 Smooth Muscle

1. Describe the general characteristics of smooth muscle.

General characteristics of smooth muscle
- Found predominantly in the walls of hollow organs and tubes.
  - Examples: Blood vessels, GI tract, bladder and uterus.
- Great structural and functional diversity.
- Compared to striated muscle, it...
  - is subjected to multiple stimuli, some excitatory, some inhibitory.
  - is capable of contraction over very wide length range.
  - can shorten to a much smaller fraction of its relaxed length than striated muscles.
  - capable of prolonged contraction with low energy (ATP) usage.

Smooth muscle cells
- Spindle-shaped.
- Single nucleus situated in the centre of the cell.
- Retains capacity to divide.
- Organisation of individual cells in smooth muscle tissue is variable and depends on the organ.

Contractile proteins in smooth muscle
- Thick filaments
  - Composed of myosin.
  - Different structure to that in striated muscle.
    → Longer than in skeletal muscle.
    → Crossbridges along entire length.
    → Lower myosin ATPase activity.
- Thin filaments
  - Actin: two-stranded helix with binding site for myosin.
  - Tropomyosin: covers myosin binding site.
  - Lacks troponin: contains Ca$^{2+}$ binding site → turns contraction on/off.

![Smooth muscle cell diagram](image)
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2. Describe the major characteristics of single-unit and multi-unit smooth muscles.

Smooth muscles can be classified into two types based on the electrical characteristics of the plasma membrane.

<table>
<thead>
<tr>
<th>Single-unit (visceral) smooth muscle</th>
<th>Multi-unit smooth muscle</th>
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<tbody>
<tr>
<td>Few nerves in relation to number of smooth muscle cells</td>
<td>Extensive neural innervation</td>
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<tr>
<td>Many gap junctions → allow cell-to-cell spread of excitation</td>
<td>Few, if any, gap junctions.</td>
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<tr>
<td>Synchronous electrical and mechanical activity → contracts as single unit.</td>
<td>Behaves as multiple independent units → allows finer control of force produced by the whole muscle.</td>
</tr>
<tr>
<td>GI tract, blood vessels, uterus.</td>
<td>Large airways, large arteries, ocular smooth muscle.</td>
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3. Describe the mechanisms that initiate and terminate smooth muscle cell contraction.

Despite differences in the arrangement of the contractile filaments, the molecular mechanism of contraction is similar to that in striated muscle. It involves:

- **Crossbridge** interactions between myosin and actin, and **relative sliding** of the actin and myosin filaments.
- **ATP** as source of energy.
- Rise in intracellular **Ca\(^{2+}\)** triggers contraction.

Increase in intracellular \([\text{Ca}^{2+}]\) → initiates smooth muscle contraction.

- Smooth muscle does not contain troponin → no **Ca\(^{2+}\)** binding site.
- Instead, **Ca\(^{2+}\)** initiates cascade of events that phosphorylates myosin → energise myosin head → attach to actin.

- **Ca\(^{2+}\)** enter cytosol from ECF or from SR → **Ca\(^{2+}\)** binds to and activates calmodulin → activated calmodulin activates myosin light chain kinase enzymes → catalyses transfer of phosphate to myosin head → activate myosin head ATPases → myosin head forms crossbridge with actin → shortening
- Crossbridge activity ends when phosphate removed from myosin heads by phosphorylase enzymes and intracellular **Ca\(^{2+}\)** levels fall.

Contraction in smooth muscle compared to in skeletal muscle.

- Myosin ATPase activity is very low → slower speed of contraction.
- Duration of contractile event (contraction and relaxation) is approximately 30 – 50 times longer.
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- Effects of Ca$^{2+}$ in contraction initiation occur at level of thick filament (cf. thin filament in striated muscle).
- Far less energy required for contraction – ~1% of energy required in striated muscle.
  - 1 ATP required during each contractile cycle.

4. Describe the major sources of calcium that initiate contraction.

- **Extracellular Ca$^{2+}$**.
- **Intracellular Ca$^{2+}$** released from the sarcoplasmic reticulum.
  - SR less well-developed in smooth muscle compared to striated muscle → limited intracellular Ca$^{2+}$ store → supplemented by extracellular Ca$^{2+}$.
- Contribution from each pool differs in different types of smooth muscle.

![Excitation-contraction coupling in smooth muscle](image)

5. Identify the major factors that regulate smooth muscle contraction.

Contractile state of smooth muscle regulated by control of the intracellular [Ca$^{2+}$].
- Multiple excitatory or inhibitory stimuli may be acting to increase or decrease [Ca$^{2+}$], contractile state reflects relative intensity of stimuli.

Stimuli

- **Spontaneous electrical activity (pacemaker cells)**
  - Some smooth muscles generate APs in the absence of neural or hormonal input.
  - RMP gradually depolarises until AP produced.
  - Repetitive sequence of APs → rhythmic contractions of smooth muscle mass.
  - Typically observed in the gut.
- **Autonomic nerves**
  - Important neurotransmitters: ACh and NA.
  - Single axon may influence multiple smooth muscle fibres.
  - Single smooth muscle cell may be influenced by both sympathetic and parasympathetic neurons.
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- Response of smooth muscle depends on:
  - Type of neurotransmitter.
  - Type of receptor that the smooth muscle cell has for the neurotransmitter.
  - Intracellular signalling pathway to which that receptor is coupled.
- Examples
  - ACh binds to receptors on bronchial smooth muscle → contraction.
  - NA binds to \( \beta \)-receptors of bronchial smooth muscle → relaxation.
  - NA binds to \( \alpha \)-receptors of vascular smooth muscle → contraction.
- **Hormones** – smooth muscles contain receptors for a variety of hormones.
  - Effects of hormones on membrane potential:
    - Excitatory: Membrane depolarisation through opening of membrane \( \text{Na}^+ \) or \( \text{Ca}^{2+} \) channels, either with or without associated APs.
    - Inhibitory” Hyperpolarisation through closure of membrane \( \text{Na}^+ \) or \( \text{Ca}^{2+} \) channels, or opening of \( \text{K}^+ \) channels.
  - Through intracellular second messengers
    - Receptor binding → production of factors → release of \( \text{Ca}^{2+} \) from SR.
    - Or produce other factors (cAMP and cGMP) inhibit contraction.
- **Local factors** (chemical and physical)
  - Released in the immediate vicinity of smooth muscle.
  - Includes paracrine agents (e.g. NO), low pH, low \( \text{O}_2 \), high \( \text{CO}_2 \).
  - Effect depends on the factor and the intracellular effects of binding.
  - Allows smooth muscle to respond to local tissue requirements independent of long-distance signals from nerves or hormones.
- **Stretch**
  - Stretch-induced contraction
    - Smooth muscle stretched → generates spontaneous APs → contraction.
    - Example: Propulsion of contents in GI tract.
  - Stress-induced relaxation.
    - Stretching causes transient contraction followed by relaxation.
    - Example: Increase in volume in urinary bladder → immediate increase in pressure → return to normal pressure as smooth muscle relaxes.