Introduction to Systems Neuroscience

Learning and memory

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Learning and memory

- Memory: storage, coding, and retrieval of information in the nervous system

- Learning: A process by which information, skills and behaviors are acquired or existing information etc. is changed

Forms of memory

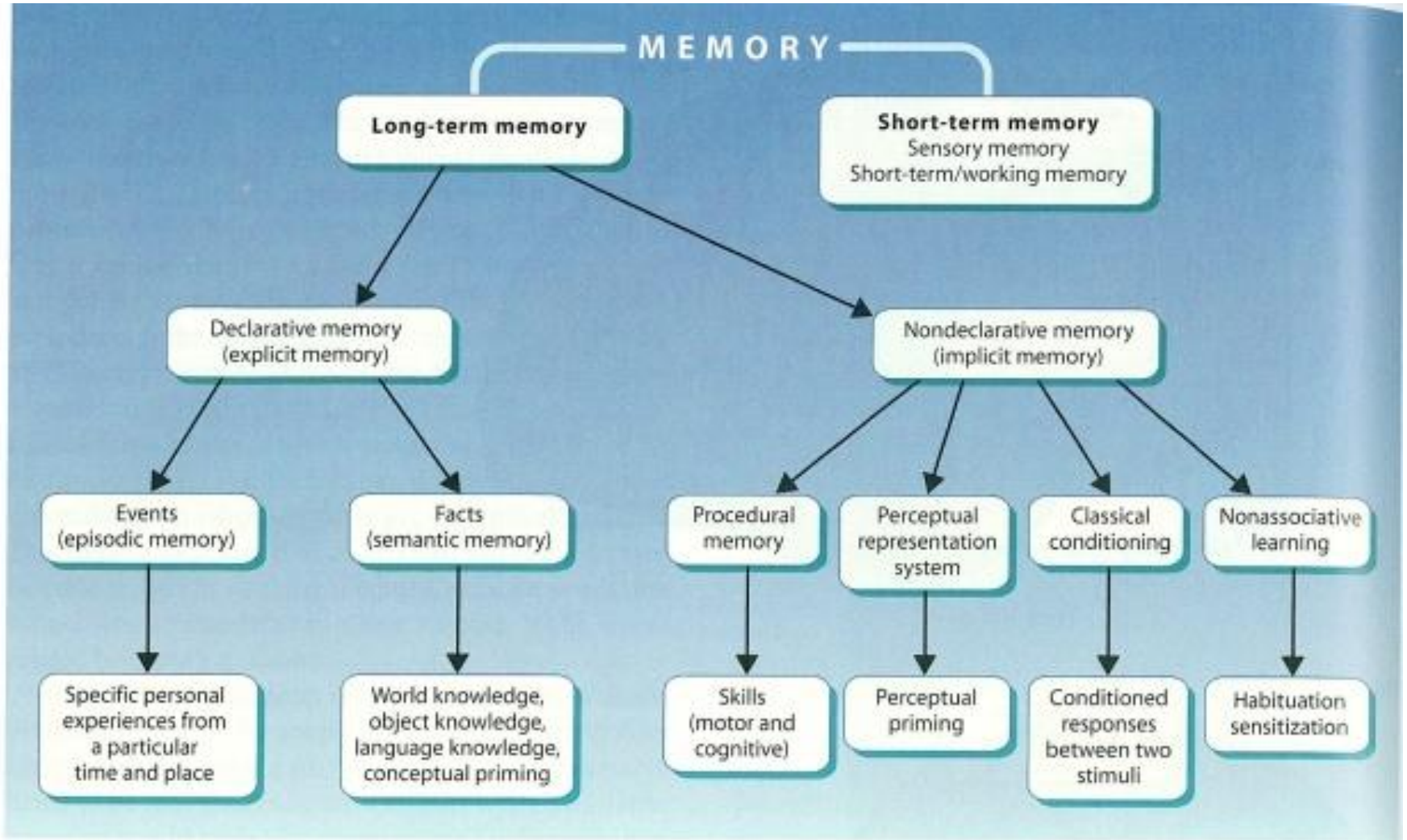
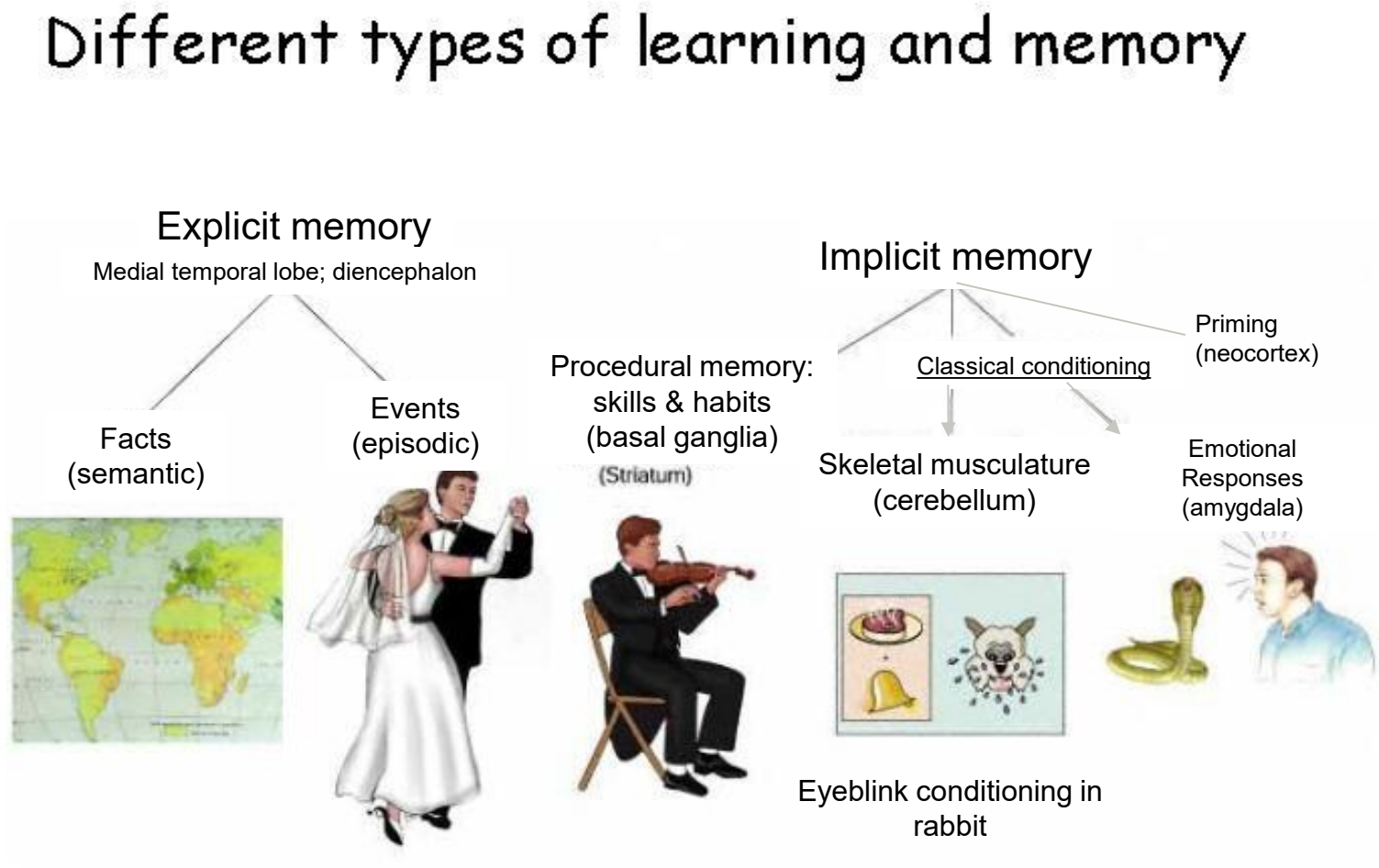


Figure 8.9 The hypothesized structure of human memory diagramming the relationship among different forms of memory.

Different types of learning & memory rely on different brain structures



Multiple memory trace theory

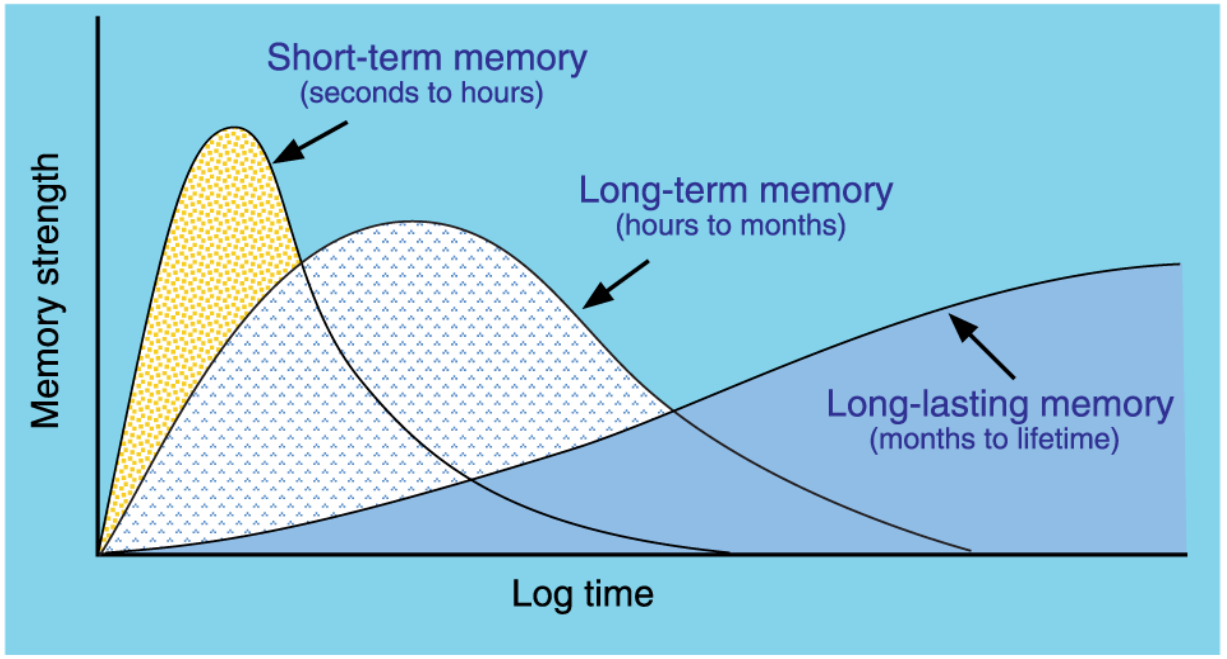


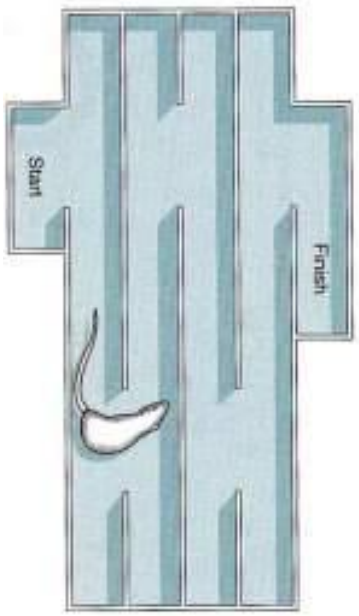
Fig. 1. Memory consolidation phases. Studies of memory and neuroplasticity support Müller and Pilzecker's hypothesis proposing that the consolidation of new memory into long-term memory is time dependent (*1*), but strongly suggest that short-term and different stages of long-term memory are not sequentially linked, as proposed by the dual-trace hypothesis (*9*). Evidence that drugs can selectively block either short-term (seconds to hours) or long-term memory (hours to months) suggests that time-dependent stages of memory are based on independent processes acting in parallel. Later stages of consolidation resulting in memory lasting a lifetime likely involve interaction of brain systems in reorganizing and stabilizing distributed connections.

McGaugh, 2000

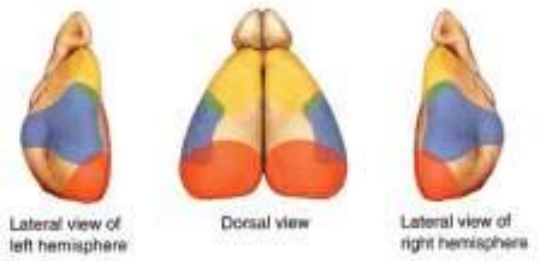
Neuroscience of memory

- Karl Lashley (1950) searched for the *engram*, the physical location of a memory.
- He destroyed progressively larger areas of monkey brain tissue after training them on a task.
- The monkeys retained the memory, suggesting it was distributed to many parts of the brain, a principle known as *equipotentiality*.

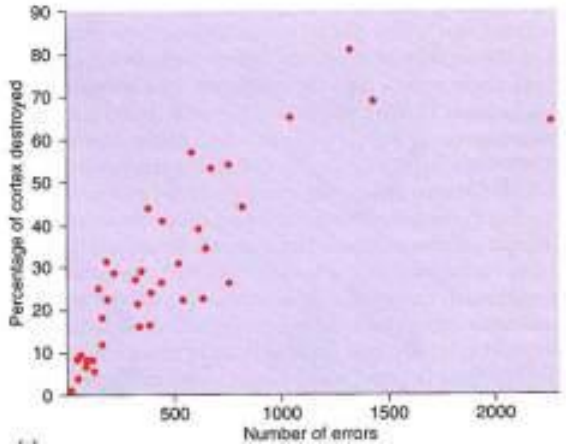
Lashley's Search for the Engram in the 1920s



Rats are trained to run through a maze without entering blind alleys.



After training, cortical lesions are made. Three different lesion locations are shown in red, blue, and yellow



Errors are associated with the size rather than the locus of the lesion.

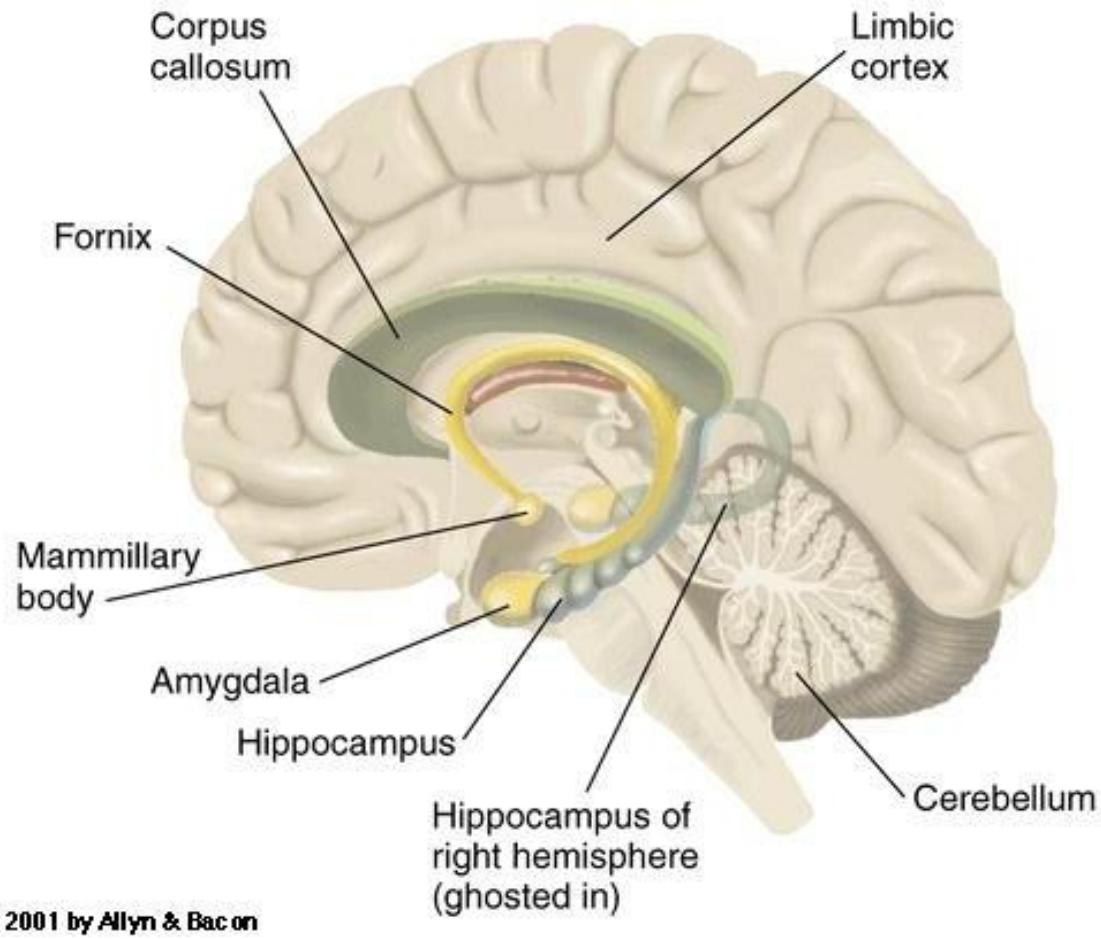
Declarative memory and learning - hippocampus

- Patient H.M.
- Bilateral resection of the Temporal lobe (notably Hippocampus) at the age of 27 (1953)

- Permanent anterograde amnesia
- No retrograde amnesia
- Non-declarative memory and learning were unaffected, working memory, abstract thinking, IQ, ability to conduct conversations etc. were unchanged

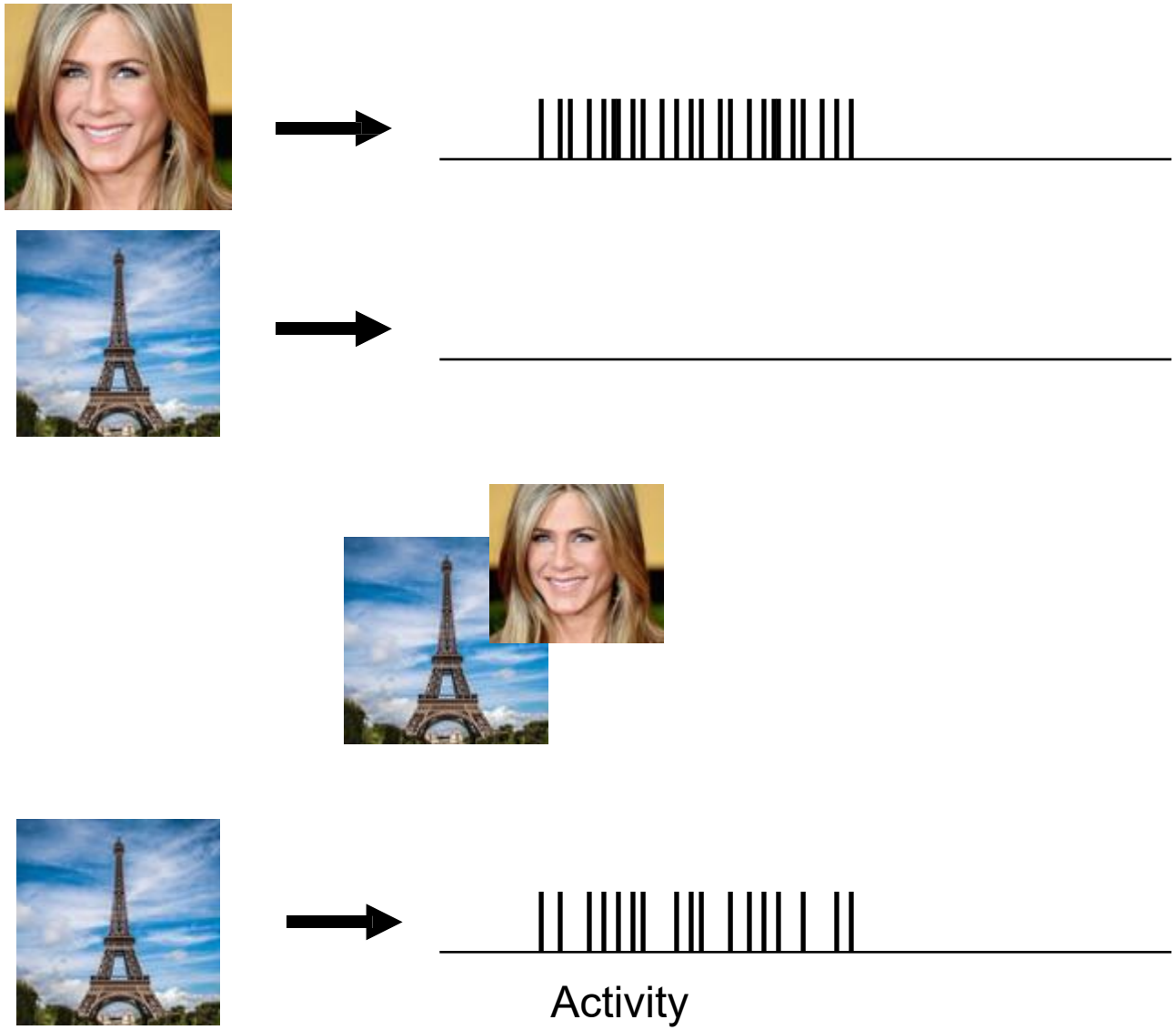
The Hippocampus

- Responsible for consolidation: the transfer of information from short-term to long-term memory.
- Damage to the hippocampus can cause anterograde amnesia, see H.M.
- ≠ retrograde amnesia



Hippocampus: Concept cells

Hippocampus: concept cells

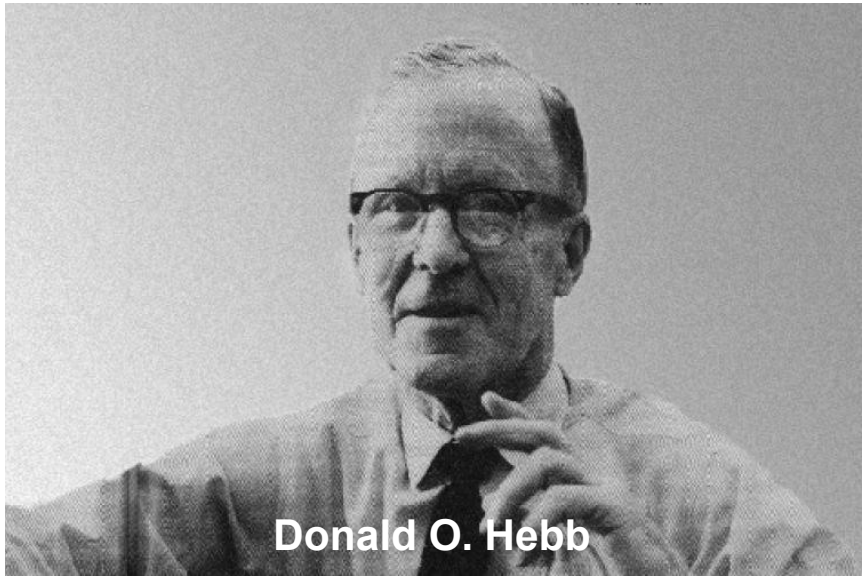


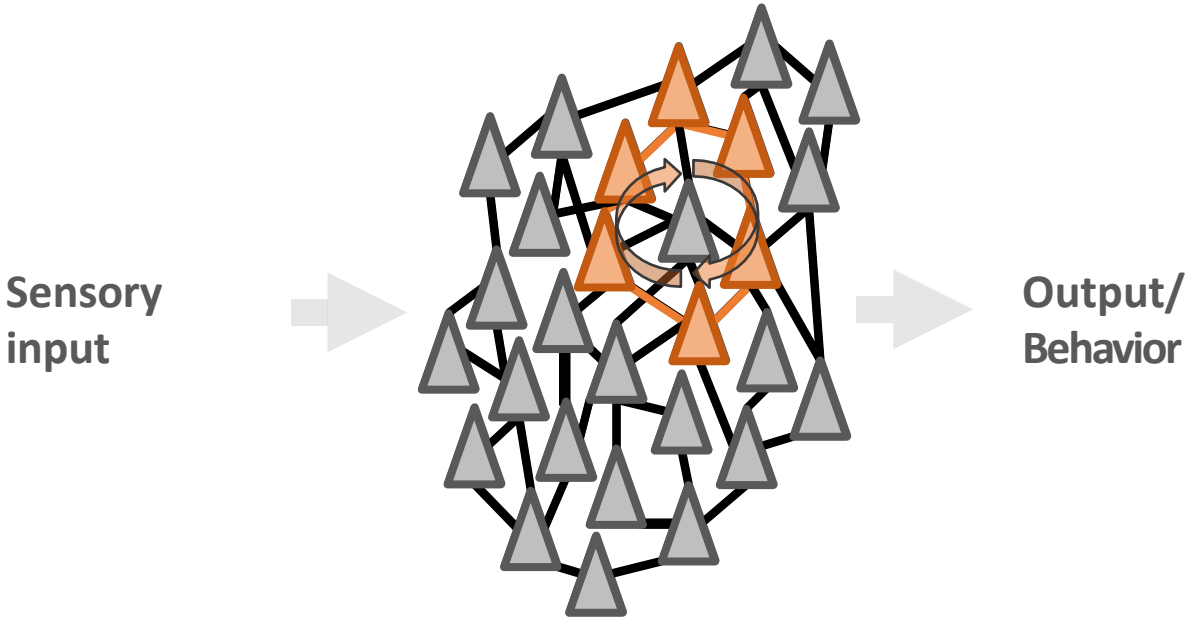
Quiroga et al., 2008

Neuronal plasticity

- Synaptic plasticity: activity-dependent change of synapse strengths
- Cellular plasticity: e.g. Formation of new synapses and loss of unused synapses
- Cortical plasticity: alteration of neuronal representations within brain areas

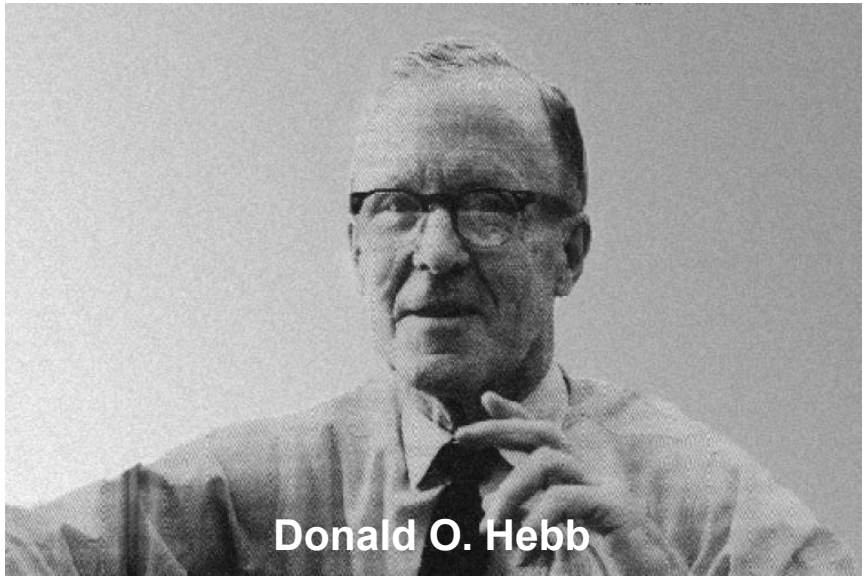
Hebb's ‚Cell Assemblies‘

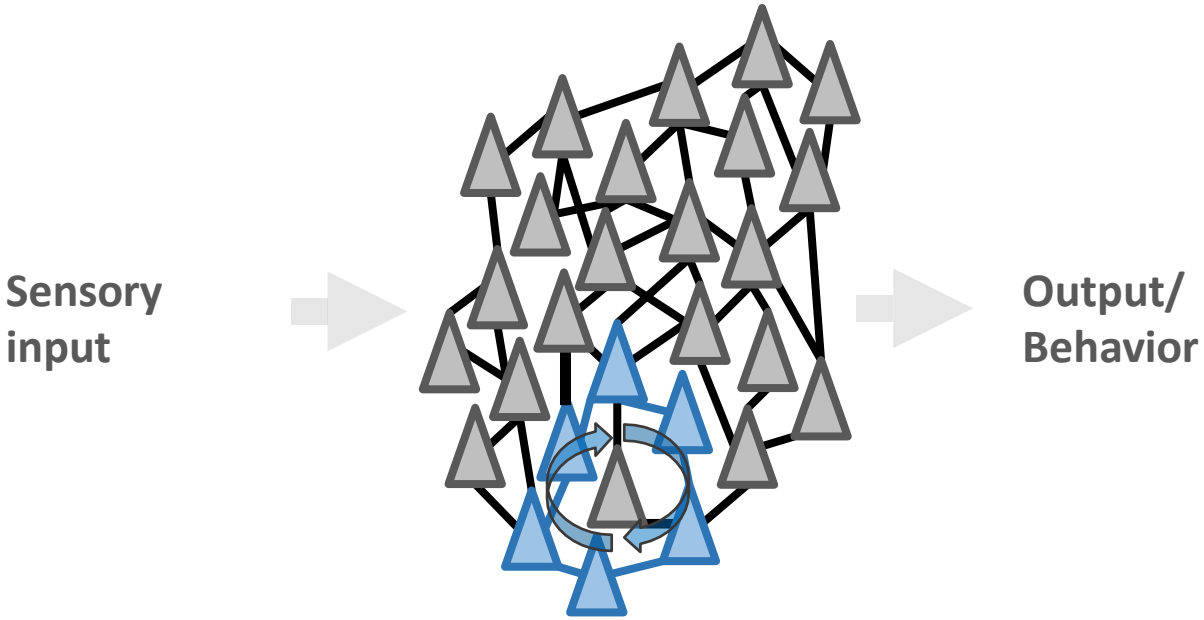




- Decentralized 'cell assemblies’ encode information (engrams)
- Short-term memory is oscillating activity in large circuits
- When the activity lasts for a long time, structural changes occur at synapses, which transfer memory to the long-term memory via the same circuits.

Hebb's ‚Cell Assemblies‘





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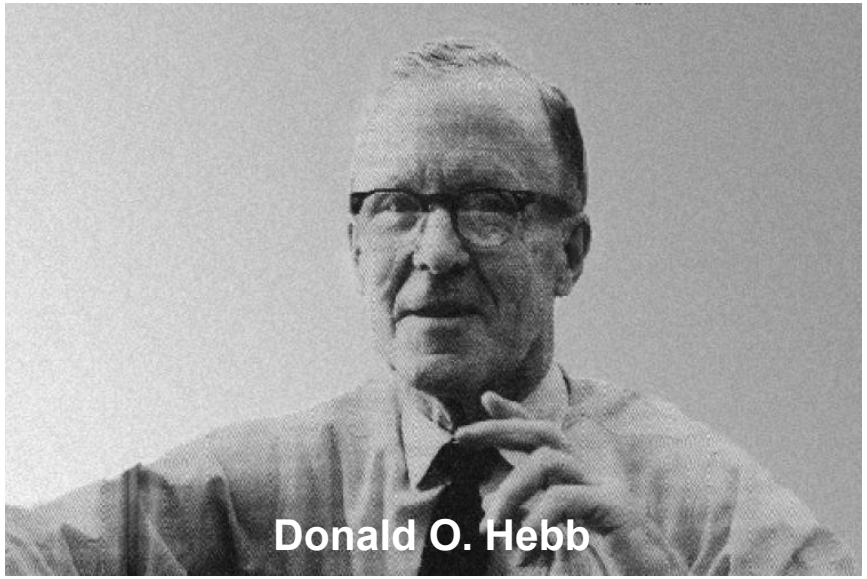

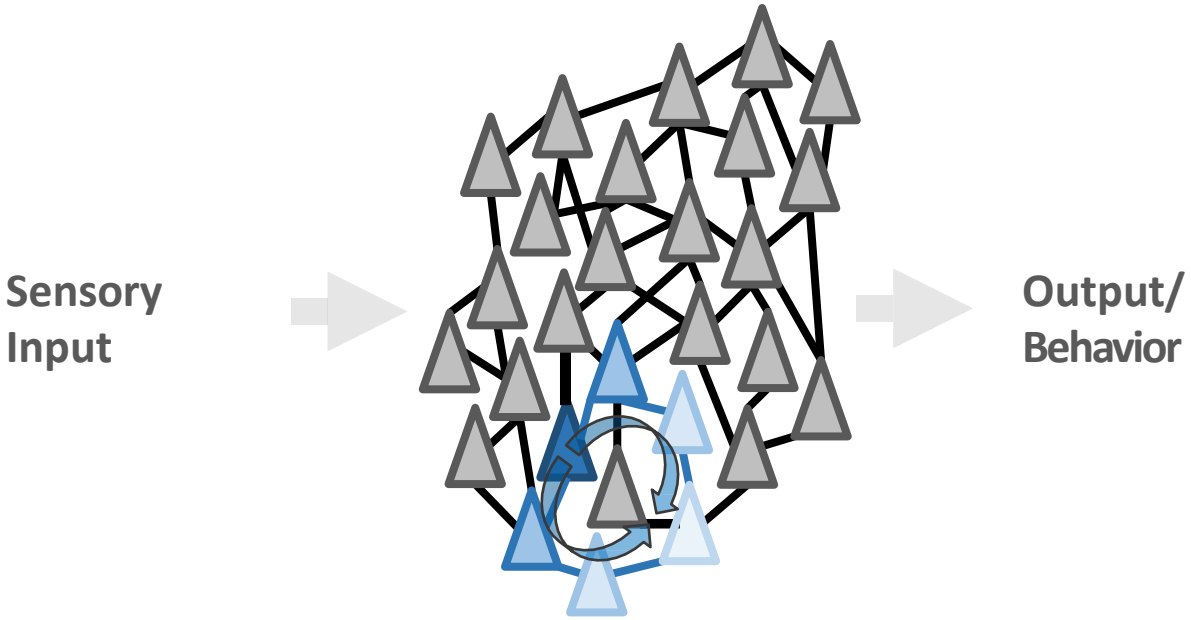

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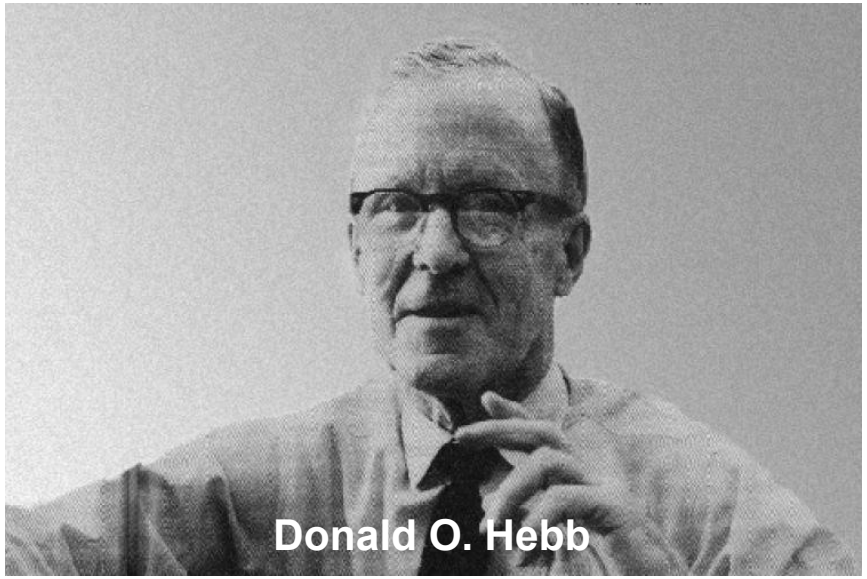
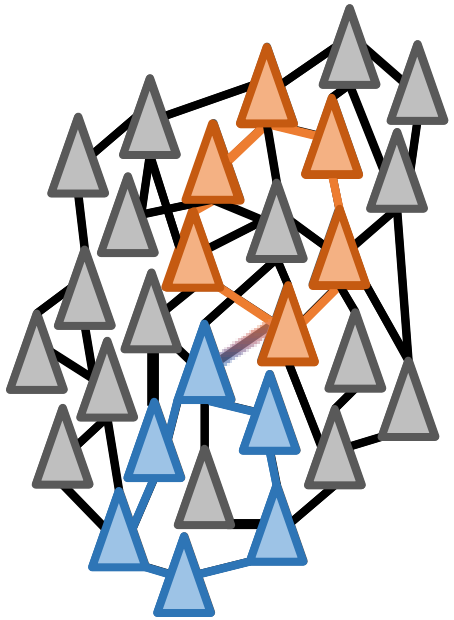
Hebb's theory of consolidation

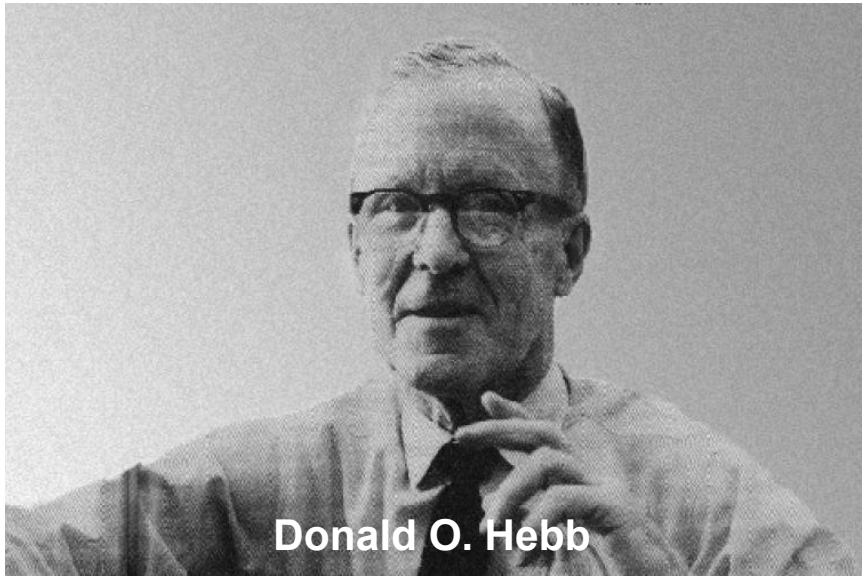


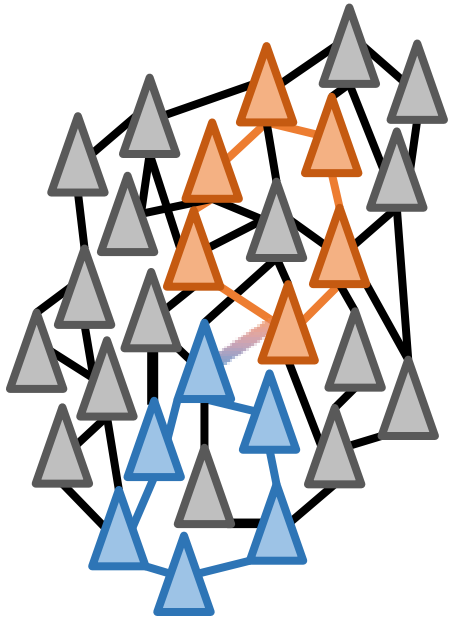


"When an axon of cell A excites cell B and repeatedly and persistently contributes to the generation of action potentials in cell B, it results in growth processes or metabolic changes in one or both cells, which cause the efficiency of cell A in terms of generating an action potential in B. “

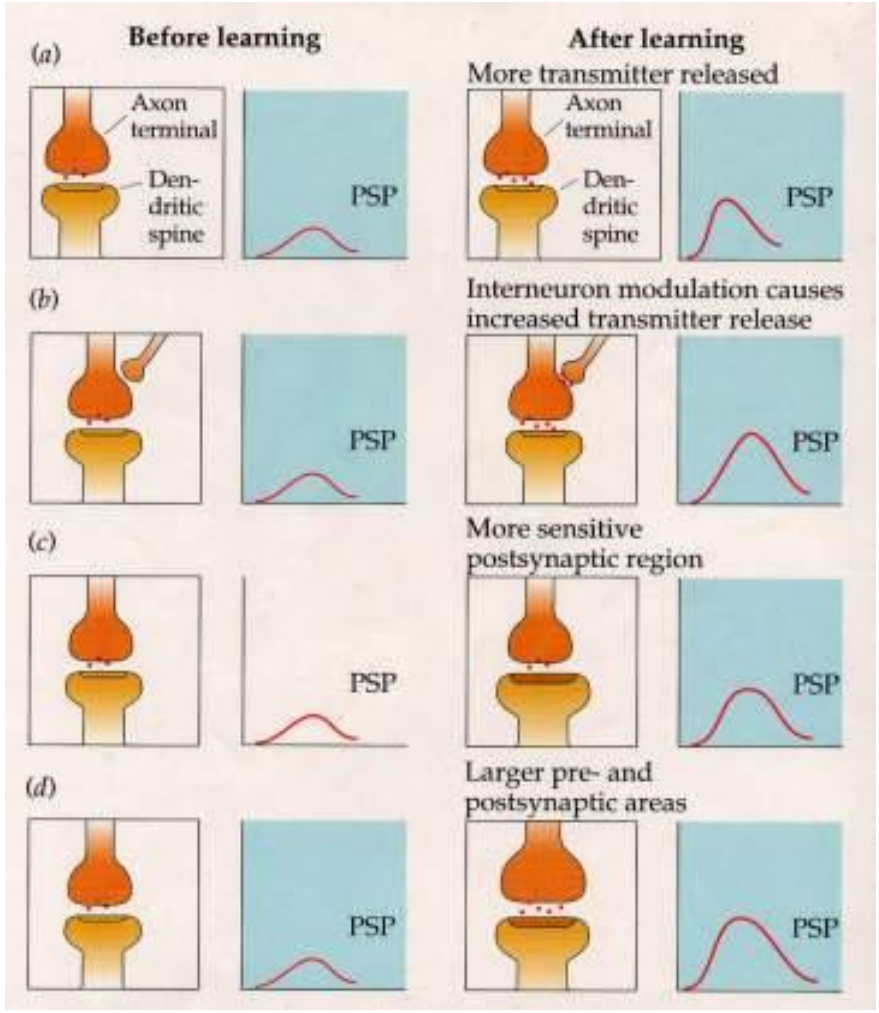
The Organization of Behavior, 1949

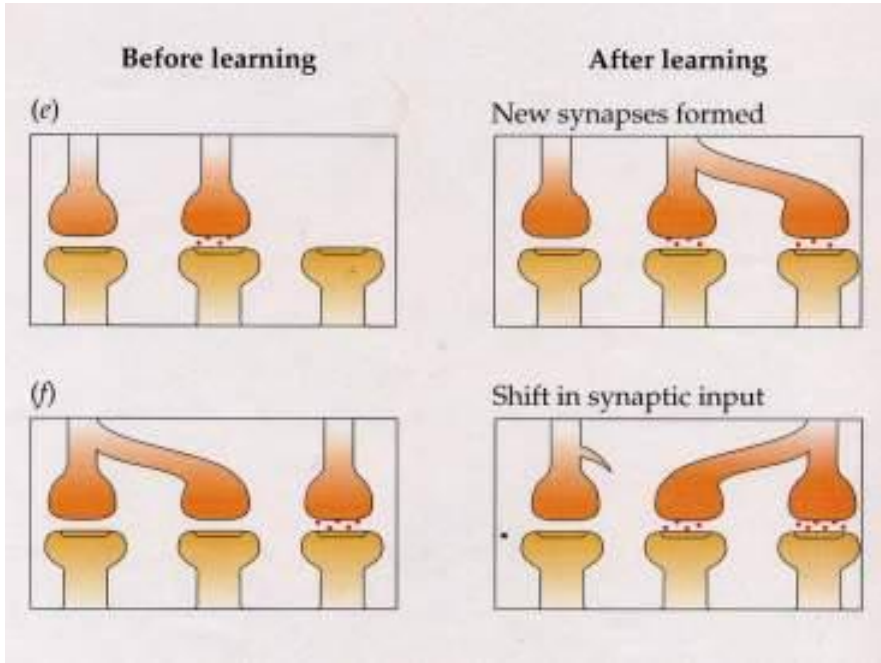
Hebb‘s theory of consolidation



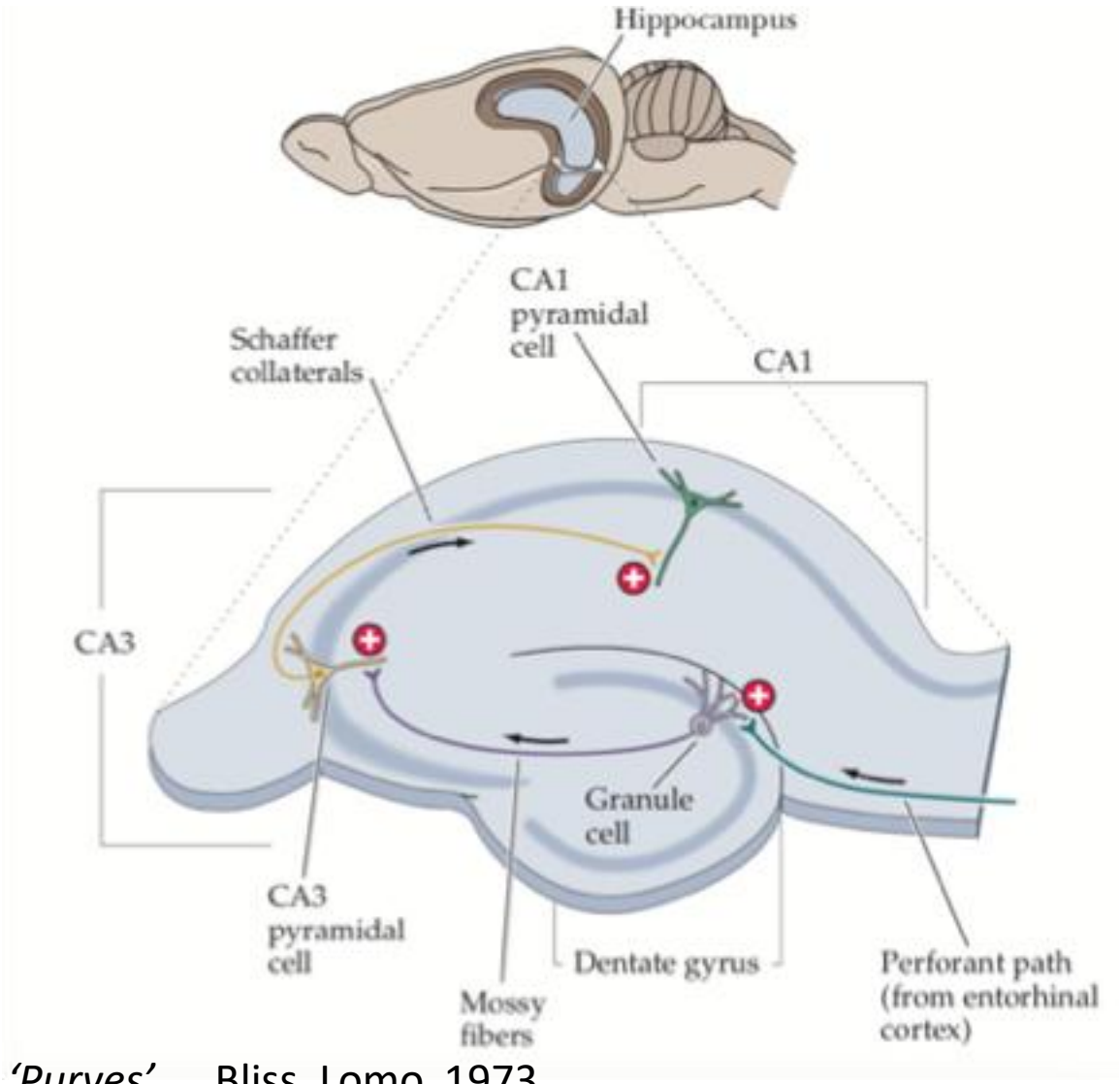


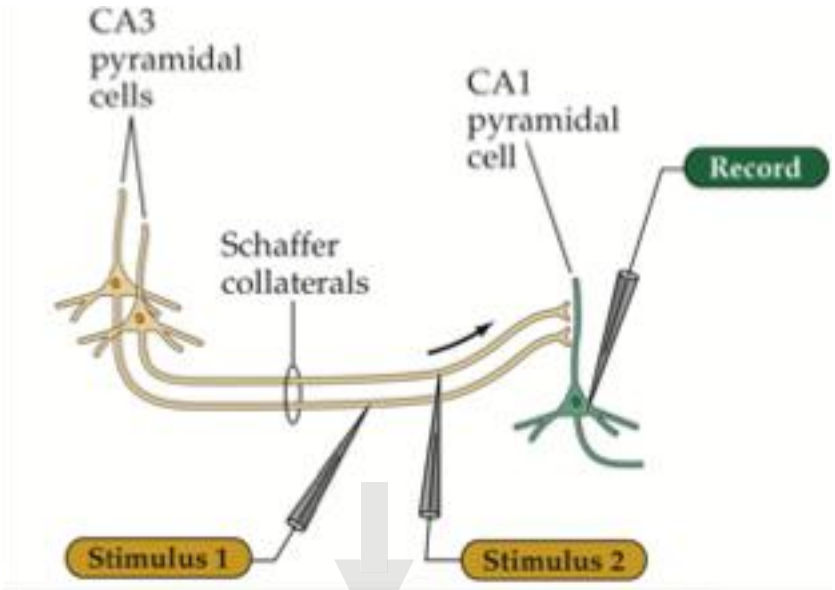
„What fires together, wires together.“


Before learning
After learning
(a)
Axon terminal
Den-dritic spine
PSP
More transmitter released
(b)
Interneuron modulation causes increased transmitter release
(c)
More sensitive postsynaptic region
(d)
Larger pre- and postsynaptic areas

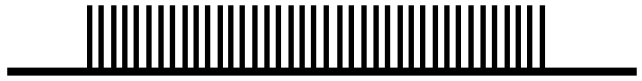

Before learning
After learning
(e)
New synapses formed
(f)
Shift in synaptic input

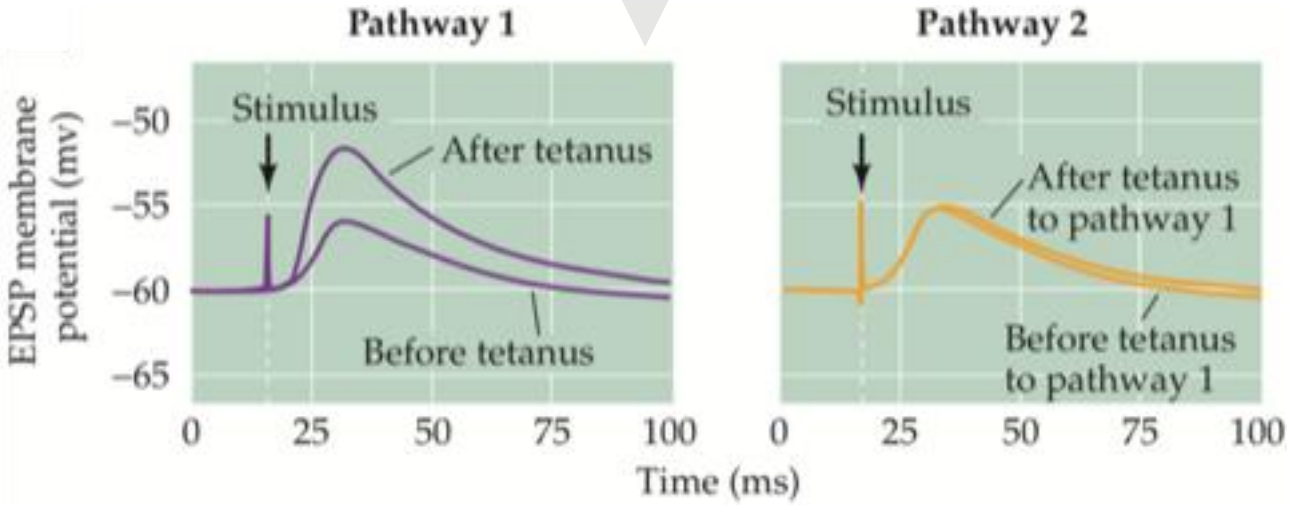
Long Time Potentiation(LTP)





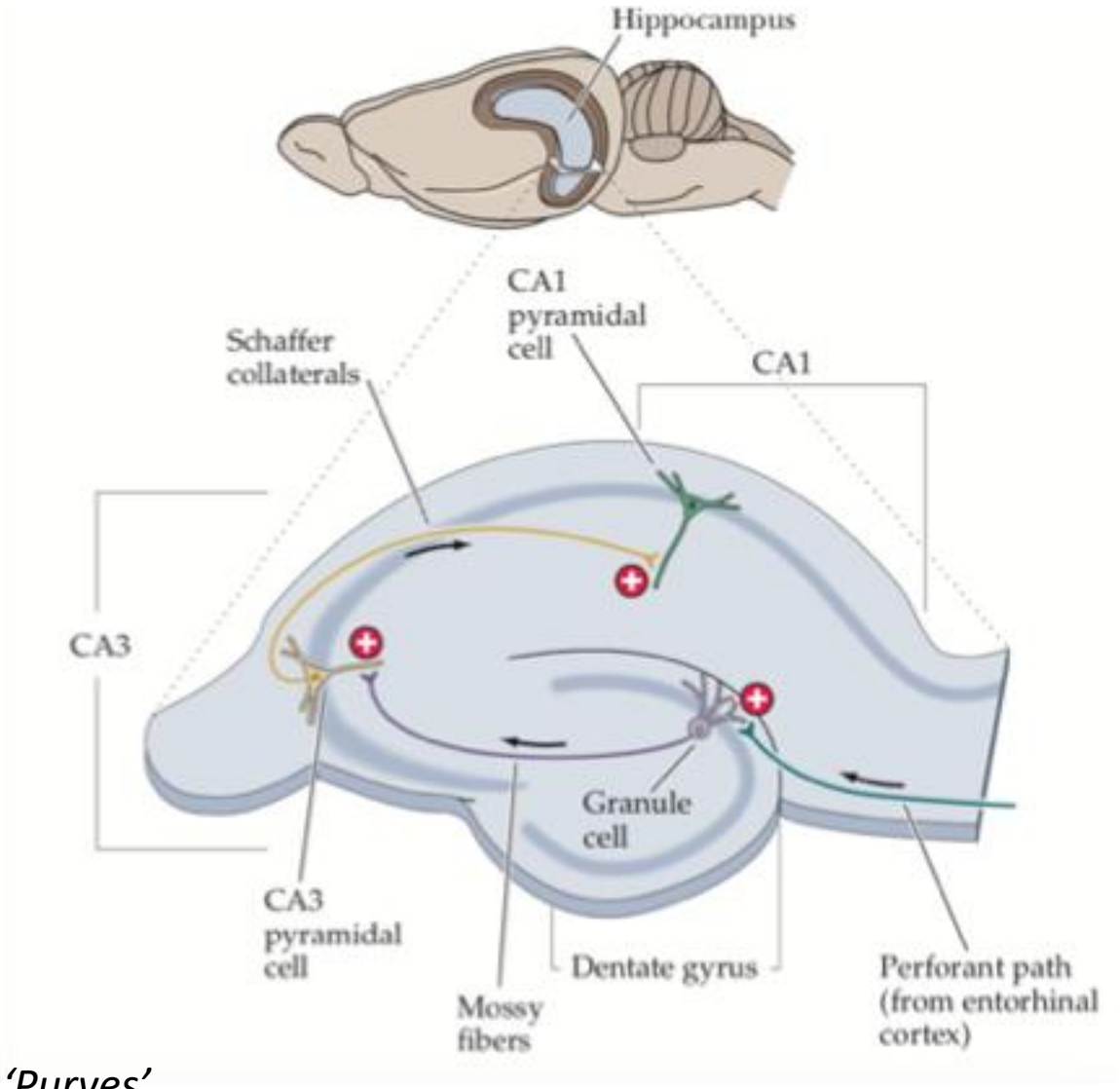
'Tetanus' of action potentials



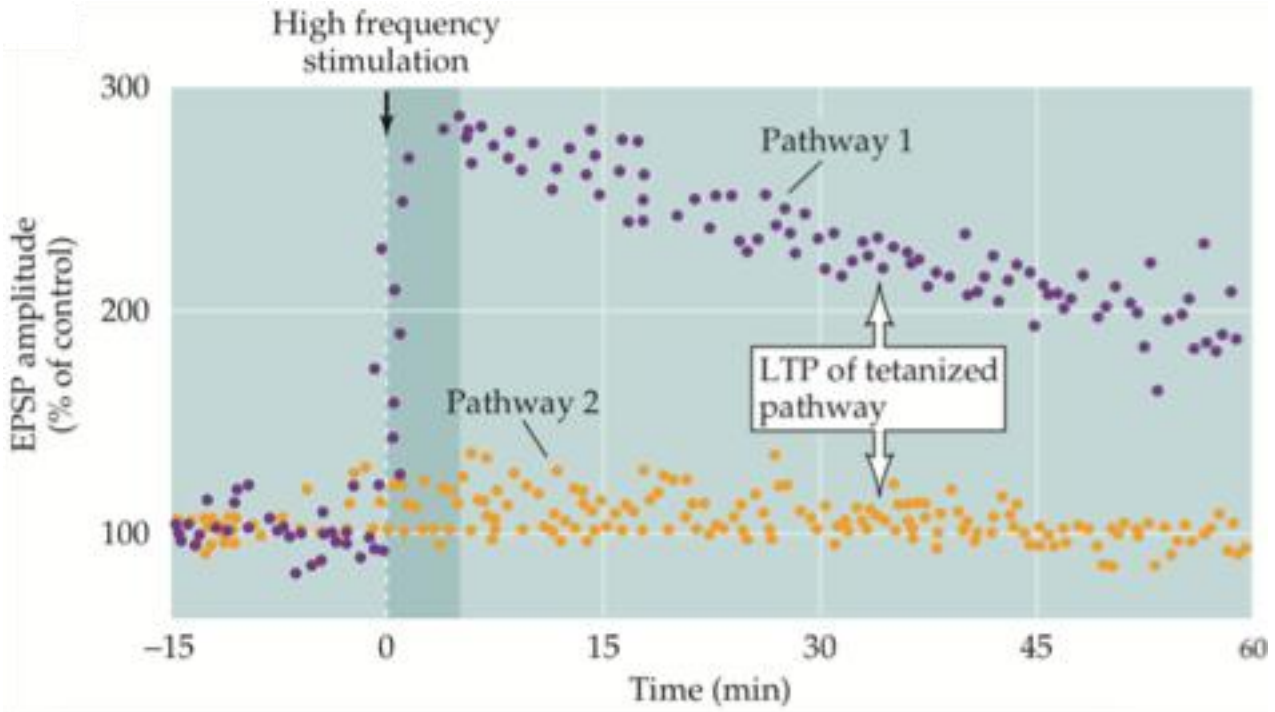


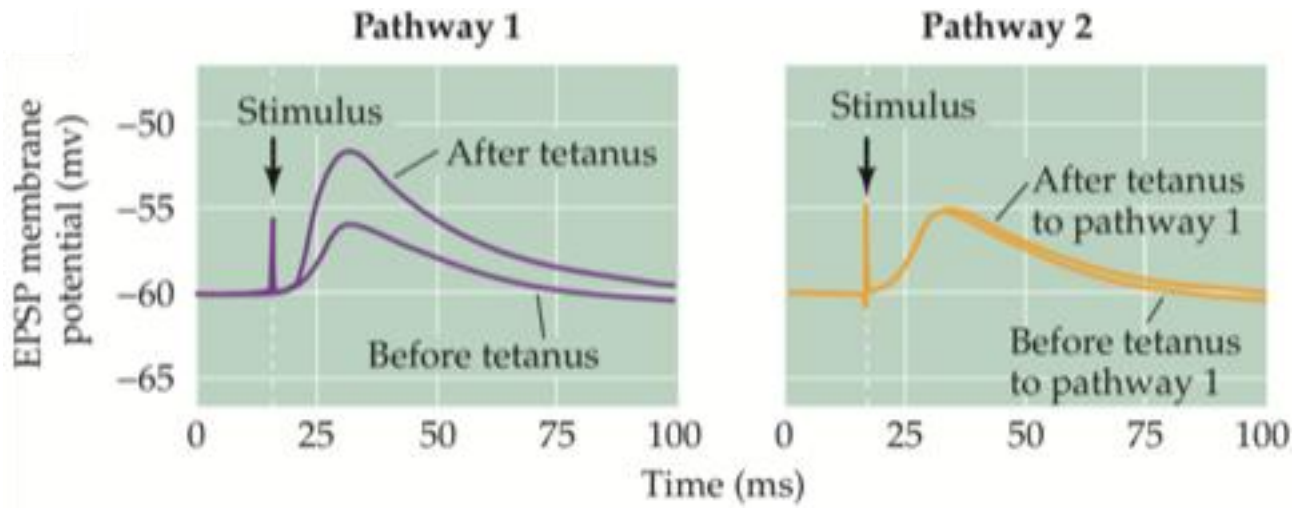
'Purves' Bliss, Lomo, 1973

Long Time Potentiation(LTP)



'Purves'





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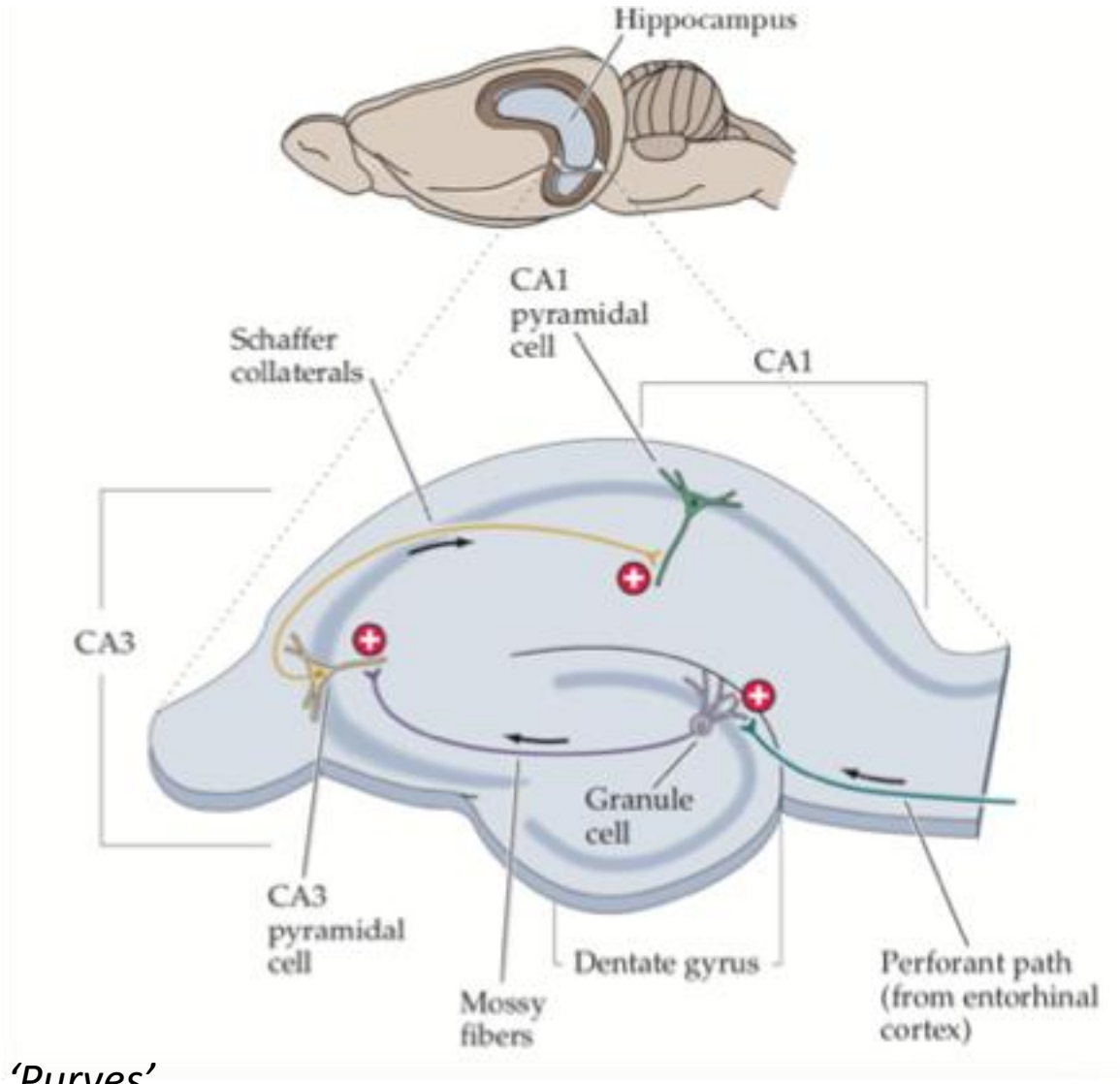
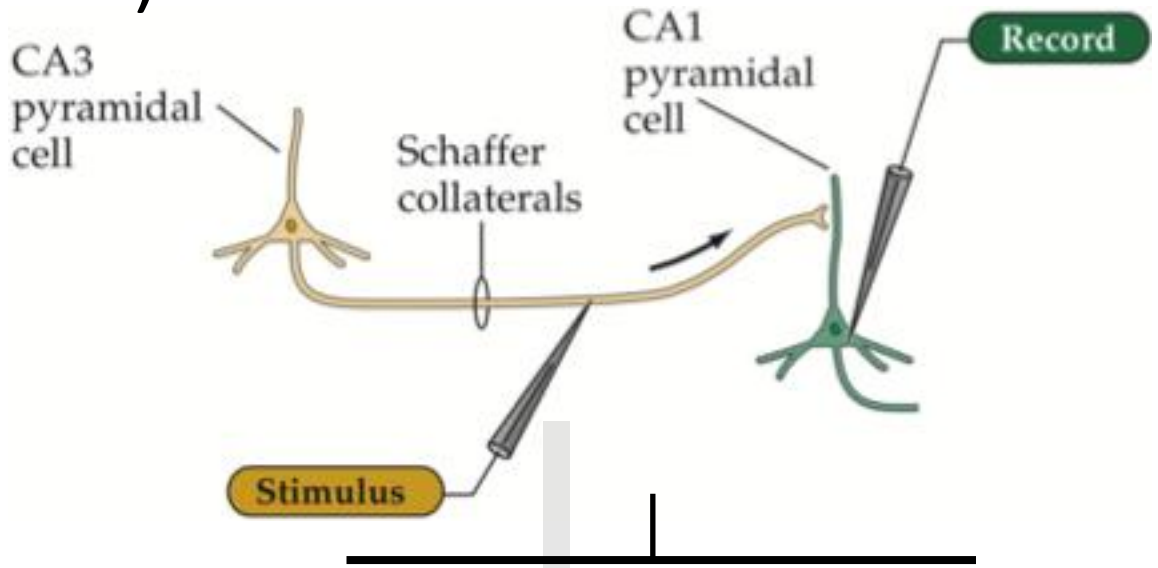
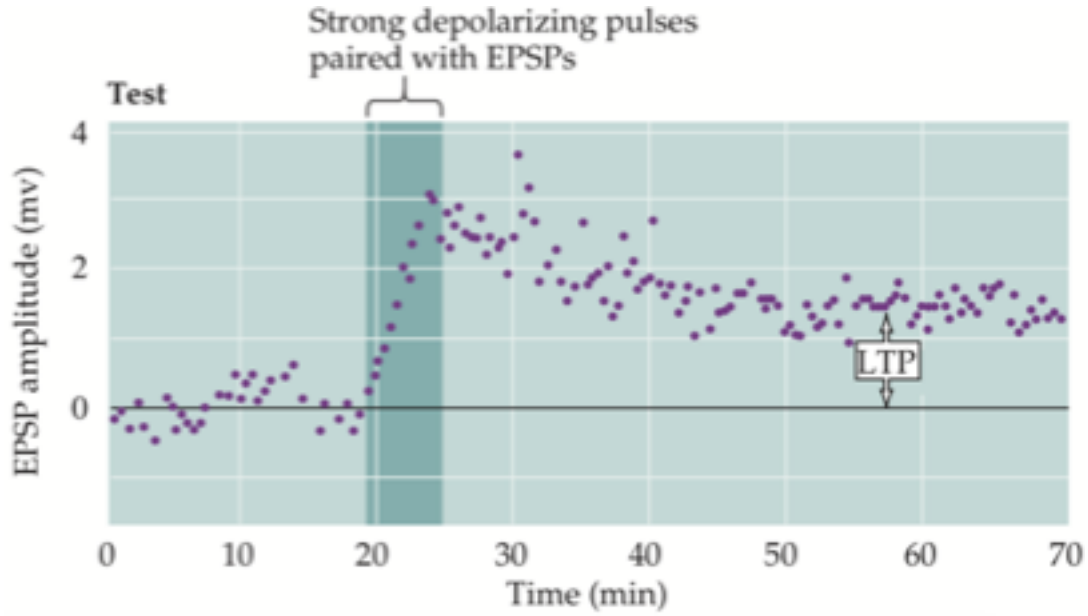
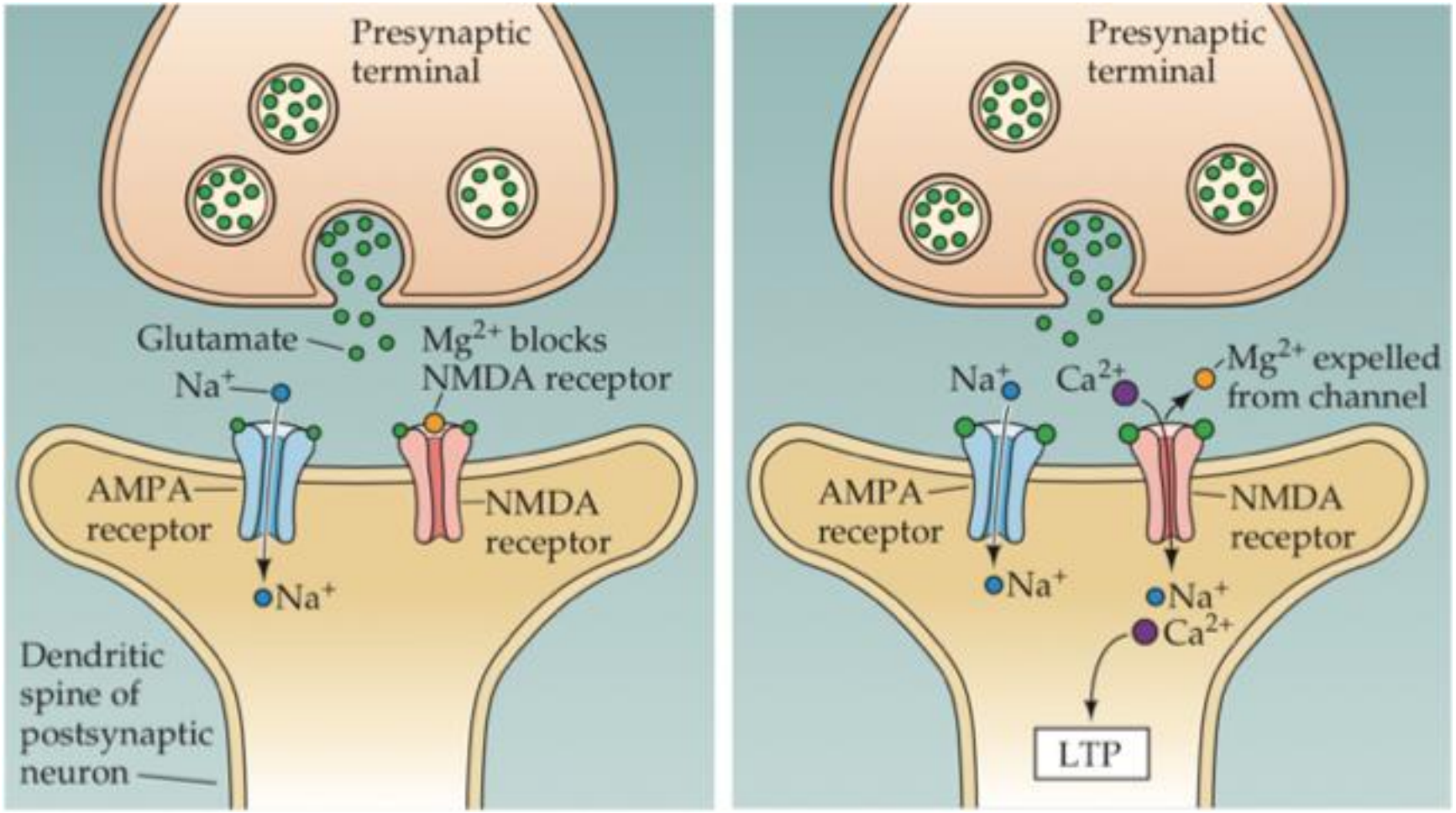






'Purves'

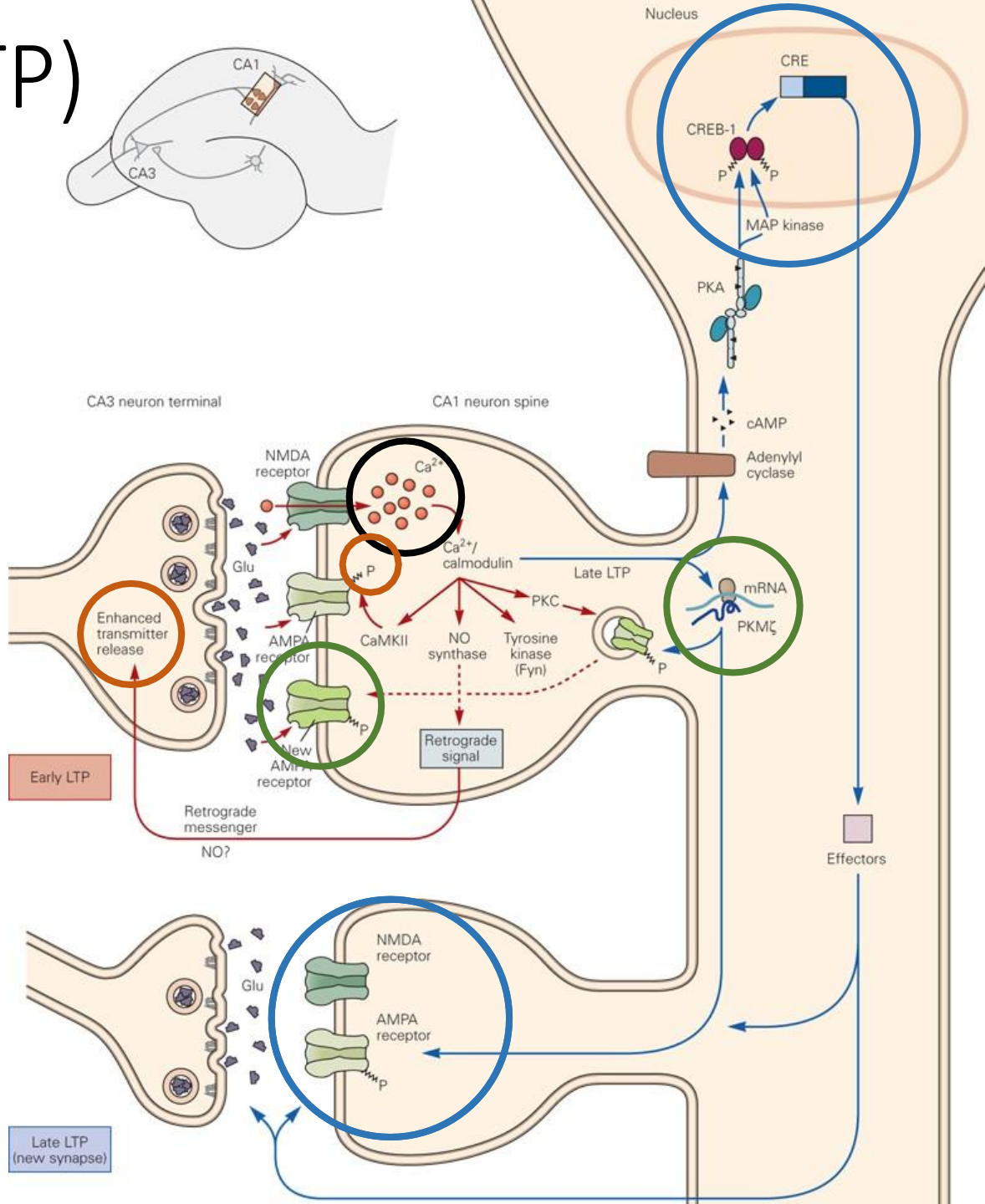
NMDA Receptors are coincidence detectors



'Purves'

Long Time Potentiation(LTP)

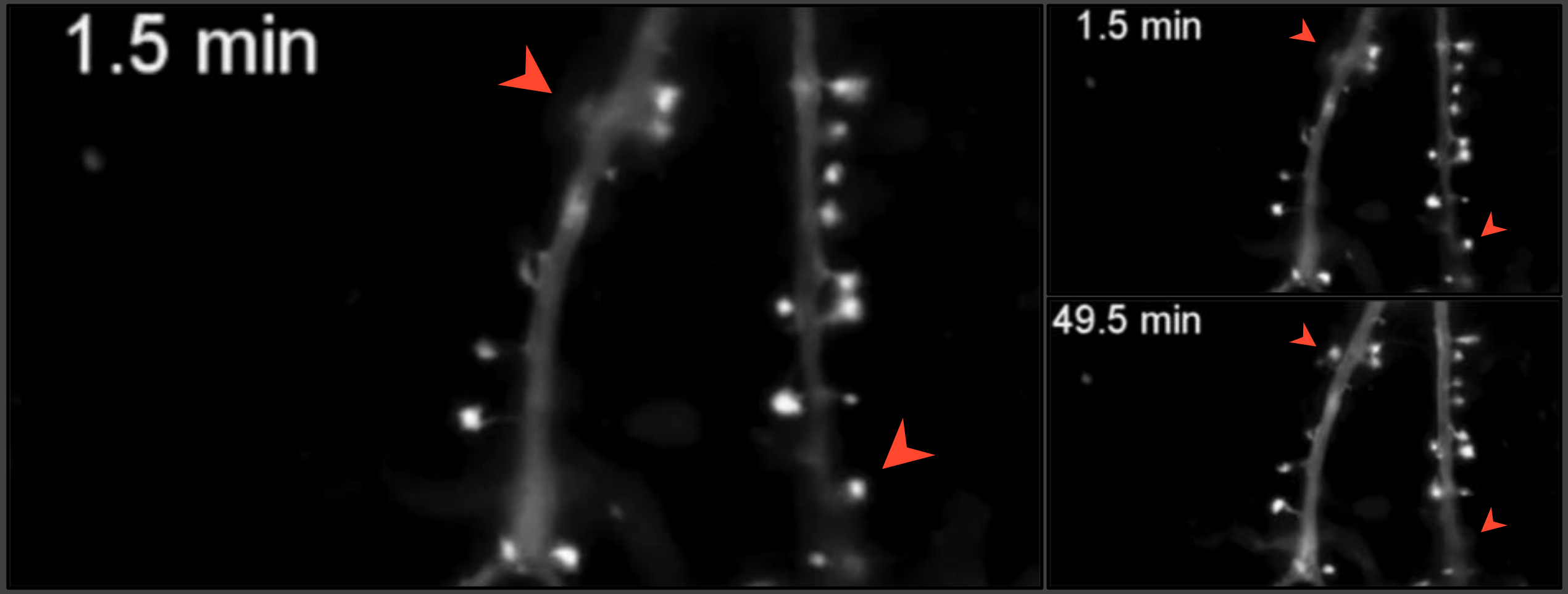
- NMDA-R -> Ca2 + as a second messenger
- Phosphorylation of AMPA-R
- Signal to presynaptic cell
- Translation of local mRNA
- Formation of new AMPA-R
- complex signaling pathways with nucleus
- Transcription of DANN
- Formation of new AMPA-R
- Formation of new synapses



LTP Phases	
Early	(sec – min)
Medium	(min – h)
Late	(h – d)

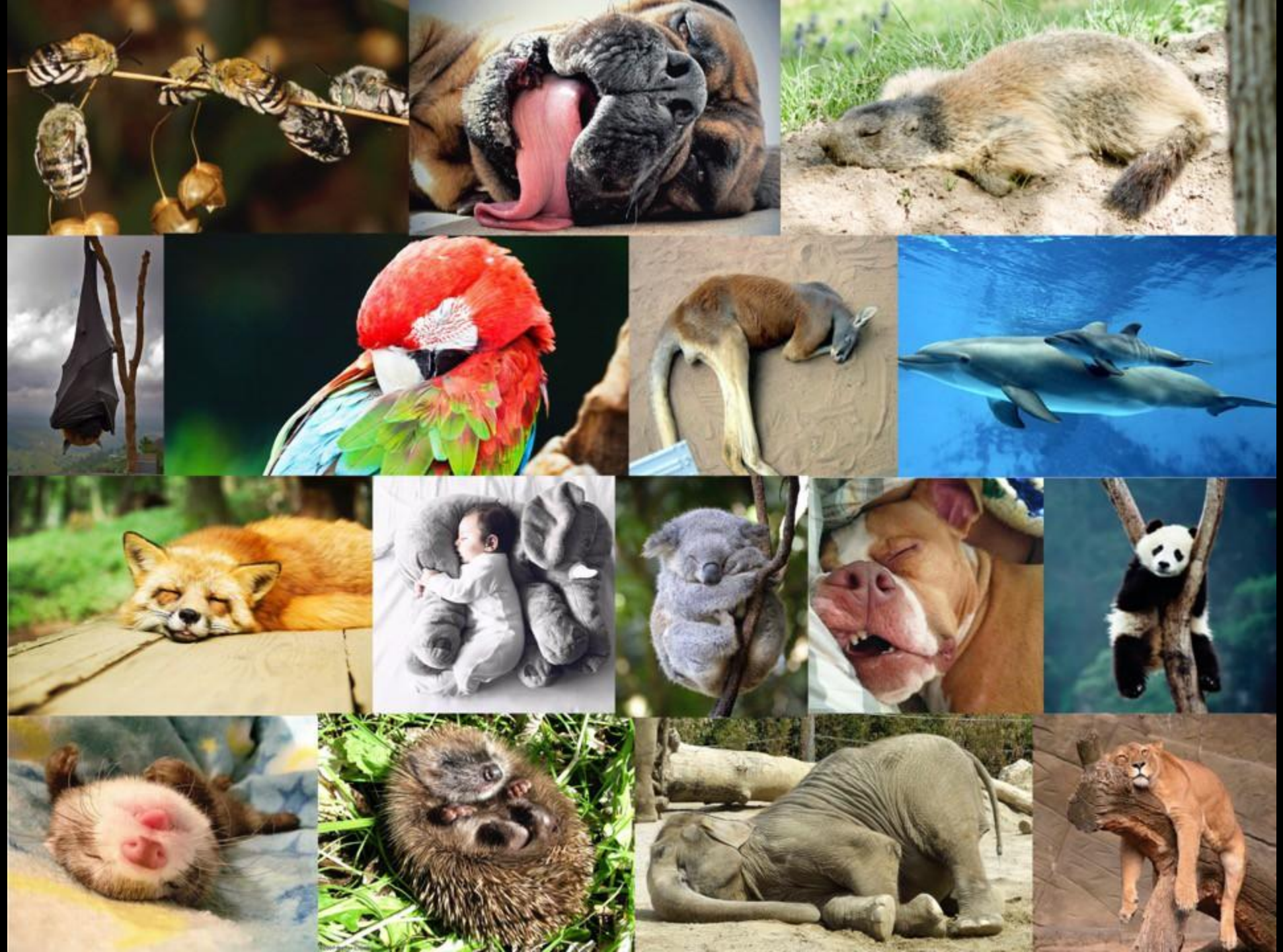
'Kandel'

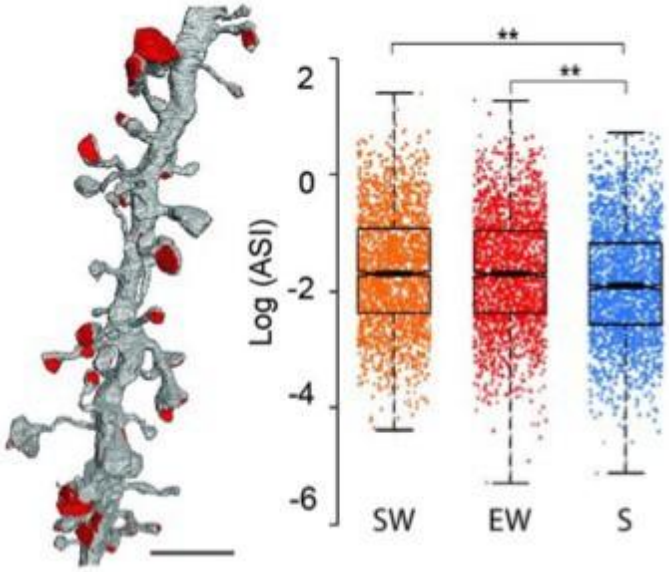
Formation and loss of synaptic spines

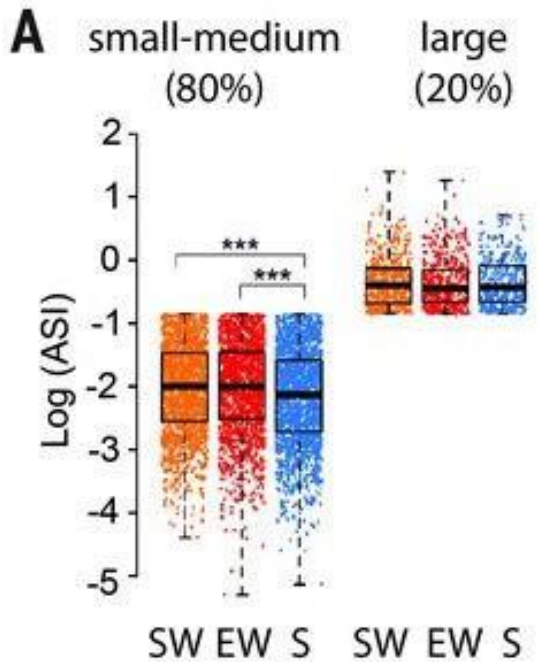


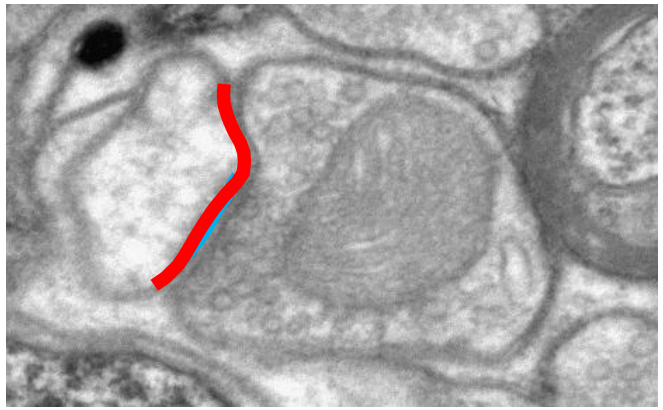
Michael J Schell, YouTube

Hippocampal primary neurons expressing F-Tractin-GFP, played at 180x real time





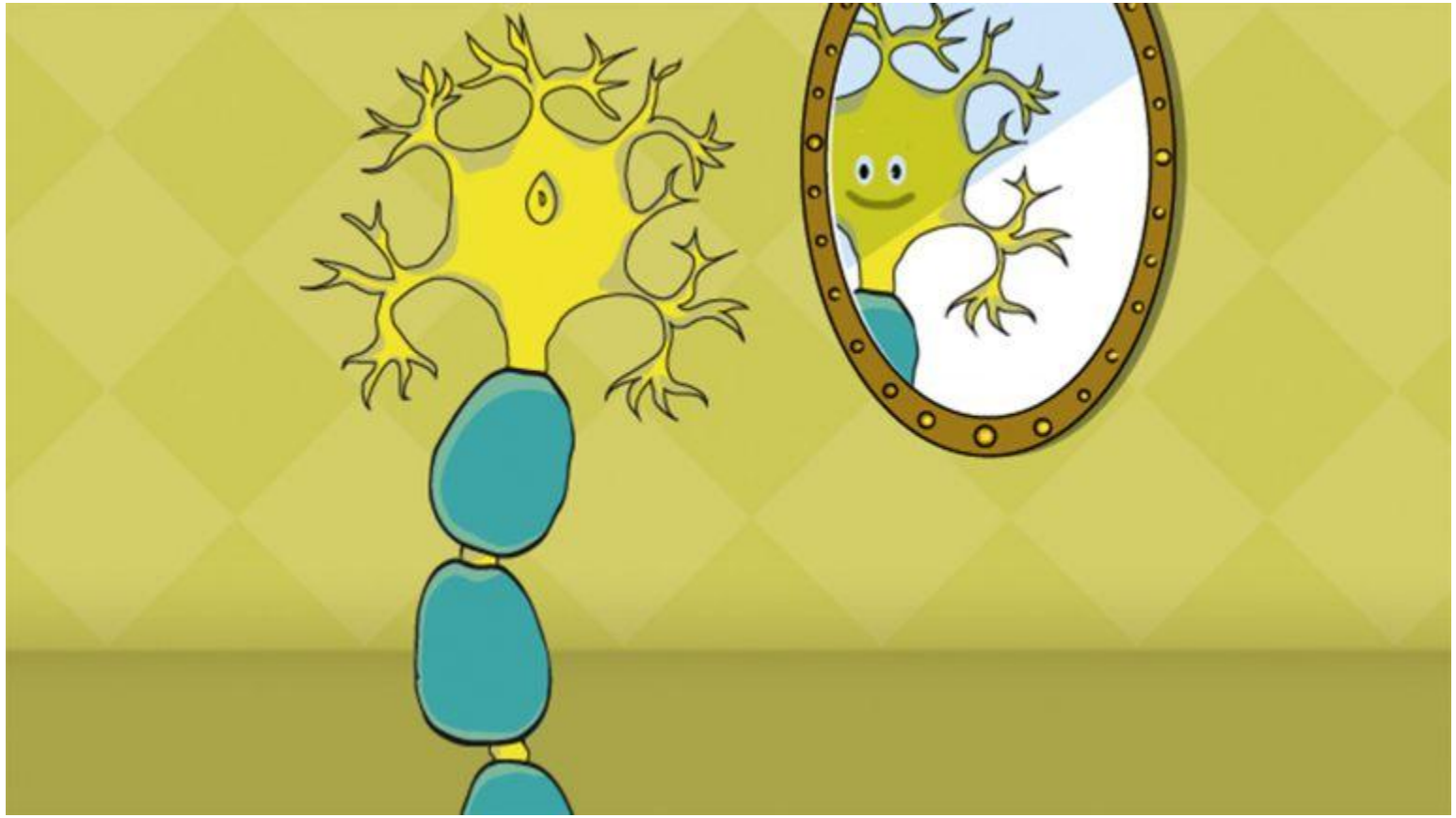




500nm

De Vivo et al., Science, 2017

Mirror neurons



Mirror neurons

The Parieto-Frontal Mirror Network

- Sensorimotor Integration
- Basis of Imitation