Synaptic Plasticity

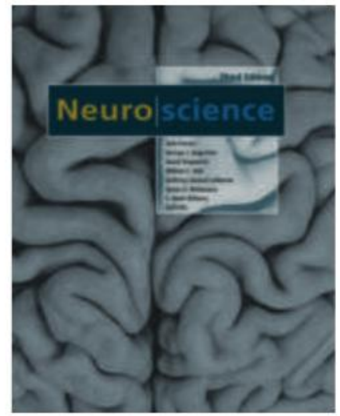
LTP and LTD

Learning and memory at the cellular level...

Topics I	Topics II
Introduction	Synaptic Transmission
Electrochemical Gradients	Electrophysiology Techniques
Passive Membrane Properties	Basic Circuits (Spinal Cord)
Action Potential	Sensory Systems Overview
Voltage-Gated Ion Channels	Synaptic Plasticity
Ligand-Gated Ion Channels	Recapitulation

Study Material

- NEUROSCIENCE Third Edition
  - Dale Purves
- Chapter 24
  - Pages 575-610



THE COVER
Dorsal view of the human brain.
(Courtesy of S. Mark Williams.)

NEUROSCIENCE: Third Edition

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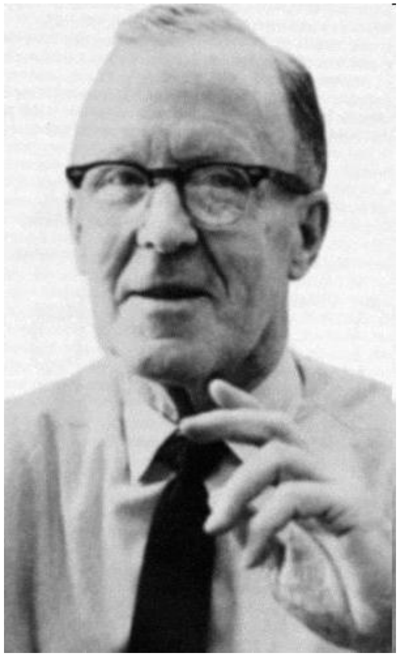
Aims for this Lecture

- Know the basic framework for associative learning.
- Know the key systems and experiments in developing cellular models for learning and memory.
- Understand the central role of calcium entry as a signal in determining synaptic plasticity.

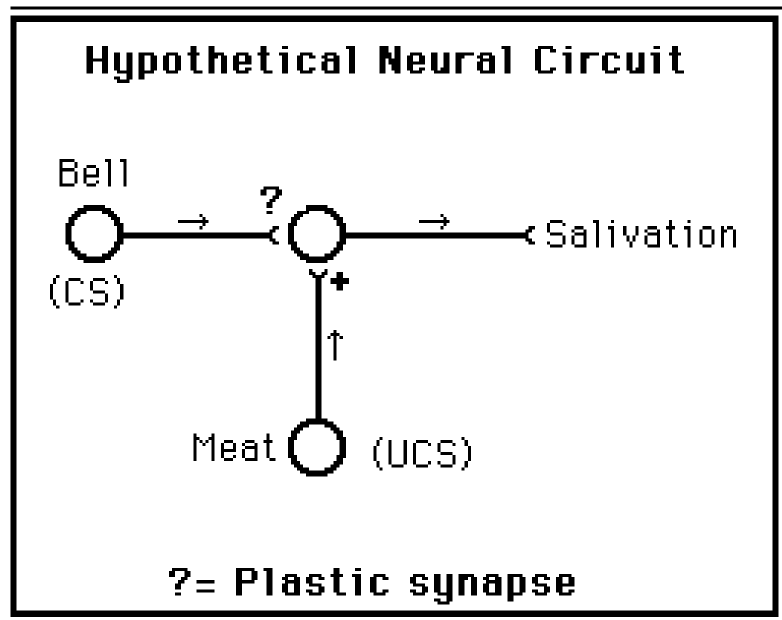
Recapitulation L11

- Specialized transducers translate signals in the environment into graded- and then action potentials.
- The brain only understands action potentials – stimulation of the afferent axons will elicit a sensation as if the proper stimulus were present.
- Feature extraction along the processing pathway is an important function of sensory systems.

Donald Hebb



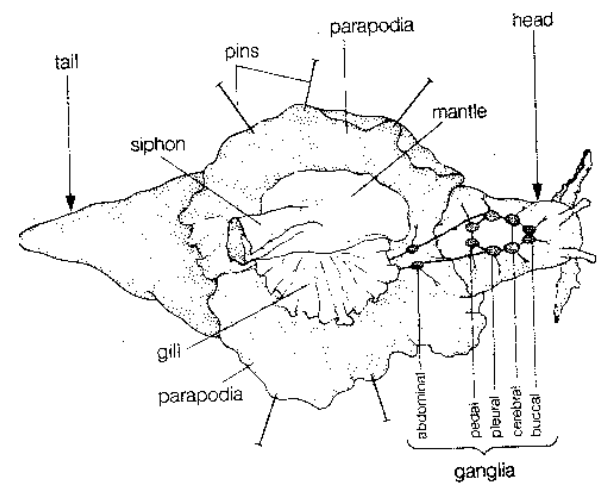
When an axon of cell A is near enough to excite cell B and repeatedly or persistently takes part in firing it, some growth process or metabolic change takes place in one or both cells such that A's efficiency, as one of the cells firing B, is increased



Pavlov: classical conditioning

The Organization of Behavior: A Neuropsychological Theory (1949)

Aplysia I



Morphological Aspects of Synaptic Plasticity in *Aplysia*

An Anatomical Substrate for Long-Term Memory[a]

CRAIG H. BAILEY[b] AND MARY CHEN

Center for Neurobiology and Behavior
Departments of Anatomy and Cell Biology and Psychiatry
College of Physicians and Surgeons
Columbia University
and
New York State Psychiatric Institute
New York, New York

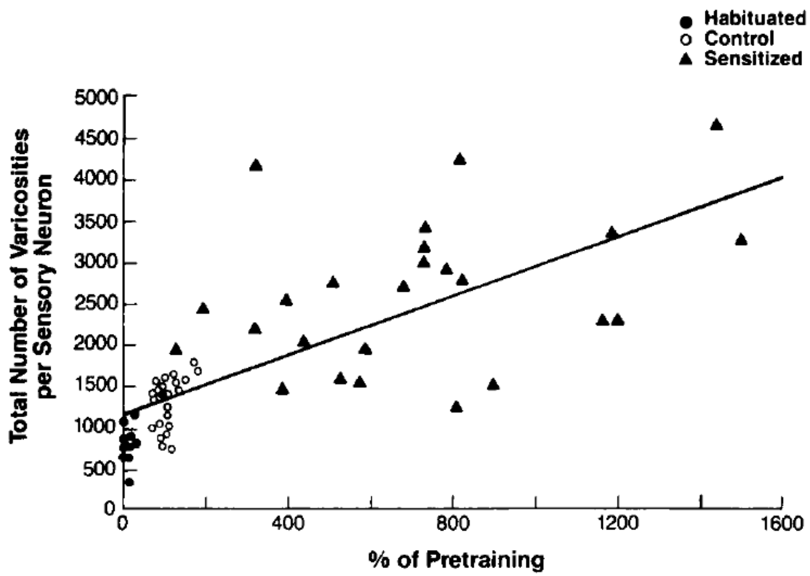


FIGURE 3. Correlation between changes in varicosity number and long-term memory. Data points represent animals trained for long-term habituation, animals trained for long-term sensitization, and untrained (control) animals. Structural changes (total number of varicosities per sensory neuron) are plotted against changes in behavioral efficacy. The responses of each 10-trial session, 24-48 hr following the completion of training, have been summed and expressed as a single median score compared to each animal's own pretraining score (Spearman's rank correlative coefficient: 0.825; $p < .001$). (From reference 32.).

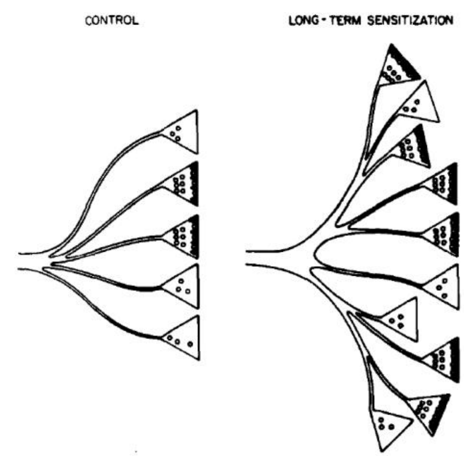
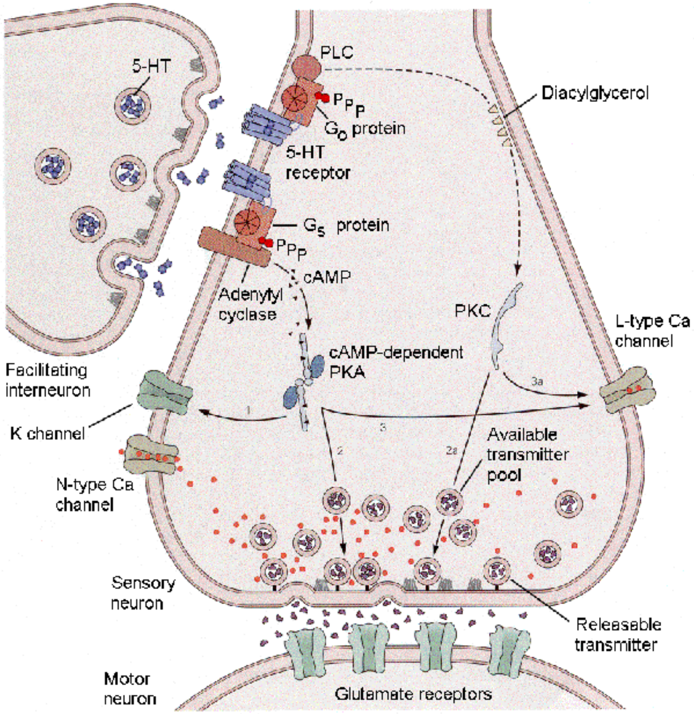
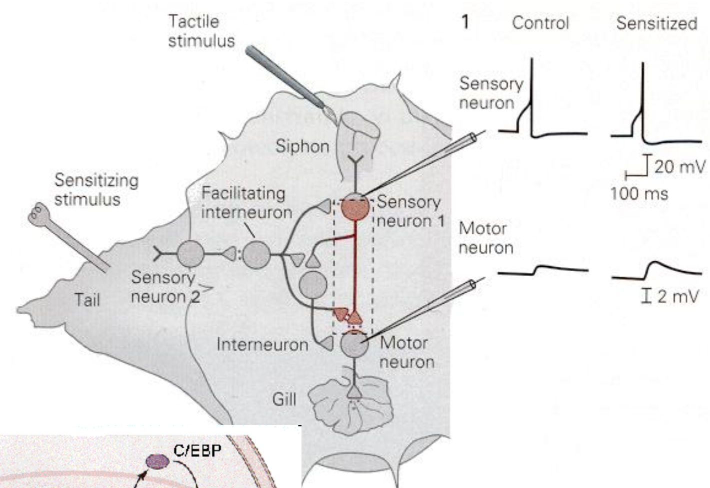
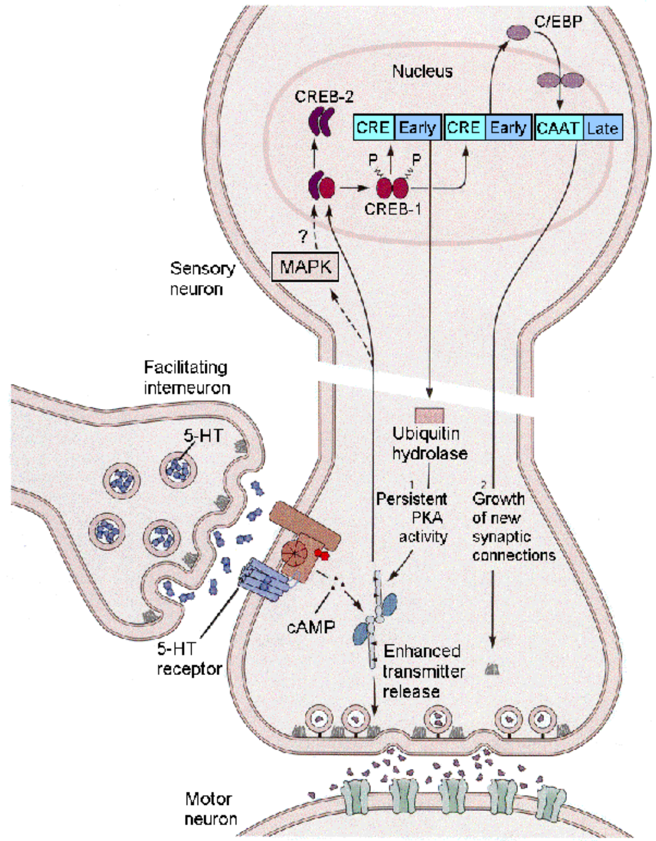


FIGURE 8. Cartoon illustrating the family of structural alterations produced by long-term sensitization. These involve a doubling in the number of sensory neuron varicosities, an increase in the incidence of their active zones, and an increase in the neuropil arbor of the sensory neurons. (Modified from reference 30.)

Aplysia II

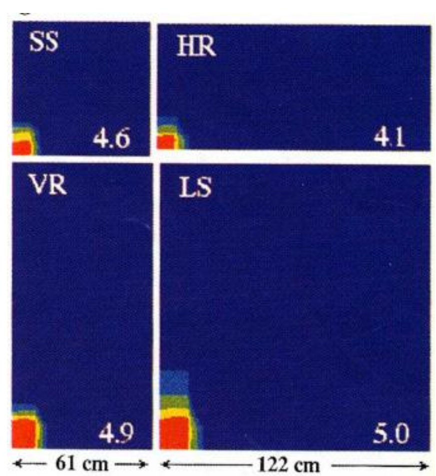

5-HT
PLC
Diacylglycerol
G$_o$ protein
5-HT receptor
G$_s$ protein
cAMP
Adenylyl cyclase
PKC
L-type Ca channel
cAMP-dependent PKA
Facilitating interneuron
K channel
N-type Ca channel
Available transmitter pool
Sensory neuron
Releasable transmitter
Motor neuron
Glutamate receptors


Tactile stimulus
1
Control
Sensitized
Sensory neuron
Siphon
20 mV
100 ms
Sensitizing stimulus
Facilitating interneuron
Sensory neuron 1
Motor neuron
Tail
Sensory neuron 2
2 mV
Interneuron
Motor neuron
Gill


C/EBP
Nucleus
CREB-2
CRE
Early
CRE
Early
CAAT
Late
CREB-1
MAPK
Sensory neuron
Facilitating interneuron
5-HT
Ubiquitin hydrolase
Persistent PKA activity
Growth of new synaptic connections
cAMP
5-HT receptor
Enhanced transmitter release
Motor neuron

Hippocampus

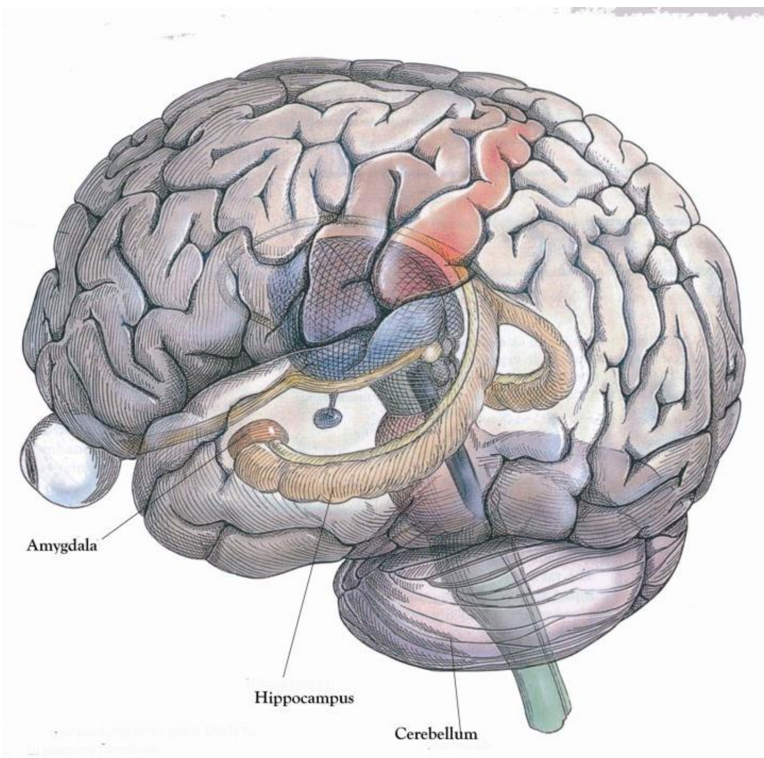
- Bilateral removal in humans causes complete anterograde amnesia.
- Best studied role in rodents is in navidation – linking places to experiences.
- Place-cells code the location of the animal – grid cells provide a coordinate system.

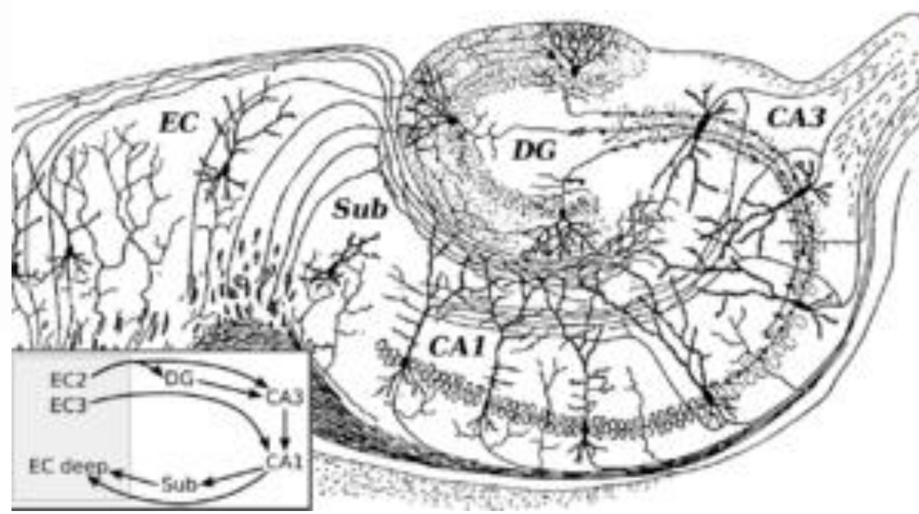


The hippocampus as a spatial map. Preliminary evidence from unit activity in the freely-moving rat

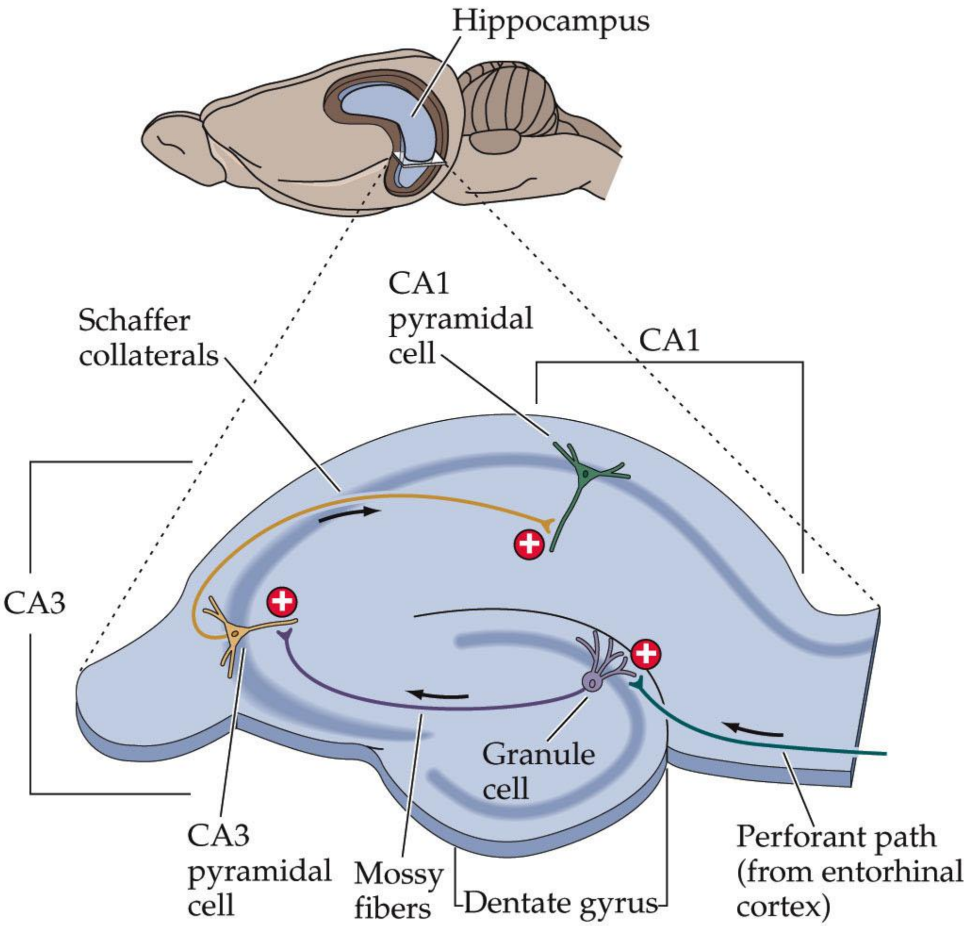
J. O'Keefea and J. Dostrovsky*, a
aM.R.C.
Brain research 1971.

Anatomy


Amygdala
Hippocampus
Cerebellum


EC
DG
CA3
Sub
CA1
EC2
EC3
DG
CA3
CA1
EC deep
Sub

Rodent Hiipocampus



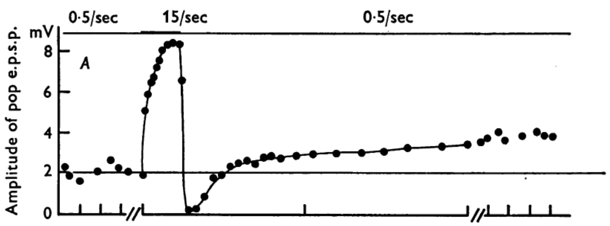
NEUROSCIENCE, Fourth Edition, Figure 8.6

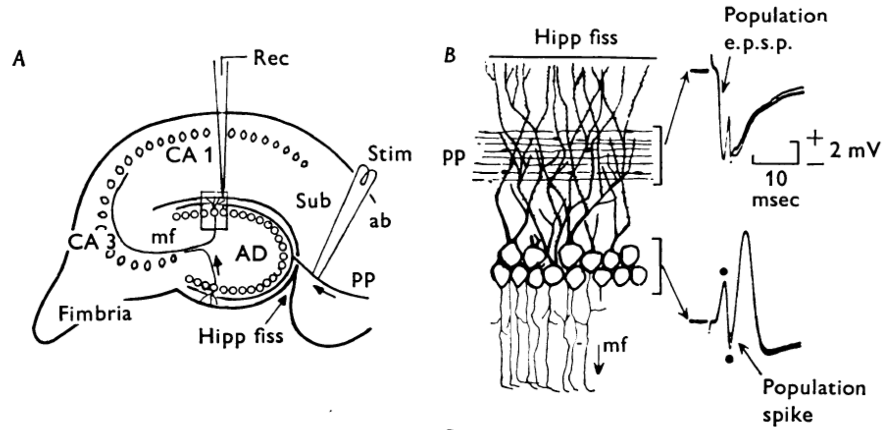
Bliss & Lømo

J. Physiol. (1973), **232**, *pp.* 331–356
With 12 text-figures
Printed in Great Britain

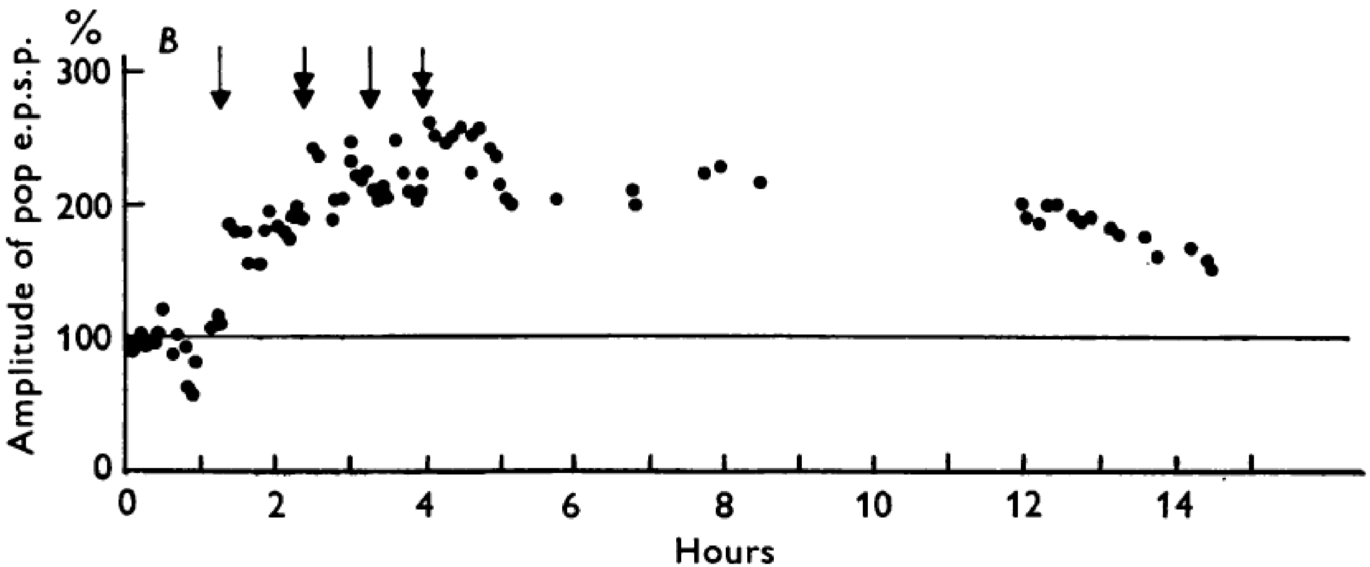
LONG-LASTING POTENTIATION OF SYNAPTIC TRANSMISSION IN THE DENTATE AREA OF THE ANAESTHETIZED RABBIT FOLLOWING STIMULATION OF THE PERFORANT PATH

By T. V. P. BLISS and T. LØMO
From the National Institute for Medical Research, Mill Hill, London NW7 1AA and the Institute of Neurophysiology, University of Oslo, Norway





LTP



LTP und LTD

- Many variants and forms of plasticity have been found since the original discovery.
- LTP ‘long-term potentiation’
  - Typically induced by intense coincident stimulation.
- LTD ‘long-term depression’
  - Typically induced by milder non-coincident stimulation.

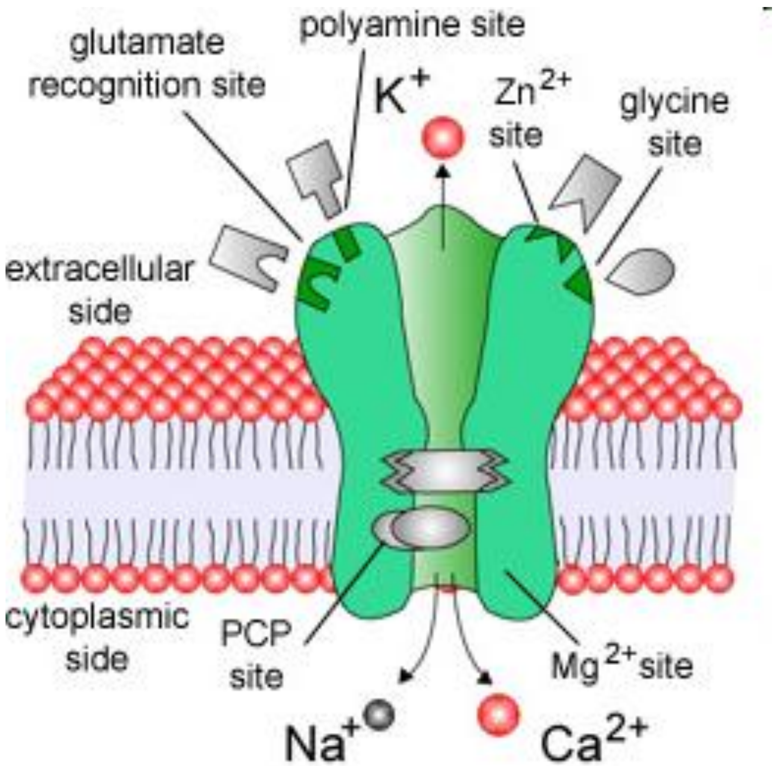
Many Forms

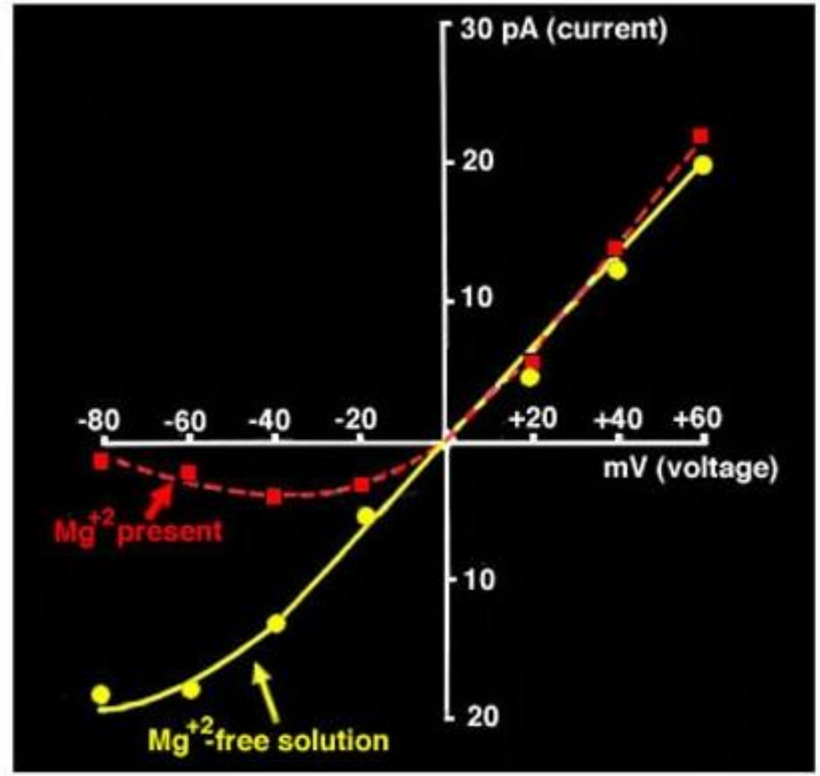
- LTP Forms can be distinguished by
  - Receptor system involvel
  - Associativity
  - Induction
    - Where is the trigger that decides whether plasticity takes place?
  - Expression
    - What molecular changes lead to a change in synaptic strength?

Associative & NMDAR Dependent

- ‘Typical’, form, most studied form of LTP.
- Occurs at the Schaffer collaterals in the CA1 region of the hippocampus.
- Presynaptic release and postsynaptic depolarization are needed for induction.

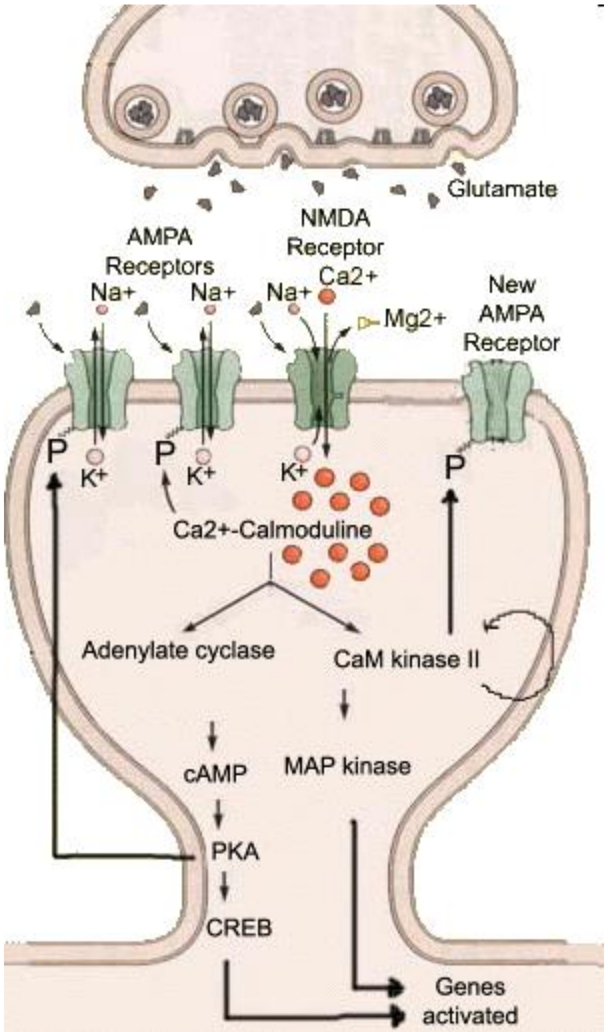
NMDA Receptors





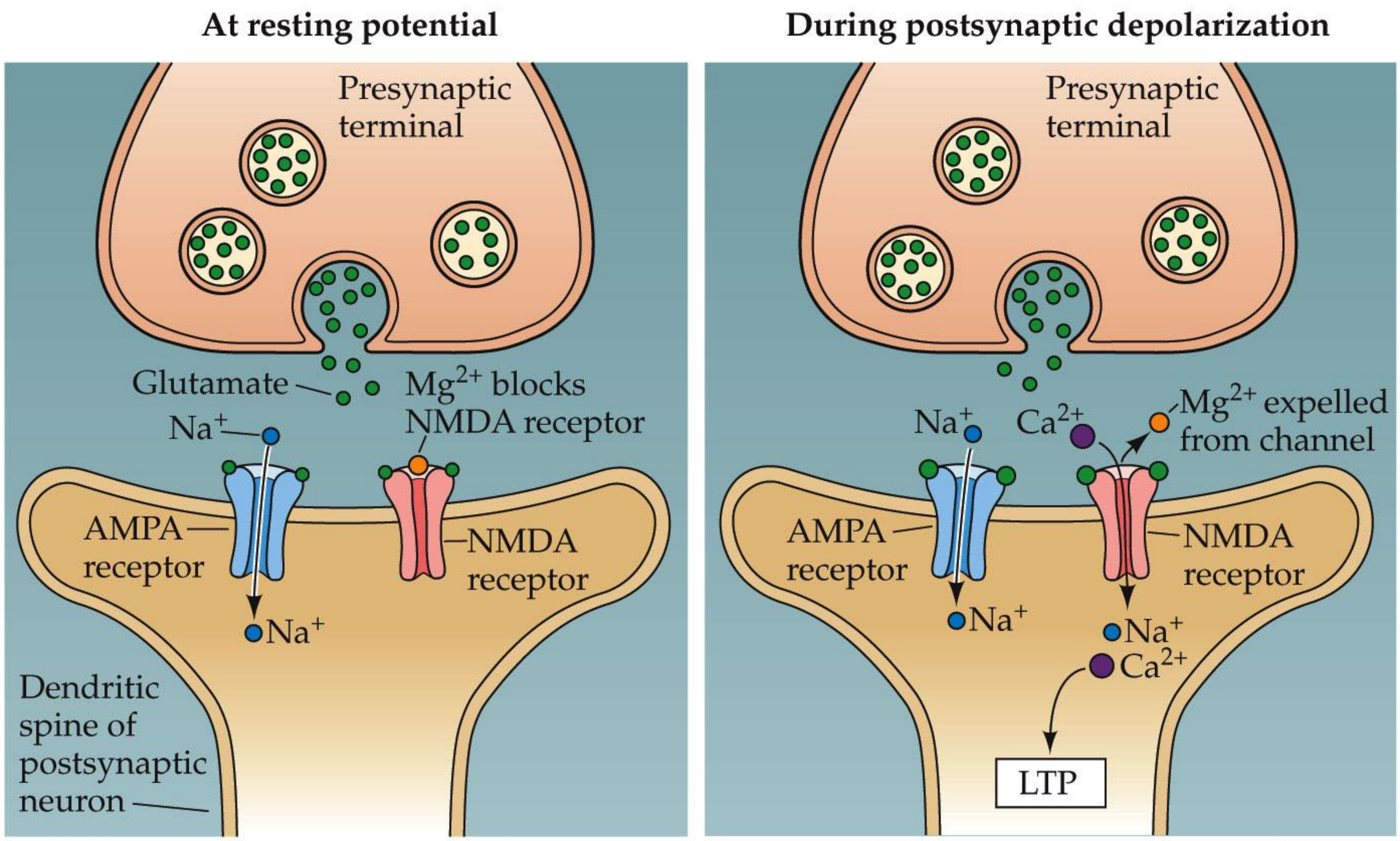
Needs glutamate (and glycine) and depolarization to conduct – in the hyperpolarized state MG ions block the flow of ions through the pore. The channel is sodium, potassium and in particular calcium permeant.

Induction



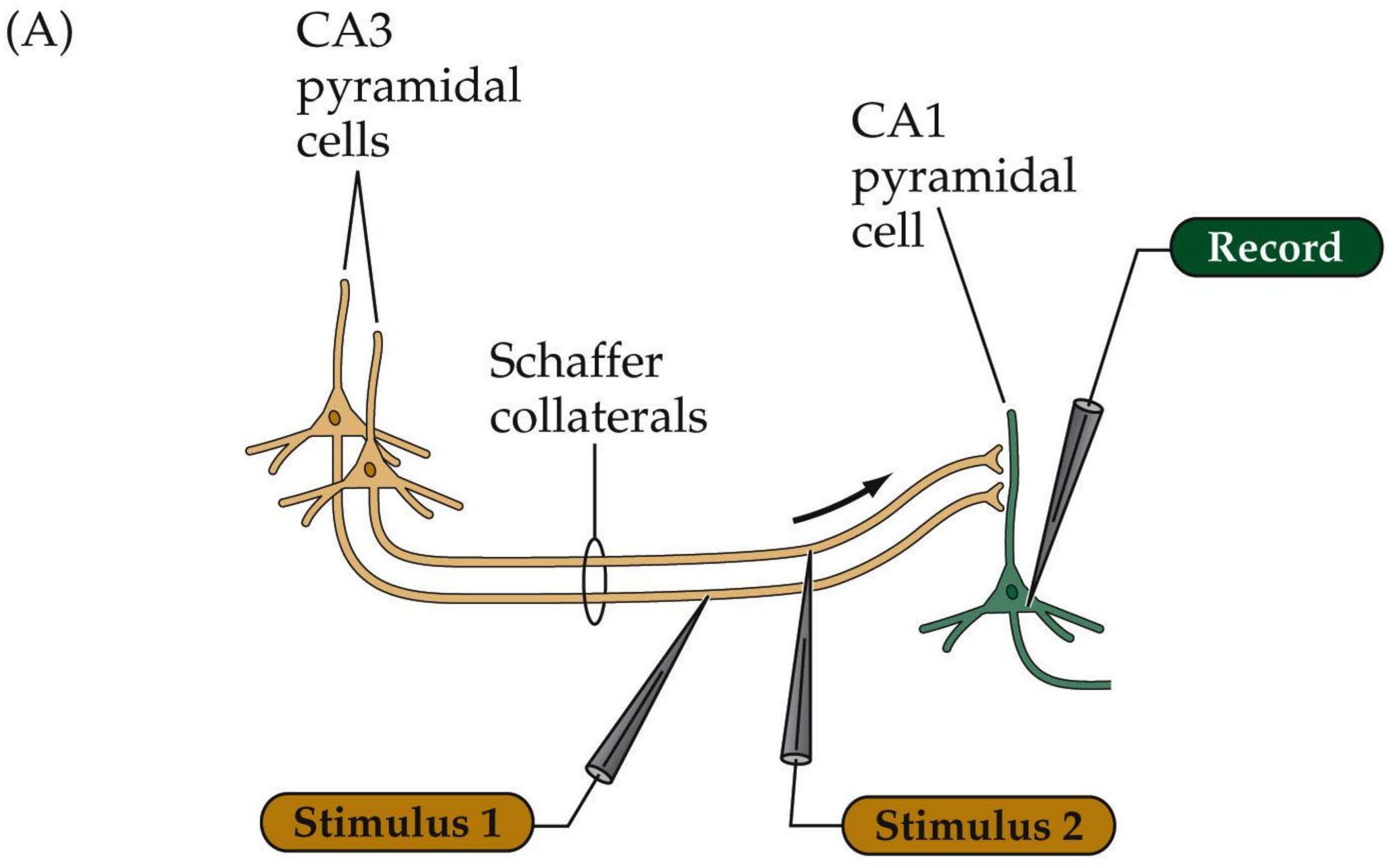
- Release of glutamate with councident postsylantic depolarozation.
- Influx of calcium and activation von CaMKII

NMDA Receptor Activation



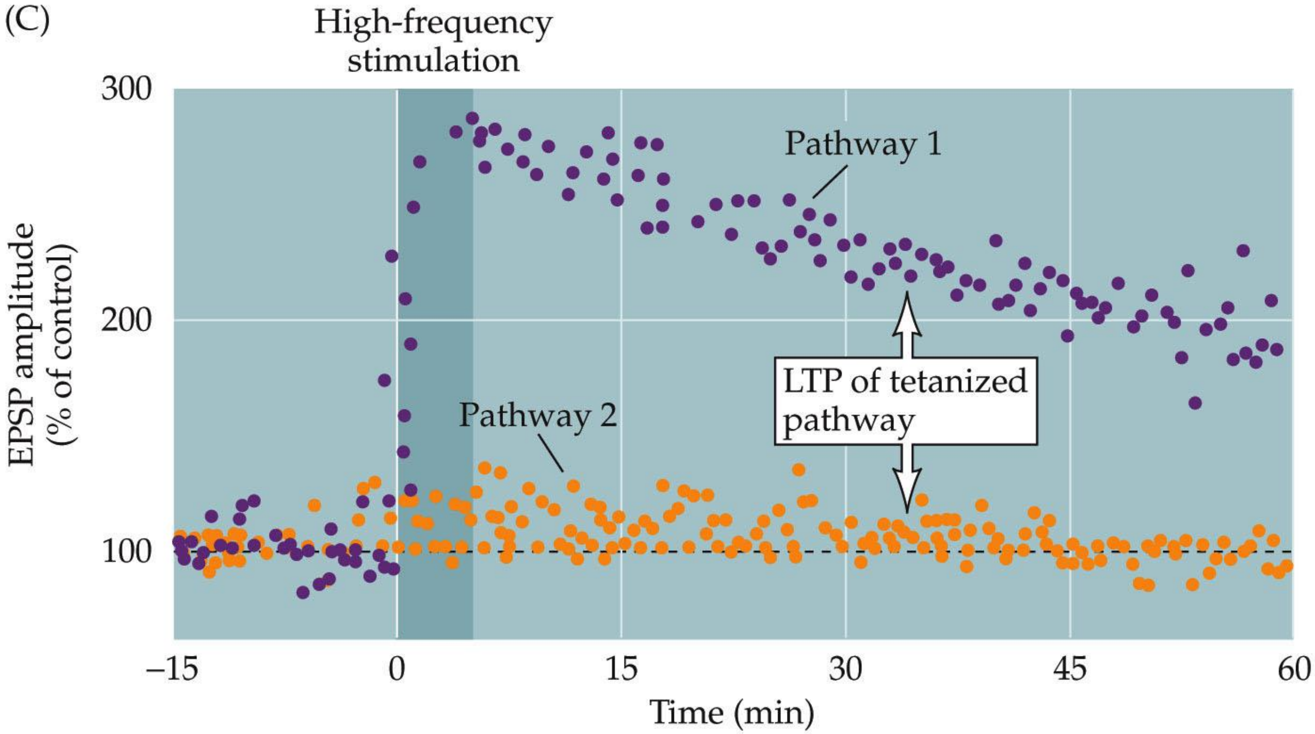
NEUROSCIENCE, Fourth Edition, Figure 8.10

Schaffer Collaterals



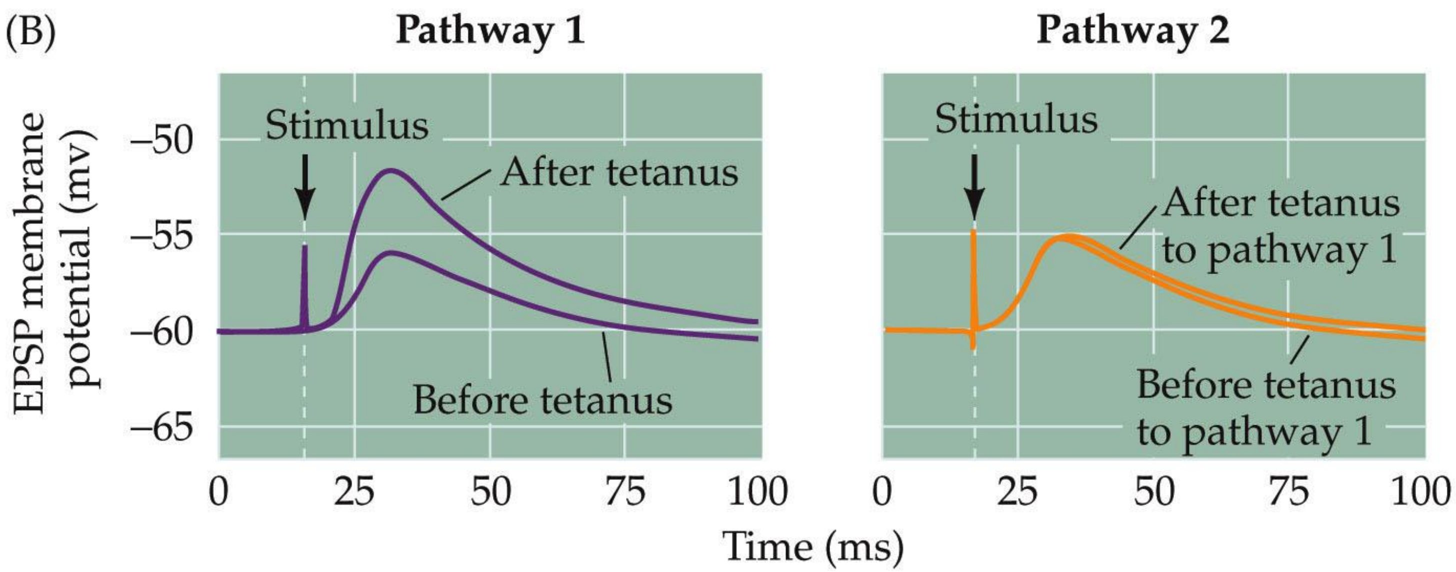
NEUROSCIENCE, Fourth Edition, Figure 8.7 (Part 1)

Schaffer Collateral LTP



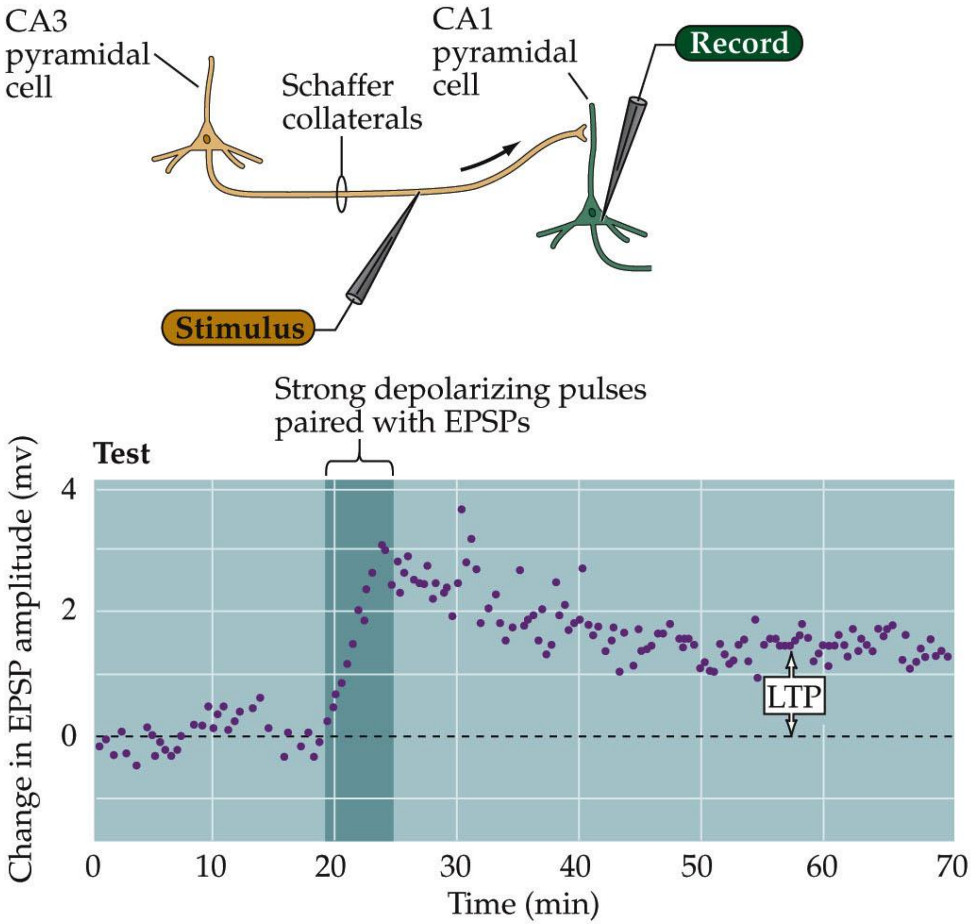
NEUROSCIENCE, Fourth Edition, **Figure 8.7 (Part 3)**

Synapse-Specifc



NEUROSCIENCE, Fourth Edition, **Figure 8.7 (Part 2)**

Pairing



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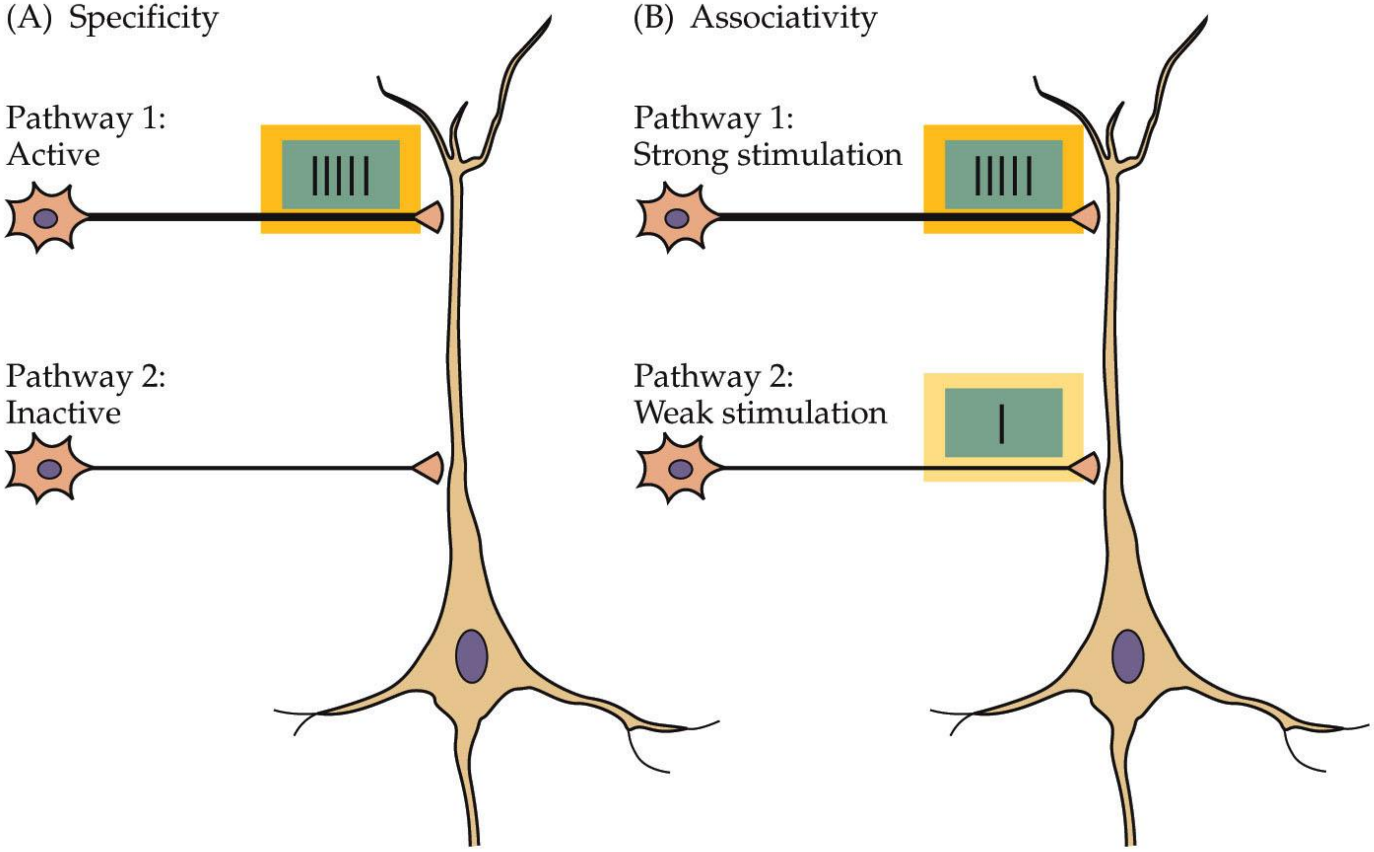
Specificity und Associativity



NEUROSCIENCE, Fourth Edition, Figure 8.9

Expression I

ARTICLES

Presynaptic mechanism for long-term potentiation in the hippocampus

John M. Bekkers & Charles F. Stevens

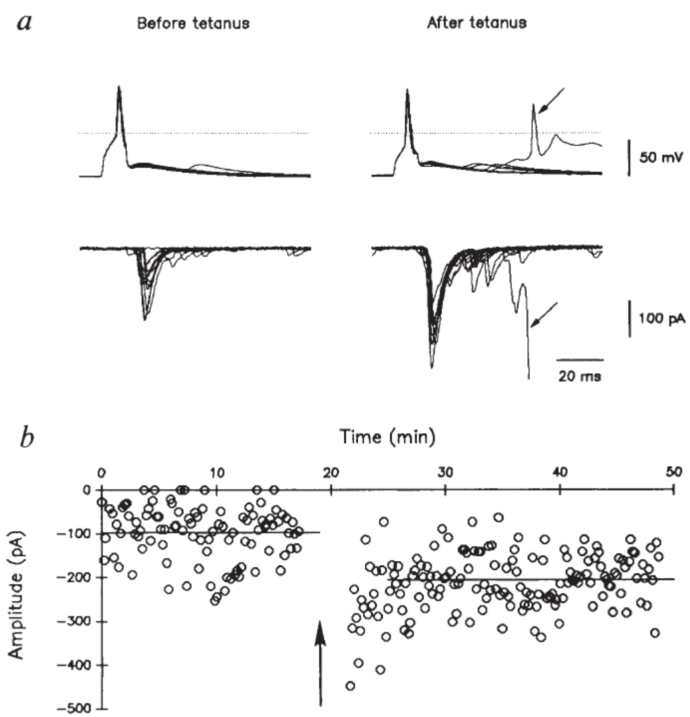
The Salk Institute, Howard Hughes Medical Institute, 10010 North Torrey Pines Road, La Jolla, California 92037, USA

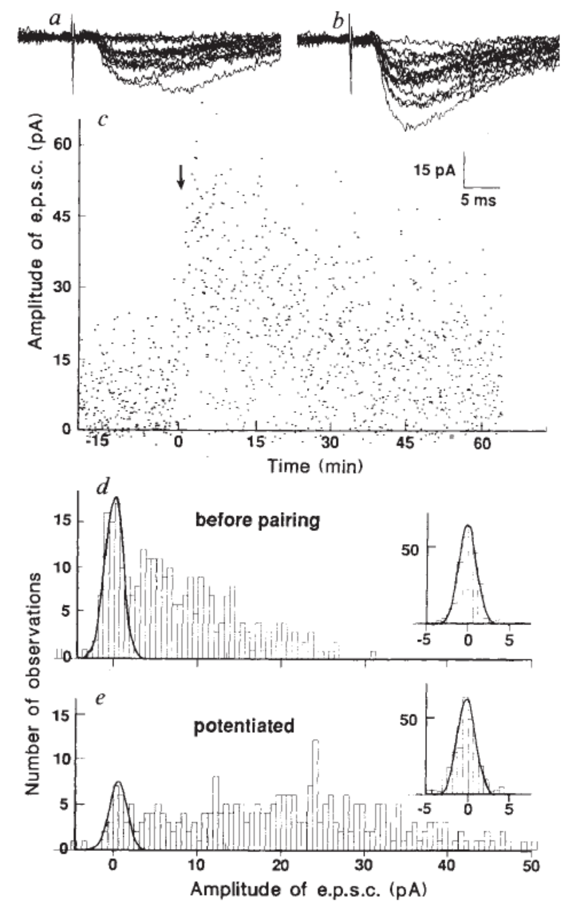
Experiments analysing the statistical properties of   reflecting the properties of a population of boutons); second,

Presynaptic enhancement shown by whole-cell recordings of long-term potentiation in hippocampal slices

Roberto Malinow* & Richard W. Tsien

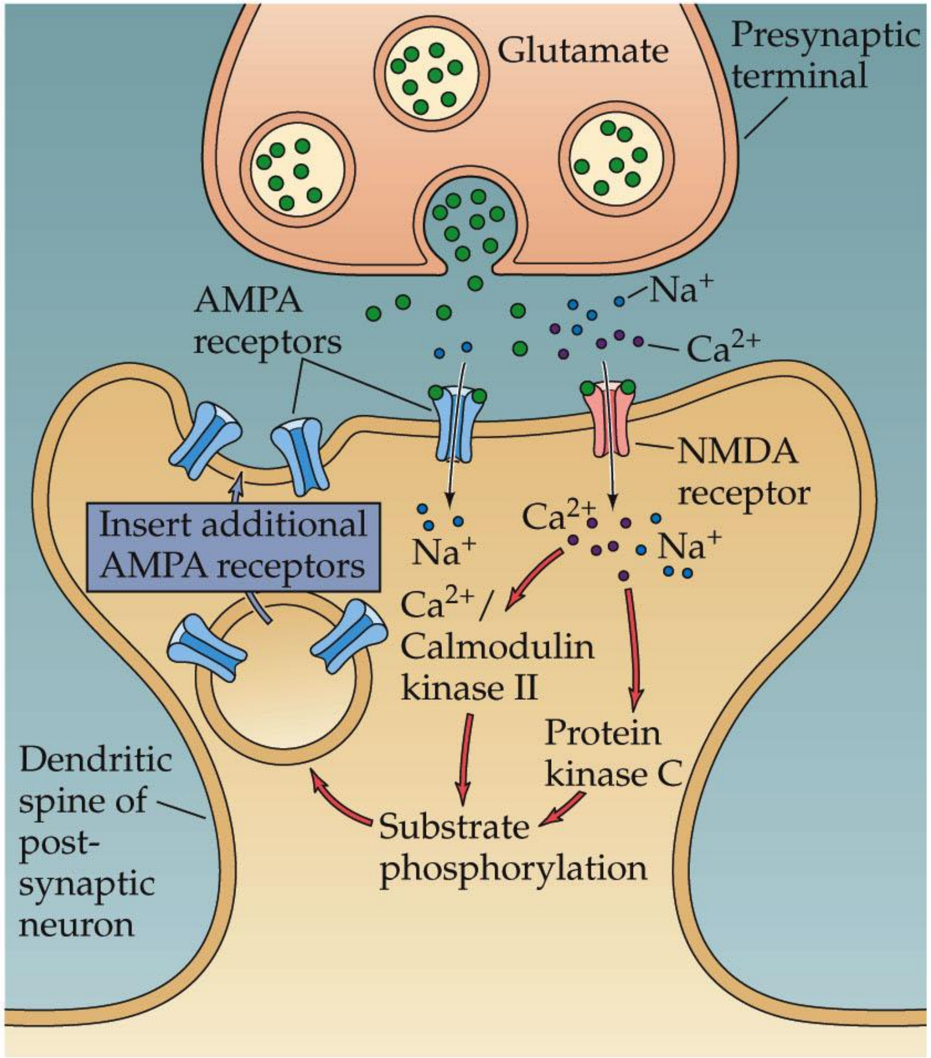
Department of Molecular and Cellular Physiology, Beckman Center, Stanford University Medical Center, Stanford, California 94305, USA





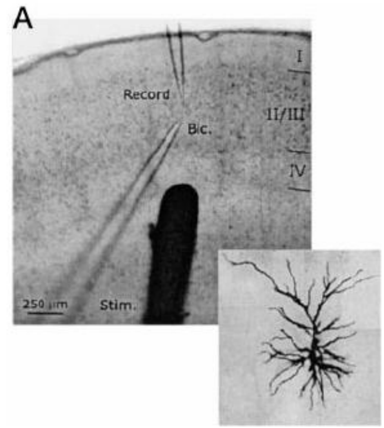
Amplitude und Zuverlässigkeit' nehmen zu

Expression II

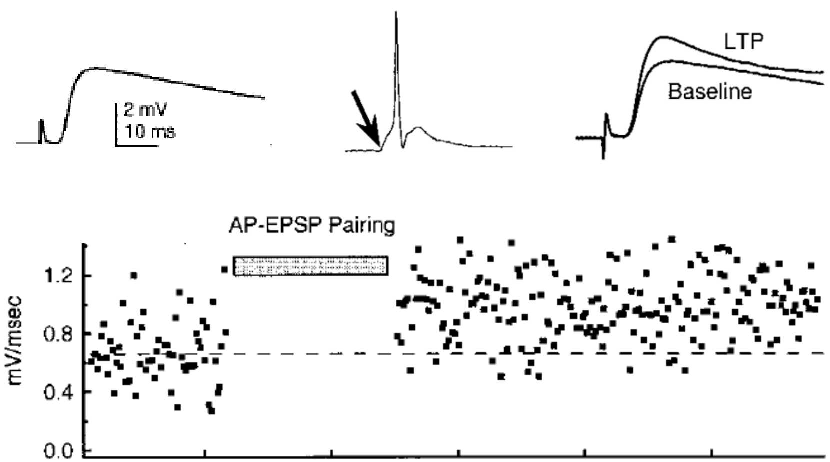


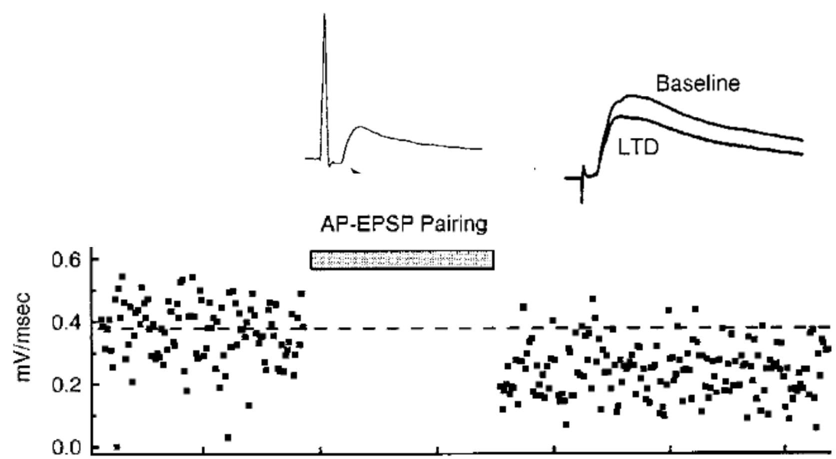
NEUROSCIENCE, Fourth Edition, Figure 8.11

Spike-Timing I



Example of Hebbian and anti-Hebbian plasticity in cortex

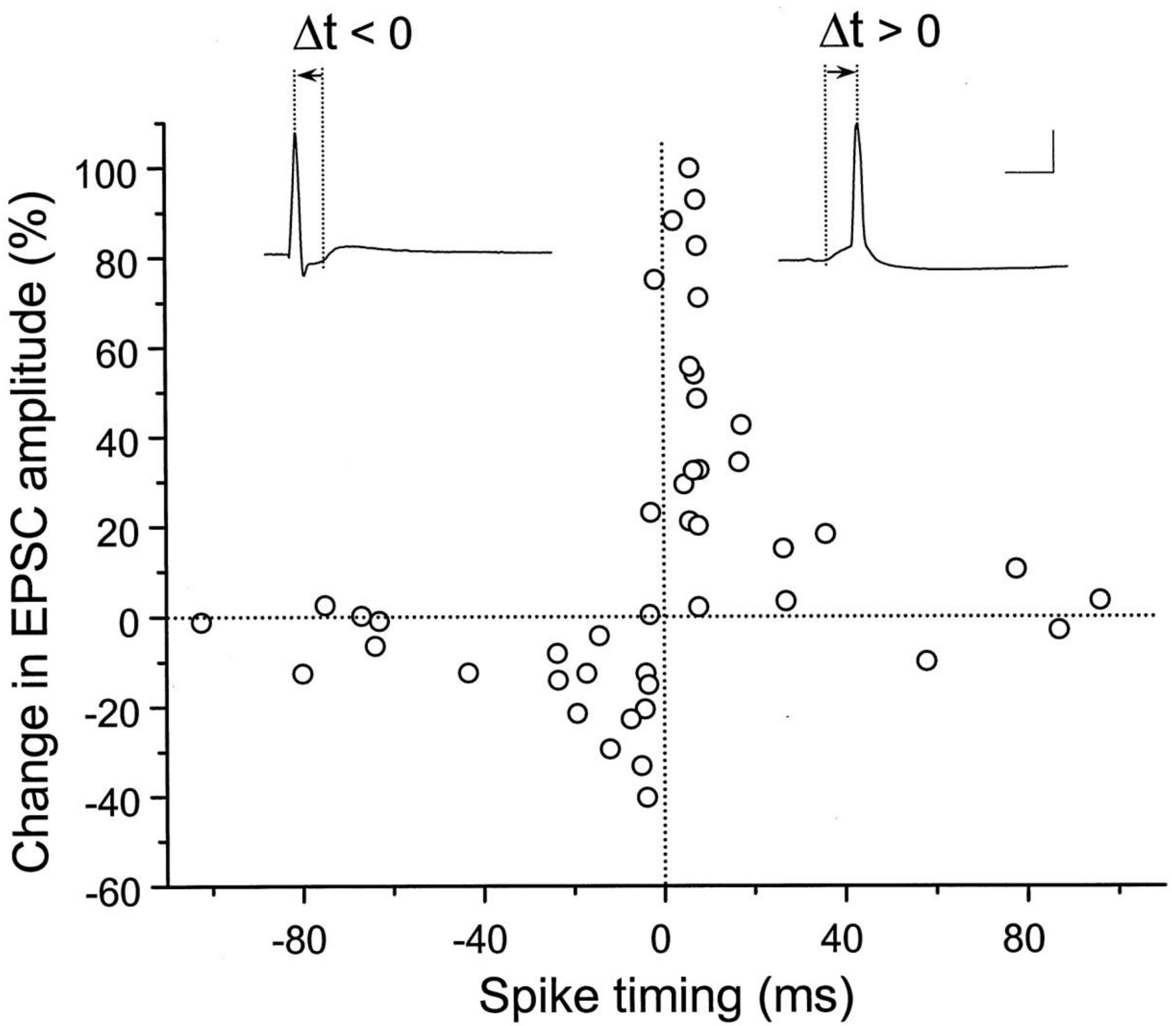




Time (10 min)

Daniel E. Feldman*
Neuron, Vol. 27, 45–56,

Spike Timing II



Bi and Poo JNS 18: 10464

Die BCM Rule

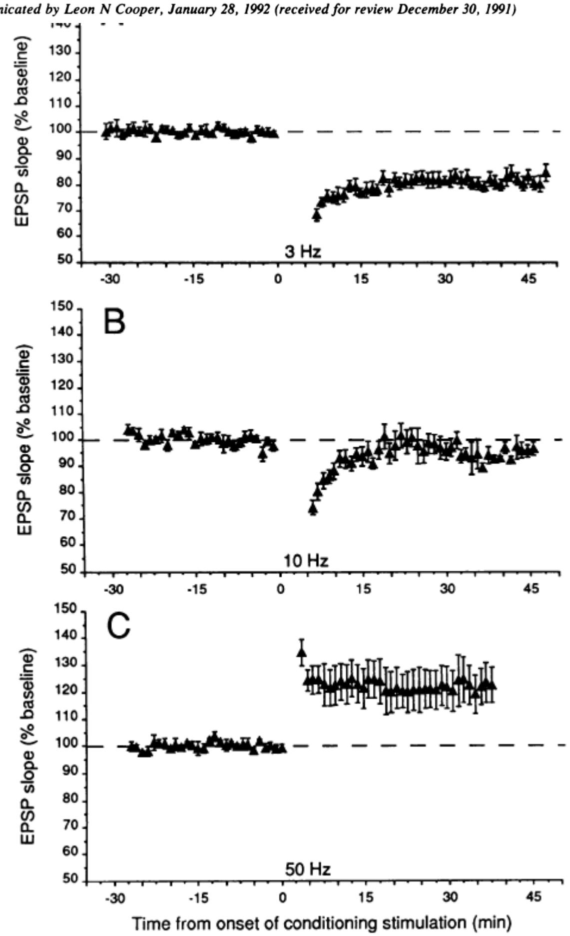
Proc. Natl. Acad. Sci. USA
Vol. 89, pp. 4363–4367, May 1992
Neurobiology

Homosynaptic long-term depression in area CA1 of hippocampus and effects of *N*-methyl-D-aspartate receptor blockade

(long-term potentiation/hippocampal slice/synaptic plasticity/learning/memory)

SERENA M. DUDEK AND MARK F. BEAR*
The Center for Neural Science, Brown University, Providence, RI 02912

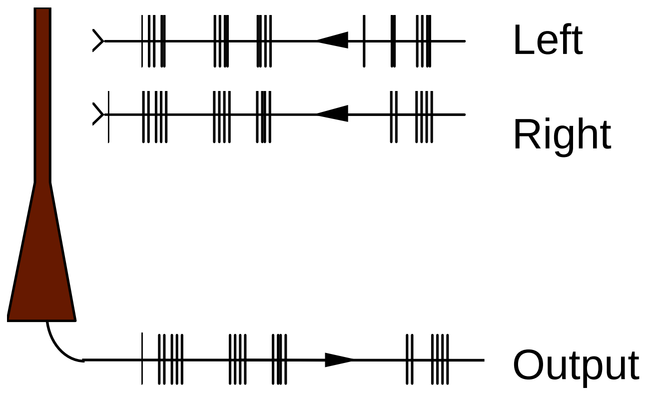
Communicated by Leon N Cooper, January 28, 1992 (received for review December 30, 1991)



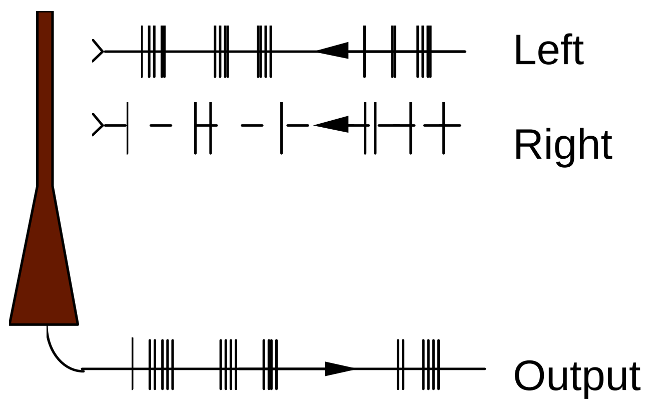
- Mild (non-coincident) stimulation leads to synaptic to depression.
- Strong (coincident) stimulation leads to potentiation.

Elie Bienenstock, Leon Cooper, and Paul Munro

Die BCM Rule



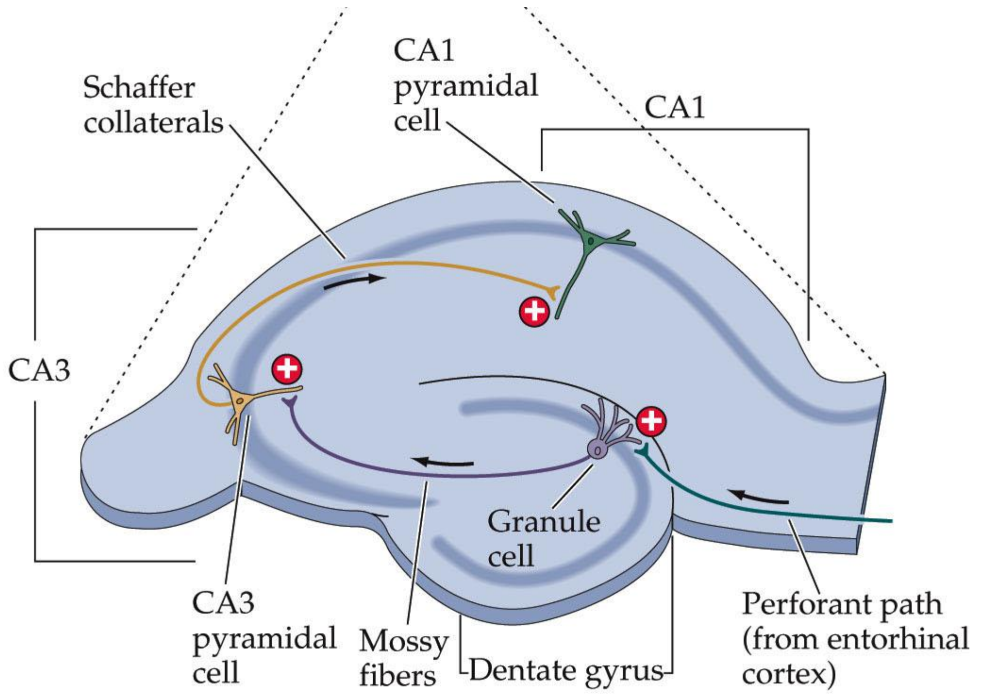
Neurons that fire together wire together.



Neurons that fire out of sync lose their link.

Non-Associative NMDAR Independent

- Typical example is the mossy fiber plasticity. (Dentate gyrus to CA3).

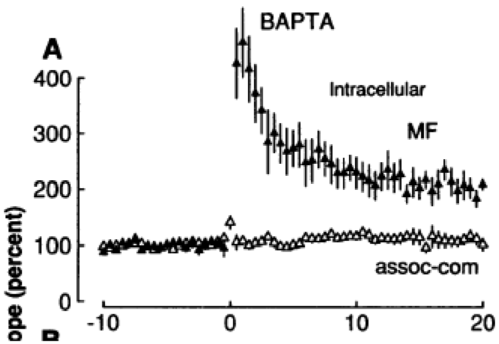


***NEUROSCIENCE*, *Fourth Edition*, Figure 8.6**

Mossy Fiber LTP

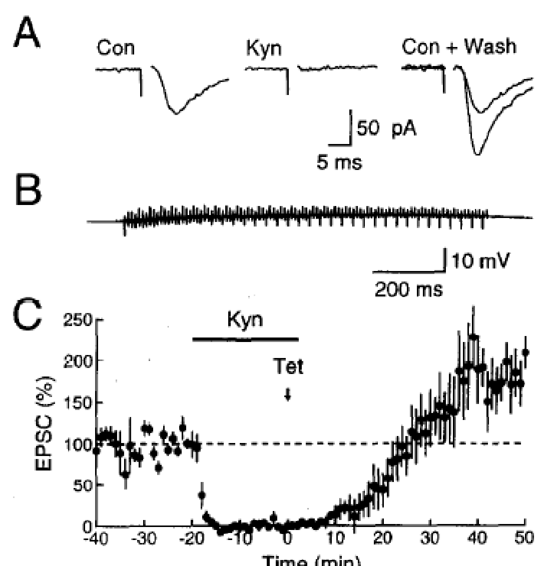
Comparison of Two Forms of Long-Term Potentiation in Single Hippocampal Neurons

ROBERT A. ZALUTSKY AND ROGER A. NICOLL*



Neuron, Vol. 12, 261-269, February, 1994, Copyright © 1994 by Cell Press

The Role of Ca^{2+} Channels in Hippocampal Mossy Fiber Synaptic Transmission and Long-Term Potentiation



Mediation of Hippocampal Mossy Fiber Long-Term Potentiation by Cyclic AMP

Marc G. Weisskopf, Pablo E. Castillo, Robert A. Zalutsky, Roger A. Nicoll*