Exercise walk-through

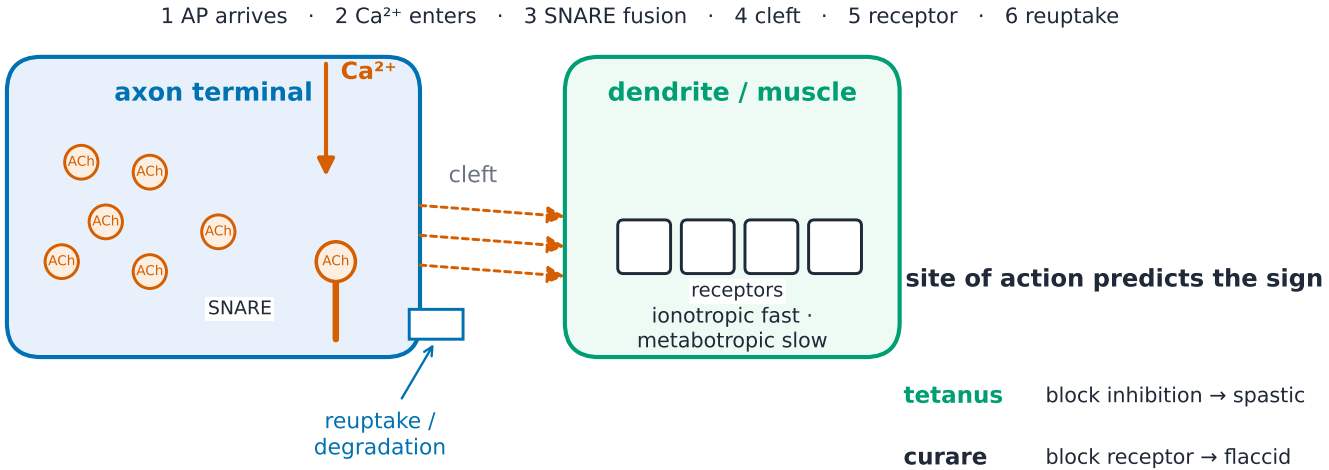
9.1 Neurons, synapses and neurotransmitters

University Medicine

Neurons, synapses and neurotransmitters: the decision point

1. **Steps** AP $\rightarrow$ Ca^{2+} channels open $\rightarrow$ SNARE fusion $\rightarrow$ cleft $\rightarrow$ receptor $\rightarrow$ **reuptake** or degradation; the NMJ releases $\sim$5,000-10,000 molecules per vesicle, $\sim$50-300 vesicles to fire.
2. **Receptors** Ionotropic open channels in ms (nicotinic, GABA-A, AMPA/NMDA); metabotropic act through G-proteins in s (muscarinic, adrenergic).
3. **Toxins** Botulinum cuts SNAREs $\rightarrow$ flaccid; curare blocks the receptor $\rightarrow$ flaccid; tetanus blocks inhibition $\rightarrow$ spastic: site predicts sign.

Synaptic transmission with its drug and toxin targets



Six steps of transmission, each a drug or toxin target.

Exercises 2.1·2.3

2.1 Name the ion that triggers vesicle fusion, and the protein machinery. [3]

2.2 Which is faster, an ionotropic or a metabotropic response – and by roughly how much? [3]

2.3 GABA on GABA-A inhibits while glutamate on AMPA excites. What decides the sign? [3]

Exercises 2.1·2.3

2.1 Name the ion that triggers vesicle fusion, and the protein machinery. [3]

2.1

- Ca^{2+} through voltage-gated channels; SNARE proteins fuse the vesicle ✓.

2.2 Which is faster, an ionotropic or a metabotropic response – and by roughly how much? [3]

2.2

- Ionotropic: channel opens in milliseconds; metabotropic works via G-proteins in seconds ✓.

2.3 GABA on GABA-A inhibits while glutamate on AMPA excites. What decides the sign? [3]

2.3

- The receptor's channel – GABA-A passes Cl^- (inhibition), AMPA passes Na^+ (excitation) ✓.

Exercise 3.1

3.1 A fictional patient given a teaching-set toxin develops flaccid paralysis; a second develops spastic paralysis.

For each toxin site (pre-synaptic release machinery, post-synaptic receptor, inhibitory interneuron release), predict the sign and justify from the six steps. Explain why weakness appears only when most end-plate receptors are occupied (the safety factor). [7]

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3.1

- Botulinum: no vesicle fusion → no release → flaccid ✓.
- Curare: release normal, receptor blocked → flaccid ✓.
- Tetanus: inhibitory release blocked → unopposed excitation → spastic ✓.
- The NMJ safety factor (~50–300 vesicles to threshold) means weakness needs most receptors occupied ✓.

Exercise 3.2

3.2 A fictional drug blocks the serotonin transporter (an SSRI).

State which of the six steps it acts on (termination by reuptake). Predict the immediate effect on the cleft (more transmitter, longer presence). Explain why it does not change synthesis. [7]

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3.2

- Step six – termination by reuptake is blocked ✓.
- Cleft serotonin persists longer and at higher concentration ✓.
- Synthesis (step three's loading of vesicles) is untouched – the drug acts after release ✓.
- Effect builds as clearance, not packing, is inhibited.