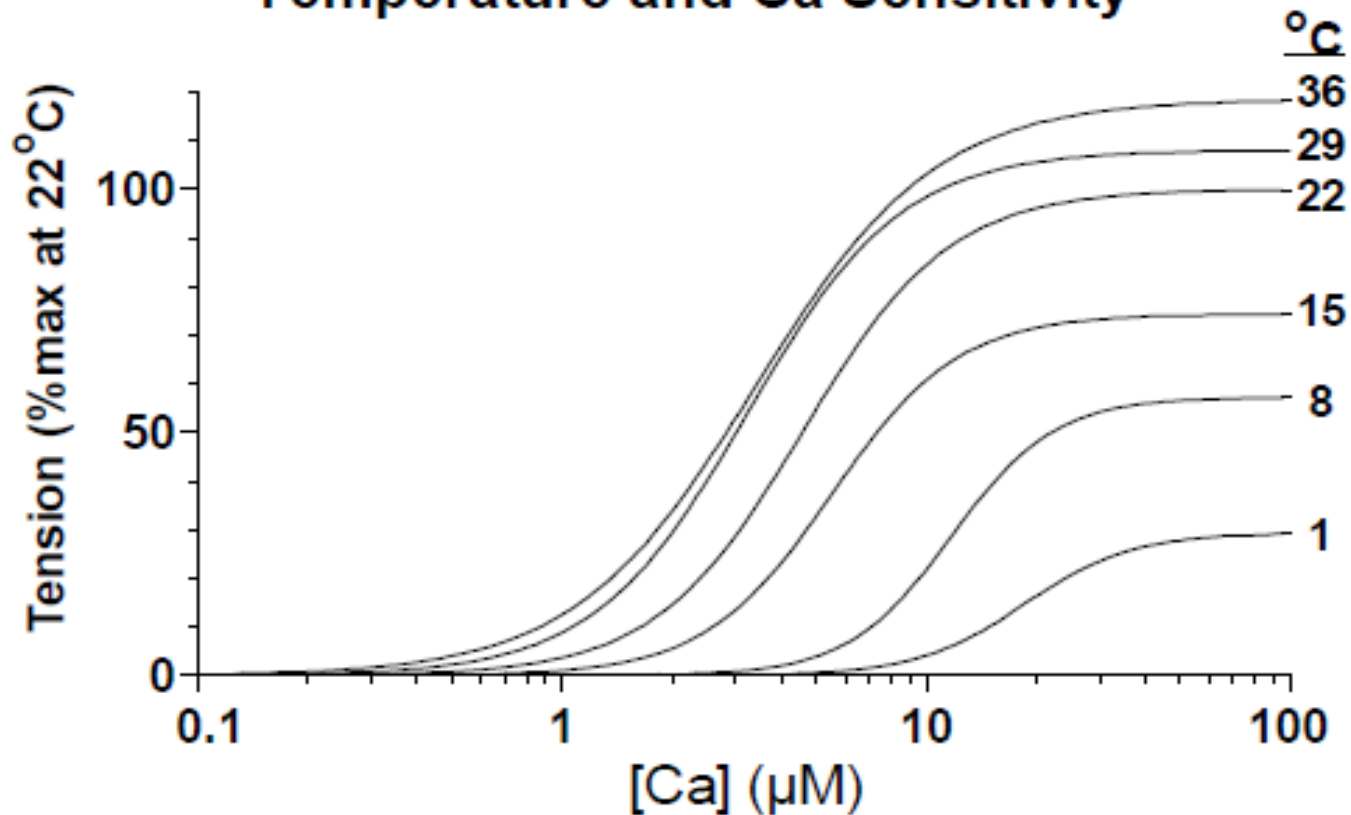
## A. Myosin



## B. Thin Filament Regulatory Proteins



## Temperature and Ca Sensitivity



The influence of temperature on the Ca sensitivity of chemically "skinned" rabbit ventricular muscle (data from Harrison and Bers, 1989a have been redrawn).

Both the Ca sensitivity and the maximum force are reduced at lower temperatures

Extracellular space

