Synaptic plasticity – correlation

- Neurons that fire together wire together.
- Neurons that fire out of sync lose their link.

$\Rightarrow$ Activity dependent synaptic rearrangement; as a result of neural activity and synaptic transmission

Ex> Visual system; we learn to see during a critical period of postnatal development (profoundly influenced by sensory experience during childhood)

Short-Term Synaptic Plasticity

1) Synaptic facilitation; a transient increase in synaptic strength that occurs when two or more action potentials invade the presynaptic terminal in close succession
   - Progressive increase of postsynaptic EPP
   - Prolonged elevation of presynaptic calcium levels (calcium builds up within the terminal)

2) Synaptic depression; diminished synaptic transmission following repeated synaptic activity
   - Progressive depletion of the pool of synaptic vesicles available for fusion

3) Synaptic integration
   - The difference between excitatory transmission at NMJ and CNS synapse?

   - Most neurons perform sophisticated computations, requiring that many EPSPs add together to produce a significant postsynaptic depolarization
   - EPSP summation; the simplest form of synaptic integration in the CNS
     (1) Spatial summation; the adding together of EPSPs generated simultaneously at many different synapses on a dendrite
     (2) Temporal summation; the adding together of EPSPs generated at the same synapse if they can occur in rapid succession, within 1-15msec of one another
Long-Term Synaptic Plasticity

- LTP (Long-term potentiation); A long-lasting increase in synaptic strength as a consequence of strong NMDA receptor activation (Strengthen synaptic transmission)

Molecular Mechanism of LTP

- Two postsynaptic glutamate-gated ion channels; AMPA and NMDA
- Unusual features of NMDA receptor

(1) NMDA R conductance is voltage-gated; the action of Mg$^{2+}$ at the channel

- At resting potential: the inward current is interrupted because of the Mg$^{2+}$ block. As the membrane is depolarized, the Mg$^{2+}$ block is displaced from the channel.

- Substantial current through the NMDA receptor channel requires the concurrent release of glutamate by the presynaptic terminal and depolarization of the postsynaptic membrane.

(2) NMDA R channel conducts Ca$^{2+}$; the magnitude of the Ca$^{2+}$ flux passing through the NMDAR channel specifically signals the level of presynaptic and postsynaptic coactivation.

- Two kinase involved in LTP induction; Ca$^{2+}$/calmodulin-dependent protein kinase (CaMKII) and protein kinase C
- Changes in the sensitivity of the postsynaptic cell to glutamate; regulate AMPA receptor activity or add new AMPA receptors to silent synapses

Cf> Long-term depression

AMPA receptors and metabotropic glutamate receptors

Two second messengers; DAG and IP3 -> PKC activation and triggers clathrin dependent internalization of postsynaptic AMPA receptors
For detail, refer to Fig. 24.10, 24.12, and 24.13

**Long-lasing Changes in a synaptic transmission during LTP**

PKA -> activation of transcriptional regulator CREB -> other transcriptional regulators and synaptic growth proteins (Fig. 24.14)

**Neurotransmitters – Three fates**