From Science Magazine, 2005

Synaptic Plasticity — Lecture 3

Long-term synaptic plasticity:

Potentiation

Neuronal Physiology and Plasticity

Aug 2018 Semester

In the previous class…

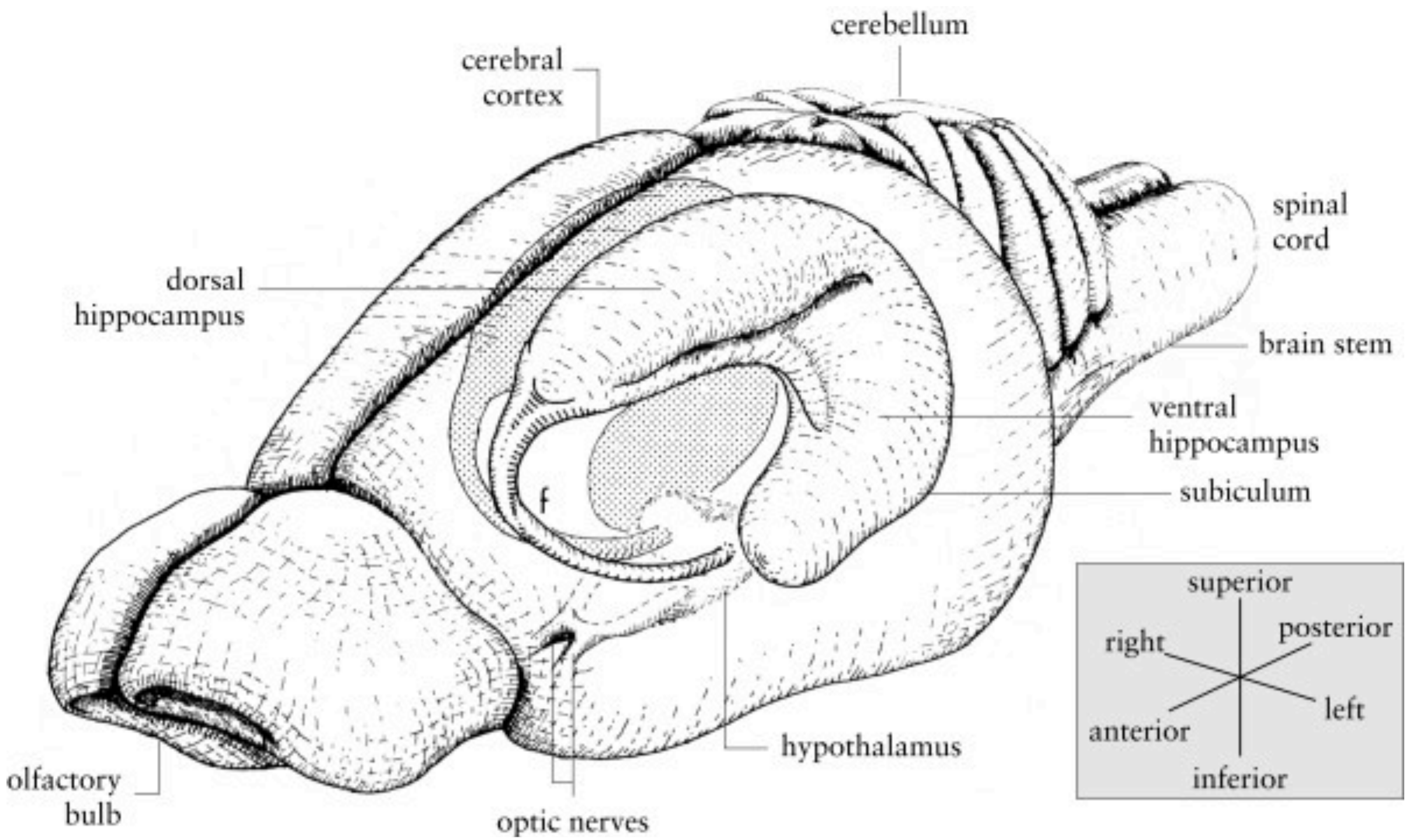
Short term plasticity: PPF/D (100s of ms), augmentation (5–10 s) and PTP (30 s – several minutes)

PPF/D, Augmentation and PTP are all presynaptic in nature and are an interplay between residual **calcium** and the amount of available vesicles for release (determined by previous releases and how fast they replenish)

PPF occurs in synapses with low initial release probability and PPD occurs in those with high initial release probability

Various parameters contribute to how STP expresses, and it is synapse dependent

The mammalian hippocampus is a good system for studying long-term synaptic plasticity

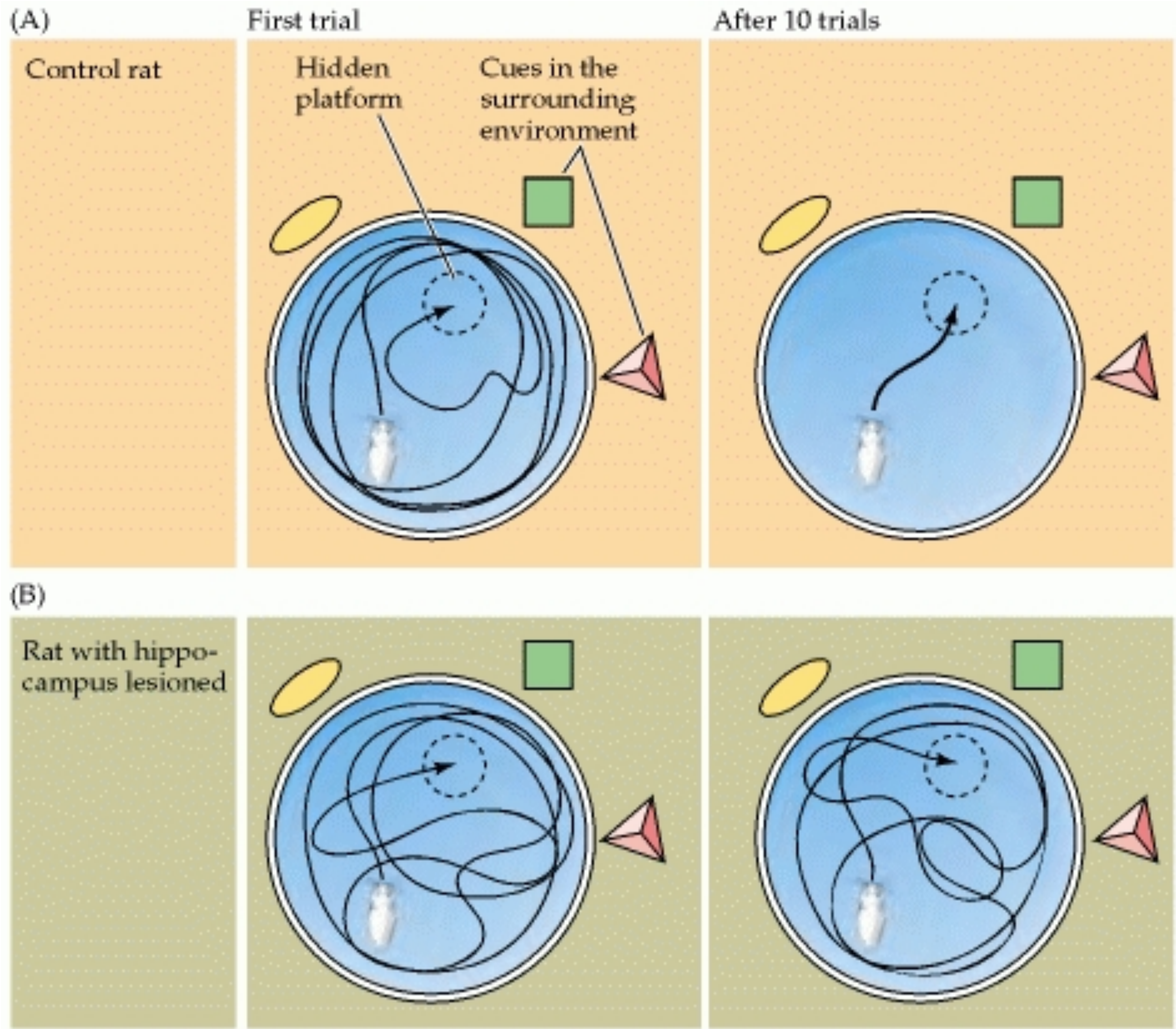


Why?

http://www.biomedcentral.com/

Hippocampus is involved in learning and memory

HM, Henry Molaison (1926–2008)

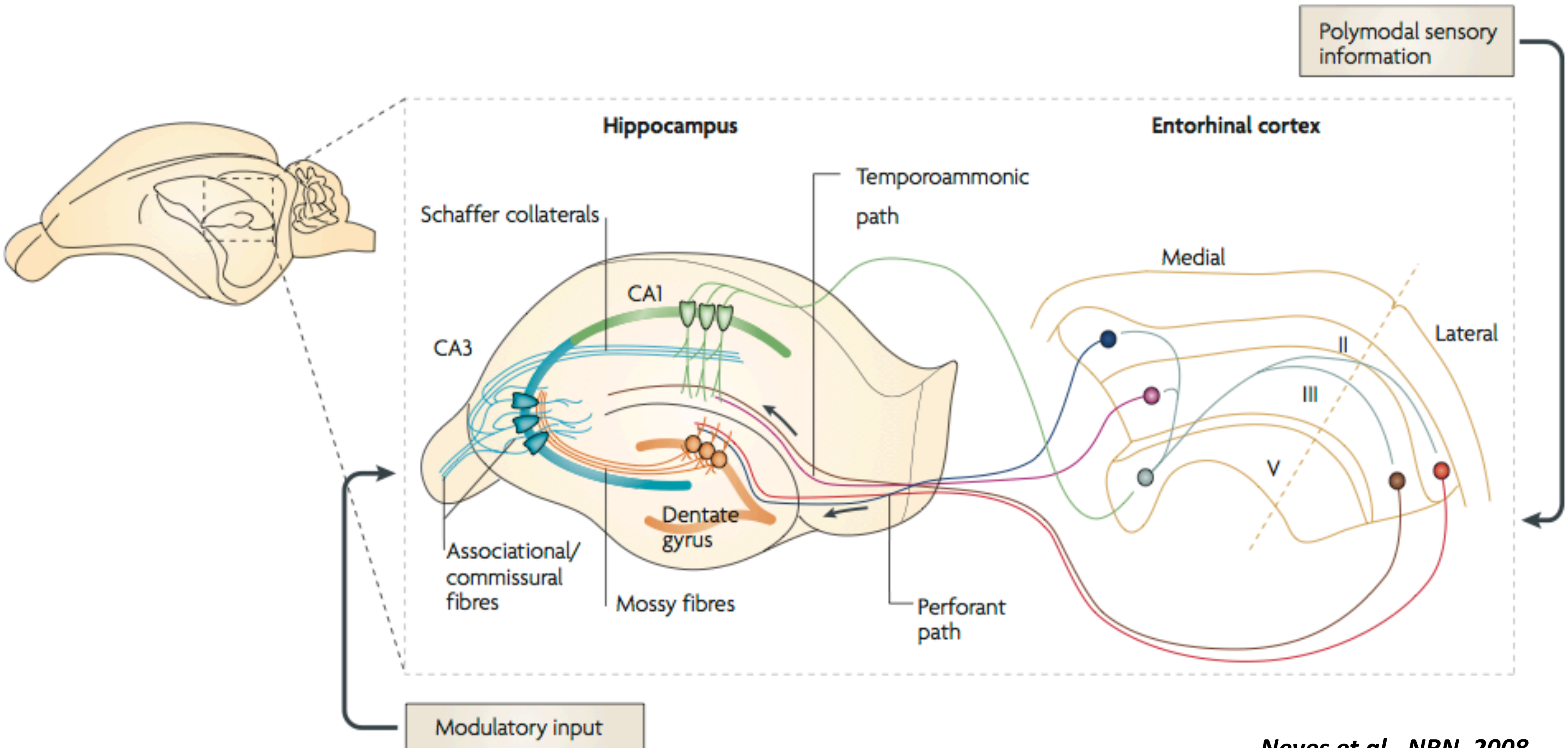


Hippocampal lesions impair the animal's ability to learn spatial tasks

Purves, Neuroscience Book

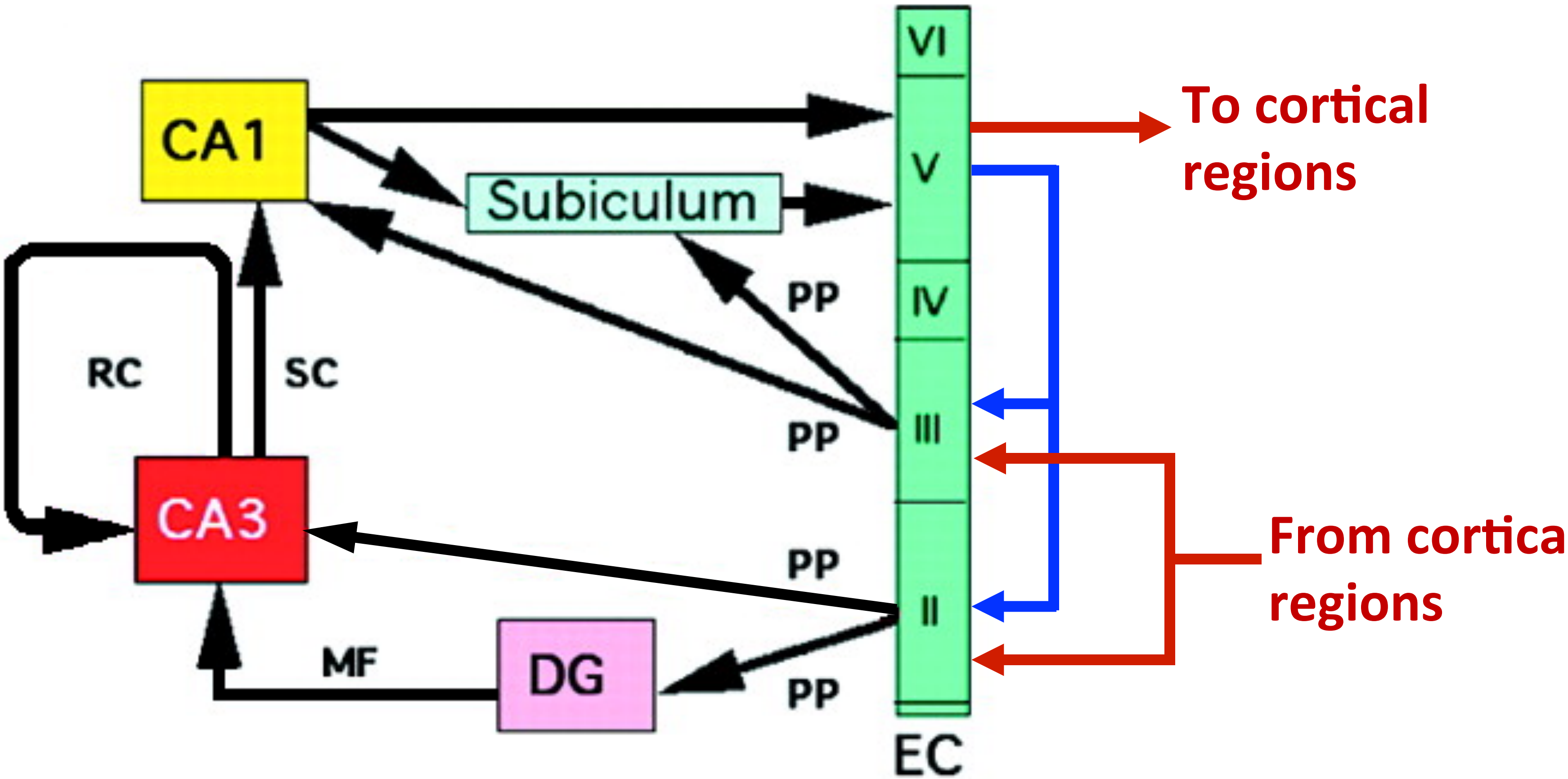
The circuitry is neatly organized making recordings and interpretations easier

The trisynaptic circuit



Neves et al., NRN, 2008

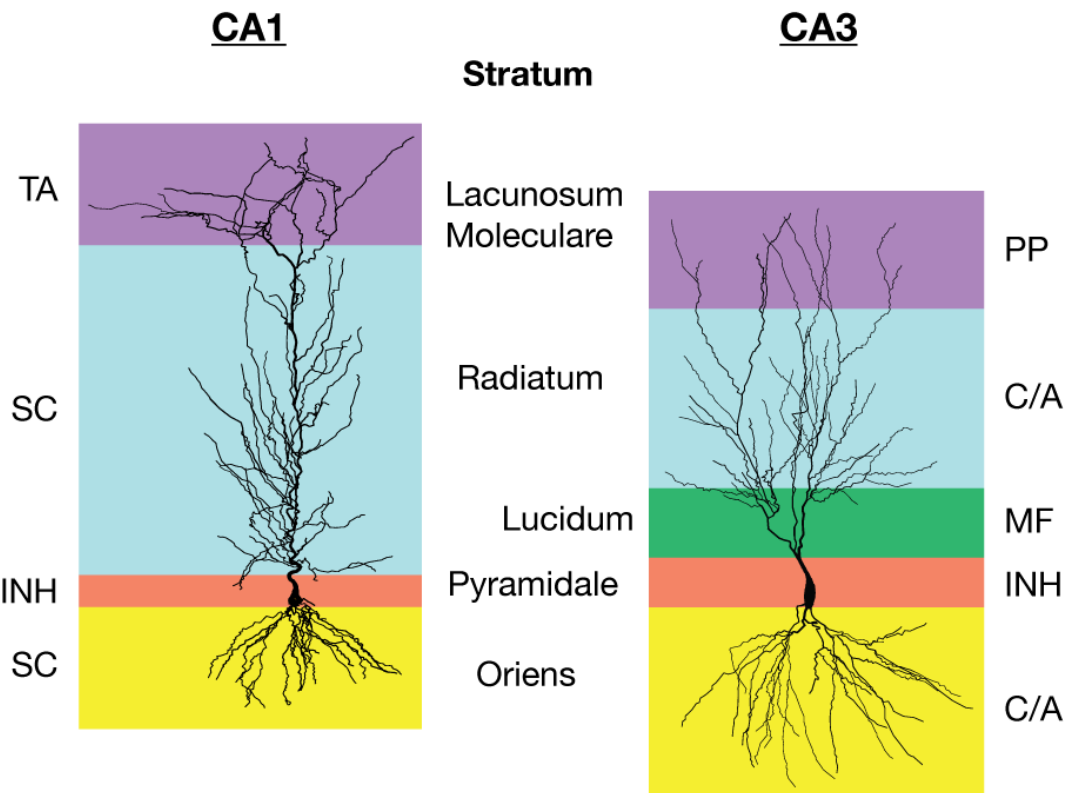
The trisynaptic circuit



Modified from Nakazawa et al. Science, 2002

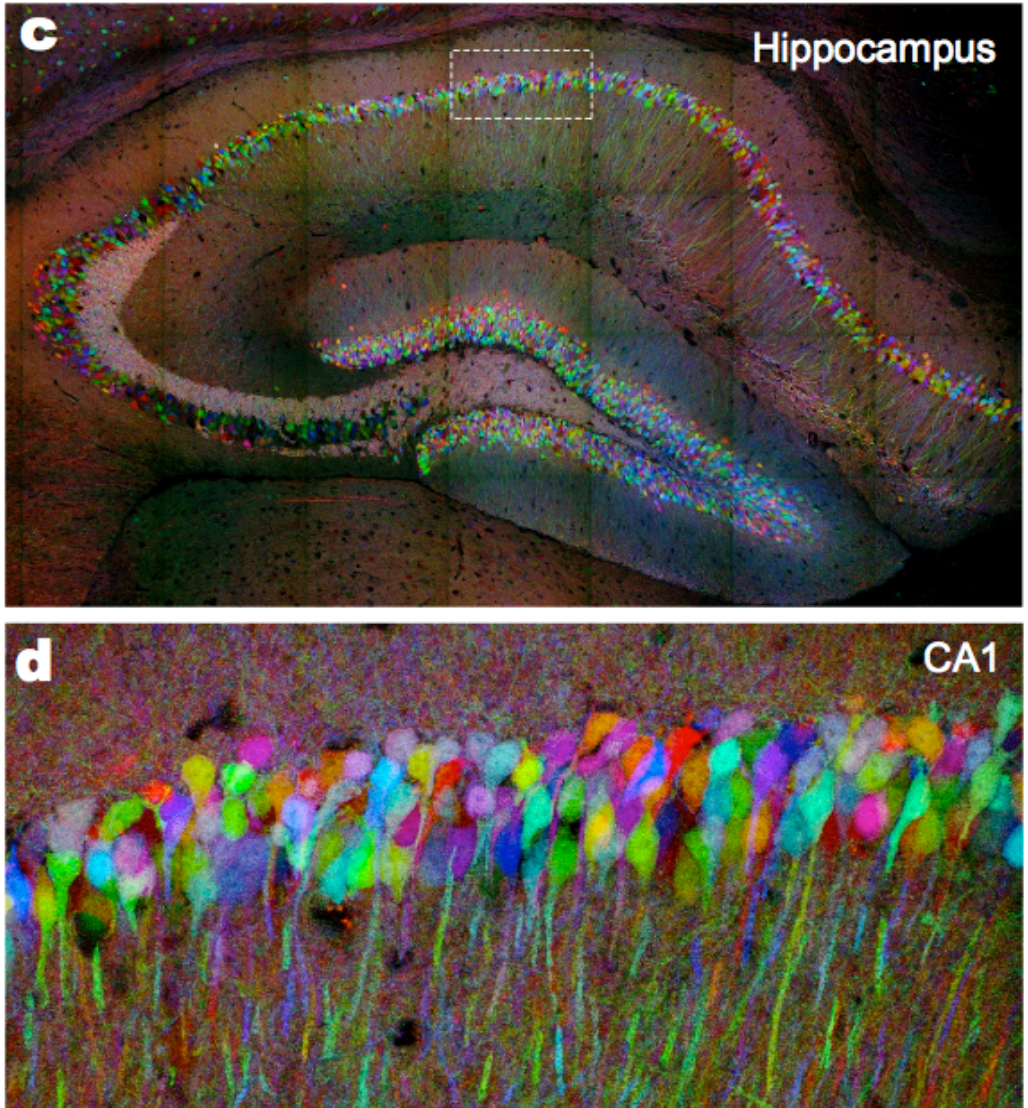
Inputs are nicely organized into different strata

There is no crossover of synapses, so studying particular synapses becomes easier

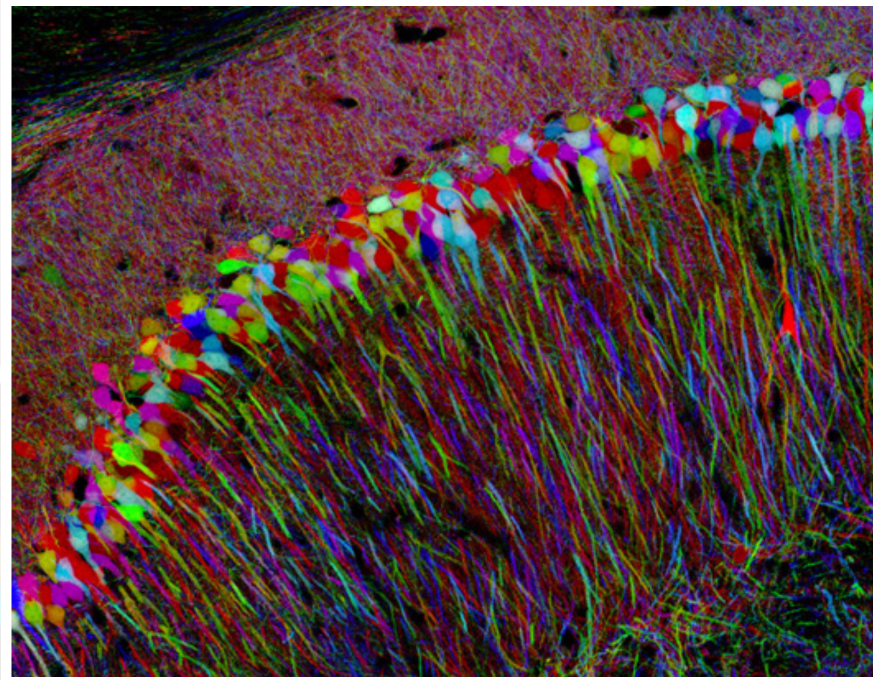


PP: Perforant pathway from entorhinal
C/A: Commissural/Associational inputs from CA3
MF: Mossy fiber inputs from DG
INH: Inhibitory inputs
SC: Schaffer collaterals from CA3
TA: Temporoammonic pathway from EC

Field recordings become easier because cells are all organized in a regular fashion



Distance measurements are also easier here with dendritic recordings!!



Brainbow mouse: each neuron has a different color!

Livet et al., Nature, 2007

Field potentials

Signals that are generated by electric fields produced by the activity of single neurons or their groups

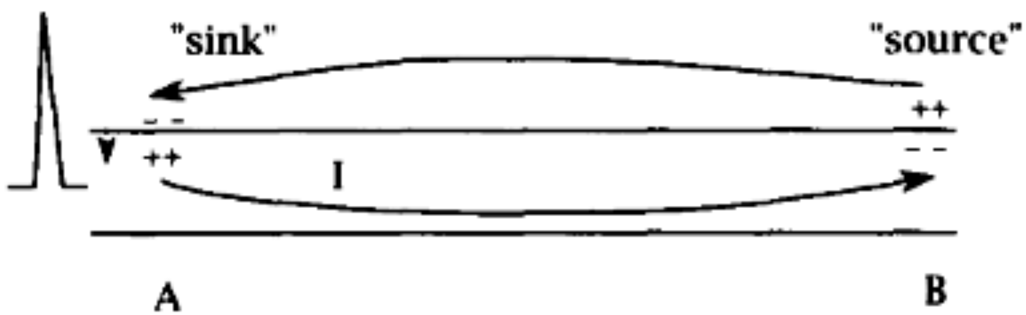
Typically measured between two points on the extracellular space rather than doing it across the membrane

Examples:

- Measuring action potential propagation from the extracellular space of a neuron,
- Measuring synaptic and spiking activity of a group of neurons,
- Electroencephalographic (EEG) recordings of gross brain activity from the scalp

Sources and sinks

At the time of action potential elicited at point A,



Rule of thumb: The point at which current enters is referred to as the sink!

Depending upon where you record in the extracellular field with respect to a distant ground electrode, you would get a negative or a positive potential with respect the same intracellular action potential

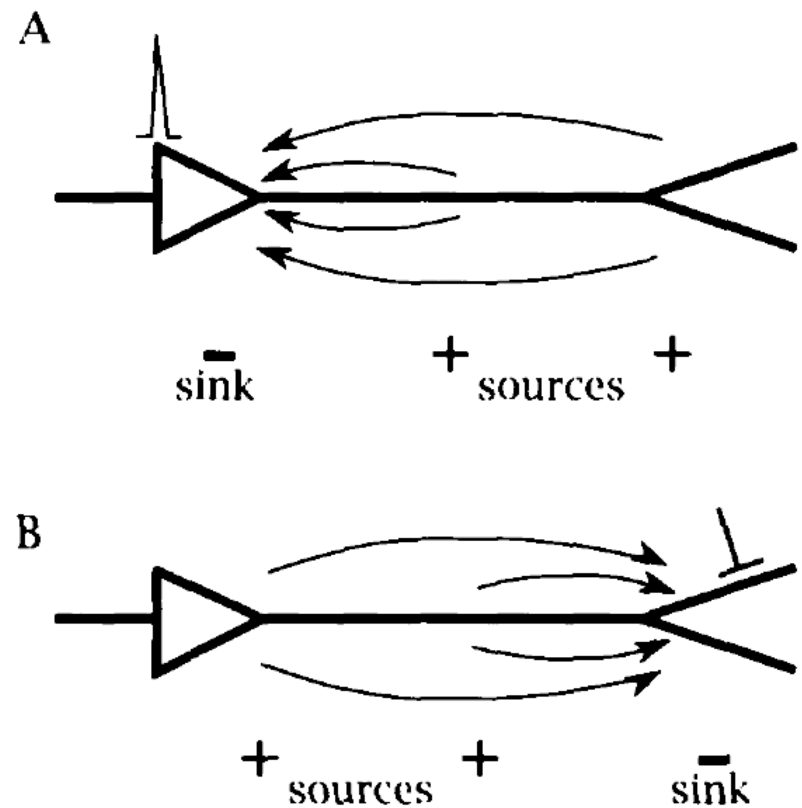
e.g., At Pt. A extracellularly it would be a –ve potential, while at Pt. B it will be +ve

Neurons as electric dipoles

Electric dipole: A quantity of positive and negative charges separated by some distance

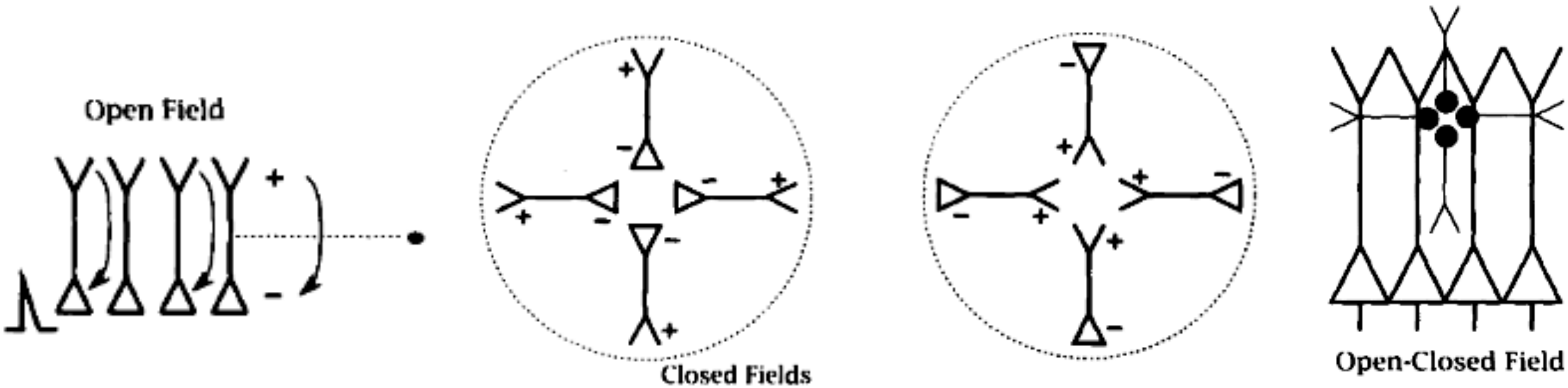
A neuron behaves as a dipole when there is an action potential initiated at the soma or a synaptic input reaches the soma or the dendrites

The location of conductance change acts as an active *sink*, while the other end acts as a passive *source*



Johnston and Wu, 1995

Open and close fields



Open fields: Nice laminar arrangement, synchronous inputs, synchronous action potentials in response to afferent inputs! Well aligned dipoles! E.g., Hippocampus, cerebellum

Close fields: Forms dipoles with spherical symmetry. Inside the sphere, the recordings will be location dependent, while outside it will be zero!

Open–Close fields: Combination of open and close. Inside the close field, the potential will be location-dependent, but outside it will be just that of the open field.

Most regions have random fields, so field potential becomes location dependent!!!

Johnston and Wu, 1995

Analyzing fields semi-quantitatively!

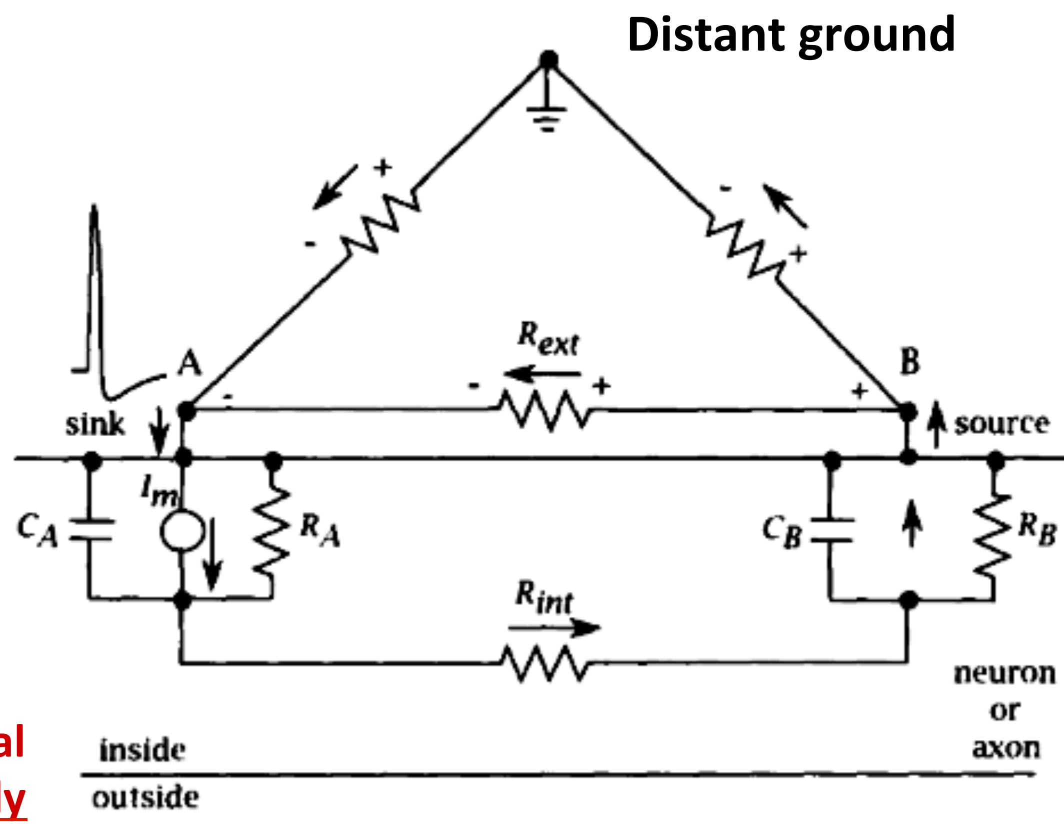
Given (a) I_m is drawn from extracellular space, (b) extracellular voltage is dependent on the transmembrane current, and (c) the polarities of V_A and V_B:

$$V_A \propto I_m \propto -V_B$$

For non-steady state fast events, I_m is largely through the capacitance:

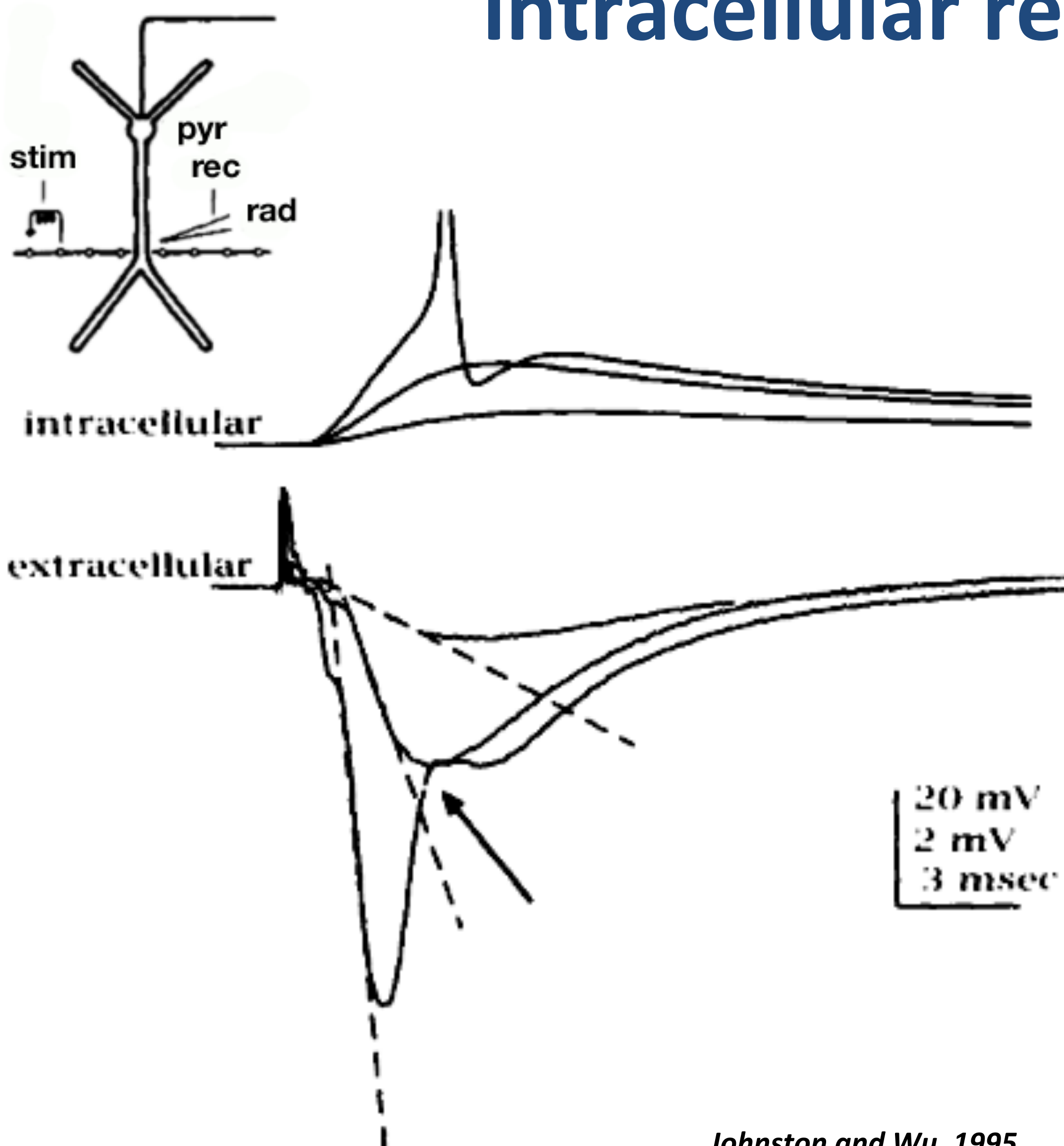
$$\therefore \quad V_A \propto \frac{dV_m}{dt} \propto -V_B$$

Thus, the extracellular field potential has a time course that is approximately equal to the transmembrane current.



Johnston and Wu, 1995

Relations between field potentials and intracellular recordings

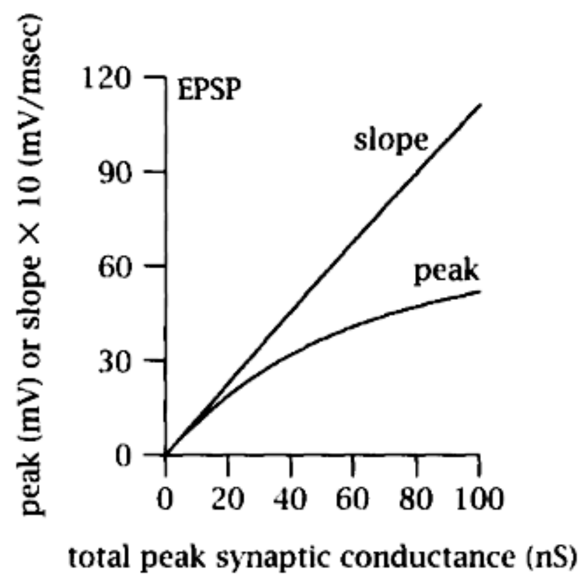


Johnston and Wu, 1995

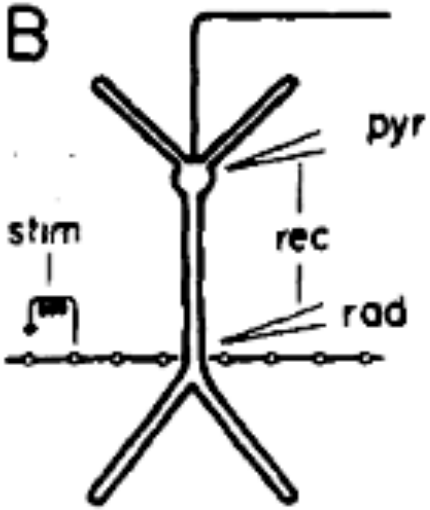
Measuring initial slope: Why?

1. Peak is usually contaminated by spikes and polysynaptic inputs; initial slope is not!

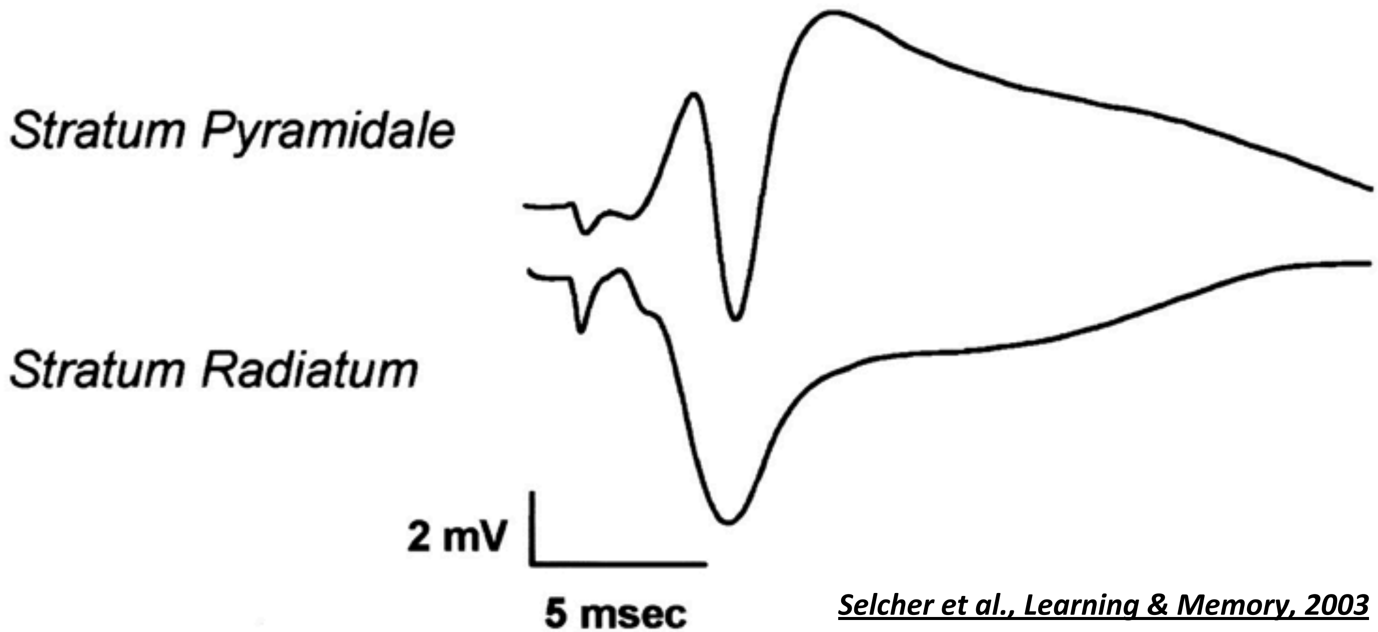
2. Slope is linearly related to synaptic conductance, while peak is not!



Dual field recordings: fEPSP and popSpike



Johnston and Wu, 1995



Selcher et al., Learning & Memory, 2003

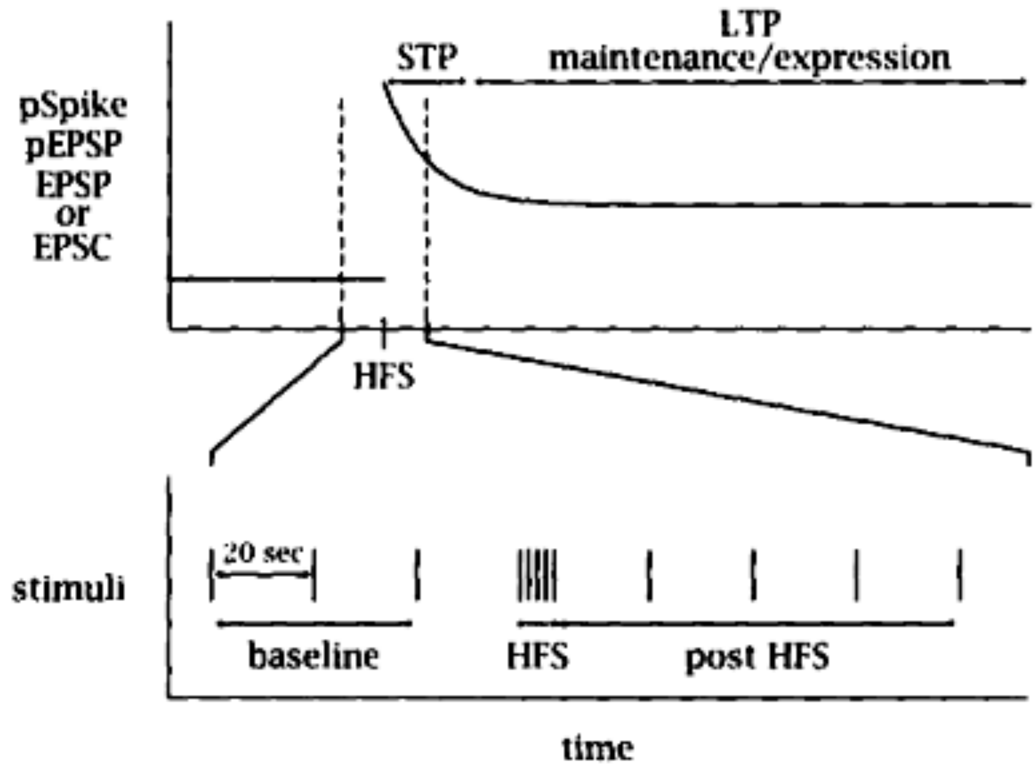
The field EPSP and population spike are dependent on the number and amplitude of individual neuronal EPSPs and action potentials, respectively

Long-term potentiation

General LTP protocol and progression

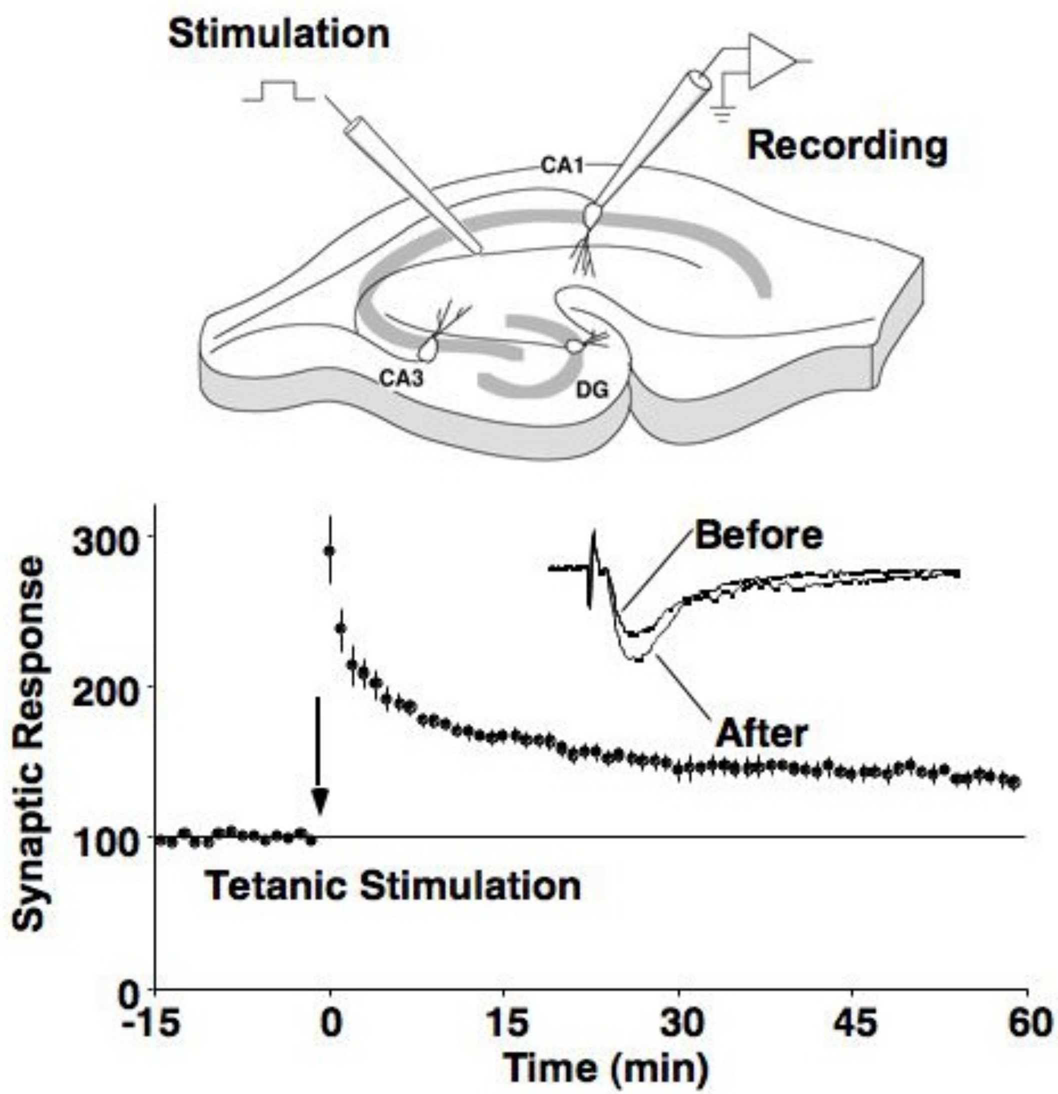
High frequency stimulation (HFS)/ Tetanus is usually a single or multiple instance(s) of 100 Hz for 1 s

But, this is variable, and LTP is dependent upon the frequency and pattern of stimulus



Johnston and Wu, 1995

A typical LTP experiment



http://glutamate.brain.riken.jp/

Modes of performing LTP experiments

In vivo

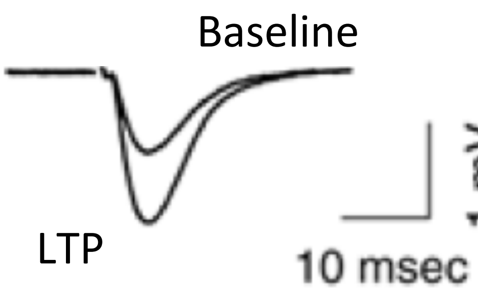
In vitro

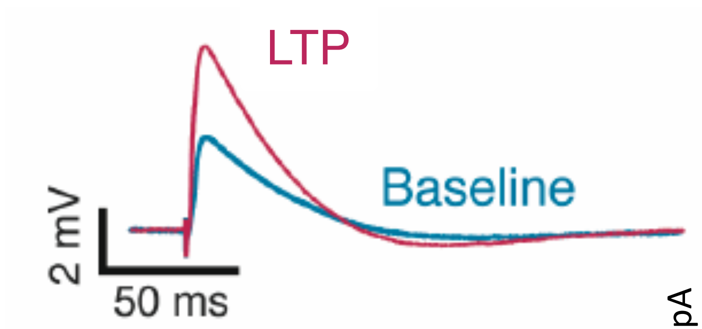
Whole-cell patch-clamp

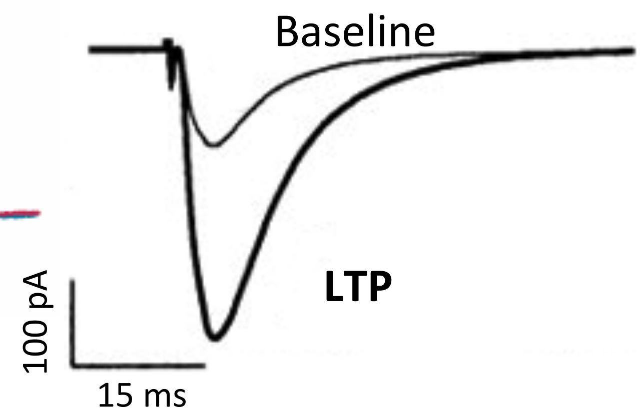
Field recordings

Current clamp

Voltage clamp





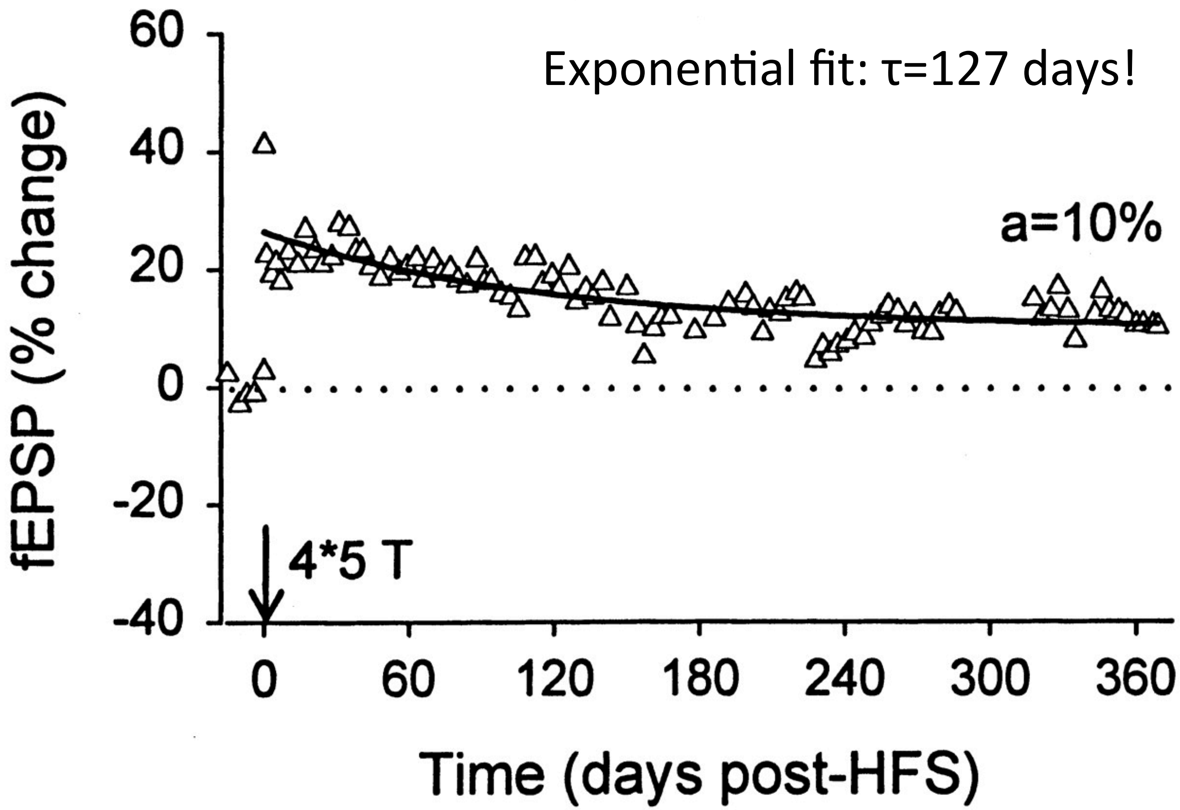


Bortolotto et al., Curr. prot. Neurosci., 2001

Narayanan and Johnston, Neuron, 2007

Kim and Lisman, J. Neuroscience, 1999

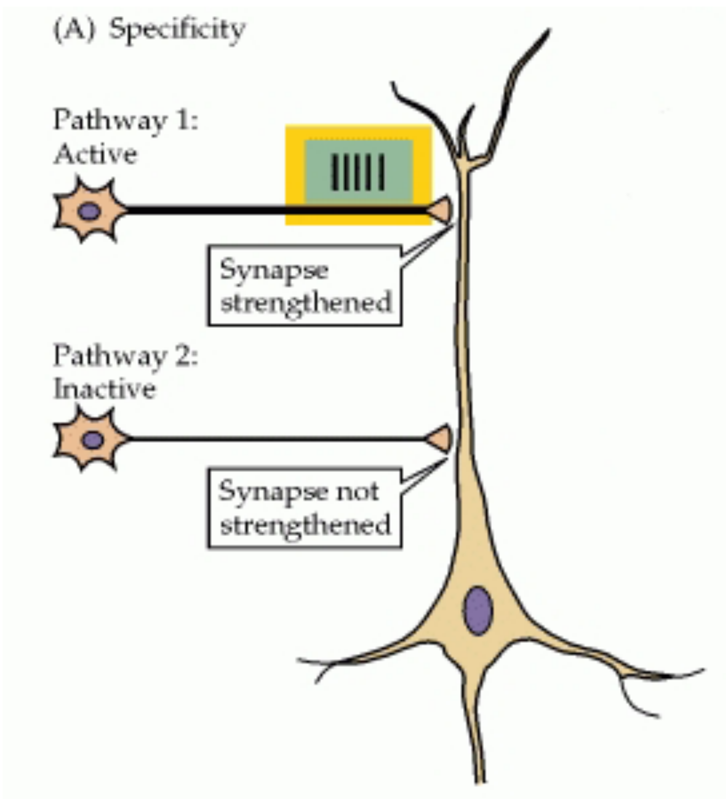
Basic Properties of LTP: Persistence

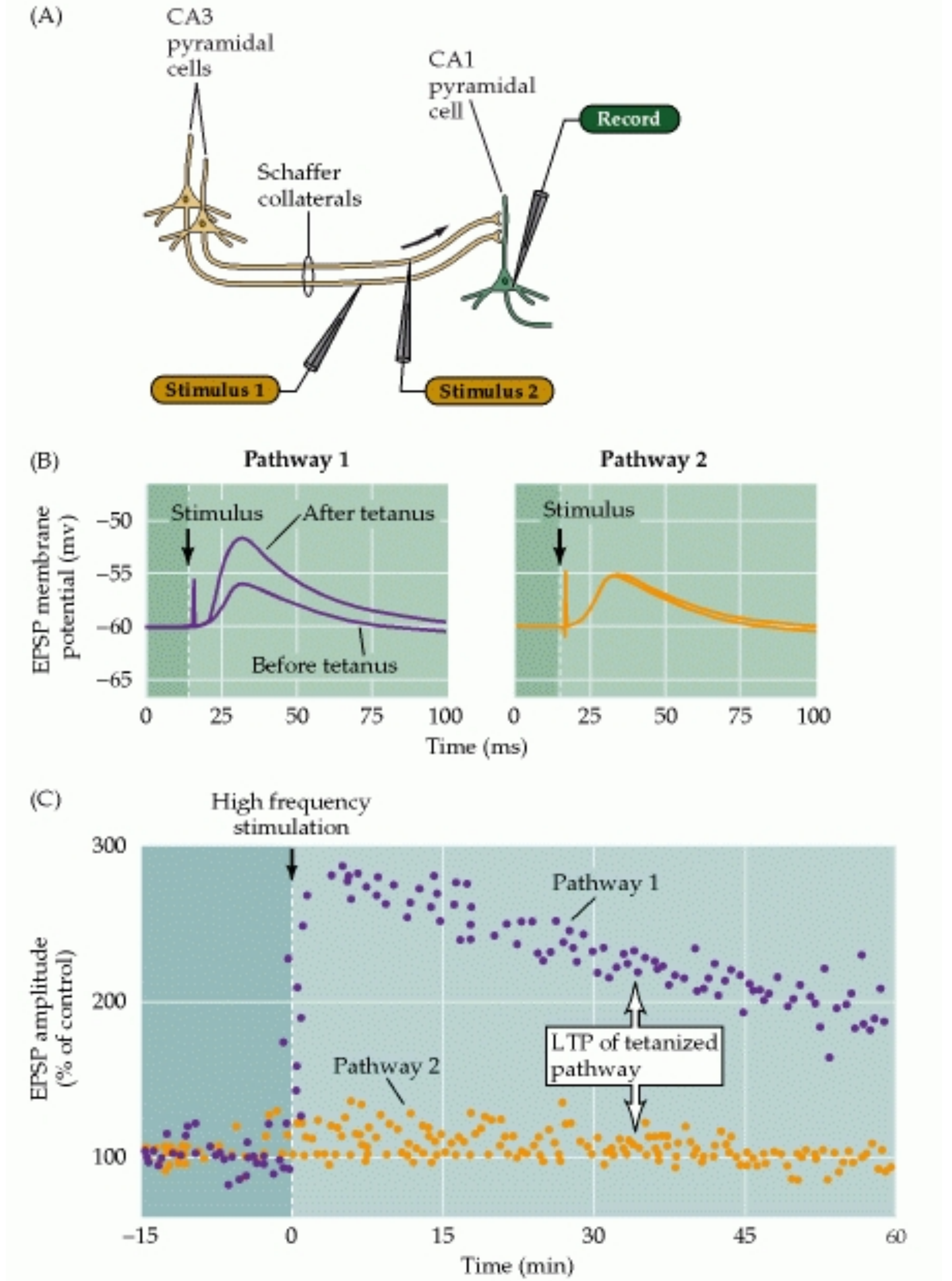


4*5 T=Four sets of five 400 Hz tetanic trains (each of 25 ms) delivered 10 min apart

Abraham et al., J. Neurosci., 2002

Basic Properties of LTP: Input specificity





__Purves, Neuroscience book__

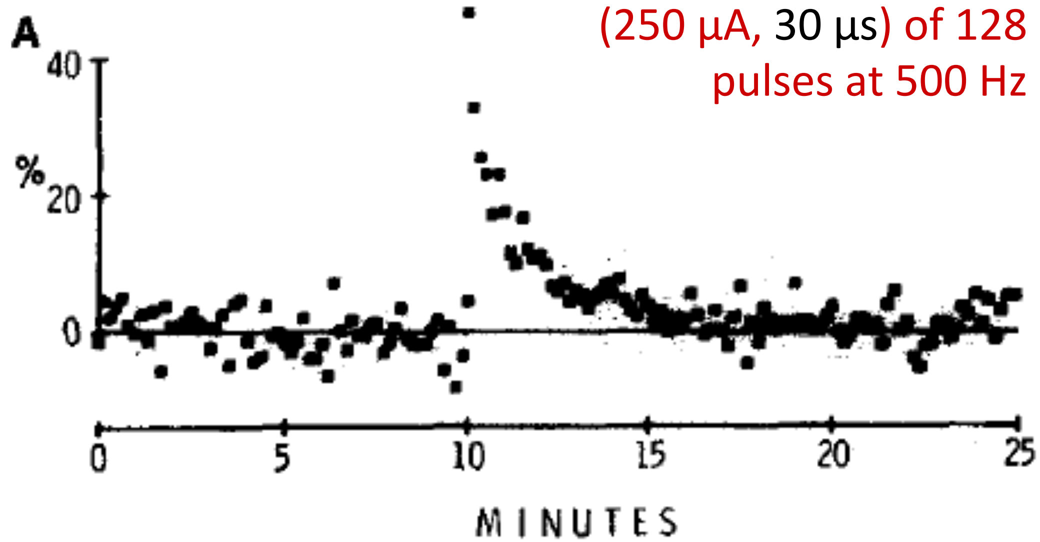
Basic properties of LTP: Cooperativity

Cooperativity describes the existence of an intensity threshold for LTP induction.

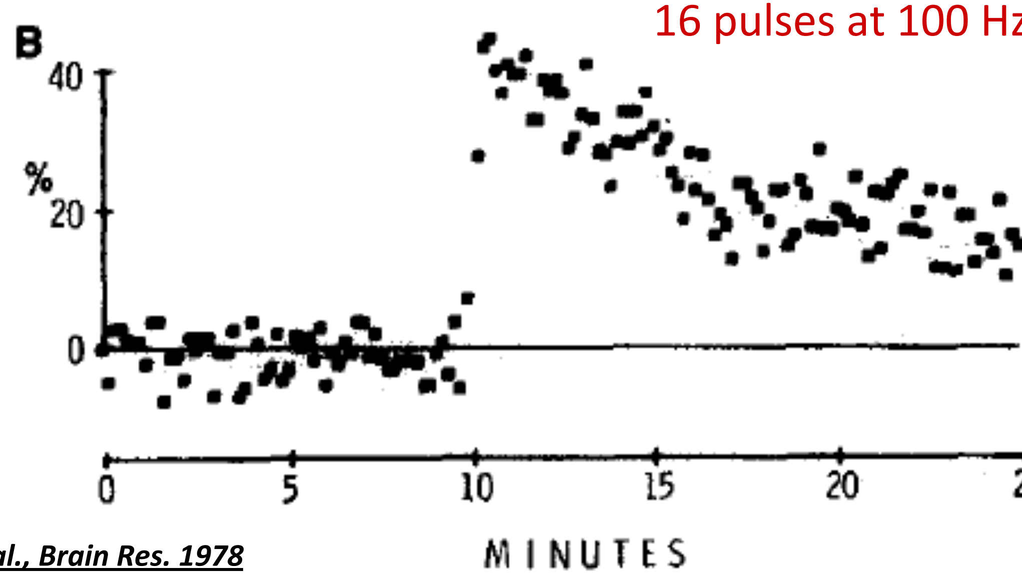
Weak tetani activating relatively few afferent fibers <u>do not</u> trigger LTP;

LTP requires cooperativity among a large set of fibers

(250 μA, 30 μs) of 128 pulses at 500 Hz

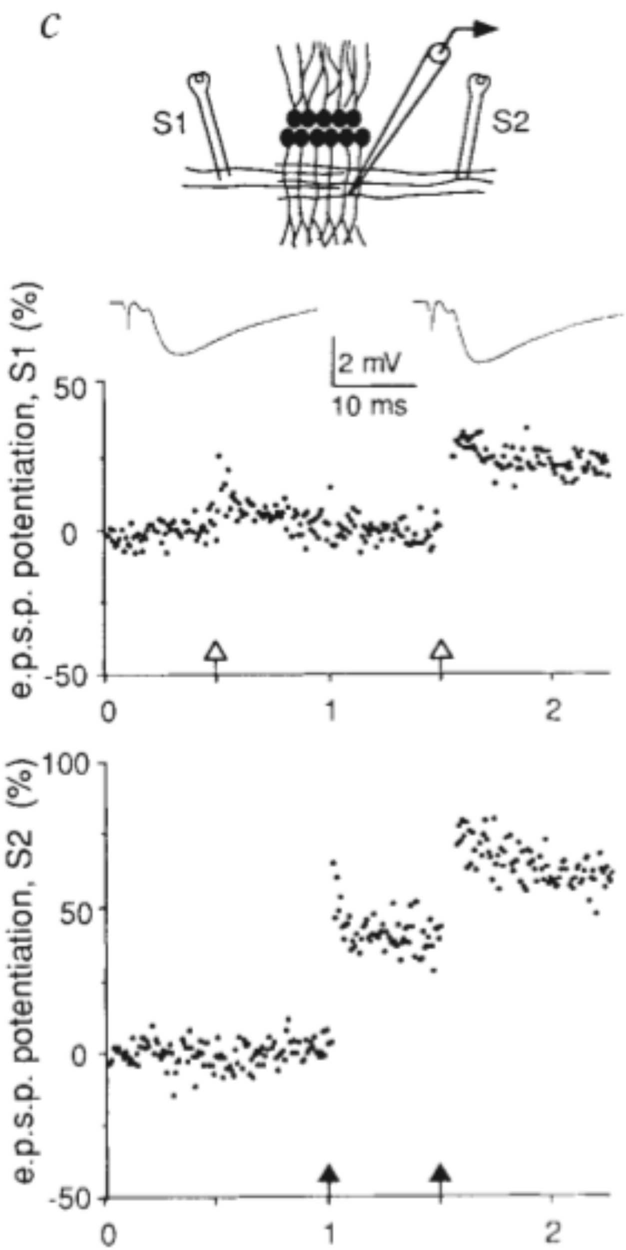


(250 μA, 255 μs) with <u>only</u> 16 pulses at 100 Hz



<u>McNaughton et al., Brain Res. 1978</u>

Basic Properties of LTP: Associativity



Linked to associative memory, where you associate one event/object with another based on some kind of similarity or co-occurrence.

Associative LTP is also referred to as <u>Heterosynaptic LTP</u>, in contrast to <u>Homosynaptic LTP</u> which does not require two synapses for induction of LTP (e.g., tetanus to the synapse produces LTP)

Open arrows: weak stimulus — low intensity;
Closed arrows: strong stimulus — high intensity.

<u>Bliss and Collingridge, Nature, 1993</u>

So, what did we learn today?

Hippocampus is a good place to study the cellular basis of learning and memory, owing to its role in learning and the nice circuitry it possesses

Field potentials are proportional to transmembrane current, and are dependent upon the organization of neurons in a given brain region — the hippocampus has advantages in terms of organization!

Method for induction of long-term potentiation — HFS!

Basic LTP properties: Persistence, input specificity, cooperativity and associativity