From Science Magazine, 2005

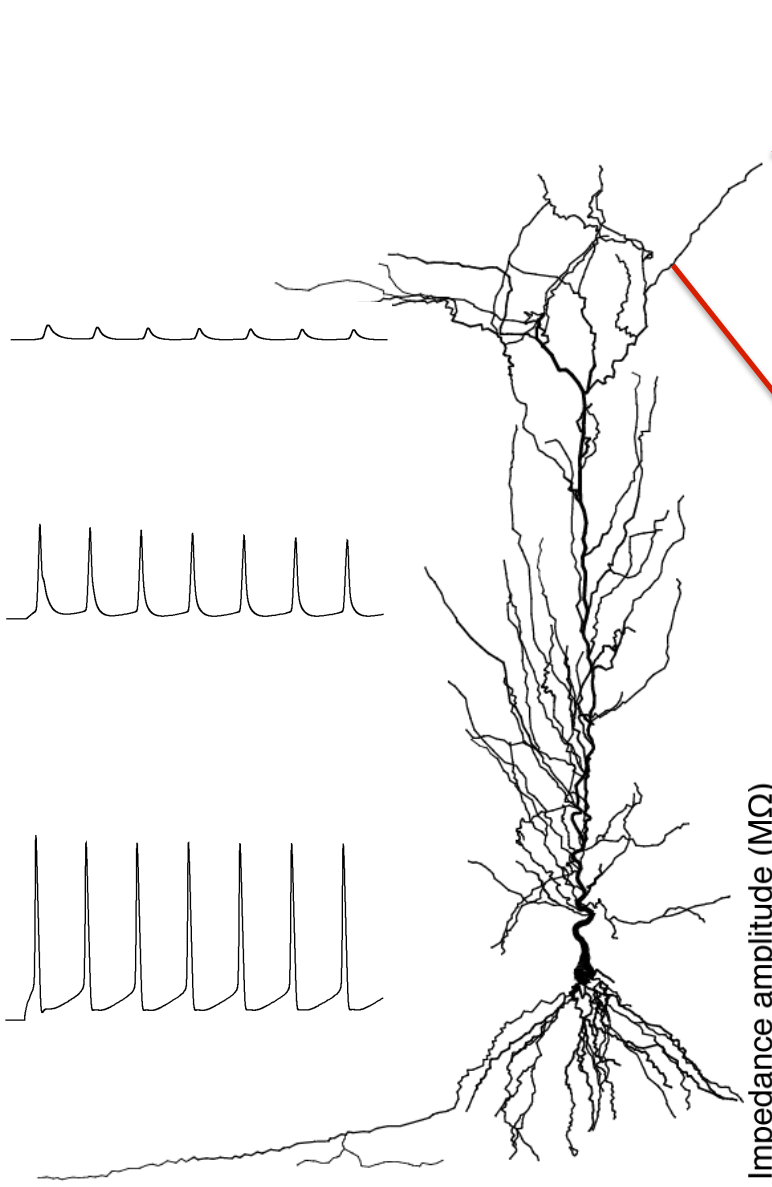
Synaptic plasticity — Lecture 1

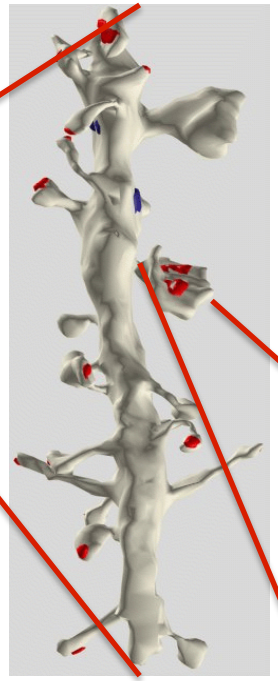
Historical perspective: Learning and memory

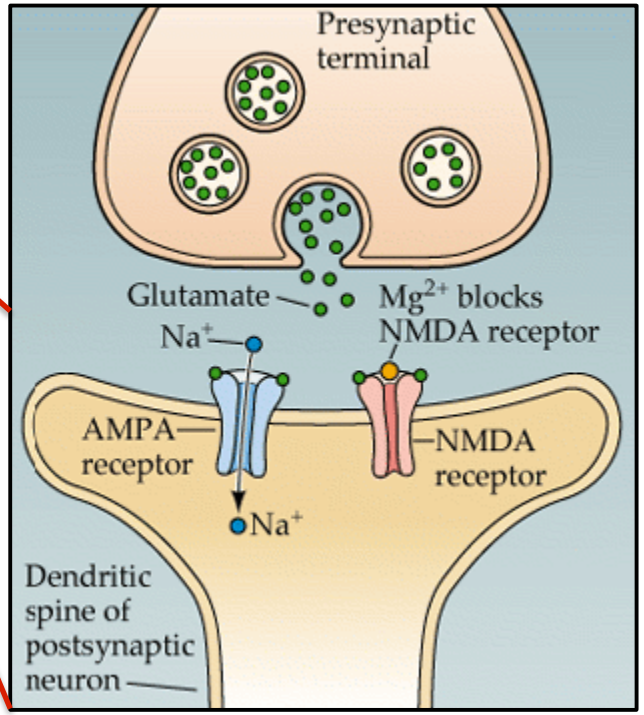
Neuronal Physiology & Plasticity

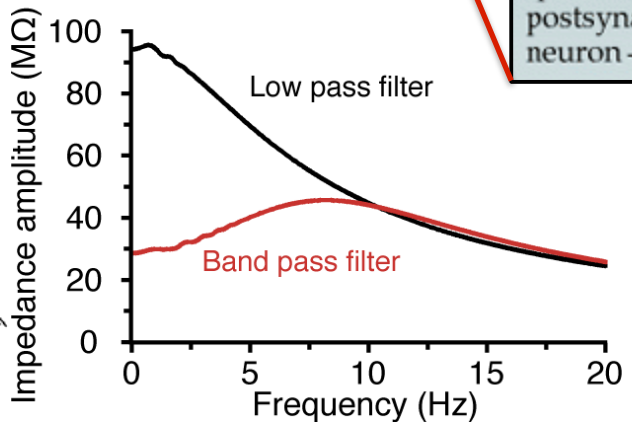
Aug 2018 Semester

Do all these remain constant?









NO!

What is plasticity?

Plasticity is the ability of a system to change or deform and thereby adapt to the environment.

In the neuronal context, the ability of a neuron or synapse to change its properties in response to incoming stimulus is referred to as plasticity

Broad types of neuronal plasticity

Synaptic plasticity: Changes pertaining to synapses

Intrinsic plasticity: Changes in properties intrinsic to neurons

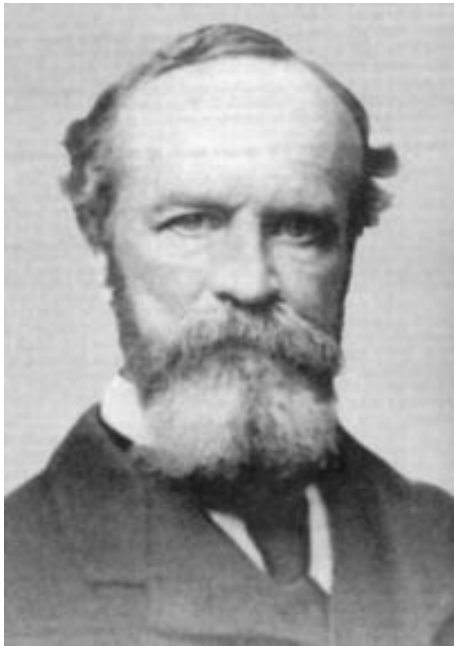
Structural plasticity: Changes in dendritic and/or spine structure

History of neural plasticity

Exp Brain Res (2009) 192:307–319. **Neuronal plasticity: historical roots and evolution of meaning G. Berlucchi · H. A. Buchtel**

The beginnings…

"Plasticity, then, in the wide sense of the word, means the possession of a structure weak enough to yield to an influence, but strong enough not to yield all at once. Each relatively stable phase of equilibrium in such a structure is marked by what we may call a new set of habits. Organic matter, especially nervous tissue, seems endowed with a very extraordinary degree of plasticity of this sort; so that we may without hesitation lay down as our first proposition the following, that the phenomena of habit in living beings are due to plasticity of the organic materials of which their bodies are composed."



Wikipedia

William James

'The Laws of Habit', *The Popular Science Monthly (Feb 1887), 434.*

Principles of psychology, 1890, vol. I, p. 105

More from William James!

***cf.* Hebb, later on!**

When two elementary brain-processes have been active together or in immediate succession, one of them, on reoccurring, tends to propagate its excitement into the other.

(James 1890, Principles of psychology, vol. I, p. 566)

"The amount of activity at any given point in the brain-cortex is the sum of the tendencies of all other points to discharge into it, such tendencies being proportionate

(1) to the number of times the excitement of each other point may have accompanied that of the point in question;
(2) to the intensity of such excitements; and
(3) to the absence of any rival point functionally disconnected with the first point, into which the discharges may be diverted.

(James, 1890, Principles of psychology, vol. II, p. 567)

***cf.* LTP protocols, later on!**

Eugenio Tanzi, a follower of Cajal

Very first hypothesis that associative memories and practice-dependent motor skills may depend on a localized facilitation of synaptic transmission

In 1893, 4 years before the term synapse came into existence

"Now, if nutrition, as in the muscle, will be accompanied by hypertrophy, and if the increase in volume will occur in the sense of length, functional exercise will decrease the distance between adjoining and contiguous neurons….If now we think that the distances between the terminal arborisation of one neuron and the body of the next neuron constitute a resistance or… a kind of difficult passage that the nervous wave must overcome not without difficulty, it is evident that the conductivity of the nervous system will stand in an inverse relation with the spaces between neurons. To the extent that exercise tends to shorten distances, it increases the conductivity of neurons that is their functional capacity."

–Tanzi, 1893

Santiago Ramon y Cajal

Coined the term “plasticity” in the neuronal context???

This plasticity of the cell processes is likely to vary in different life periods: conspicuous in youngsters, it decreases in adults and disappears almost completely in old age.

(Ramón y Cajal, 1894)

Santiago Ramon y Cajal

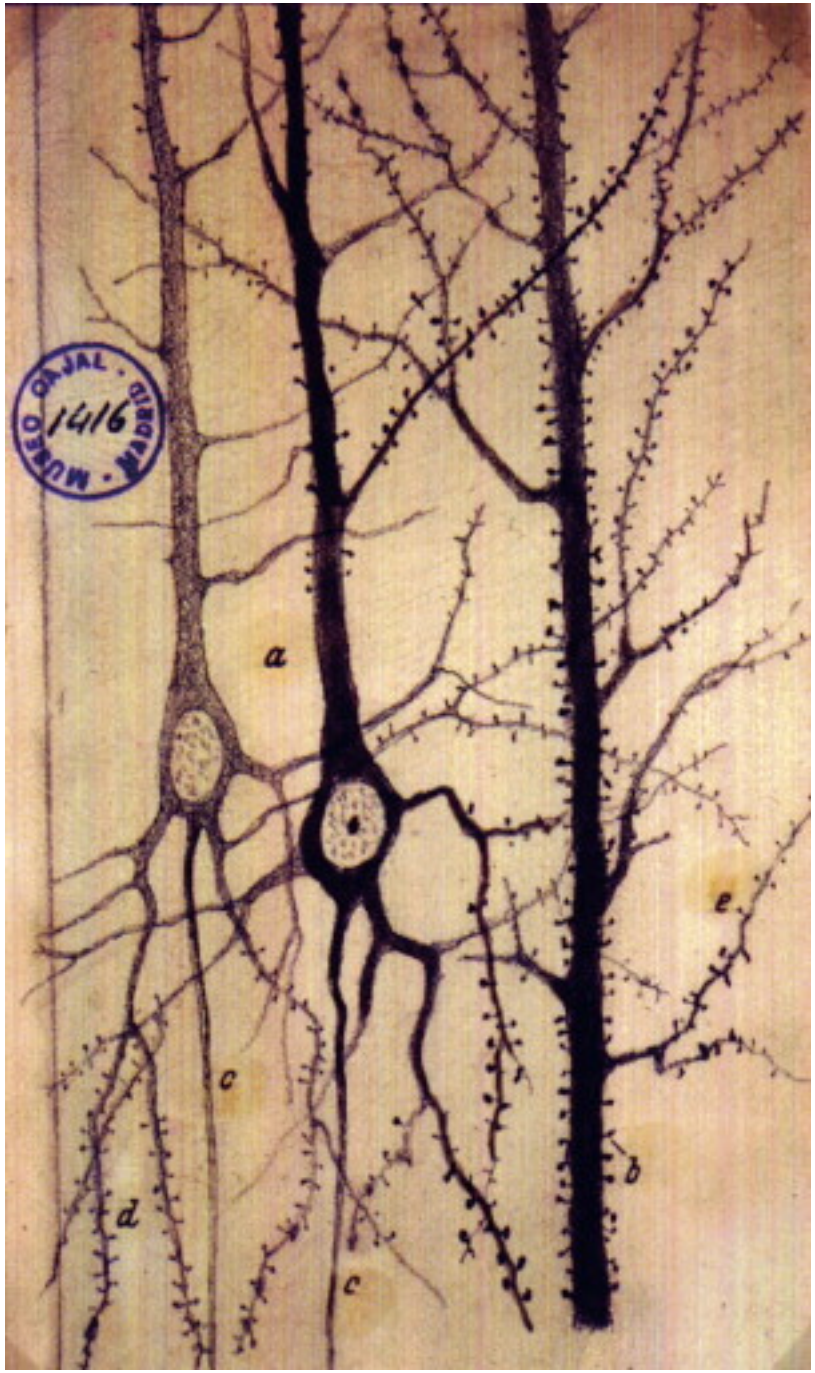
Spines were dismissed as artifacts of the silver nitrate staining technique!

Cajal asked:

Why are they not in interneurons and axons?

And proved that spines show up with other (Mercury chloride, Methylene blue) staining techniques as well!

"… that by virtue of the aforesaid spines, dendritic branches increase their receptive surface and establish more intimate contacts with the axonal terminal arborizations"



S.R. Cajal, Rev Trimestr, Micrograf. 1 (1896), pp. 5–19.

Sir Charles Scott Sherrington

Coins the term synapse (1897)

From "synaptein", from the Greek "syn-" ("together") and "haptein" ("to clasp").

Wikipedia

Ernesto Lugaro

Ernesto Lugaro (1898, 1905, 1909) expanded on Tanzi's hypothesis by applying the term plasticity to practice-related synaptic changes

Also had the visionary intuition of the chemical nature of synaptic transmission in the central nervous system.

Eugenio Tanzi (left) and Ernesto Lugaro (both seated)

http://www.ibro.org

Two psychology textbooks of that time concurred, and reworded William James

This permanent lowering of resistance, or increase in permeability of synapses seems to be the essential condition of the formation of neural habits, and is therefore an effect of the highest importance. (McDougall 1905)

cf. **James, earlier!**

Whenever two neurones are active at the same time some change is induced in the synapse that makes it act more readily later. (Pillsbury 1911)

cf. **James, earlier, and Hebb later on!**

Karl Spencer Lashley

Very influential psychologist and behaviorist with pioneering contributions!

Neurotree

Argued for a distributed representation of memory, and used rat cortical lesions (removal) — but reached erroneous conclusions (like visual cortex is the site for learning and memory)

His attack on synaptic learning was based on two kinds of evidence:

(1) A learned response could be performed by means of neural paths that had never been used during the learning process and were completely separated from the trained path (based on his flawed studies!);

(2) In higher animals and especially in humans there are many instances of temporary associations or one-trial learning, which by definition do not require any repetition of stimuli and responses.

Killed the field for some time from 1920s to 1940s.

Jerzy Konorski

- developed the work of Ivan Pavlov by discovering secondary conditioned reflexes and also operant conditioning.

- proposed the concepts of grandmother cell and ideas similar to Donald Hebb on neural plasticity.

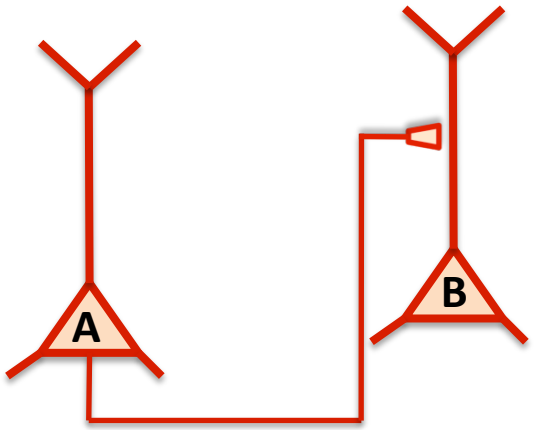
"Plastic changes would be related to the formation and multiplication of new synaptic junctions between the axon terminals of one nerve cell and the soma (i.e. the body and the dendrites) of the other."

(Konorski 1948)

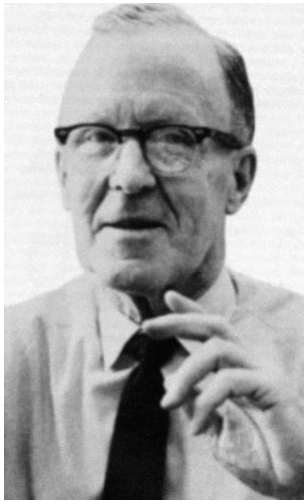
www.nencki.gov.pl

Donald Hebb's postulate

"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."



cf. James, earlier!



- Repeated simultaneous activation of two cells *strengthens* the synapses that link them

- *"Cells that fire together wire together"*

Proposed in 1949

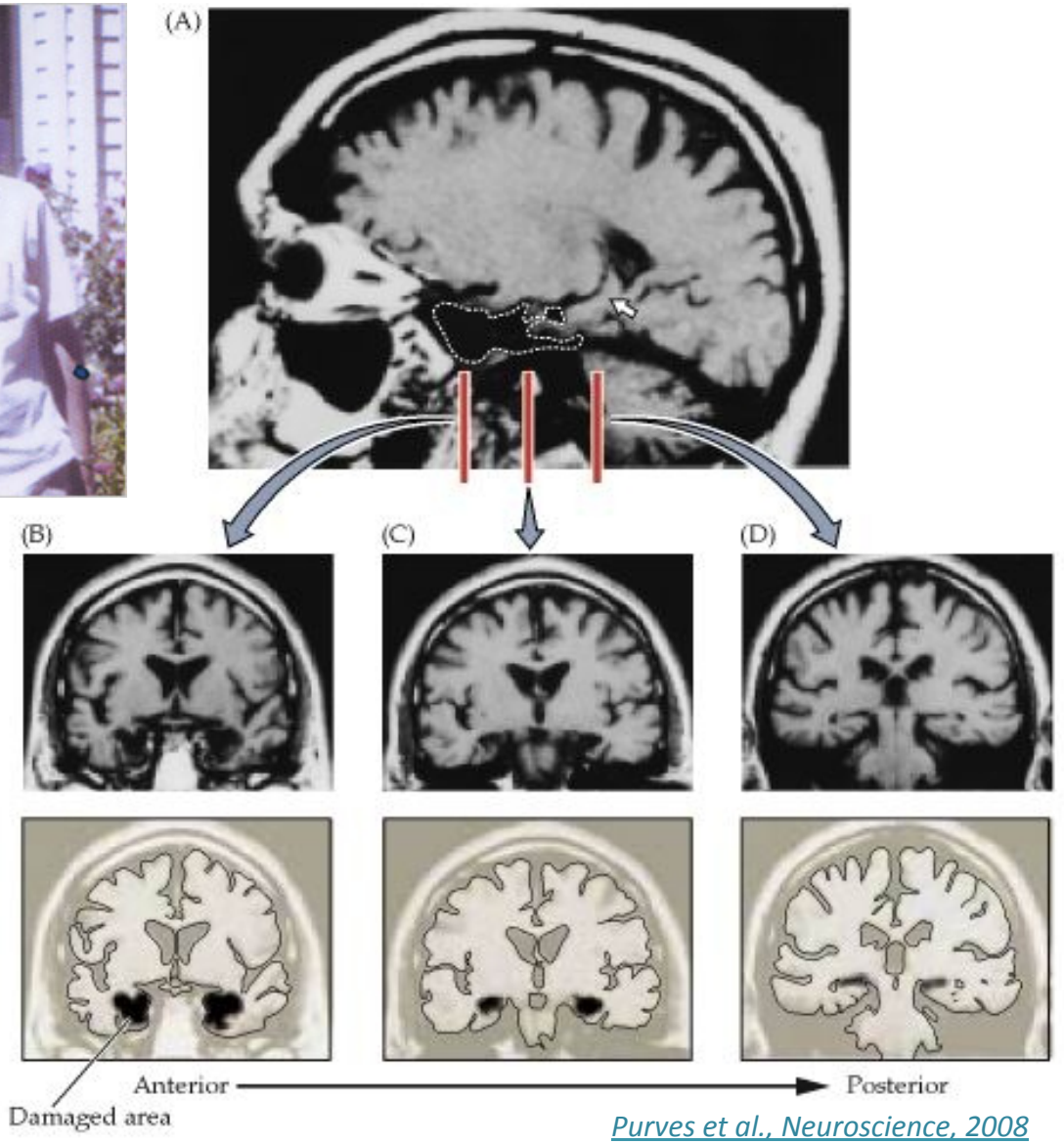
The hippocampus and memory — 1950's

HM, Henry Molaison (1926–2008)

Bilateral surgical resection of the MTL, following epilepsy

HM lost two-thirds of his hippocampus, parahippocampal gyrus and amygdala

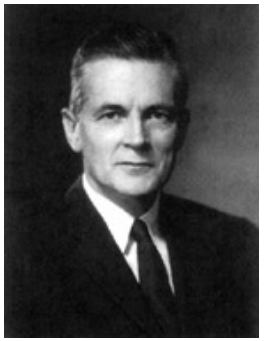
Lost ability to form new semantic knowledge, and to encode episodic memory, but working memory and motor learning were intact



Purves et al., Neuroscience, 2008

The hippocampus and memory

J. Neurol. Neurosurg. Psychiat., 1957, **20**, 11.



LOSS OF RECENT MEMORY AFTER BILATERAL HIPPOCAMPAL LESIONS

BY

WILLIAM BEECHER SCOVILLE and BRENDA MILNER

From the Department of Neurosurgery, Hartford Hospital, and the Department of Neurology and Neurosurgery, McGill University, and the Montreal Neurological Institute, Canada

The role of the hippocampus in declarative and episodic memory was established after this landmark study on H.M., and the hippocampus became an area for intense investigation

The hippocampus

Named so by Julius Caesar Aranzi (1587). Latin: *hippocampus, from Greek: ἵππος, "horse" and Greek: κάμπος, "sea monster")*

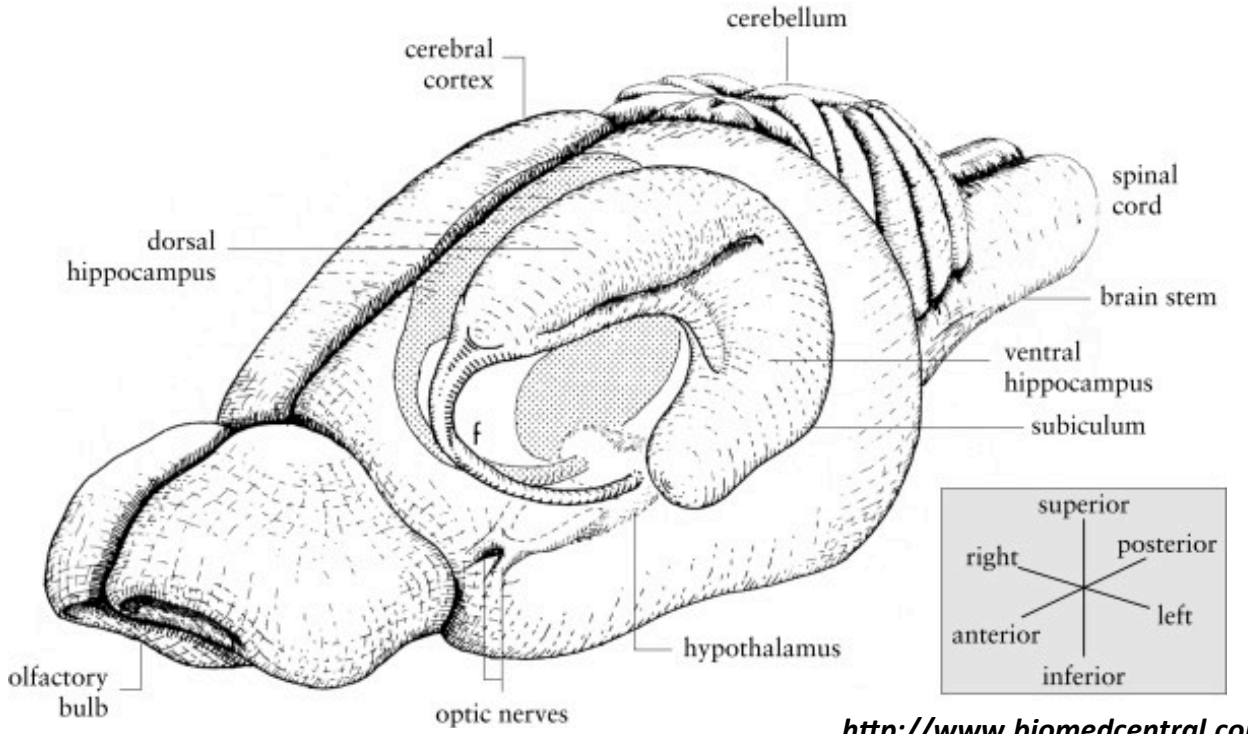
Also named by de Garengeot, as "cornu Ammonis", meaning horn of (the ancient Egyptian god) Amun

Histological divisions of hippocampus are still called CA1, CA2 and CA3

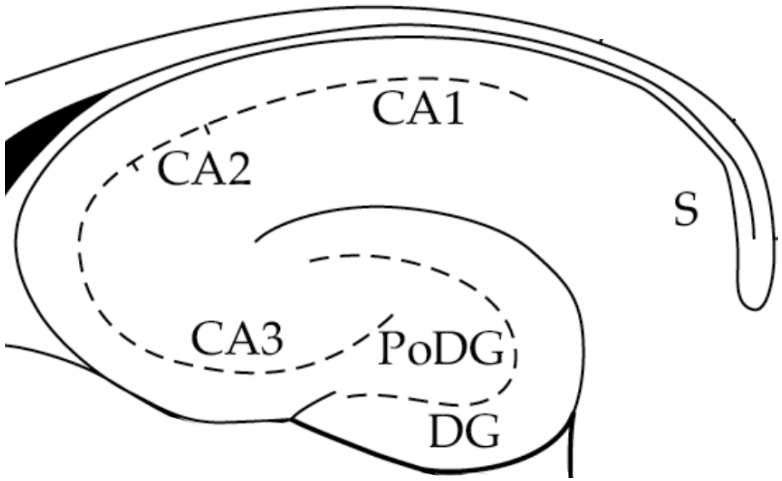
Wikipedia

Plays important functions in learning and memory, and incorporates a spatial map of the environment using place cells

The hippocampus



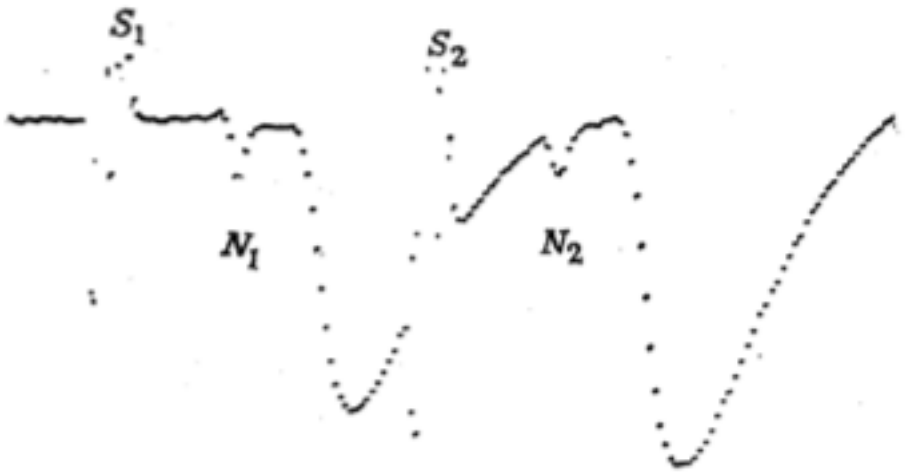
http://www.biomedcentral.com/



Bernard Katz

Nothing much happened from 1950's to 1970's except for Katz and others decoding the synapses and understanding short-term plasticity mechanisms, apart from some other things happening in parallel (H-H, Hubel-Wiesel, etc.)

Neuromuscular junction EPPs



Katz and Miledi, 1965

Paired pulse facilitation

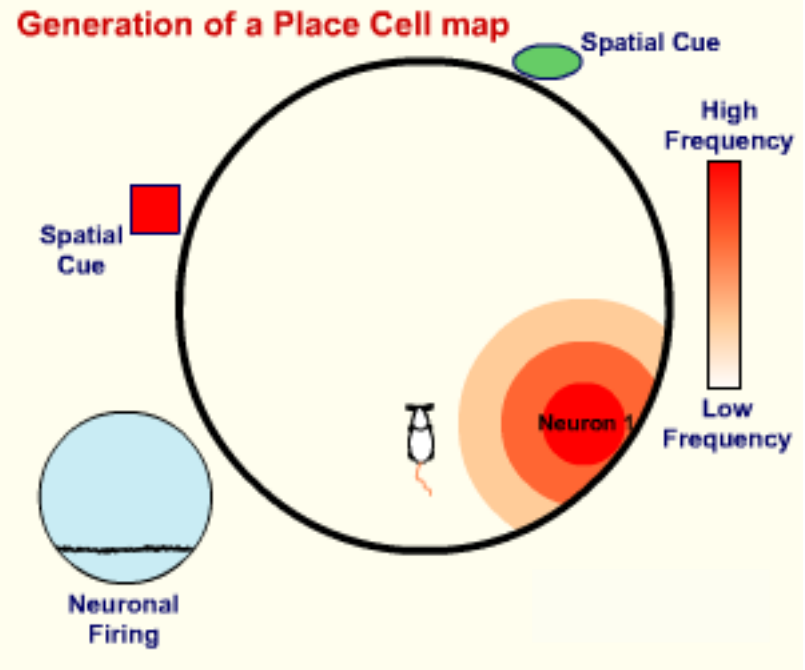
Residual Calcium Hypothesis

Post-tetanic potentiation, another form of short term plasticity, was also studied around the same time.

The hippocampus, spatial learning and memory

Place cells are neurons in the hippocampus that exhibit a high rate of firing whenever an animal is in a specific location in an environment.

Found originally by O'Keefe and Dostrovsky, 1971



1970's — The Hippocampal era of learning and memory began and the hippocampus became the center piece of the show, in so many ways!!!!

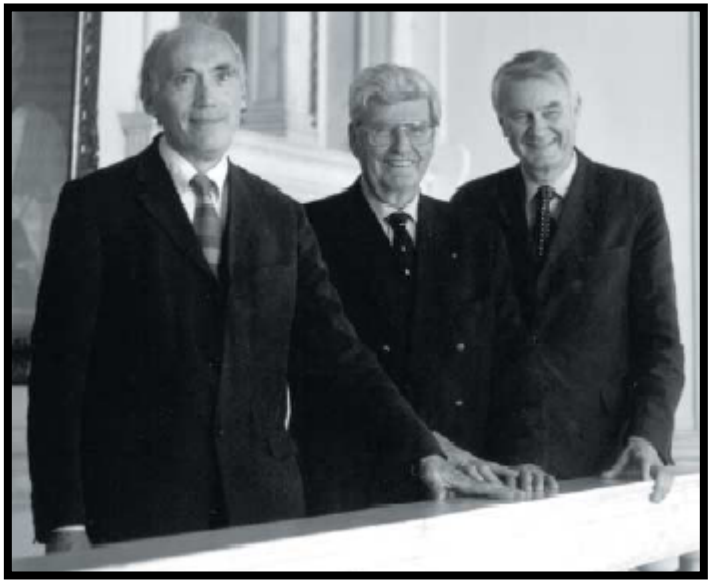
Nobel Prize in Physiology or Medicine, 2014

http://www.bris.ac.uk/synaptic/research/projects/memory/spatialmem.htm

Long-term potentiation (LTP)

~30 years after Hebb's postulate, in 1973…

Tim Bliss, Per Andersen and Terje Lømo



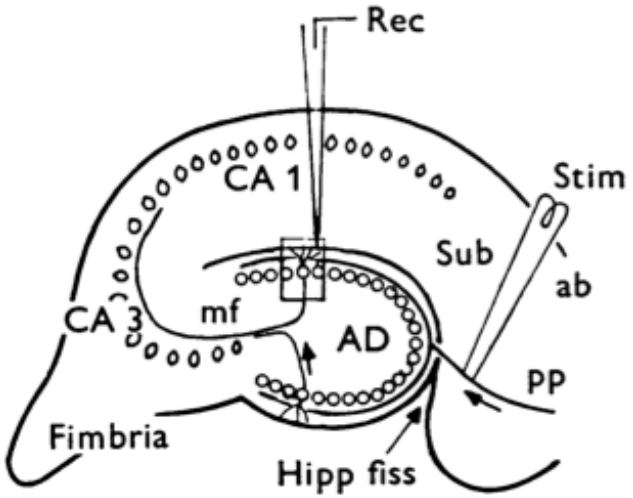
- Tim Bliss and Terje Lømo discover long-term potentiation while working in Per Anderson's laboratory

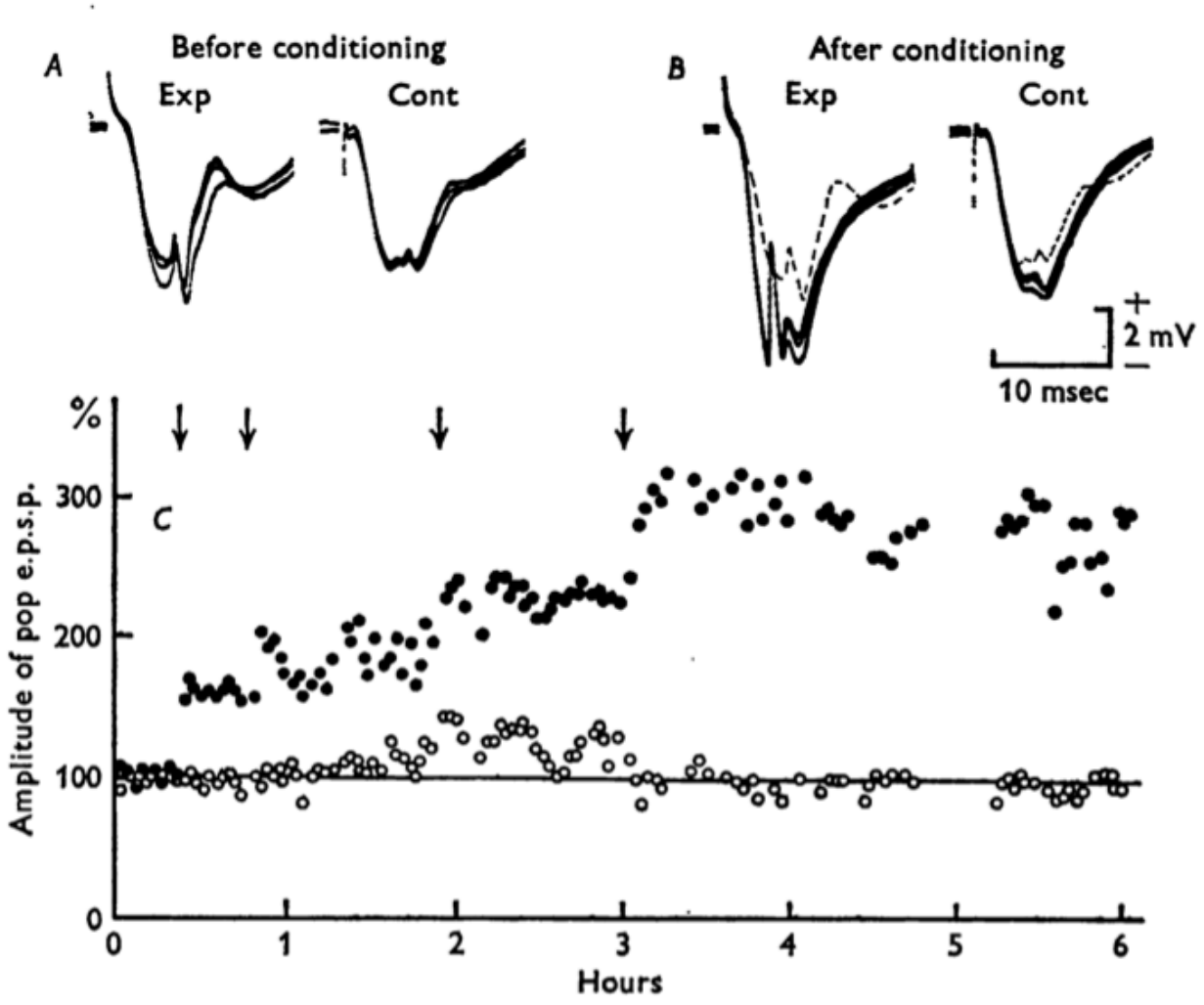
- LTP: Refers to a long-lasting strengthening of synapses that can be triggered by particular patterns of stimulation

- Other patterns can produce a long-term weakening or depression of the same synapses.

- Together they are referred to **synaptic plasticity**, and form a candidate cellular mechanism behind learning and memory

Bliss and Lomo, 1973



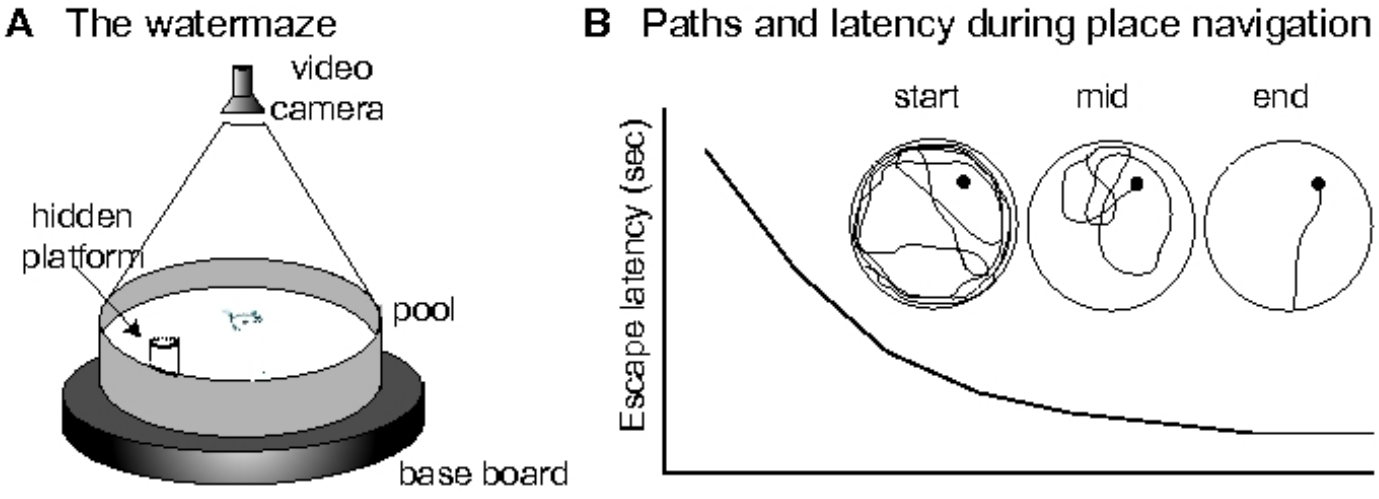


(15/s for 10 s)

Theorists, electrophysiologists, behaviorists, molecular biologists, everybody went after this!!!

Bliss and Lomo, J. Physiology, 1973

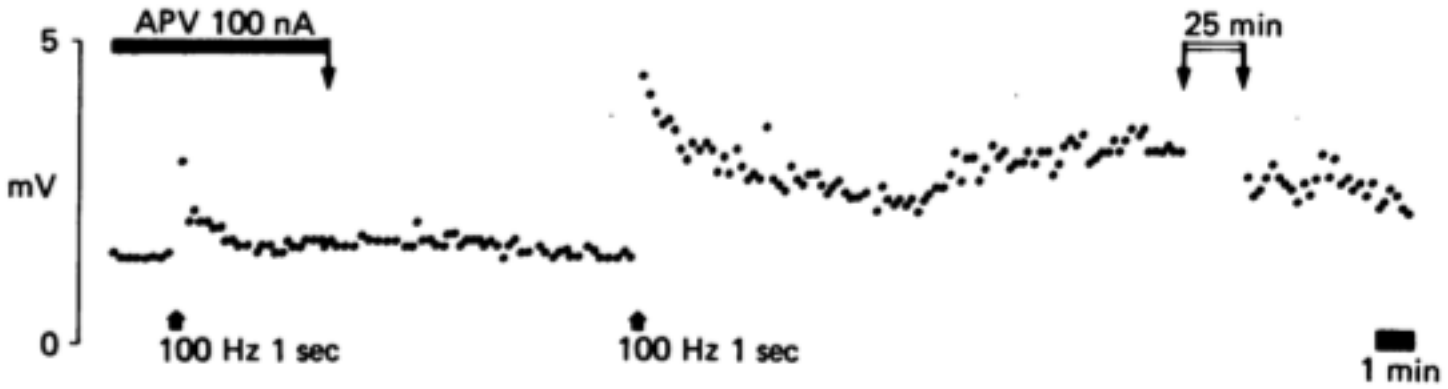
The hippocampus, spatial learning and memory



Hippocampal lesions affect the animal's ability to learn spatial tasks like those that involve the Morris water maze.

Morris et al., Nature, 1982

LTP molecular mechanisms — NMDAR



Collingridge et al., J. Phys. 1983

Learning and synapses — first connections?

A Cellular Mechanism of Classical Conditioning in Aplysia: Activity-Dependent Amplification of Presynaptic Facilitation
Author(s): R. D. Hawkins, T. W. Abrams, T. J. Carew and E. R. Kandel
Source: *Science*, New Series, Vol. 219, No. 4583 (Jan. 28, 1983), pp. 400-405

A Critical Period for Macromolecular Synthesis in Long-Term Heterosynaptic Facilitation in Aplysia
Author(s): P. G. Montarolo, P. Goelet, V. F. Castellucci, J. Morgan, E. R. Kandel and S. Schacher
Source: *Science*, New Series, Vol. 234, No. 4781 (Dec. 5, 1986), pp. 1249-1254

Molecular Biology of Learning: Modulation of Transmitter Release
Author(s): Eric R. Kandel and James H. Schwartz
Source: *Science*, New Series, Vol. 218, No. 4571 (Oct. 29, 1982), pp. 433-443

Injection of the cAMP-responsive element into the nucleus of *Aplysia* sensory neurons blocks long-term facilitation

Pramod K. Dash, Binyamin Hochner* & Eric R. Kandel

NATURE · VOL 345 · 21 JUNE 1990

Eric Kandel
Nobel Prize, 2000

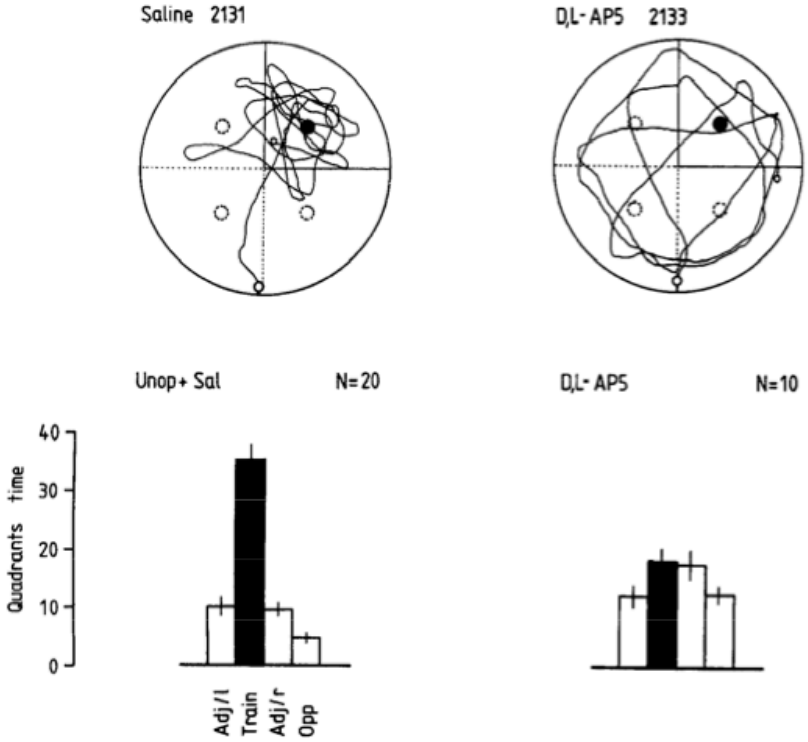
LTP and learning — first connections?

The Journal of Neuroscience, September 1989, 9(9): 3040–3057

Synaptic Plasticity and Learning: Selective Impairment of Learning in Rats and Blockade of Long-Term Potentiation *in vivo* by the *N*-Methyl-D-Aspartate Receptor Antagonist AP5

R. G. M. Morris

Department of Pharmacology, University of Edinburgh Medical School, Edinburgh EH8 9JZ, Scotland



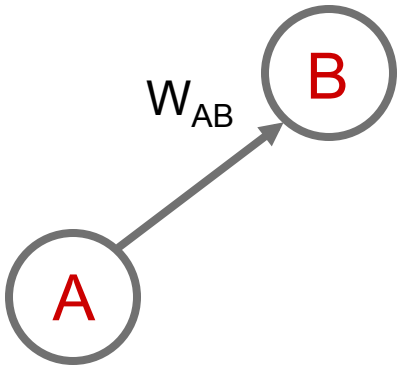
Both LTP *in vivo* and water maze learning were impaired by infusing D,L-AP5 specifically to the hippocampus through a canula.

Bidirectional synaptic plasticity — theory and experimental evidence

If positive correlations (as postulated by Hebb) lead to increase in potentiation, what do negative corrrelations mean? Depression??

$\Delta w_{AB} = k. f_A f_B$

Terry Sejnowski, Covariance Rule, J. Math. Biol.1977



- Postsynaptic activity greater than threshold => potentiation of active synapses
- Postsynaptic activity lesser than threshold => depression of active synapses

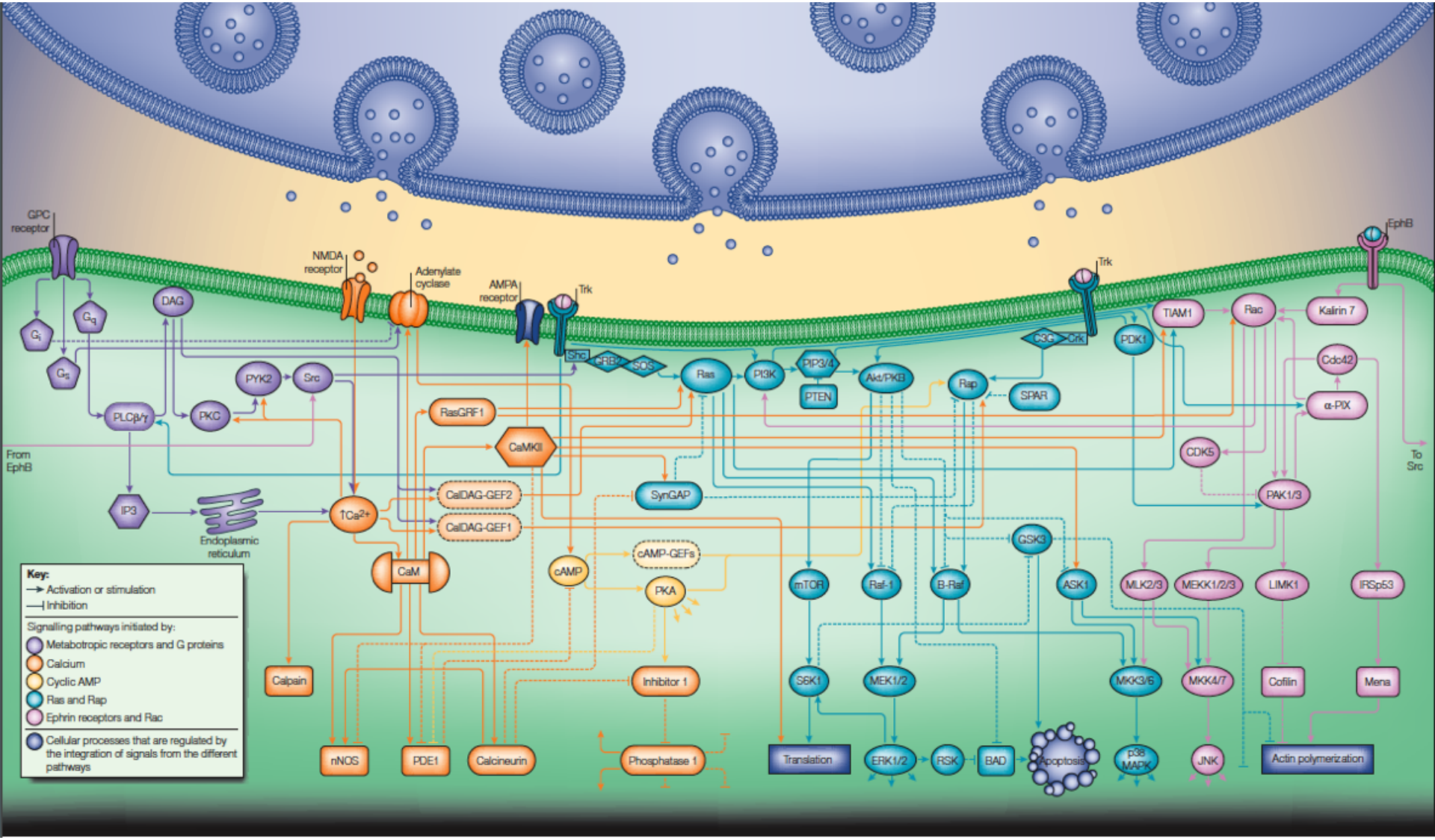
Cooper et al., Biological cybernetics, 1979

See Cooper and Bear, *Nature Reviews Neuroscience* (November 2012), for a 30-year historical perspective on the contributions of theory to synaptic plasticity literature

Experimental evidence: LTD

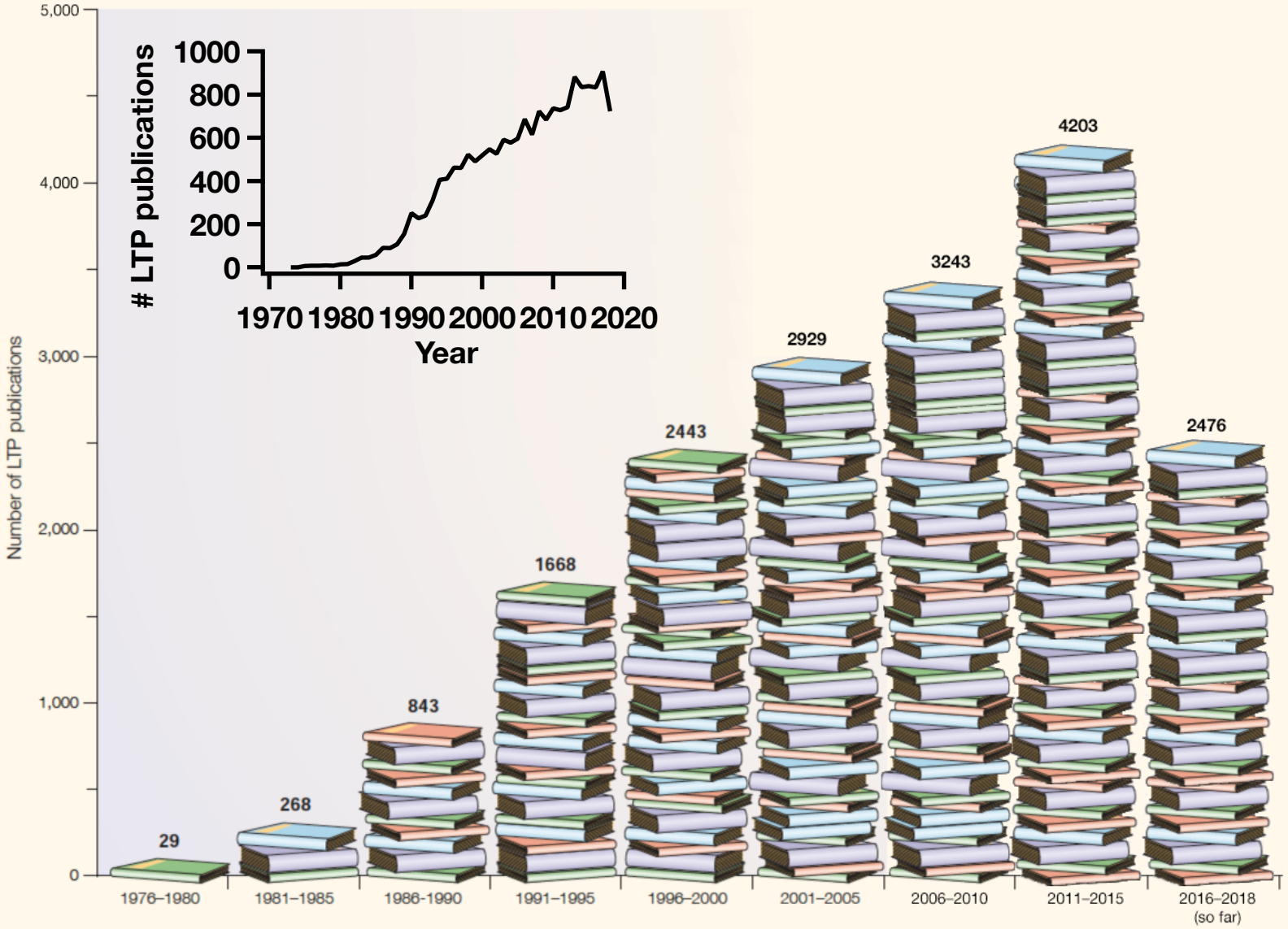
Dudek and Bear, 1992

Quantitative electrophysiology, imaging and molecular biology happened …



Kennedy et al., NRN, 2003

And, the field exploded…!



Modified from Malenka, Nature Rev. Neurosci., 2003