


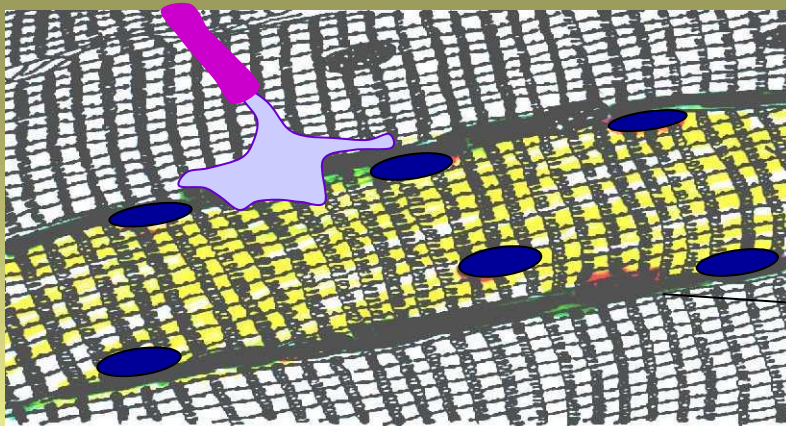
SKELETAL, CARDIAC, AND SMOOTH MUSCLES

This presentation includes only the most important terms and facts. Its content by itself is not a sufficient source of information required to pass the Physiology exam.

SKELETAL, CARDIAC, AND SMOOTH MUSCLES

-  ● **Structural characteristics**
- **Electrical and mechanical activities**
- **Molecular mechanisms of contraction**
- **Biophysical properties of muscle as a whole**
- **Mechanisms of gradation/modulation of contraction**
- **Overview of characteristic properties of skeletal, cardiac, and smooth muscles**

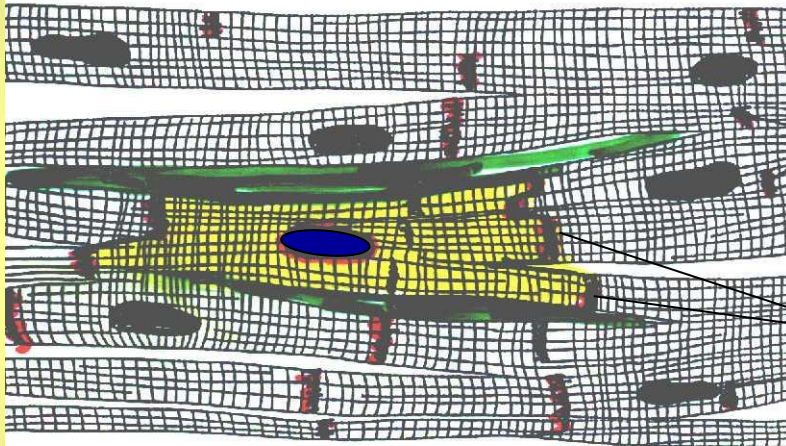
30 μm



SKELETAL MUSCLE

sarcolemma

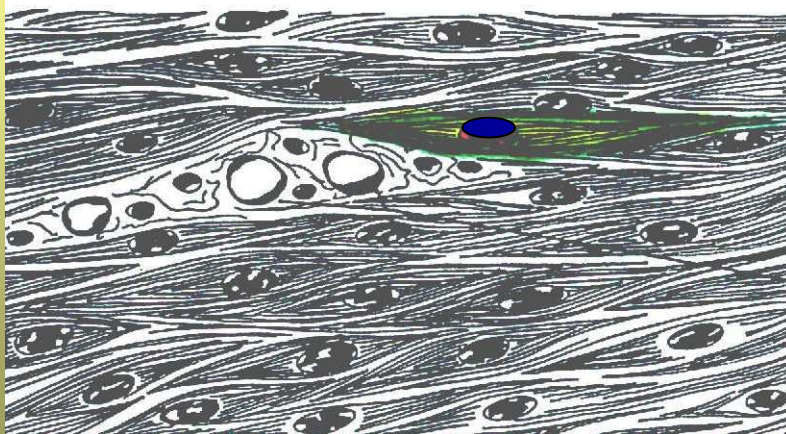
20 μm



CARDIAC MUSCLE

intercalated discs

3 μm



SMOOTH MUSCLE

(vascular system, airways, gastrointestinal and urogenital systems)

ELECTRICAL CONNECTIONS „GAP JUNCTIONS“

BASIC STRUCTURAL ELEMENTS OF FUNCTIONAL SYNCYTIUM

GAP JUNCTION UNIT

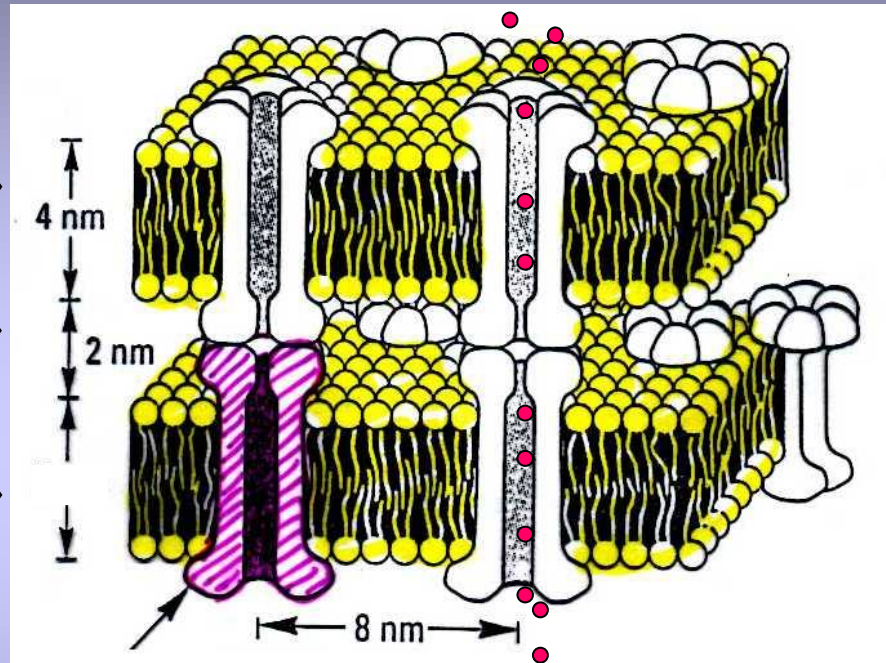
CONNEXON 1

„gap“
(extracellular space)

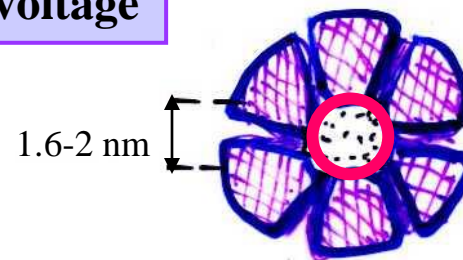
CONNEXON 2

MYOCARDIUM

SMOOTH MUSCLE



pH
 $[Ca^{2+}]_i$
membrane voltage



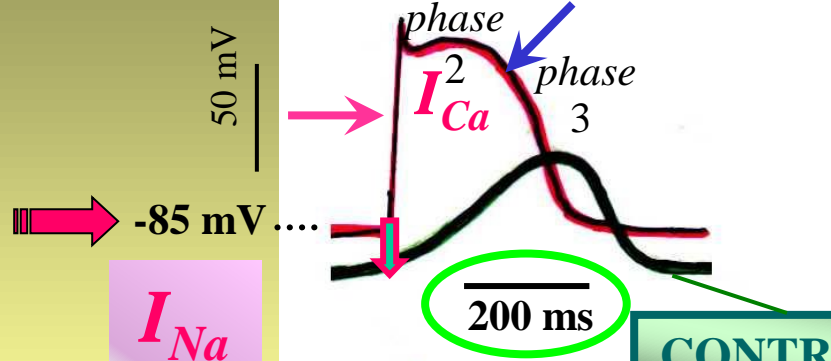
SKELETAL, CARDIAC, AND SMOOTH MUSCLES

- **Structural characteristics**
- ● **Electrical and mechanical activity**
- **Molecular mechanisms of contraction**
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DEPOLARIZATION

REPOLARIZATION

HEART



I_{Na}

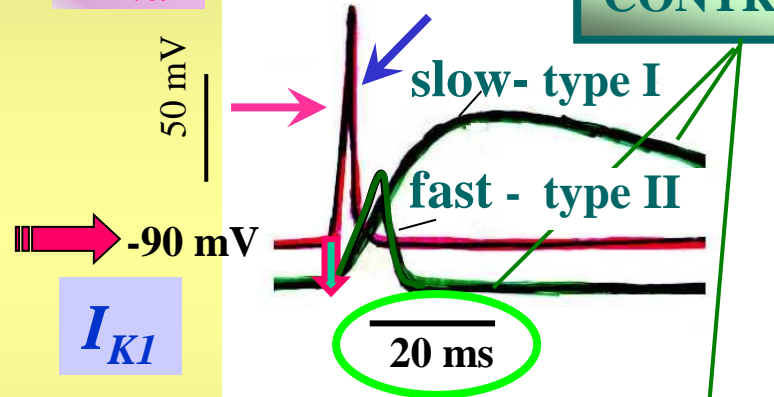
I_{Ca}^{inact}

family of K currents

regular pacemaker activity (SA, AV nodes)

CONTRACTION

SKELETAL MUSCLE



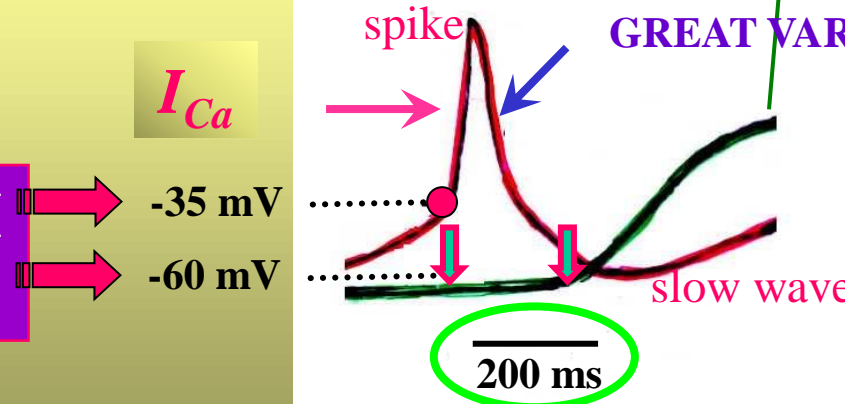
I_{K1}

I_{Na}^{inact}

I_K

GREAT VARIETY IN REPOLARIZATION

SMOOTH MUSCLE



I_{Ca}

I_{Ca}^{inact}

$I_{K(Ca)}$

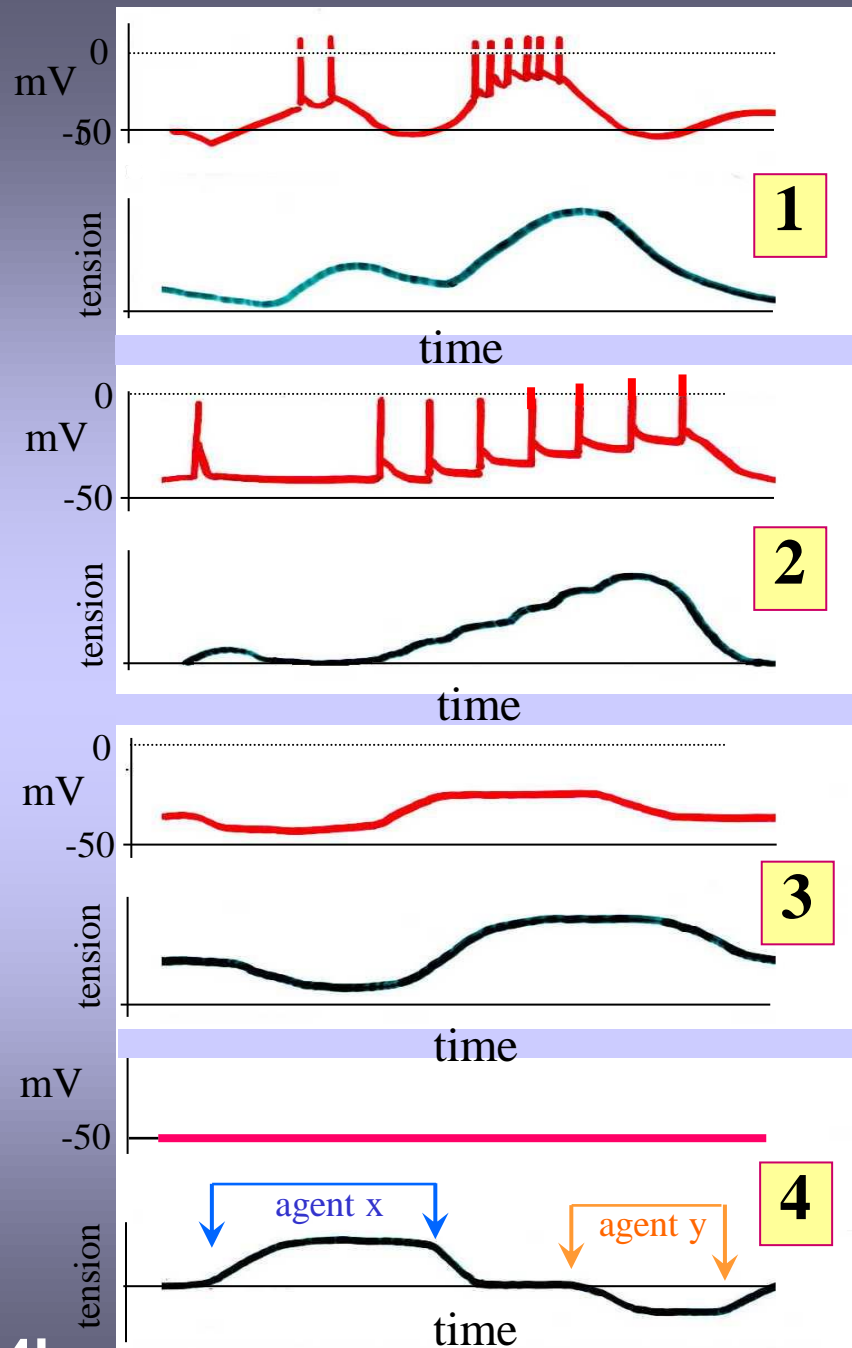
irregular pacemaker activities of unstable foci

SMOOTH MUSCLE CELL

TRIGGERING AND MODULATION OF MECHANICAL RESPONSES

**GREAT VARIETY IN
ELECTRO-MECHANICAL RELATIONS**





ELECTRO-MECHANICAL COUPLING

SLOW IRREGULAR WAVES in membrane voltage with APs



SLOW WAVES IN CONTRACTION

(GIT)

↑ frequency of APs



TETANIC CONTRACTION

(ureter, gall duct, uterus)

SLOW CHANGES in membrane voltage



SLOW CHANGES IN TONE

(smooth muscles of eye, arterioles)

CONSTANT MEMBRANE VOLTAGE

SLOW CHANGES IN TONE

(vascular smooth muscle)

NEUROHUMORAL STIMULATION

e.g. via LIGAND-RECEPTOR activation pathways

SMOOTH MUSCLE CELL

MECHANICAL RESPONSES can be triggered/modulated

- by different patterns of **ELECTRICAL ACTIVITY**
ELECTRO-MECHANICAL COUPLING

ELECTRICAL STIMULATION

- by different **NEUROHUMORAL STIMULATION**

NEUROTRANSMITTERS (acetylcholine, noradrenaline, ...)

NEURAL STIMULATION

HORMONES (e.g. progesterone, oxytocin, angiotensin II, ...)

LOCAL TISSUE FACTORS (NO, adenosine, P_{CO_2} , P_{O_2} , pH, ...)

HUMORAL STIMULATION

- by **STRETCH** of the smooth muscle cell (**STRETCH-ACTIVATED CHANNELS**)

MECHANICAL STIMULATION

SKELETAL, CARDIAC, AND SMOOTH MUSCLES

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CROSS STRIATED MUSCLES

CONTRACTILE ELEMENTS



**THICK MYOSIN
FILAMENT**

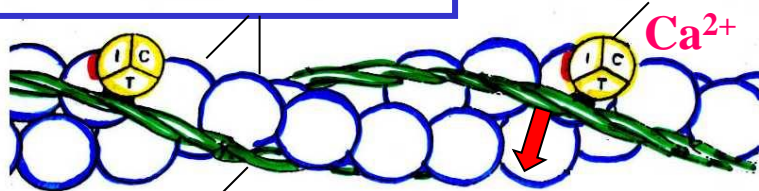
**MOLECULE
OF MYOSIN II**

ACTIN binding site
ATP binding site
(ATP → ADP + P_i)

~400

**G-ACTIN
MOLECULES**

**troponin
complex**



tropomyosin

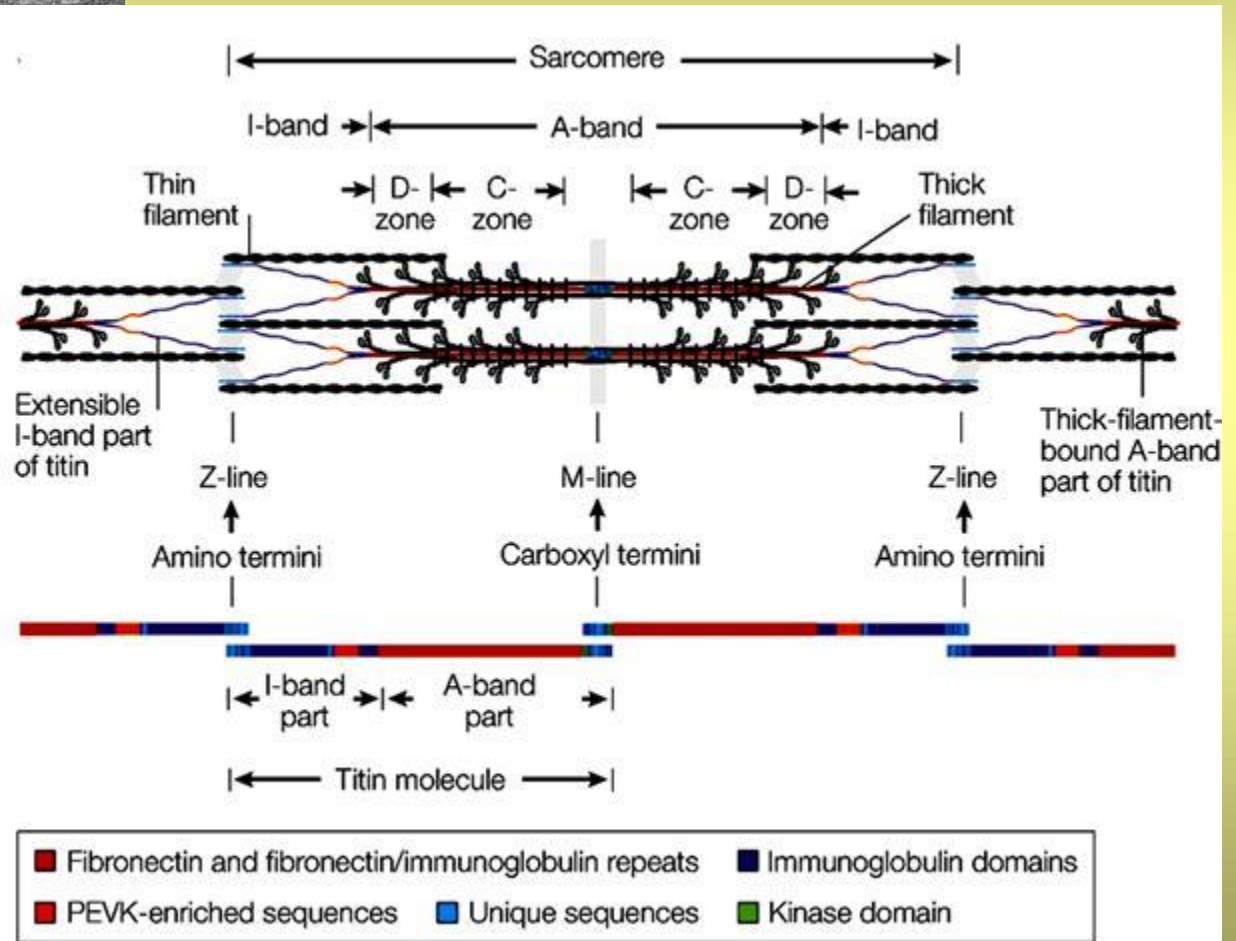
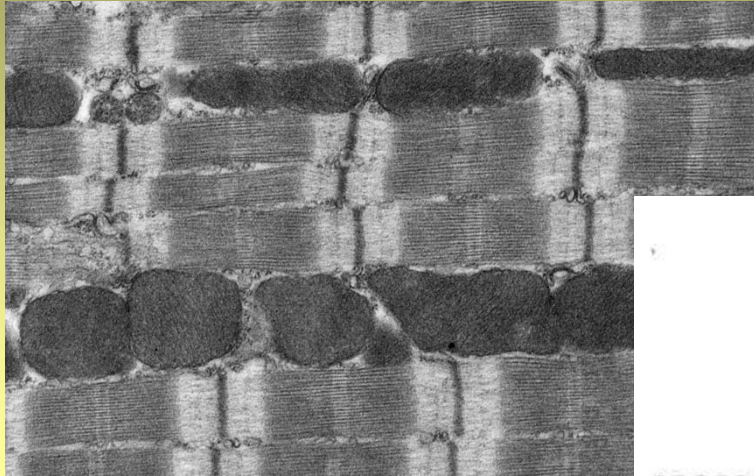
40 nm

**THIN ACTIN
FILAMENT**

**REGULATORY
PROTEINS**

**TROPOMYOSIN - TROPONIN
COMPLEX**

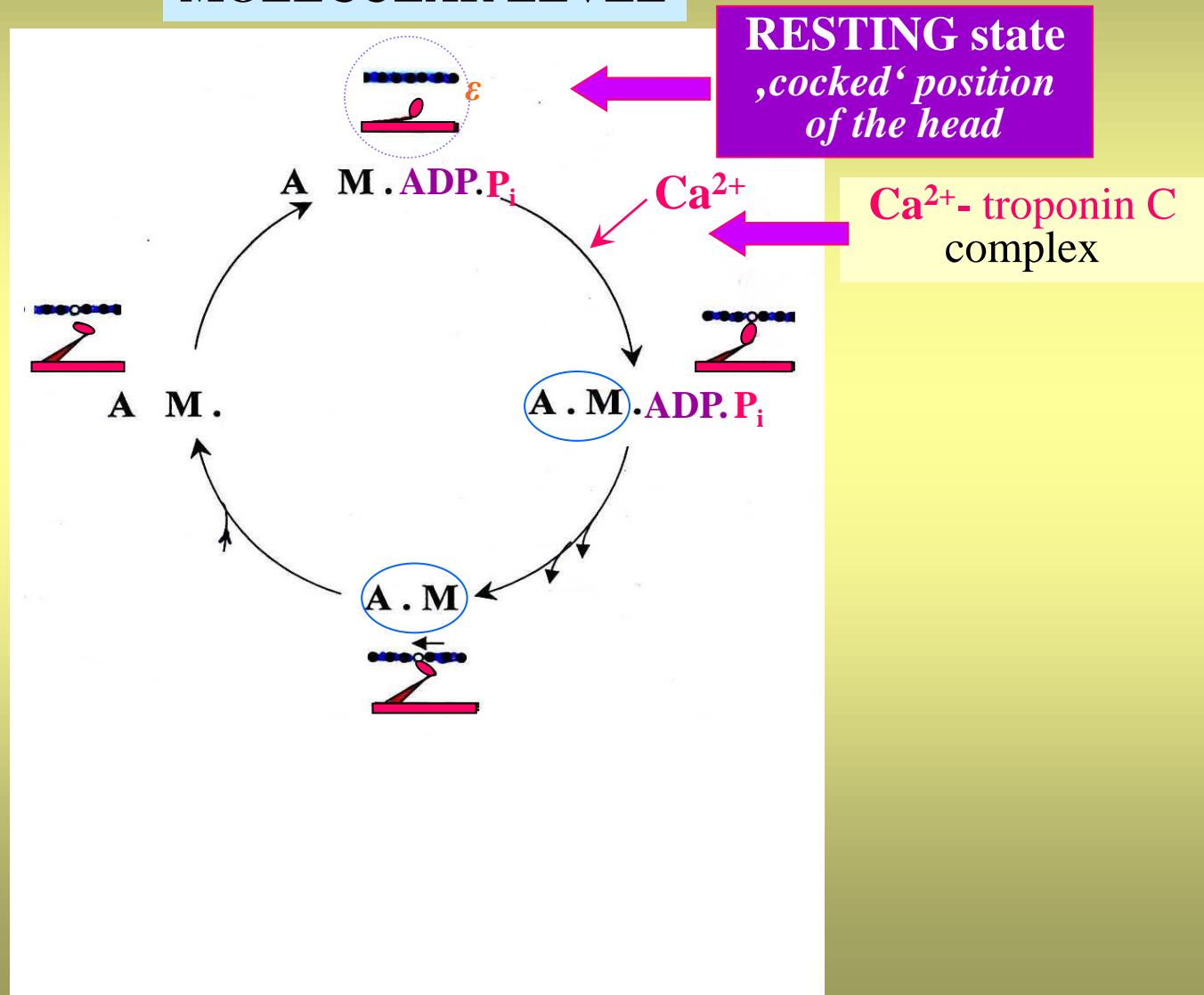
CROSS STRIATED MUSCLES



CROSS-STRIATED MUSCLE

ONE ELEMENTARY CYCLE OF CONTRACTION AND RELAXATION

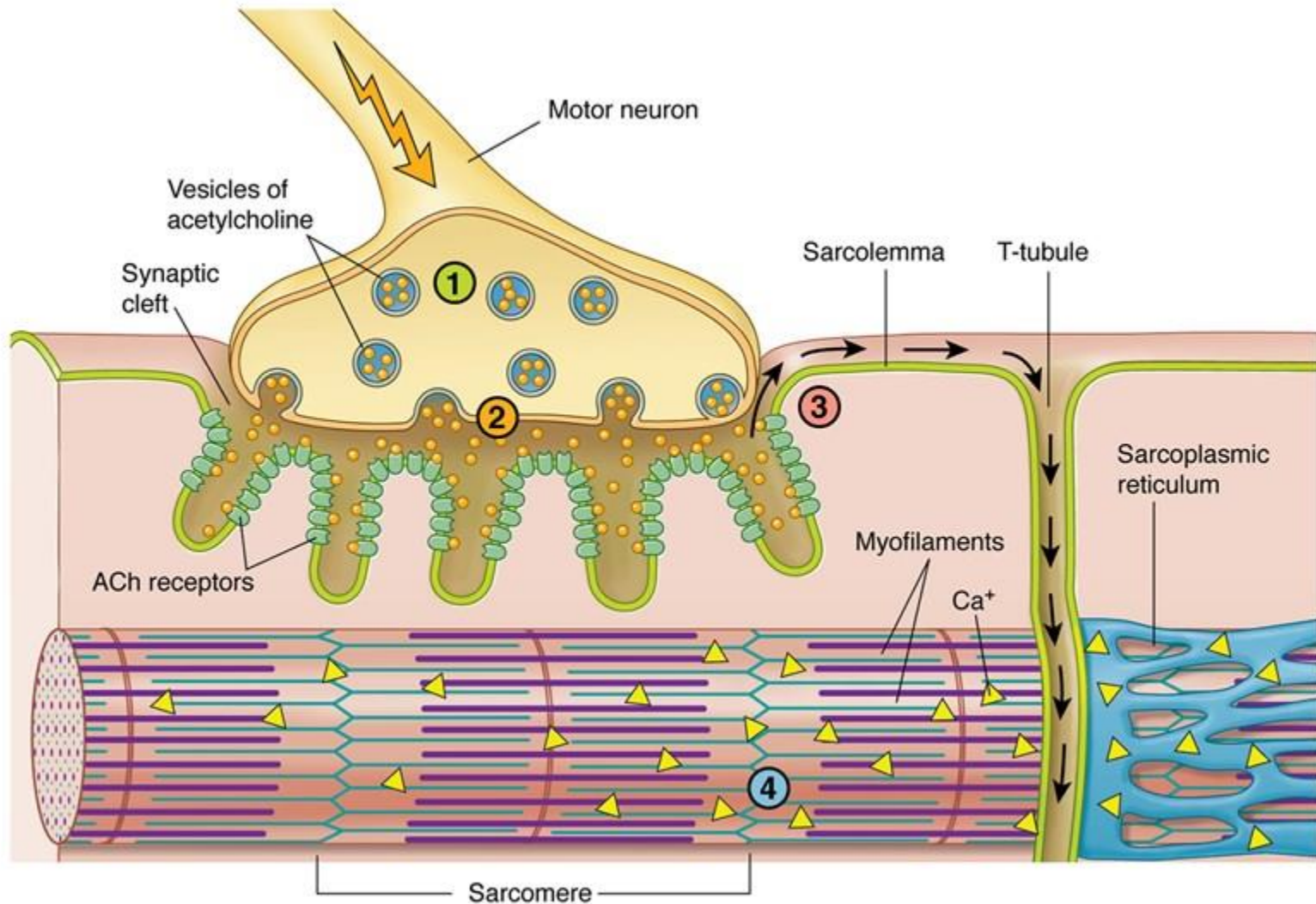
MOLECULAR LEVEL



CROSS-STRIATED MUSCLE

ONE ELEMENTARY CYCLE OF CONTRACTION AND RELAXATION

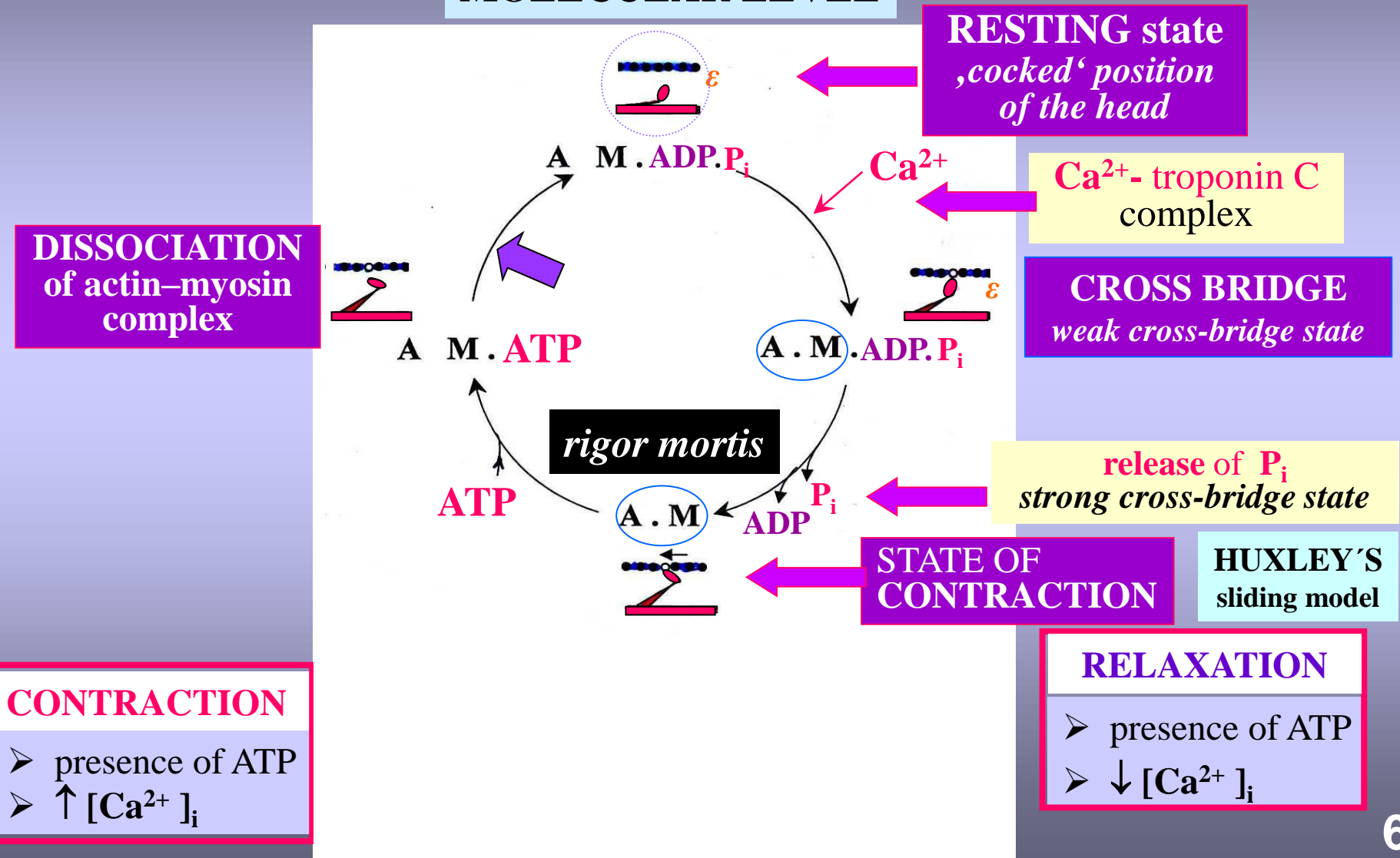
MOLECULAR LEVEL



CROSS-STRIATED MUSCLE

ONE ELEMENTARY CYCLE OF CONTRACTION AND RELAXATION

MOLECULAR LEVEL



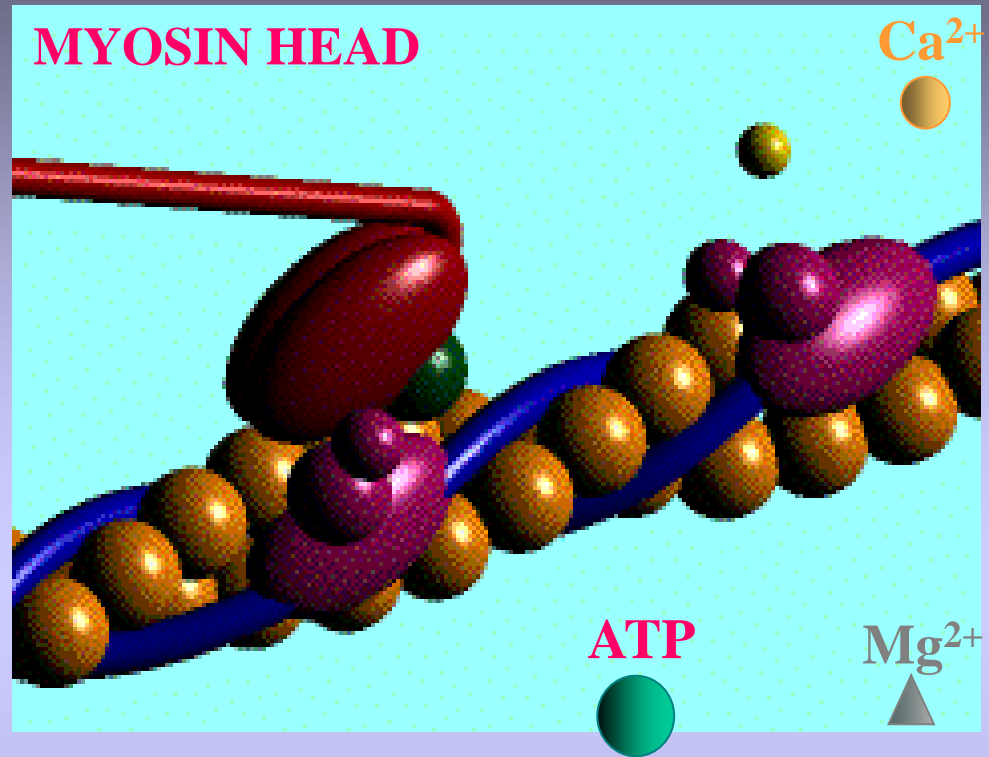
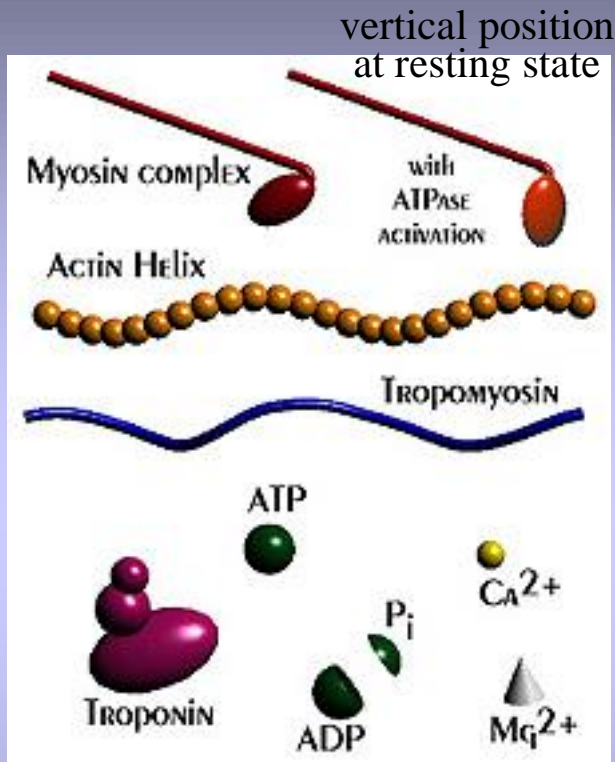
CONTRACTION

- presence of ATP
- $\uparrow [Ca^{2+}]_i$

RELAXATION

- presence of ATP
- $\downarrow [Ca^{2+}]_i$

CROSS-STRIATED MUSCLE



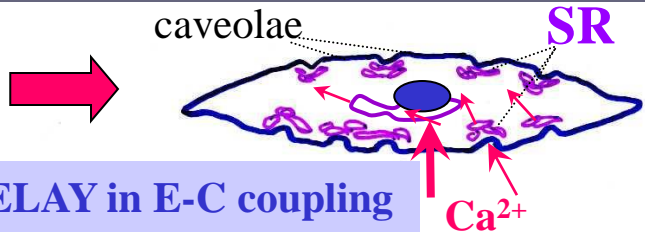
Animated model of interaction of myosin head with actin filament („ paddling “)

Myosin – MOLECULAR MOTOR

It consumes chemical energy released from **hydrolysis of ATP** and converts it into the motion (**mechanical work**)

troponin – tropomyosin complex

SMOOTH MUSCLE



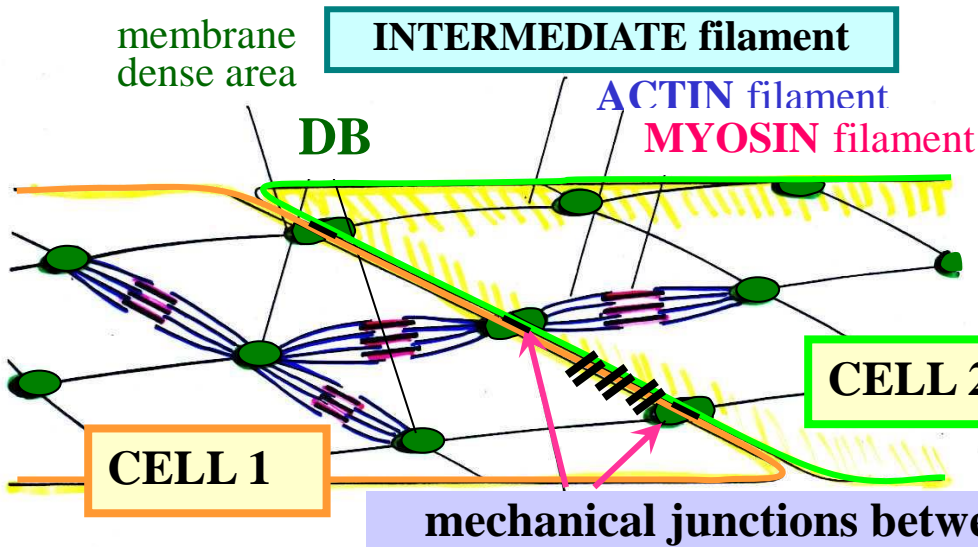
DELAY in E-C coupling

SLOW DEVELOPMENT of contraction and relaxation

?

- myosin ATP-ase
- Ca²⁺ transport systems

ORGANIZATION OF CYTOSKELETON AND MYOFILAMENTS



DB - DENSE BODIES

|| gap junctions

TROPONIN IS ABSENT !!

REGULATORY PROTEINS

TROPOMYOSIN

CALMODULIN (TNC)

CALPONIN

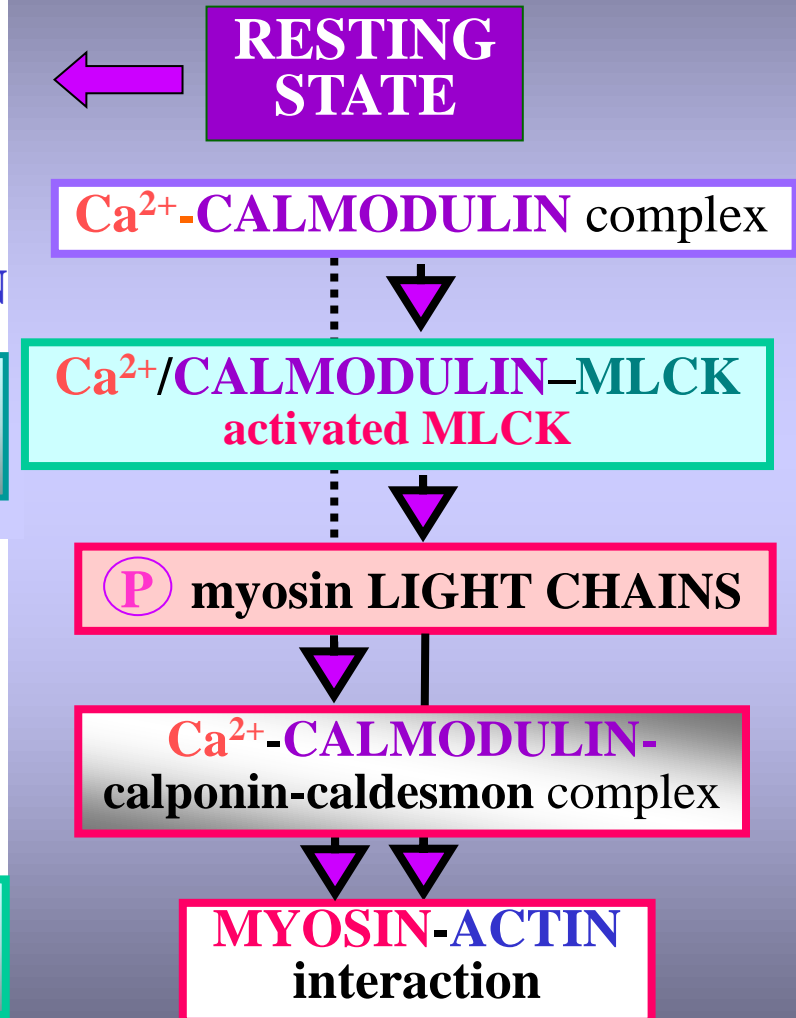
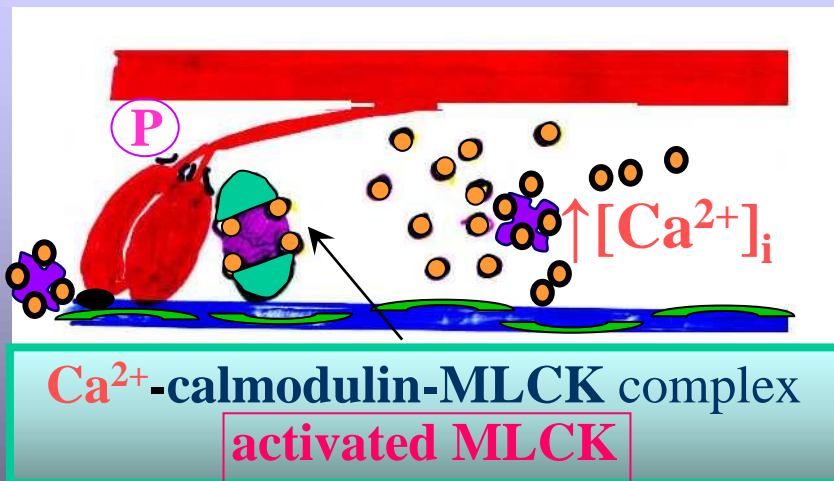
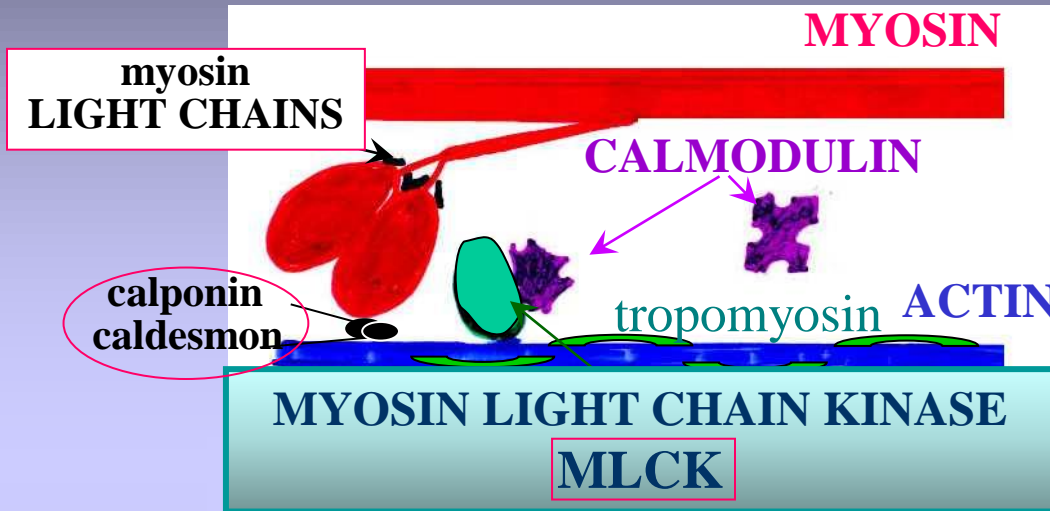
CALDESMON

SMOOTH MUSCLE

TROPONIN COMPLEX is not present

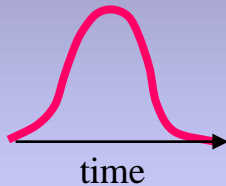
CALMODULIN

2 ROLES OF Ca^{2+} -CALMODULIN COMPLEX



CONTRACTION VARIANTS OF SMOOTH MUSCLE CELL

1 PHASIC variant of CONTRACTION - mode of CYCLING



- **P** of **myosin light chains (RMLCs)** is a prerequisite of **PHASIC** contraction
- **ATP is consumed**



2 TONIC variant of CONTRACTION - LATCH BRIDGES



At the state of **CONTRACTION**
RMLCs are **dephosphorylated** by **MLCP**



SLOW dissociation
of **M.A** complex



SUSTAINED TONIC CONTRACTION

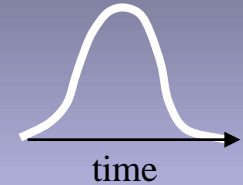
ATP is spared

P

SMOOTH MUSCLE

1

PHASIC variant of CONTRACTION - mode of cycling



Ca^{2+} -calmodulin complex

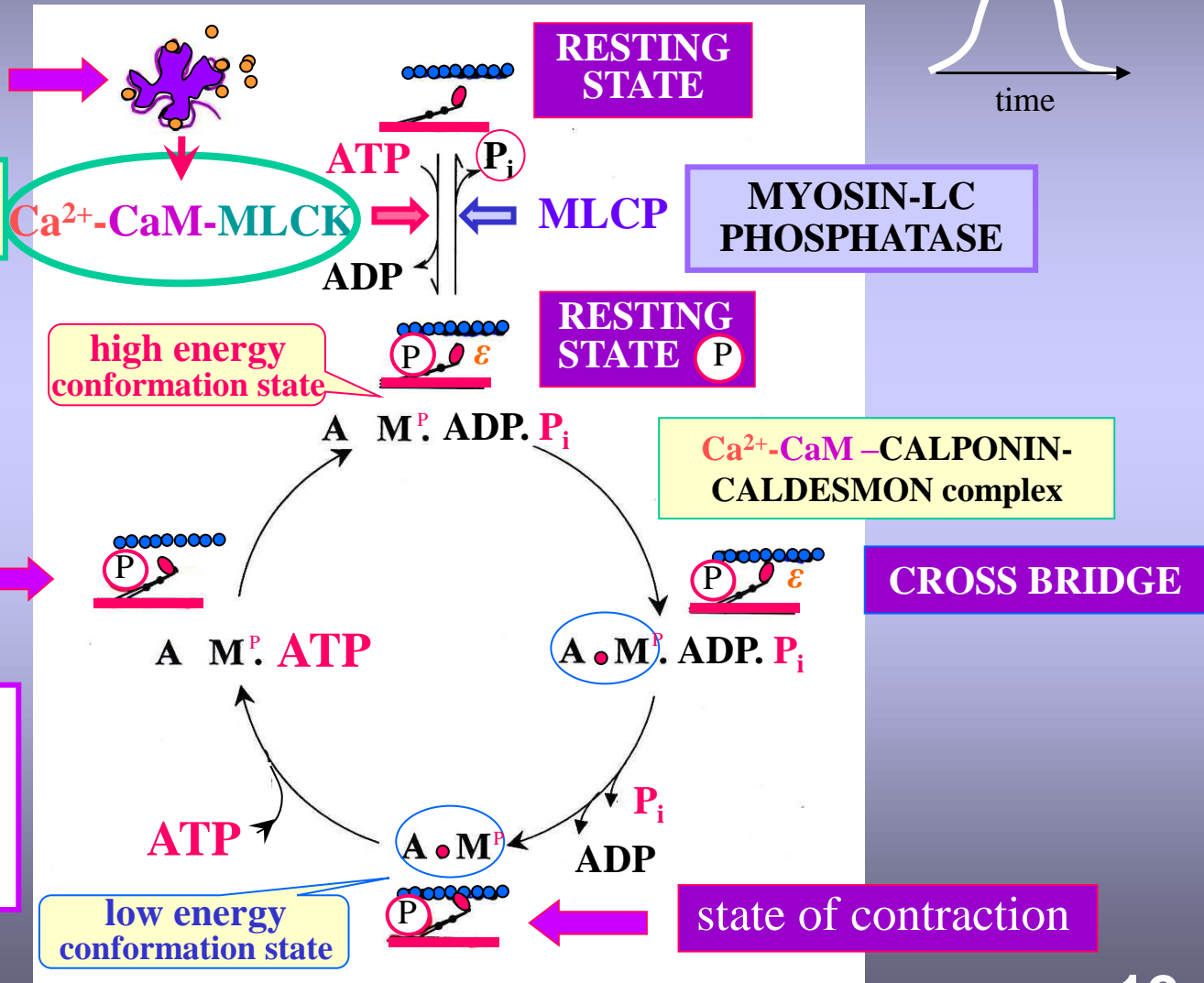
MYOSIN-LC KINASE activated

MLCK* / MLCP

dissociation of actin-myosin complex

PHOSPHORYLATION of myosin light chains is a prerequisite of PHASIC CONTRACTION

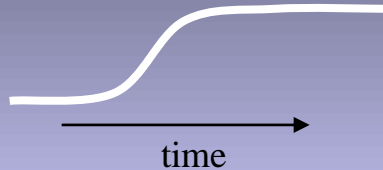
ATP is consumed



SMOOTH MUSCLE

2

TONIC variant of CONTRACTION - LATCH BRIDGE



↓ **MLCK*** / **MLCP**

DEPHOSPHORYLATION of **MLCs**
at the **STATE OF CONTRACTION**

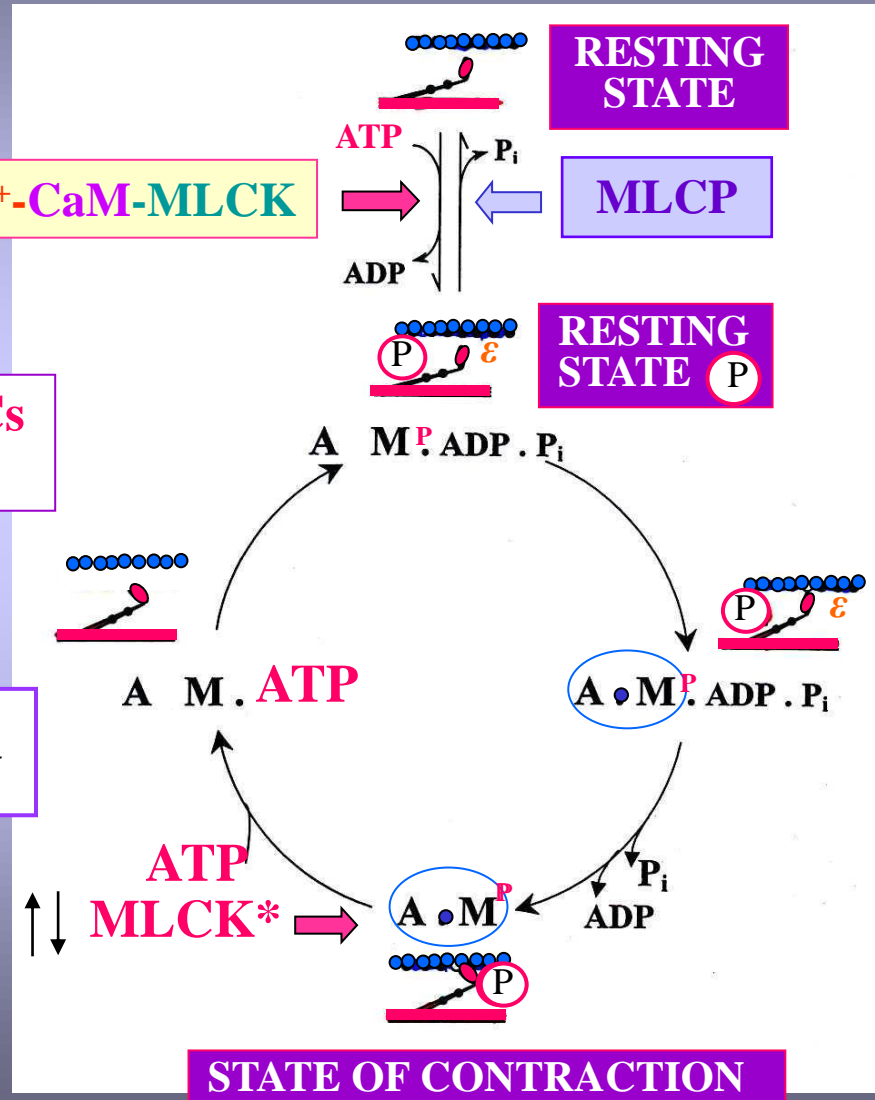
very slow **DISSOCIATION**
of **M.A** complex

LATCH BRIDGE mechanism
of sustained **TONIC CONTRACTION**

ATP is spared

↑ **MLCK*** / **MLCP**

Ca²⁺-CaM-MLCK



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ISOMETRIC AND ISOTONIC CONTRACTION

SKELETAL MUSCLE

RESTING TENSION

IMC

ISOMETRIC CONTRACTION

at constant **LENGTH**
changes in **TENSION**
are measured by tensiometer

ITC

ISOTONIC CONTRACTION

at constant **TENSION**
changes in **LENGTH**
are measured

AUXOTONIC CONTRACTION

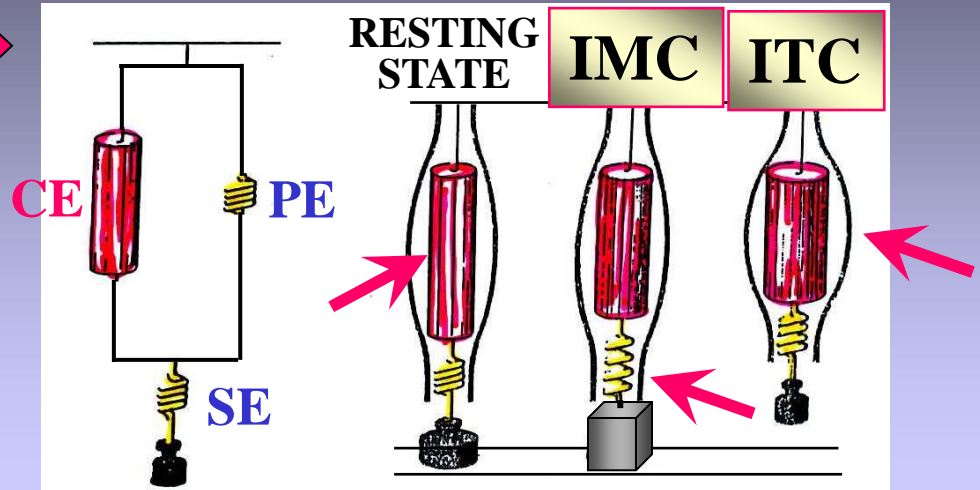
HEART

ISOVOLUMIC PHASE (ISOMETRIC)

EJECTION PHASE (ISOTONIC) **AUXOTONIC**

SMOOTH MUSCLE

TONIC CONTRACTION (*tone of blood vessels*)
PHASIC CONTRACTION (*contraction of urinary bladder*)



CE – **contractile elements**

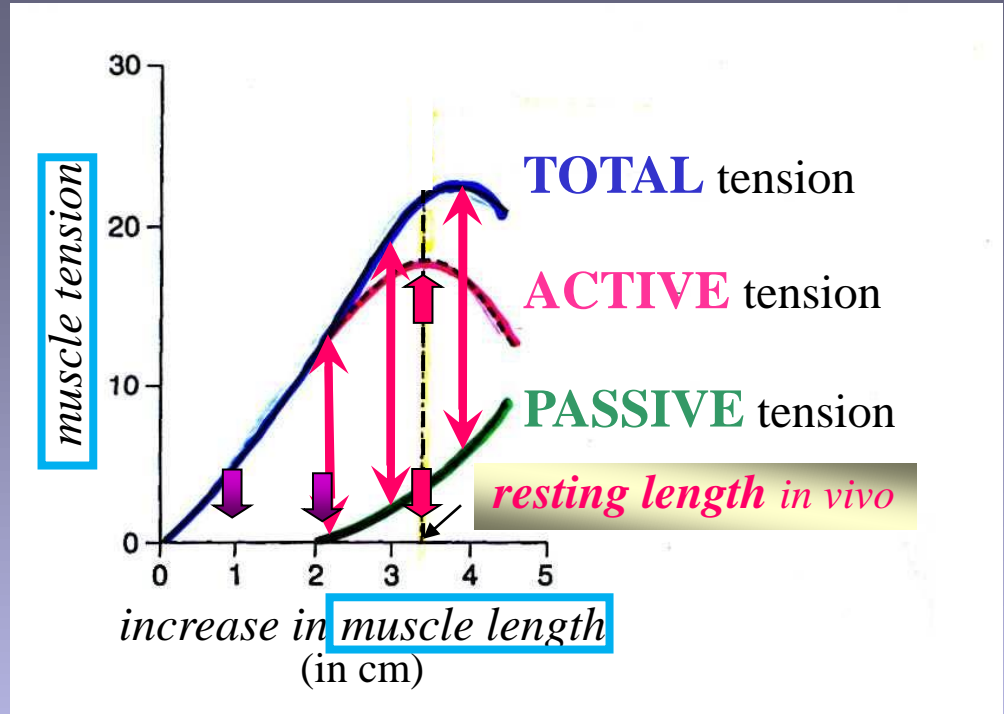
PE, SE - **parallel and series elasticity**
(in relation to contractile elements)

PE – *extracellular* and *intracellular* elasticity
(*titin* connecting Z and M lines in the sarcomere)

SE – elasticity of fibrous tissue - *tendon*

TENSION-LENGTH RELATIONSHIP

SKELETAL MUSCLE



PASSIVE tension

tension of *unstimulated muscle* at gradual stretching
(**ELASTIC COMPONENTS**)

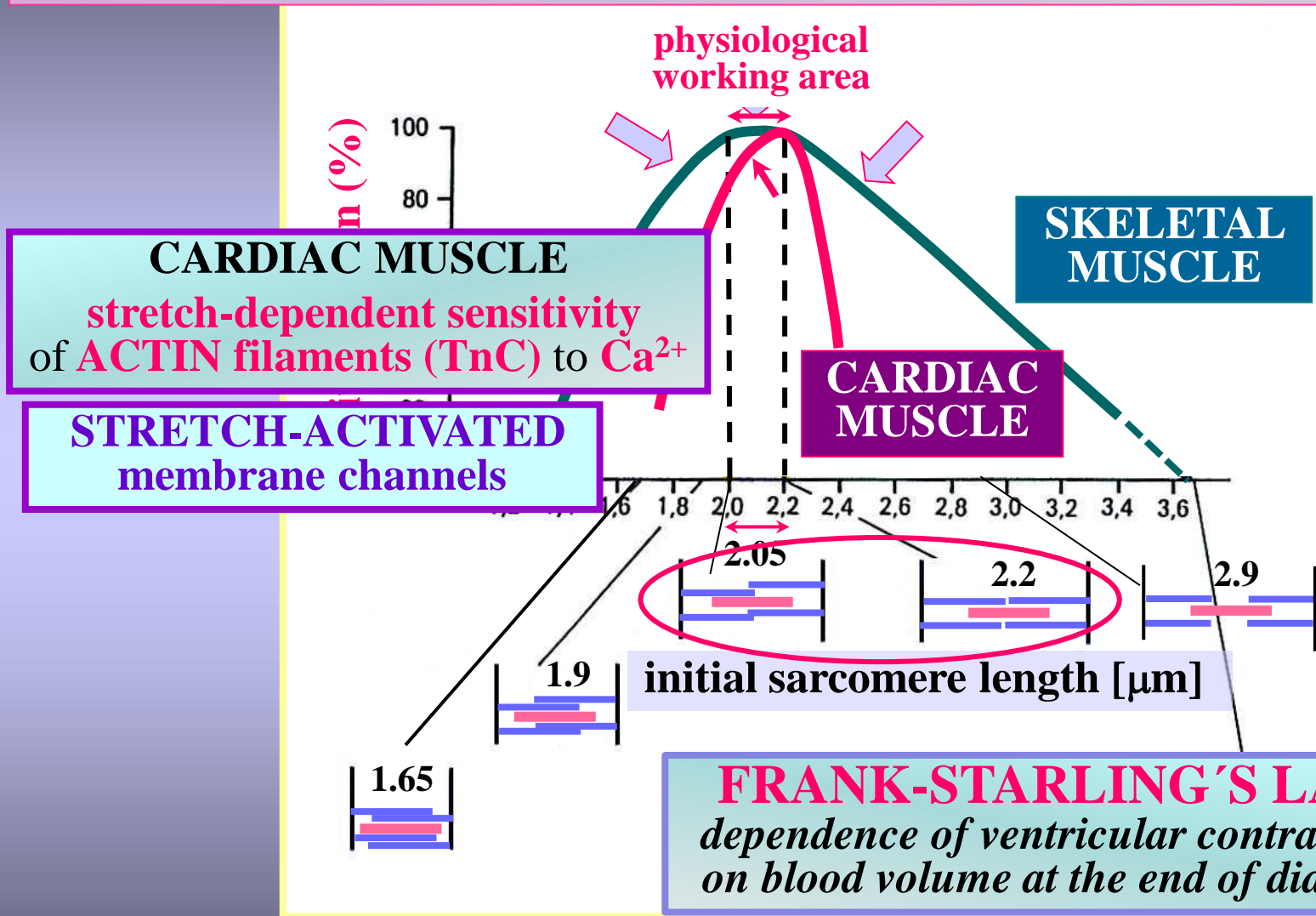
TOTAL tension

ISOMETRIC CONTRACTIONS of *stimulated muscle* at gradually increased *initial (resting) length*

ACTIVE tension

difference between **TOTAL** and **PASSIVE** tension curves at any length (*tension actually generated by contractile elements*)

ACTIVE TENSION of cross striated muscles as a function of INITIAL LENGTH of SARCOMERE



SMOOTH MUSCLE

CHARACTERISTIC FEATURES

- **GREAT EXTENSIBILITY**

(e.g. myocytes of urinary bladder can lengthen up to **200%**, myocytes of uterus even up to **1000%** at the end of pregnancy in relation to their original state)

- **PLASTICITY**

No direct relation between the **LENGTH** and **TENSION** in smooth muscle cells. Stretch-induced increased tension almost *immediately spontaneously decreases*.

Analogous relation is valid between **VOLUME** and **PRESSURE** in hollow organs (*stomach, intestines, urinary bladder, ...*).

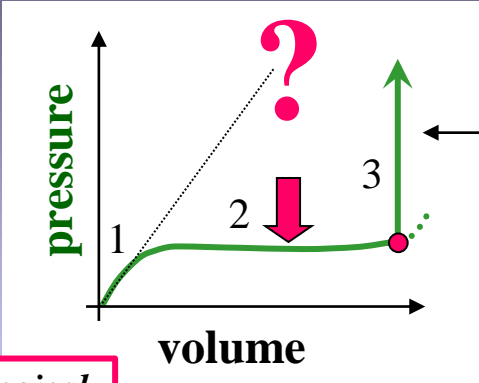


PLASTICITY OF SMOOTH MUSCLE

CYSTOMETROGRAM

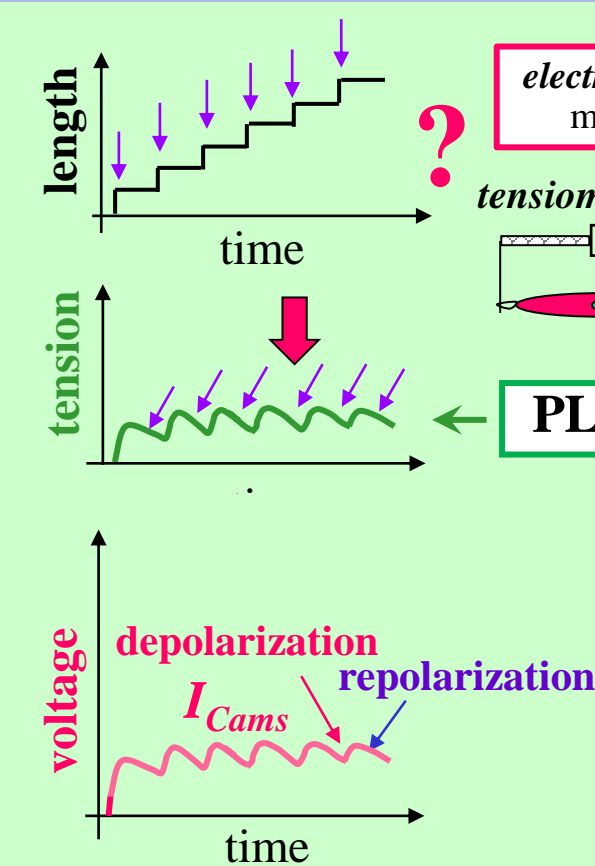
urinary bladder

ISOLATED MYOCYTE
(human jejunum)

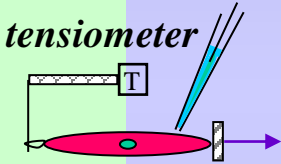


micturition reflex is triggered

$P = 2T/r$ LAPLACE LAW



electrophysiological measurements



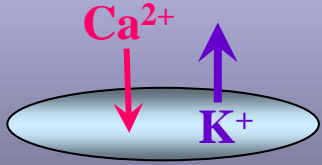
STRETCH-activated Ca^{2+} -channels
(mechano-sensitive channels)

$I_{Ca ms}$ ↓ **DEPOLARIZATION**

↑ $[Ca^{2+}]_i$

↑ **TENSION**

calcium-activated $[Ca^{2+}]_i$ -sensitive K^+ -channels



↓ I_{KCa}
REPOLARIZATION

↓ **TENSION**

↓ $[Ca^{2+}]_i$

PLASTICITY

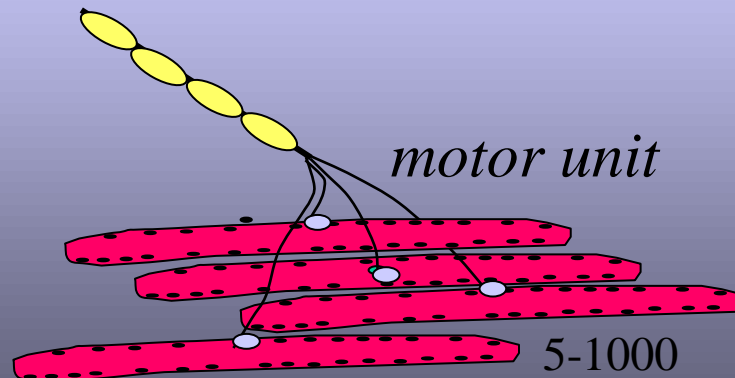
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SKELETAL MUSCLE

MAIN FACTORS IN GRADATION OF CONTRACTION

- ↑ *frequency* of discharges in *motor neuron* ⇒ **FREQUENCY SUMMATION** of contractions in skeletal muscle fibre (TETANIC CONTRACTION)
- ↑ *number* of activated **MOTOR UNITS** by increasing voluntary effort ⇒ **SPATIAL SUMMATION** (multiple fibre summation) - **RECRUITMENT OF MOTOR UNITS**



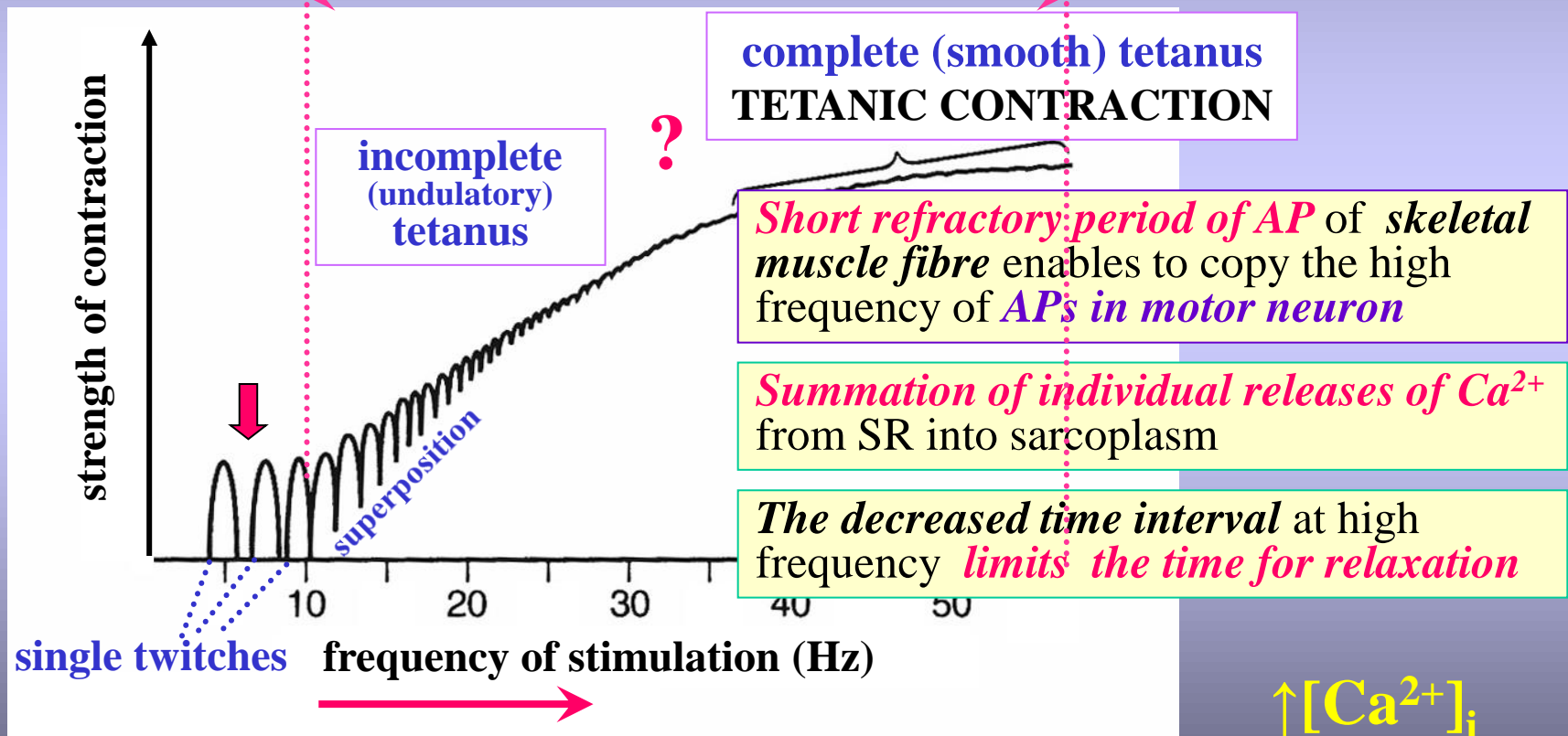
SKELETAL MUSCLE

GRADATION of CONTRACTION by \uparrow FREQUENCY of STIMULATION

SINGLE MUSCLE FIBRE

RANGE OF SUMMATION

physiological behaviour of skeletal myocyte



1 Hz = 1 impulse/sec

CARDIAC MUSCLE

MAIN FACTORS IN GRADATION OF CONTRACTION

- **↑ DIASTOLIC FILLING** of ventricles *in vivo* („preload“)
⇒ **↑ contraction of ventricles proportionate to the stretching of cardiomyocytes at the end of diastole**

FRANK-STARLING'S LAW

- **↑ FREQUENCY of electrical activity** of cardiac cells *via* modulation of **pacemaker activity of SA node** by **sympathetic nerves** - **positive FREQUENCY EFFECT**

- **LIGAND-RECEPTOR ACTIVATION CASCADES**
leading to **↑ [Ca²⁺]_i** (noradrenalin, adrenalin, thyroxine, ...)



↑ [Ca²⁺]_i

SMOOTH MUSCLE

MAIN FACTORS IN GRADATION OF CONTRACTION / TONUS

- **DEPOLARIZATION** of the smooth muscle membrane with or without triggering of action potentials via opening of the *voltage dependent calcium channels* $\Rightarrow \uparrow [Ca^{2+}]_i$
- **FACTORS independent** on membrane depolarization
 - *Ligand-receptor activation cascades* leading to $\uparrow [Ca^{2+}]_i$ (e.g. via *activation* of PLC $\Rightarrow \uparrow IP_3$ releasing Ca^{2+} from SR)
 - *Stretching of the smooth muscle cell* \Rightarrow opening of the *stretch-activated channels* $\Rightarrow \uparrow [Ca^{2+}]_i$



$\uparrow Ca^{2+}$ -calmodulin complex

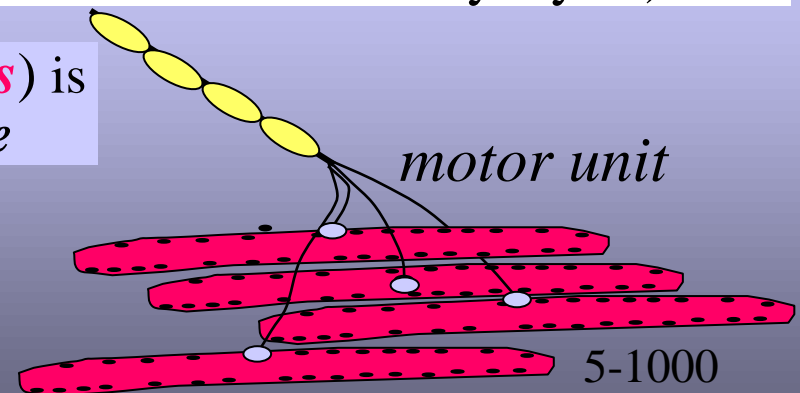
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- ➔ ● **Overview of characteristic properties of skeletal, cardiac, and smooth muscles**

SKELETAL MUSCLE

MAIN CHARACTERISTIC FEATURES

- **Multinucleated** long cylindrical cells (max. length up to 20 cm)
- **Rich** sarcoplasmic reticulum
- **Regular arrangement** of thick and thin filaments in sarcomeres (**cross striation**)
- Activity strongly dependent on **motor nerve supply** (excitation transmitted via **motor end-plate**)
- Without intercellular connections (**no** gap junctions between muscle cells)
- Motor neurons branch to innervate more muscle cells (**motor unit** defined as one motor neuron with 5-1000 myocytes)
- **Summation of contractions** (**tetanus**) is a physiological property of muscle fibre
- Activity under **voluntary control**



MAIN TYPES OF SKELETAL MUSCLE FIBRES

TYPE I

SLOW - RED

e.g. muscles of the back, soleus m.

- *Slow* (posture-maintaining) *contractions*
- *Motor units* contain *slowly conducting motor neurons*

High **OXIDATIVE CAPACITY** and **high** resistance to fatigue

TYPE II

FAST (RED /WHITE)

*e.g. extraocular muscles,
muscles of the hand*

- *Short twitches* for fine skilled movements
- *Motor units* with *rapidly conducting motor neurons*

TYPE IIa (FAST-RED) and **TYPE IIb (FAST-WHITE)**

Proportion of **OXIDATIVE** and **GLYCOLYTIC** metabolism determines the **resistance to fatigue**

Sport activities cause gradual transformation from IIb into IIa

CARDIAC MUSCLE

MAIN CHARACTERISTIC FEATURES

- ***Branched*** and ***interconnected cells*** with ***one nucleus*** in the centre (length ~100 μm)
- ***Well (moderately) developed*** sarcoplasmic reticulum
- ***Regular arrangement*** of **thick** and **thin filaments** in sarcomeres (***cross striation***)
- **Excitations (contractions)** are **independent** on nerve supply (***specialized pacemaker cells***)
- **Functional syncytium** (electrical connections - ***gap junctions***)
- ***Receptors*** for ***neurotransmitters*** (released from neuron endings) and ***hormones*** (brought by circulation); activity is ***modulated*** by ***local mediators***
- ***Long refractory period*** ***prevents*** cells from **tetanic contraction** (which would be life threatening)
- Activity is **not** under ***voluntary*** control

SMOOTH MUSCLE

MAIN CHARACTERISTIC FEATURES

- Thin *spindle-shaped* cells of various length (20-200 μm) with *one nucleus* in the centre
- *Irregular arrangement* of thick and thin filaments; **no** cross striation
- *Poorly developed* sarcoplasmic reticulum, *TT system* is missing
- Contractions of *visceral muscles* can be triggered independently on nerve supply (*slow irregular unstable pacemaker activity*); **functional syncytium** (*gap junctions*)
- **Slow phasic**, often *tonic*, even *tetanic* contractions
- Numerous *receptors* for *neurotransmitters* (released from neuron endings) and *hormones* (brought by circulation). Activity is greatly modulated by *local mediators* (local tissue factors)
- **Activity can be triggered by stretch** (*stretch activated channels*)
- **Great extensibility and plasticity**
- **Activity without** voluntary control

TYPES OF SMOOTH MUSCLE

VISCERAL „SINGLE UNIT“

e.g. stomach, intestine, uterus, ureter, ...

- *Functional syncytium (gap junctions)*
- Excitation and contraction can be evoked *in the absence of nerve supply (slow irregular pacemakers in multiple foci* shifting from place to place, *gap junctions*)
- Contraction evoked by **stretching** (*stretch-activated channels*)

MULTIUNIT- stimulated by neurons

e.g. arterioles, m. ciliaris, muscle of iris, ...

- Myocytes need the stimulation by autonomic “motor” neurons releasing *acetylcholine / norepinephrine, ... (AUTONOMIC „MOTOR UNITS“)*
- Cells are **not** interconnected by **gap junctions**, APs are **not** triggered
- **Synapses „en passant“** in the course of the neuron endings
- **Contractions** are *finely graded* and *localized*

