From Science Magazine, 2005

Synaptic Plasticity — Lecture 5

Bidirectionality

Neuronal Physiology and Plasticity

Aug 2018 Semester

In the previous class…

HFS leads to LTP through depolarization followed by influx of calcium into the postsynaptic neuron

Multiple sources of calcium could mediate LTP induction: NMDAR, CP-AMPAR, VGCCs, stores

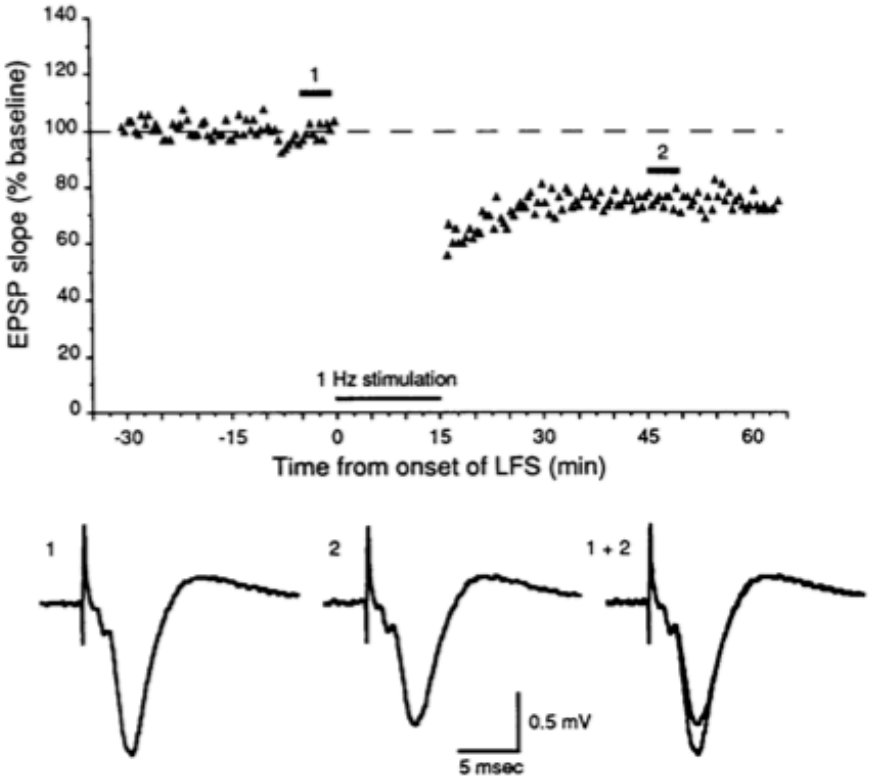
In reality, multiple calcium sources could synergistically contribute to various forms of LTP

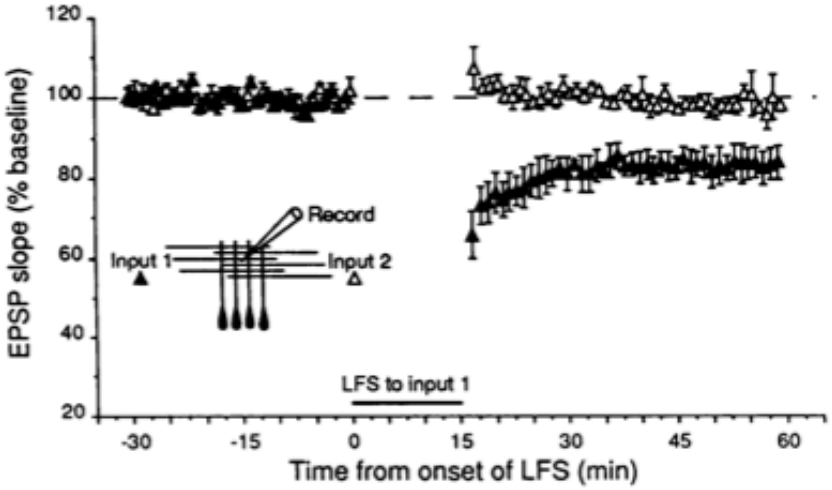
Backpropagating action potentials and dendritic spikes can provide depolarization required for the induction of synapse-specific LTP

Question 1: Shouldn't plasticity be bidirectional for stability??

Question 2: What comes after calcium in inducing LTP??

Long-term depression

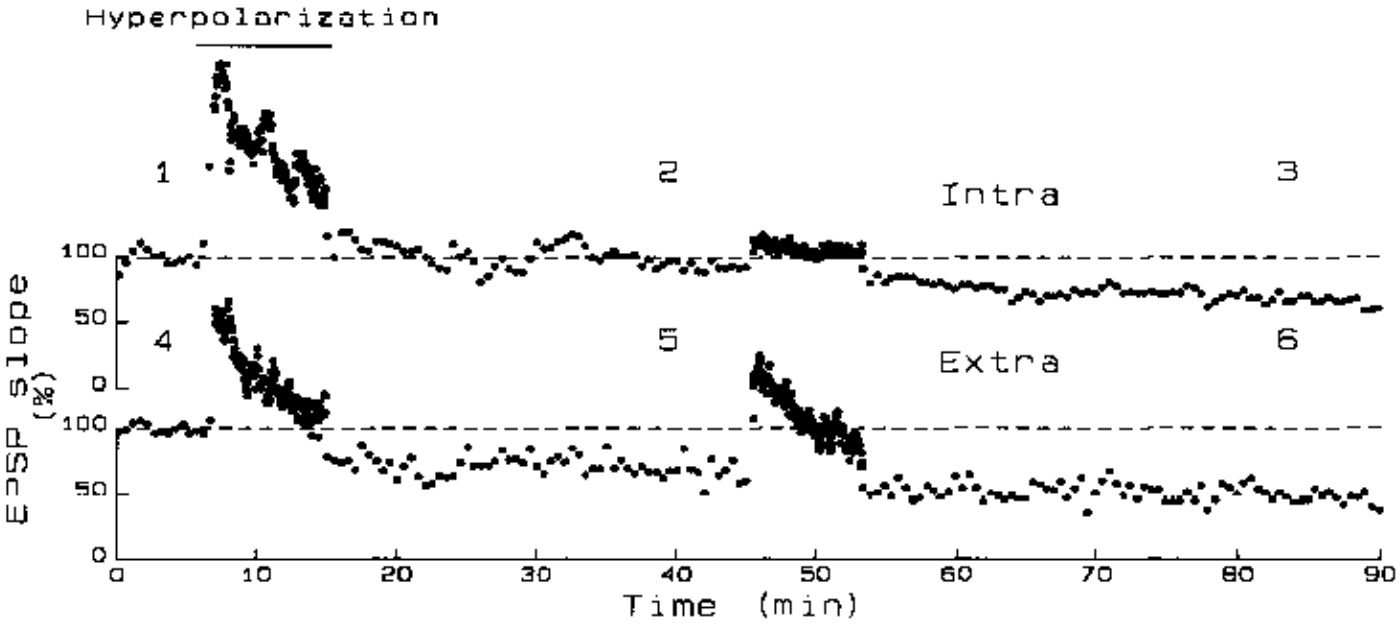




Long-term depression also exhibits input specificity

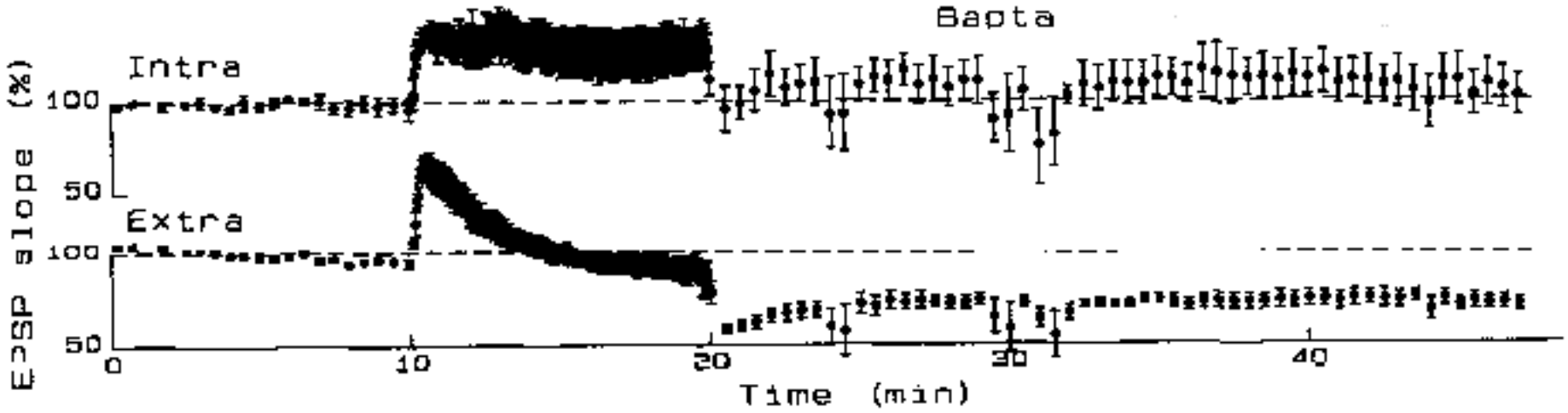
Dudek and Bear, PNAS, 1991

LTD is depolarization-dependent, too!!!



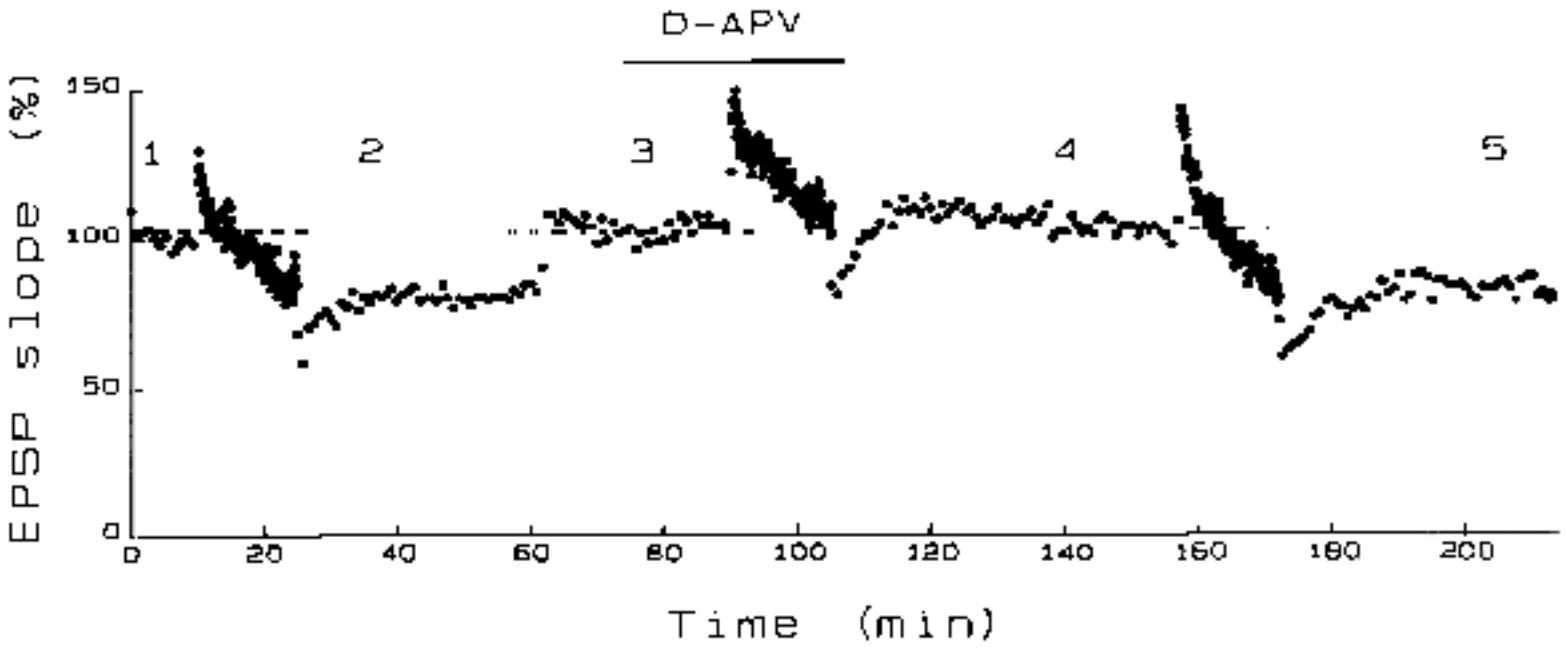
Mulkey and Malenka, Neuron, 1992

Surprise! Surprise!! LTD is $[Ca^{2+}]_i$ dependent, too!!!



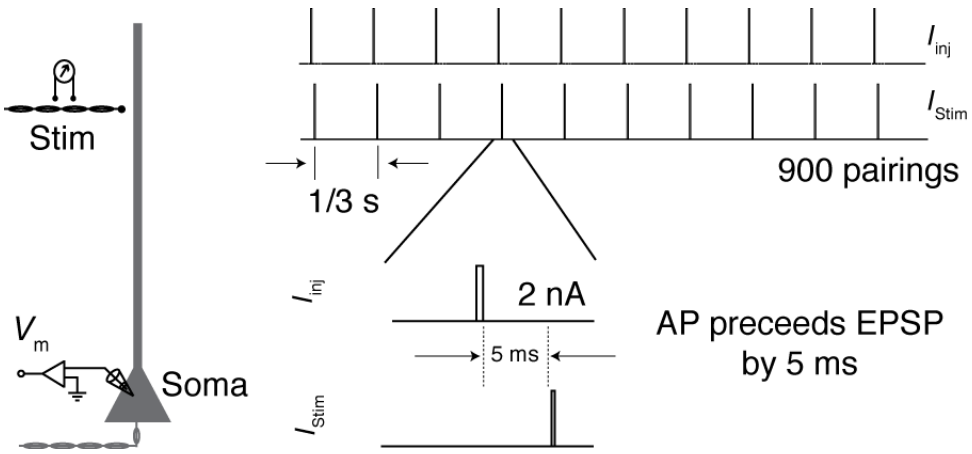
Mulkey and Malenka, Neuron, 1992

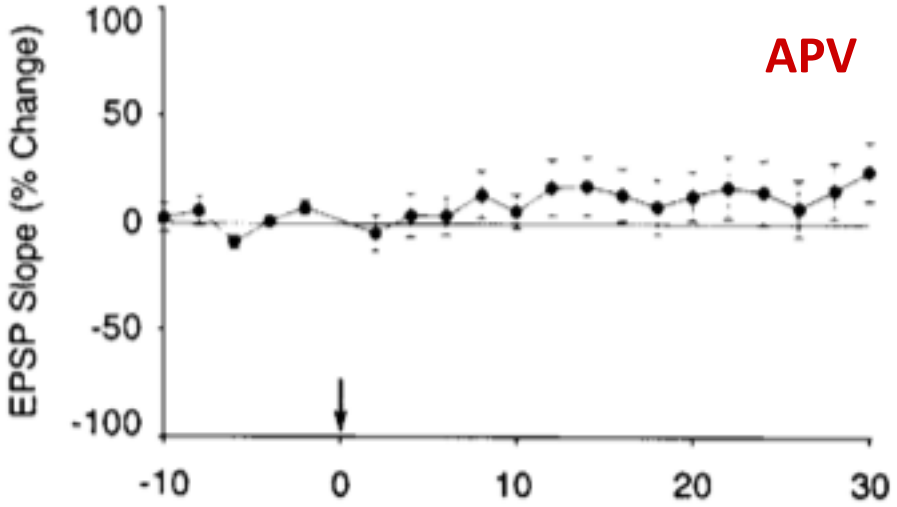
Calcium can come from NMDARs

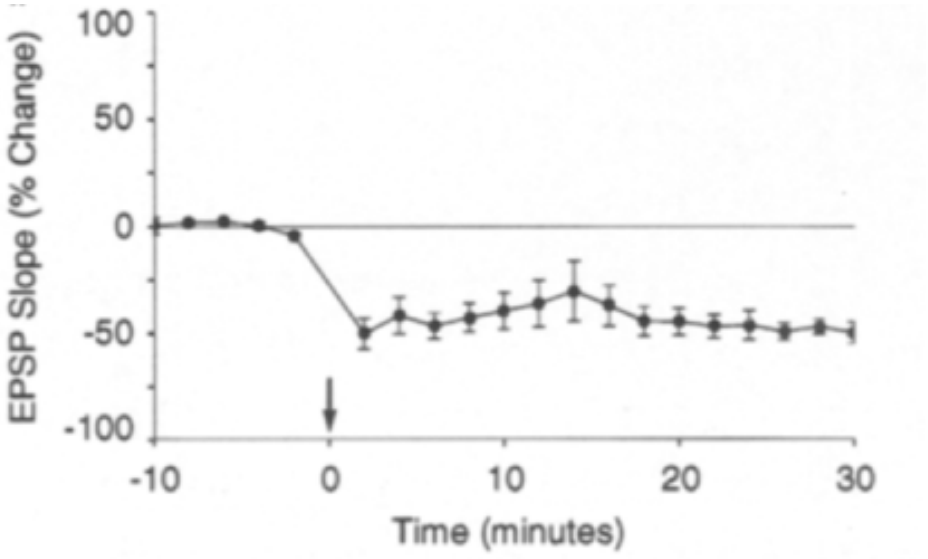


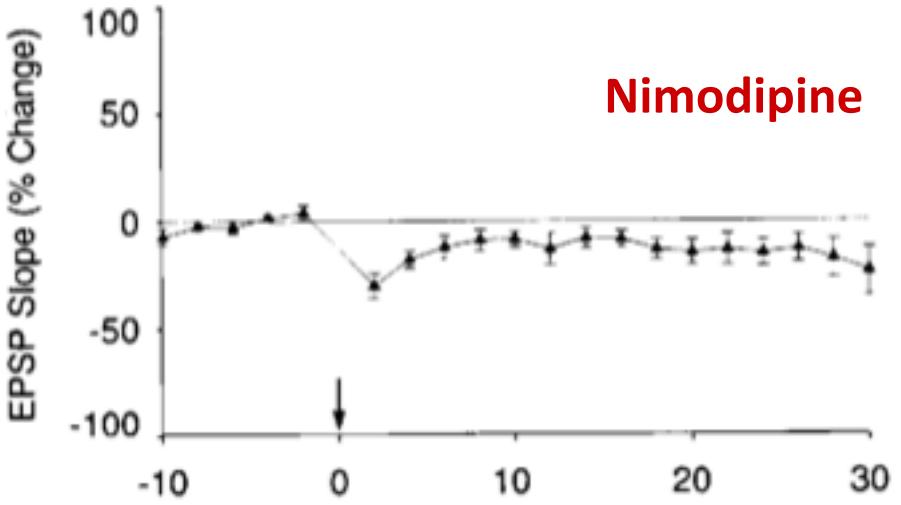
Mulkey and Malenka, Neuron, 1992

Or, from both NMDARs and VGCCs



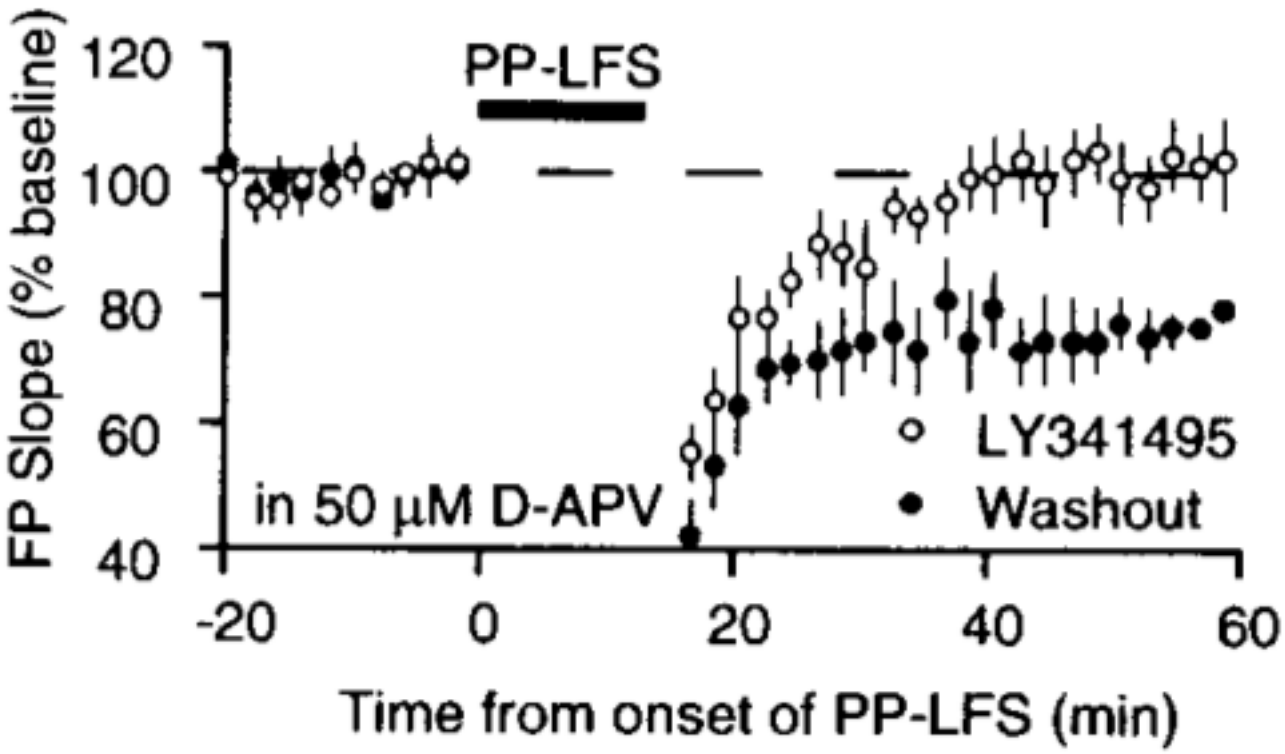






Christie et al., Learning and Memory, 1996

Or, mGluRs



LY341495: mGluR antagonist
Washout: After washing out LY

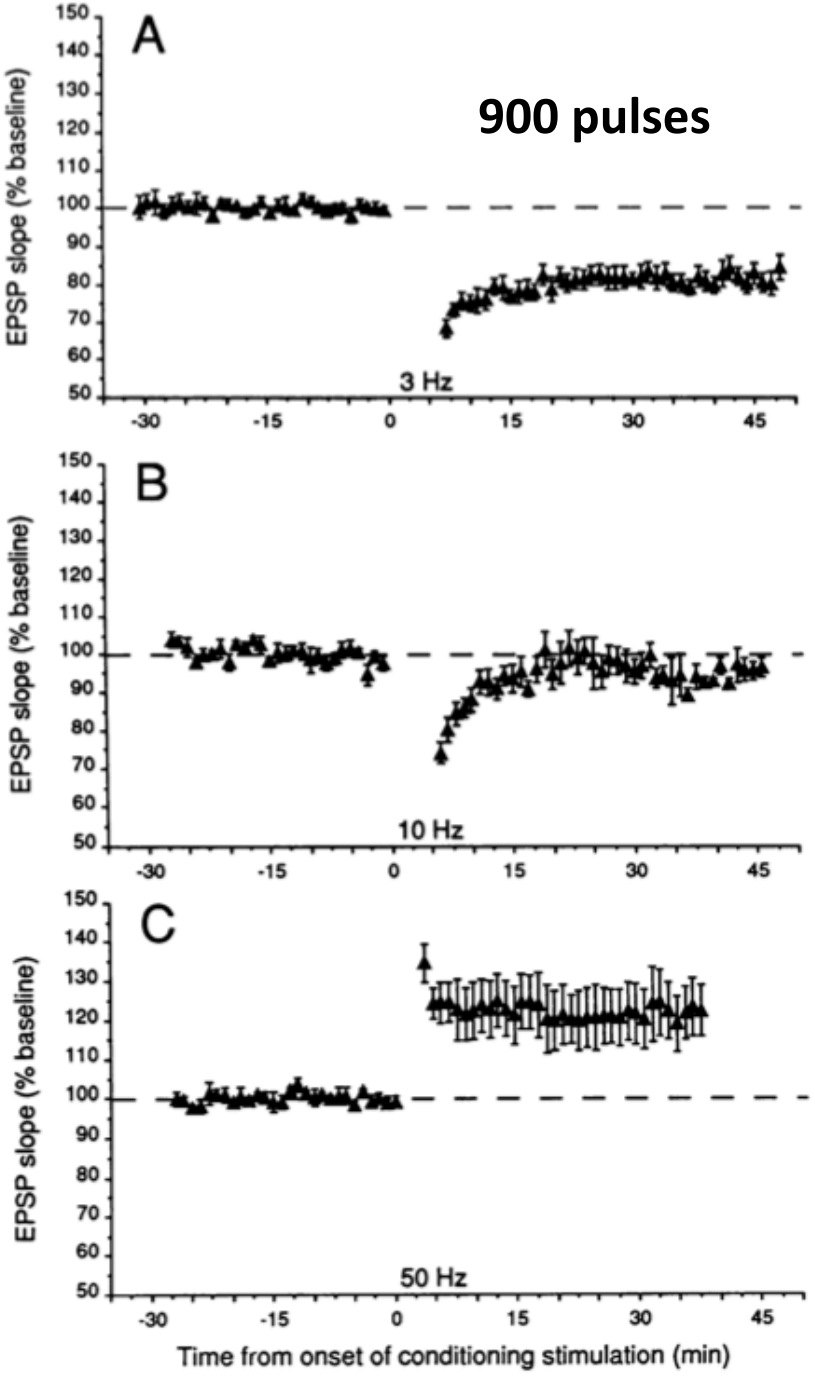
Huber et al., Science, 2000

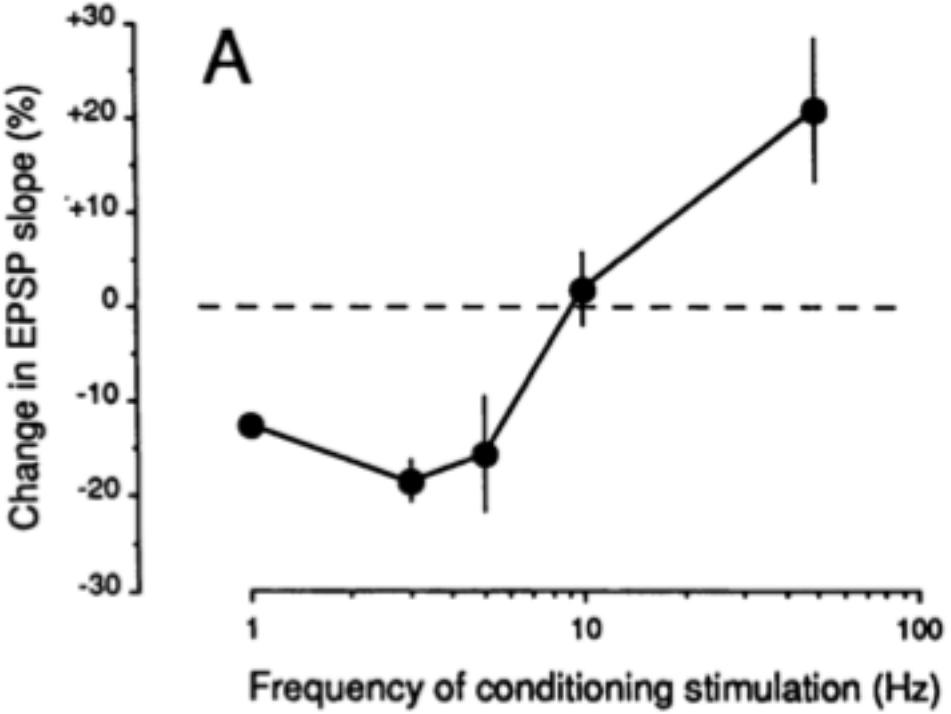
LTP is dependent on depolarization, elevation of postsynaptic calcium through NMDAR's/VGCC's/ mGluR's!!

So is LTD!!!

So, what property of the induction stimulus determines whether it is LTP/LTD?

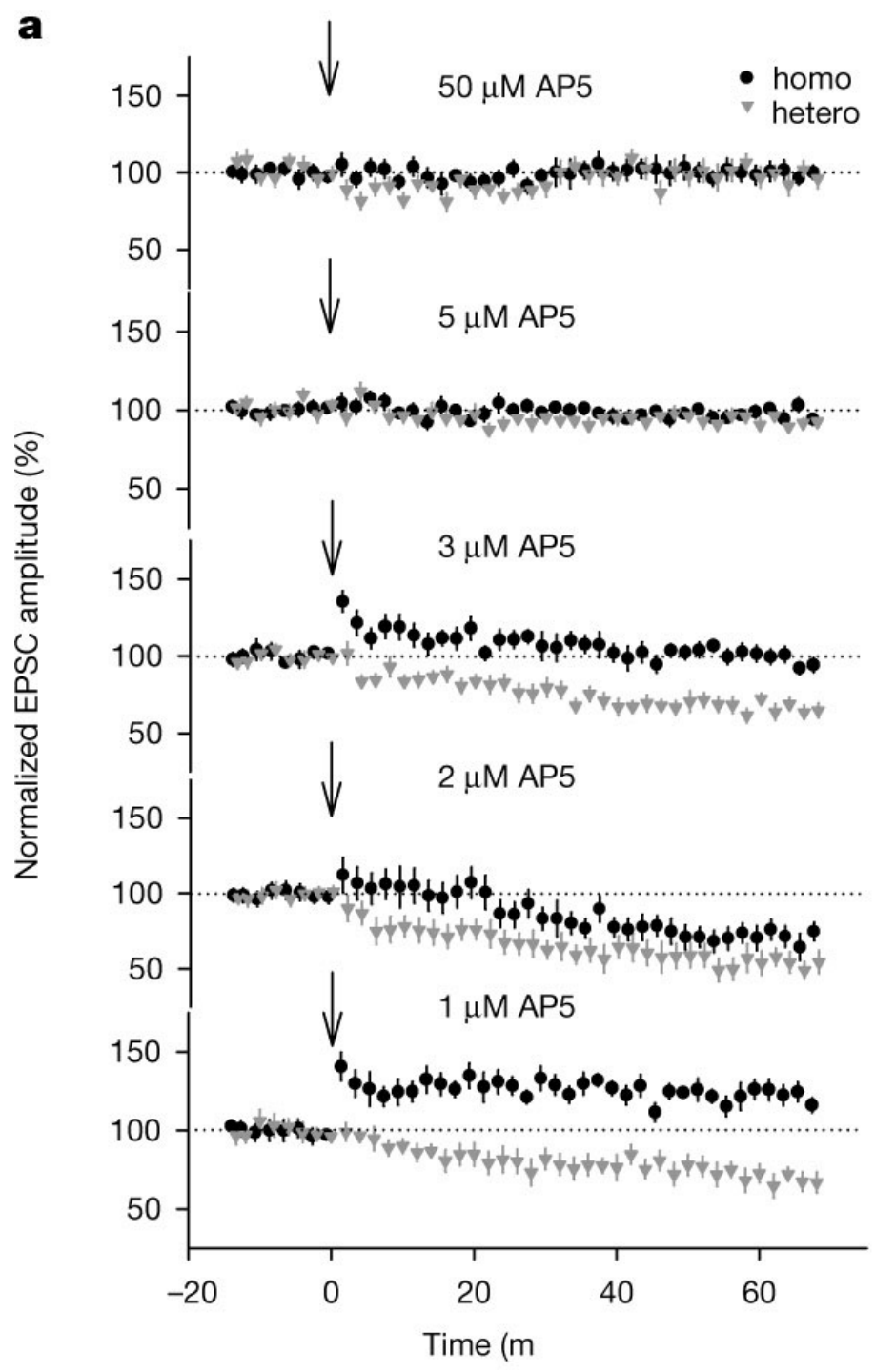
Frequency of stimulus?

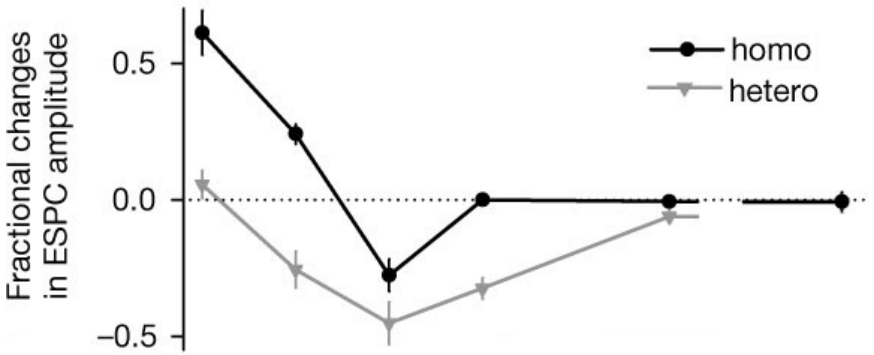




Dudek and Bear, PNAS, 1991

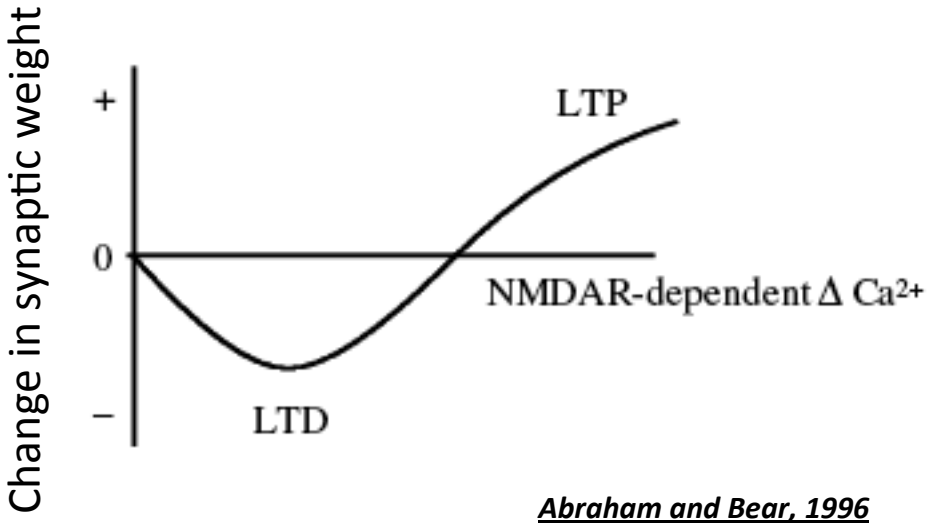
Amount of calcium?



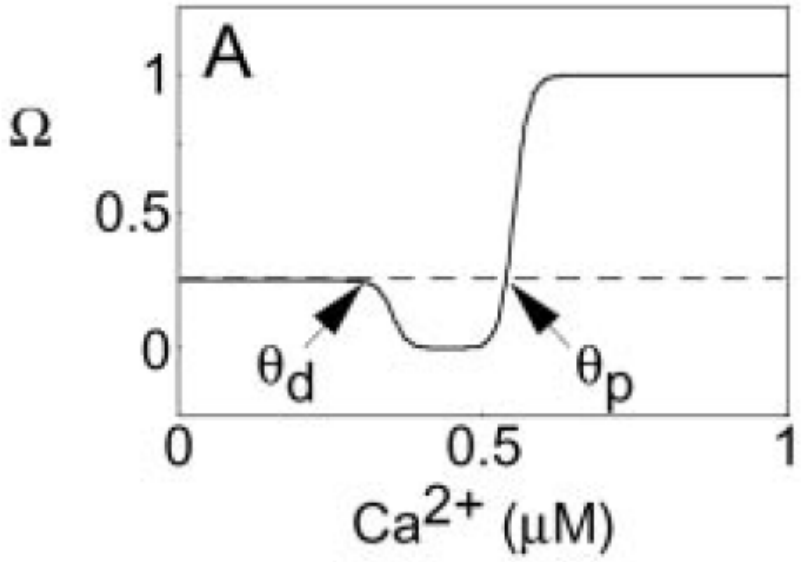


Nishiyama et al., Nature, 2000

Amount of calcium entering?



Abraham and Bear, 1996



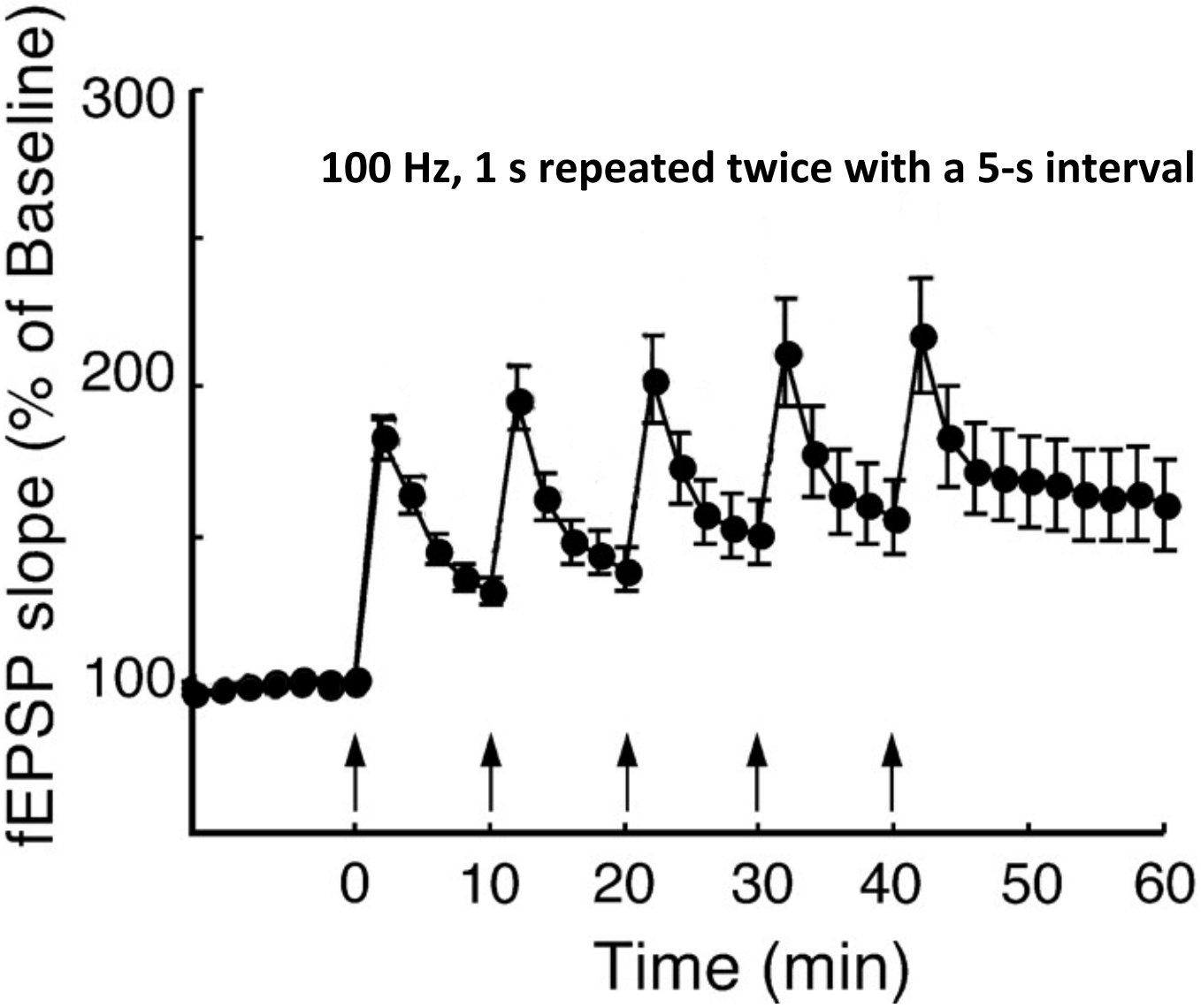
Shouval, Bear and Cooper, PNAS, 2002

General consensus?: Low-levels of longer lasting calcium leads to LTD, while high-levels of short-lasting calcium leads to LTP

Both amplitude and kinetics of calcium matter, apart from a 1000 other things!

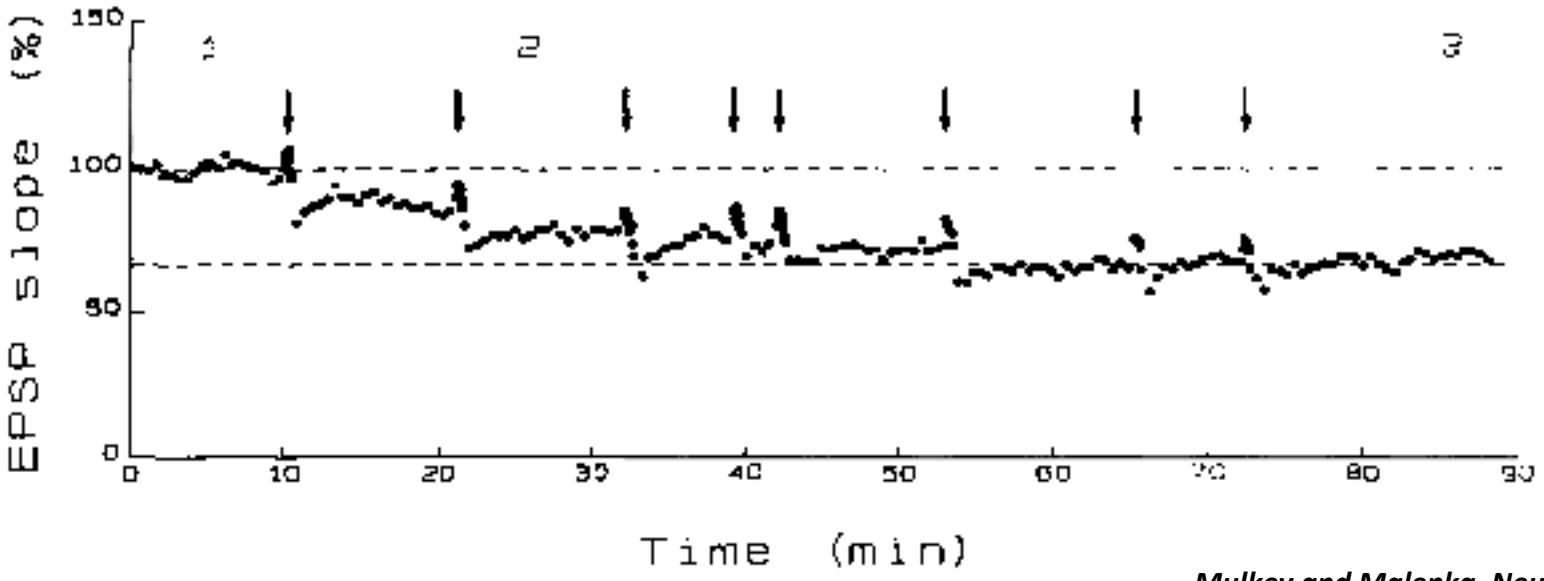
Multiple inductions, one after another!

Saturation of LTP



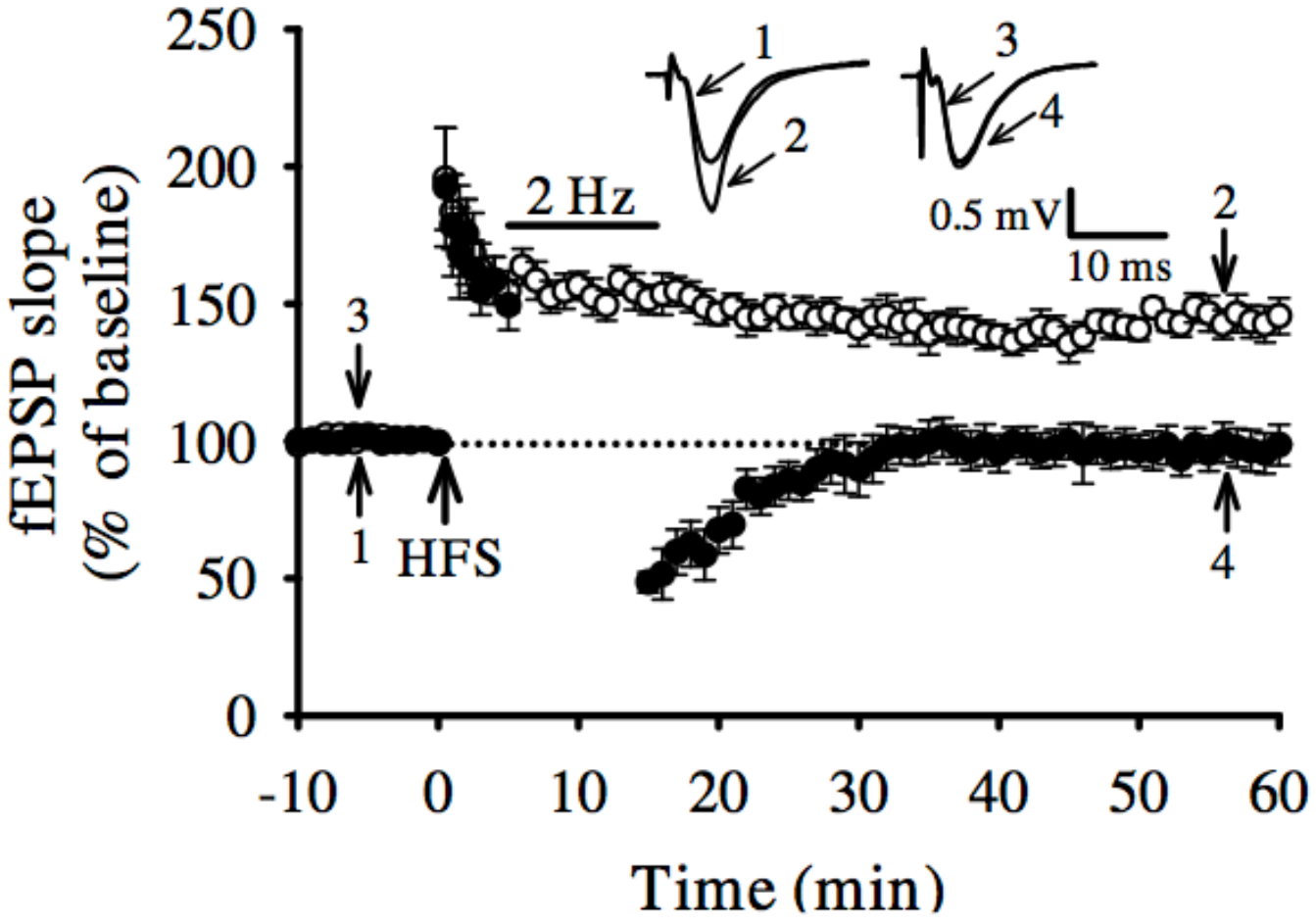
Modified from Nishiyama et al., PNAS, 2002

Saturation of LTD



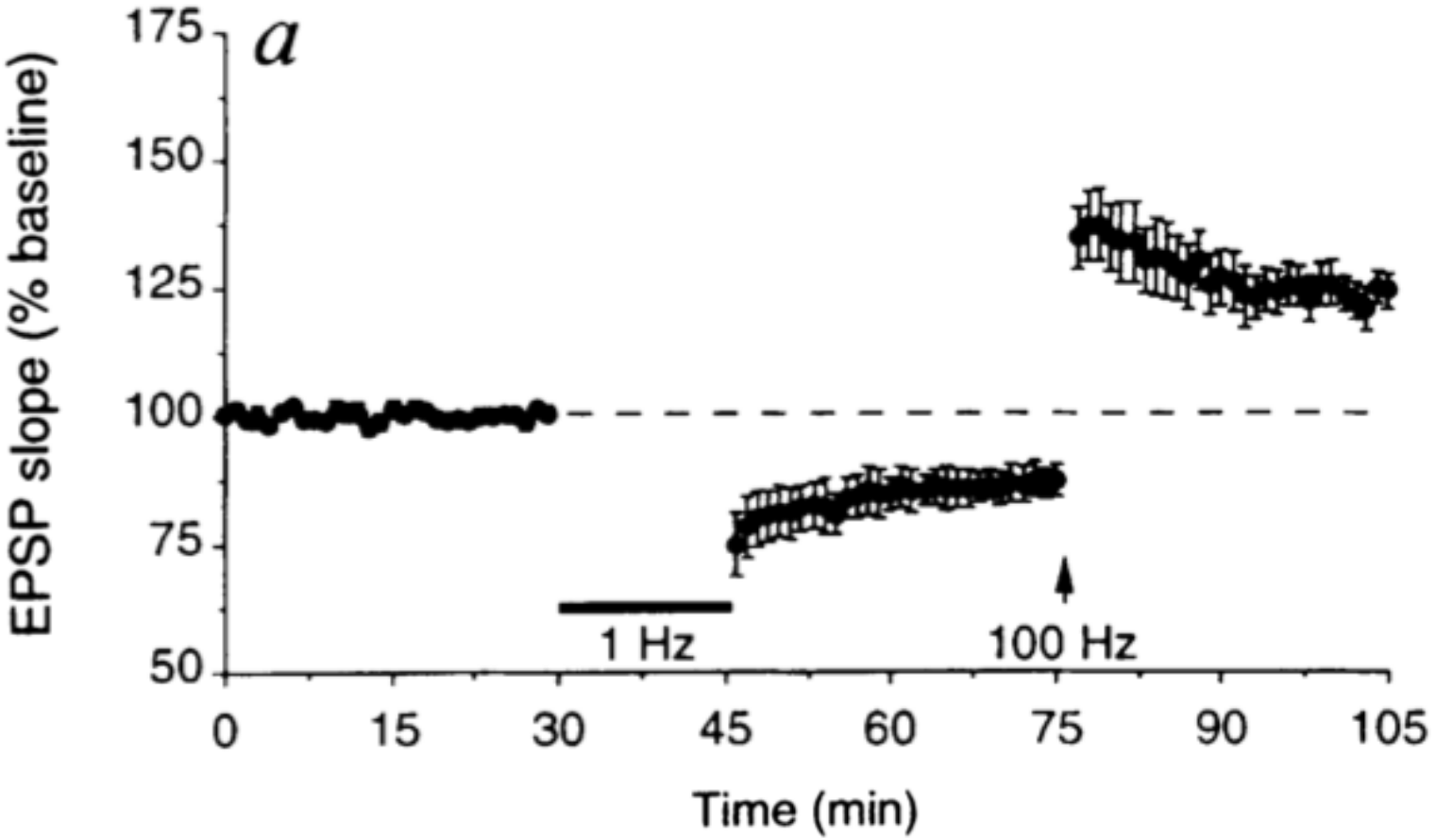
Mulkey and Malenka, Neuron, 1992

Depotentiation



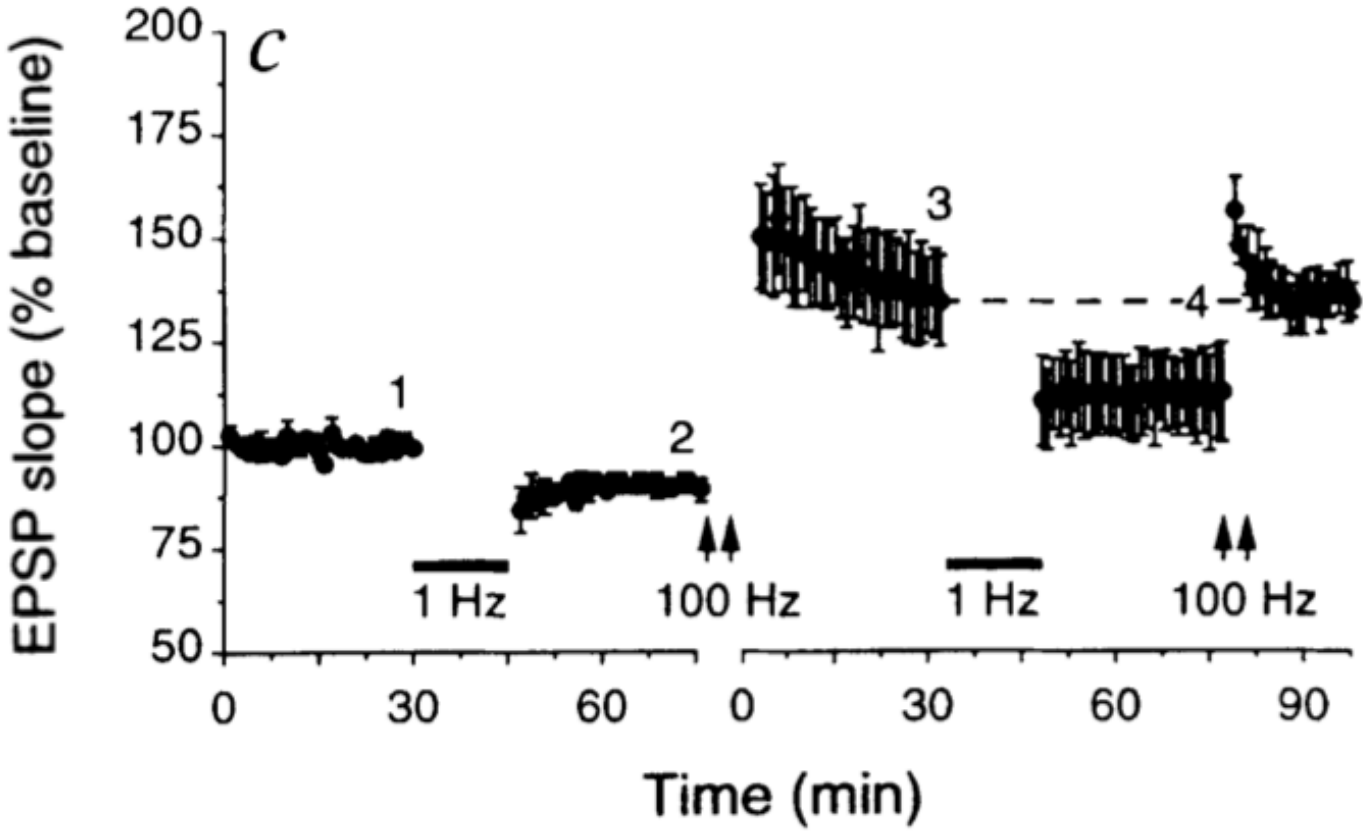
Liang et al., Molecular Brain, 2008

Dedepression



Heynen et al., Nature, 1996

Or, as many!

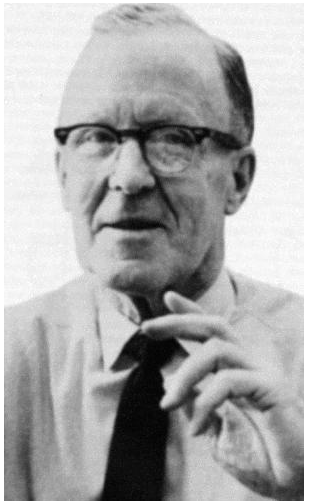


Heynen et al., Nature, 1996

Spike timing dependent plasticity

What did Hebb really say?

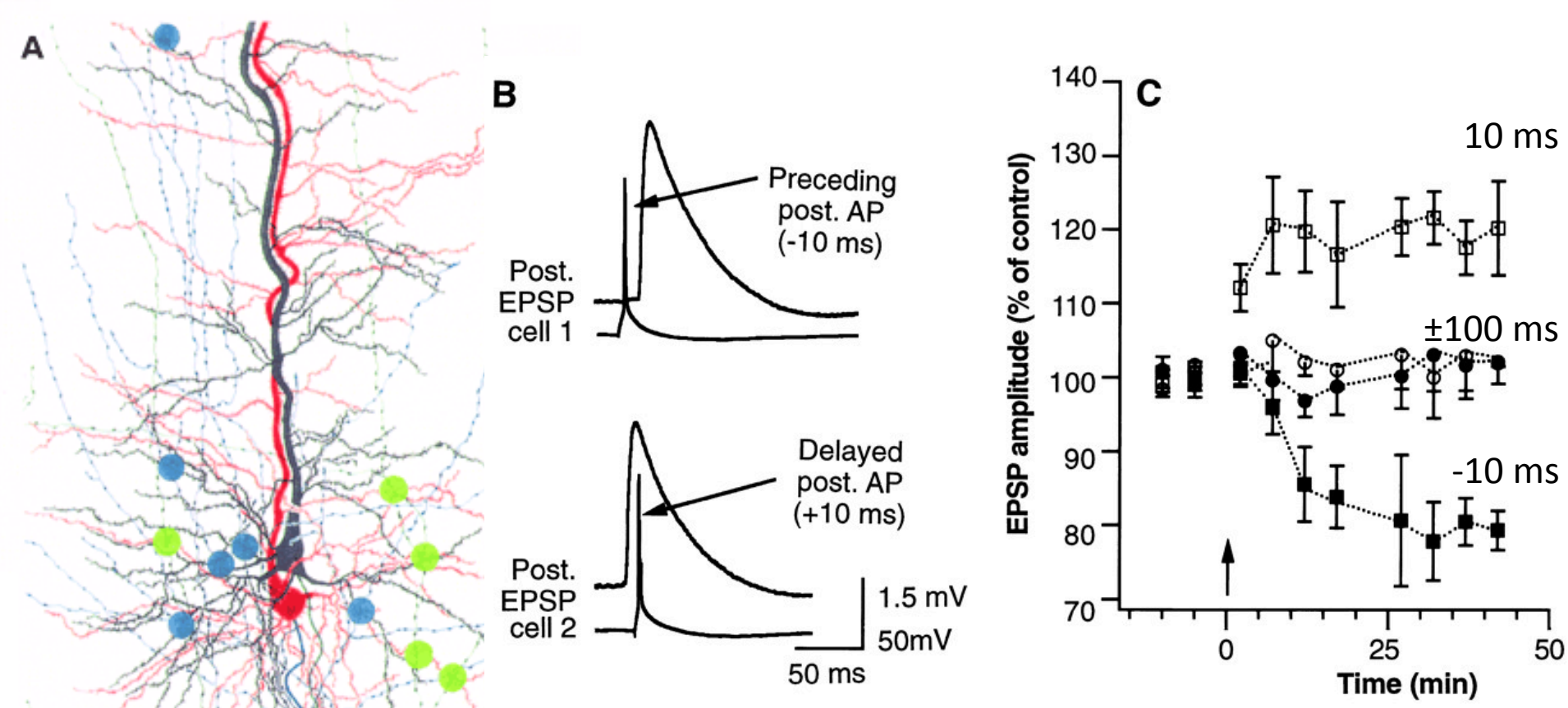
"When an axon of cell A is near enough to excite a cell B and repeatedly and persistently takes part in firing it, some growth process or metabolic change takes place in one or both cells, such that A's efficiency, as one of the cells firing B, increases."



Donald Hebb

There is a mention about temporal relationship between the action potentials of cell A and cell B

STDP



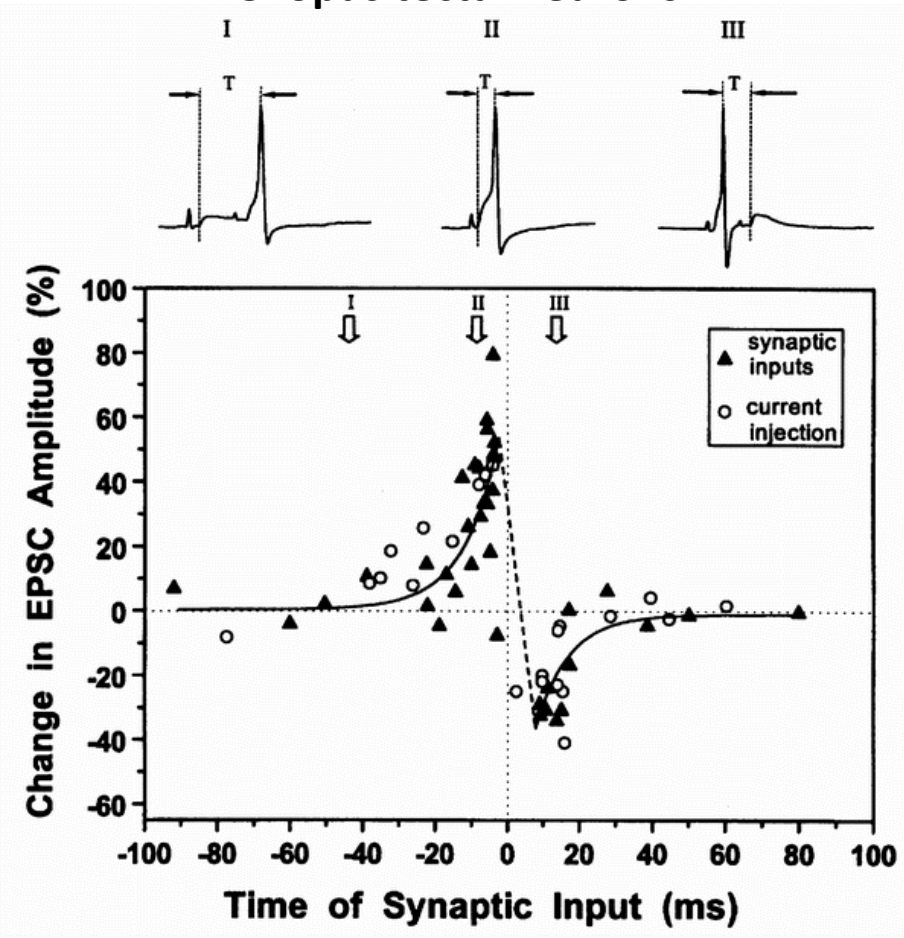
10-Hz train of 5 APs repeated 10 to 15 times every 4 s

Markram et al., Science, 1997

Two bidirectionally connected cells in Layer V neocortex made to fire APs with a 10 ms

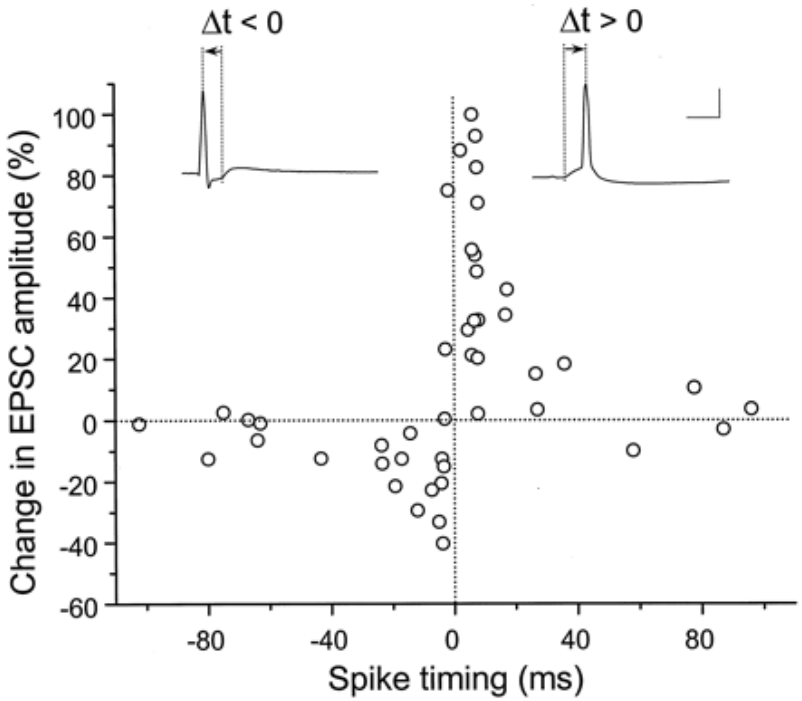
STDP

Xenopus tectal neurons



Zhang et al., Nature, 1998

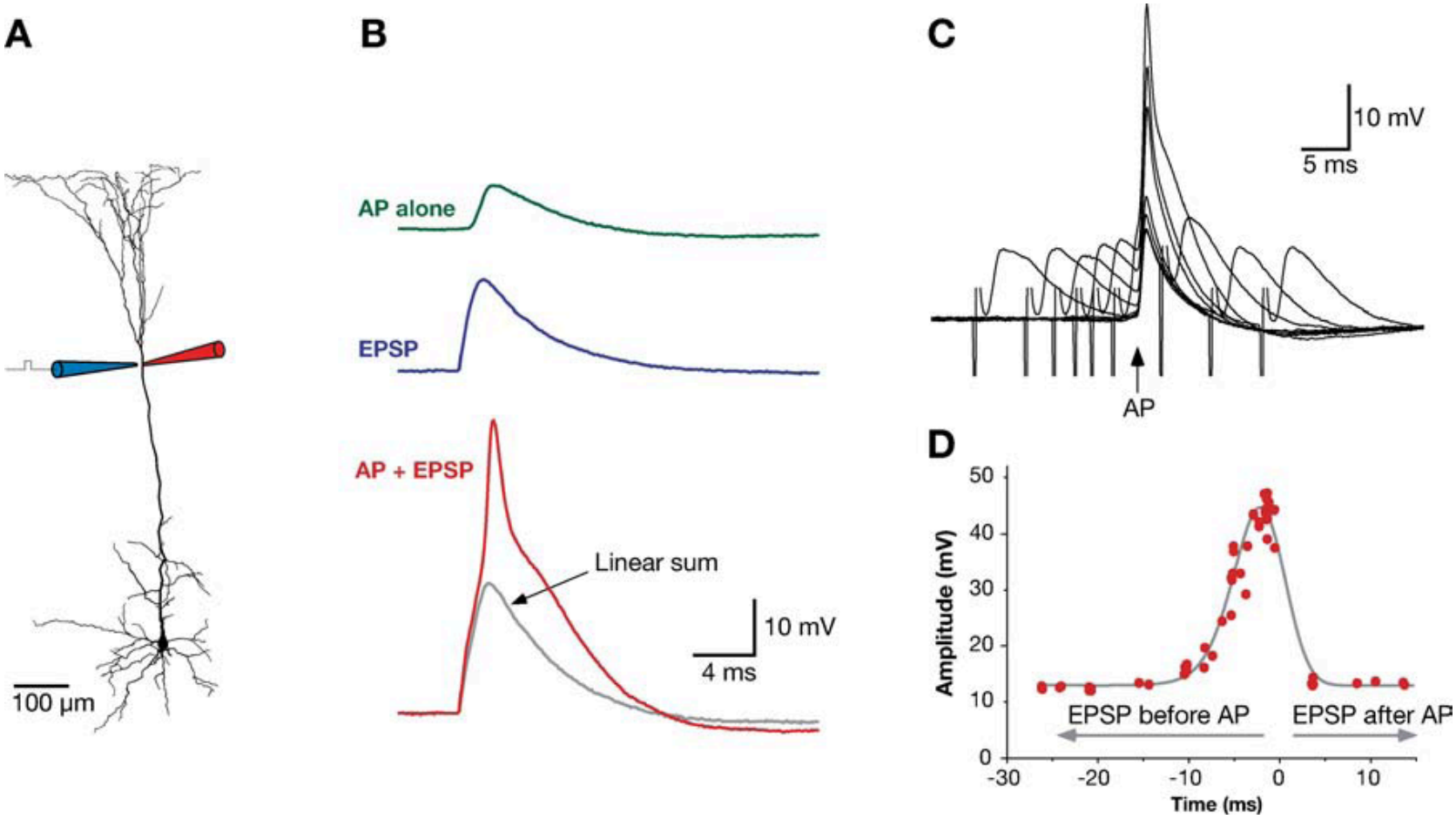
Rat Hippocampal culture neurons



Bi and Poo, JNS, 1998

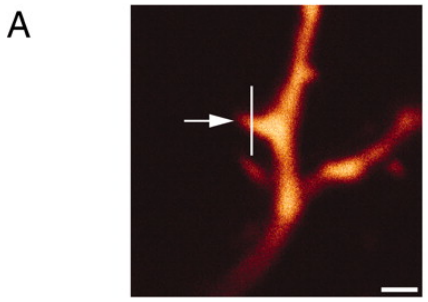
Coincidence detection

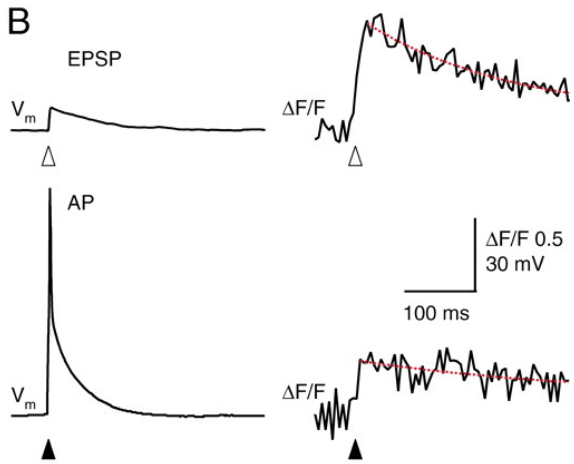
We saw this slide in the second lecture on dendrites!

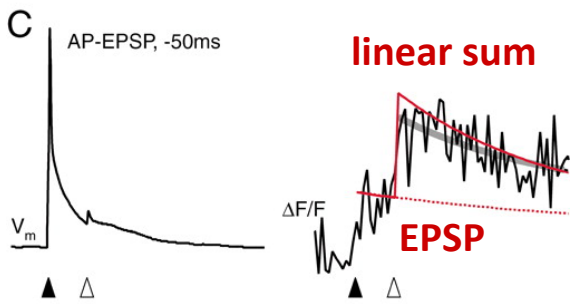


Stuart and Hausser, Nat. Neurosci., 2001

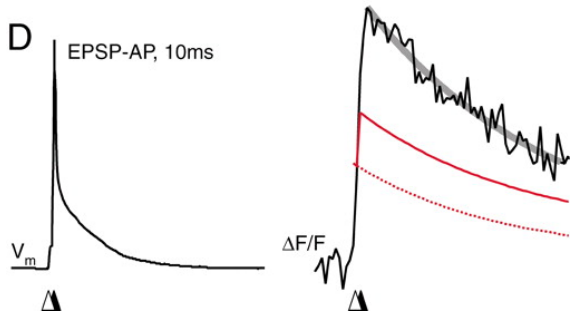
Calcium detection of positive and negative timing



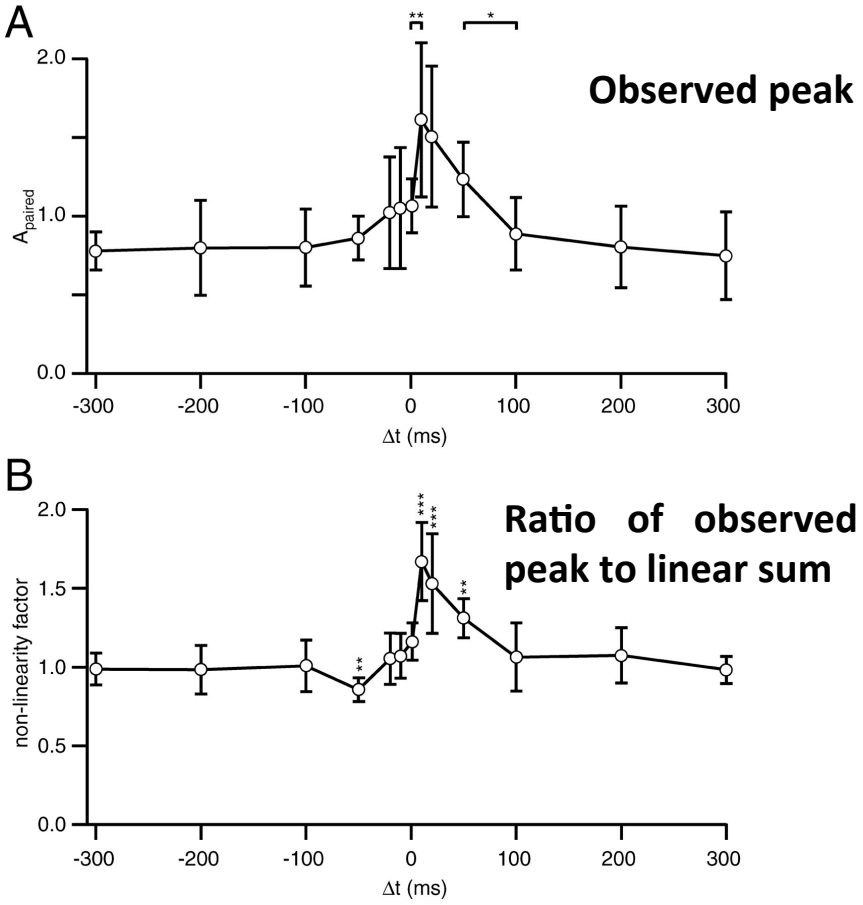




Sublinear

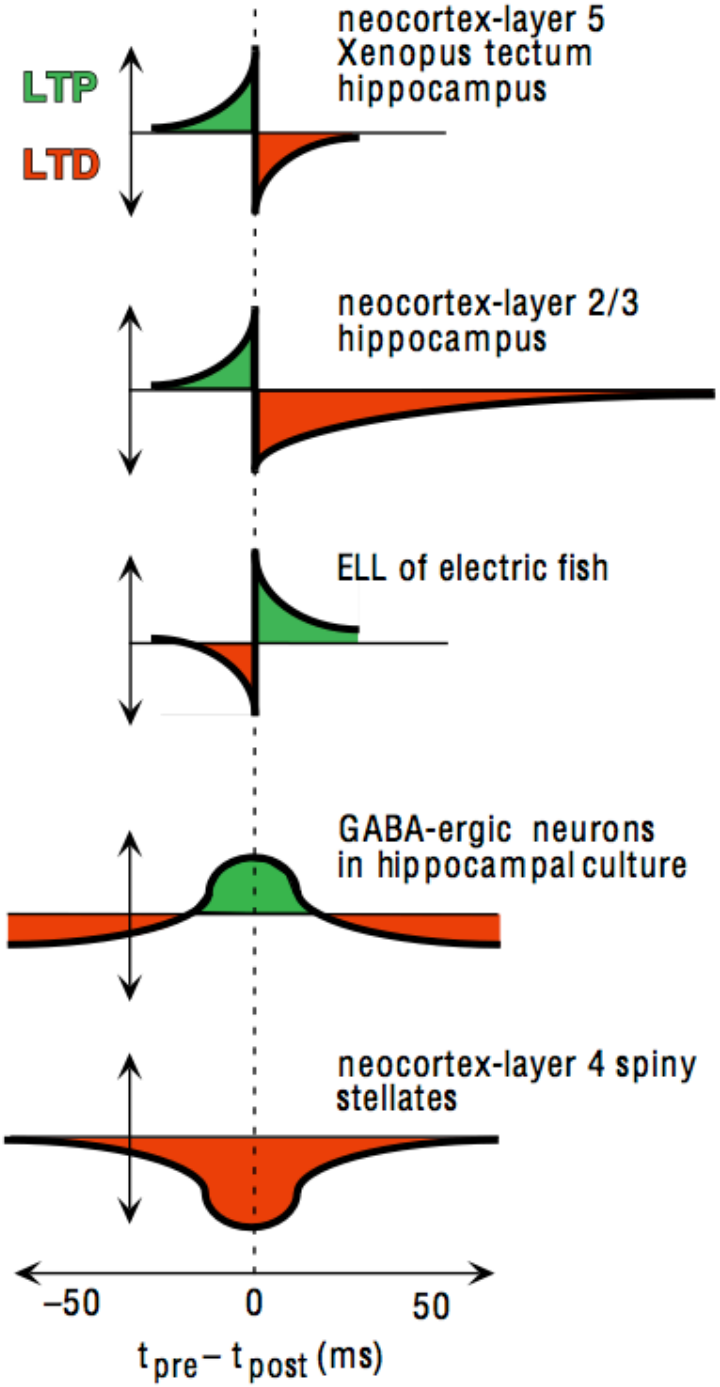


Supralinear



Nevian and Sakmann, JNS, 2004

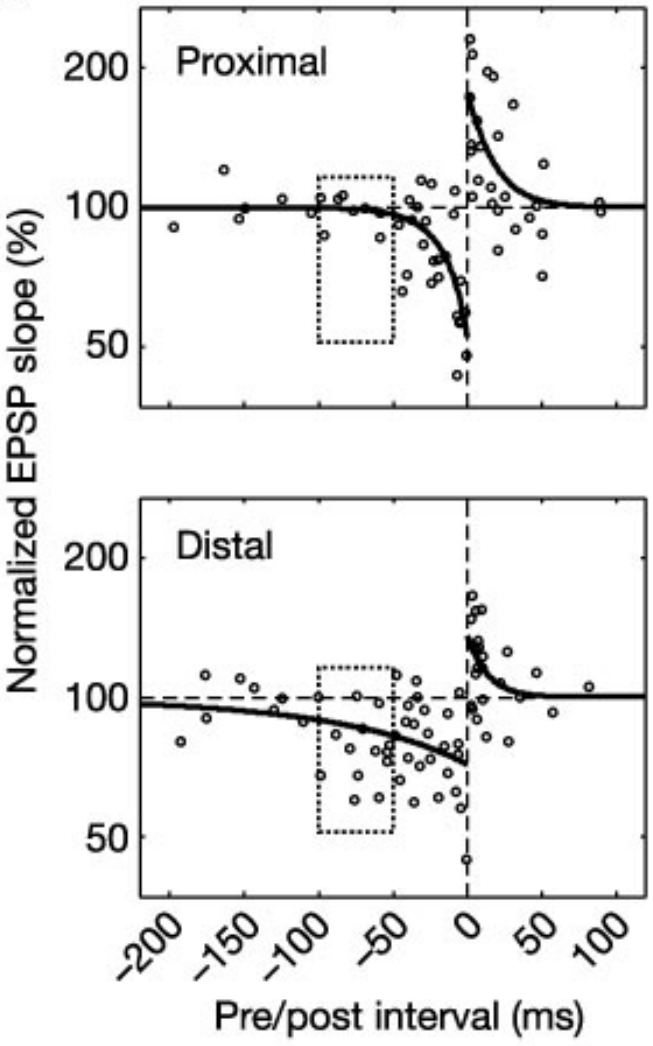
Different synapses have different plasticity profiles!



Nelson and Abbott, Nat Neurosci., 2000

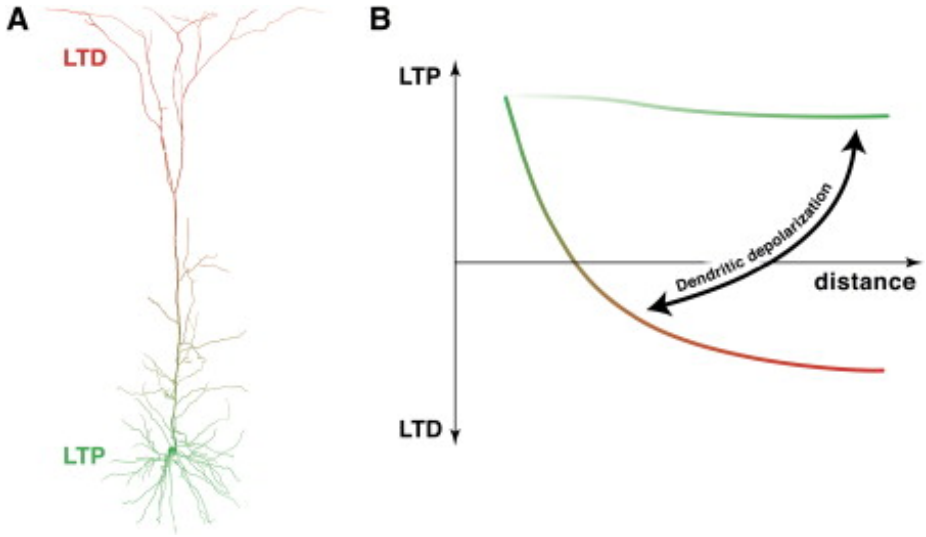
Plasticity is also dependent on dendritic location

Layer 2/3 neocortex



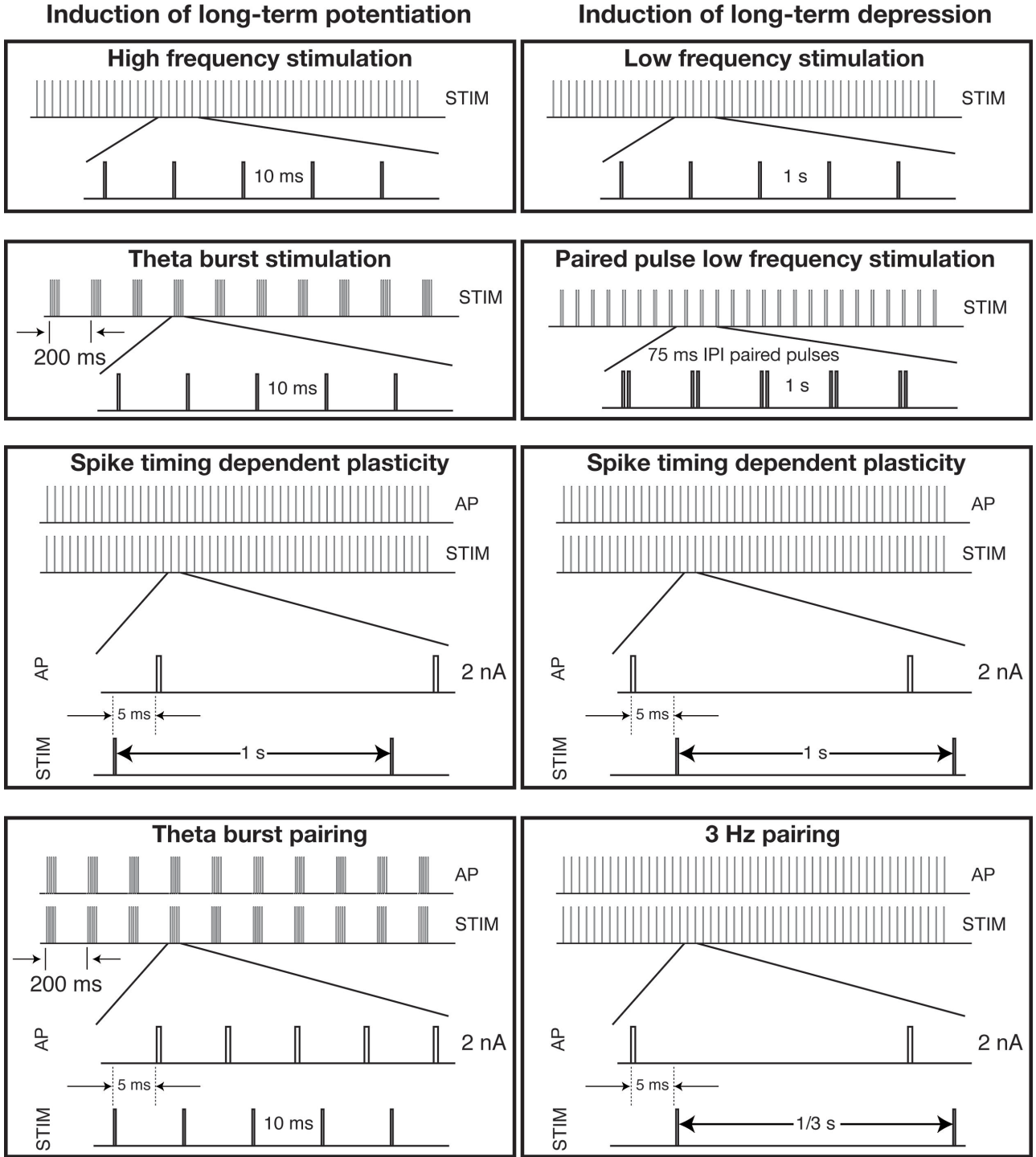
Froemke et al., Nature, 2005

Layer 5 neocortex



Sjostrom and Hausser, Neuron, 2006

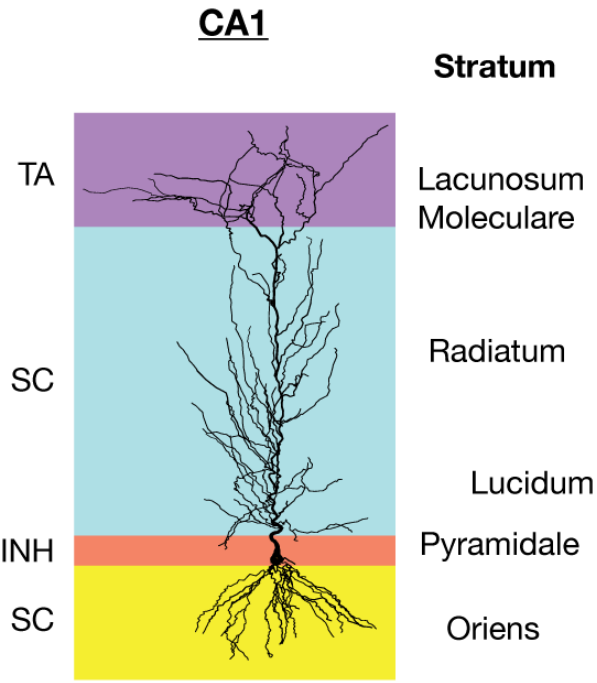
Both are controlled by the spread of backpropagating action potentials

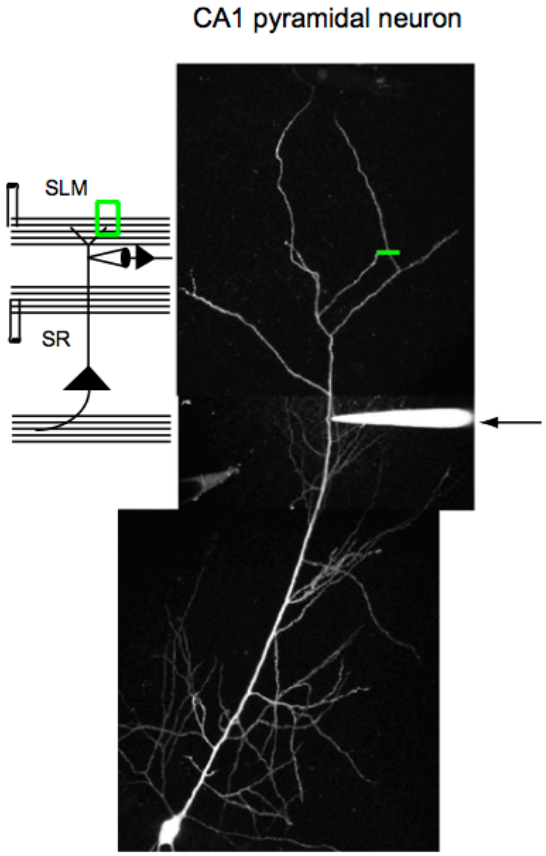


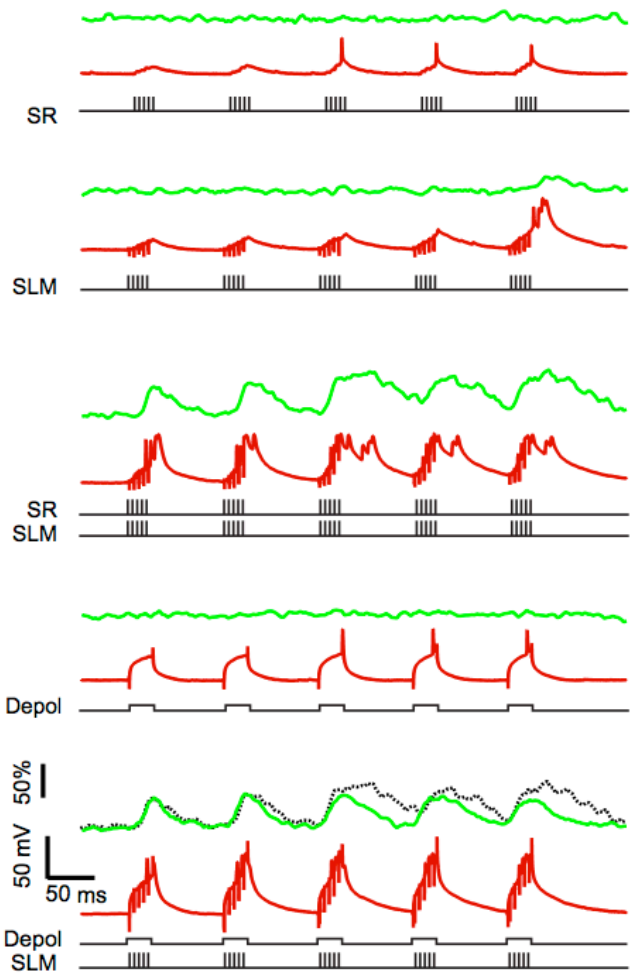
Several induction protocols!!

Plateau potential based LTP protocols

Means to get dendritic spikes in hippocampal pyramids

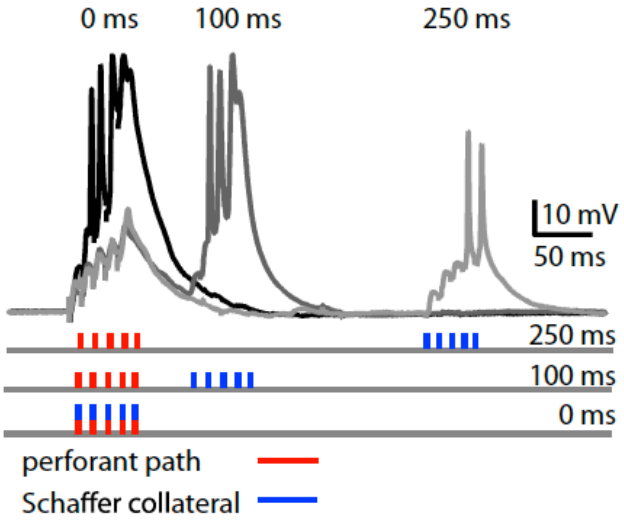


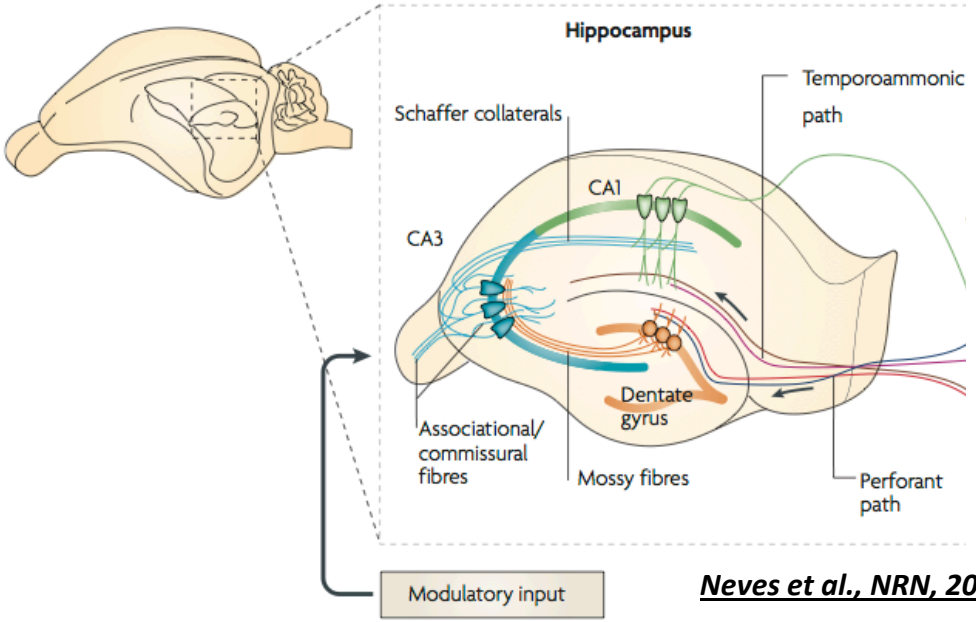




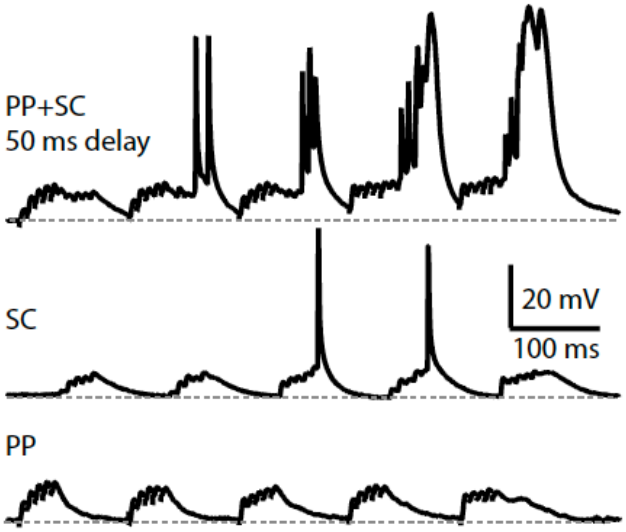
Takahashi and Magee, Neuron, 2009

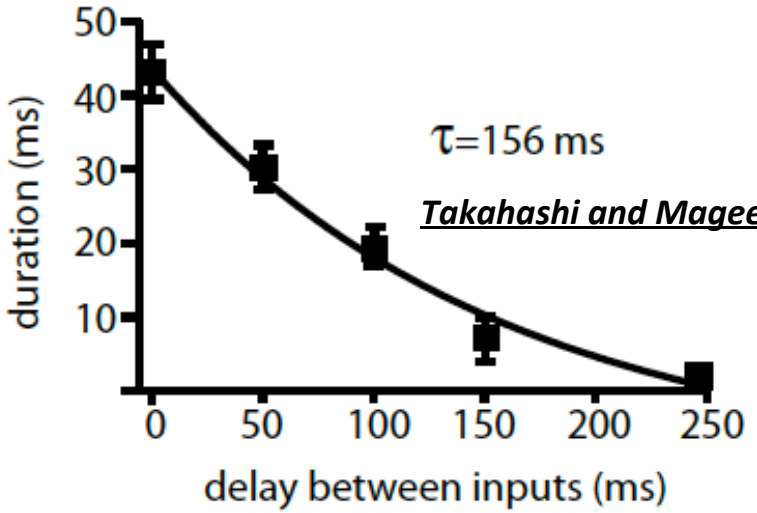
Pathway interactions to obtain dendritic plateau potentials in hippocampal pyramids





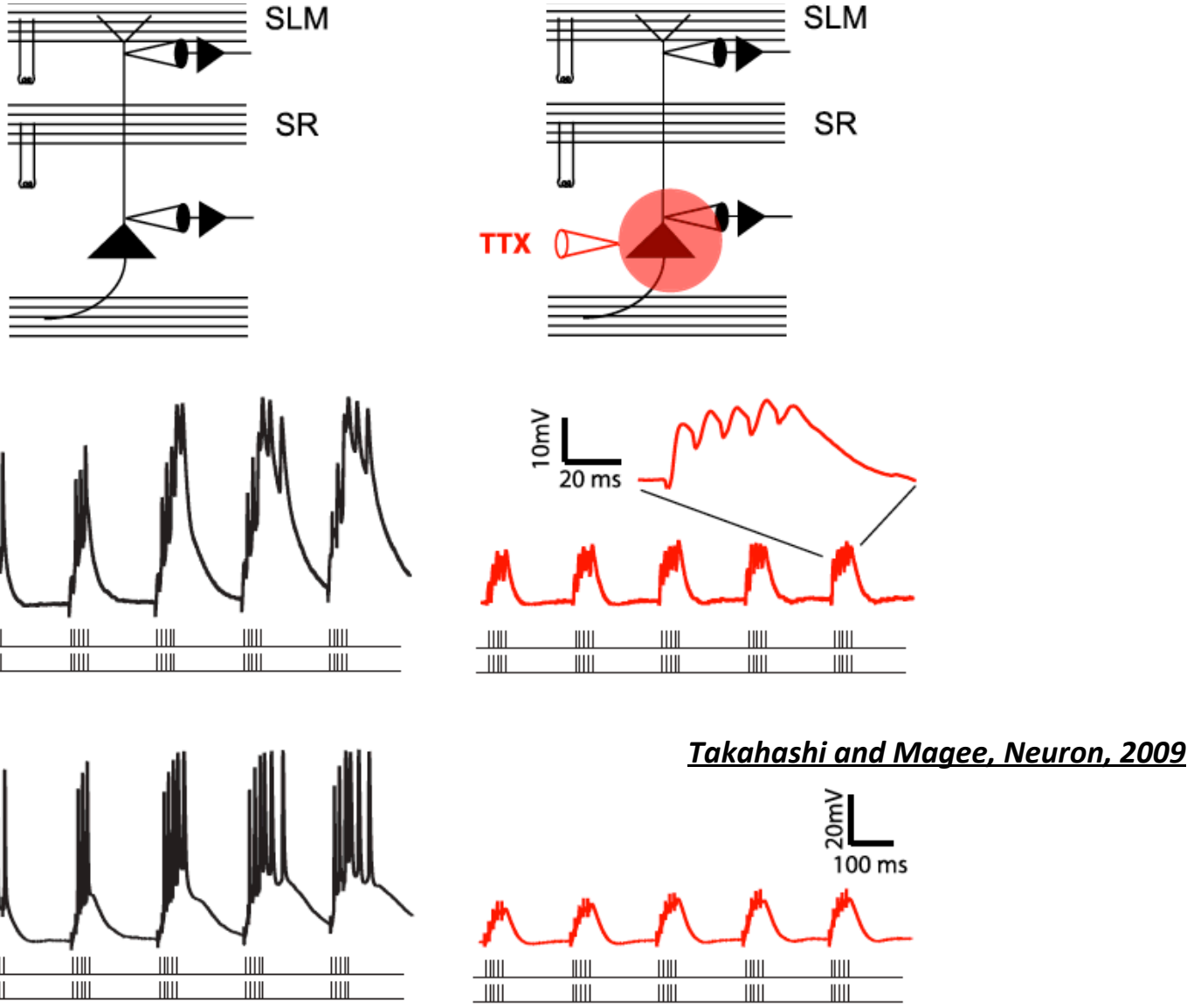
Neves et al., NRN, 2008



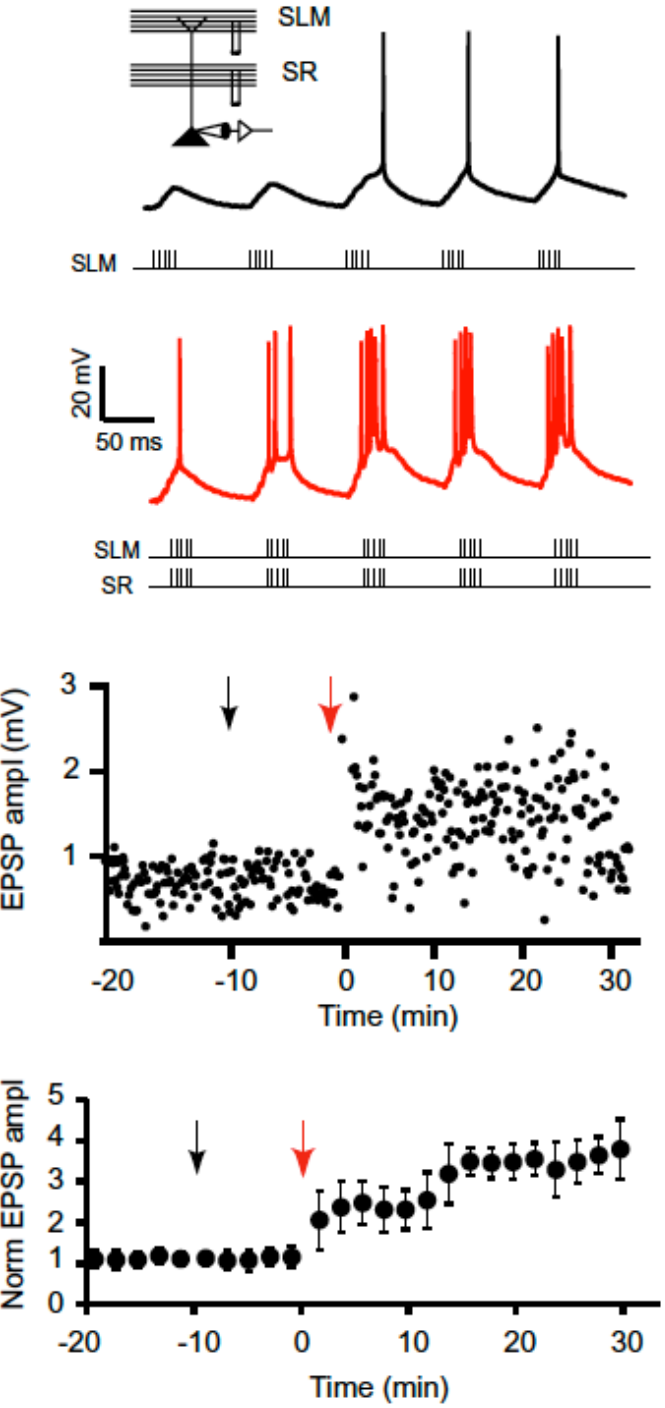


Takahashi and Magee, Neuron, 2009

Backpropagating action potentials contribute to plateau potentials



Takahashi and Magee, Neuron, 2009



Plateau potentials resulting from pathway interactions result in perforant path LTP

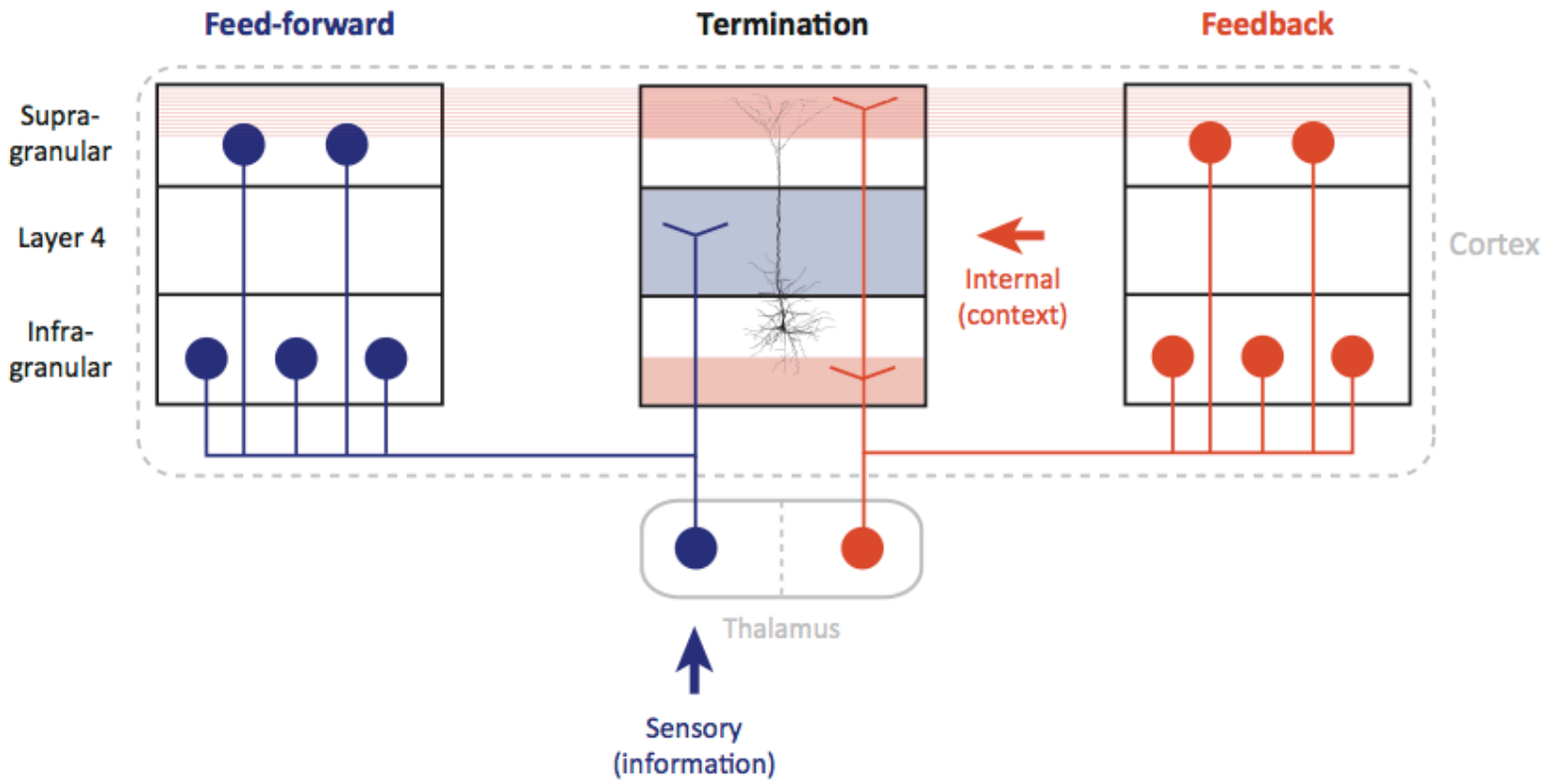
Takahashi and Magee, Neuron, 2009

An interesting synthesis

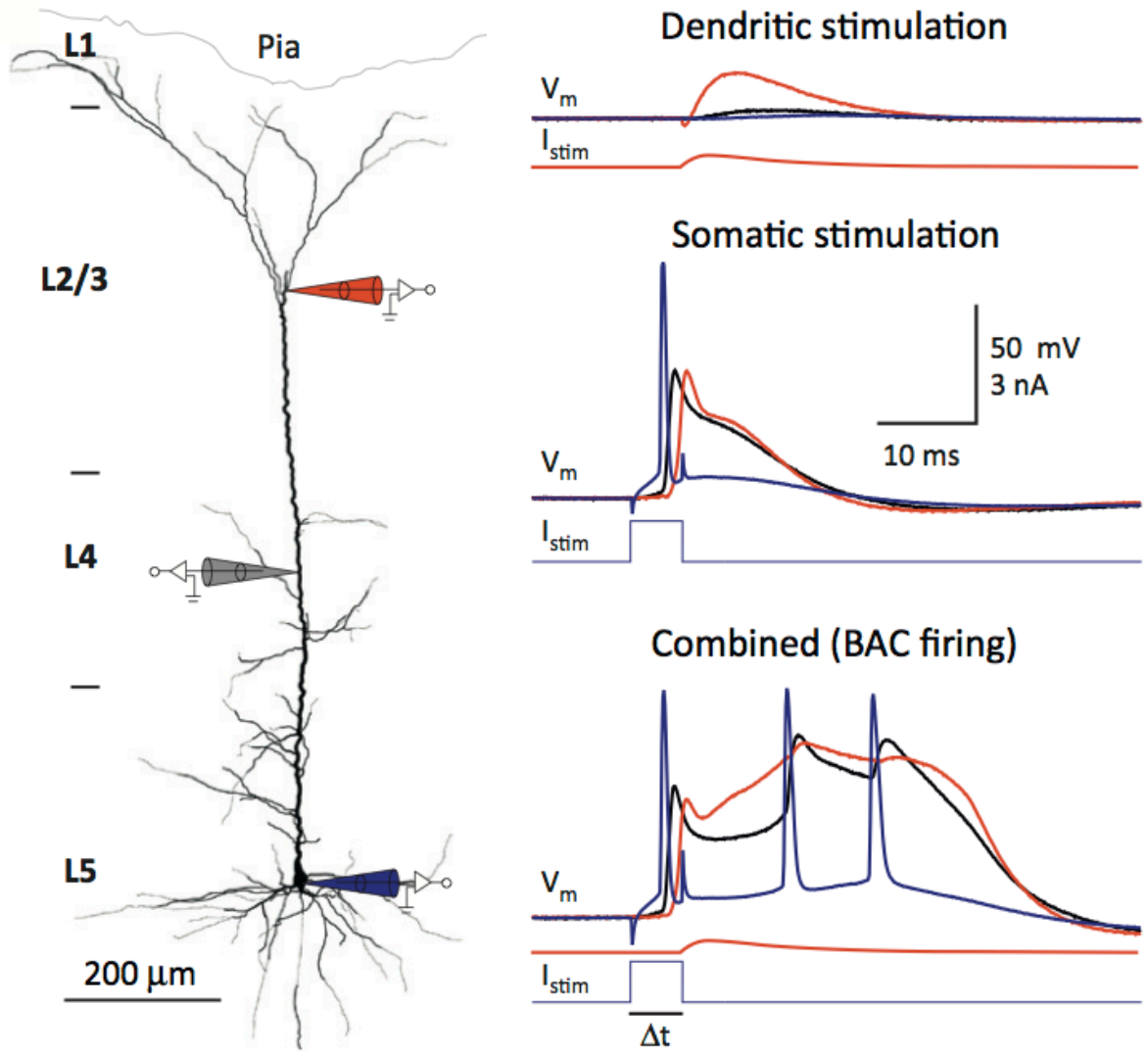
A cellular mechanism for cortical associations: an organizing principle for the cerebral cortex

Trends in Neurosciences (2012)

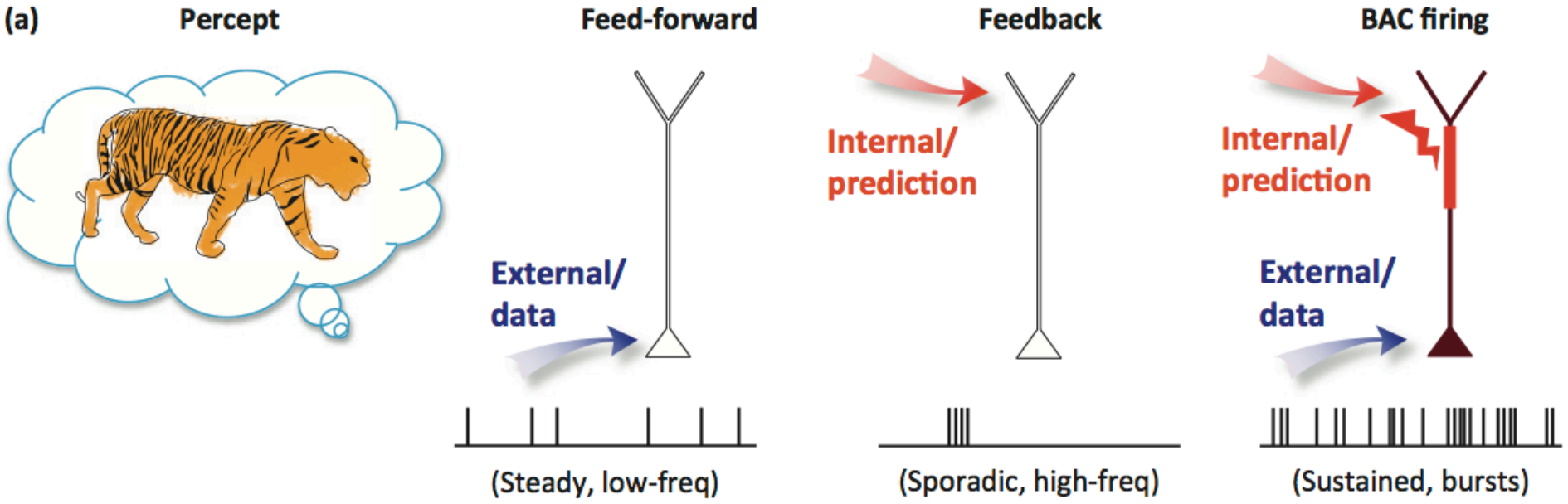
Matthew Larkum



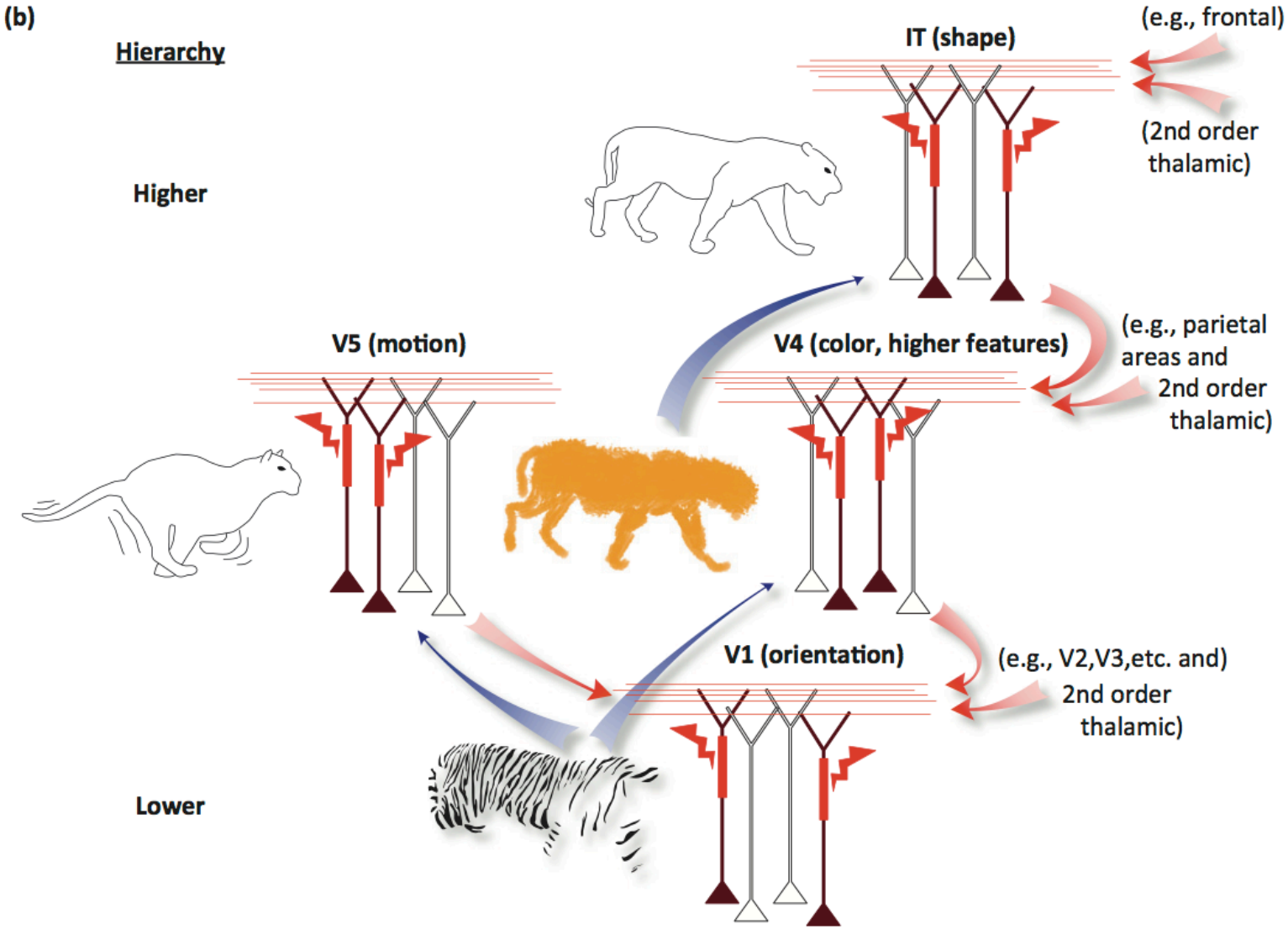
An interesting synthesis of cross-pathway interactions



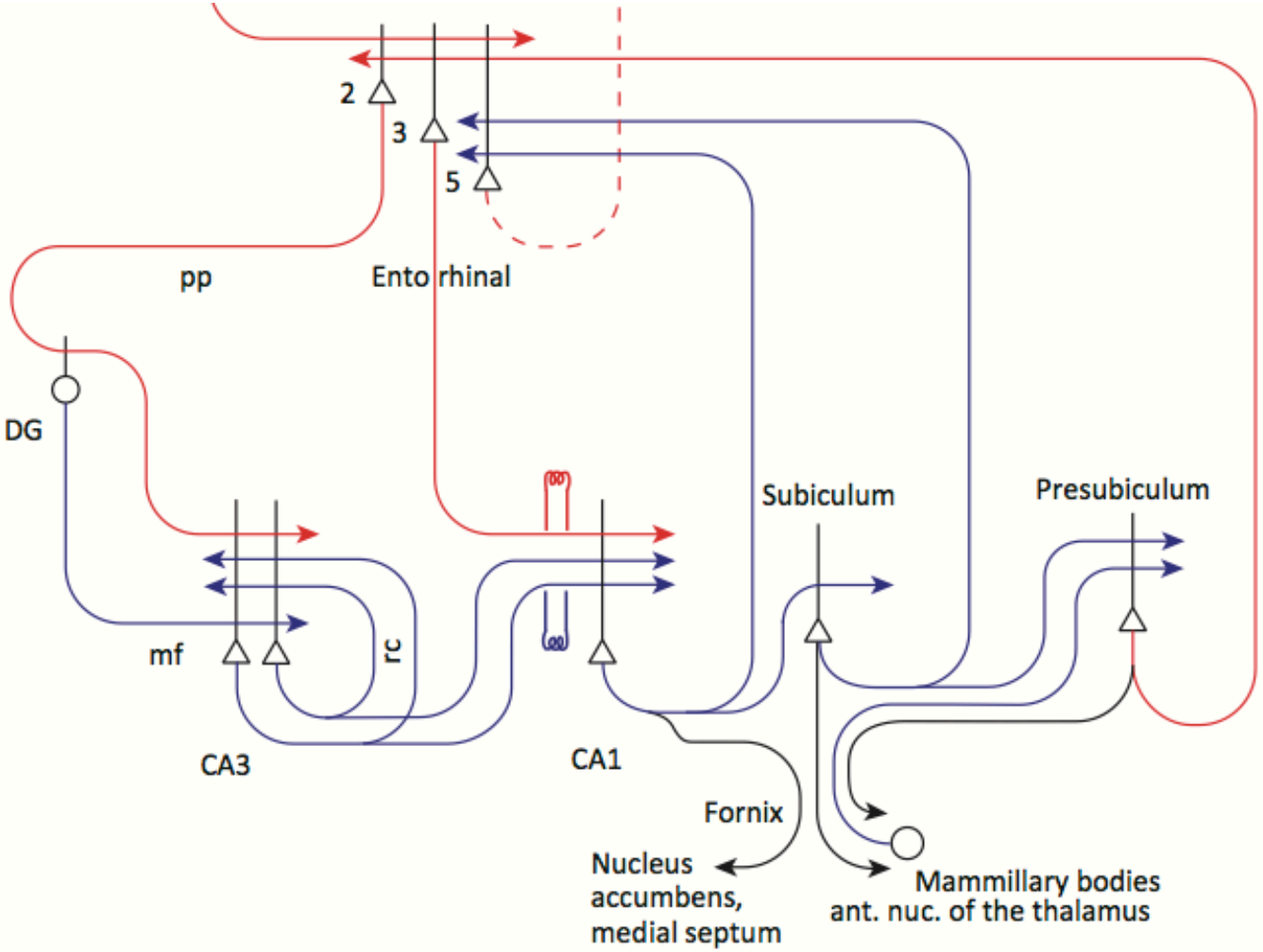
An interesting synthesis of cross-pathway interactions

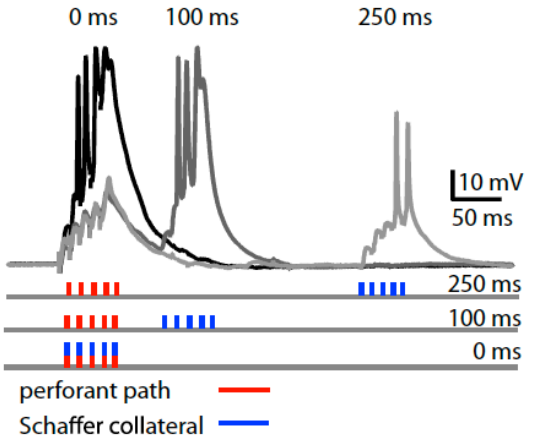


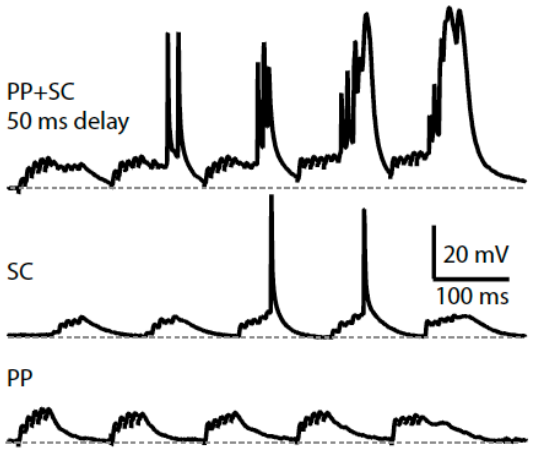
An interesting synthesis of cross-pathway interactions



An interesting synthesis: the hippocampus also has a similar organization





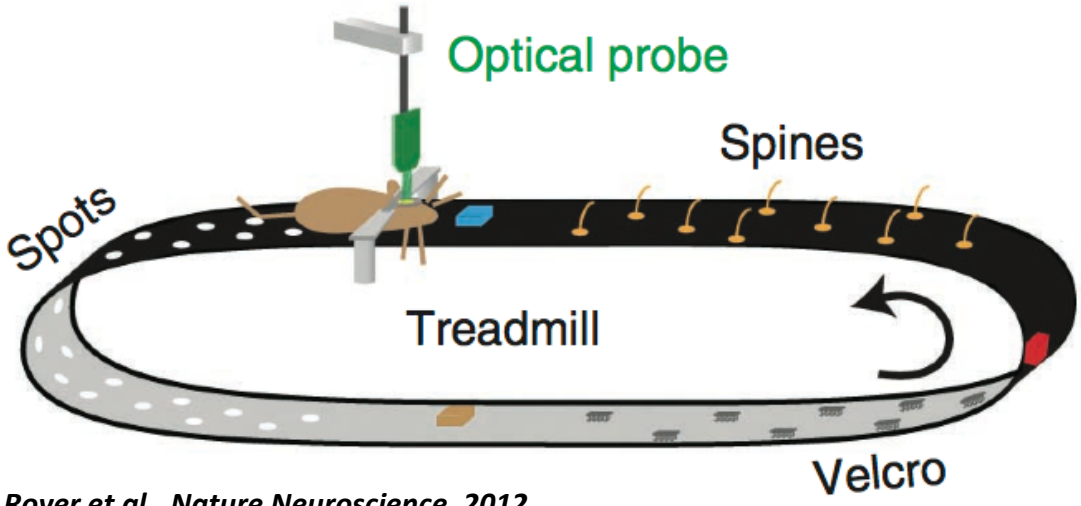


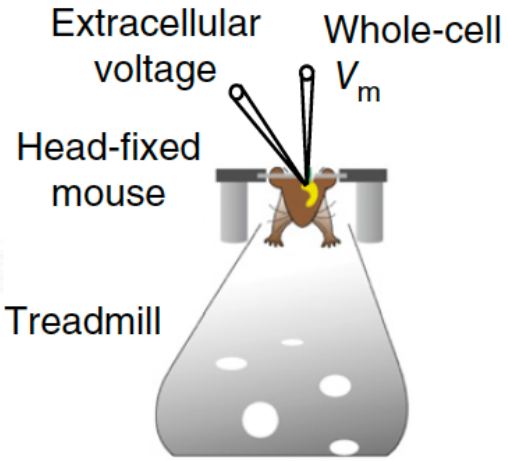
Place cells and plateau potentials

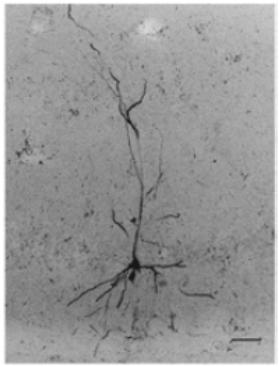
Conjunctive input processing drives feature selectivity in hippocampal CA1 neurons

Katie C Bittner[1], Christine Grienberger[1], Sachin P Vaidya[1], Aaron D Milstein[1], John J Macklin[1], Junghyup Suh[2,3], Susumu Tonegawa[2,3] & Jeffrey C Magee[1]

Nature Neuroscience 18, 1133–1142 (2015).

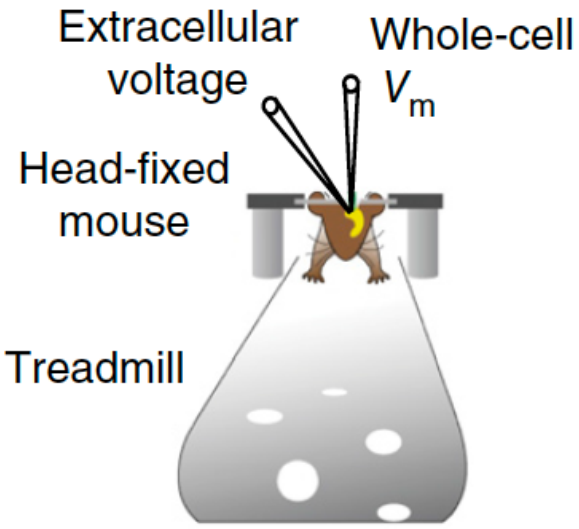


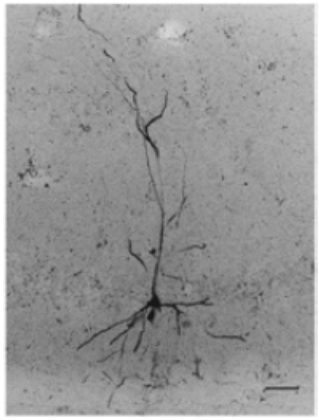


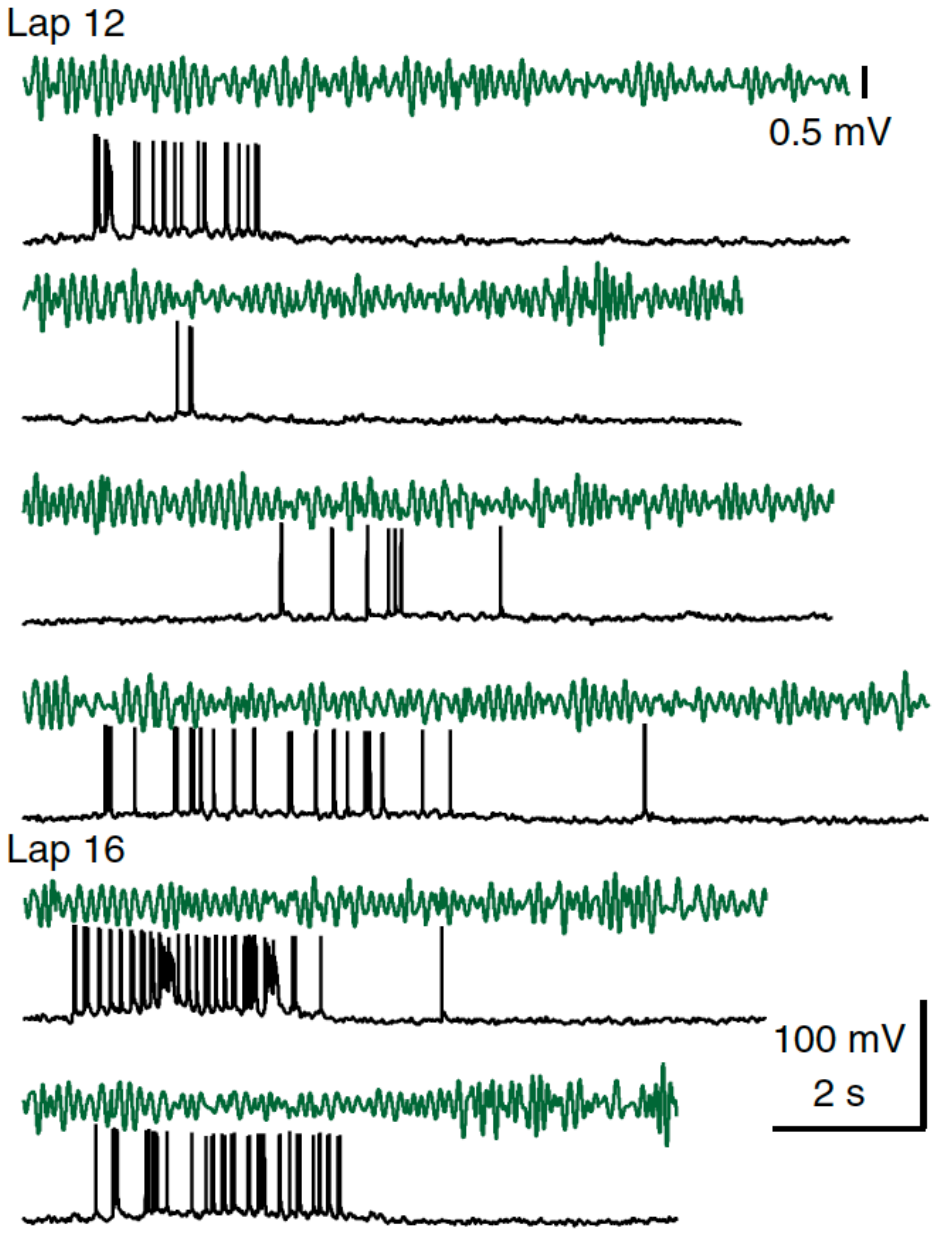


Royer et al., Nature Neuroscience, 2012

Typical place cell on the treadmill

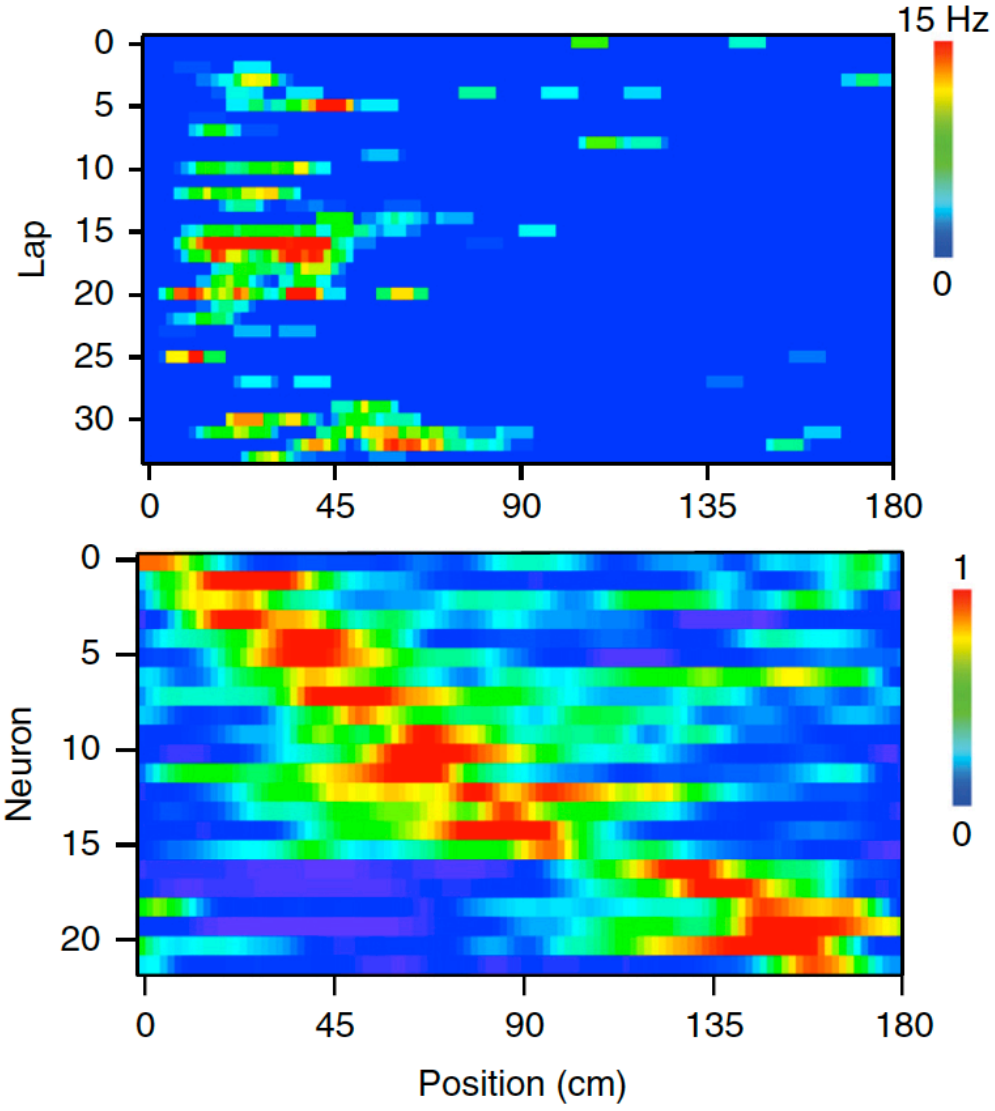






Bittner et al., Nature Neuroscience, 2015

Different cells, different place.



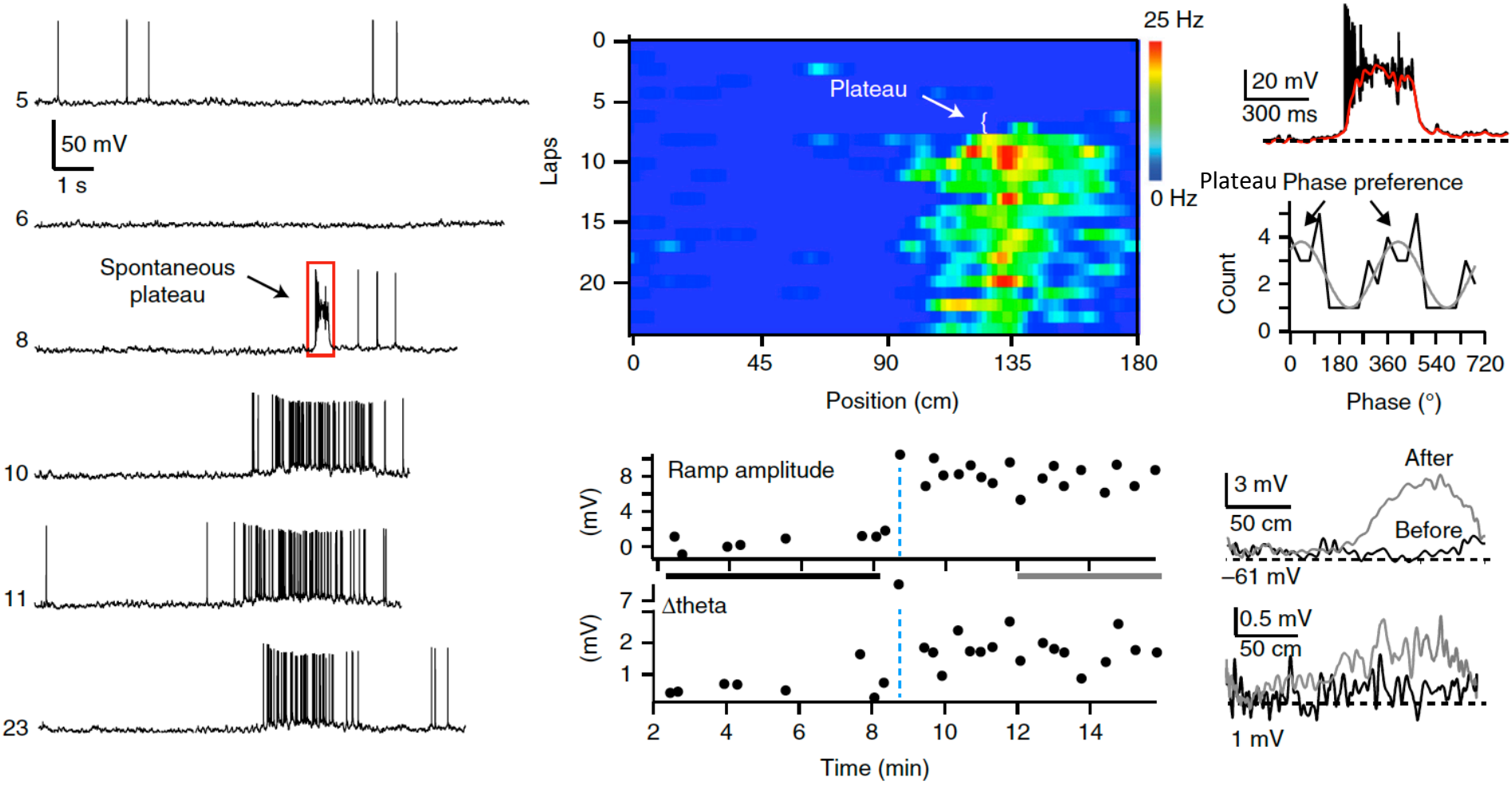
Single place cell, different laps

22 place cells from 21 mice

Bittner et al., Nature Neuroscience, 2015

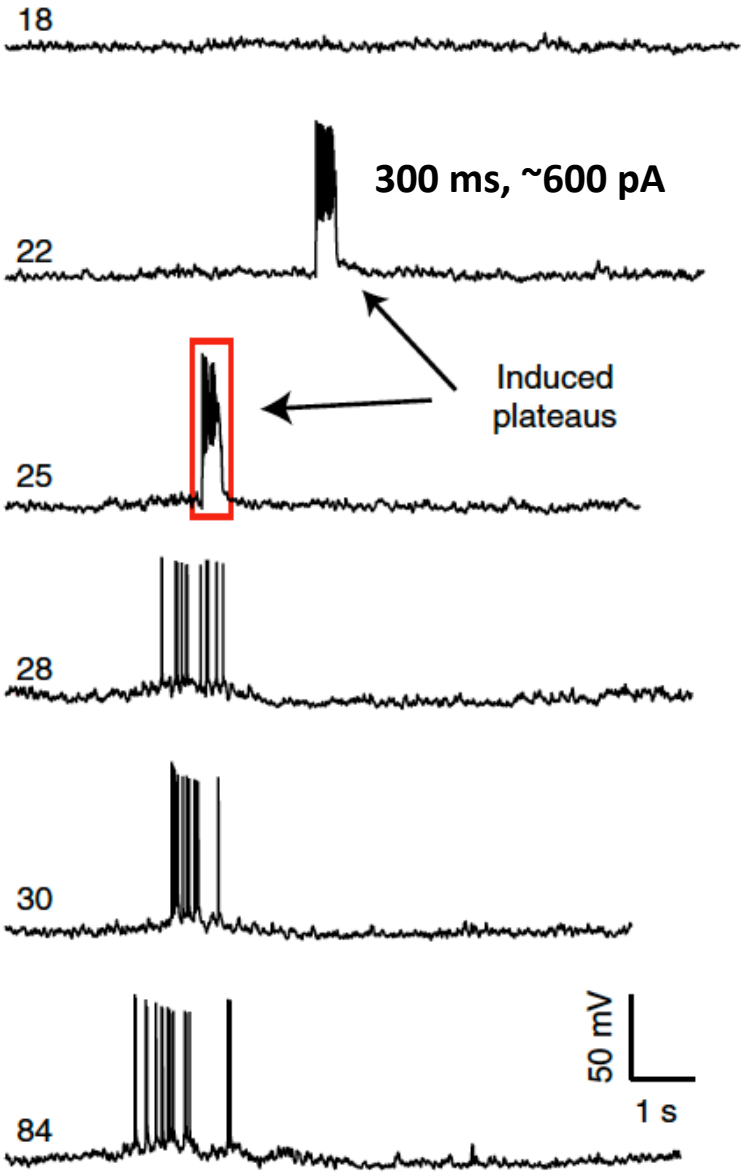
Spontaneous plateaus are associated with new place field formation

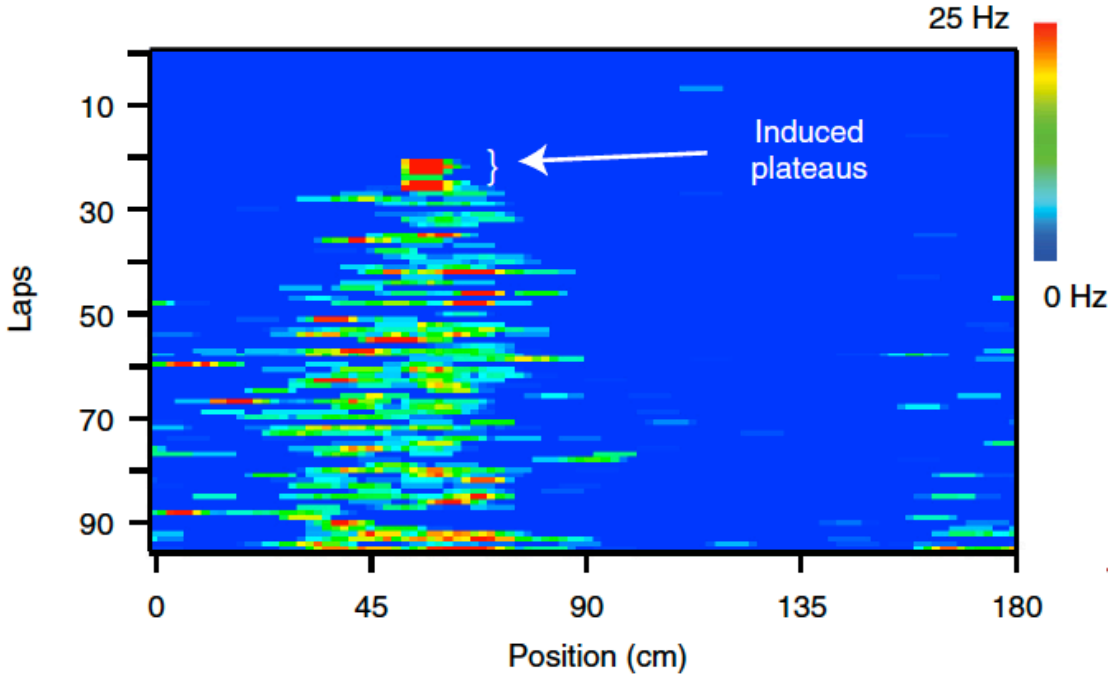
Place fields in silent cells formed after appearance of a large plateau potential



Bittner et al., Nature Neuroscience, 2015

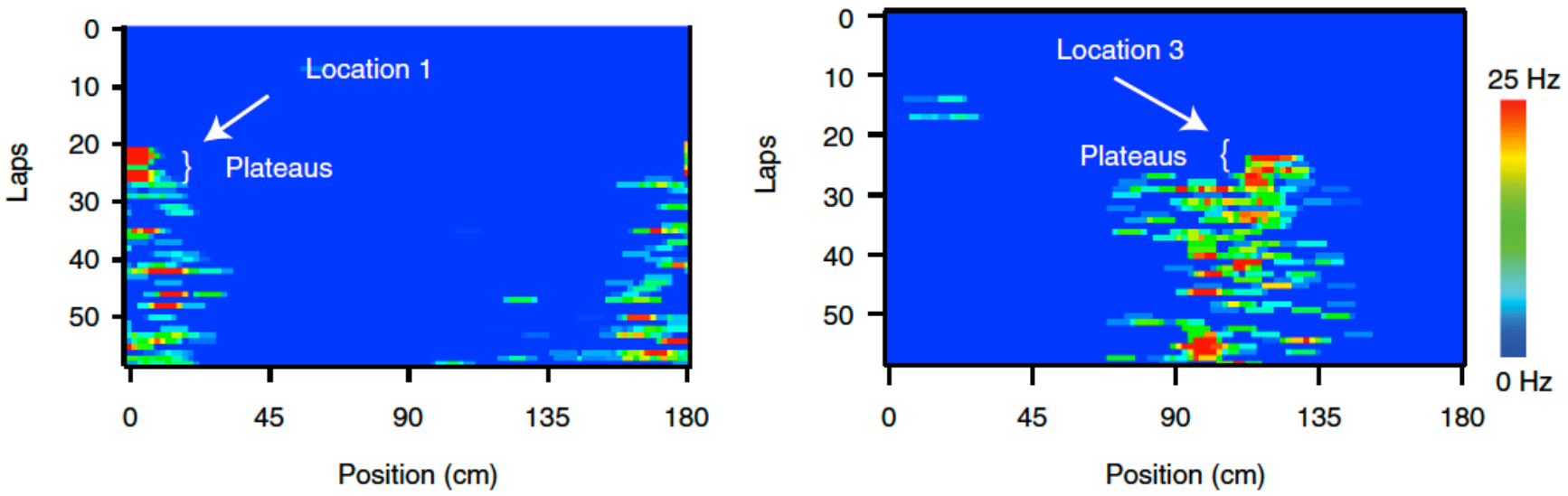
Artificial plateaus are sufficient to drive new place field formation





Bittner et al., Nature Neuroscience, 2015

Artificial plateaus are sufficient to drive new place field formation at any arbitrarily chosen location



Implication: CA1 pyramidal neurons receive proportional amounts of input from presynaptic cells that are tuned to all possible spatial locations and as a result are equally capable of expressing place-specific firing at any potential position.

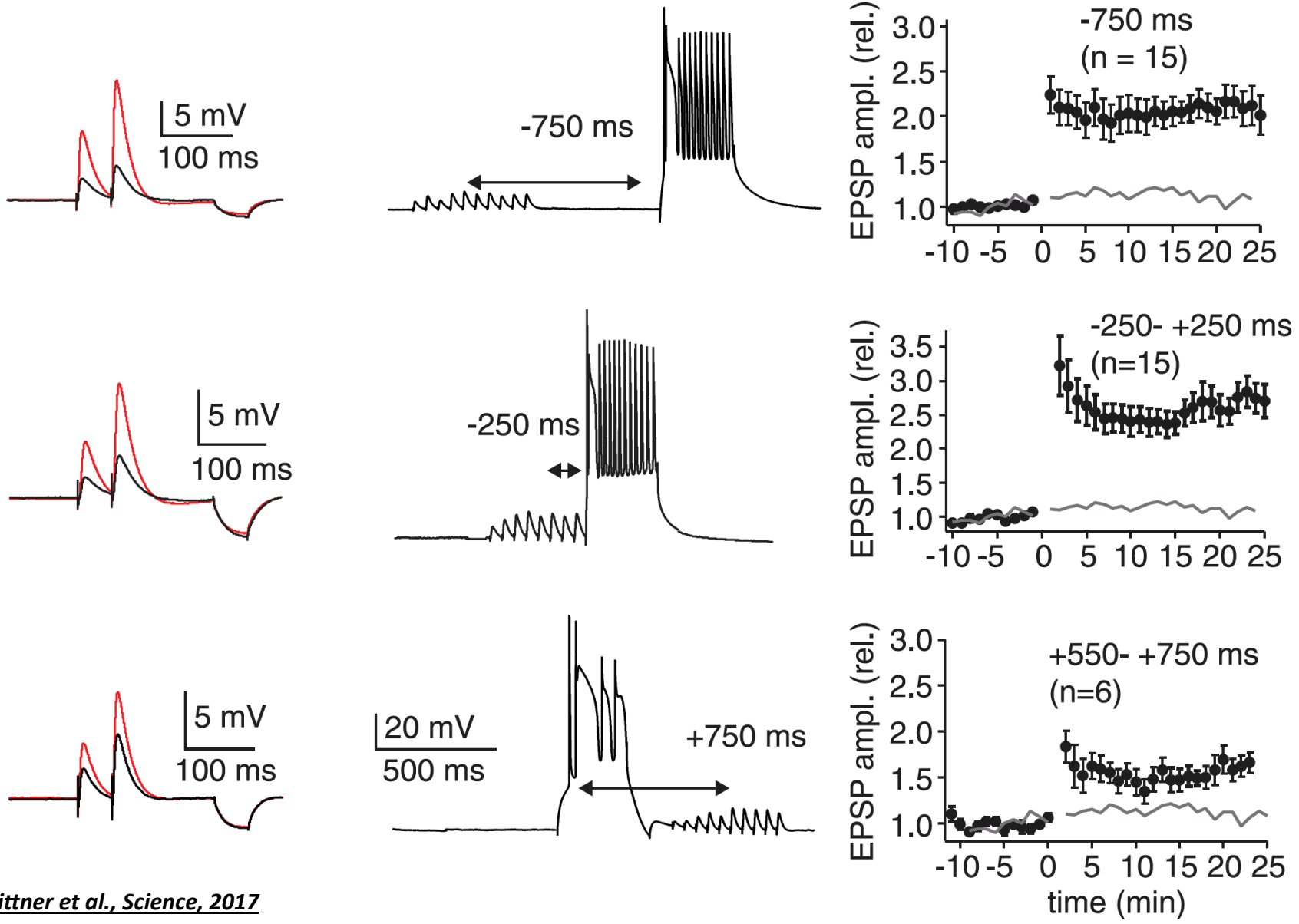
Bittner et al., Nature Neuroscience, 2015

Behavioral time scale synaptic plasticity underlies CA1 place fields

Katie C. Bittner,[1]* Aaron D. Milstein,[1,2]* Christine Grienberger,[1]
Sandro Romani,[1] Jeffrey C. Magee[1]†

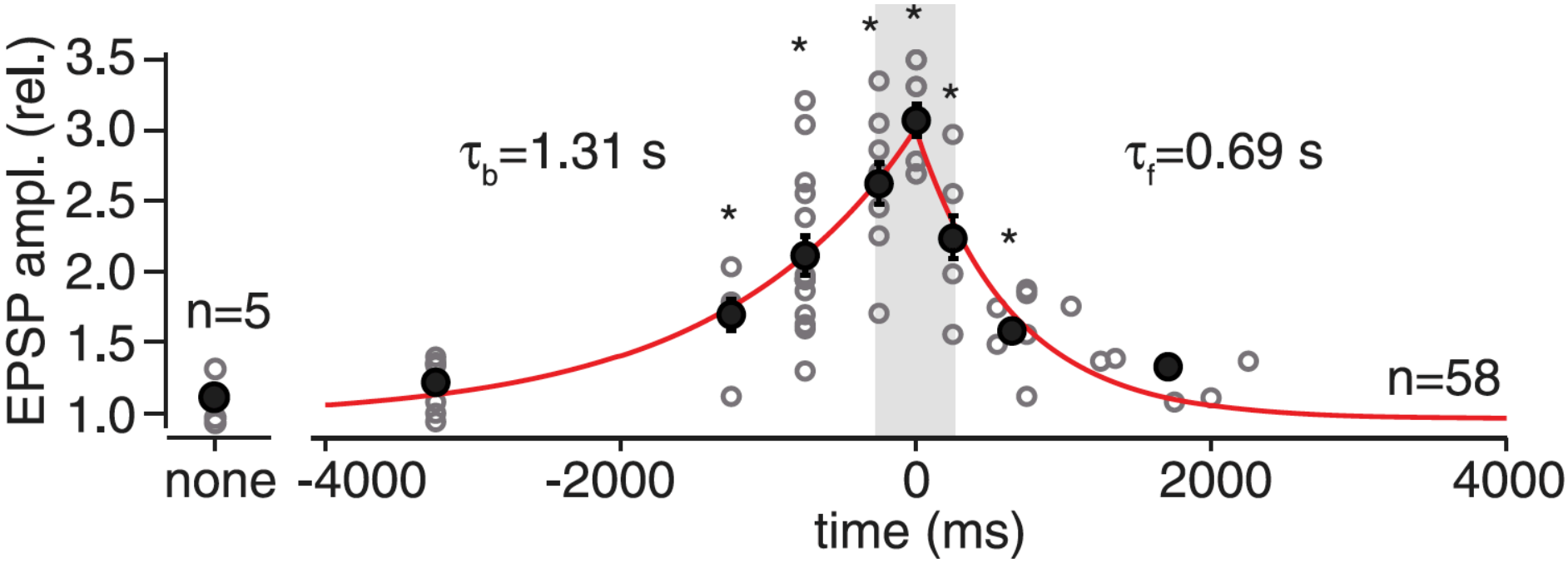
Science 357, 1033–1036 (2017)

Artificial plateaus are sufficient to drive LTP over long delays



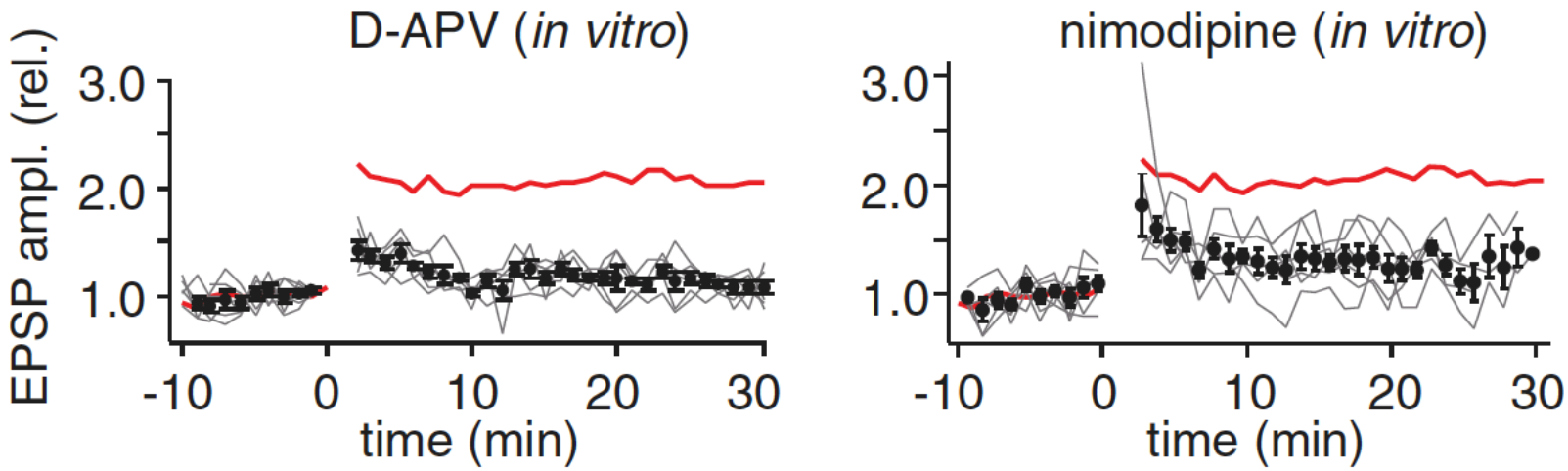
Bittner et al., Science, 2017

Artificial Plateaus are sufficient to drive LTP over long delays



Bittner et al., Science, 2017

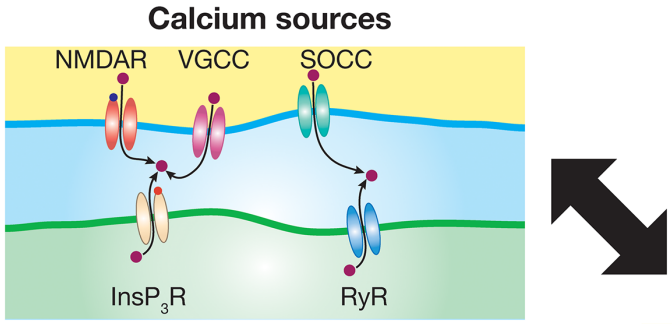
Plateau-based LTP was dependent on NMDARs and L-type calcium channels

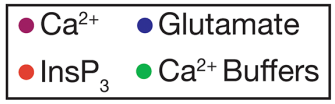


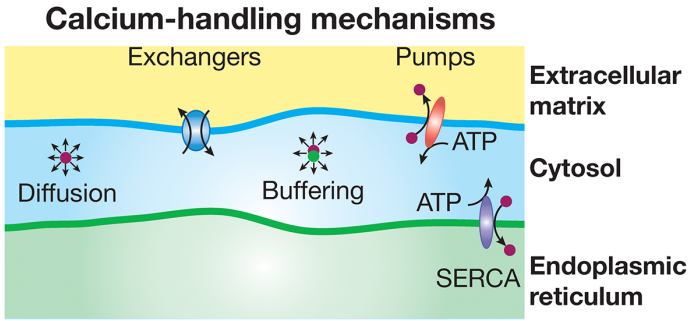
Bittner et al., Science, 2017

Several mechanisms governing LTP induction and calcium elevation

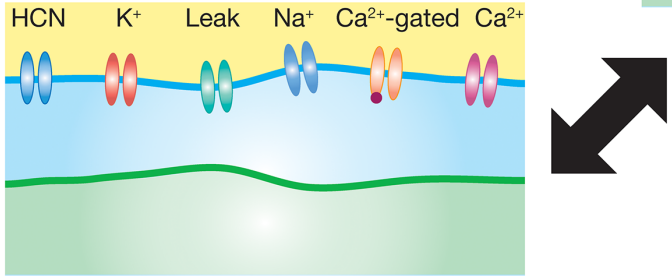
High frequency stimulation
Theta burst stimulation
Theta burst pairing
Spike-timing dependent plasticity
Plateau potentials
Pathway interactions
Pharmacological depolarization







Synergistic Interactions



What did we learn today?

Synaptic plasticity is bidirectional — just as there is LTP, there is LTD

LTD has similar properties as LTP — dependent on depolarization and calcium influx through NMDAR/VGCC/stores

Rule of thumb: Slowly decaying low-levels of calcium leads to LTD, whereas fast decaying high-levels of calcium leads to LTP

Spike timing dependent plasticity: true implementation of Hebb's postulate?

Plateau-based LTP: Behavioral scale plasticity?

All plasticity properties are synapse dependent, and are subject to change — DO NOT GENERALIZE