Synaptic Transmission

Transmission of signals (excitatory or inhibitory) between two nerve cells or nerve to muscle cell. Can be electrical or chemical.

A. Electrical

Gap junctions form aqueous pores linking cells. Direct electrical current flow from one cell to the other.

Does not allow for synaptic inhibition.
B) **Chemical**

Signaling is via a chemical (neurotransmitter) released by an action potential in the presynaptic terminal, which acts on receptors in the postsynaptic cell to produce an electrical response.

i) Pre- and post-synaptic terminals are differentially specialized

ii) Transmission goes only one way

iii) Action of neurotransmitter can be excitatory or inhibitory, depending on nature of transmitter and its receptor.
Stages in chemical synaptic transmission

1. Action potential in presynaptic nerve

2. Ca\(^{2+}\) ions flow into nerve terminal and ...

3. Trigger release of neurotransmitter

4. Transmitter diffuses across synaptic cleft and ..... 

5. Acts on postsynaptic receptors to allow current flow through ion channels

6. Transmitter is destroyed or removed
**Quantal Nature of Transmitter Release**

Fatt & Katz - early 1950's

- Stimulate nerve
- End-plate (synapse)
- Record from muscle with microelectrode
- Frog muscle fibre

**e.p.p.s and m.e.p.p.s**

- Miniature end-plate potentials (m.e.p.p.s)
- End-plate potential (e.p.p.)

**Membrane potential (mV)**

- +50
- 0
- -90
- 1 mV

**Stim. nerve**
Stimulating nerve evokes large depolarization of muscle end-plate (e.p.p.) which normally triggers action potential, causing muscle to contract. e.p.p. due to massive release of transmitter (acetylcholine: ACh) from nerve terminal.

Also see tiny (1mV) spontaneous depolarization even without stimulating nerve - miniature e.p.p.s.

These are due to spontaneous release of ACh from nerve - m.e.p.p.s get bigger if apply drug that stops breakdown of ACh.
e.p.p. evoked by release of ~ 100 quanta of transmitter

In normal solution (2 mM Ca\(^{2+}\)) e.p.p. is about 100x bigger than m.e.p.p.

But - if [Ca\(^{2+}\)] lowered, size of epp gets smaller and epps occur as multiples of size of m.e.p.p.

![Diagram showing epps evoked by successive stimuli](image)
size distributions of mepps and epps.

Fig. 5.7

...number of observations

size of mepp.

size of epp.

number of observations

size of epp.

multiples of mepp. size

apps are quantized — transmitter is released in 'packets' (quanta) corresponding to the amount of transmitter in a mepp.

$\text{Ca}^{2+}$ entering the nerve terminal increases the probability of release of quanta — the more $\text{Ca}^{2+}$ the greater the average number of quanta released.

Believed that 1 quantum = 1 vesicle e.g. drugs (Black Widow spider venom) that cause massive release of transmitter deplete number of vesicles.
Vesicular nature of transmitter release

Transmitter stored in vesicles—membrane sacks containing a few thousand molecules of transmitter.

Vesicle and cell membranes contain special proteins.

$Ca^{2+}$ causes proteins in vesicle and cell membrane to interact, forming fusion pore.

Pore enlarges and bursts open, allowing vesicle to fuse with cell membrane.
(B) Vesicle docks

(1) Vesicle docks

(2) SNARE complexes form to pull membranes together

(3) Entering Ca^{2+} binds to synaptotagmin

(4) Ca^{2+}-bound synaptotagmin catalyzes membrane fusion
Evidence

1. Synaptic transmission stops if extracellular Ca\textsuperscript{2+} removed. Transmitter release varies very steeply (fourth power) with [Ca\textsuperscript{2+}], so Ca\textsuperscript{2+} in blood and CSF regulated tightly.

2. Can mimic synaptic transmission by injecting Ca\textsuperscript{2+} into nerve terminal.

Fig. 5.11B
Ca\textsuperscript{2+} and transmitter release

very low (0.1\textmu M) [Ca\textsuperscript{2+}] inside

high (2mM) [Ca\textsuperscript{2+}] outside

nerve membrane impermeable to Ca\textsuperscript{2+} at rest.

Voltage-gated Ca\textsuperscript{2+} channels open during action potential allowing Ca\textsuperscript{2+} influx

Ca\textsuperscript{2+} ions entering the terminal carry a 'chemical' message. It is the rise in intracellular [Ca\textsuperscript{2+}] that triggers transmitter release, not the electrical current carried by Ca\textsuperscript{2+} ions.