LTP: a three step process involving specific signalling pathways and events:

Induction of LTP involves NMDA receptors

- induction requires the influx of extracellular Ca^{2+} into postsynaptic neurons via NMDA receptors (coincidence detector)

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During normal synaptic transmission, glutamate (Glu) is released from the presynaptic bouton and acts on both AMPA receptors (AMPARs) and NMDA receptors (NMDARs). However, Na^{+} flows only through the AMPA receptor, but not the NMDA receptor, because Mg^{2+} blocks the channel of the NMDA receptor. Depolarization of the postsynaptic cell relieves the Mg^{2+} block of the NMDA receptor channel, allowing Na^{+} and Ca^{2+} to flow into the dendritic spine by means of the NMDA receptor. The resultant rise in Ca^{2+} within the dendritic spine is the critical trigger for LTP.

Expression of LTP:

1) Early phase expression:

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- second messenger-mediated activation of Ca^{2+}/calmodulin-dependent kinase (CaMKII) phosphorylates AMPA receptors, which
  - increases their affinity for glutamate
  - increases the single-channel conductance of GluR1 (GluR1 at amino acid S831)
- PKA phosphorylation of S845 in GluR1 increases the peak open probability
- protein trafficking/ increase in surface AMPAR number
  - acquisition of AMPA receptors by previously 'Silent' synapses
  - phosphorylation of S845 accompanies the surface reinsertion of GluR1
- increased pre-synaptic release of glutamate
  - triggered by retrograde messengers such as NO

2) Late phase expression/maintenance:

1) protein synthesis
2) gene transcription
3) PKA/MAPK/CamKIV activates key transcription factor: CREB

Other forms of LTP:

1) Growth of new dendritic spines
2) Enlargement of existing spines and their associated postsynaptic densities
3) Splitting of single PSDs and spines into 2 functional synapses

LTD:

Induction:
requires activation of NMDARs, a rise in postsynaptic calcium ion concentration, and activation of a serine-threonine protein phosphatase cascade

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Expression:

1) GluR1 s845 dephosphorylation (PKA site) by PP1
2) LTD induction in previously potentiated synapses leads to dephosphorylation of the CaMKII site, S831
3) GluR2 regulated receptor endocytosis via a dynamin- and clathrin-dependent mechanism
4) Lost of "slot protein", PSD 95
5) NMDAR activation leads to ubiquitination and proteasome degradation of PSD95

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Maintenance:

- requires protein synthesis for stable expression
- translation of preexisting mRNA

Other forms of LTP:

1) Elimination of dendritic spines
2) Shrinkage of existing spines