Synaptic plasticity

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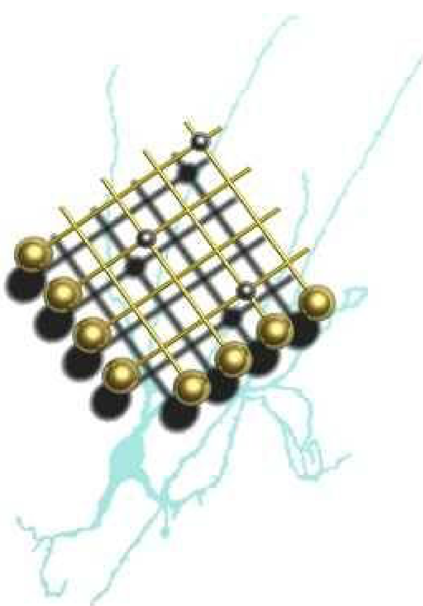


Human memory systems

Psychologists have split up memory in:

Declarative memory

* Episodic memory (personal what, when, where memories)
  - recollection
  - familiarity
  - hippocampus (patient HM)

* Semantic memory: General facts about the world (cortex)

Non-declarative memory (cortex, cerebellum,..)

Motor skills, sensory processing, ...

Working memory (prefrontal, not discussed here)

Testing animal memory

(Classical) conditioning

Pavlov's dog

Aplysia gill reflex

Mazes and environments for rodents

- water maze
- place avoidance
- fear
- food location

Long term synaptic plasticity

What is (activity dependent, long term) synaptic plasticity?

Long term, semi-permanent changes in the synaptic efficacy, induced by neural activity.

In contrast to:

- some aspects of development
- short term changes
- excitability changes

Memory systems

Declarative memory

* Episodic memory
  - recollection
  - familiarity
  - hippocampus (patient HM)

* Semantic memory: General facts

Non-declarative memory

Motor skills, sensory processing, ...

} Synaptic plasticity

More reading

Reviews of experimental LTP:
- Kandel and Schwartz book
- Hippocampus book

Theory of Hopfield networks and Backpropagation
- Herz, Krogh and Palmer

Neural computation theory
- Dayan & Abbott
- Trappenberg

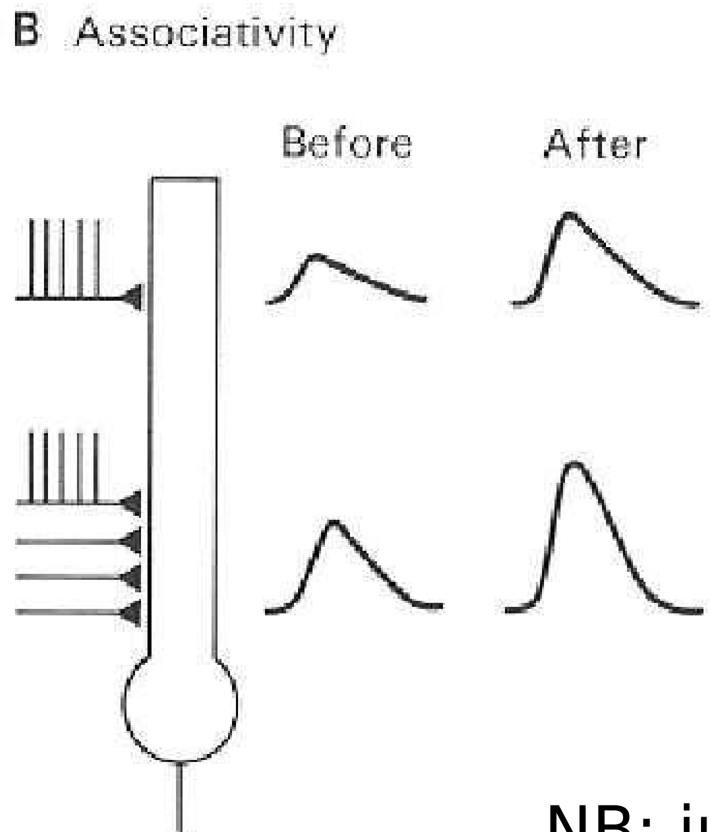
Basis of classical conditioning?

conditioned stimulus

Bell

unconditioned stimulus

Food



Saliva

NB: just a cartoon!

For Aplysia see Kandel book

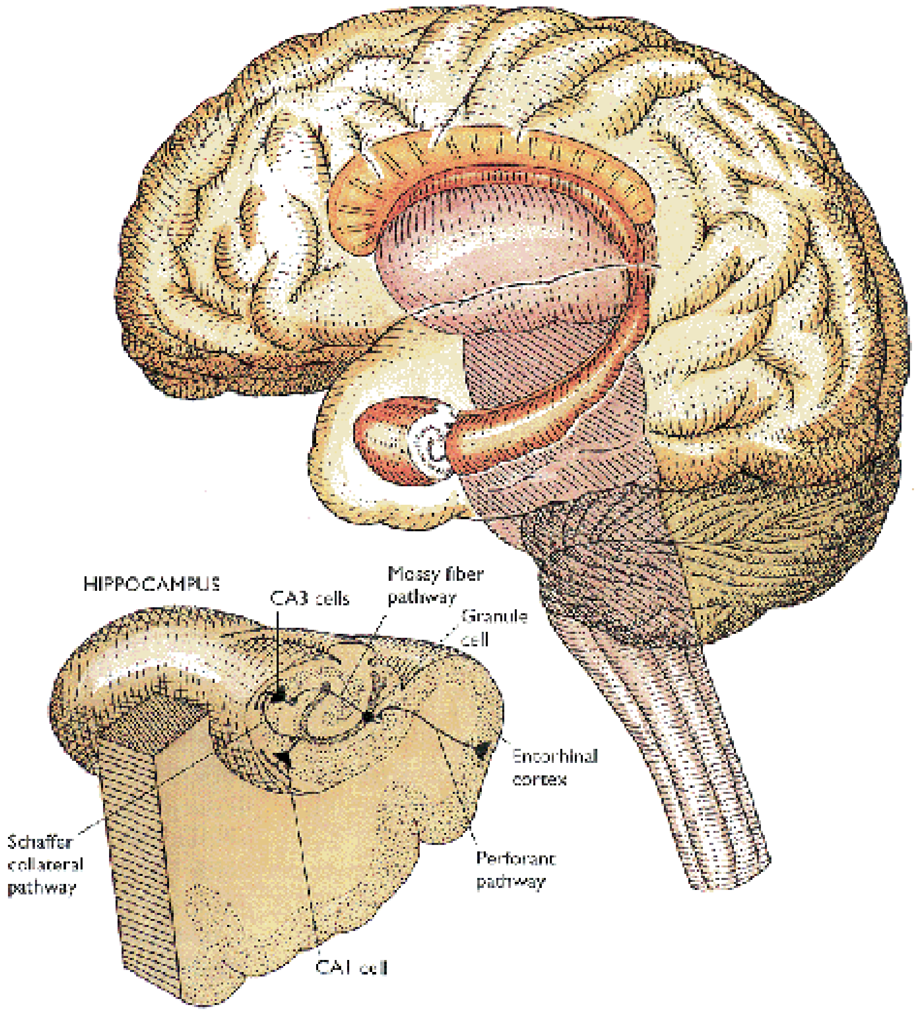
Donald Hebb (1949)

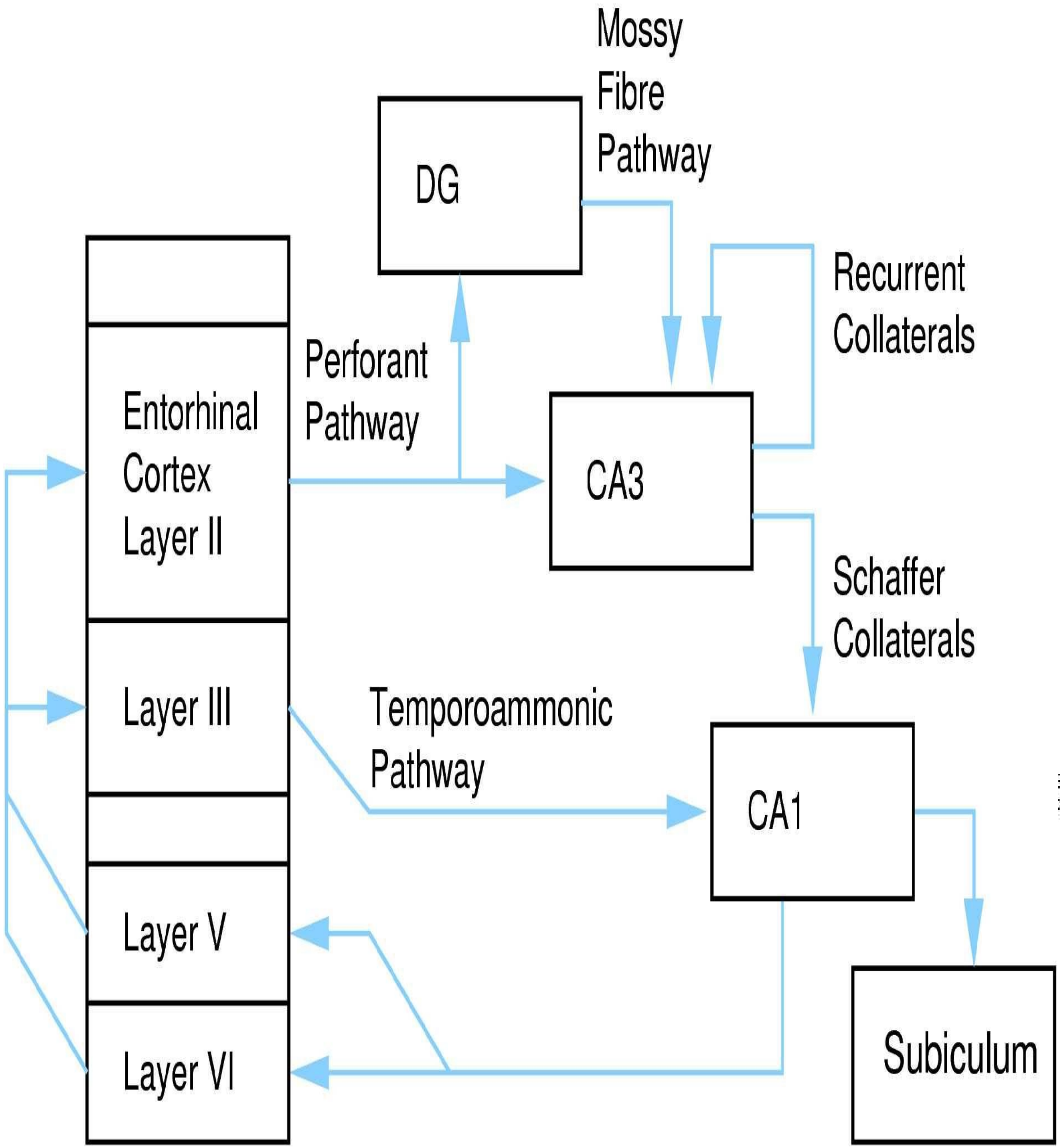
Let us assume that the persistence or repetition of a reverberatory activity (or "trace") tends to induce lasting cellular changes that add to its stability. . . . When an axon of cell A is near enough to excite a cell B and repeatedly or persistently takes part in firing it, some growth process or metabolic change takes place in one or both cells such that A's efficiency, as one of the cells firing B, is increased.

"What fires together, wires together"

Hippocampus

- Essential for declarative memory
- cylindrical structure
- longitudinal axis surrounds thalamus





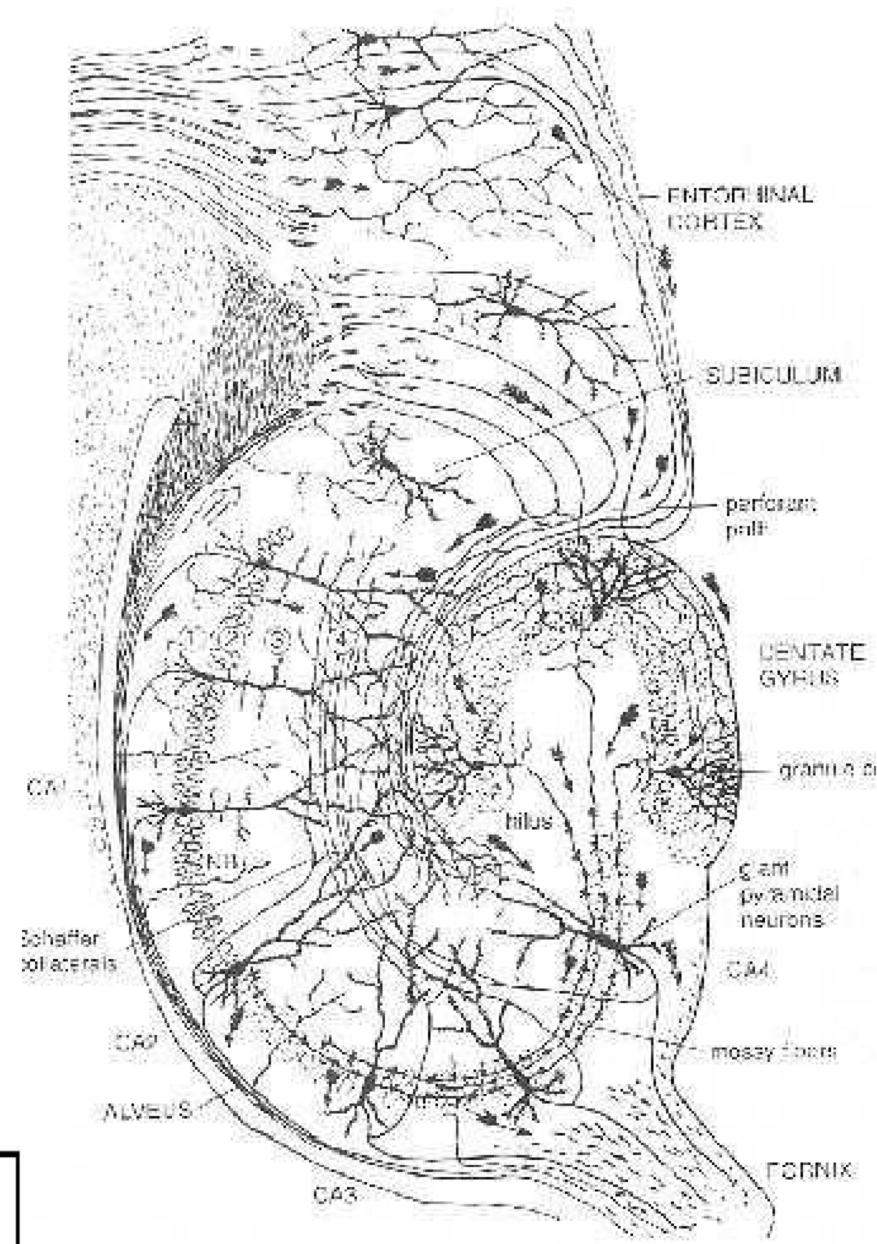
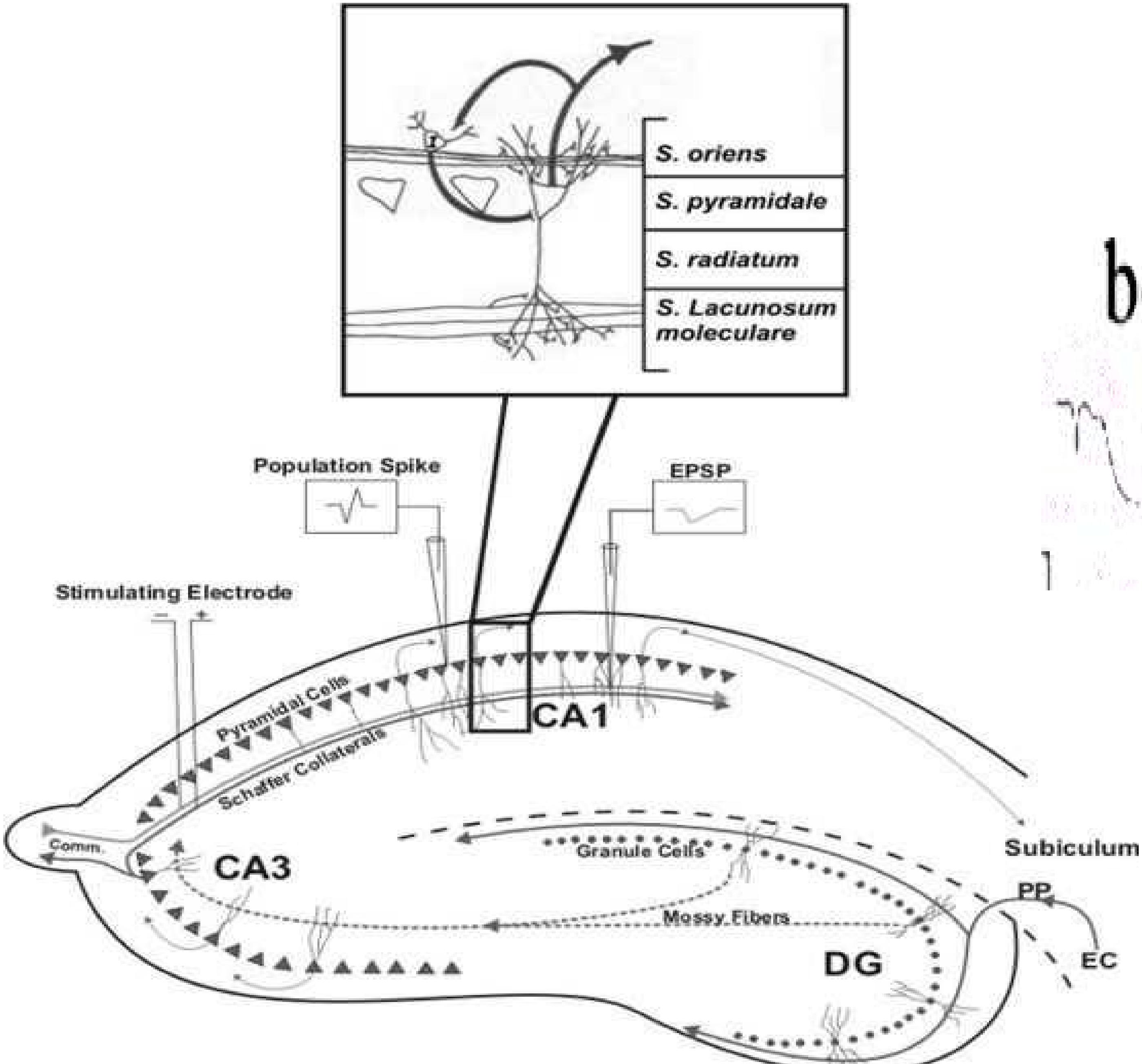
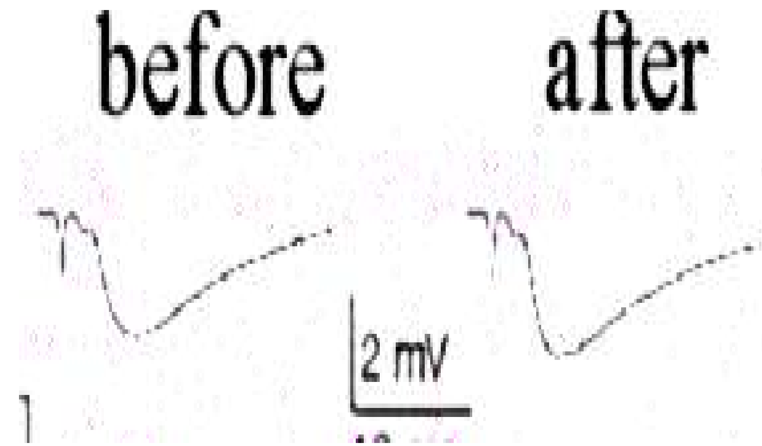
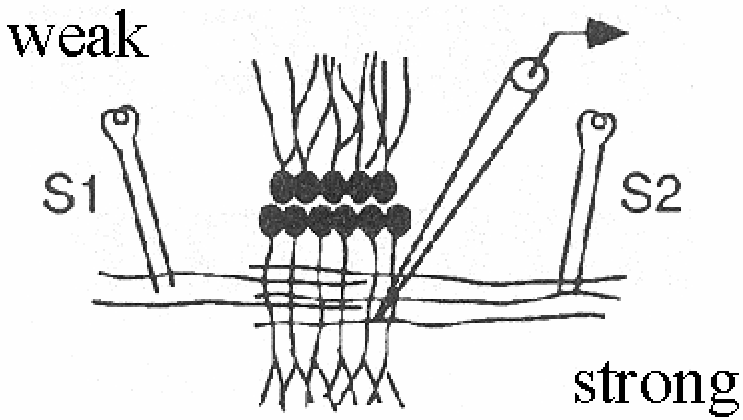


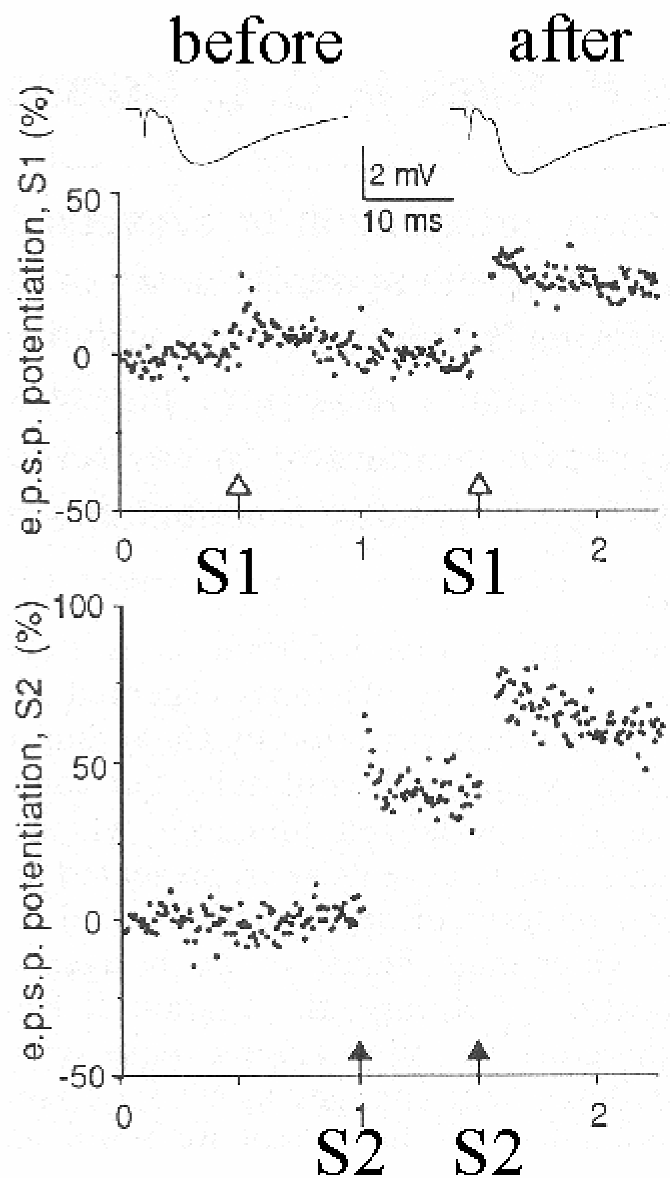
Diagram: Kit Longden


S. oriens
S. pyramidale
S. radiatum
S. Lacunosum moleculare
Population Spike
EPSP
Stimulating Electrode
Pyramidal Cells
Schaffer Collaterals
CA1
Comm.
CA3
Granule Cells
Mossy Fibers
DG
Subiculum
PP
EC


before
after
2 mV

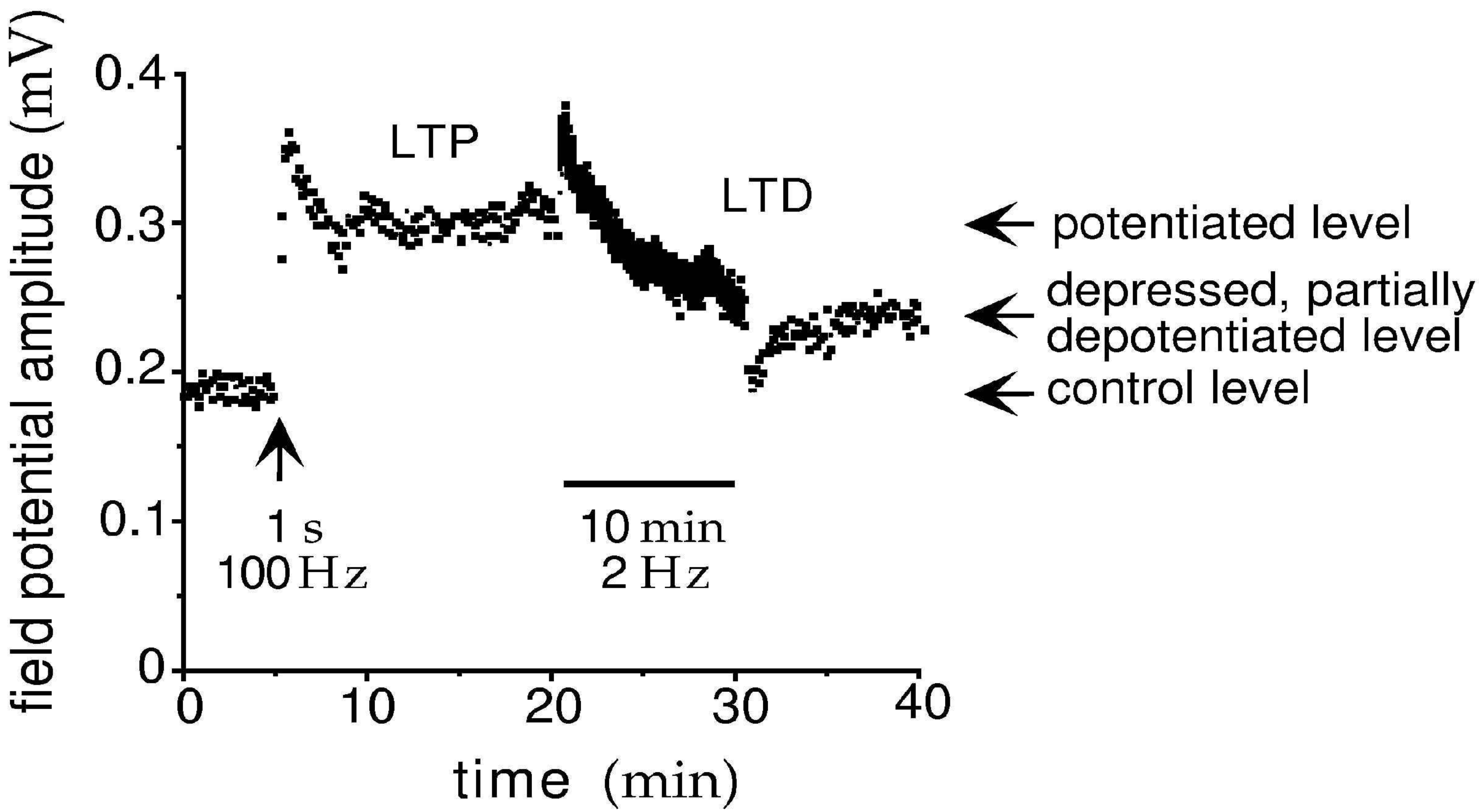
Schaffer collateral LTP (in vitro)





alternate at 15 sec intervals

tetanic stimulation
S1: cooperative
S2: input-specific
S1+S2: associative



field potential amplitude (mV)
0.4
0.3
0.2
0.1
0
LTP
LTD
1 s
100 Hz
10 min
2 Hz
0
10
20
30
40
time (min)
potentiated level
depressed, partially
depotentiated level
control level

Synaptic plasticity = memory? Criteria

•Detectability
changes in behaviour and synaptic efficacy should be correlated
Yes

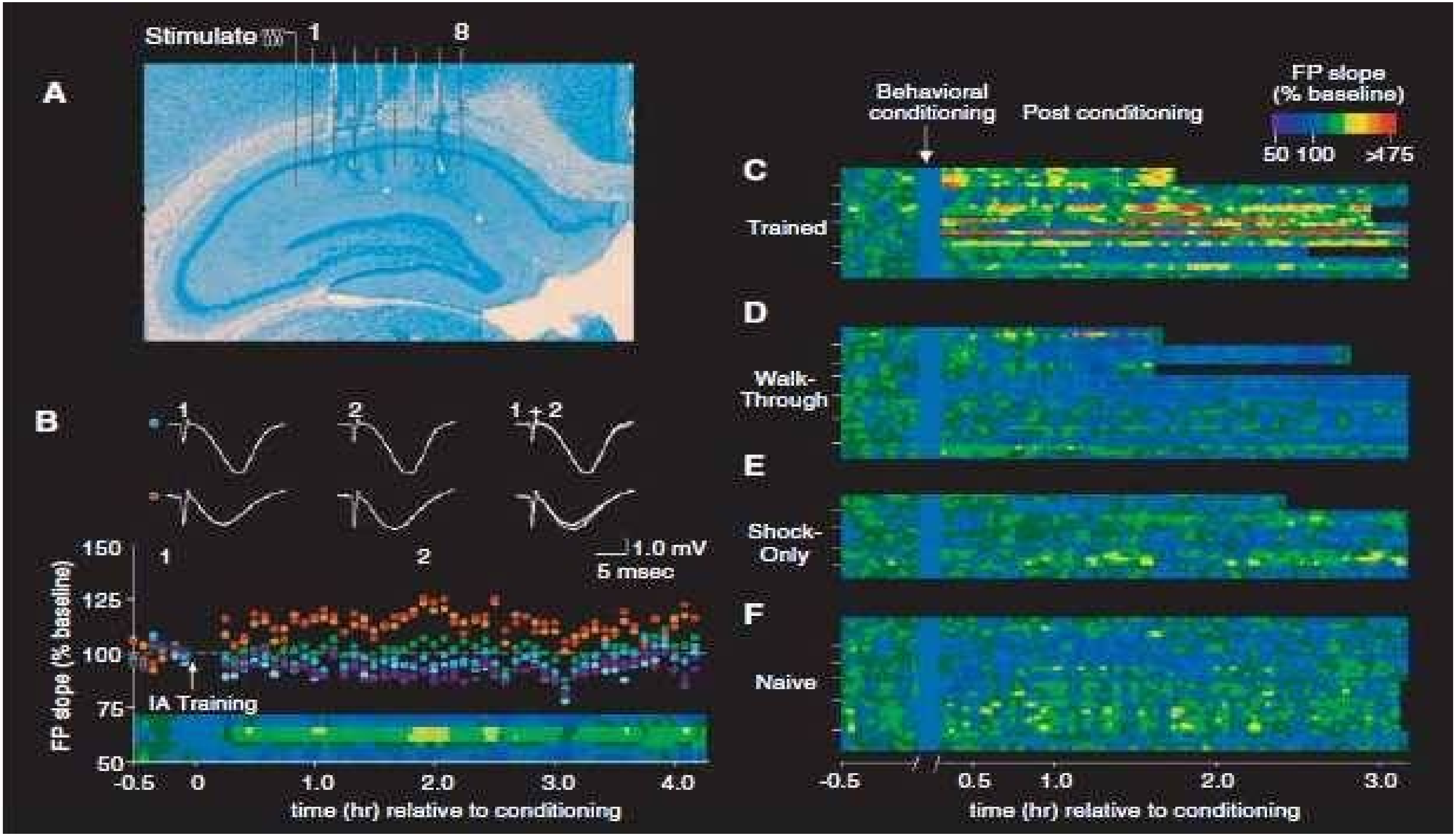
•Mimicry
change synaptic efficacies → new ‘apparent’ memory
Rudimentary

•Anterograde alteration
prevent synaptic plasticity → anterograde amnesia
Yes (e.g. NMDA block)

•Retrograde alteration
alter synaptic efficacies → retrograde amnesia
Yes (e.g. PKMz), but...

[Martin, Greenwood, Morris '04]

Synaptic plasticity=memory?



[Whitlock,.. and Bear '06]

LTP stages

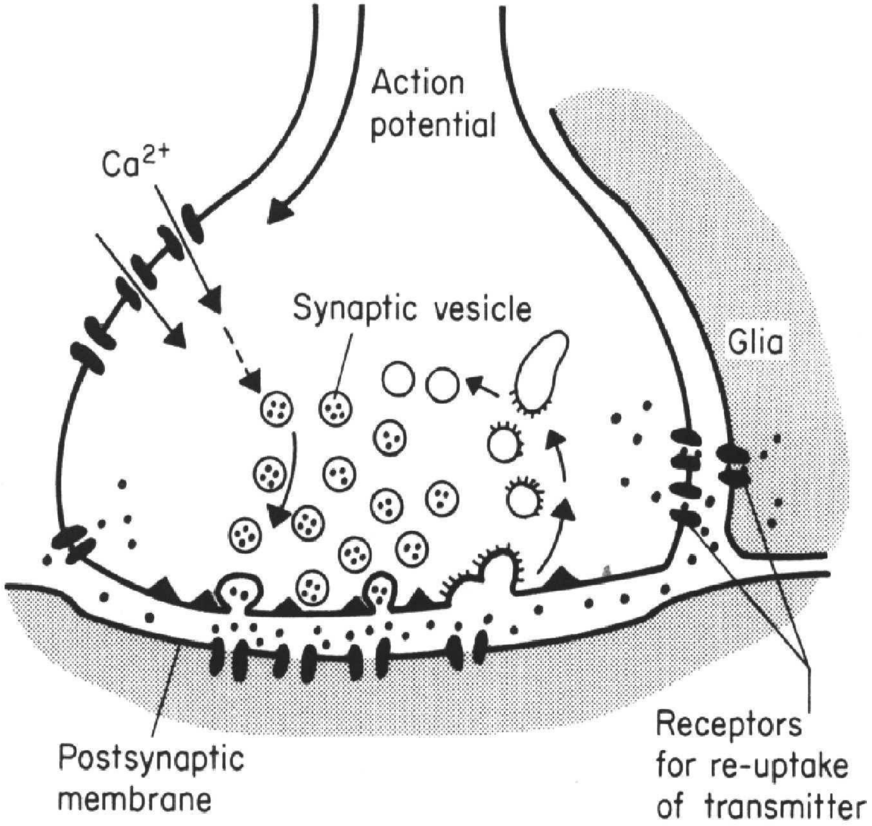
Induction:

- Requires pre- and post synaptic activity.
- Mechanism: NMDA and Ca influx

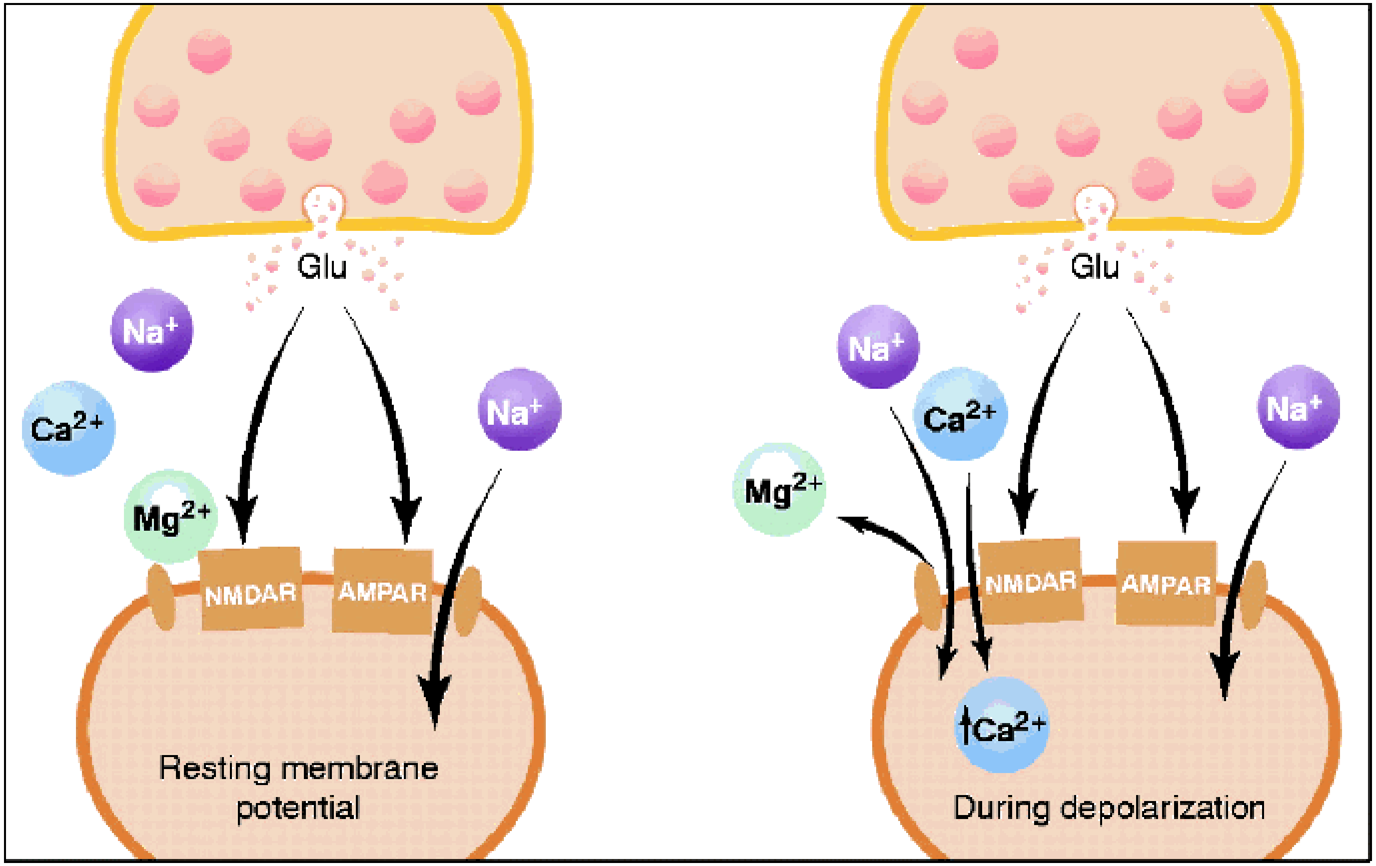
Expression

- Early LTP
- Late LTP

Maintainance

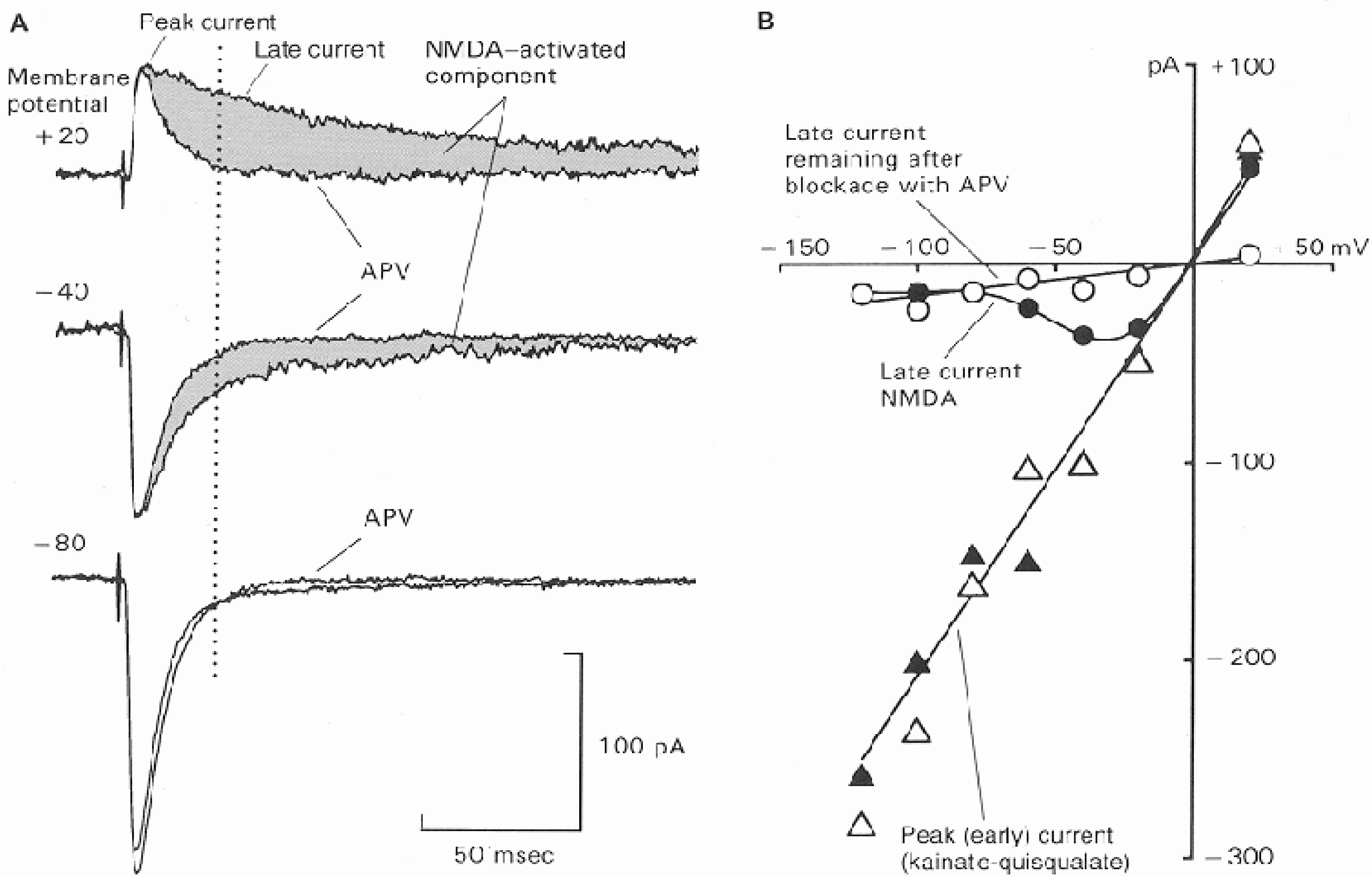


Model for LTP induction

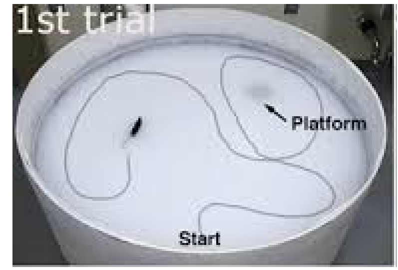


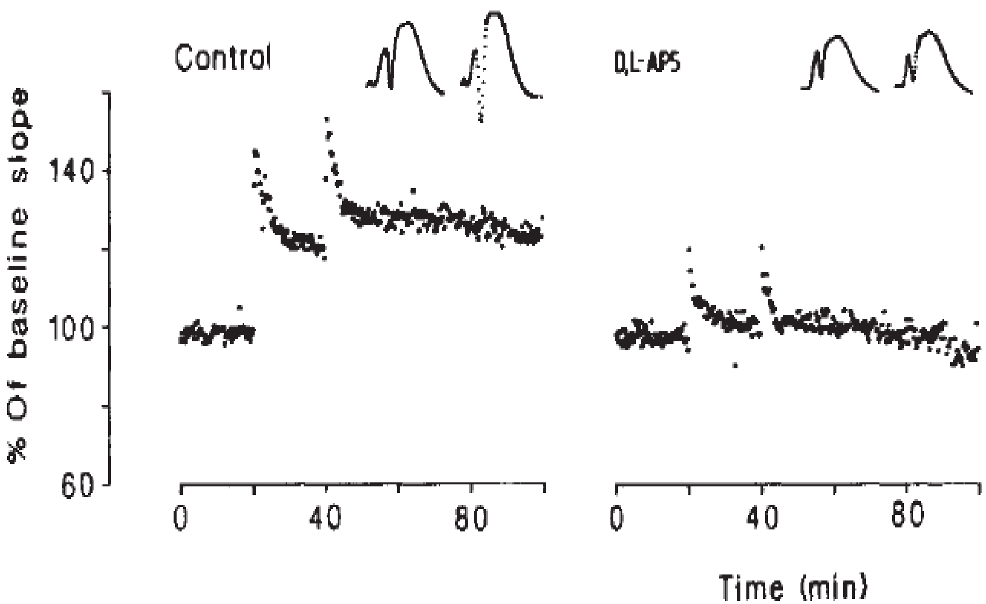
NMDA requires pre and post activity, hence ideal for Hebbian Learning

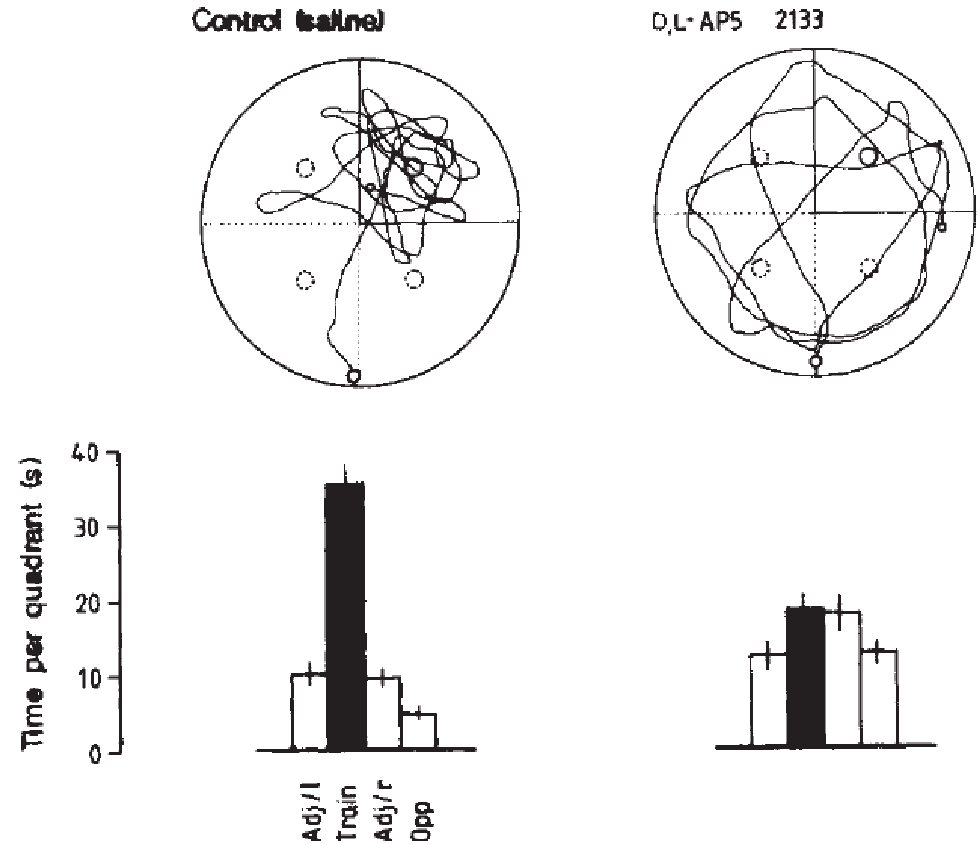
AP5 is a selective blocker



AP5 blocks learning







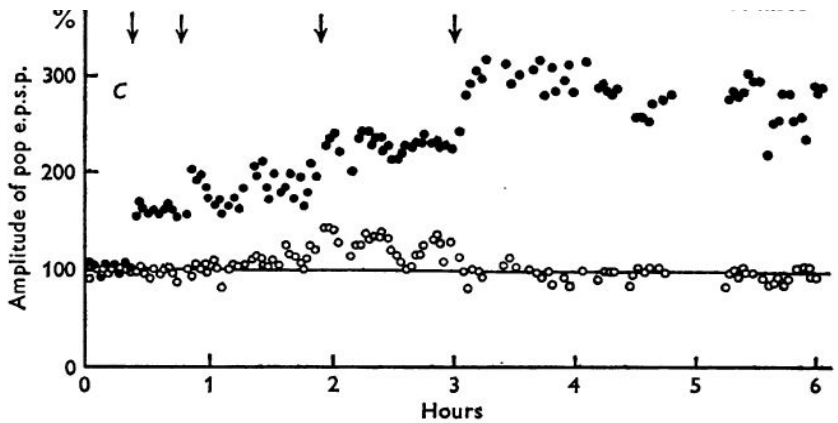
NMDA- block

NMDA- block

[Morris et al 86]

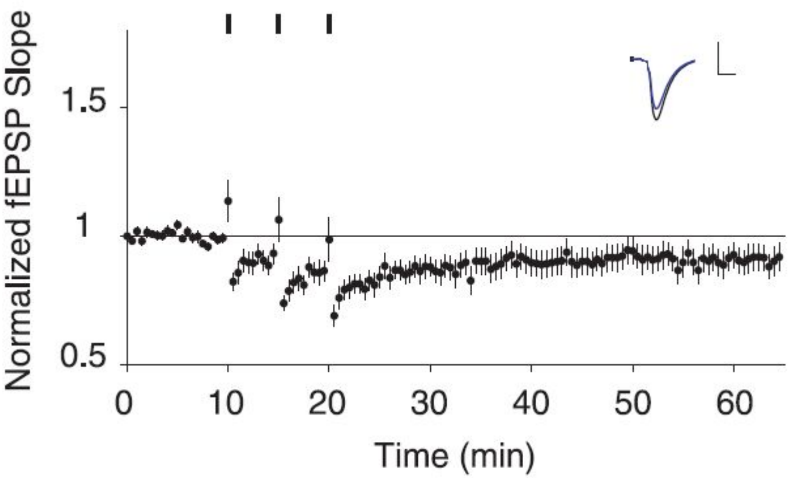
Ca hypothesis

LTP

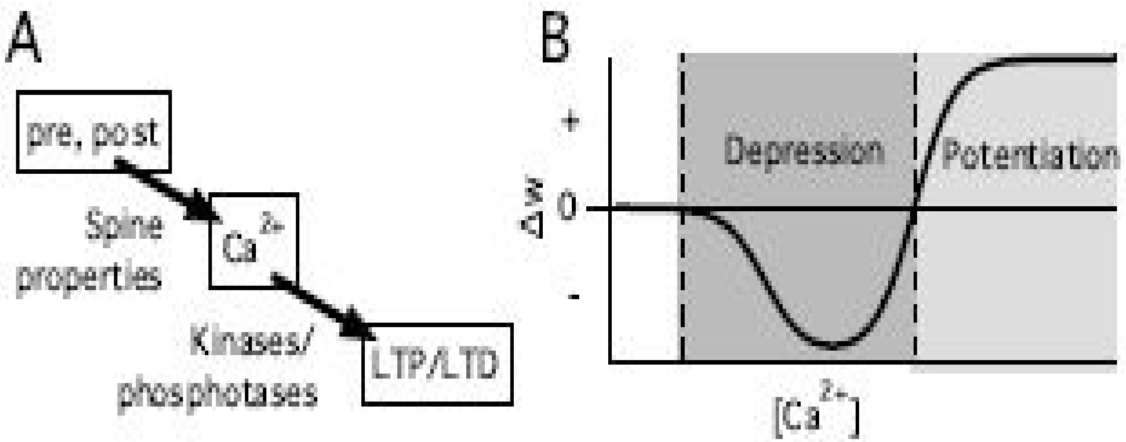


[Bliss & Lomo '73]

LTD



[O'Connor & Wang '05]



Pairing high pre- and post synaptic activity => LTP
Pairing with low activity => Long term depression

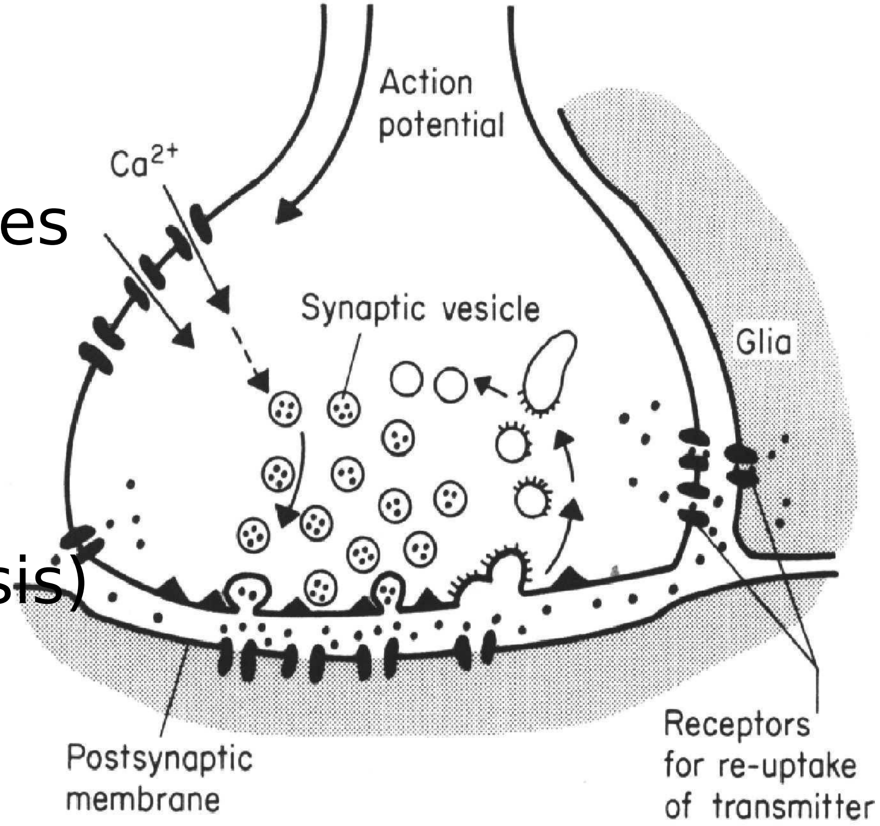
LTP stages

Induction:

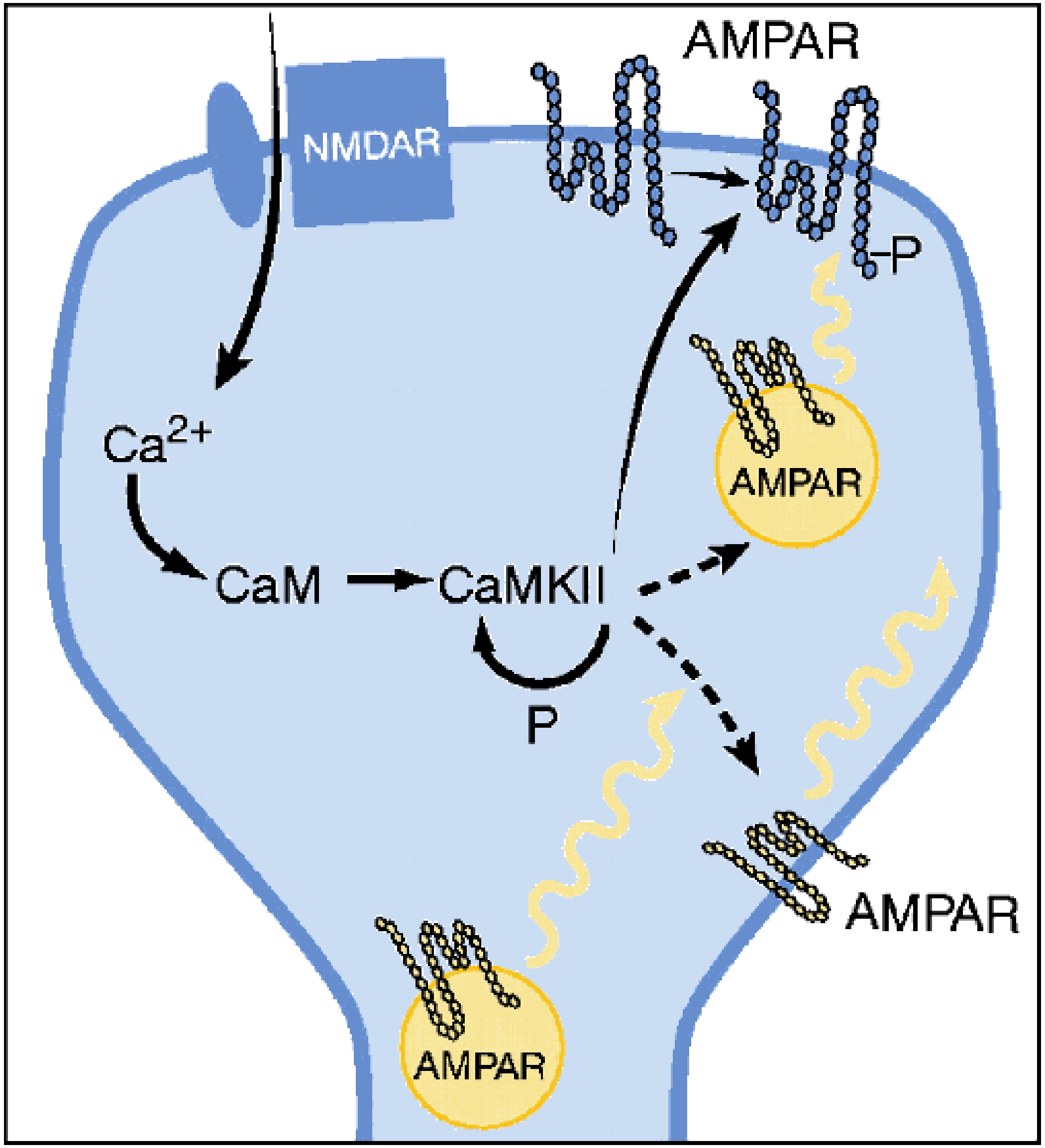
- Requires pre- and postsynaptic activity.
- Mechanism: NMDA and Ca influx

Expression:

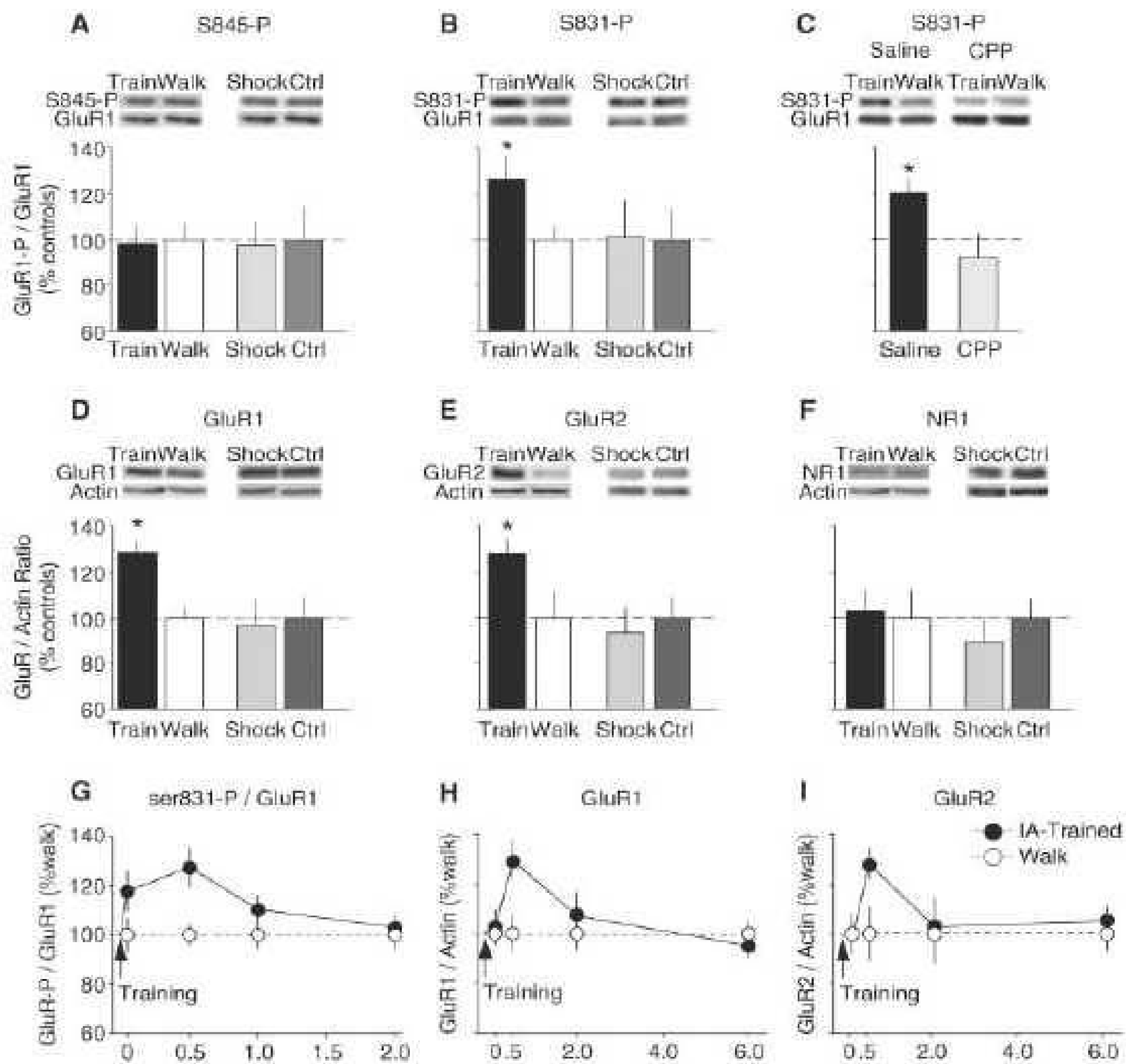
- Early LTP (1 hr):
  - partly pre-synaptic changes
  - AMPAR phosphorylation
  - AMPAR insertion
- Late LTP
  - ? (requires protein synthesis)



"Post-" model for expression

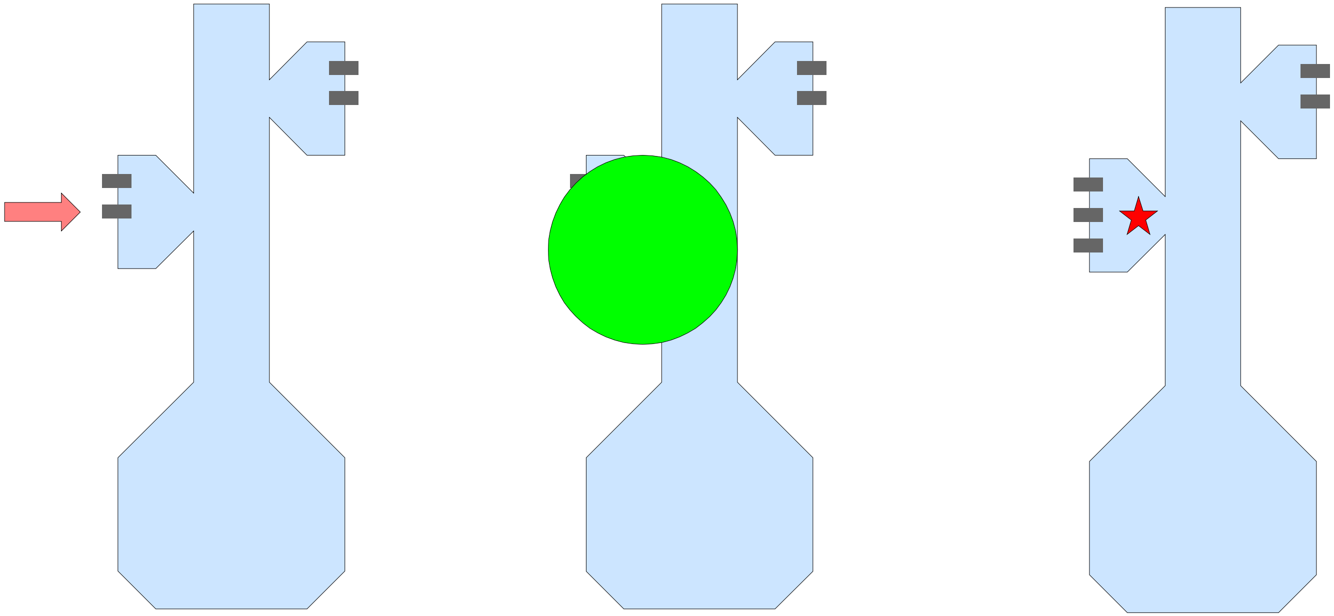


Changes in AMPA receptor phosphorilation

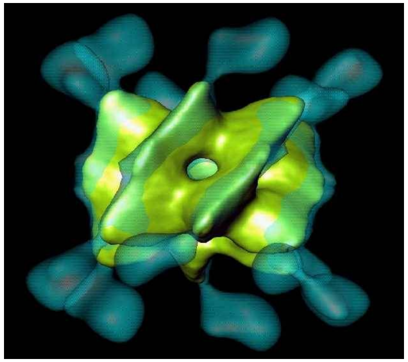


[Whitlock,
.. and Bear '06]

Early phase LTP



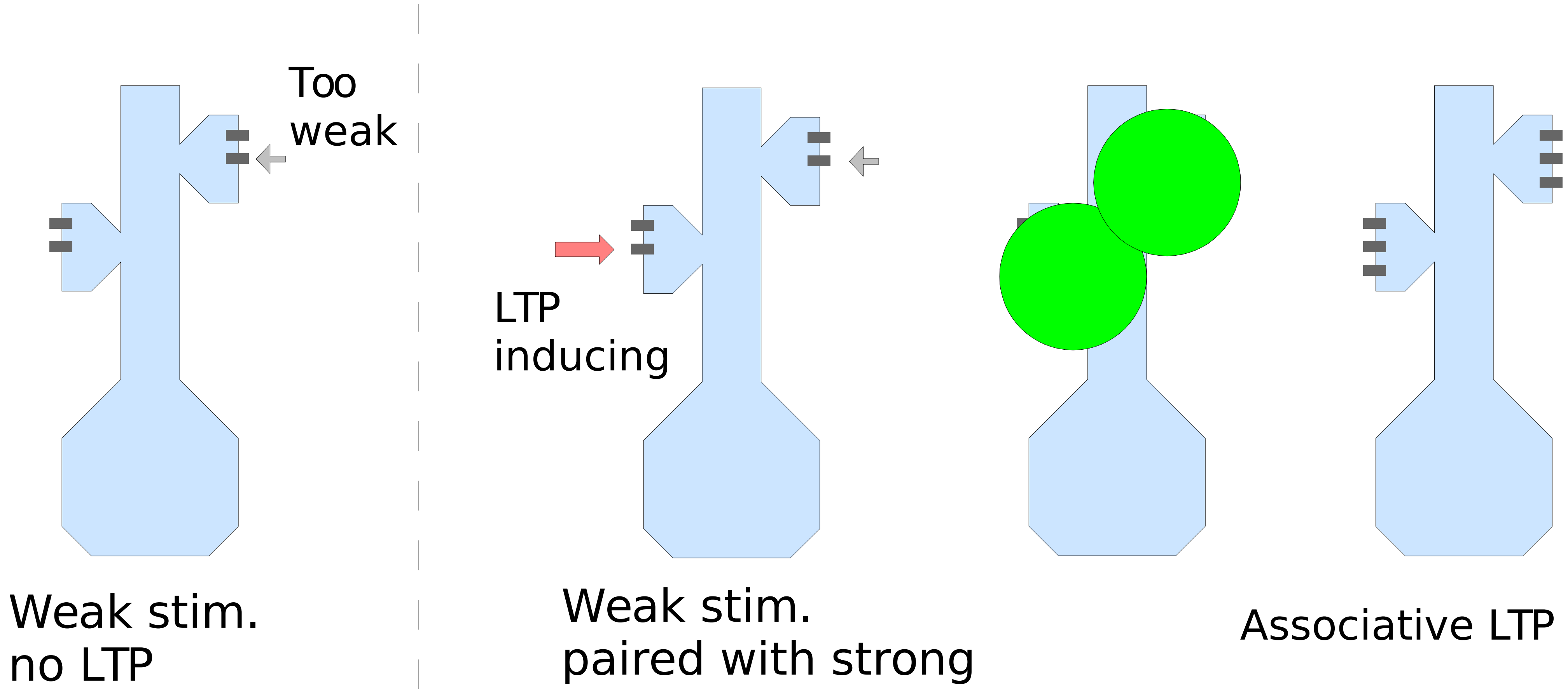
★ CaMKII



Stim.:
1 s @ 100Hz

Rapid and local
change

Associativity



- Can be explained with voltage dependence of NMDA
- Associative learning such as Classical conditioning (Pavlov)

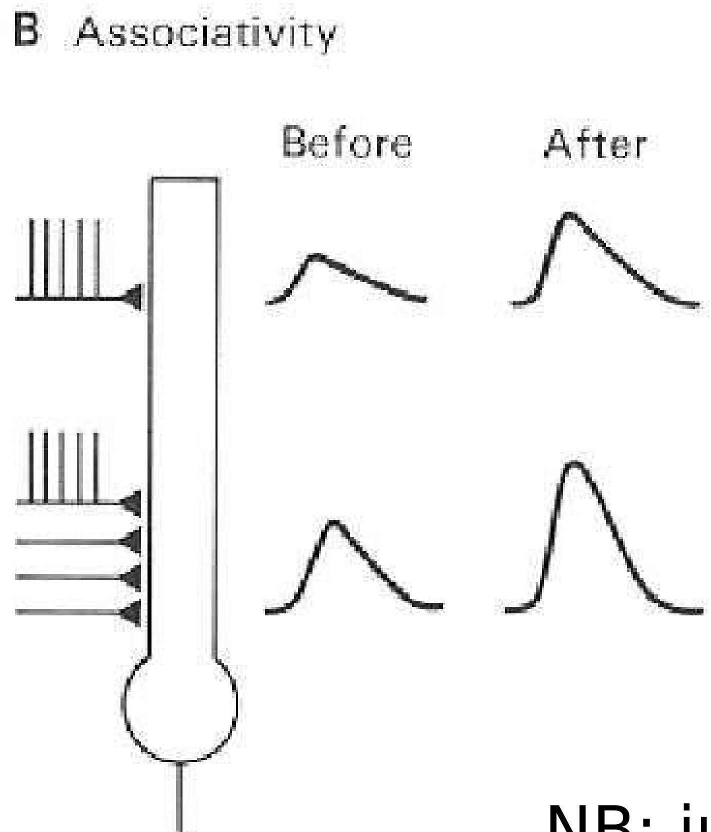
Basis of classical conditioning?

conditioned stimulus

Bell

unconditioned stimulus

Food

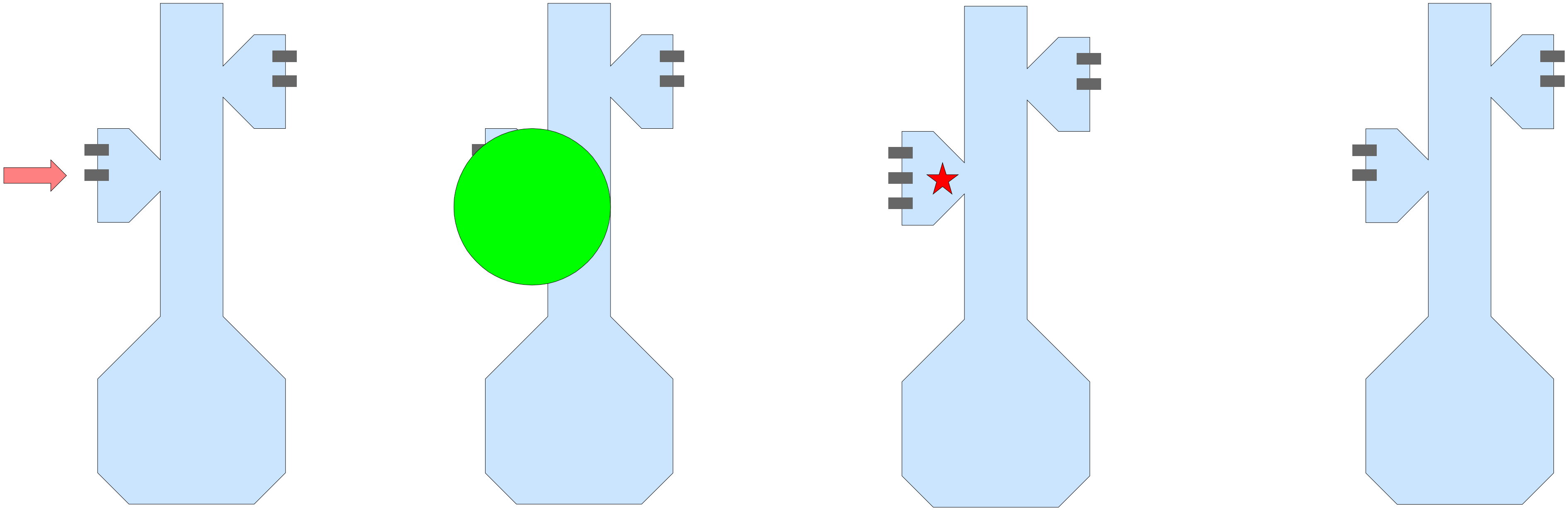


Saliva

NB: just a cartoon!

For Aplysia see Kandel book

Early phase LTP

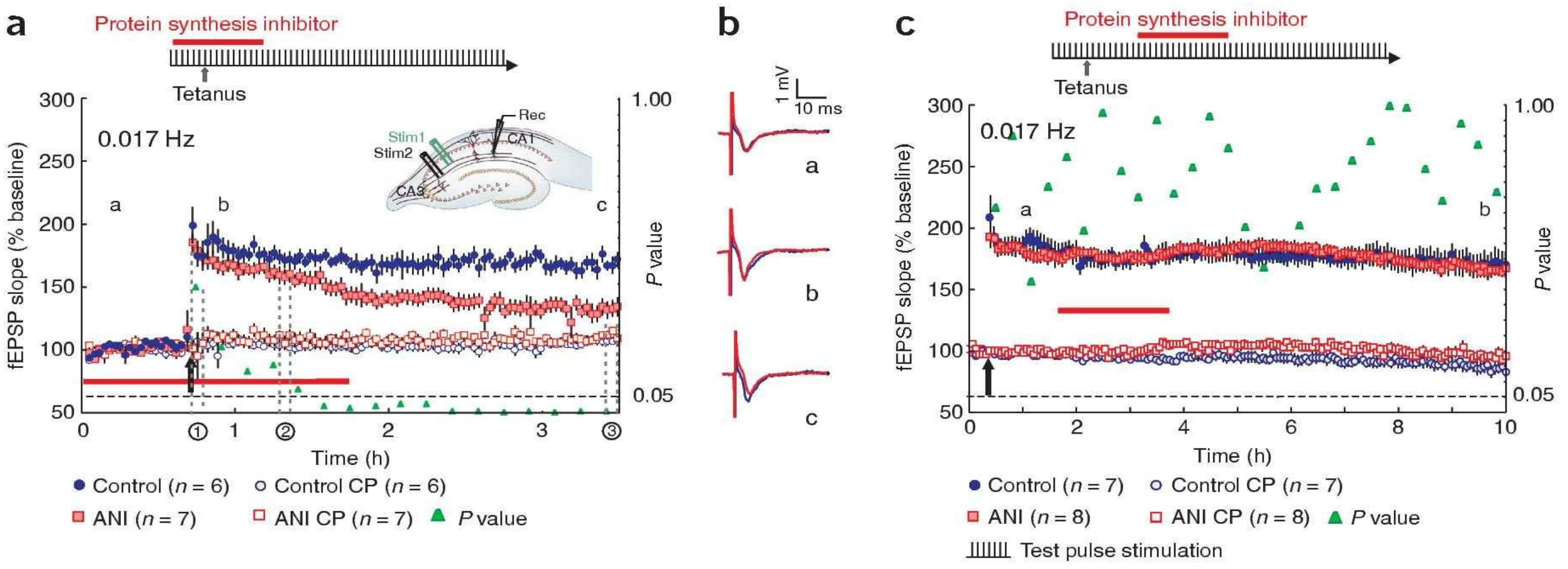


Stim.:
1 s @ 100Hz

Rapid and local
change

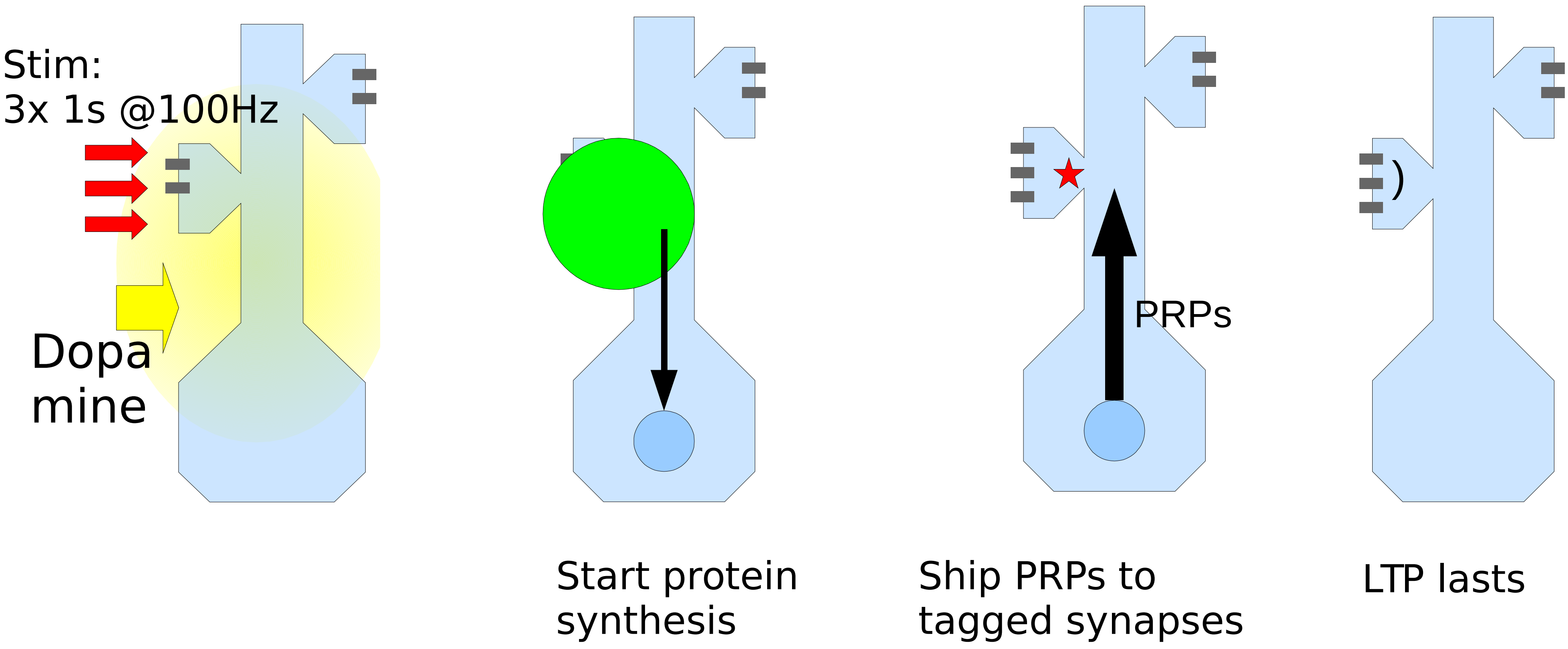
But gone
after few hours

Late LTP requires protein synthesis



[Fonseca et al 06]

Late phase LTP



LTP stages

Induction:

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- Mechanism: NMDA and Ca influx

Expression:

- Early LTP (1 hr):
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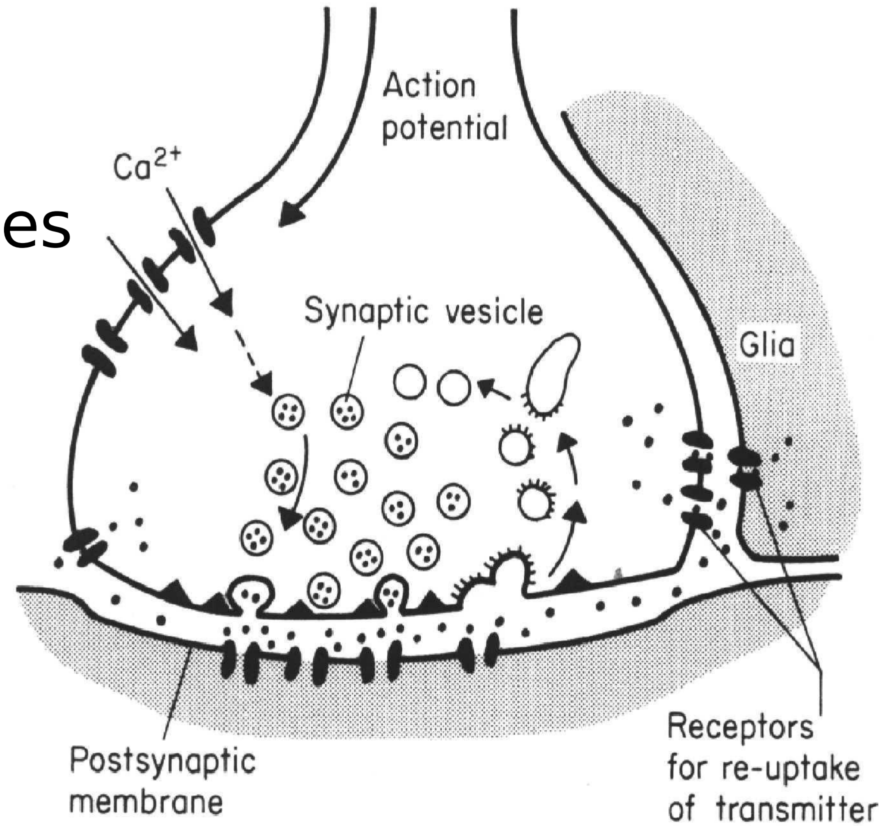
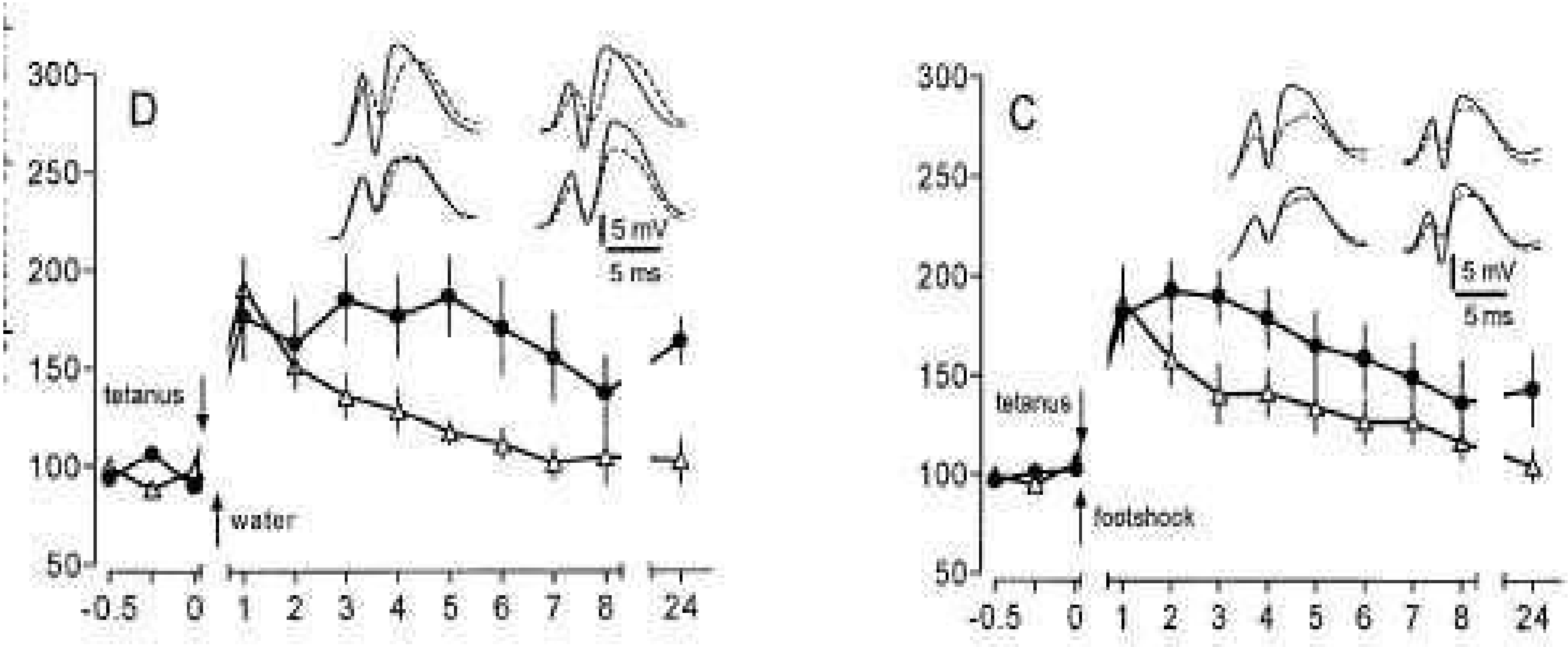
    - AMPAR phosphorylation
    - AMPAR insertion
- **-Late phase LTP**
    - -requires protein synthesis



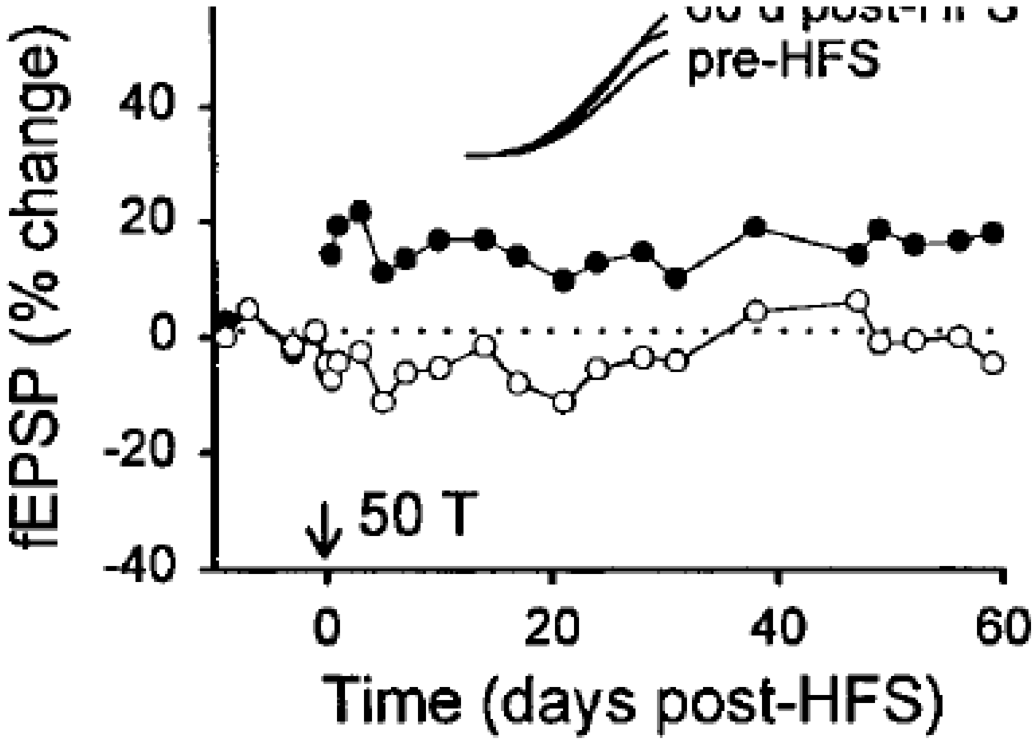
What determines if LTP lasts?

Reward and punishment



[Seidenbecher '95]

Longevity: In vivo physiology

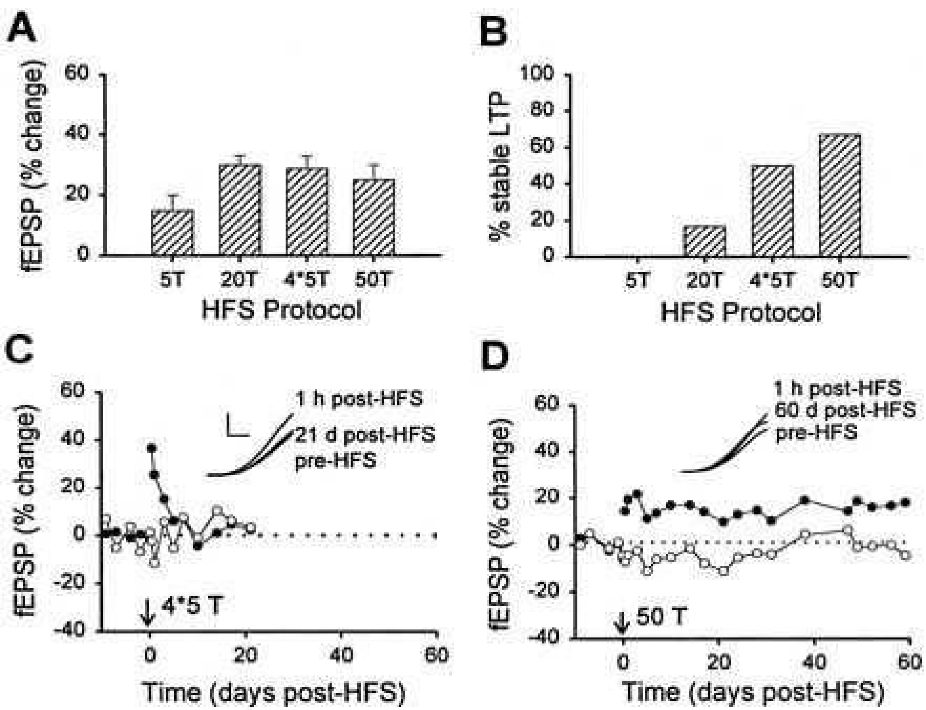


[Abraham '02]

- Strong extracellular stimulation, leads to long lasting strengthening of synapse [Bliss and Lomo '73]

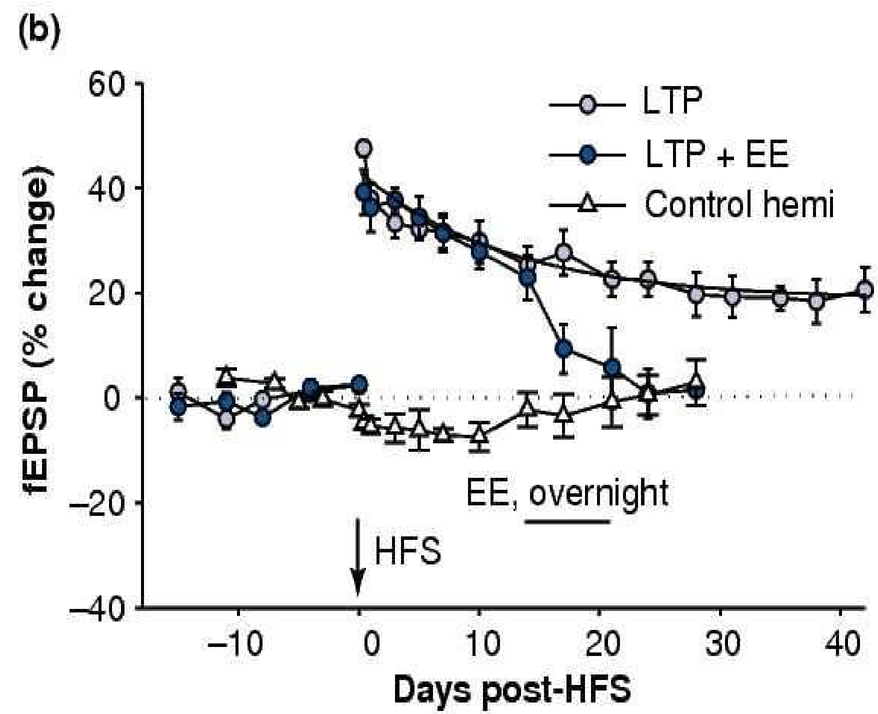
What determines if LTP lasts?

Stimulus protocol



[Abraham '00]

Environment



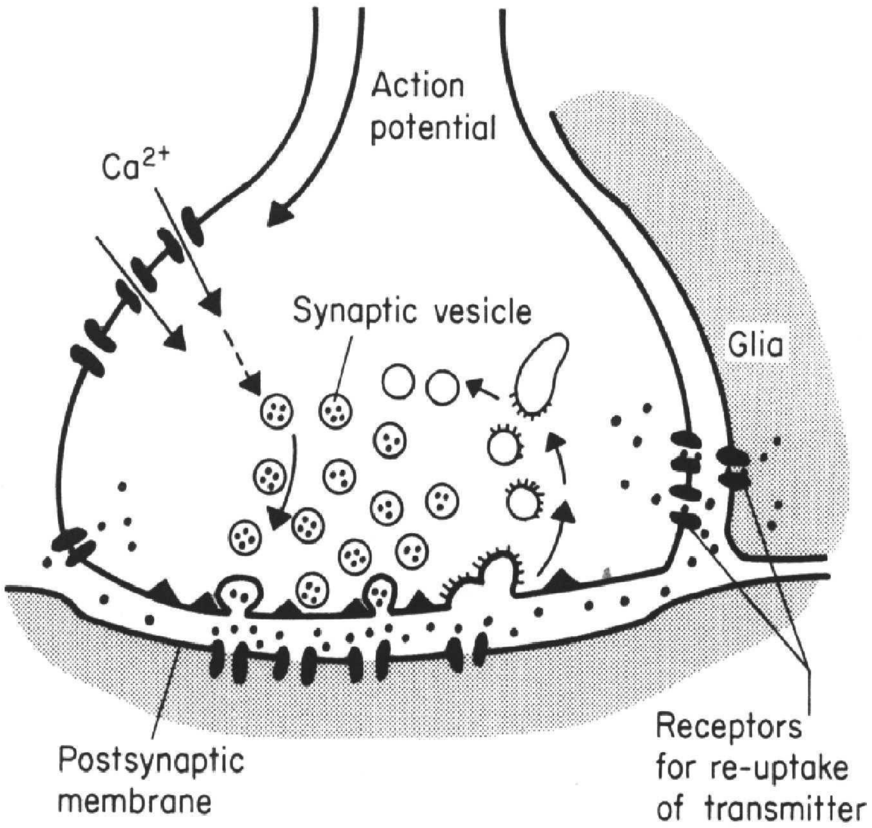
[Abraham '02, Li & Rowan '00]
(Dopamine mediated)
Does a novel environment 'reset' hippocampal learning?

LTP stages

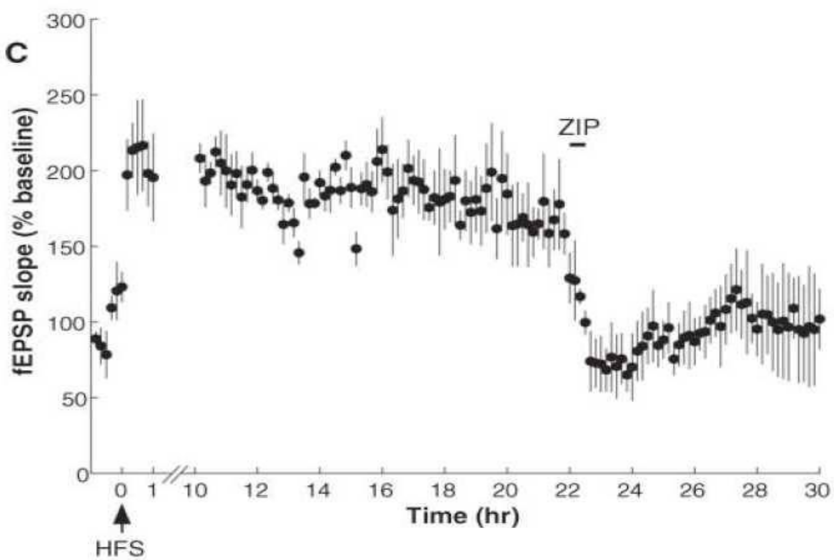
Induction

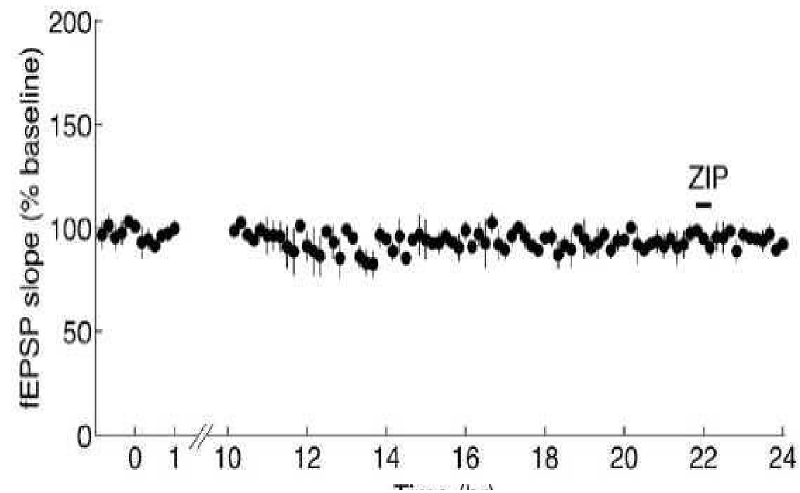
Expression

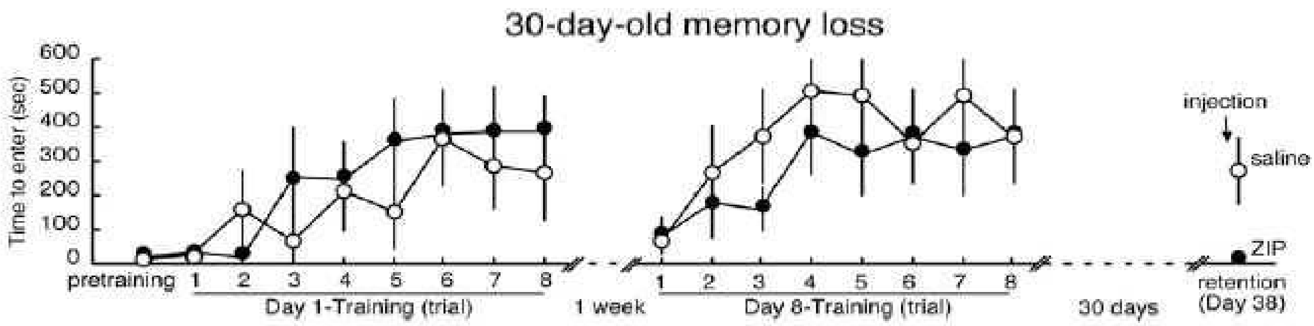
Maintainance



LTP maintenance as an active process







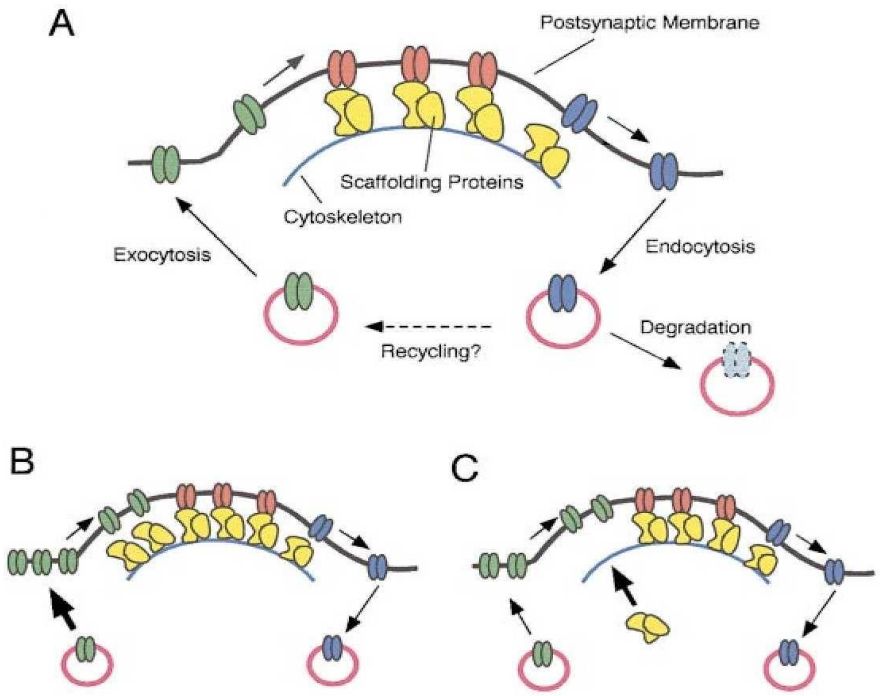
ZIP disrupts one month old memory [Pastalkova et al '06]

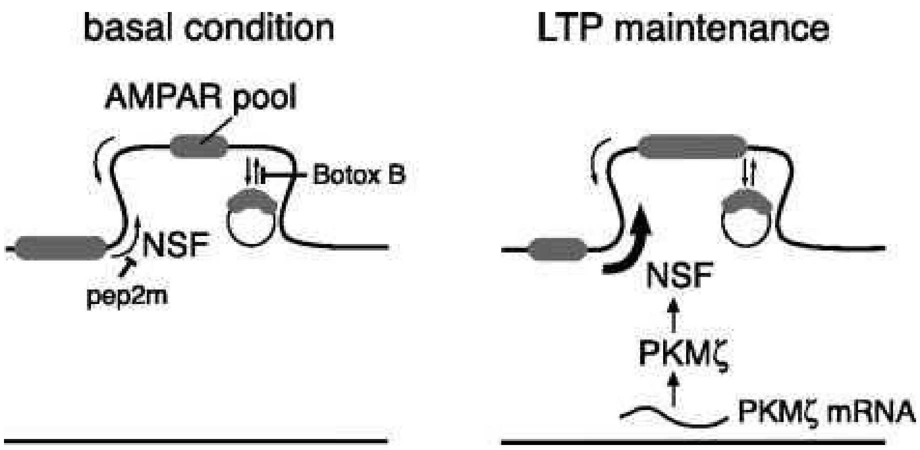
[movie demo]

Hypotheses for maintaince / long term stability

Slots for AMPA receptors

GluR2 trafficking

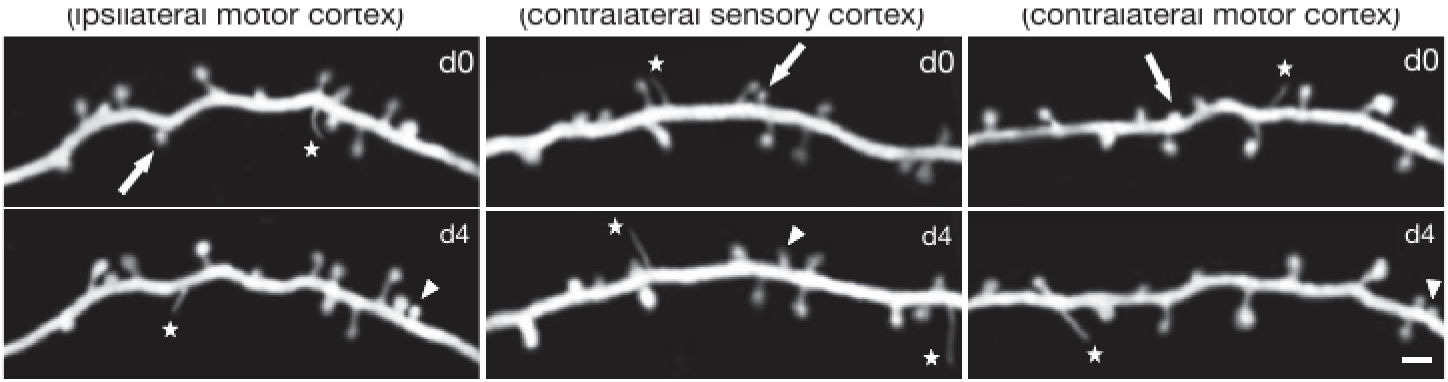


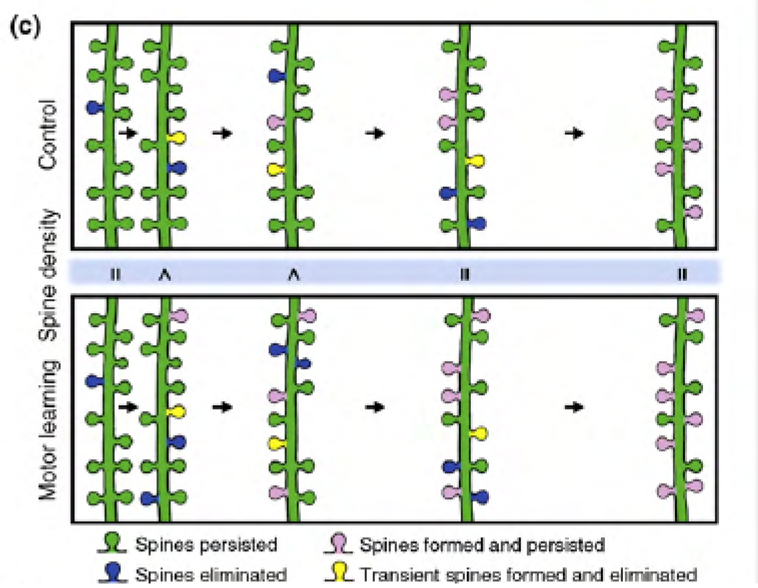


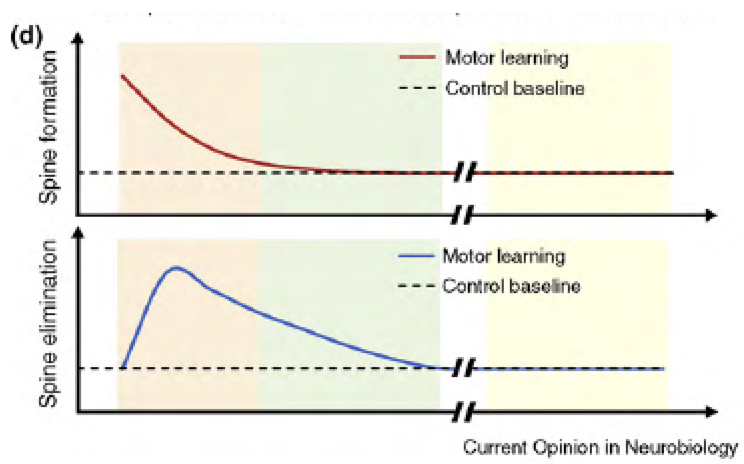
[Turrigiano '02]

[Yao & Sacktor '08]

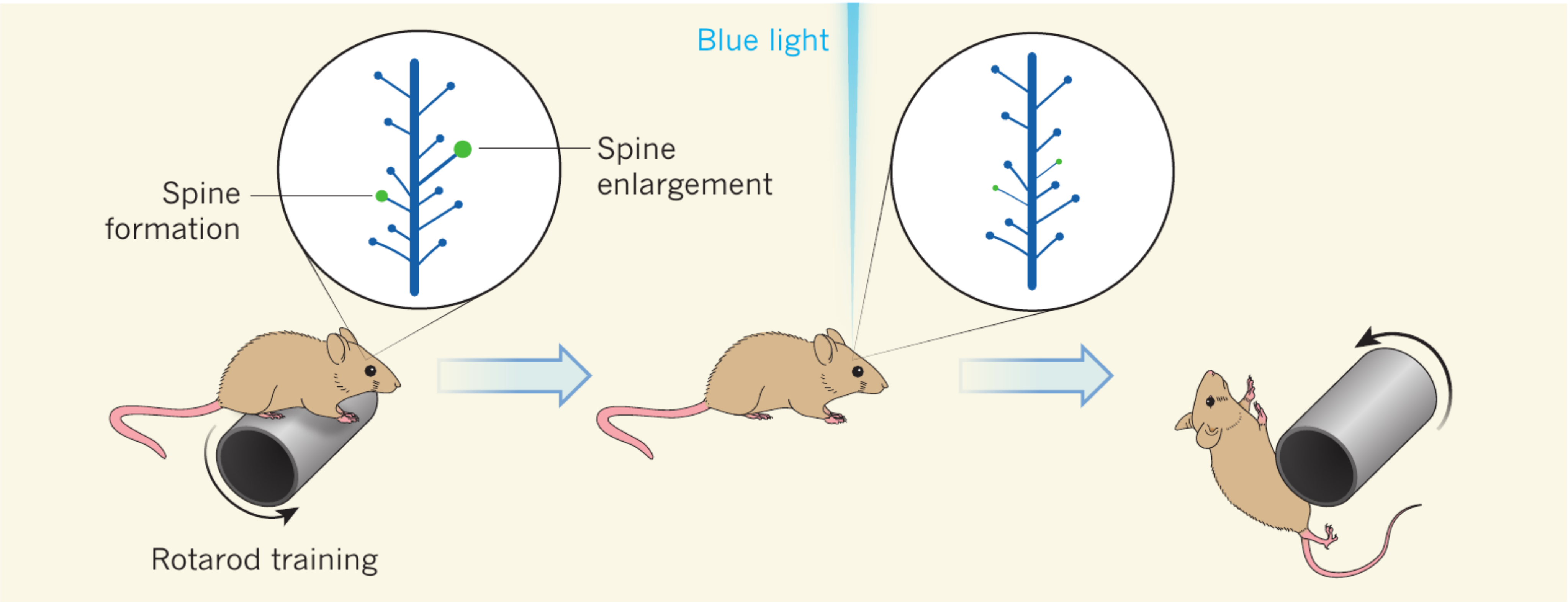
Spine plasticity







Yu Zuo Curr Opin Neurobiol (2010)


Blue light
Spine formation
Spine enlargement
Rotarod training