Theoretical & computational Neuroscience:
Programming the Brain

(BM 6140)

2-credit

Levels of abstraction in Neuroscience

Behaviour	Responses to stimuli, choices etc
Systems	e.g. Visual, Auditory, Motor
Areas	e.g. Frontal, Temporal lobes
Circuit	e.g. cortical column
Neurons	A Cell
Synapse	Connection between cells
Molecule	Molecules, ions entering/leaving the cell

Learning, memory and plasticity

- Can be studied and modeled at different levels
  - *Behaviour*
  - *Network*
  - *Cellular or synaptic*
  - *All are interwoven*

Behaviour

- Implicit memories
  - *E.g. walking, swimming*
- Explicit memories
  - *Can explicitly state e.g. name, place etc.*

- Habituation and Sensitization are also learning
  - *Habituation to noise*
  - *Increased or decreased sensitivity in the face of exposure to stimuli*
  - *e.g. We don't feel the chair we sit on, or the weight of clothes after some time*

Hebb’s rule

When an axon of cell *A* is near enough to excite a cell *B* and repeatedly or persistently takes part in firing it, some growth process or metabolic change takes place in one or both cells such that *A*'s efficiency, as one of the cells firing *B*, is increased.“

- Hebb (1949) *The Organization of Behavior*

Fire together, wire together

Crude network level learning rules

- Neurons firing together get strongly connected
- Once strong enough, even if subset fires, the whole set fires, because of strong interconnections : Associative memories

Synaptic plasticity

- Basis of higher level plasticity schemes
- Short- term plasticity : milliseconds – minutes
- Long term plasticity : minutes to years
- Underlying Mechanisms vary

Short term plasticity

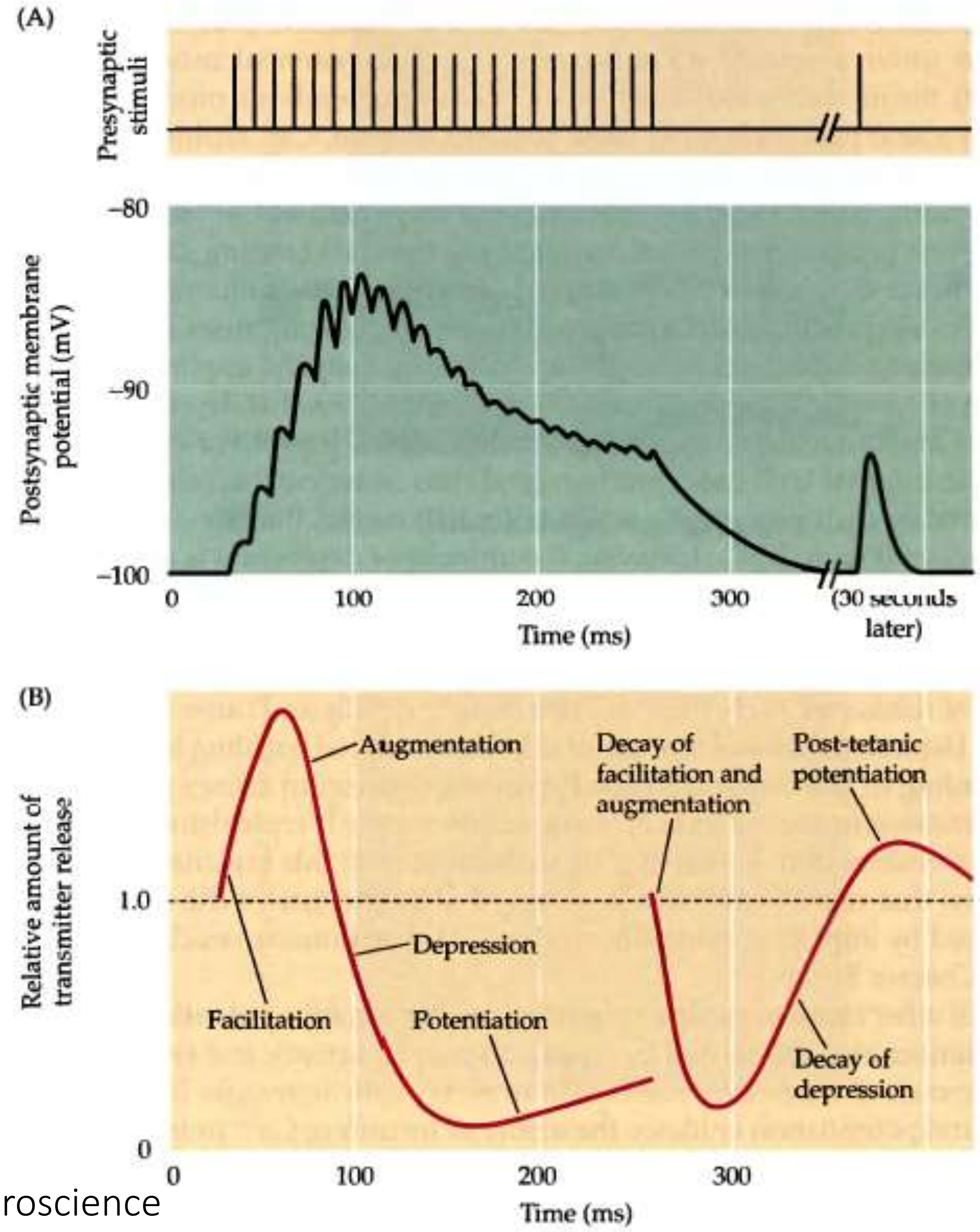
Facilitation :

Calcium buildup in presynapse => increased transmitter release => larger epsp

Depression :

Depletion of transmitter available => reduced epsp

Types of short term plasticity



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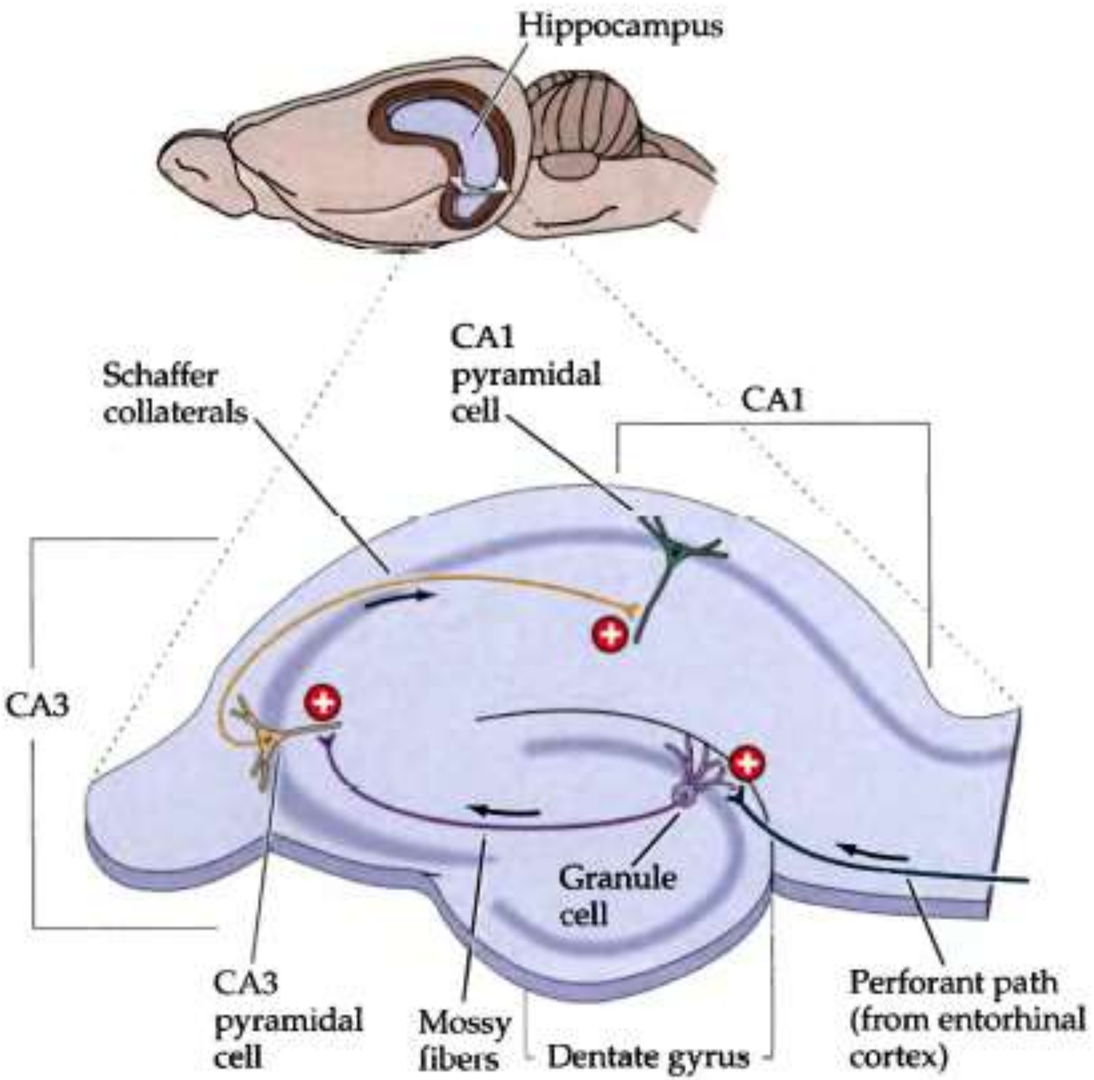
Long term plasticity

- Long term potentiation(LTP) and Long term depression(LTD)
- Seconds to hours and beyond

Hippocampal tri-synaptic circuit



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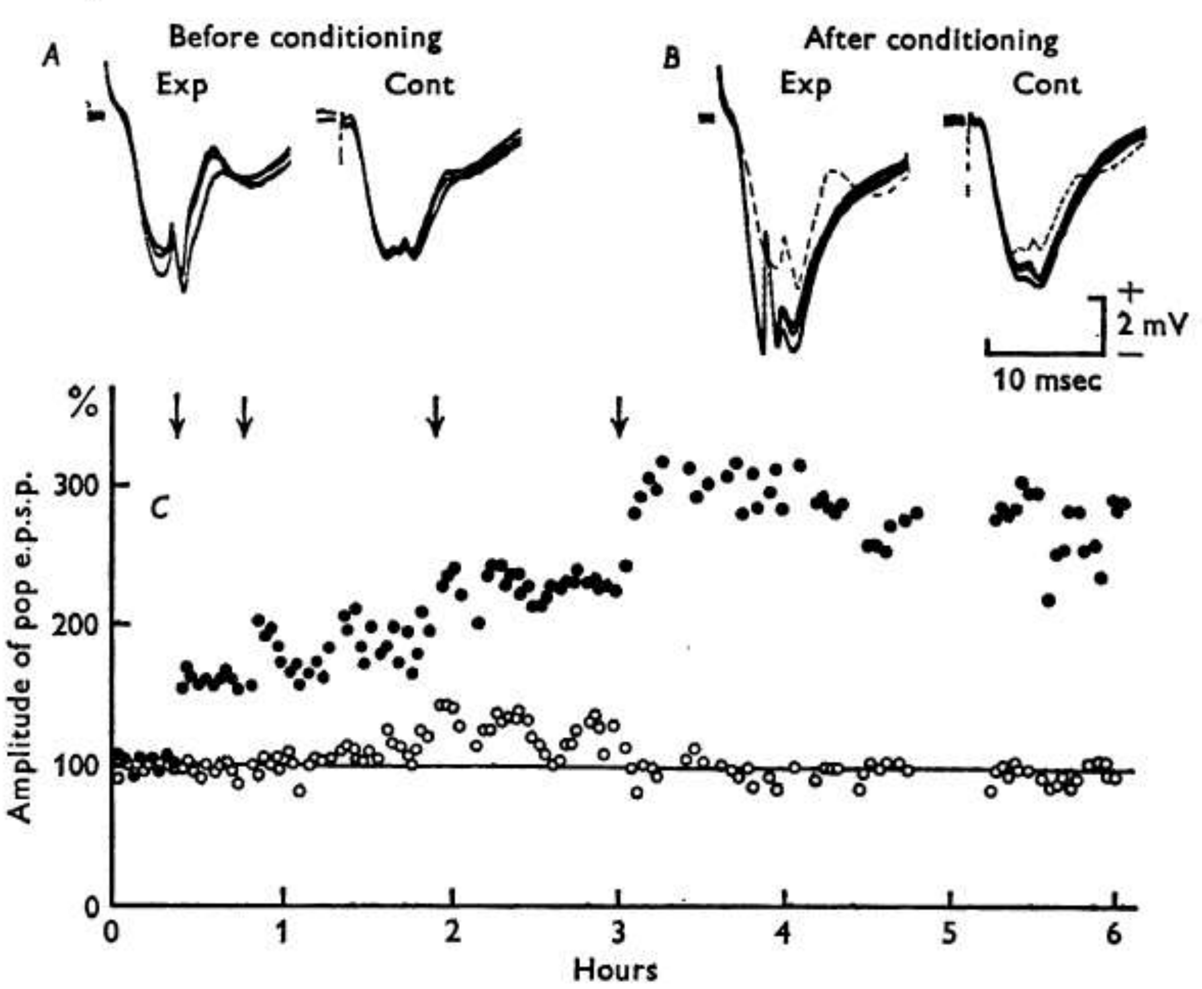
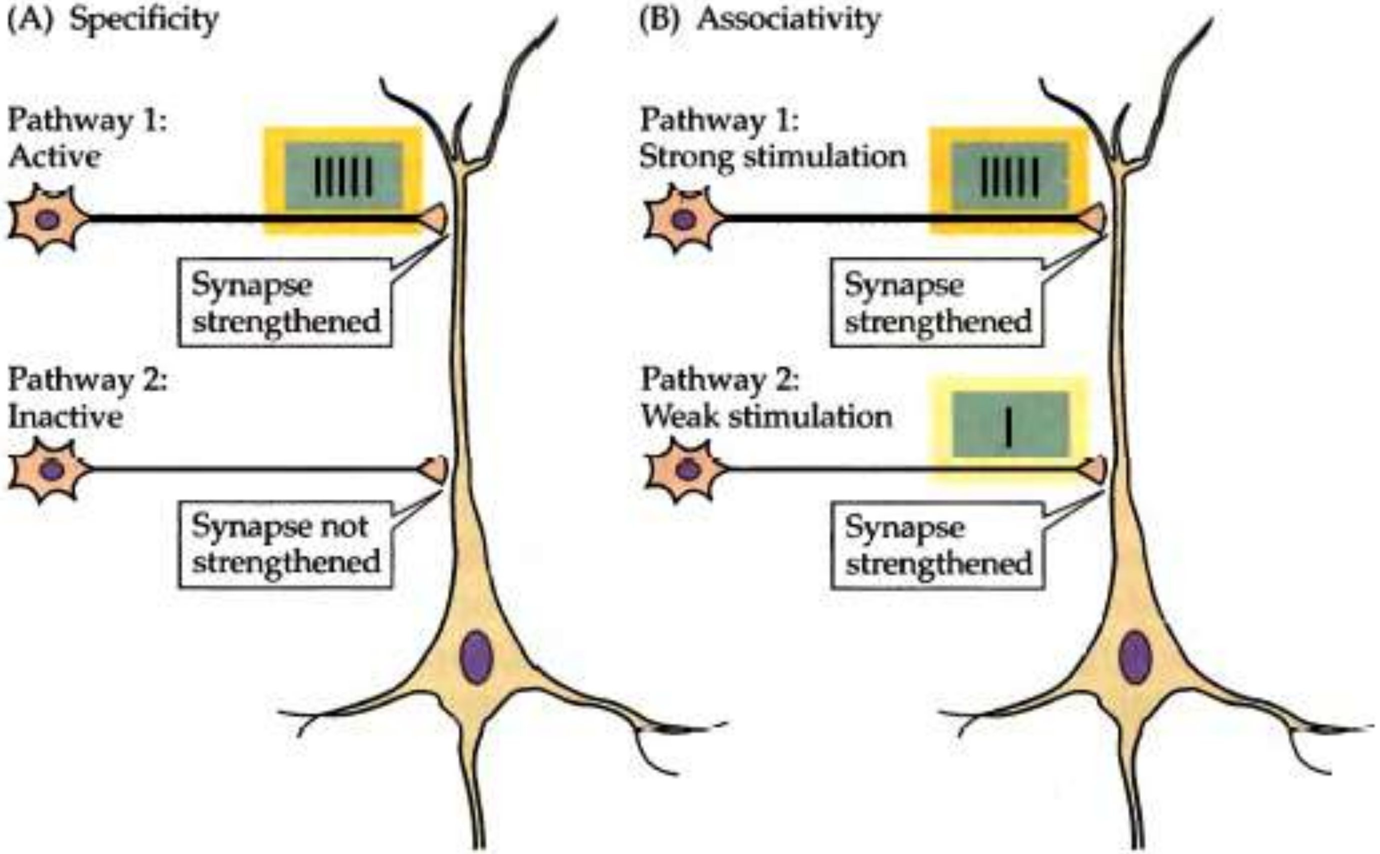
LTP (Long term potentiation)
NOT to be confused with long term plasticity

- tetanic stimulation



Input specificity and Associativity

Figure 8.9 Properties of LTP at a CA1 pyramidal neuron receiving synaptic inputs from two independent sets of Schaffer collateral axons. (A) Strong activity initiates LTP at active synapses (pathway 1) without initiating LTP at nearby inactive synapses (pathway 2). (B) Weak stimulation of pathway 2 alone does not trigger LTP. However, when the same weak stimulus to pathway 2 is activated together with strong stimulation of pathway 1, both sets of synapses are strengthened.



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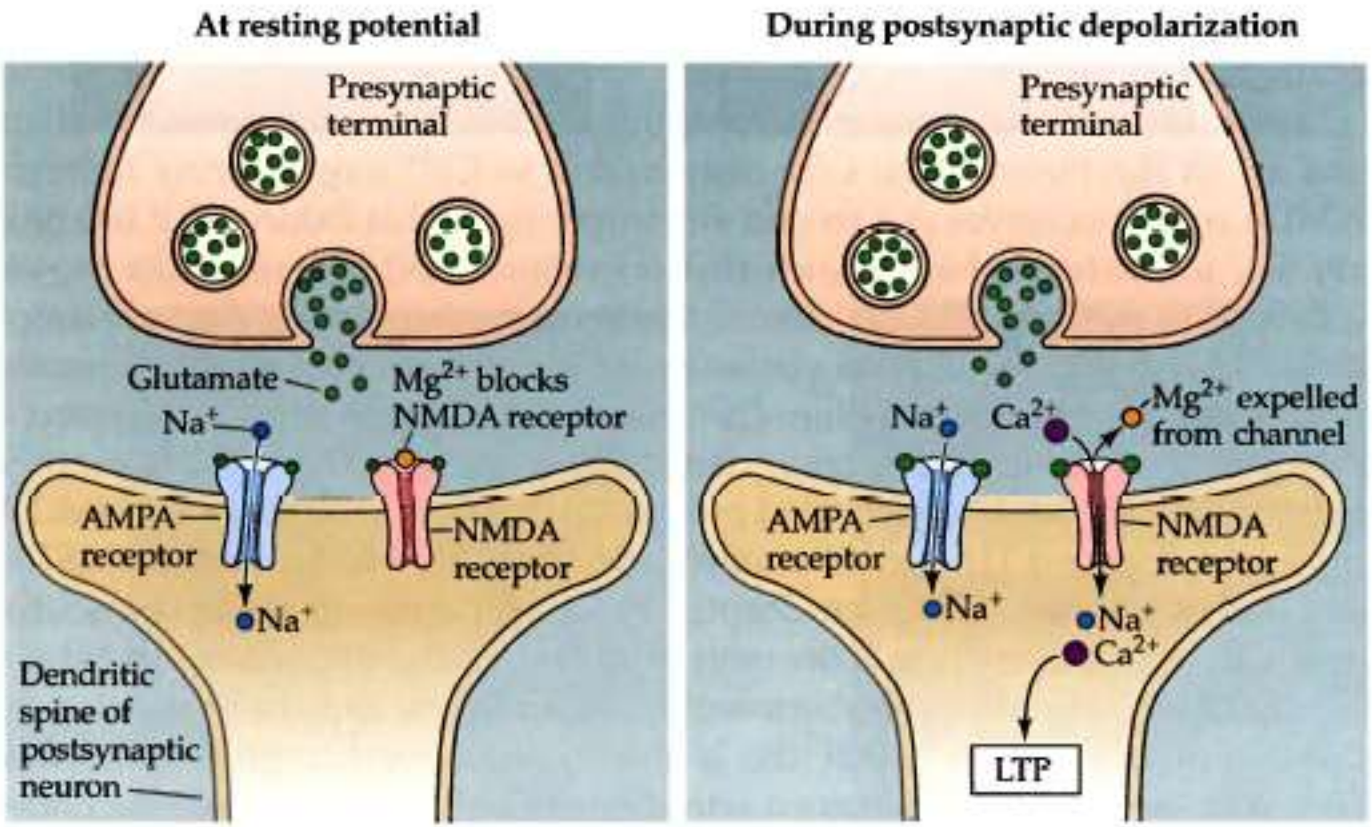
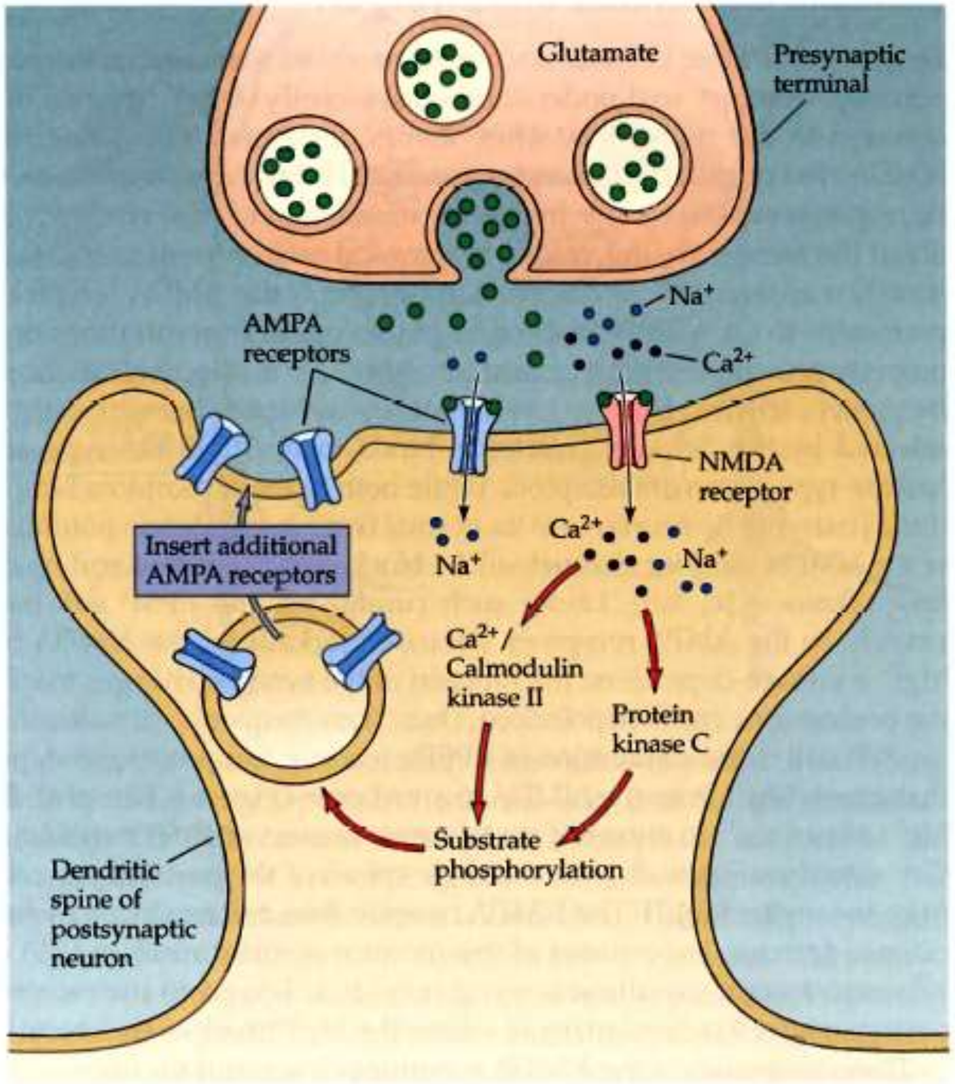
Cooperativity

Similar to associativity, but no single stimulus can elicit LTP, but all together can !

Mechanism of LTP



Induction



Maintenance

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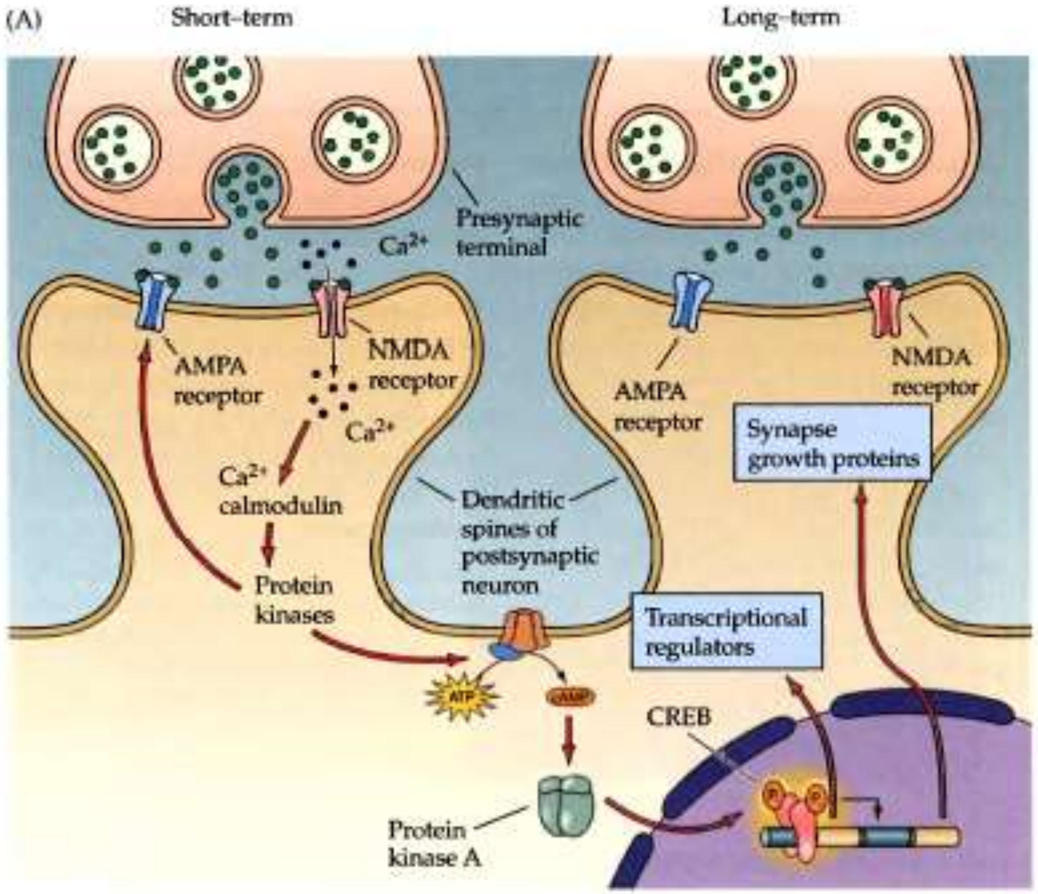
Structural change induced LTP



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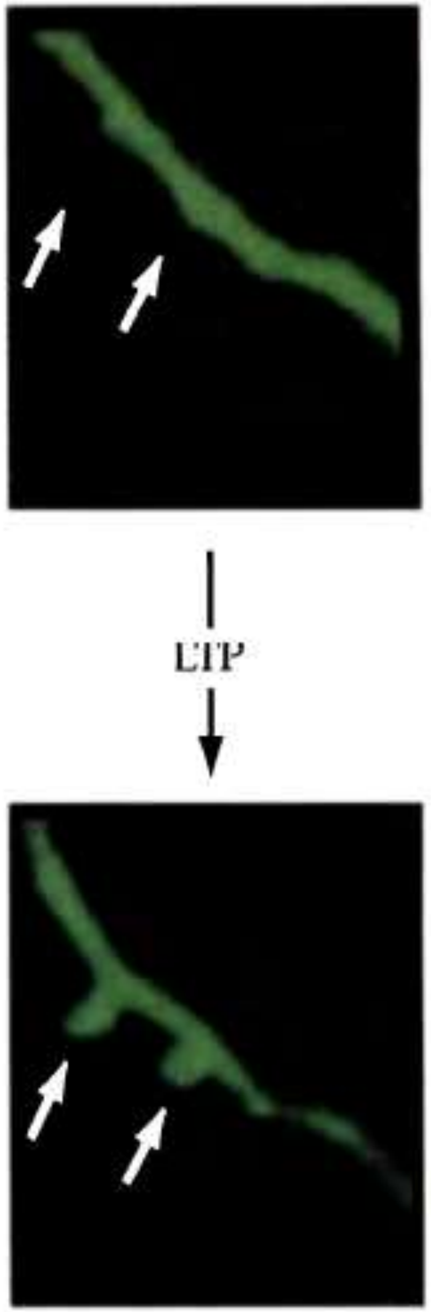


This is not the only mechanism ! Think !

- What if there is no NMDA receptor ?
- Can fewer spikes evoke LTP ?
- Is tetanic stimulus essential ?

Plasticity : Key take away

- Need both Pre and post synaptic activity
- *Pre synaptic activity to release glutamate*
- *Post synaptic activity for depolarization*
- *Depolarisation needed for CA^{2+} influx : !! Calcium is the King !!*
- *Devil is in the details !! Biochemistry !!*

Long term depression

- Induced in a protocol similar to LTP, but with lower frequency stimulus
- LTD also needs Ca^{2+} influx but slow, low influx, while LTP needs faster Ca^{2+} influx

Modeling plasticity

$$\tau_r \frac{dv}{dt} = -v + \mathbf{w} \cdot \mathbf{u} = -v + \sum_{b=1}^{N_u} w_b u_b$$

$$\tau_w \frac{d\mathbf{w}}{dt} = \langle v\mathbf{u} \rangle$$

u : vector of presynaptic firing rates

v : post synaptic firing rates

W : vector of weights

<> : Ensemble average over all possible combinations

Modeling plasticity

When input changes slowly with respect to time constant (eq 1) , v = **w**.**u** and

$$\tau_w \frac{d\mathbf{w}}{dt} = \mathbf{Q} \cdot \mathbf{w}$$

Q is input correlation matrix $$Q_{bb'} = \langle u_b u_{b'} \rangle$$

Problems : Unbounded growth ?

BCM rule

$$\tau_w \frac{d\mathbf{w}}{dt} = v\mathbf{u}\,(v - \theta_v)\ .$$

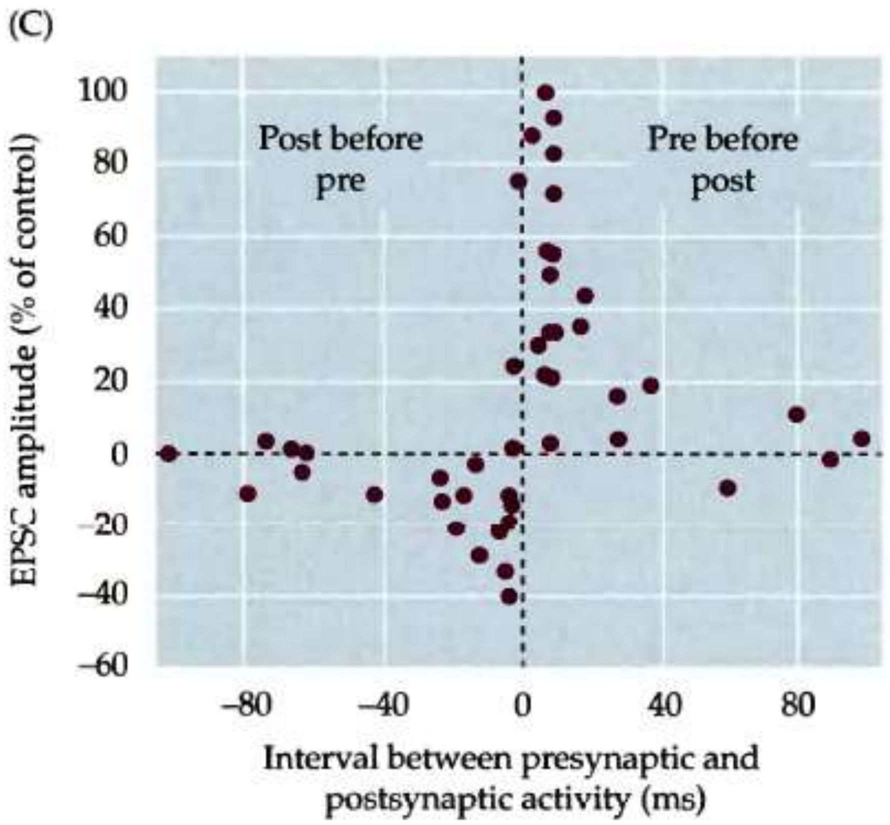
Comparing v with a variable sliding threshold : e.g using $\tau_\theta \frac{d\theta_v}{dt} = v^2 - \theta_v$

- induces competition

- Normalisation of synaptic weights

STDP : Spike timing dependent plasticity

- Bi and Poo (1998)



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