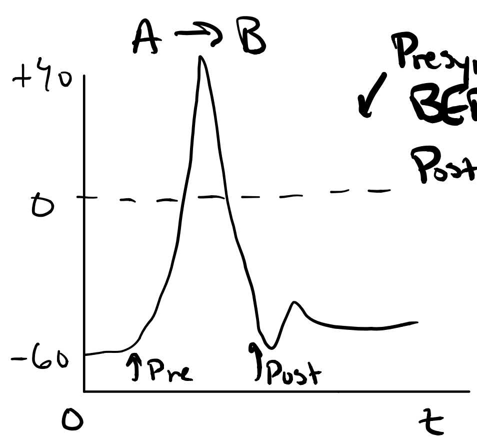
Pre-Lecture Video

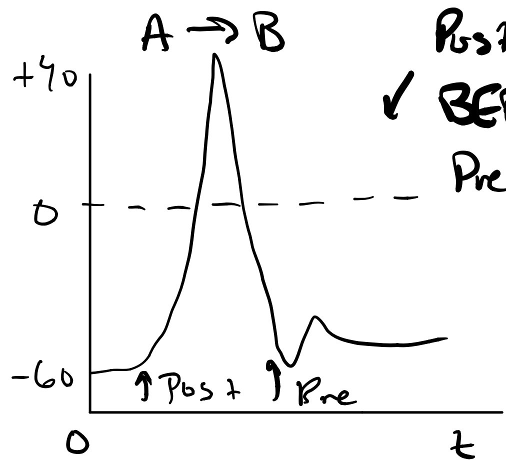
- Neural activity triggers the activation of postsynaptic, second messenger symptoms
- Trigger is usually an alteration in the level of intracellular Ca^{2+} in postsynaptic neuron.
- Ca-dependent second messenger systems alter activity of protein kinases + phosphatases
- alterations in protein phosphorylation mediates early stages of long-term synaptic plasticity.

Spike-Timing Dependent Plasticity

A framework for understanding plasticity one postsynaptic spike at a time.



✓ Presynaptic **BEFORE** Postsynaptic



✓ Postsynaptic **BEFORE** Presynaptic

Lecture 19. Learning 4- Spike Timing Synaptic Plasticity

Professor Christiane Linster

Pre-lecture preparation

(1) Watch pre lecture video on spike-timing dependent plasticity
(2) Read pages 889-891, Figure 25.18
(3) Optional read Box 25.3 pages 880 -881
(4) Read Box 25.2 page 878 and text associated with Figure 25.12 page 882
(5) Read pages 846-852; Figures 24.19-22.

Learning Objectives

To understand the nature of spike-timing-dependent plasticity (STDP) and its role in learning

(1) Be able to understand how spike timing dependent plasticity was discovered
(2) Be able to compare and contrast STDP and LTP/LTD and understand how they relate to each other
(3) Be able to understand the relative computational advantages of STDP
(4) Be able to apply STDP to a simple experimental example

Lecture Outline

(1) Classic LTP/LTD experiments use relatively unnatural stimulation patterns to induce plasticity which do not correspond to natural spike trains (Page 880: Weakening synapses).
(2) More detailed experiments show that the timing between pre and postsynaptic activation can be important for the induction of plasticity; these findings are called spike timing dependent plasticity or STDP (Box 25.2 page 878 and Figure 25.12 page 882
(3) STPD creates a self normalizing learning rule for spike trains in which synaptic weights are stabilized and the rule is resistant to noise
(4) We review experiments using naturalistic spike trains to illustrate how plasticity might occur in nature.
(5) This type of plasticity might be especially relevant for learning of temporal sequences such as path integration.
(6) We review the concept of place cells and place fields in hippocampal cells and illustrate how STDP could contribute to their formation (Figure 24.21 and associated text).

Study Questions

(1) When pre and postsynaptic spike trains occur randomly at different average frequencies, how would LTP or LTD dominate in a classical view (correlation) or in the STDP framework?
(2) How could you determine to what degree only nearest neighbor action potentials (closest in time) contribute to plasticity in STDP?
(3) How would you choose parameters of the STDP rule to avoid all synapses growing or all synapses shrinking?
(4) How would parameters of STDP vary for learning paradigms with different time scales?

Lecture 19: Spike timing dependent plasticity

Christiane Linster
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Office hours Wed. 1:30-2:30 or by appointment

Lectures 16-21: Learning and memory

Lecture 16 NMDA receptor allows to “associate” two events at the level of a synapse

Lecture 17 Learning at the synaptic level: LTP and LTD

Lecture 18 Learning at the network level: how are LTP and LTD involved in changing networks ?

Lecture 19 **Learning while behaving: sequences of events and STDP**

Lecture 20 Remembering: Consolidation of what has been learned

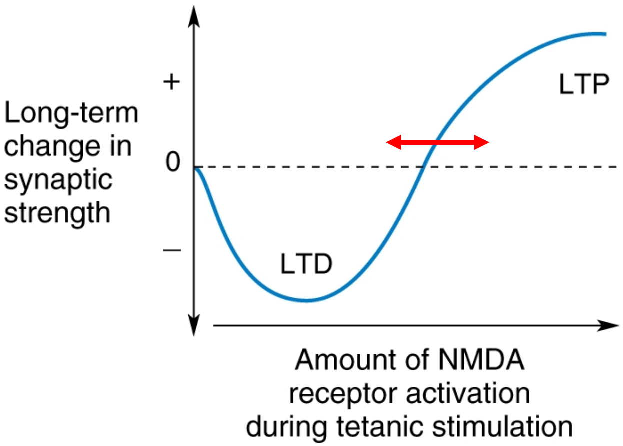
Lecture 21 What is a memory?

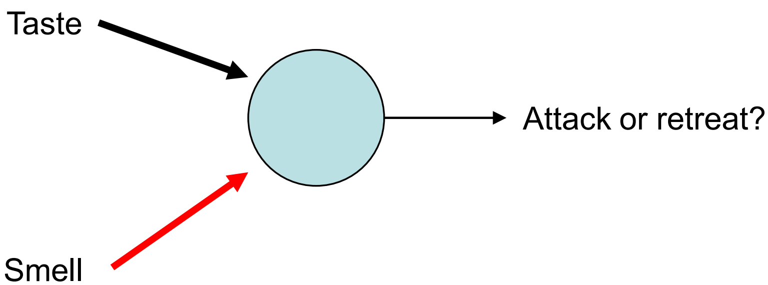
Lecture 18: Learning 3

Synaptic plasticity and learning

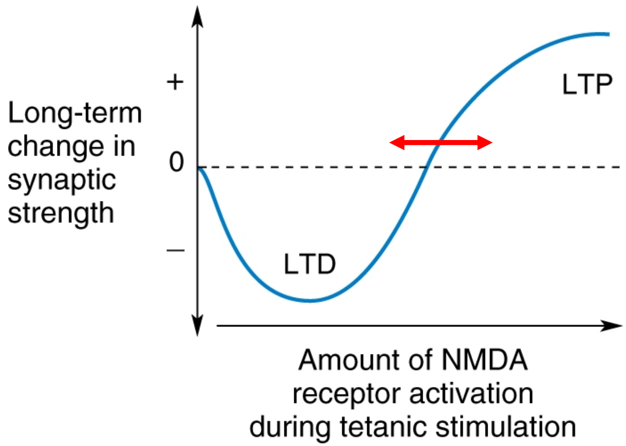
(1) Be able to understand how spike timing dependent plasticity was discovered
(2) Be able to compare and contrast STDP and LTP/LTD and understand how they relate to each other
(3) Be able to understand the relative computational advantages of STDP
(4) Be able to apply STDP to a simple experimental example

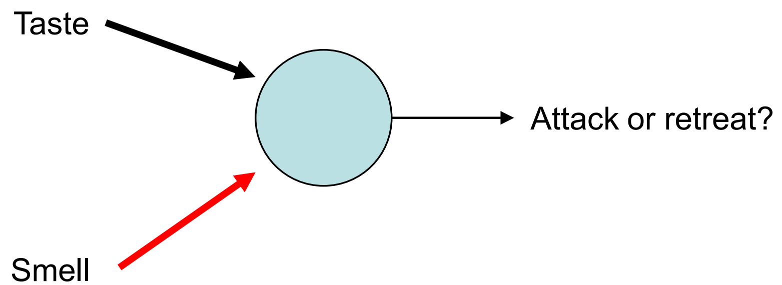
Increased and decreased synaptic strength : computational power and issues





Clicker question





Modulation of short term synaptic plasticity can move the LTP induction threshold

A. True

B. False

Hebbian learning : pro and cons?

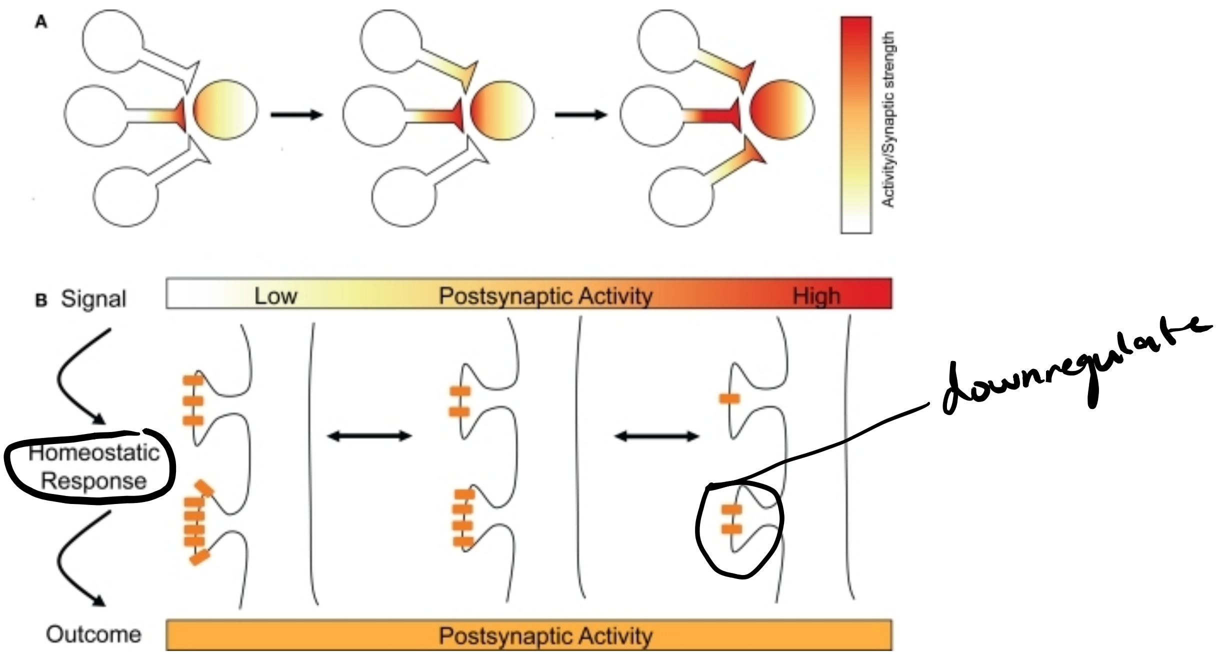
Pros

- local computations
- create associations

Cons

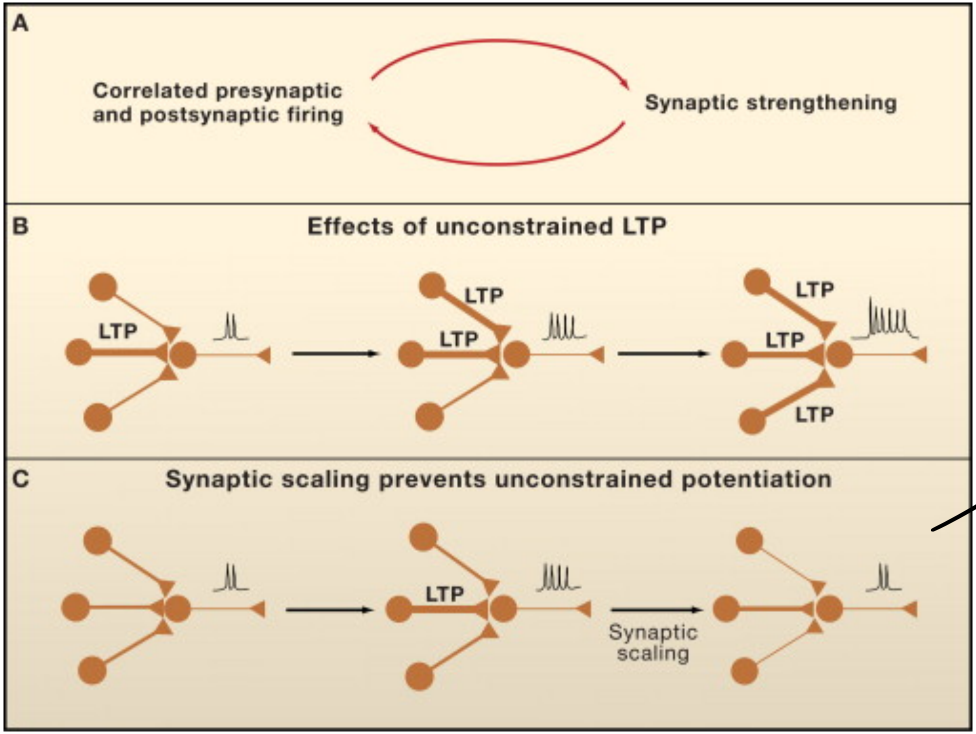
- energy cost
- unwanted associations
- "explosions"

(1) Run-away synaptic plasticity and a need for normalization



Watt AJ, Desai NS - Frontiers in synaptic neuroscience (2010)

(1) Run-away synaptic plasticity



↑ strength
ratios maintained

DOI:https://doi.org/10.1016/j.cell.2008.10.008

Homeostasis is needed to keep activity balanced

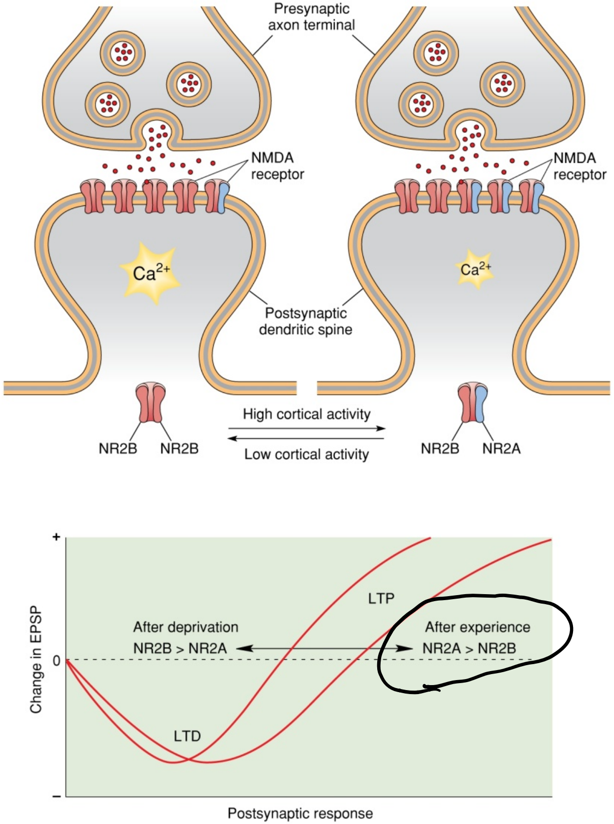
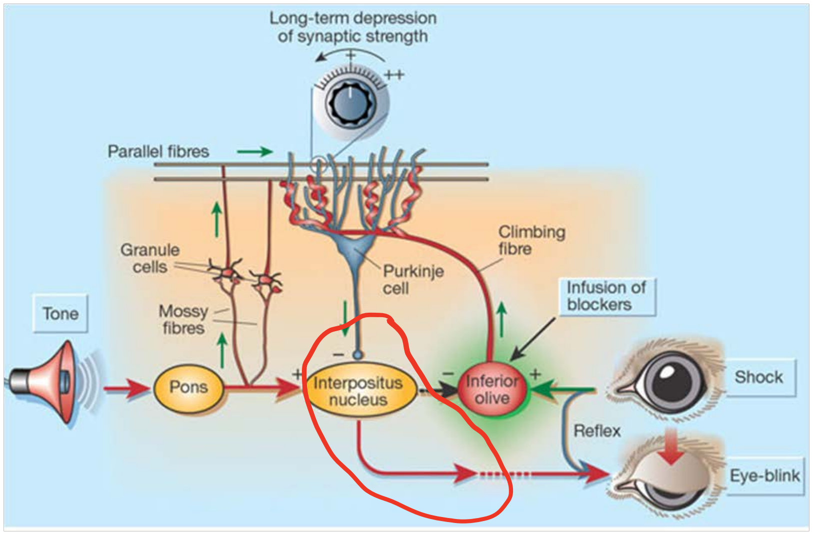
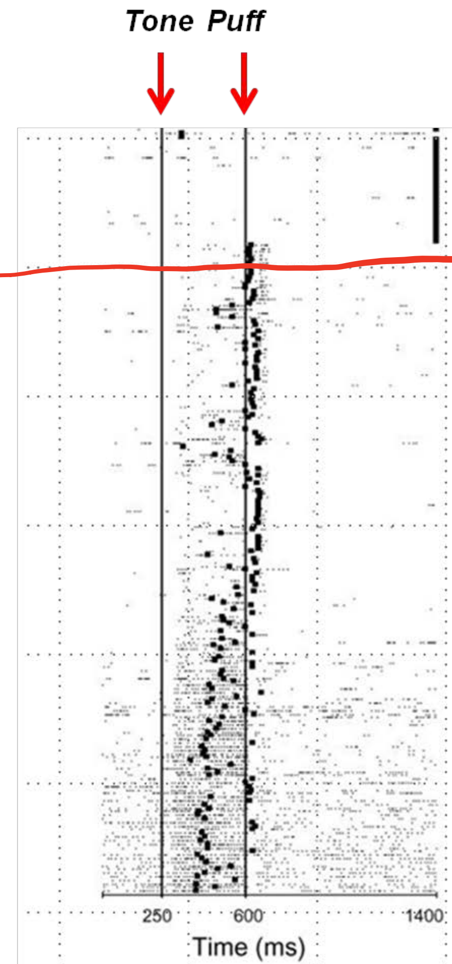


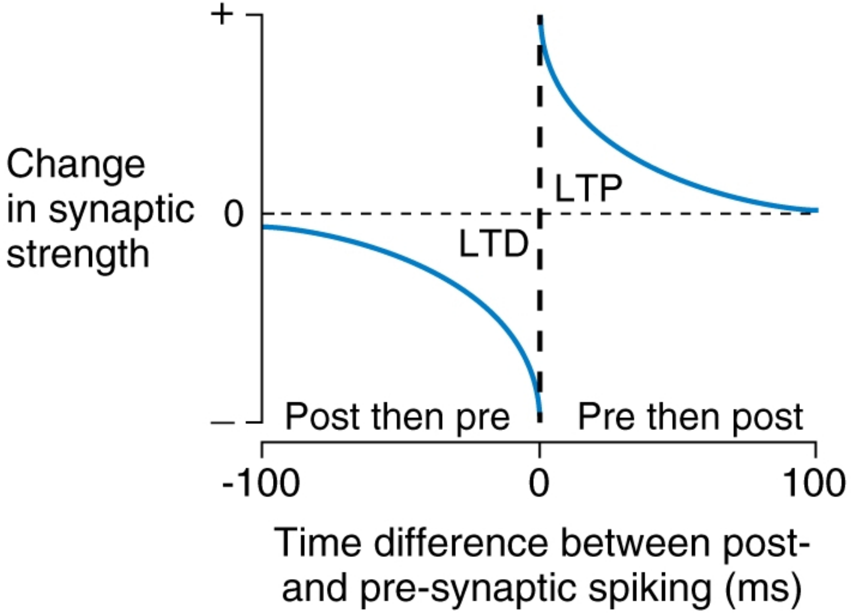
Figure 25.18

(2) Real life spike trains are noisy!

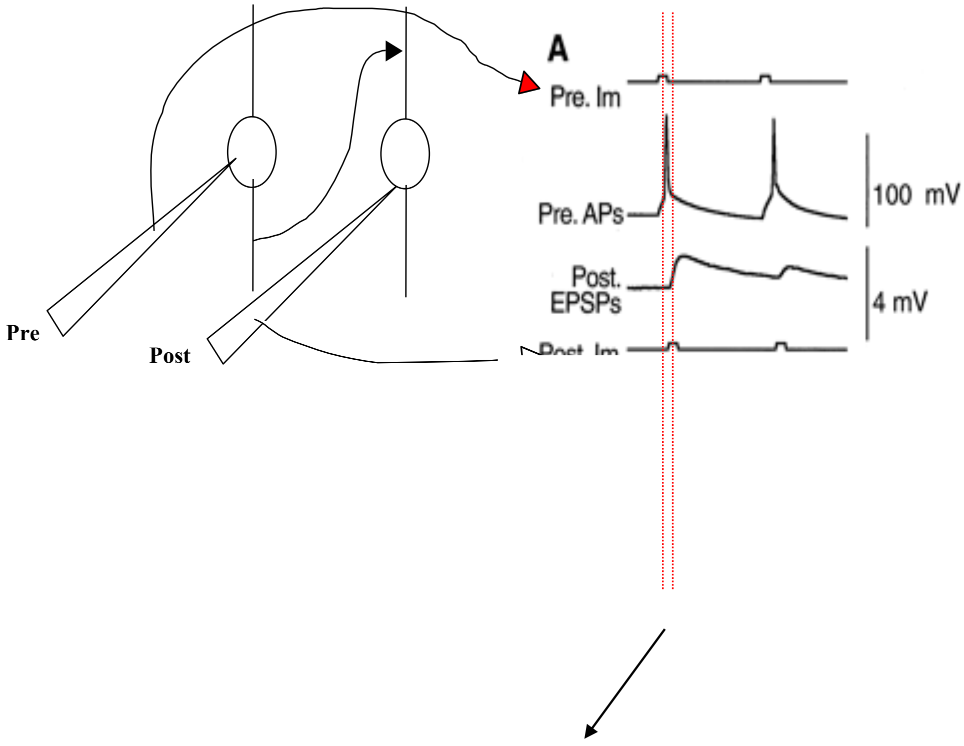




Real life plasticity does not follow simple "active at the same time" rule

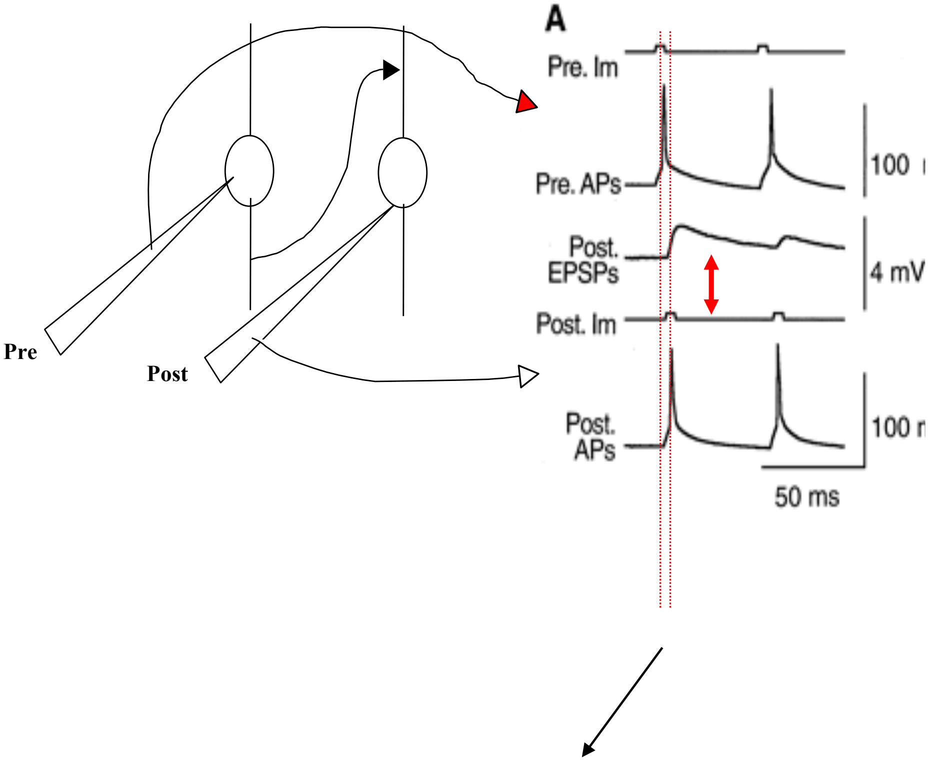


Real life plasticity does not follow simple "active at the same time" rule



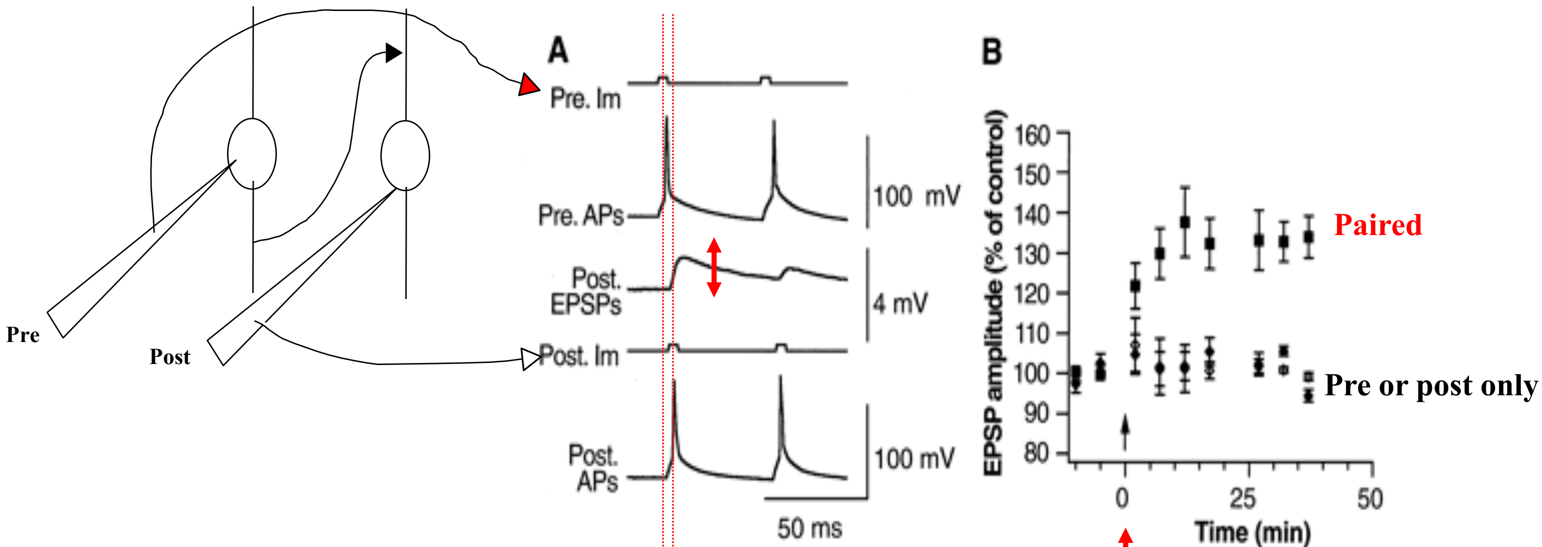
$t_{post} - t_{pre} = 5ms$

Real life plasticity does not follow simple “active at the same time” rule



$t_{post} - t_{pre} = 5ms$

Real life plasticity does not follow simple “active at the same time” rule



$t_{post} - t_{pre} = 5ms$

Repeated pairing (20x)

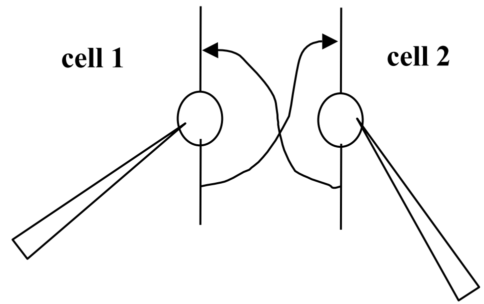
Due to pre AP

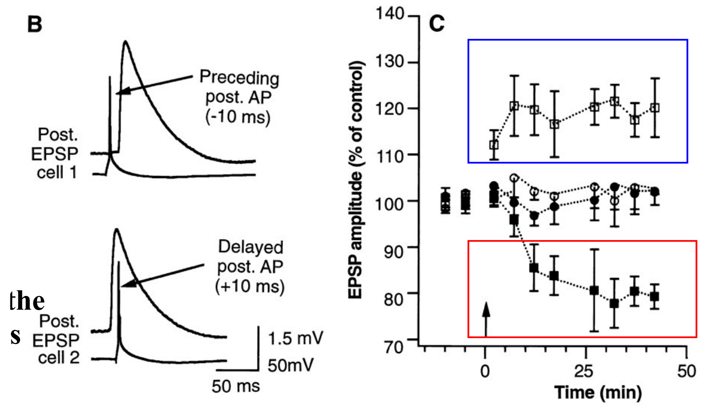
AP before EPSP: weakening of synaptic strength

EPSP before AP: strengthening of synaptic strength

Pre → Post LTP

Post → Pre LTD





Bursts of AP triggered 10 ms apart

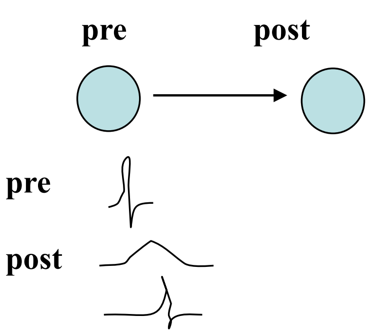
KNOW THIS

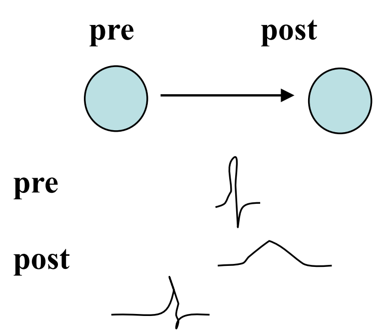
Summary:

1) If a pre-synaptic cell fires BEFORE a connected postsynaptic cell, the synapse connecting them increases in strength LTP

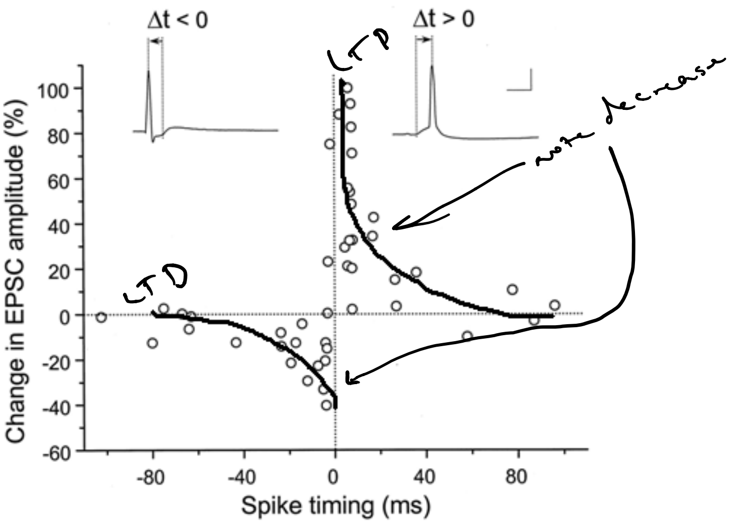
2) If pre-synaptic cell fires AFTER a connected postsynaptic cell, the synapse between them decreases in strength

LTD

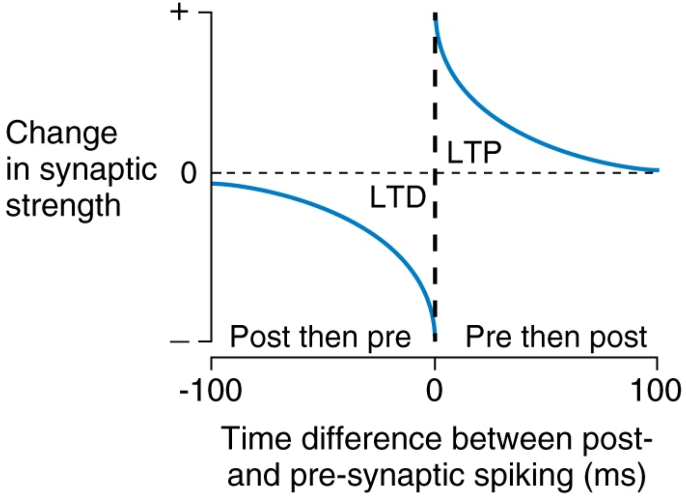




Spike timing dependent plasticity rule

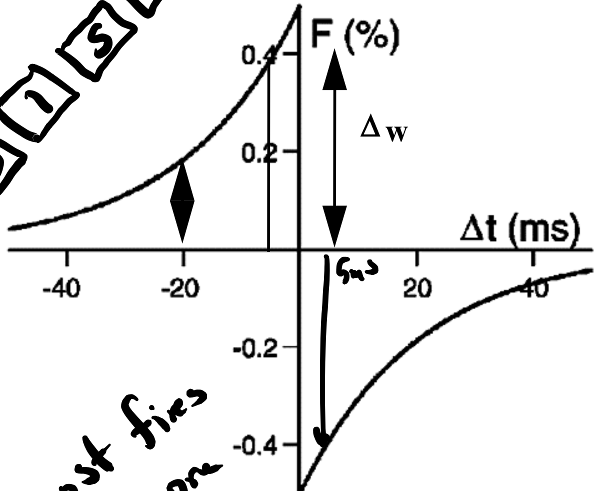


Bi, GQ and Poo, MM. Synaptic modifications in cultured hippocampal neurons: dependence on spike timing, synaptic strength, and postsynaptic cell type.
J Neurosci. 1998 Dec 15;18(24):10464-72.



Clicker question

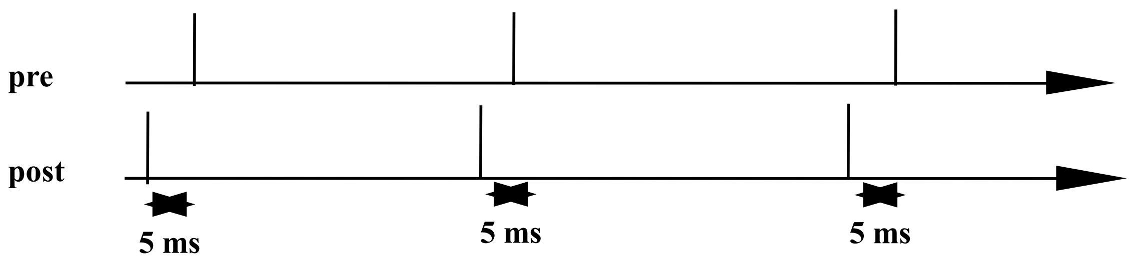
N O I S Y B O Y



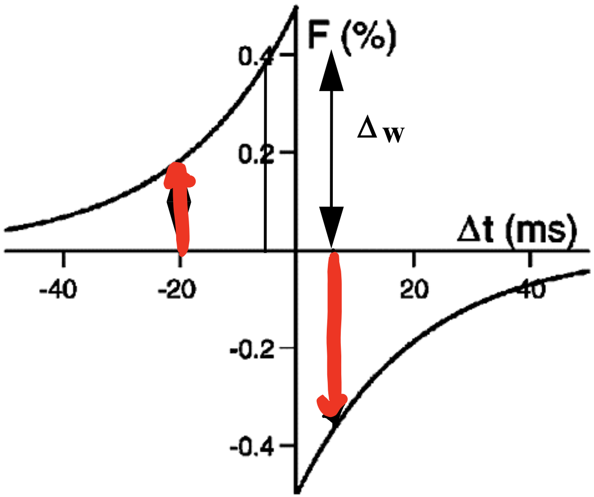
Given the pre and postsynaptic action potential sequence depicted below, you would expect a

A. 1.2 % increase in synaptic weight
B. 1.2 % decrease in synaptic weight
C. No change

Note post fires before pre

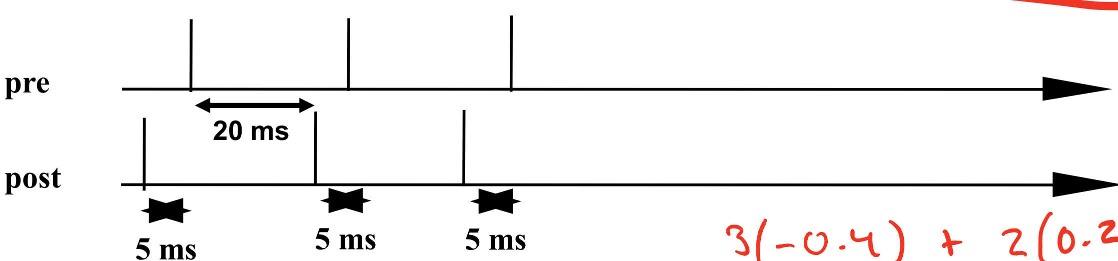


Clicker question



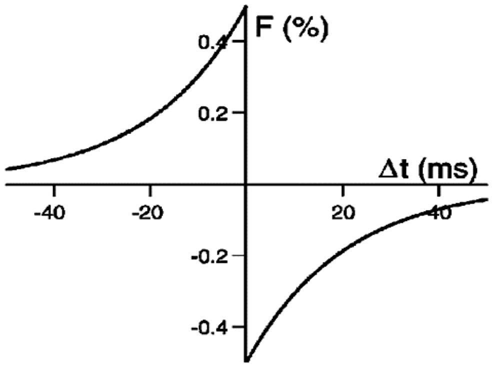
Given the pre and postsynaptic action potential sequence depicted below, you would expect a

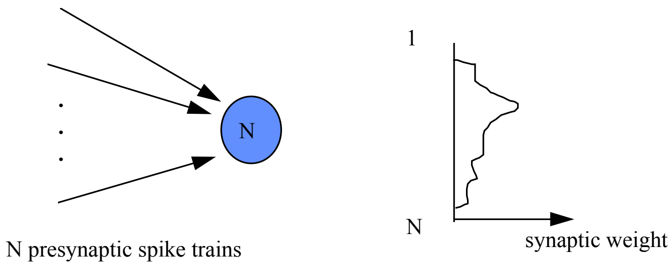
A. 0,4 % increase in synaptic weight
B. 1.2 % decrease in synaptic weight
C. 0.4 decrease in synaptic weight
D. 0.4 increase in synaptic weight
E. No change



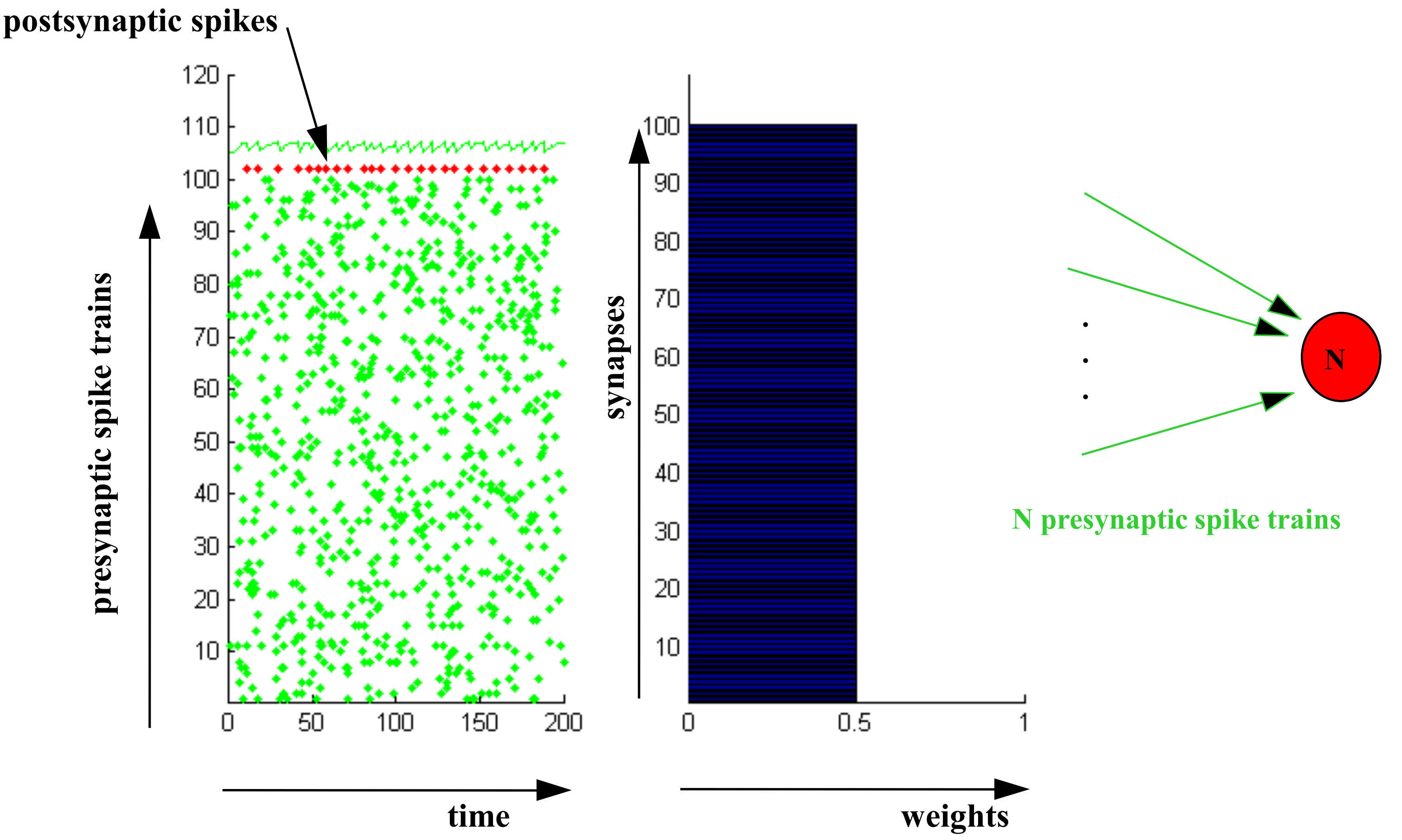
$3(-0.4) + 2(0.2) = 0.8\% \downarrow$

STDP has a built-in normalization function





STDP has a built-in normalization function



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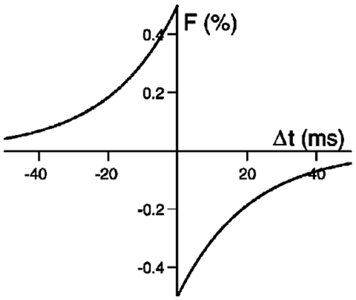
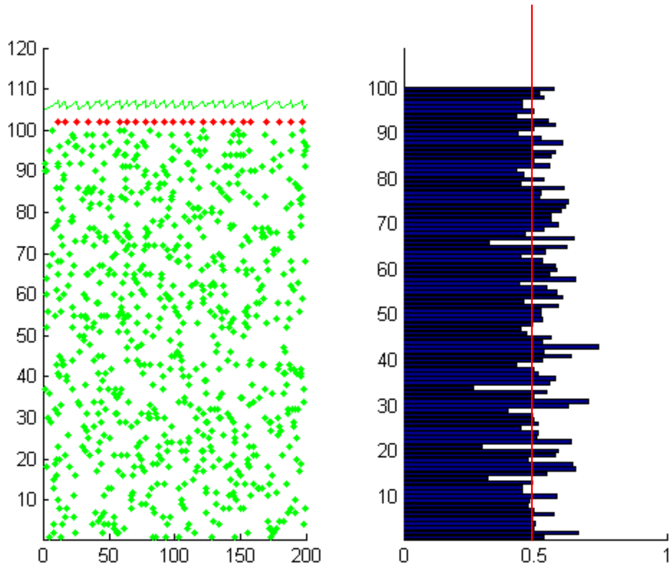
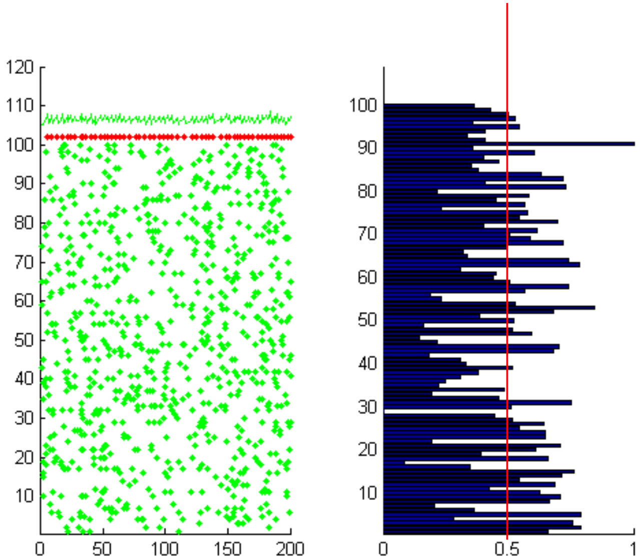
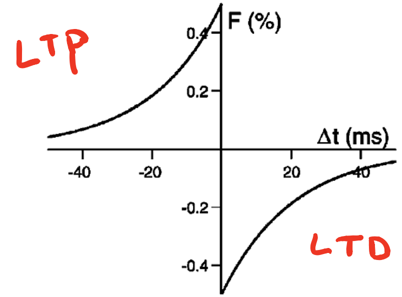






Clicker question



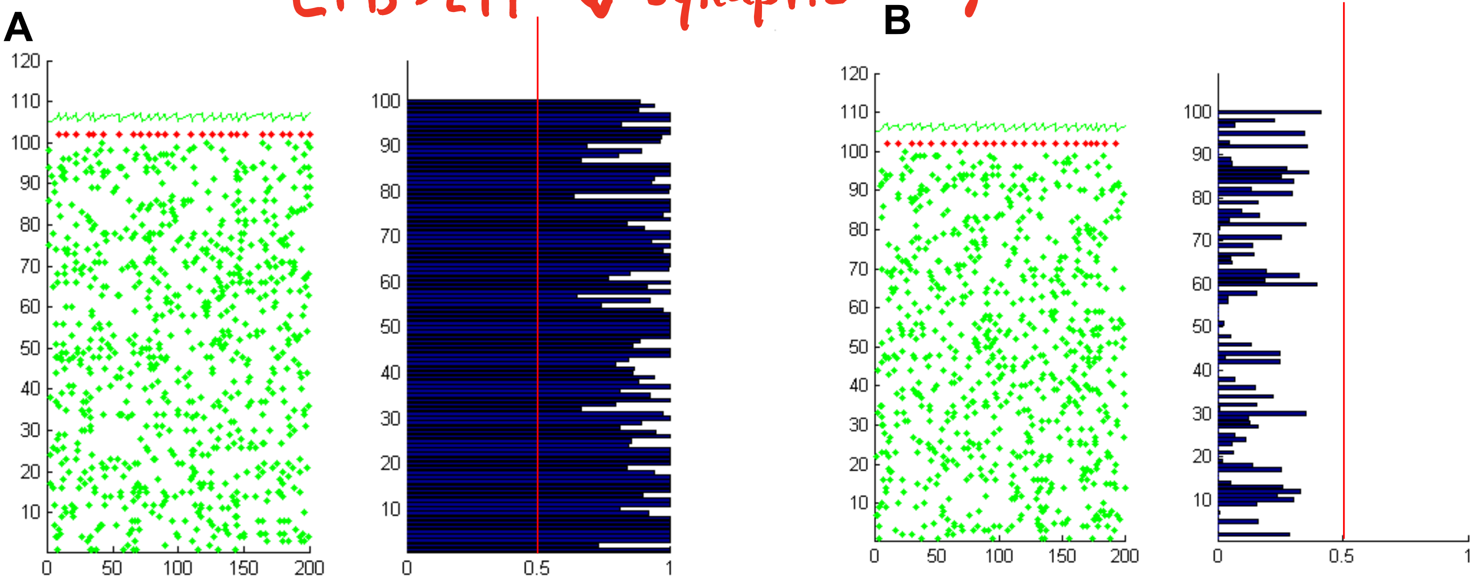
Results in B happen when

A. The areas under both curves are equal

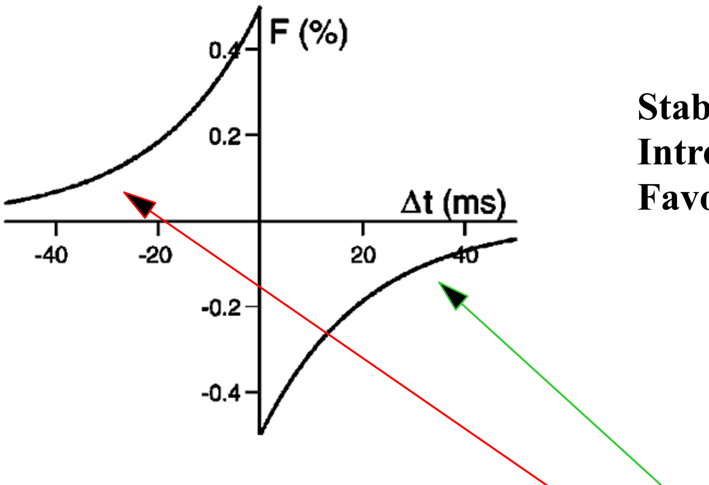
B. The area under the LTD part of the curve is larger

C. The area under the LTP part of the curve is larger

LTD > LTP ↓ synaptic weights

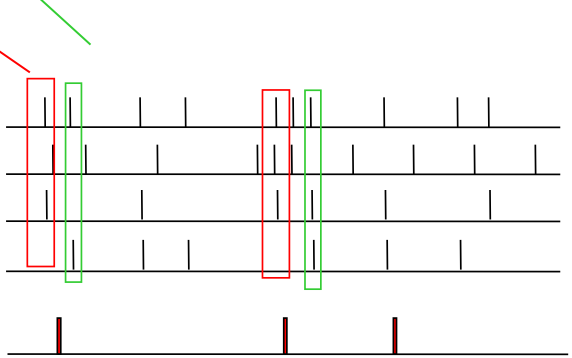


STDP has a built-in normalization function

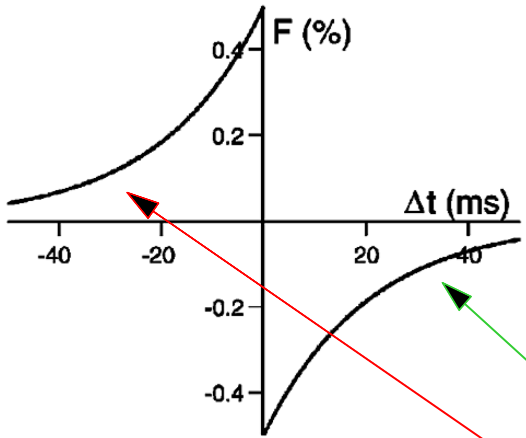


Stabilizes Hebbian learning
Introduces competition
Favors synchronous presynaptic events

$\Delta t = \text{time}_{pre} - \text{time}_{post}$



STDP has a built-in normalization function



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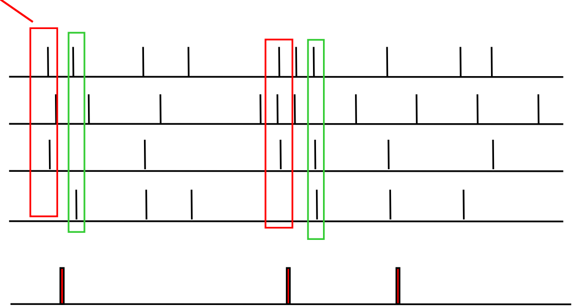
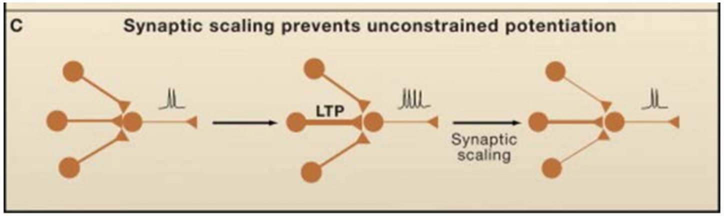
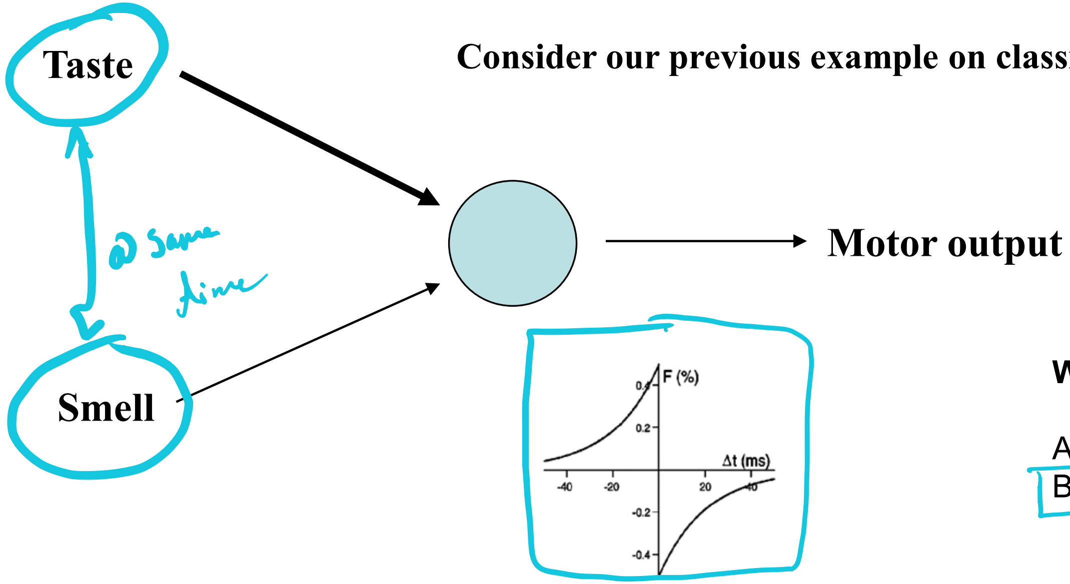




Clicker question

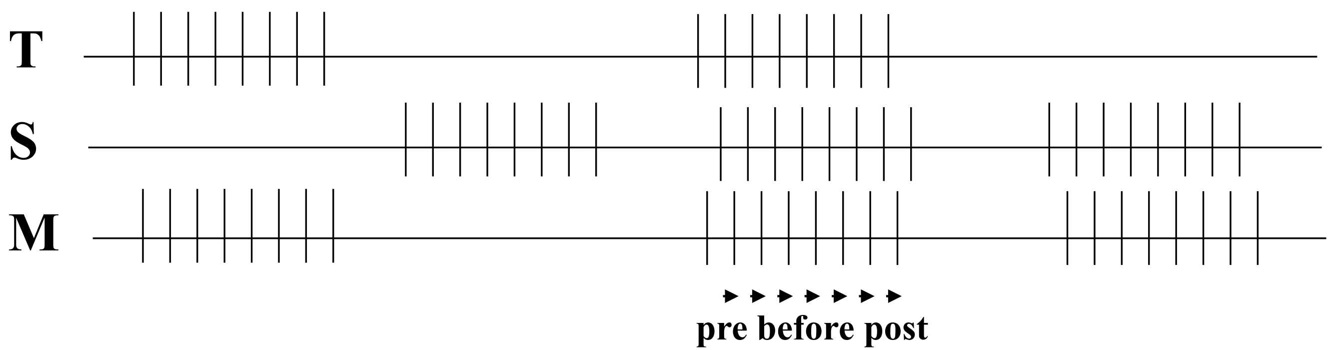
Consider our previous example on classical conditioning:



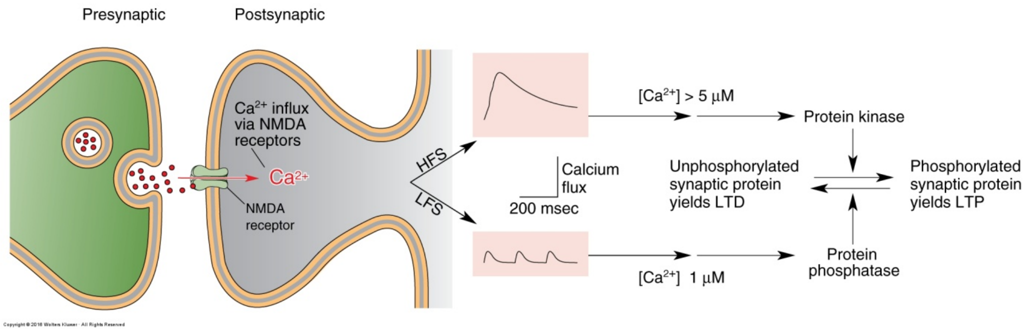
Will this work?

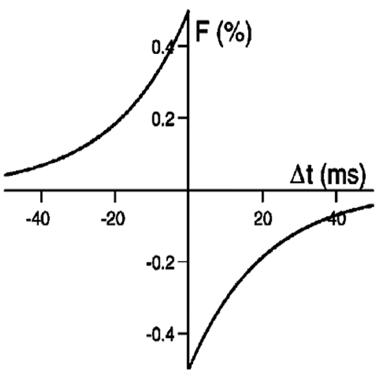
A. Yes ← depends on exact temporal structure

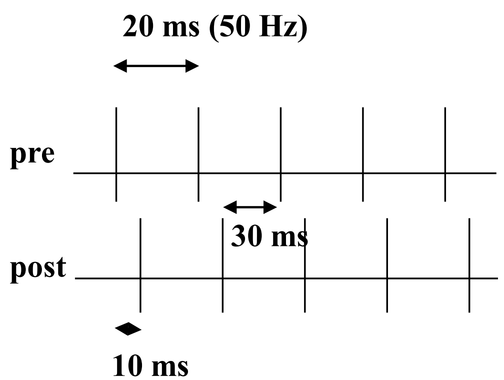
B. No



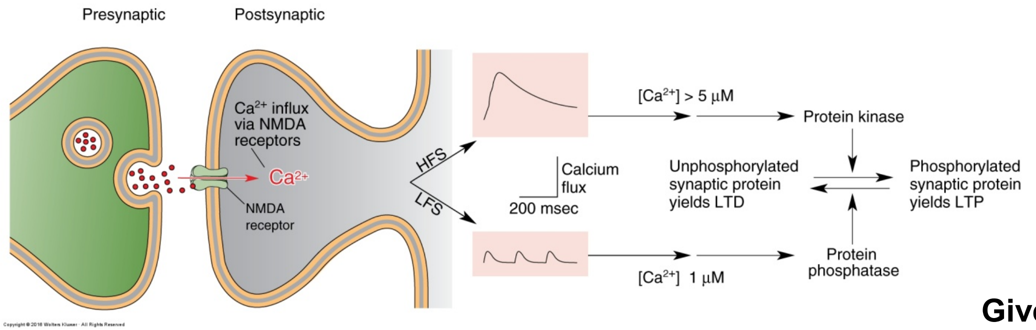
How can we look at this in the light of what we know about LTP/LTD?

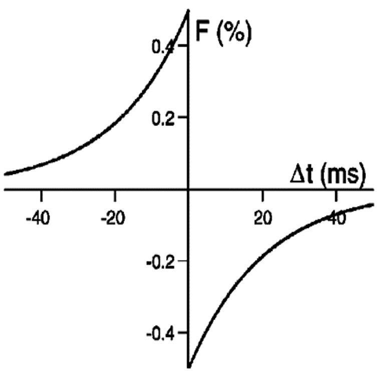


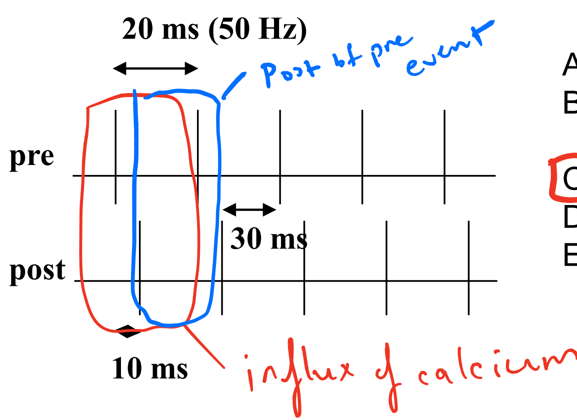




Clicker question





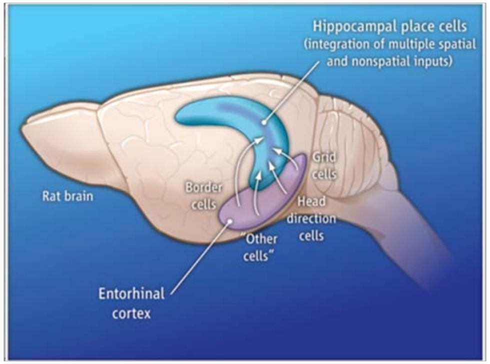


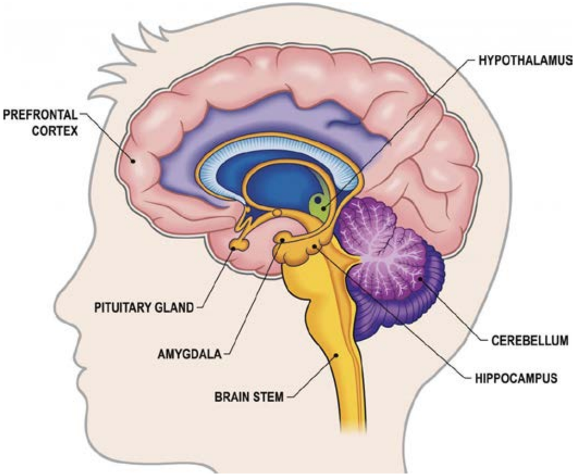
Given what you have learned about calcium, LTP and LTD, which hypothesis do you support?

A. Spike time effects add up linearly
B. Only nearest neighbor spikes have an effect
C. LTP overrides LTD
D. LTD overrides LTP
E. OTHER

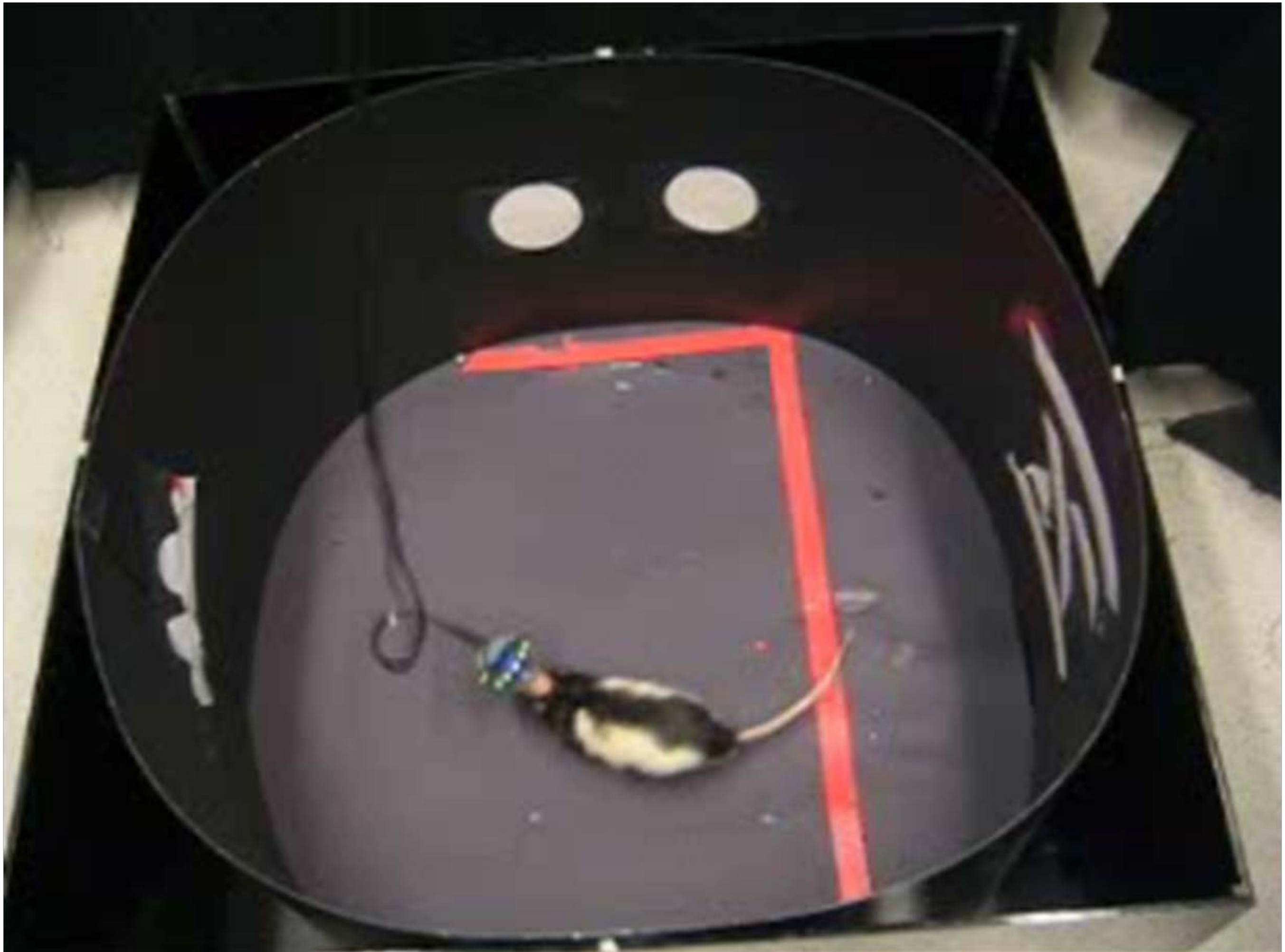
- Ca is only added, not removed

STDP learning rule and sequence learning

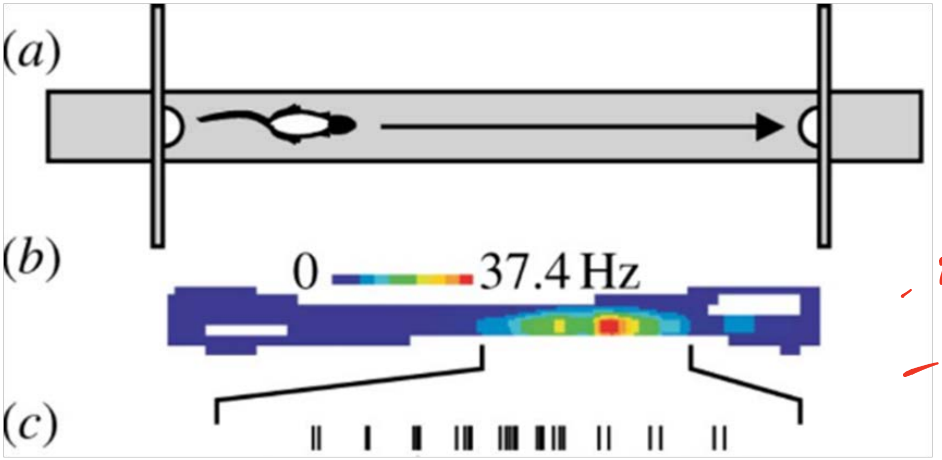




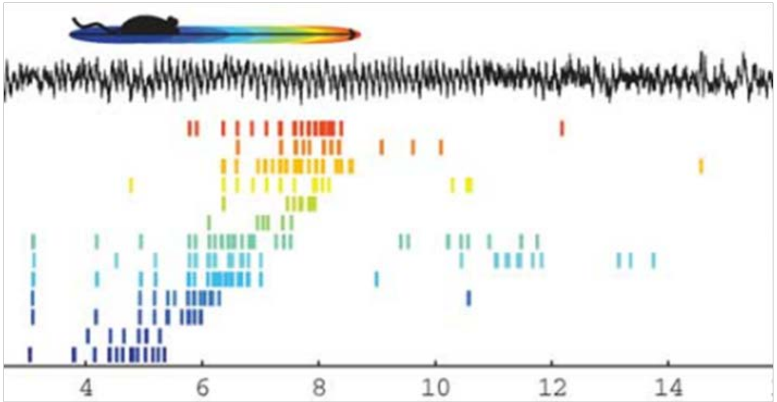
Some cells in the hippocampus fire preferentially when a rat (mouse) in a specific spatial location



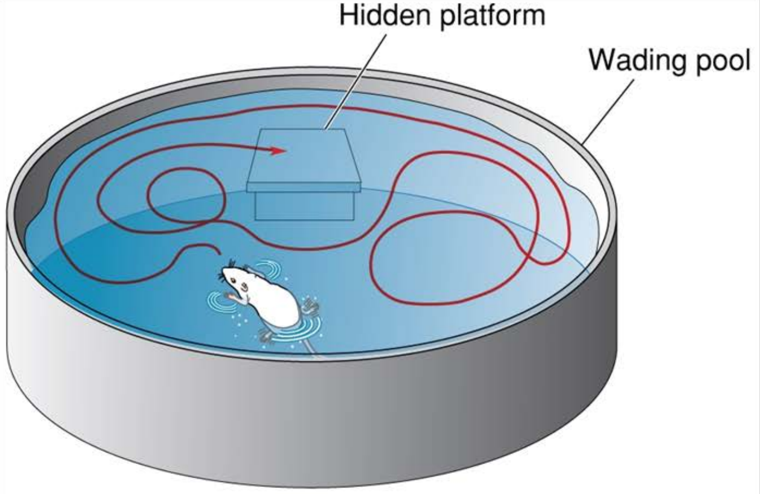
Hippocampal place cells fire in sequence as rats moves



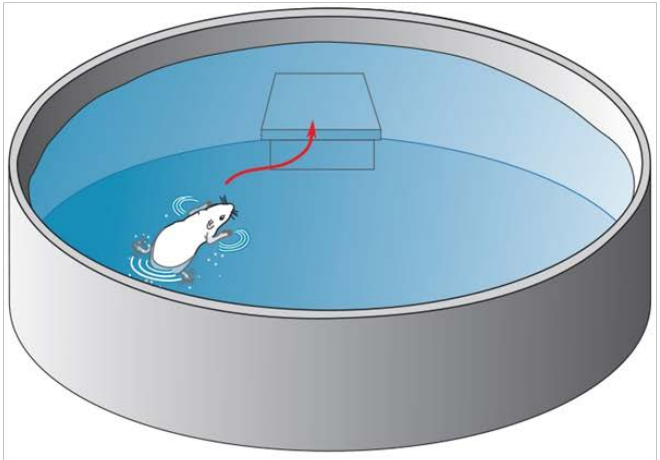
- place cells
- place fields



Hippocampal lesions impair spatial learning



(a) Before learning

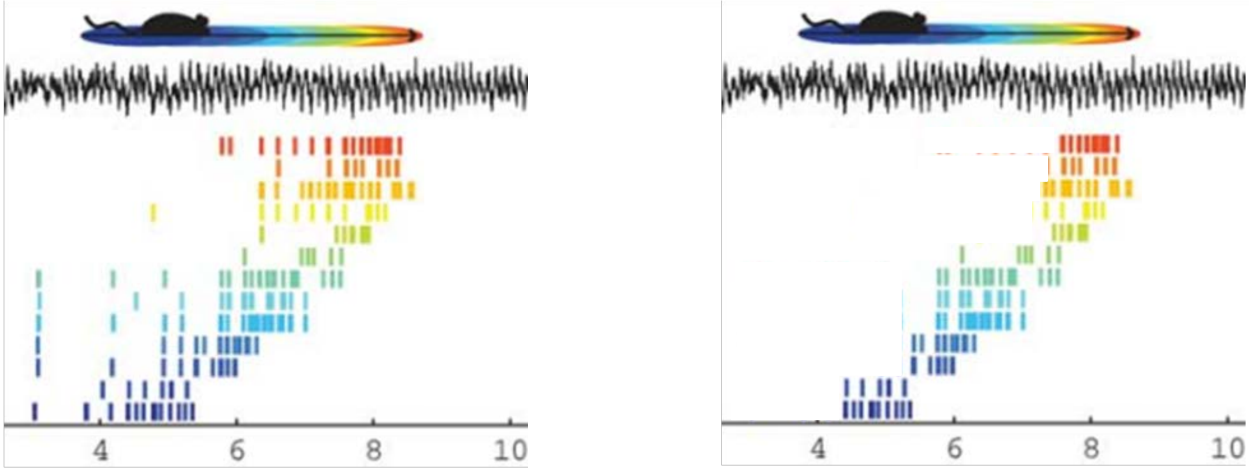


(b) After learning

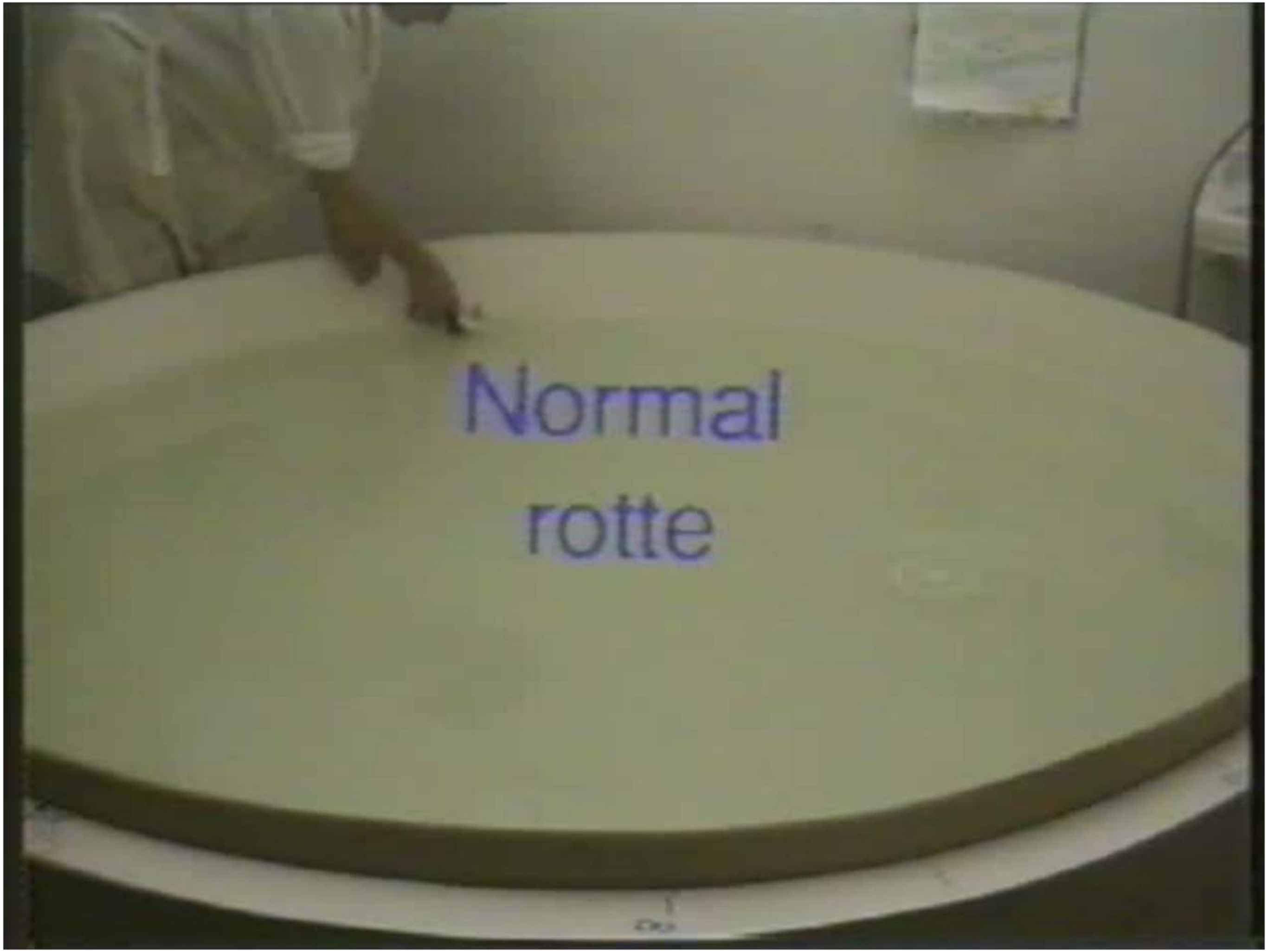
* Experience-dependent changes of place fields could result from the LTP and LTD of NMDA-dependent synapses.

•NMDA-dependent synapses are strengthened if postsynaptic activity lags behind presynaptic spiking and depotentiated if the converse is true

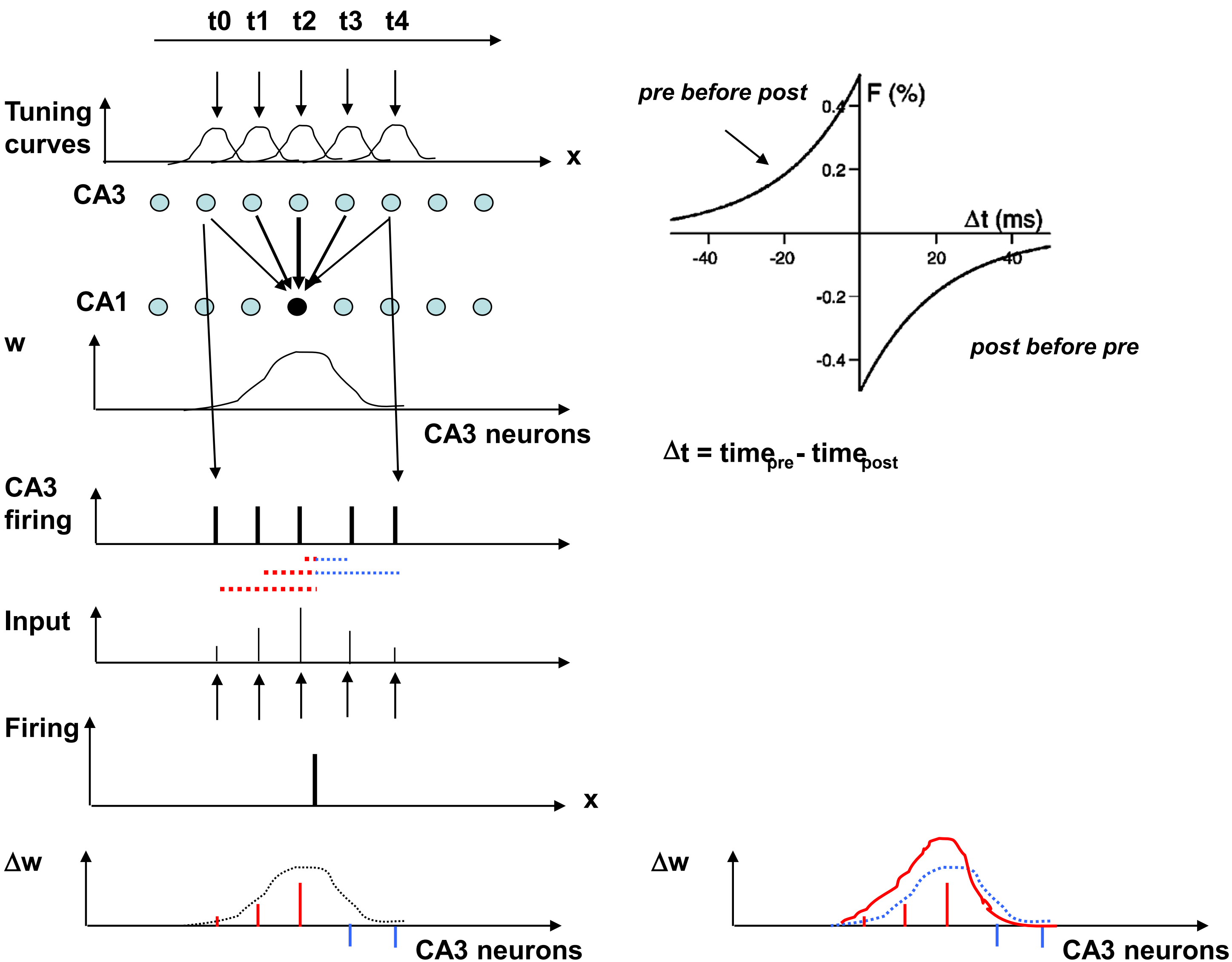
•STDP can explain how sequences of place cells fire as animal moves along the path



Place cells become more narrowly tuned as animals learns the path.
This could happen through STDP because STDP favors preceeding spikes


Normal
rotte


Hippocampus-skadet
rotte


t0 t1 t2 t3 t4
Tuning curves
x
CA3
CA1
w
CA3 neurons
CA3 firing
Input
Firing
x
Δw
CA3 neurons
pre before post
F (%)
0.4
0.2
Δt (ms)
-40
-20
20
40
-0.2
-0.4
post before pre
Δt = time_pre - time_post
Δw
CA3 neurons

What you should remember

(1) STDP is an extension of simple LTP/LTD
(2) In STDP, synapses are
 - strengthened when a pre-synaptic spike is followed by a postsynaptic response
 - weakened when a postsynaptic response is followed by a presynaptic spike
(3) STDP is self normalizing in that some synapses will be strengthened and others weakened
(4) In realistic spike trains, LTP will override LTD
(5) STDP can naturally lead to sequence learning