

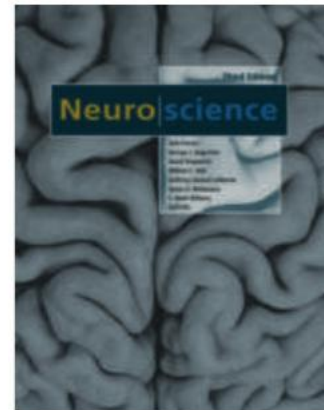
# Synaptic Plasticity

Learning and  
Remembering...

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

# 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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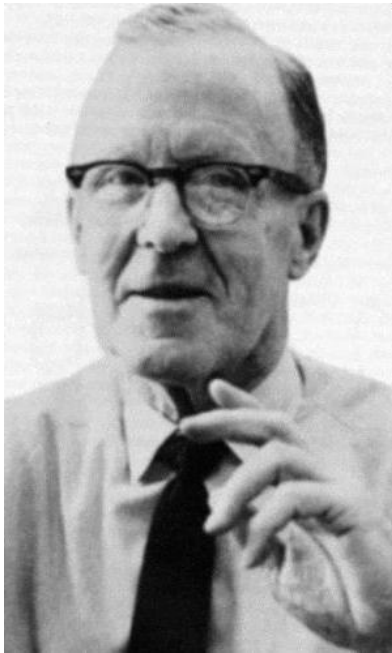
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# Aims for this Lecture

- 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.

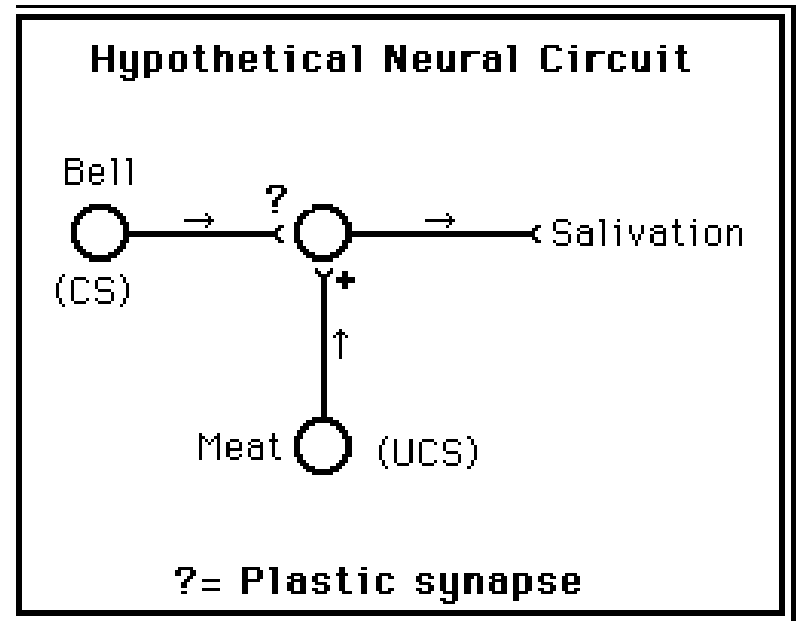
# Recapitulation L9

- 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

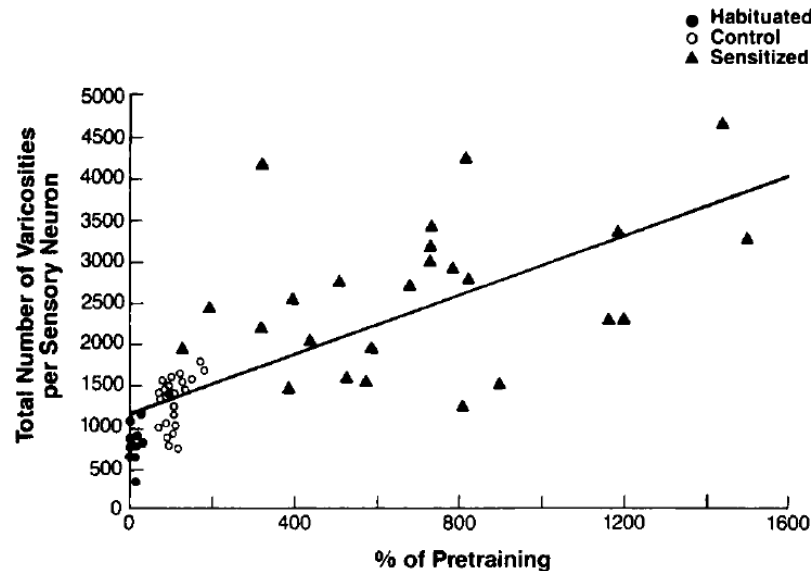
# Aplysia I

## Morphological Aspects of Synaptic Plasticity in *Aplysia*

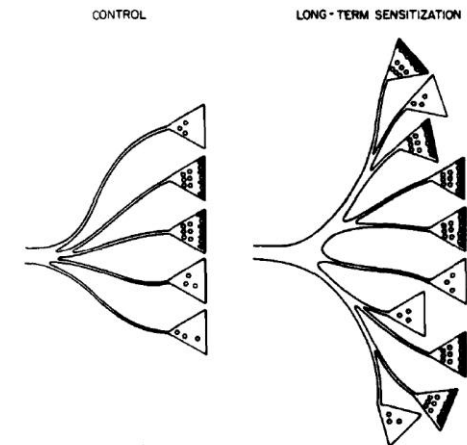
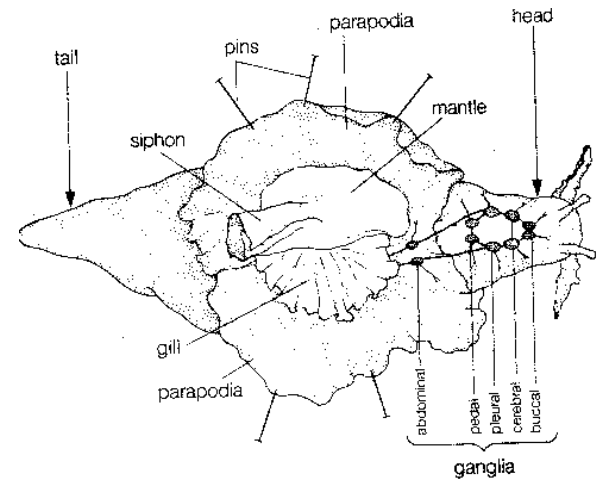
### An Anatomical Substrate for Long-Term Memory<sup>a</sup>

CRAIG H. BAILEY<sup>b</sup> 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

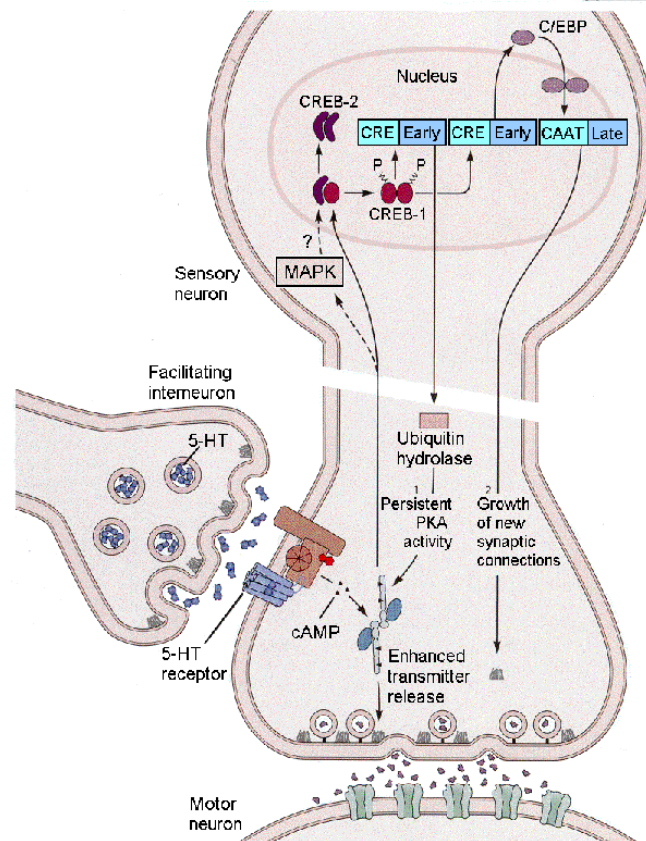
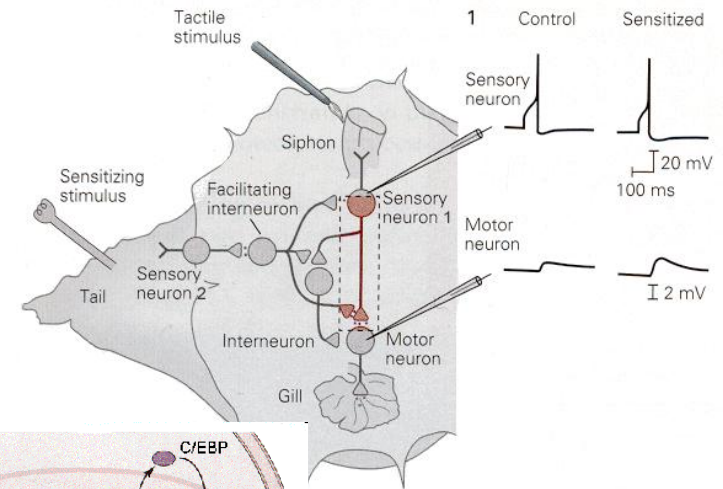
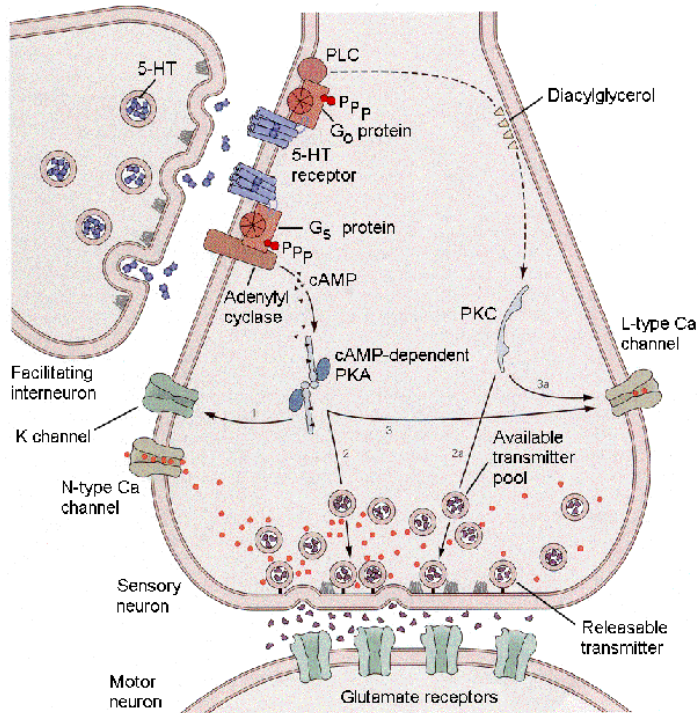


**FIGURE 3.** Correlation between changes in varicosity number and long-term memory. Data points represent animals trained for long-term habituation, animals trained for long-term sensitization, and untrained (control) animals. Structural changes (total number of varicosities per sensory neuron) are 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.)



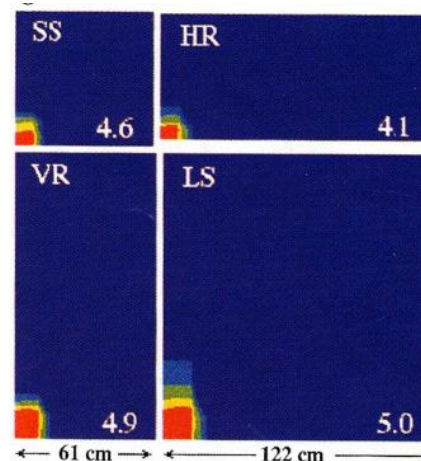
**FIGURE 8.** Cartoon illustrating the family of structural alterations produced by long-term sensitization. These involve a doubling in the number of sensory neuron varicosities, an increase in the incidence of their active zones, and an increase in the neuropil arbor of the sensory neurons. (Modified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

# Aplysia II



# Hippocampus

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

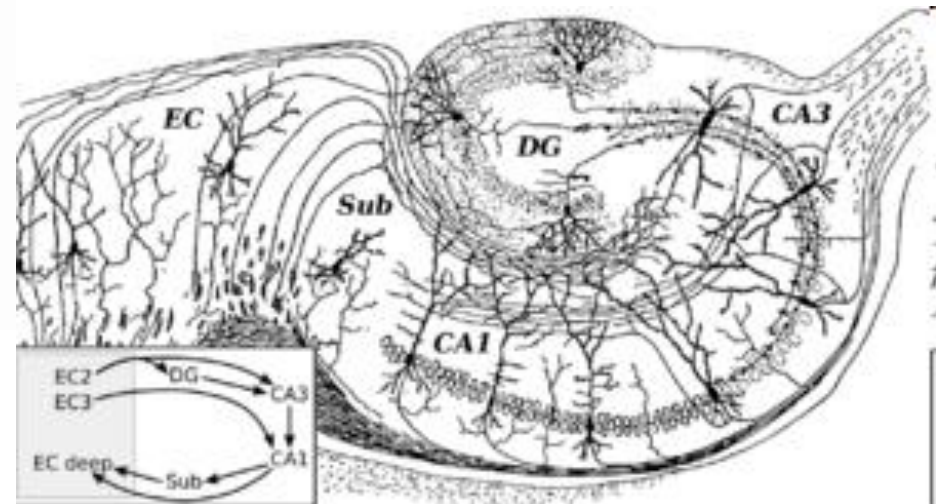
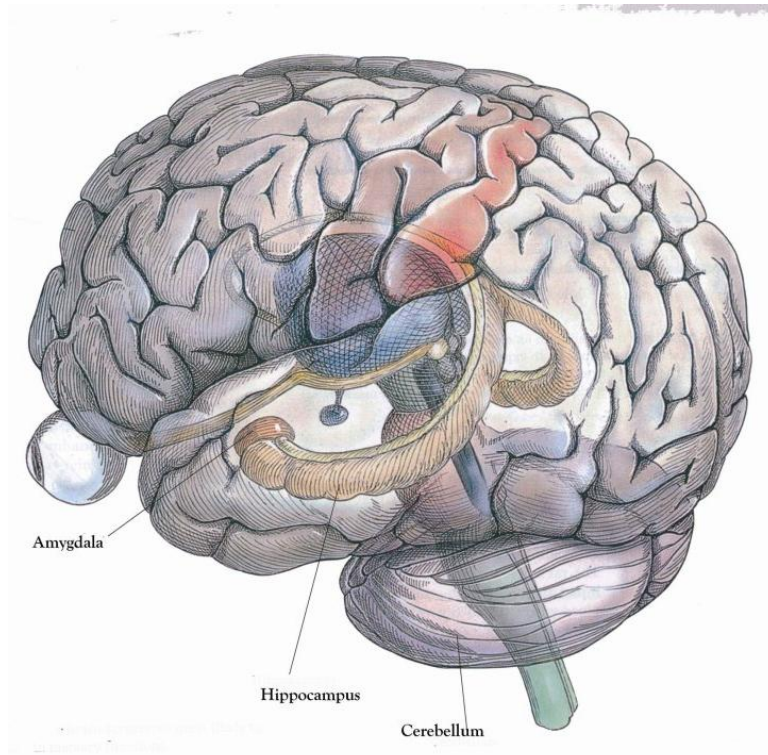


The hippocampus as a spatial map.  
Preliminary evidence from unit activity in the  
freely-moving rat

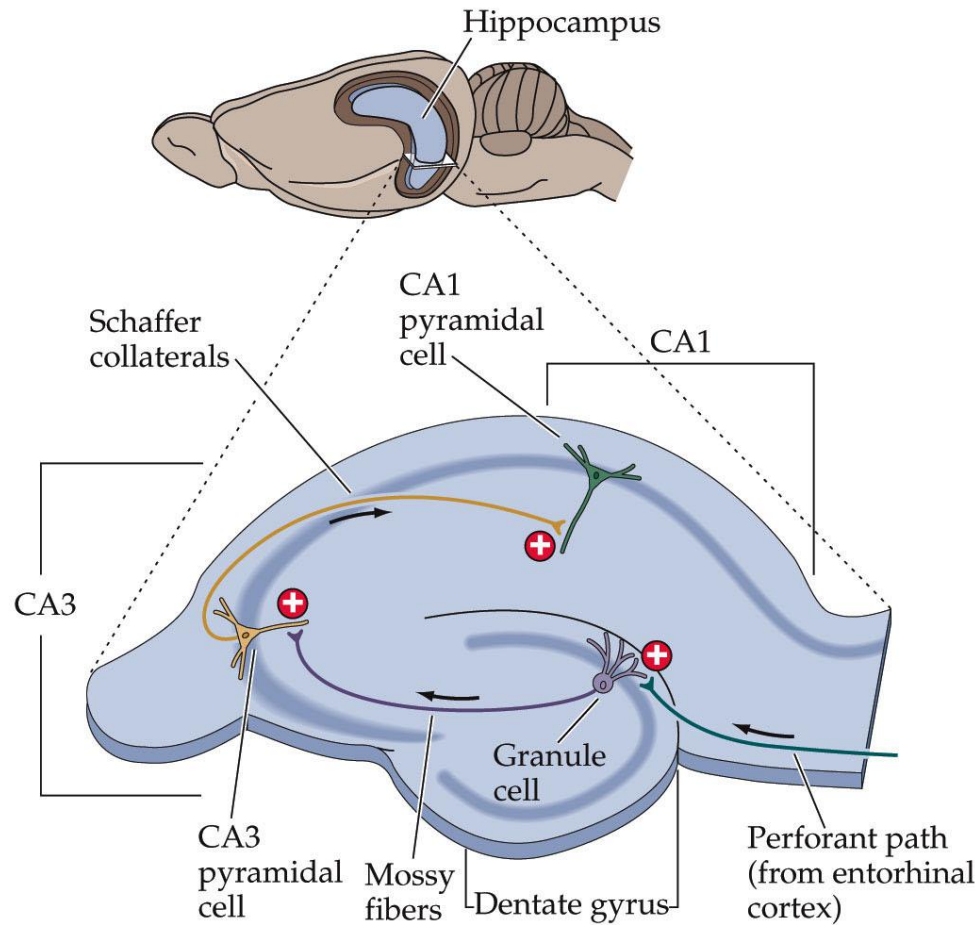
J. O'Keefe<sup>a</sup> and J. Dostrovsky<sup>\*, a</sup>  
aM.R.C.  
Brain research 1971.



# Anatomy



# Rodent Hippocampus



**NEUROSCIENCE, Fourth Edition, Figure 8.6**

# Bliss & Lømo

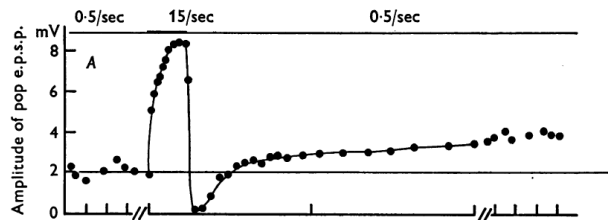
*J. Physiol.* (1973), **232**, pp. 331-356  
With 12 text-figures  
Printed in Great Britain

331

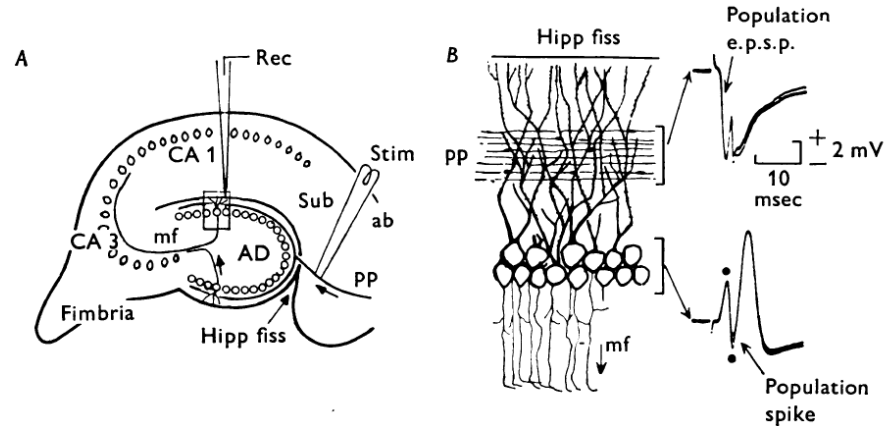
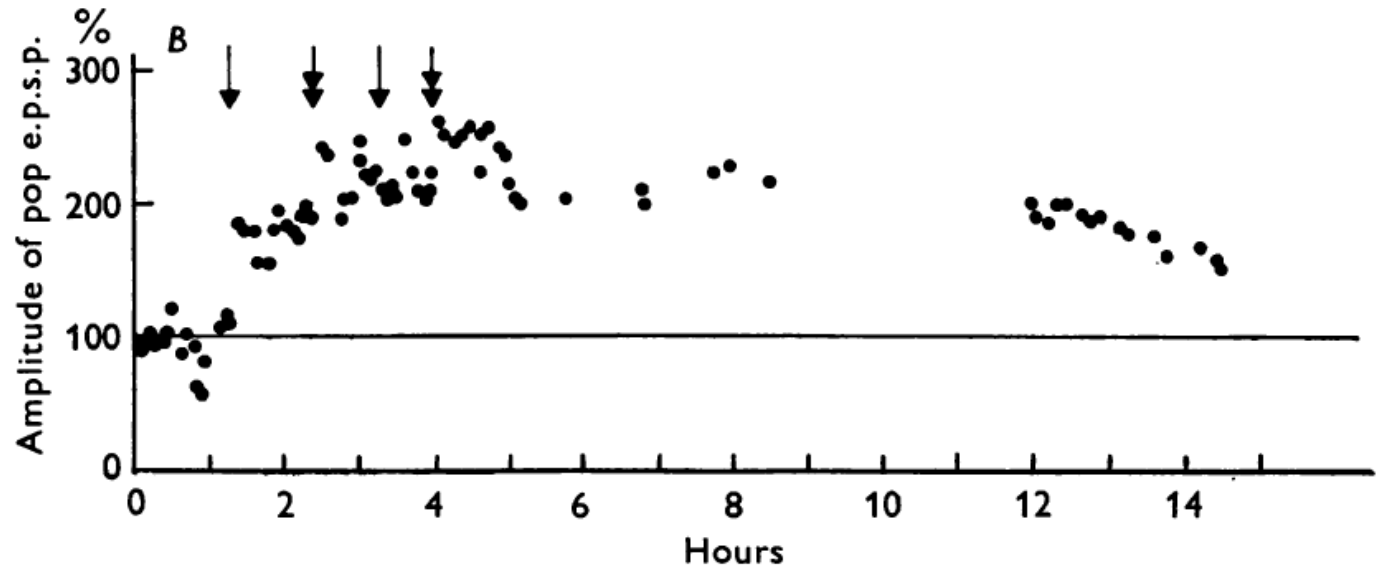
## LONG-LASTING POTENTIATION OF SYNAPTIC TRANSMISSION IN THE DENTATE AREA OF THE ANAESTHETIZED RABBIT FOLLOWING STIMULATION OF THE PERFORANT PATH

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.

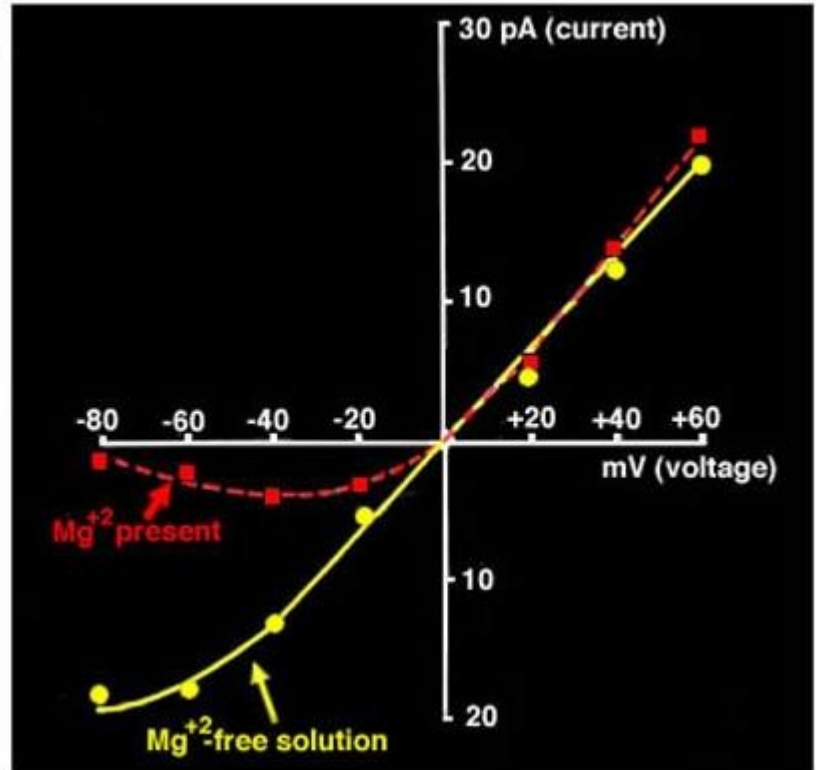
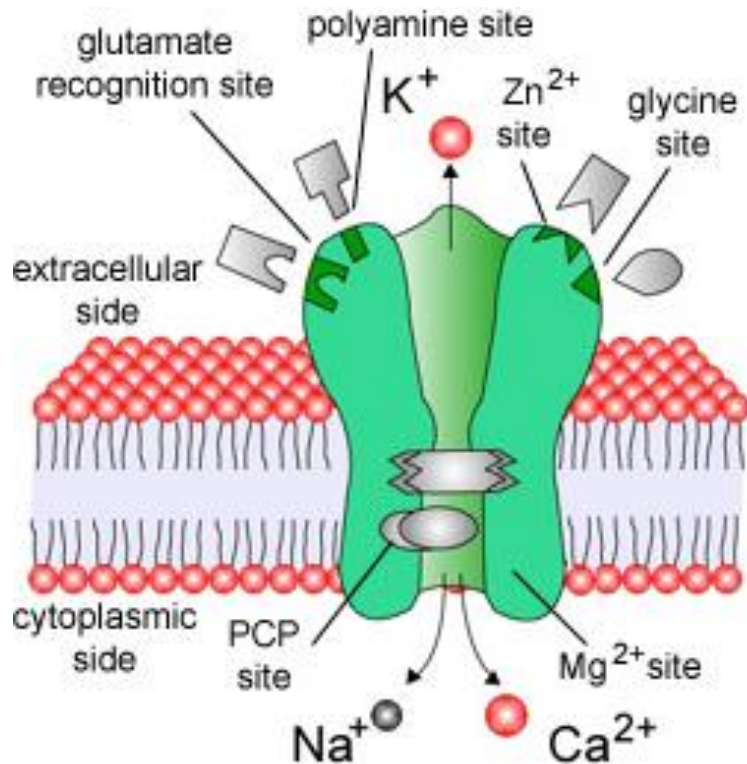
# Many Forms

- LTP Forms can be distinguished by
  - Receptor system involved
  - 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.

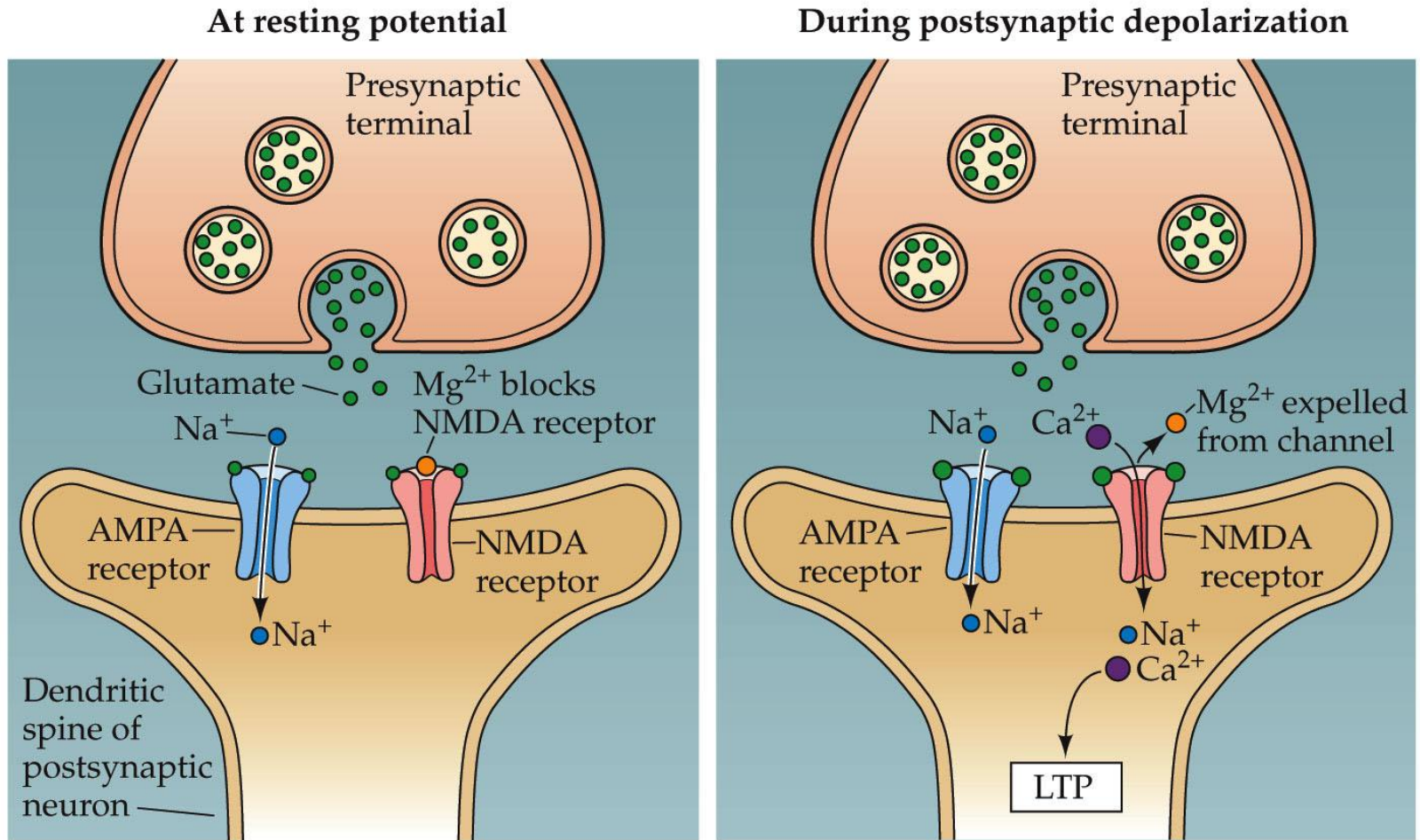
# NMDA Receptors



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.

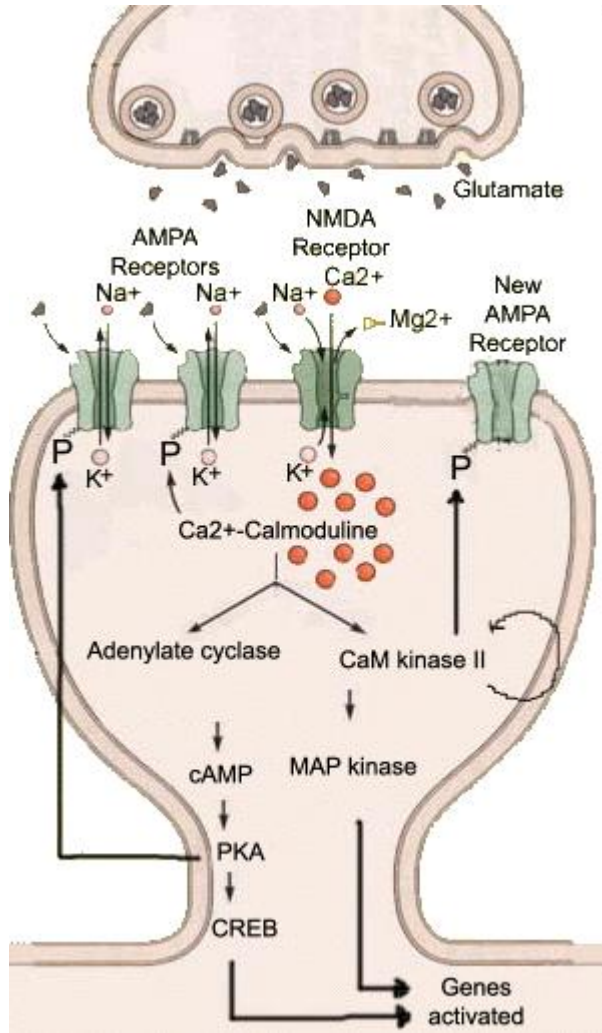


# NMDA Receptor Activation



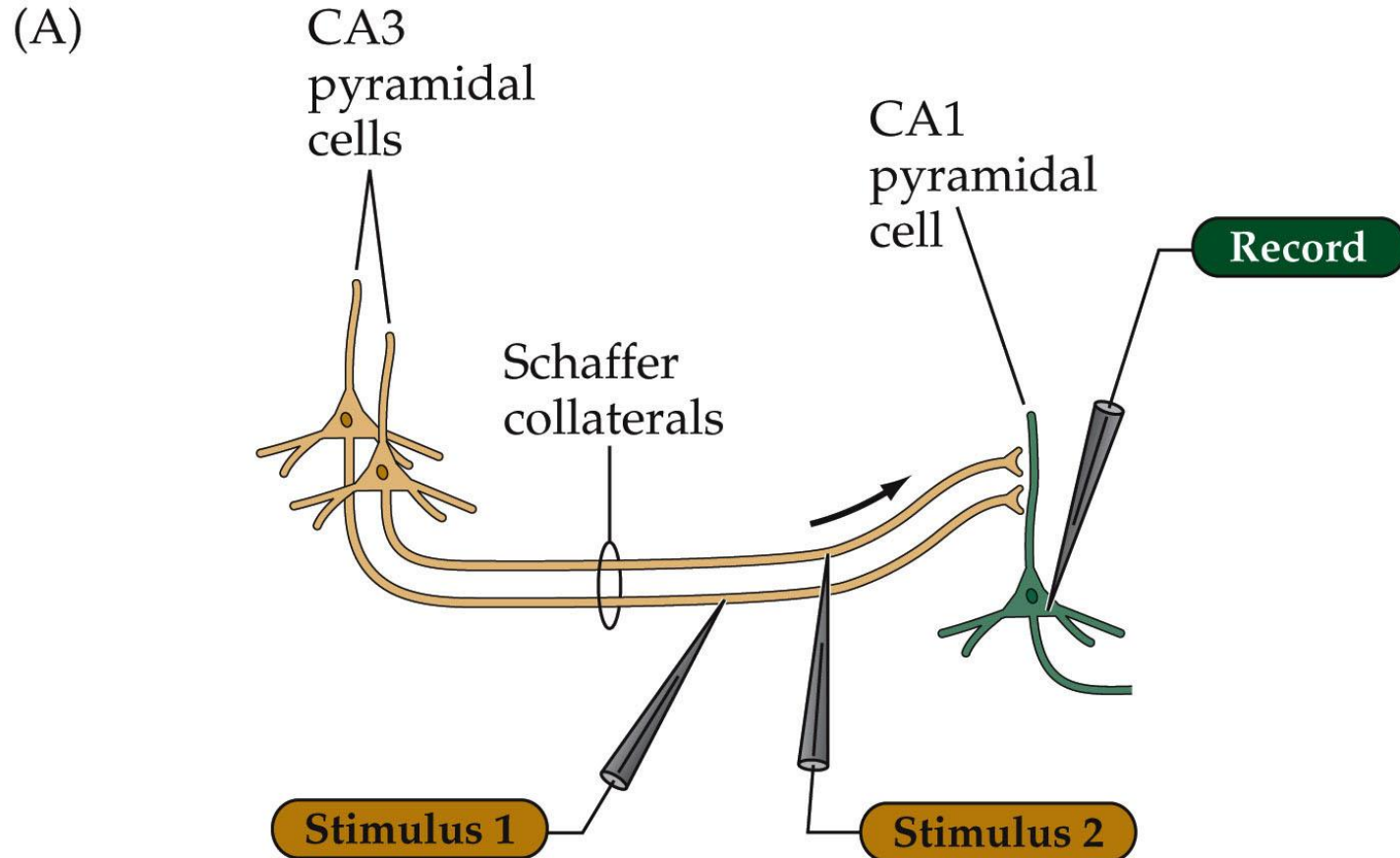


# Induction

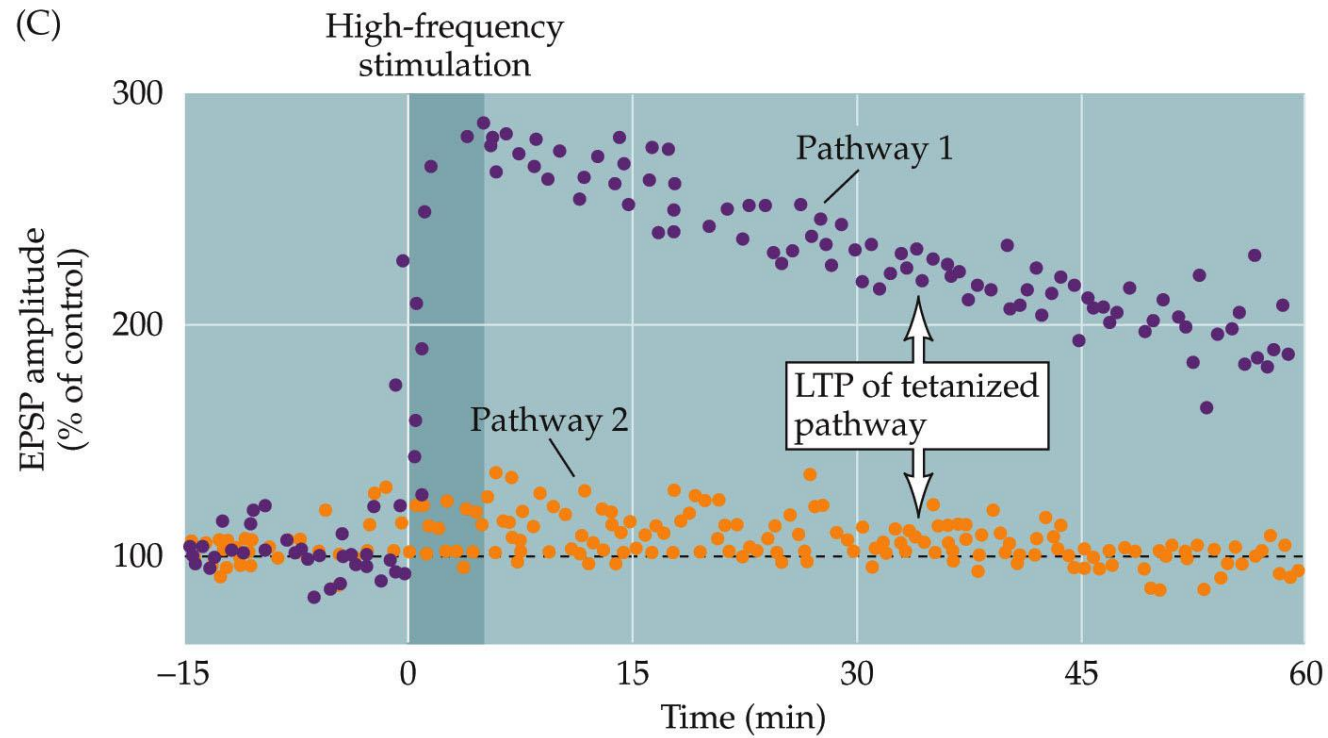


- Release of glutamate with coincident postsynaptic depolarization.
- Influx of calcium and activation von CaMKII

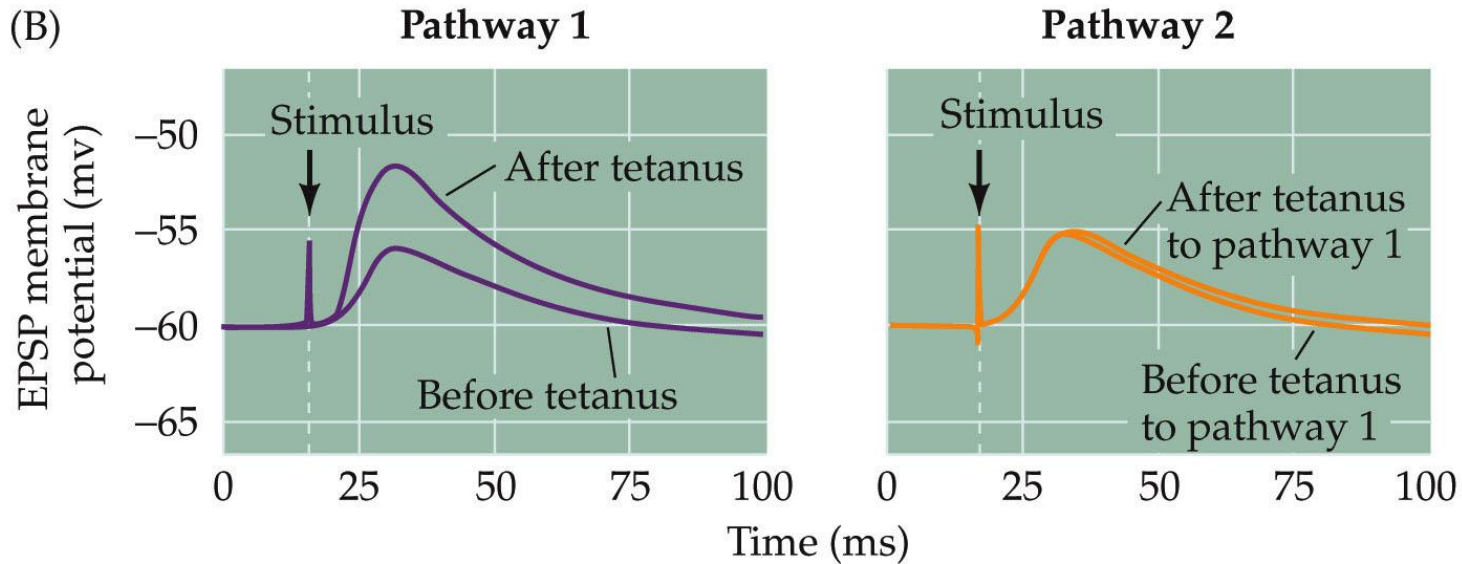
# Schaffer Collaterals



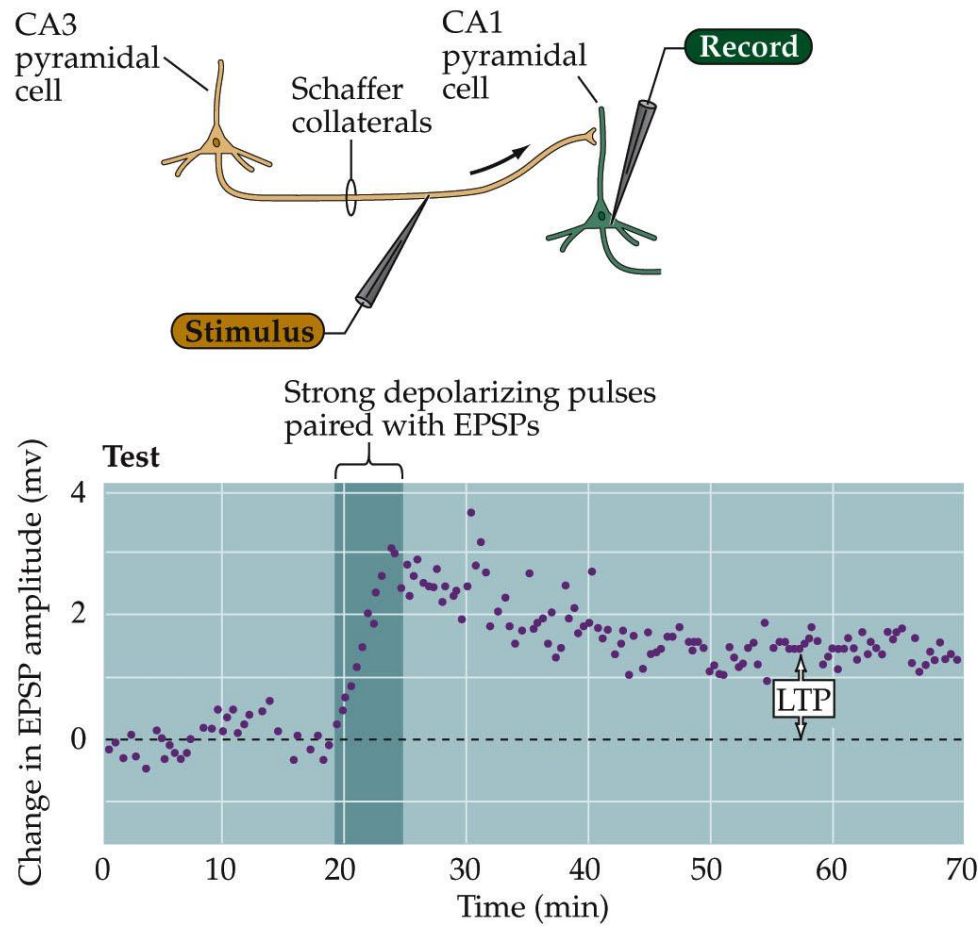
# Schaffer Collateral LTP



# Synapse-Specific



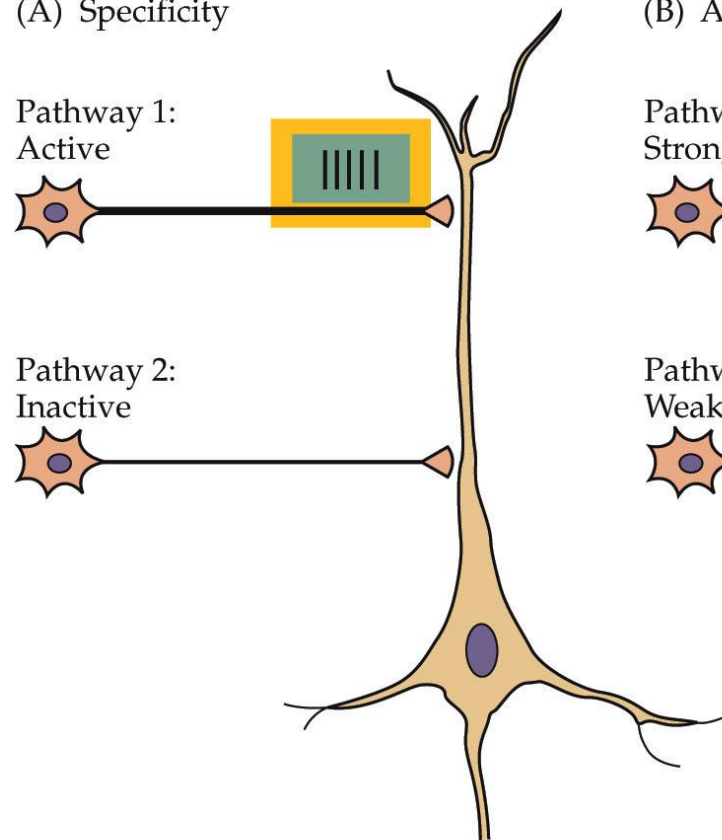
# Pairing



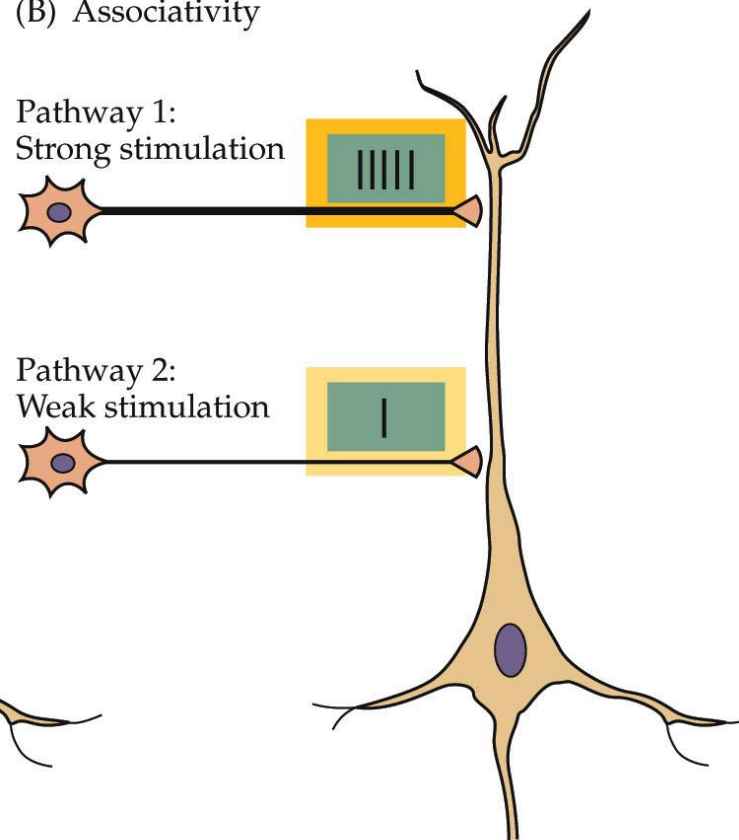
**NEUROSCIENCE, Fourth Edition, Figure 8.8**

# Specificity und Associativity

(A) Specificity



(B) Associativity



# Expression I

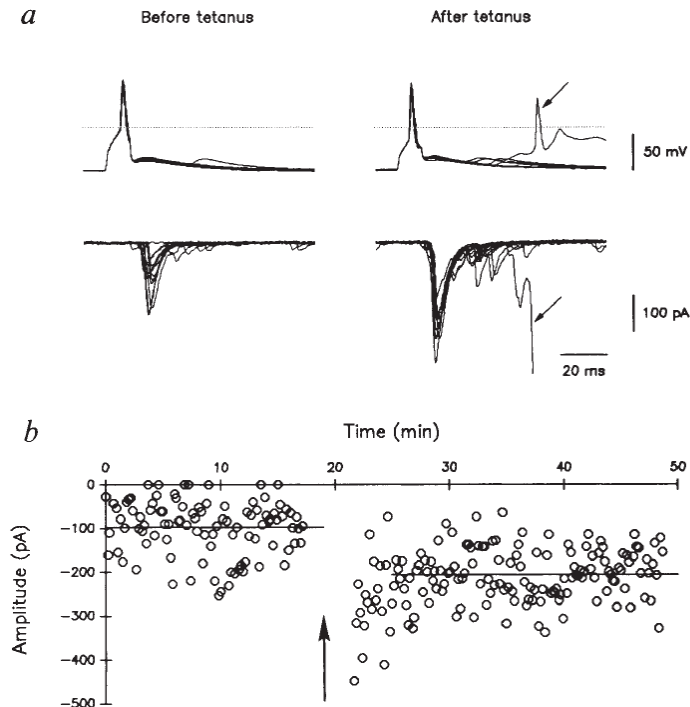
ARTICLES

## 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,

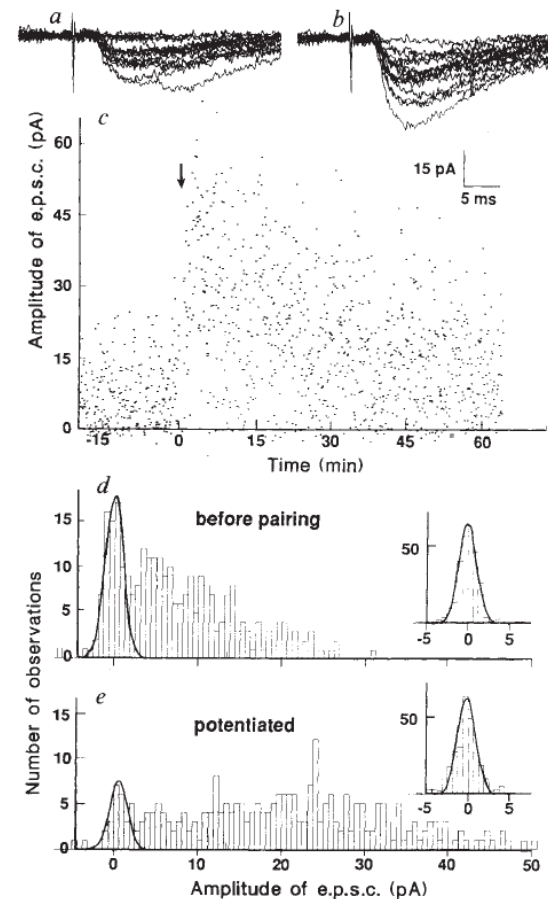


Amplitude und Zuverlässigkeit'  
nehmen zu

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

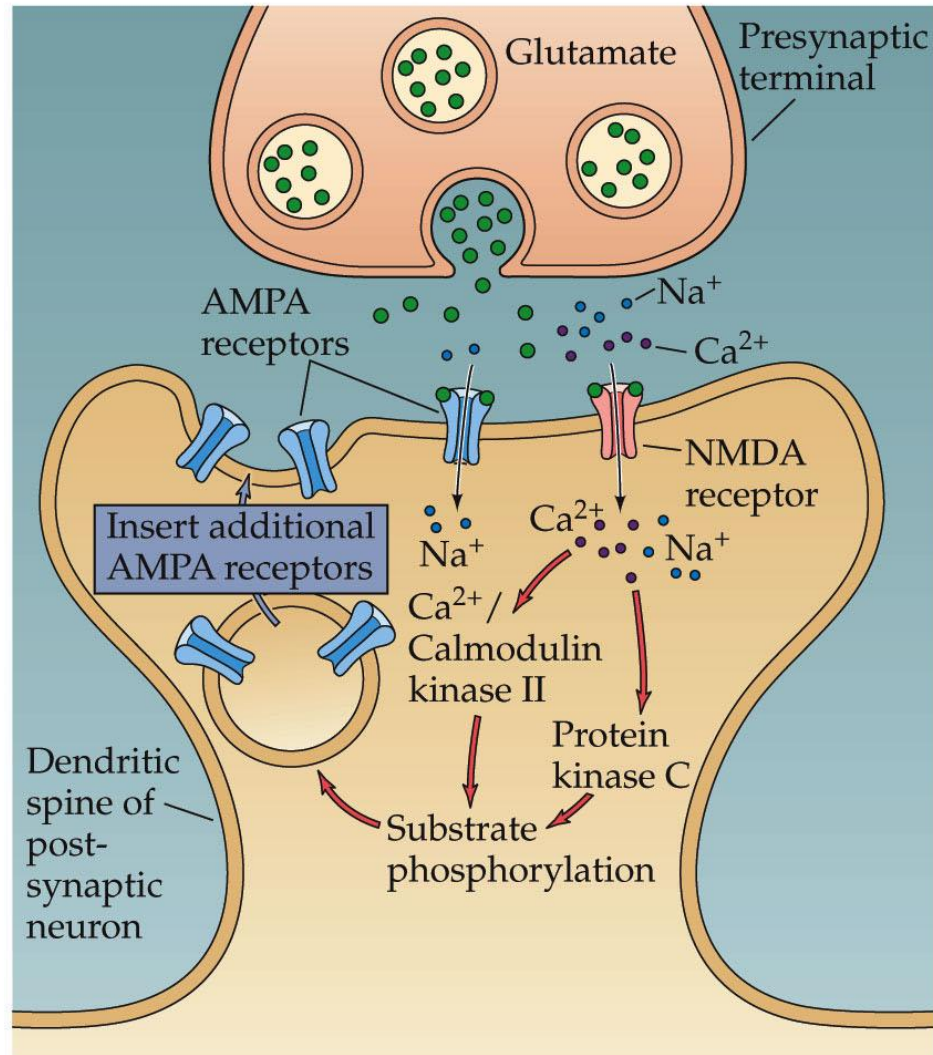
Roberto Malinow\* & Richard W. Tsien

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



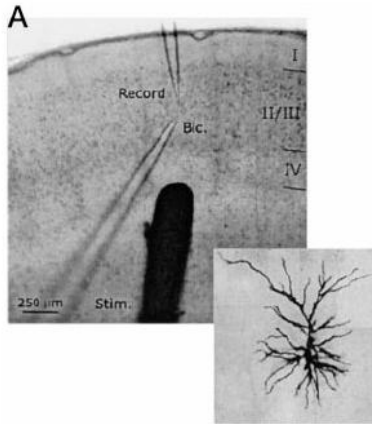


# Expression II

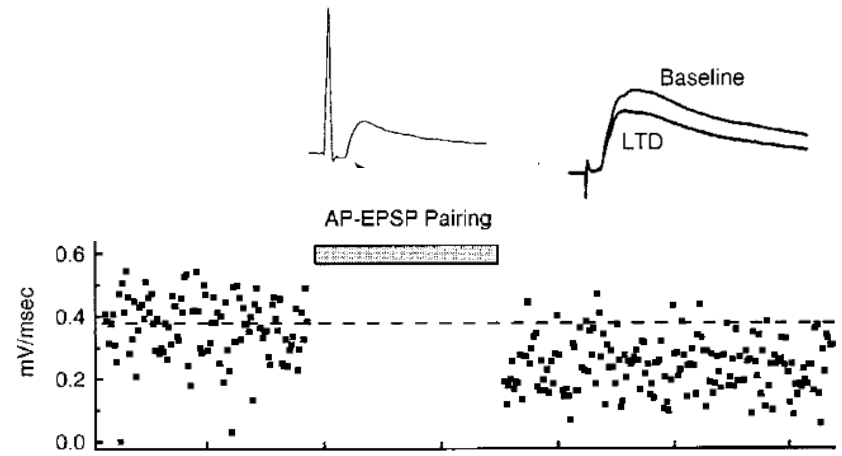
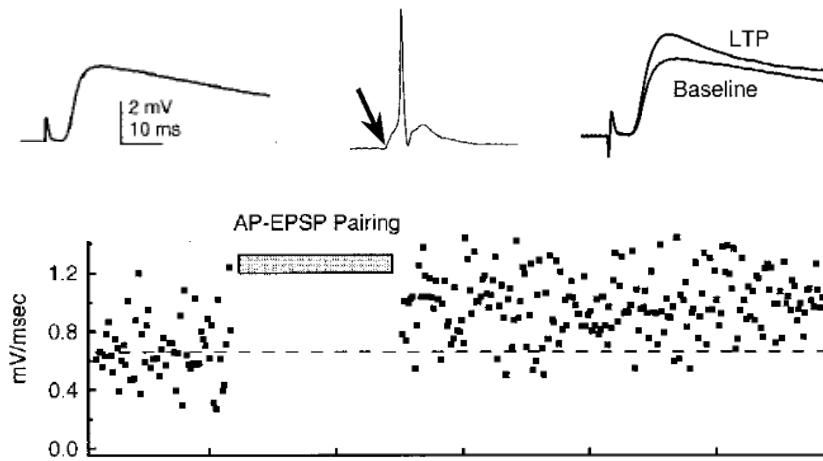




# Spike-Timing I

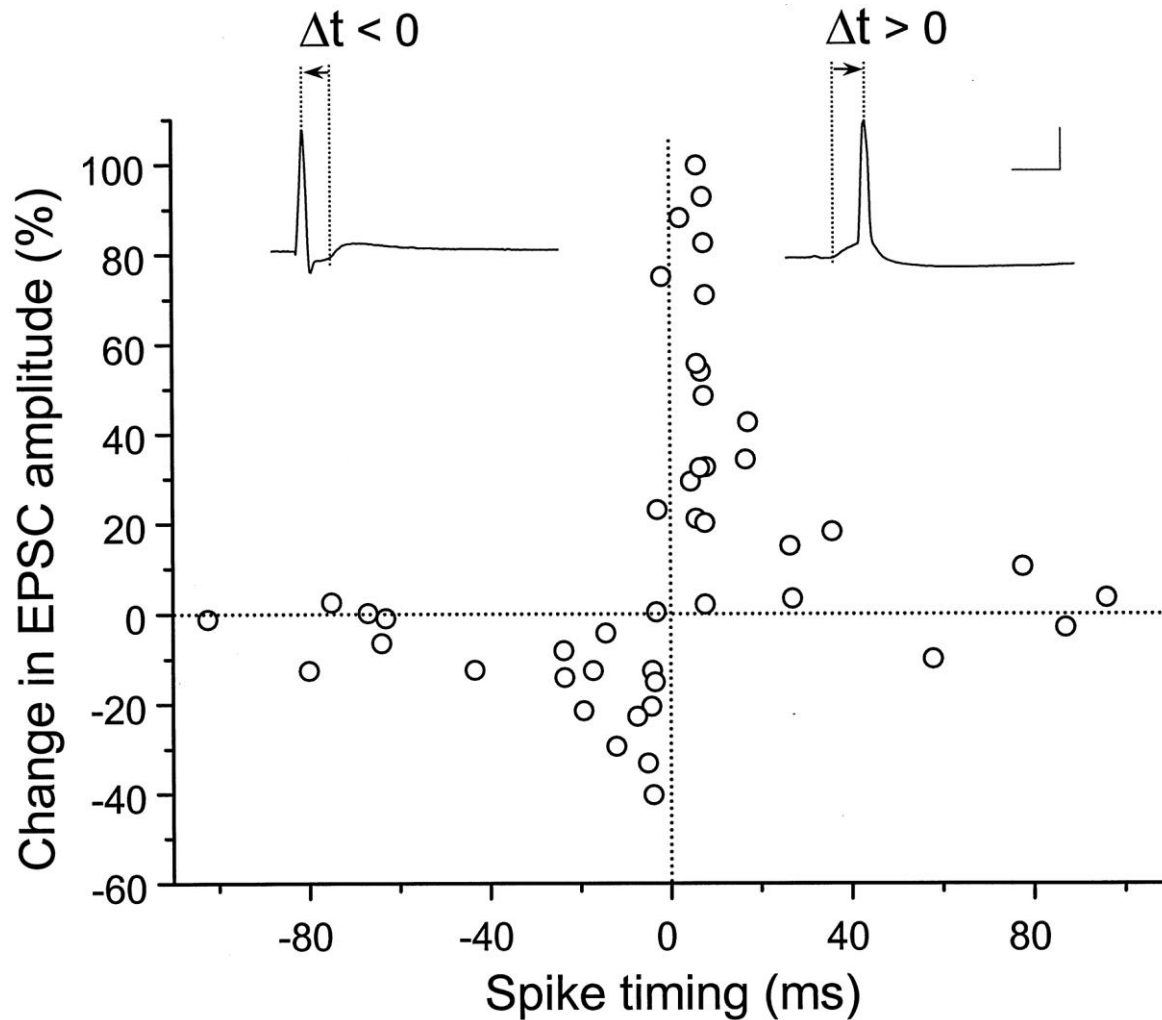


Example of Hebbian and anti-Hebbian plasticity in cortex



Time (10 min)

# Spike Timing II



# The BCM Rule

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

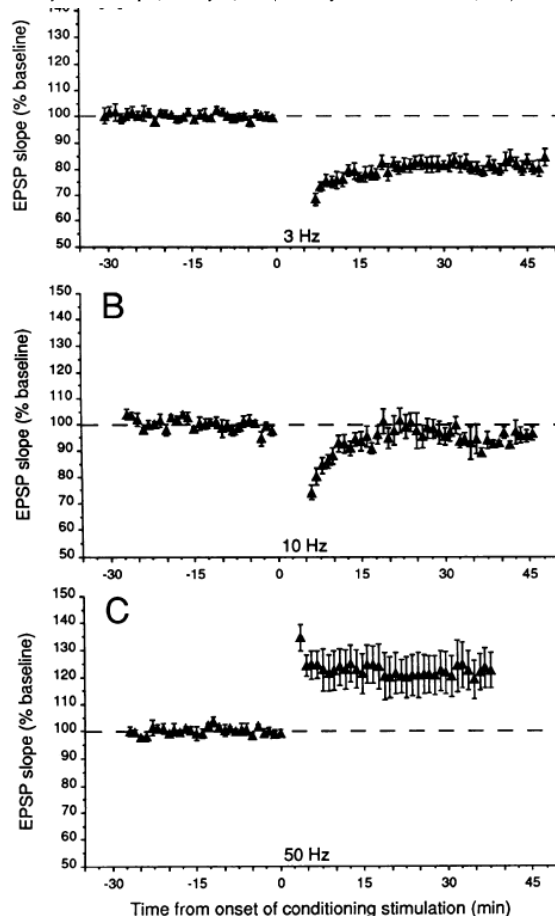
## Homosynaptic long-term depression in area CA1 of hippocampus and effects of *N*-methyl-D-aspartate receptor blockade

(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 depression.
- Strong (coincident) stimulation leads to potentiation.

Elie Bienenstock, Leon Cooper, and Paul Munro