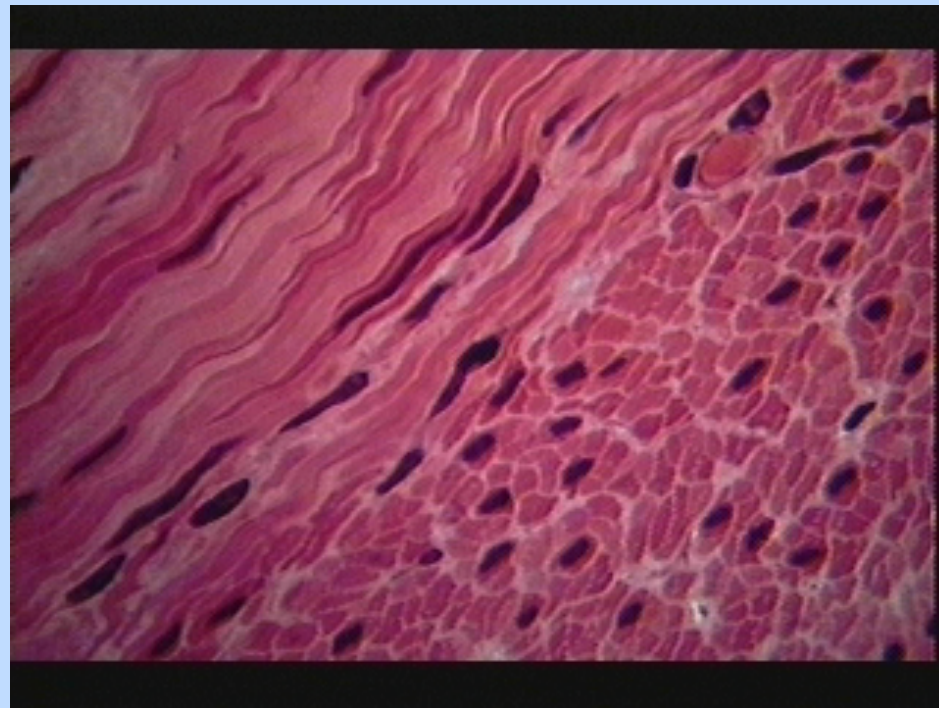


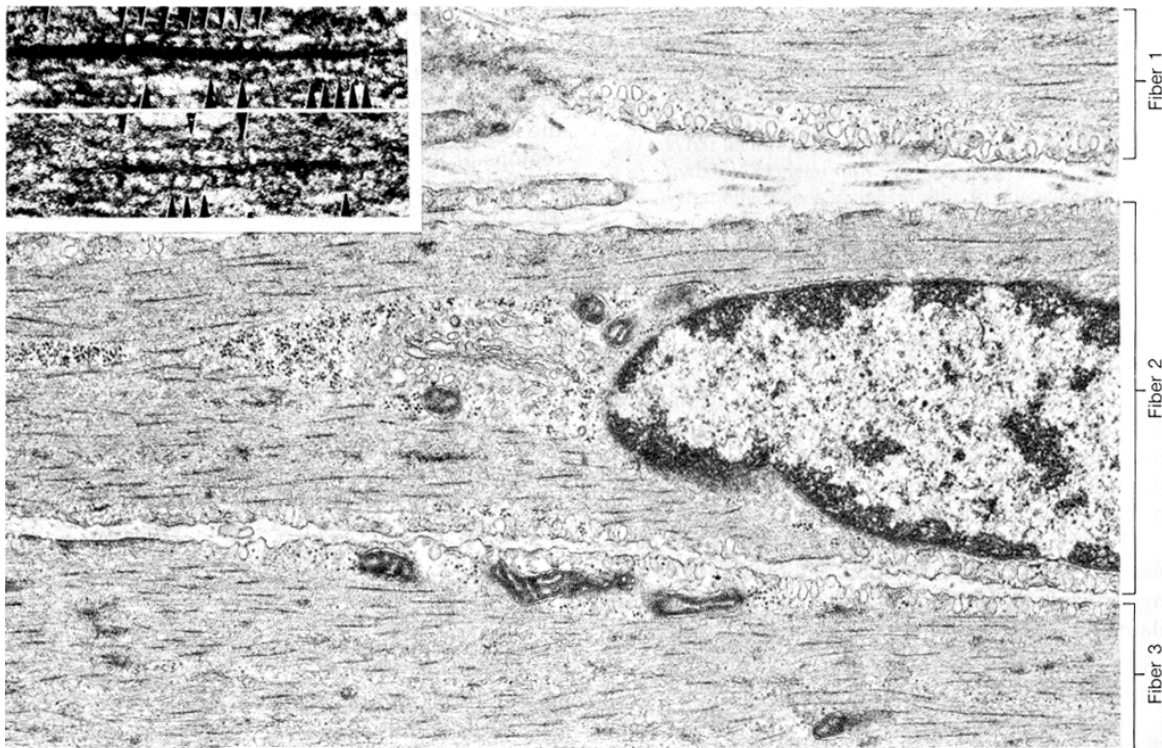
# Fundamentals of Neurosciences

## Smooth Muscle

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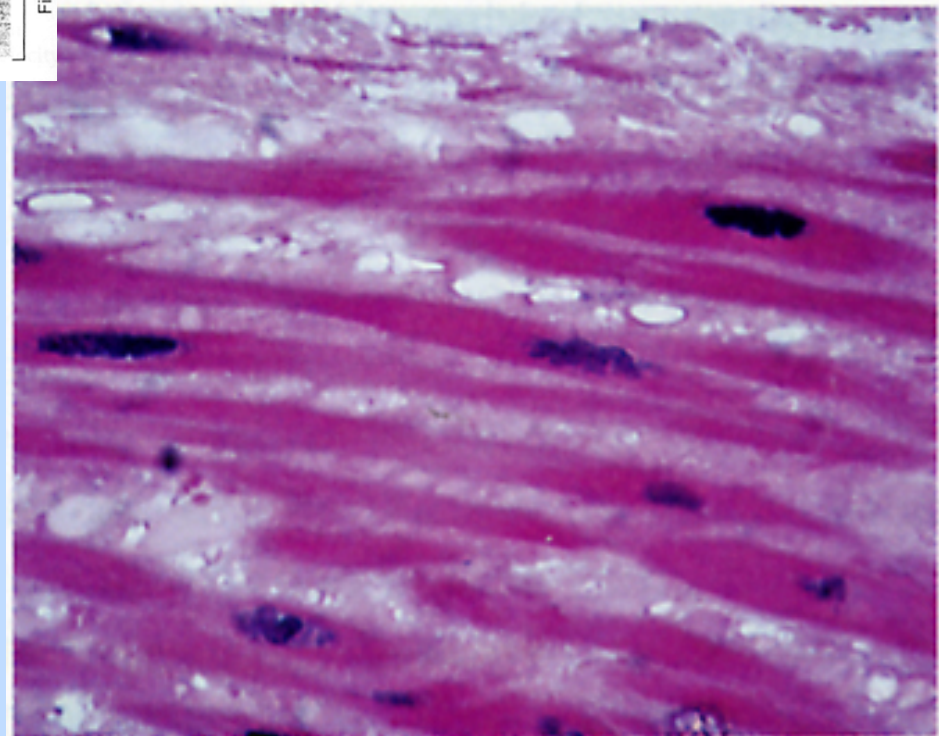




adapted from: Vander et al; © McGraw Hill Co.

# Smooth Muscle Structure

- Cells much smaller than skeletal muscle
  - (2-5 $\mu$ M diam, 100-400 $\mu$ M long)
- Single central nucleus
- Tapering spindle shape
- No visible striations with light microscope

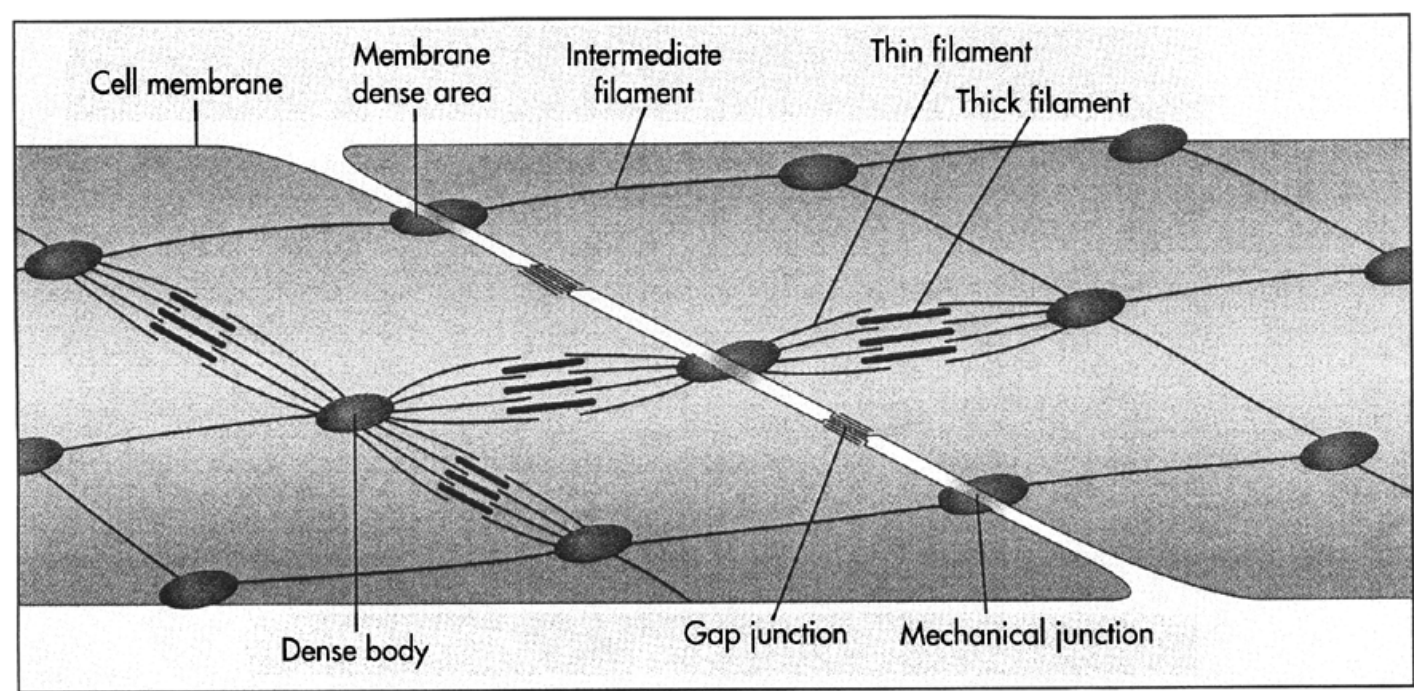


adapted from: Widmaier et al; © McGraw Hill Co.



# Myofilament Organization

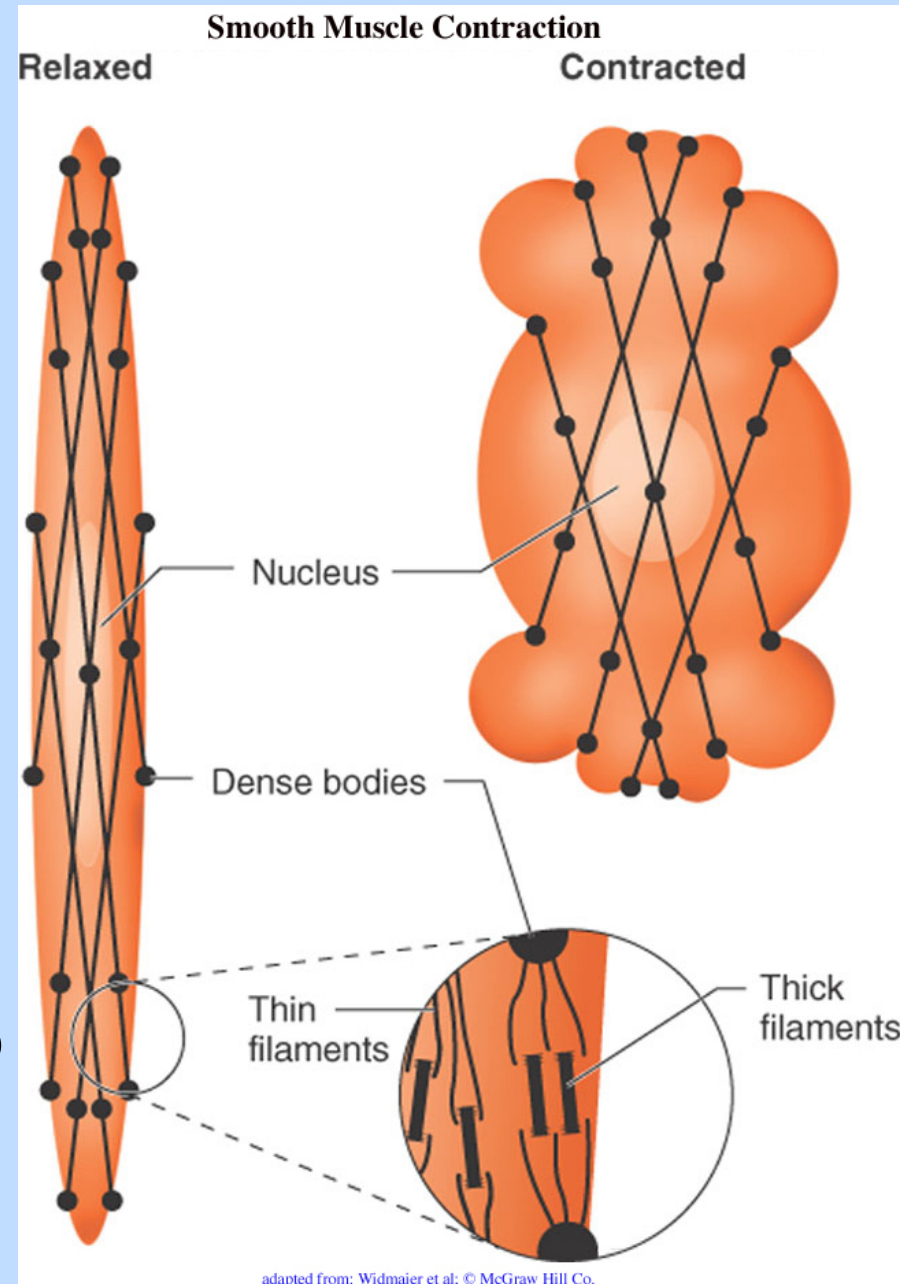
- Contains both actin & myosin
- More actin and less myosin than skeletal Muscle
- Lower contractile force

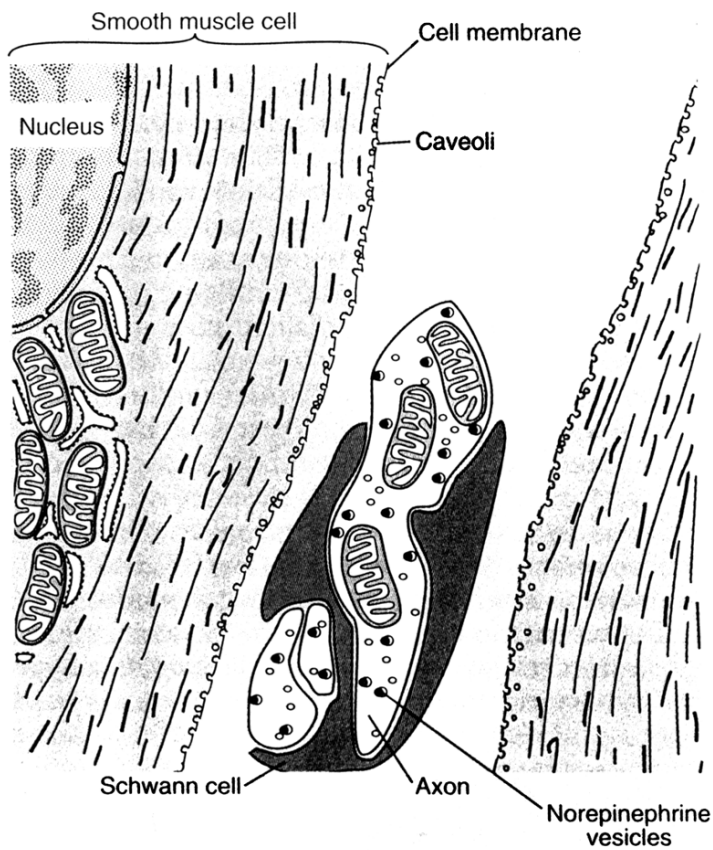


- Myofilaments loosely oriented in long axis of cell
- Force transferred to cell membrane by intermediate filaments
- Meshwork linked together at dense bodies

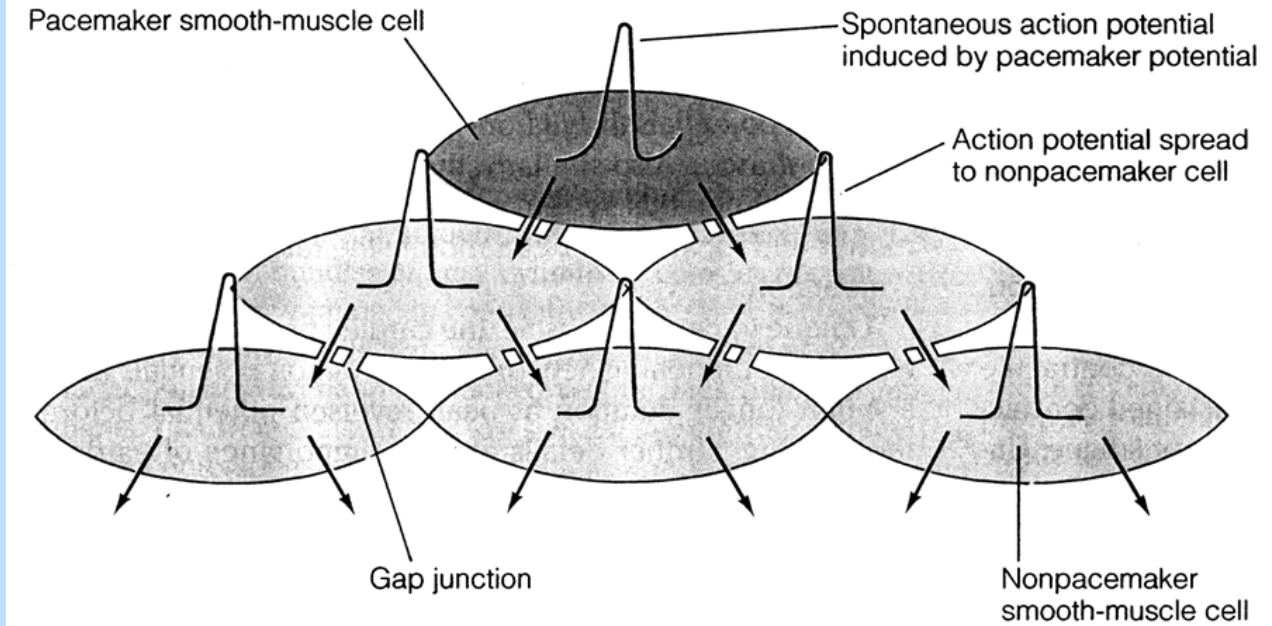
# Shortening in Smooth Muscle

- Actin & myosin overlap
- Slide along each other during contraction
- Meshwork becomes more compact
- Cell shortens and fattens
- Increase in intracellular free  $\text{Ca}^{++}$  is necessary for contraction
  
- Much  $\text{Ca}^{++}$  comes from extracellular fluid (ECF)
  - Entry through cell membrane
- Some  $\text{Ca}^{++}$  released from internal vesicles (SR)
- Mechanisms to trigger  $\text{Ca}$  increase:
  - Spontaneous Membrane depolarization
  - Depol. By Extrinsic nerve supply (autonomics)
  - Chemical messengers
    - Local & blood-borne; Hormones , metabolites





# Membrane specializations



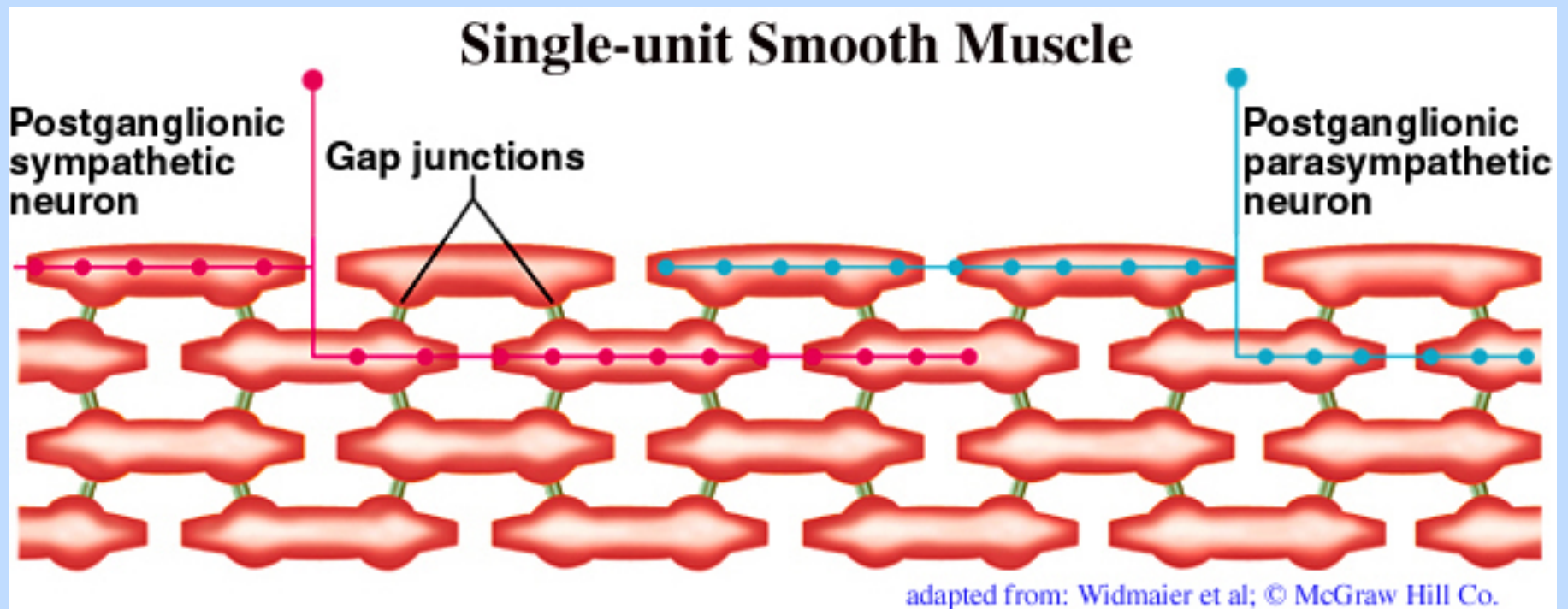
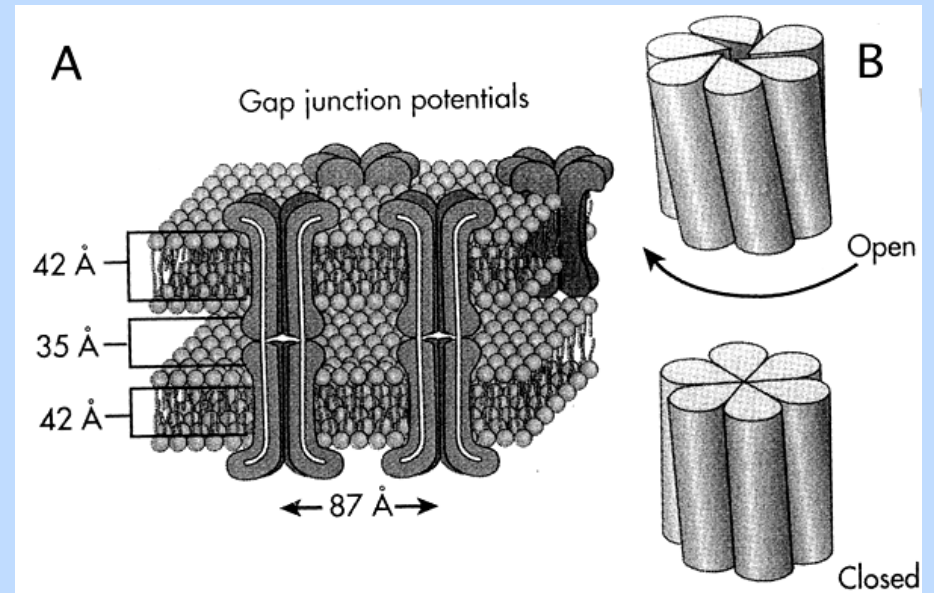
- Caveoli - small membrane pits
  - Possible role in  $\text{Ca}^{++}$  entry
- Sarcoplasmic reticulum less extensive than skel. Musc.

- Gap junctions
  - Between most smooth Muscle cells
- Allow spread of ions and depolarization between cells
- Many cells act as syncytial unit
  - All cells contract together



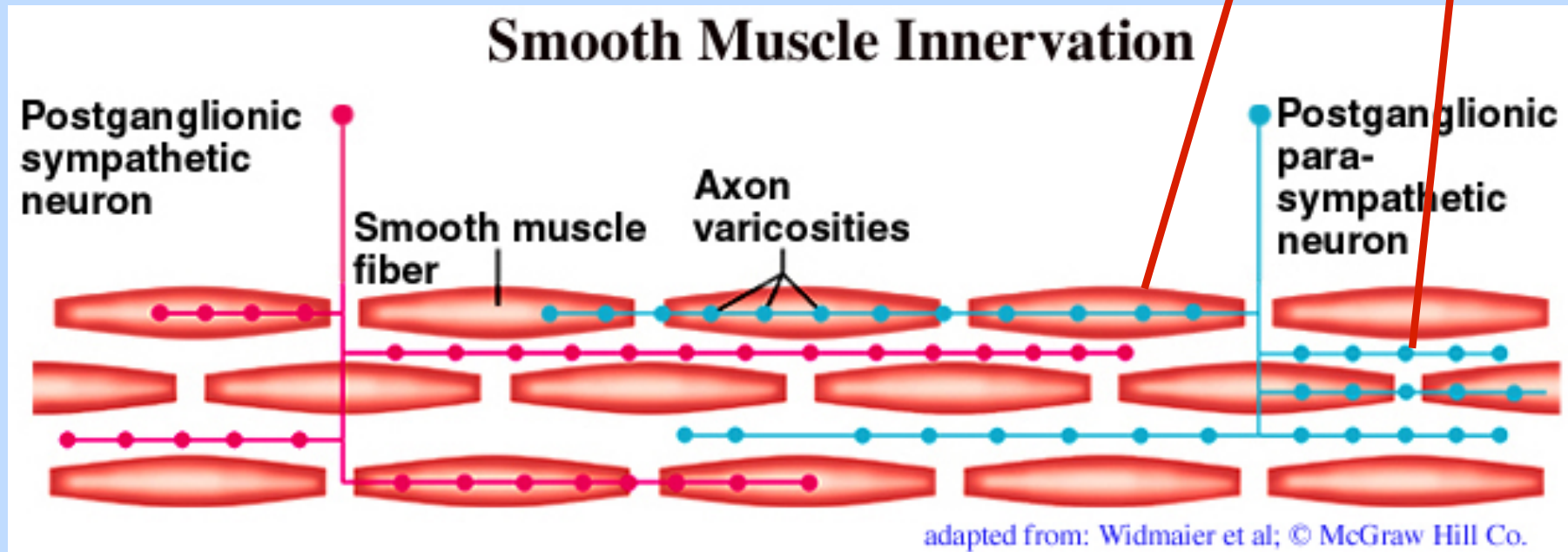
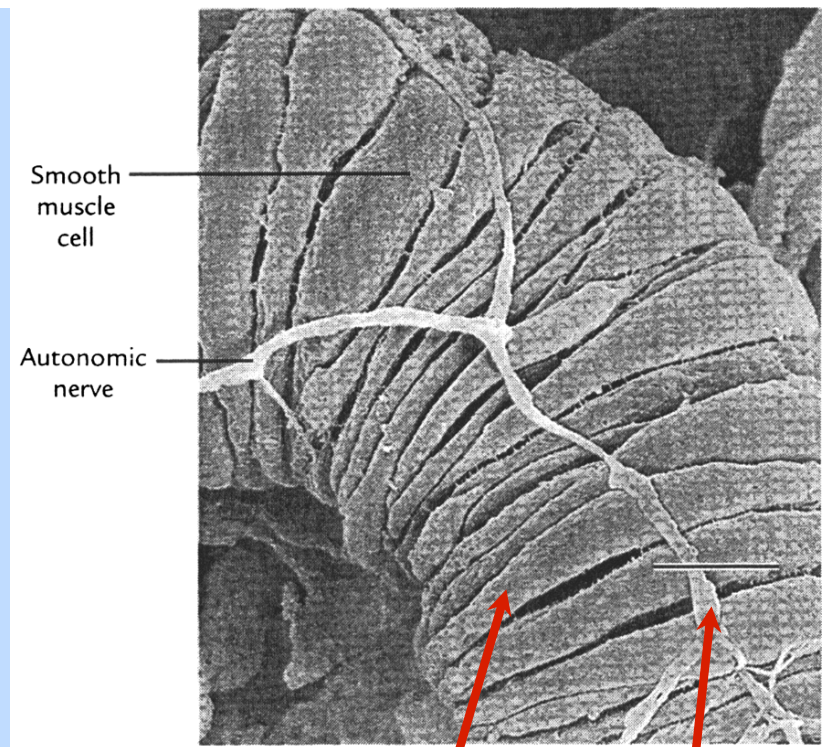
# Single-Unit Smooth Muscle

- Gap junctions
  - Between most smooth Muscle cells
- Allow spread of ions and depolarization between cells
- Many cells act as syncytial unit
  - All cells contract together

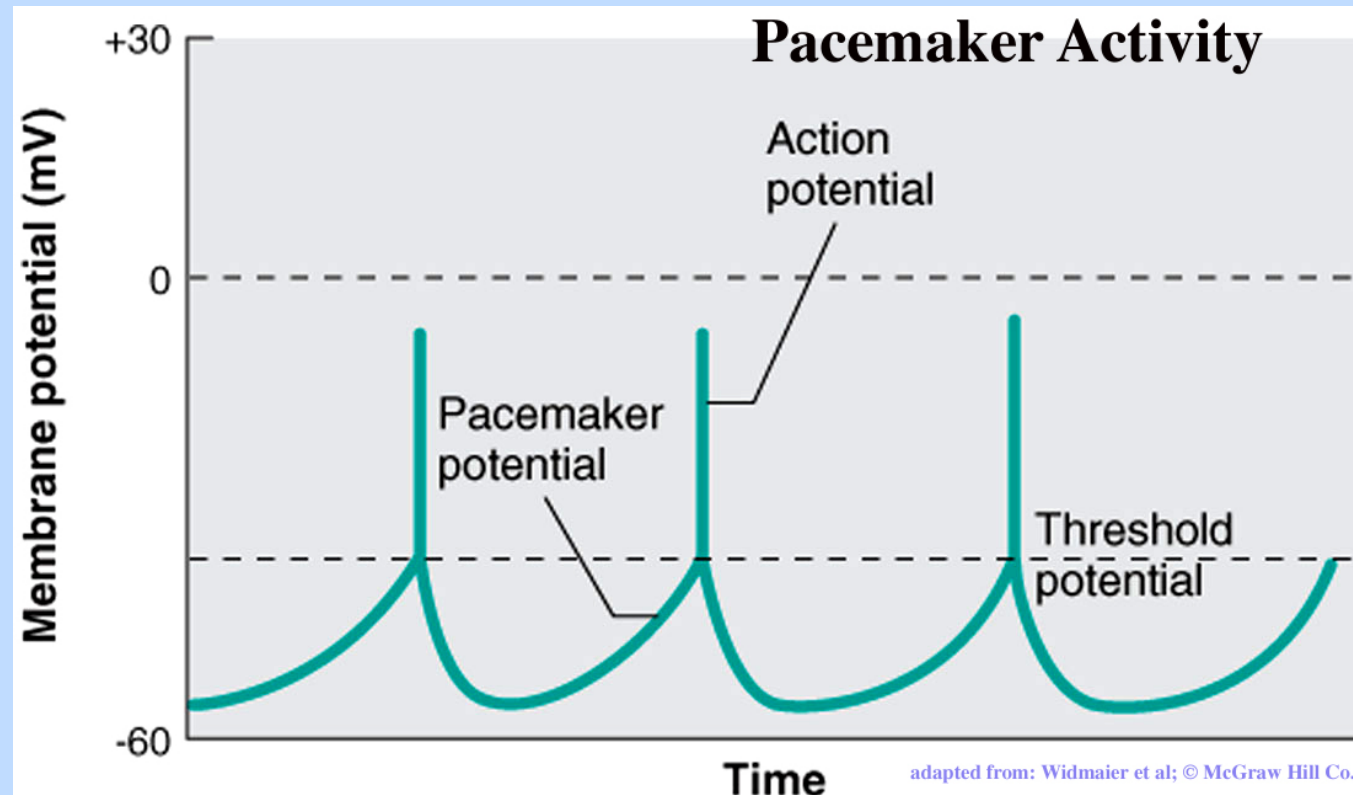


# Autonomic Innervation

- NT released from synaptic varicosities
- Effects many cells at once
- **Two divisions:**
  - Sympathetic - nor-epi. & Epi.
  - Parasympathetic - Acetylcholine
- **Most cells have dual reciprocal innervation**
- **Diff. Transmitters have diff. Effects at diff. sites**



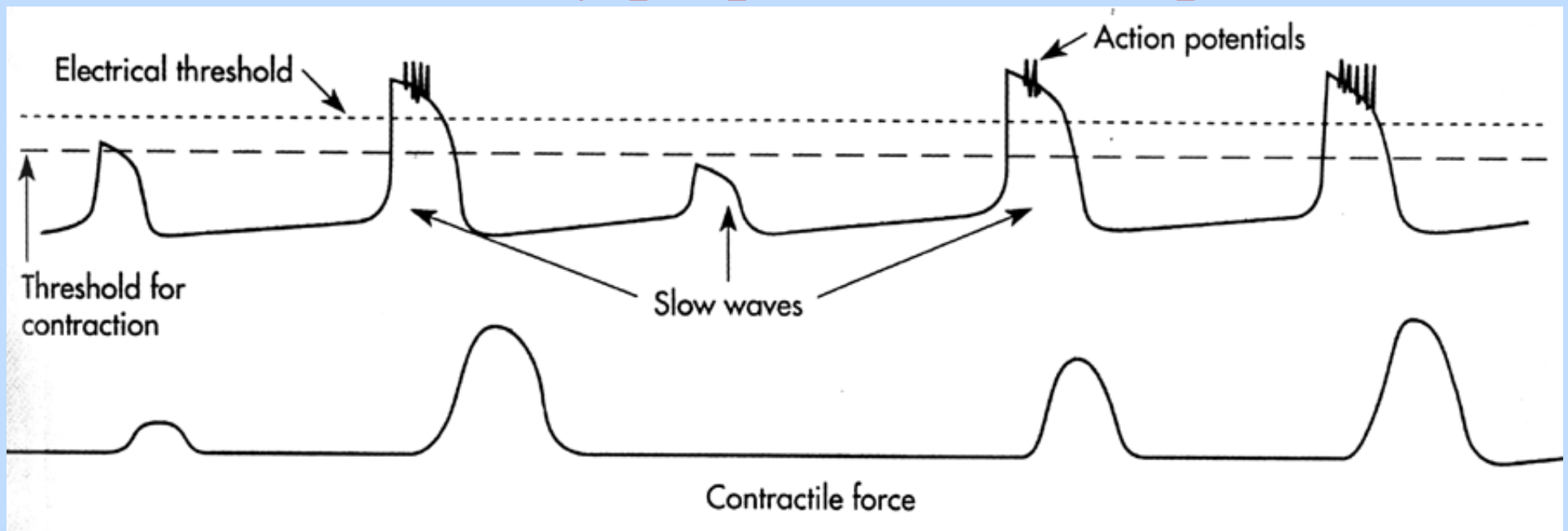
# Spontaneous Depolarization - Pacemaker Potentials



- Typical smooth muscle cell has oscillating membrane potential
  - Spontaneous rhythmicity
- Subthreshold -slow wave potentials
- Above threshold - triggers action potentials



# Contractile activity proportional to Depolarization



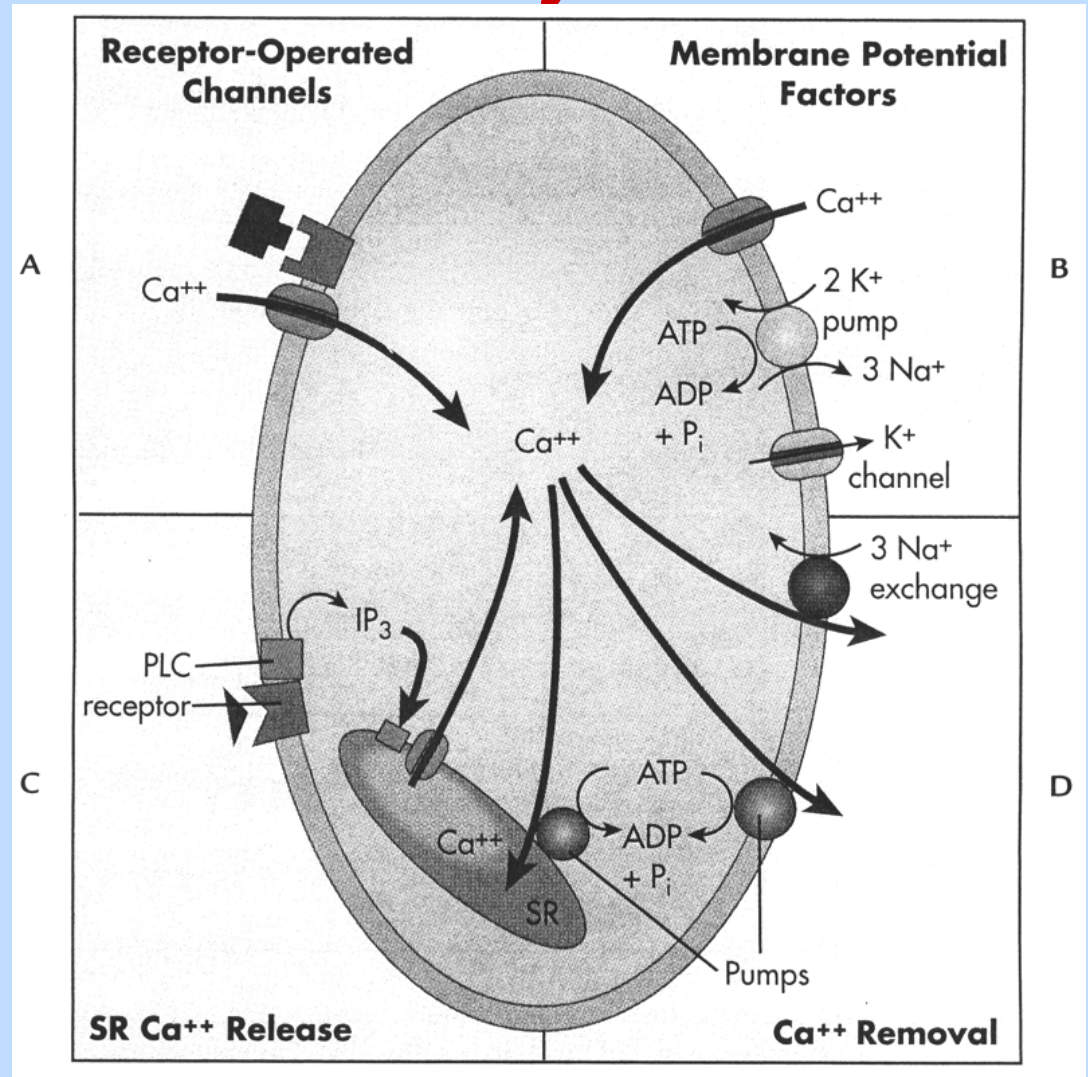
- Has contractile activity in absence of direct nerve supply
- Contractile force proportional to depolarization
  - Subthreshold depol. - low contraction force
  - Depol. Above threshold - produces action potentials - Results in large contractile force

# Sources of $\text{Ca}^{++}$ and Contraction

- Two sources:
- Sarcoplasmic reticular stores (intracellular)
  - Rapid release
  - Phasic contraction
  - Limited amount
- Entry from ECF
  - Slower response
- Large amounts - prolonged availability
  - Tonic activity
- Stretch can directly result in entry of  $\text{Ca}^{++}$  and contraction

# Regulation of Contraction by $\text{Ca}^{++}$

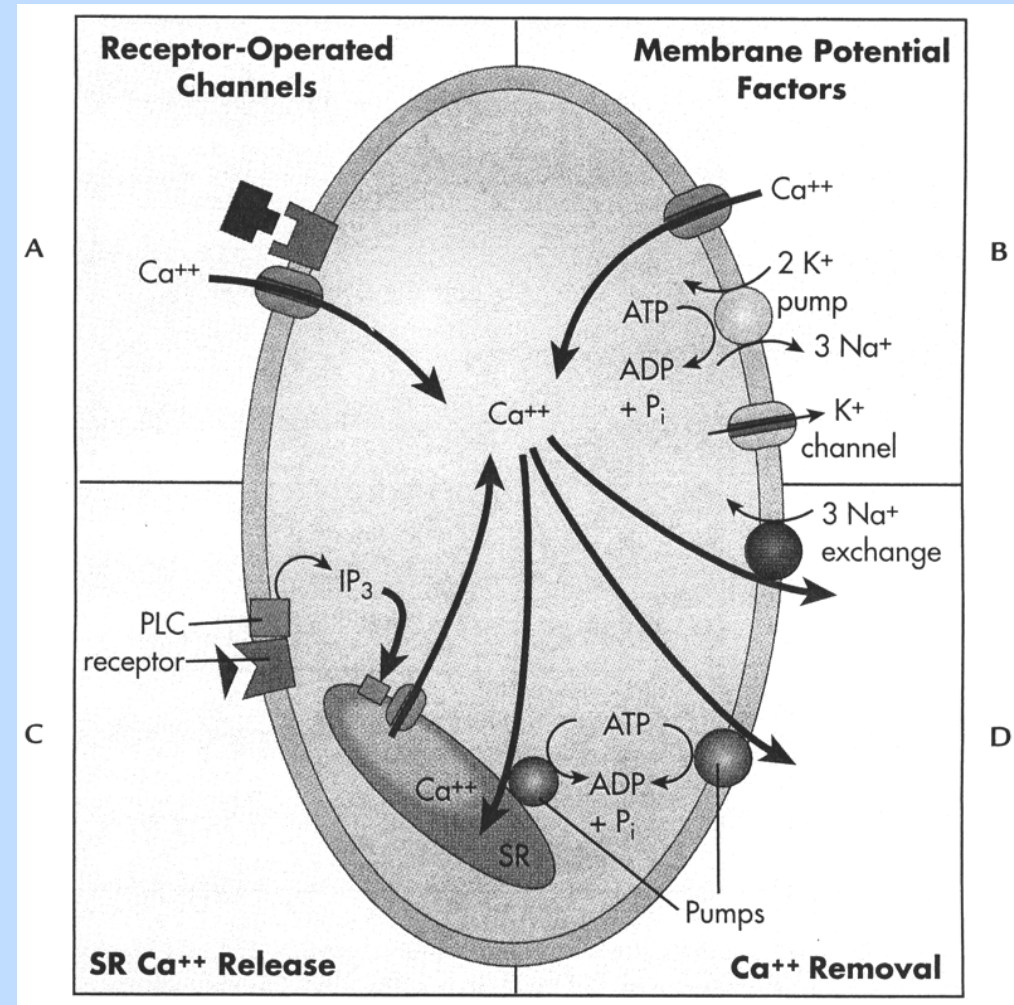
- Intracellular  $\text{Ca}^{++}$  conc. regulates contractile force
- Much  $\text{Ca}^{++}$  comes from ECF
  - Entry through cell membrane
- Some  $\text{Ca}^{++}$  released from internal vesicles (SR)
- Mechanisms to trigger  $\text{Ca}$  increase:
  - Membrane depolarization
  - Extrinsic nerve supply (autonomics)
  - Chemical messengers
    - Local & blood-borne
    - Hormones, metabolites





# Regulation of $[Ca^{++}]_i$

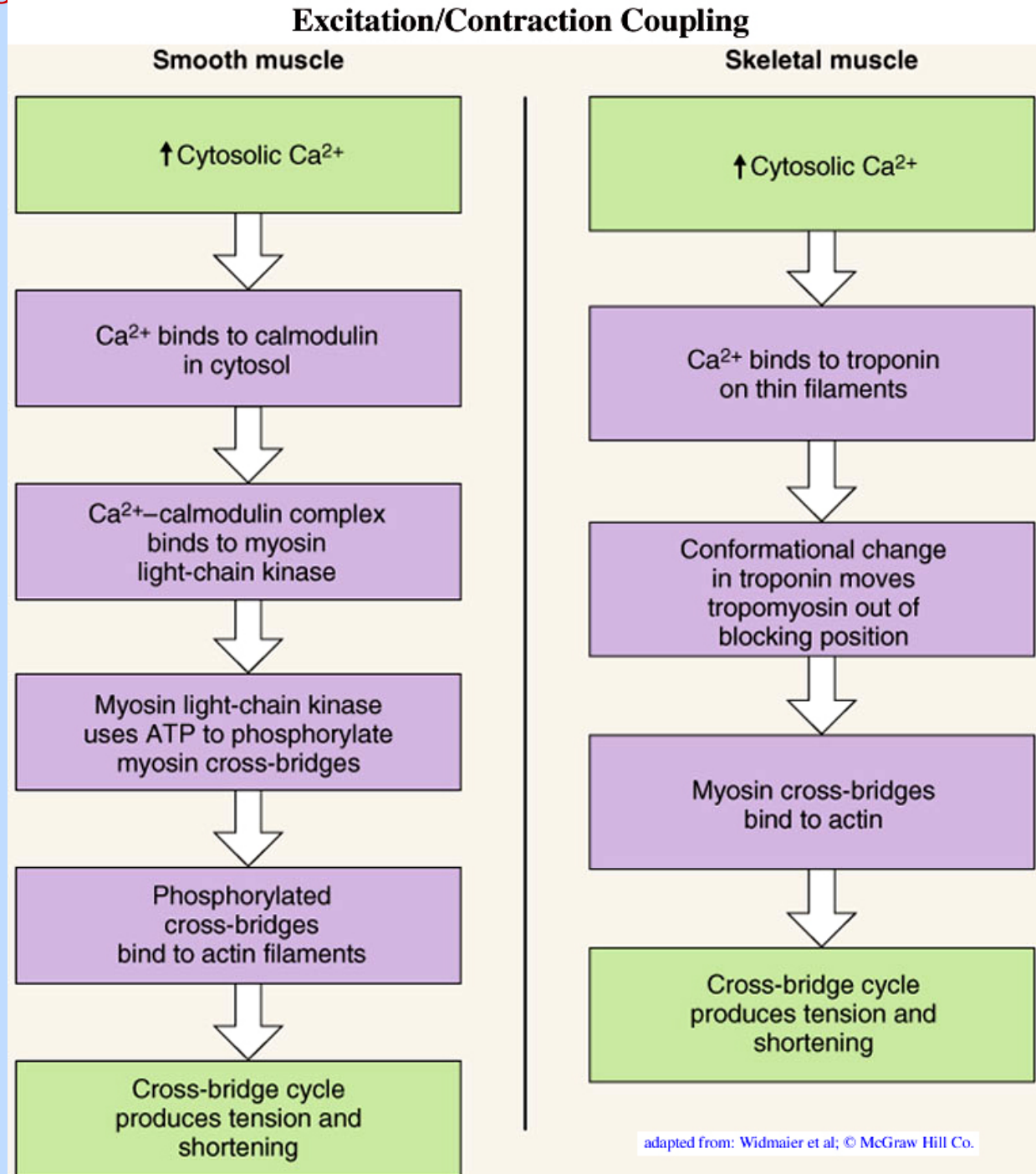
- ICF concentration is balance between entry and removal
- Entry:
  - Membrane depolarization
    - V-gated  $Ca^{++}$  channels
  - Hormones, metabolites
    - Receptor activated channels
  - Second messengers cause release from SR stores



- Removal: Outward across cell membrane & into SR vesicles
  - 1) Active transport, 2) Na/ Ca exchange

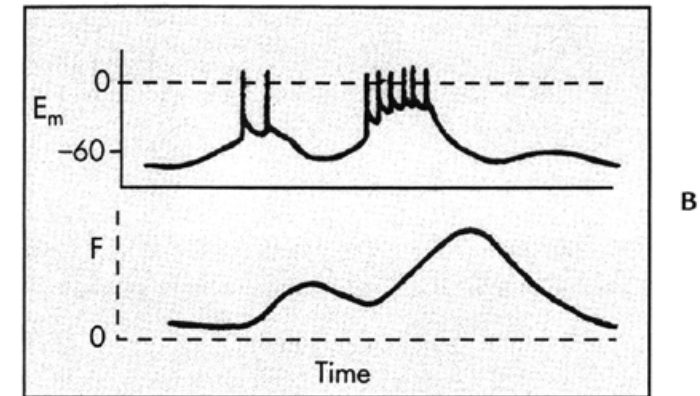
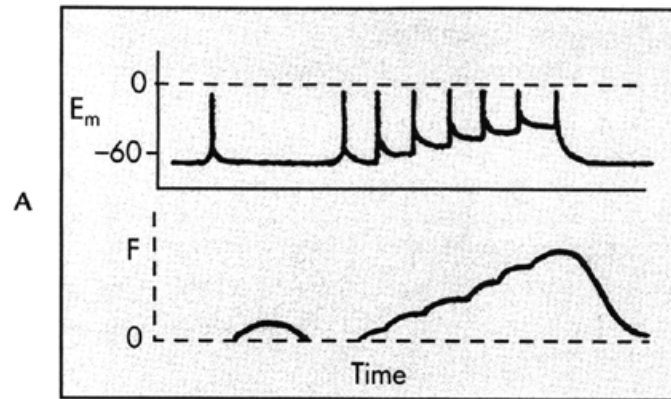
# Regulation of Cross-bridge activity

- Smooth muscle lacks Troponin
- Cross-bridges activated (phosphorylated) by myosin kinase
- Myosin kinase activated by  $\text{Ca}^{++}$  binding to calmodulin

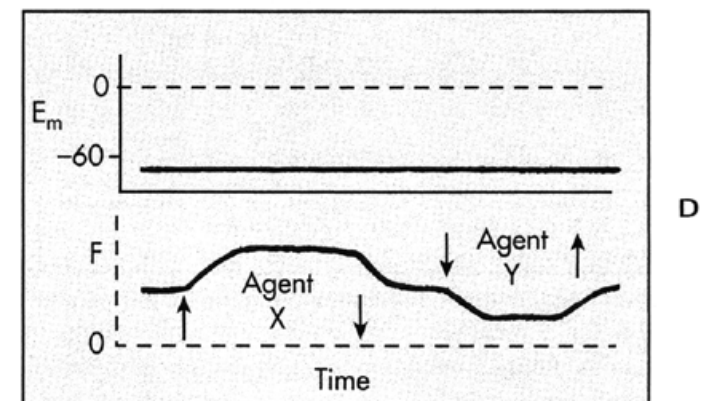
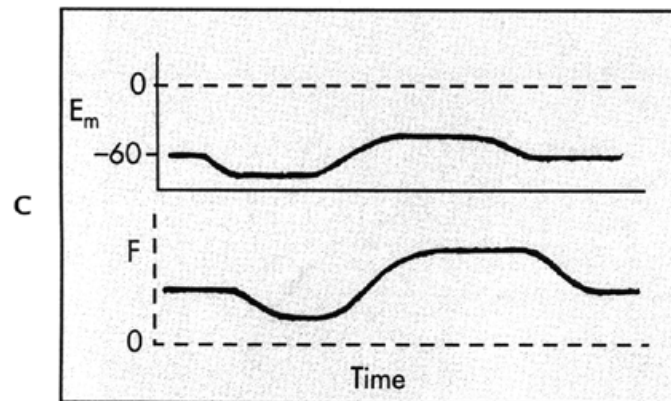


# Relationship between contraction force and membrane Potential

- Action potentials - greater contractile force (A&B)



- Slow potentials - low contractile force (B&C)



- Humoral agents - can produce force without change in membrane potential (D)



# Comparison of muscle types

	<b>Skeletal</b>	<b>Cardiac</b>	<b>Smooth</b>
<b>Location</b>	<b>Attached to bones</b>	<b>Heart</b>	<b>Visceral organs</b>
<b>Innervation</b>	<b>Somatic; Voluntary</b>	<b>Autonomic; Involuntary</b>	<b>Autonomic; Involuntary</b>
<b>Appearance</b>	<b>Striated</b>	<b>Striated</b>	<b>Non-striated</b>
<b>Fibre Diameter</b>	<b>80-100 <math>\mu</math> m</b>	<b>10-15 <math>\mu</math> m</b>	<b>2-5 <math>\mu</math> m</b>
<b>Fibre Length</b>	<b>&lt; 340 mm</b>	<b>200 <math>\mu</math> m</b>	<b>100-400 <math>\mu</math> m</b>
<b>Fibre Appearance</b>	<b>Large, solitary bands</b>	<b>branched network</b>	<b>small spindles</b>
<b>Nuclei</b>	<b>Multi Peripheral</b>	<b>Single Central</b>	<b>Single Central</b>
	<b>Relatively small</b>	<b>Large, oval</b>	<b>largest</b>

# Characteristics of Muscle fibers

	Skeletal	Single unit	Multiunit	Cardiac
Sarcomere	Y	N	N	Y
Trans. Tub.	Y	N	N	Y
Sarc. Ret.	High	Low	Low	Inter
Gap junct.	N	Y	Few	Y
Ca <sup>++</sup> source	SR	SR/ECF	SR/ECF	SR/ECF
Ca <sup>++</sup> Target	Troponin	Myosin	Myosin	Troponin
Pacemaker	N	Y	N	Some
Tone	N	Y	N	N
Nerve stimulation	Ex	Ex/Inh	Ex/Inh	Ex/Inh
Hormone effect	N	Y	Y	Y
Stretch	N	Y	N	N

# Summary

- Smooth muscles are uninucleate spindle-shaped cells lacking striations. Actin myosin units distributed along long axis linked to dense bodies ( $\alpha$ -actinin) and use intermediate filaments.
- Cause contraction by actin-myosin sliding, but trigger is by extracellular and intracellular  $\text{Ca}^{++}$ .
- $\text{Ca}^{++}$ -calmodulin activates kinase to phosphorylate myosin.
- Classified to single and multiunit. Gap junctions connect single unit, innervated at one place, mostly close to pacemaker. Multiunit richly innervated.
- Autonomic nervous system innervates smooth muscle with one neuron signaling to multiple muscles via varicosities and each fiber can get inputs from both sympathetic and parasympathetic pathways.



# Major Questions

1. What kind of muscle is used to create force and movement in most hollow organs?
2. What are the characteristics of smooth muscle? How is it different from skeletal (striated) muscle? What is its structural organization?
3. What is the function of gap junctions in smooth muscle? What is *single-unit* smooth muscle? Why is it significant that this is the main type of muscle found in the gut?
4. What are the mechanisms by which contraction in smooth muscle can be regulated?
5. What is the source of the spontaneous rhythmicity of G.I. tract smooth muscle?
6. What is the relationship of membrane potential and contractile force in smooth muscle?
7. What is the effect of rapid stretch on smooth muscle membrane potential? What functional role does this have?
8. What are the mechanisms of coupling between stimulation and force generation in smooth muscle? How is intracellular  $\text{Ca}^{++}$  regulated?