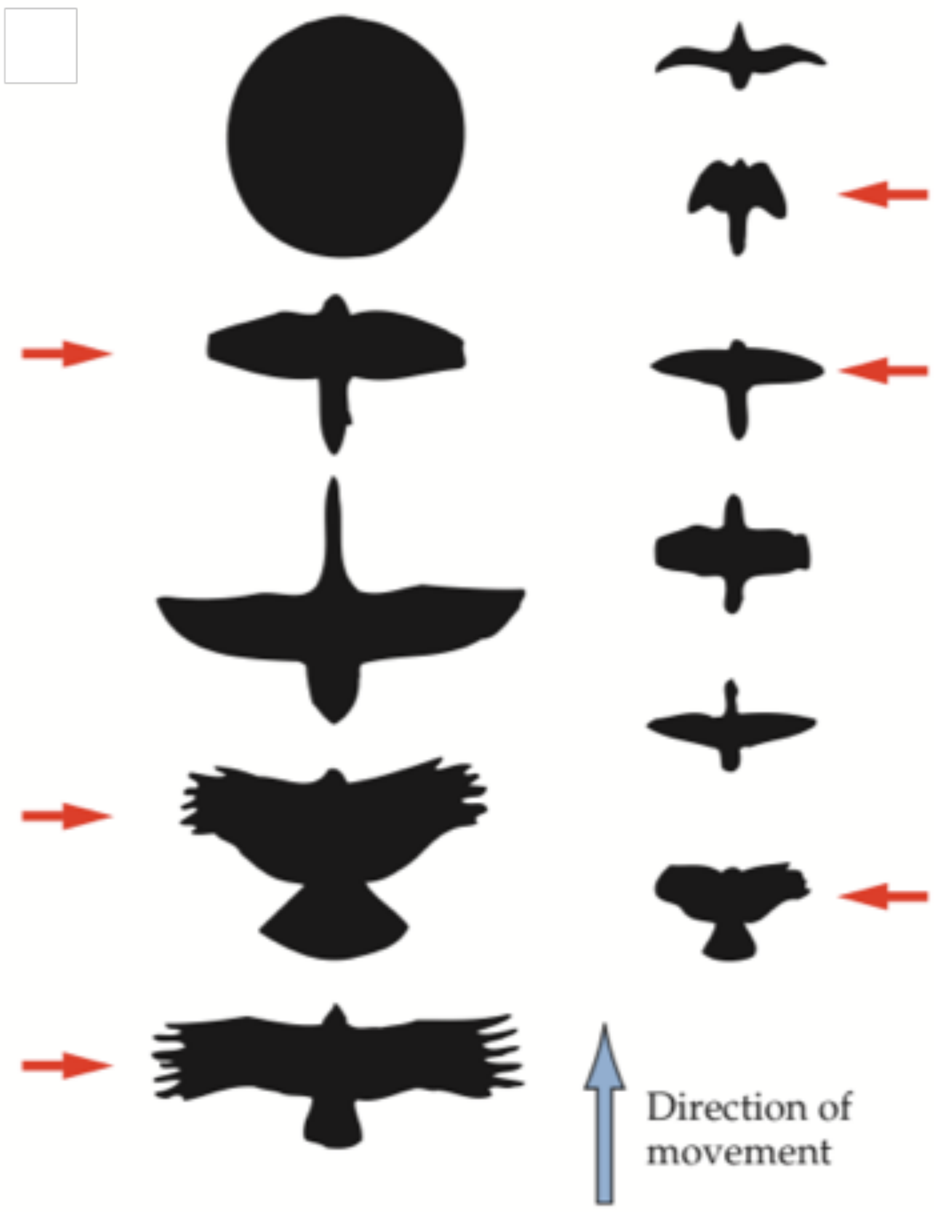
Systems Neuroscience

Sep. 25, 2018

Gregor Schuhknecht
sgregor@ethz.ch

http:www.ini.unizh.ch/~kiper/system_neurosci.html



Niko Tinbergen, Konrad Lorenz

Human memory

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

- Learning: process by which information, skills, behaviours are acquired, or existing information, skills, etc. changed

Schedule

- Human forms of memory
- Declarative (explicit) memory systems
- Non-declarative (implicit) memory systems
- Cellular mechanisms of memory/learning

- Memory and Sleep
- Biological memory versus computer memory
- Artificial neural networks and AI

Qualitative forms of memory

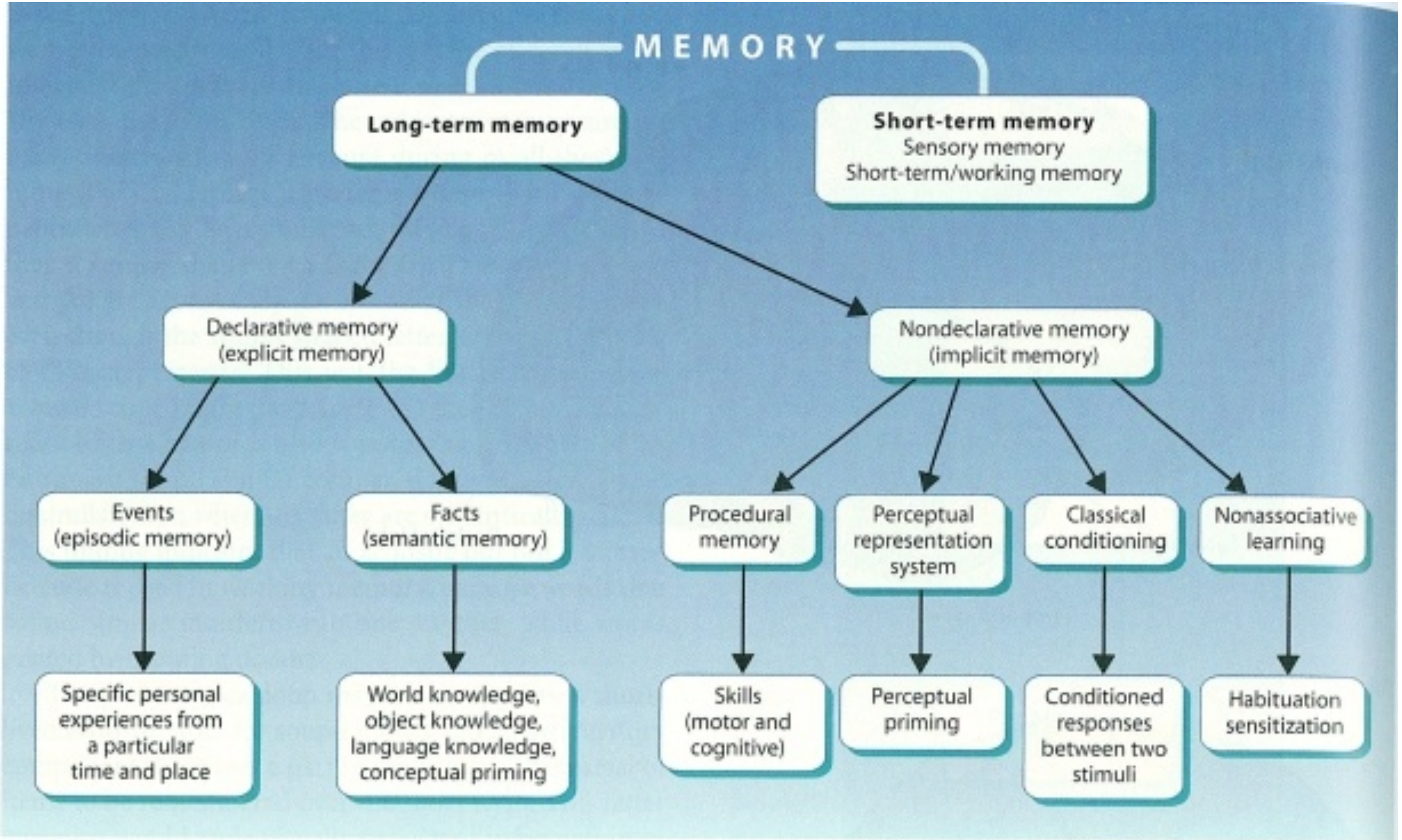
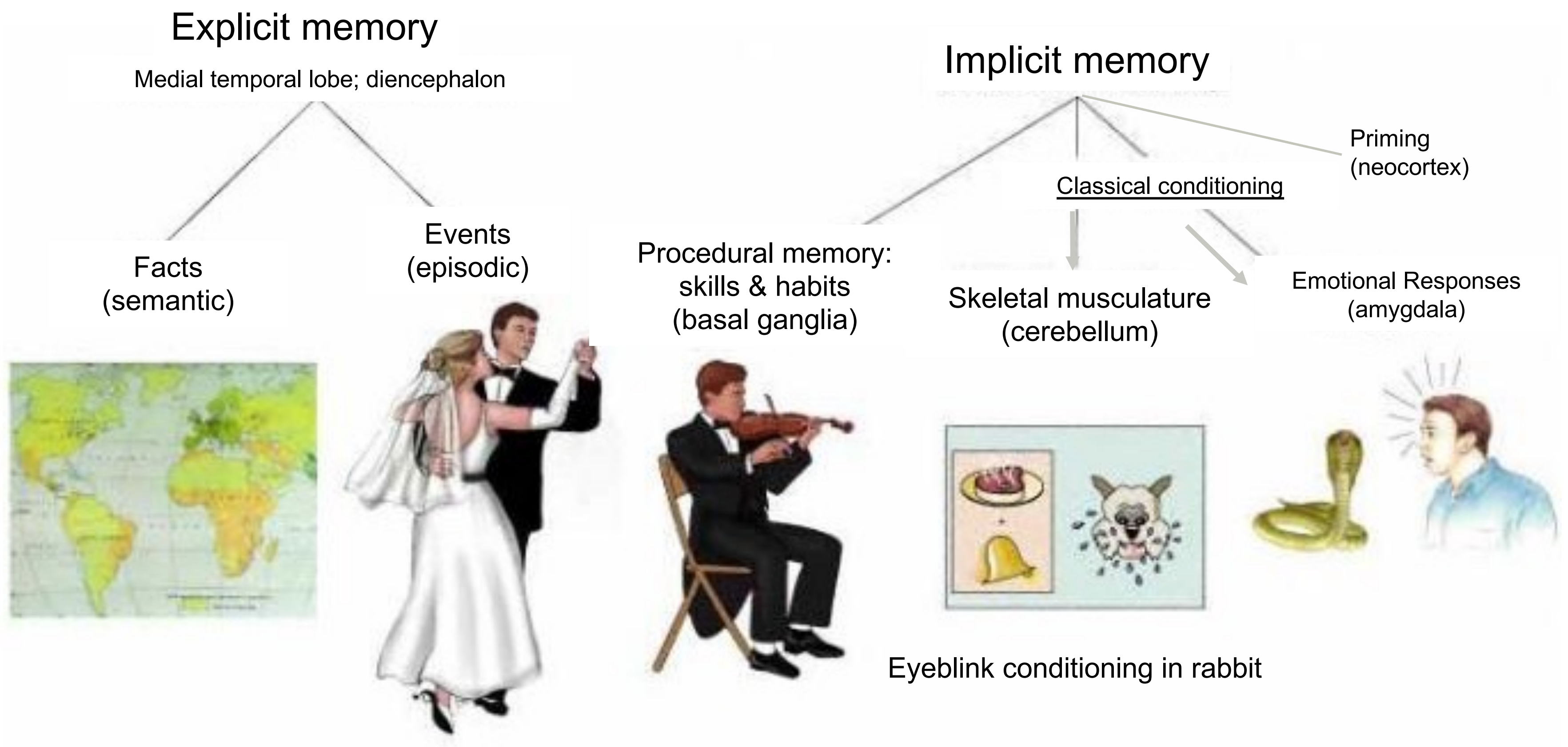


Figure 8.9 The hypothesized structure of human memory diagramming the relationship among different forms of memory.

Different types of learning & memory rely on different brain structures



Anatomical substrates of declarative memory

- Patient H.M.
- Bilateral removal of the temporal lobes, (amygdala, hippocampus) at age 27

- Persisting Anterograde Amnesia
- No retrograde amnesia!
- Unaffected formation of non-declarative memories and skills, working memory, no deficits in abstract thinking, IQ, leading conversations,…

Multiple memory trace theory

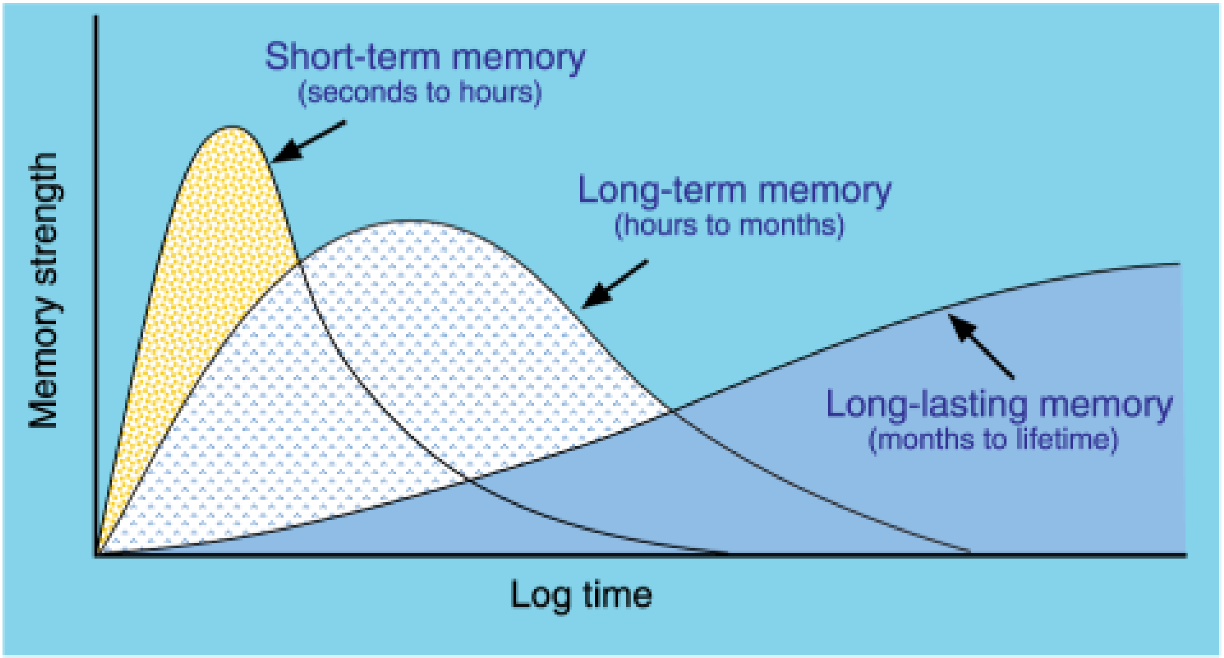


Fig. 1. Memory consolidation phases. Studies of memory and neuroplasticity support Müller and Pilzecker's hypothesis proposing that the consolidation of new memory into long-term memory is time dependent (*1*), but strongly suggest that short-term and different stages of long-term memory are not sequentially 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

Forms of Long Term Memory

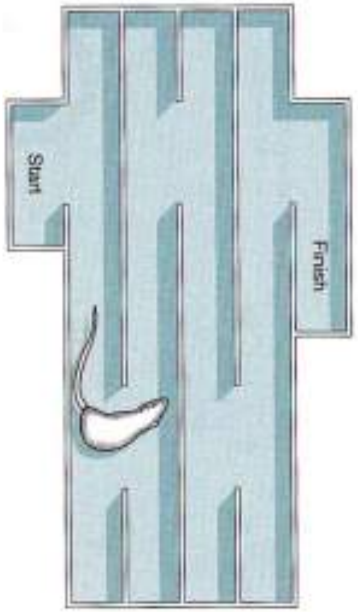
Declarative/explicit

- Semantic (facts)
- Episodic (events)
- (medial temporal lobe, hippocampus and cortex)

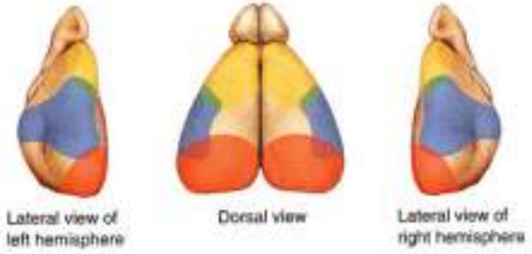
Non-declarative/implicit

- Procedural (Skill learning: basal ganglia and motor cortex)
- Priming (cortex)
- Conditioning (classical cond.: amygdala, cortex)
- Nonassociative (sensitization and habituation)

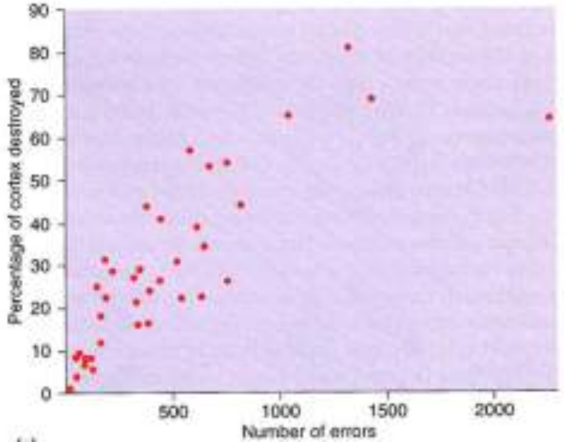
Lashley's Search for the Engram in the 1920s



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

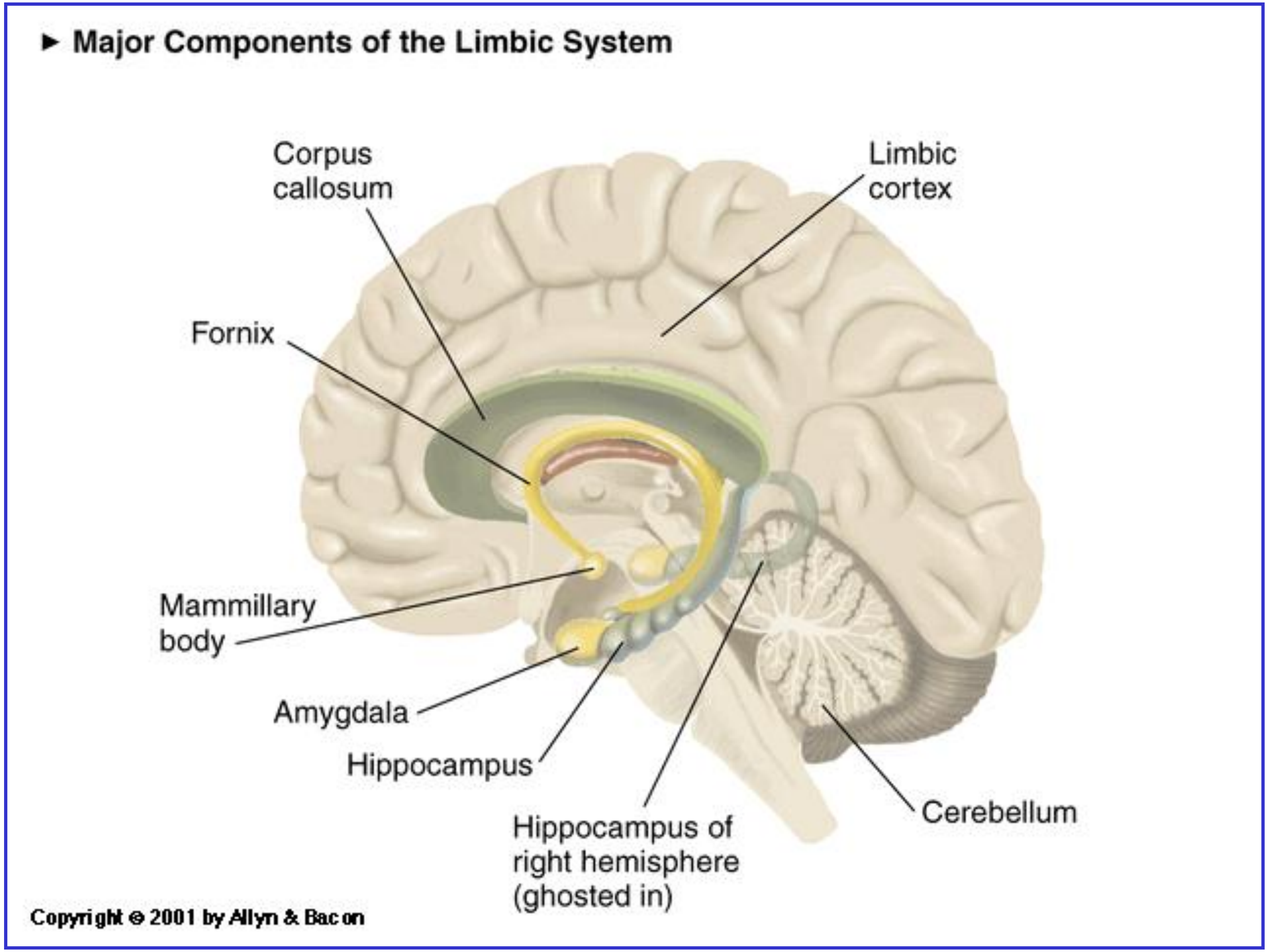


Errors are associated with the size rather than the locus of the lesion.

Neuroscience of memory

- Karl Lashley (1920s) searched for the *engram*, the physical location of a memory.
- He destroyed progressively larger areas of monkey and rat brain tissue after training them on a task.
- The monkeys/rats retained the memory, suggesting it was distributed to many parts of the brain, a principle known as *equipotentiality*.

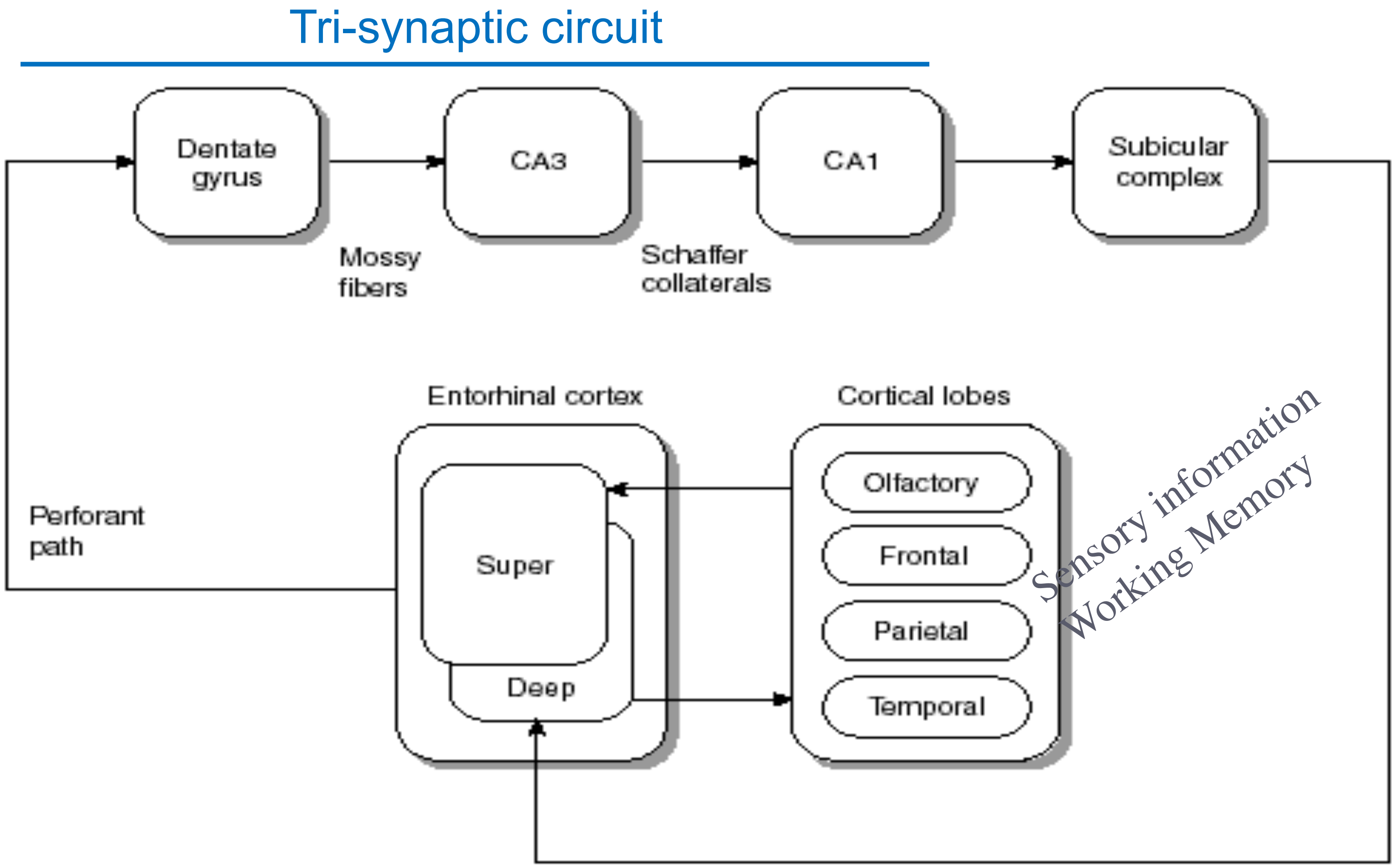
The limbic system



The hippocampus

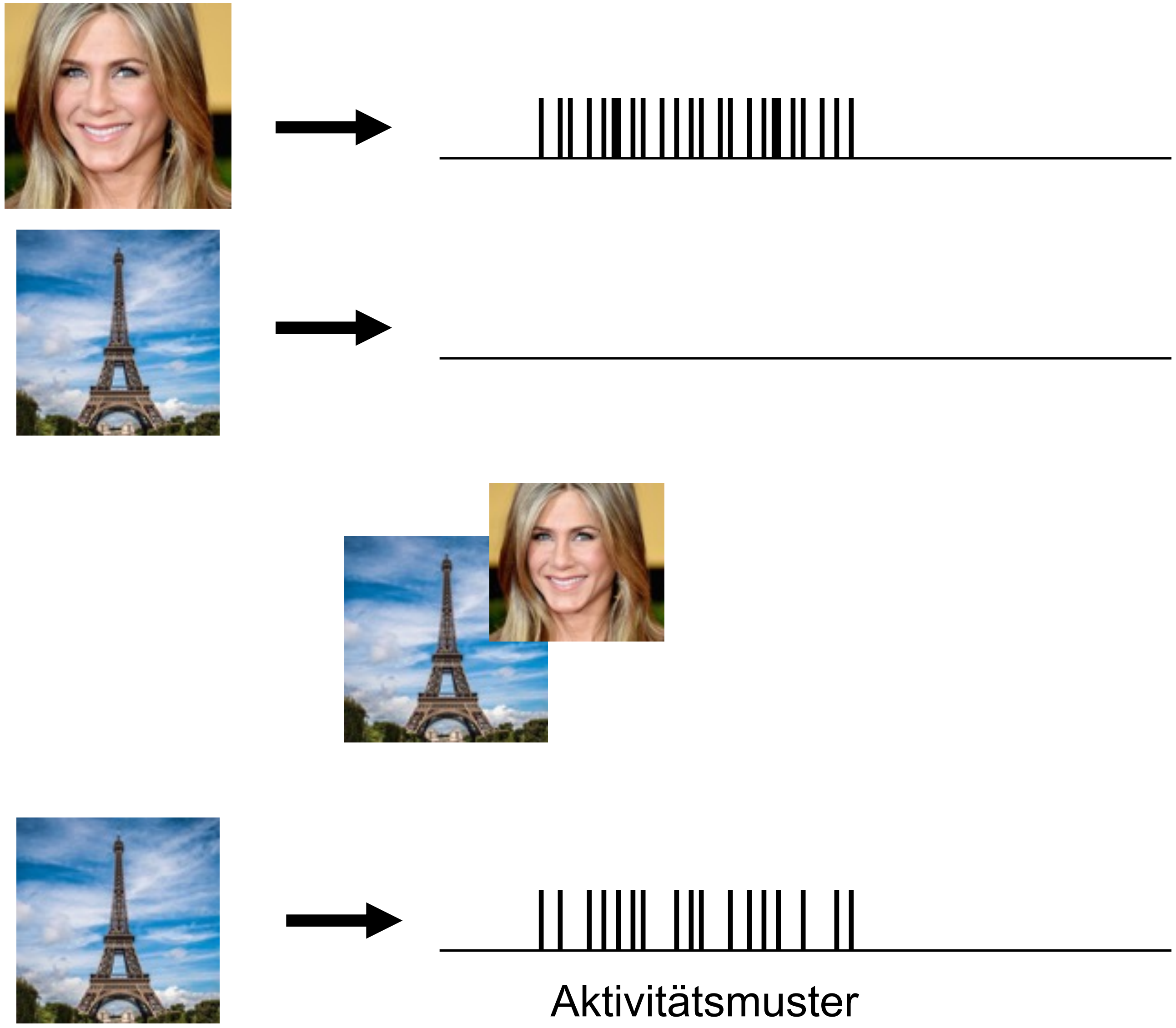
- This brain structure is responsible for *consolidation*, the transfer of information from STM to LTM.
- Damage to the hippocampus results in *anterograde amnesia*, an inability to retain new information subsequent to the damage. Example: The tragic case of H.M.
- This should be distinguished from *retrograde amnesia*, in which it is difficult to remember information learned prior to a traumatic incident.

Hippocampal structure and function



Hippocampus: Concept-'cells'

Hippocampus: Concept-’cells’



Quiroga et al., 2008

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Memory systems in implicit/non-declarative memory

- Not all implicit memory is independent of the hippocampus

- Not all implicit memory depends on the basal ganglia, e.g., emotional learning, priming, certain motor responses

- Cortical systems (e.g., priming)
- Amygdala (fear conditioning)
- Cerebellum (eyeblink conditioning)

…etc

Basal Ganglia

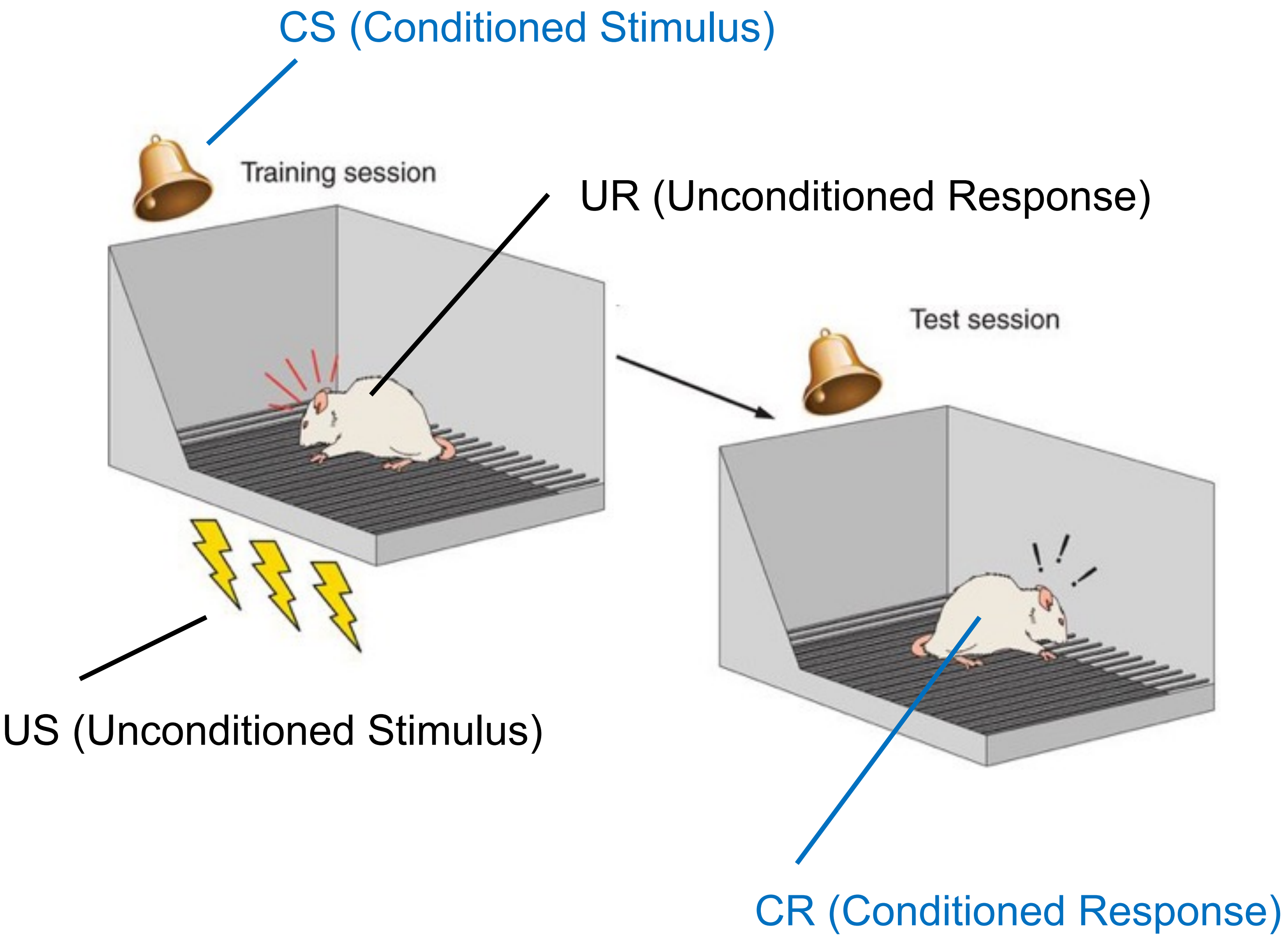
- Can examine Parkinson’s & early Huntington’s Disease
- no apparent amnesia (declarative memory ok)

But implicit memory problems in “procedural memory”:

- Perceptual-Motor Learning
- Habits
- Skills

Separate from motor disorders

Classical (Pavlovian) conditioning and memory



Classical (Pavlovian) conditioning and memory

There are many different forms of classical conditioning and the responsible brain structure depends on the form

Examples:

a) Pavlovian fear conditioning:

Tone --> Shock (CS) (US) Then: Tone --> freeze (CS) (CR)

- Depends on the amygdala
- + the hippocampus with trace procedure
- + the hippocampus if the CS is a context

b) Eyeblink conditioning

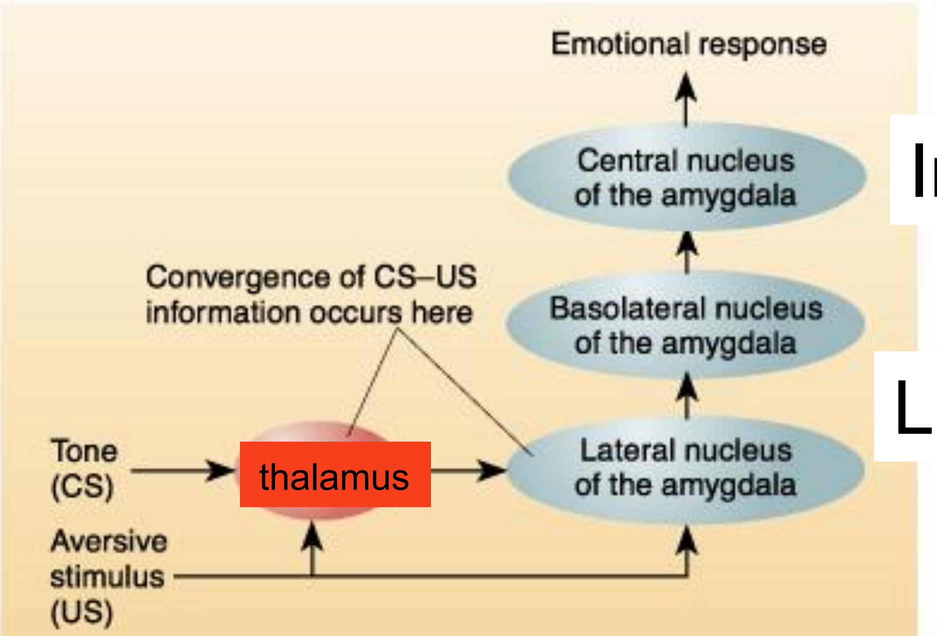
Tone --> puff of air to eye (CS) (US) Then: Tone --> eyeblink (CS) (CR)

- Depends on cerebellum
- + hippocampus with trace procedure

- Declarative knowledge of task always depends on hippocampus

Basic model that has emerged for Pavlovian fear conditioning

▶ **The Probable Location of the Changes in Synaptic Strength Produced by the Classically Conditioned Emotional Response That Results from Pairing a Tone with a Foot Shock**

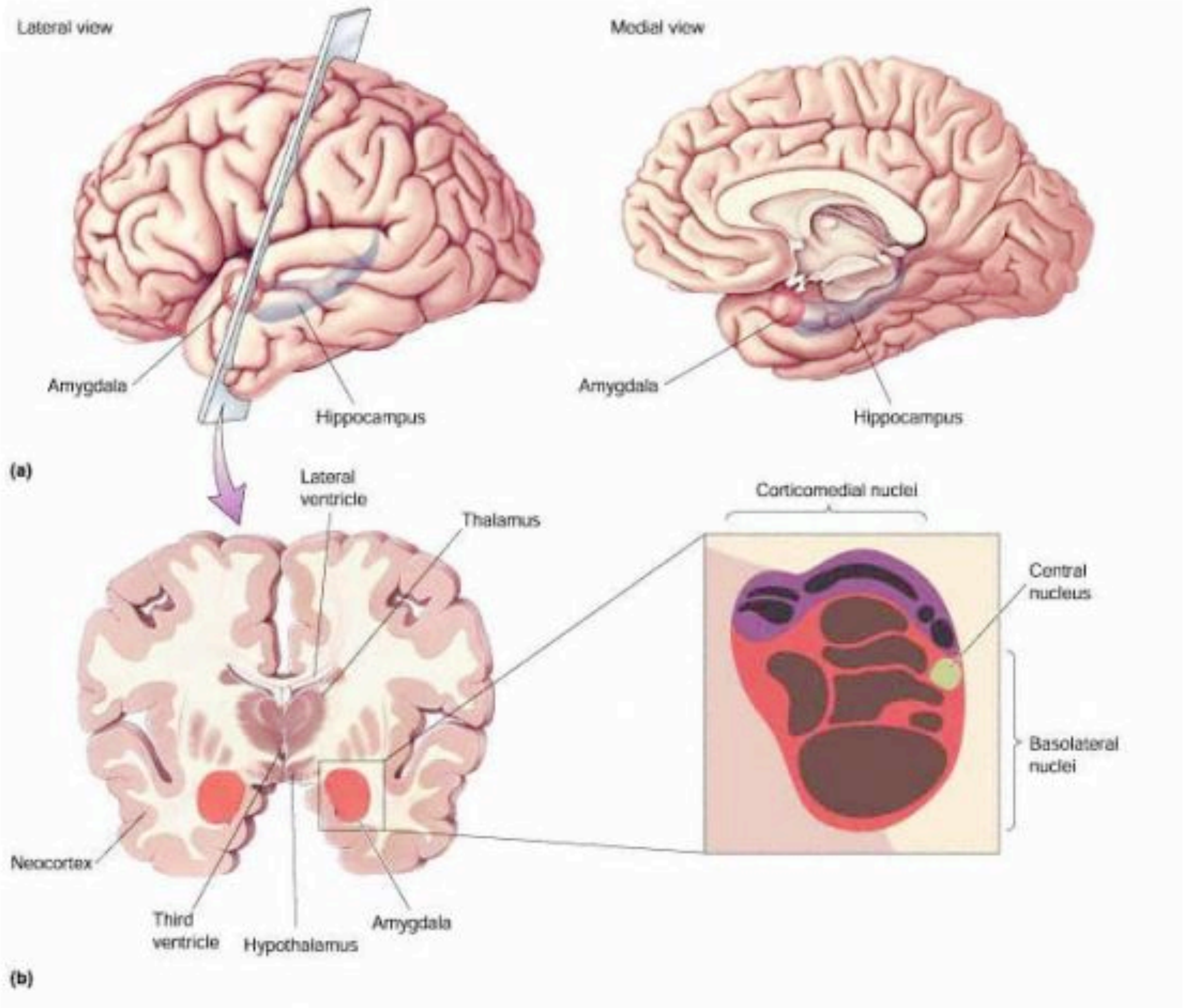


Innate fear

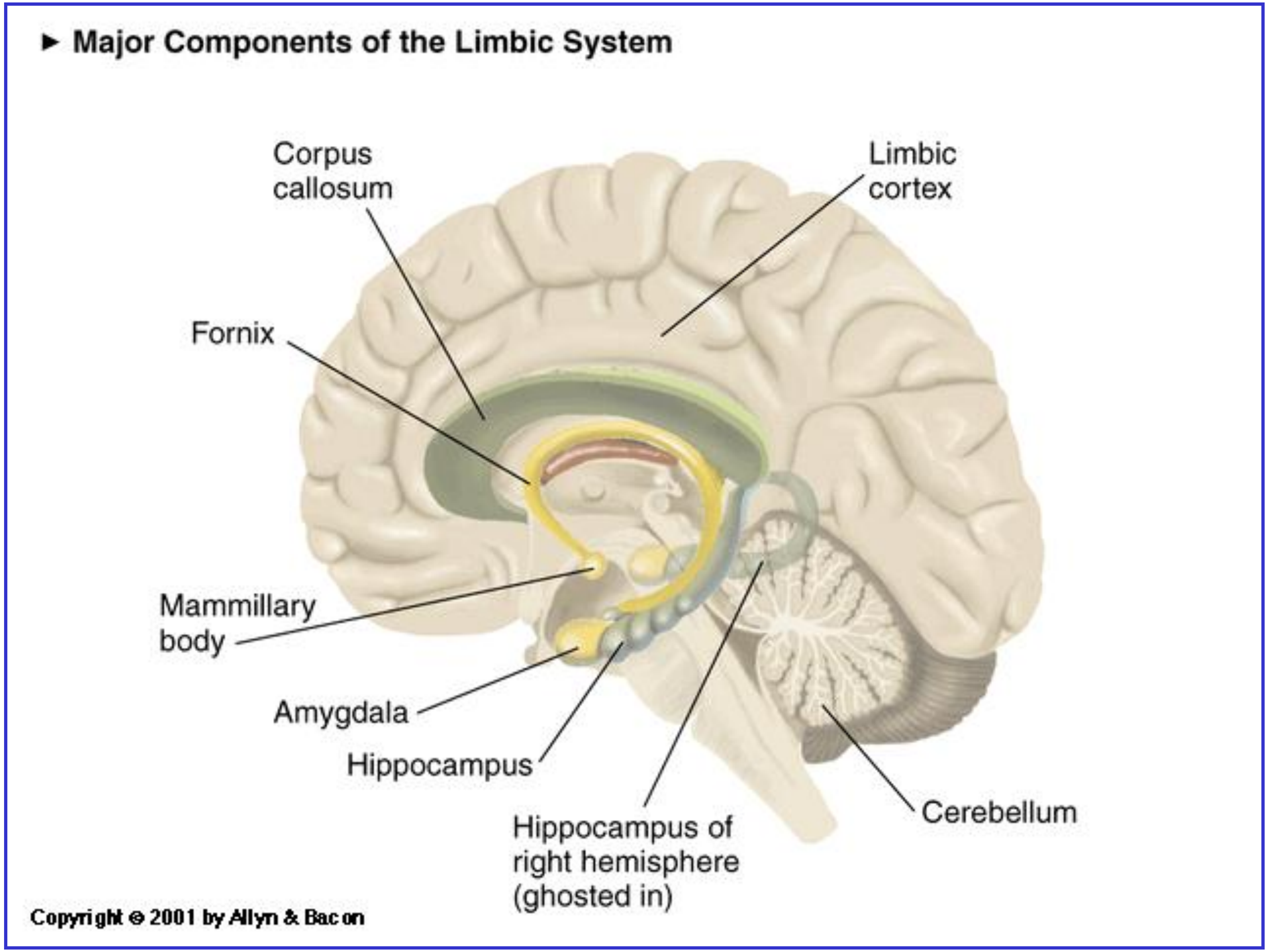
Learned fear

Central nucleus = output of fear/unlearned fear
Basolateral/lateral nucleus = learned fear

Amygdala is a key structure in fear and anxiety

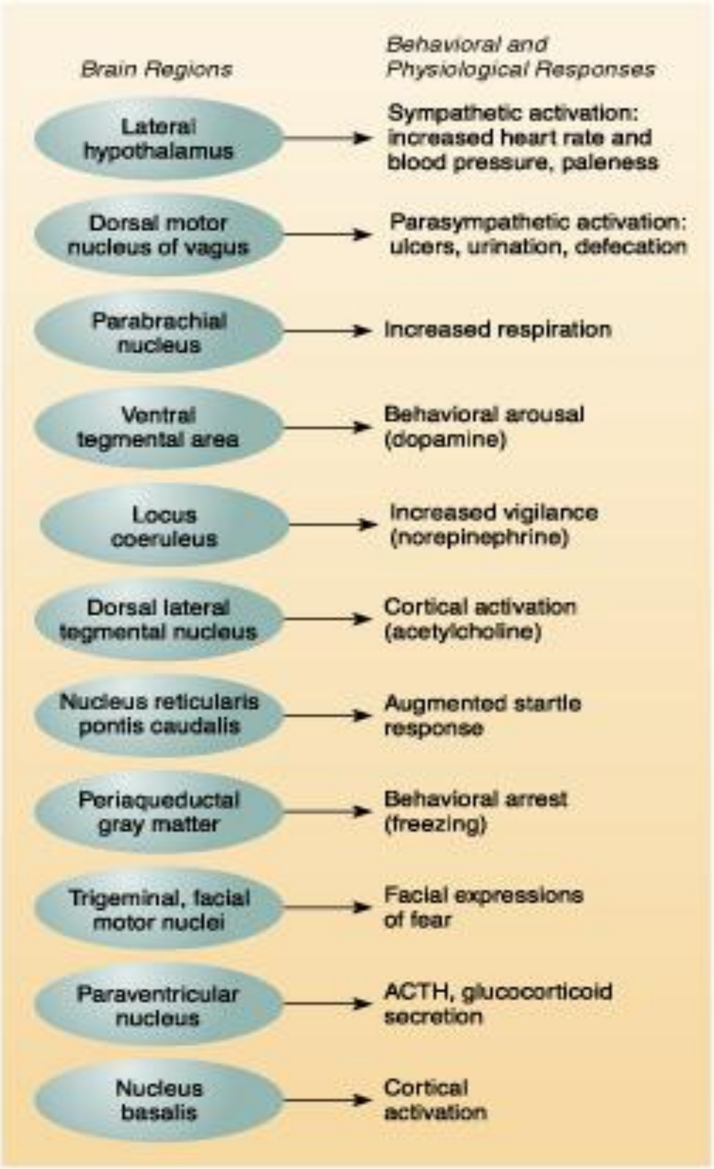


Unconditioned Fear Circuit: Central Nucleus of the Amygdala and its Outputs



Unconditioned Fear Circuit: Central Nucleus of the Amygdala and its Outputs

▶ **Some Important Brain Regions That Receive Input from the Central Nucleus of the Amygdala and the Emotional Responses Controlled by These Regions**



Central nucleus outputs coordinate all of the defensive responses (learned and innate).

Source: Adapted from Davis, M., Trends in Pharmacological Sciences, 1992, 13, 35-41.

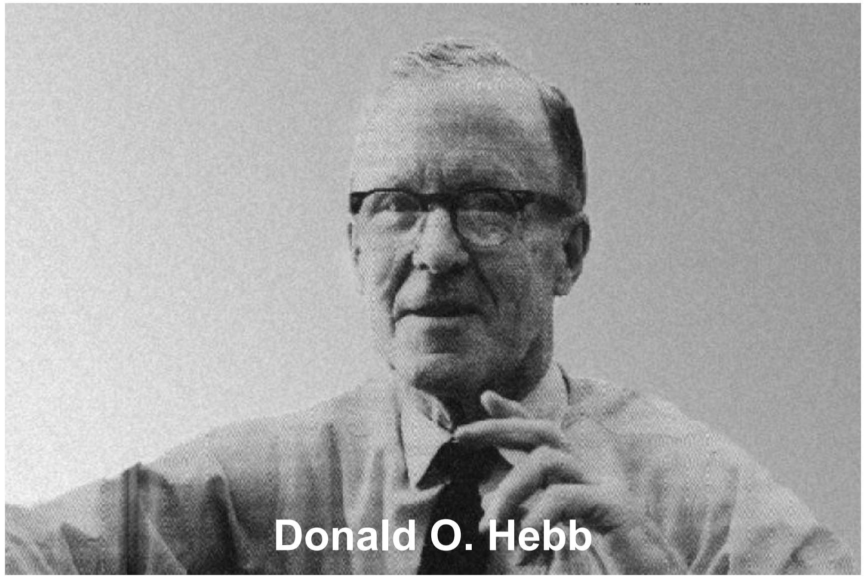
Neural substrates of working/ short-term memory

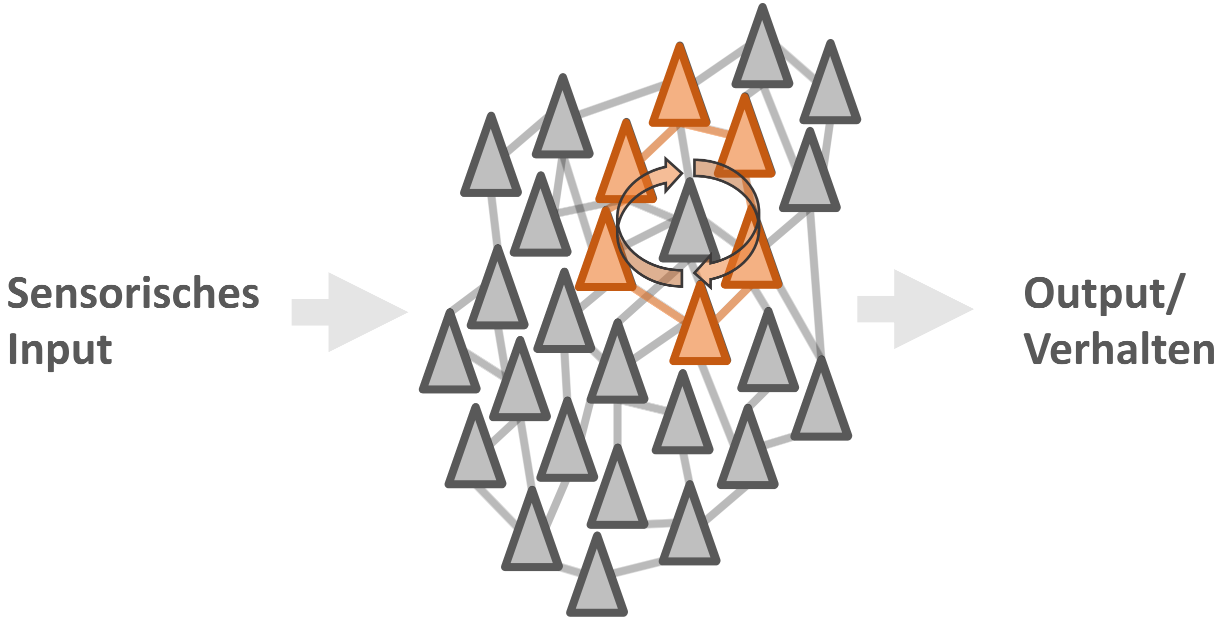
- Storage of verbal material: posterior parietal cortex in left hemisphere.
- Rehearsal of verbal material: prefrontal cortex.
- Storage of spatial information: posterior parietal cortex in right hemisphere.
- Maintenance of spatial information: dorsolateral prefrontal cortex.

Cellular substrates of memory

- *Learning* is a change in the nervous system caused by some event that in turn causes a change in behaviour.
- Learning in a nervous system requires a change in the structure or biochemistry of a synapse, what is called *synaptic plasticity*, or change in connections, which is called *structural plasticity*.
- If a group of neurons is repeatedly activated, the synaptic connections between them will be strengthened. This circuit will then contain the new information.

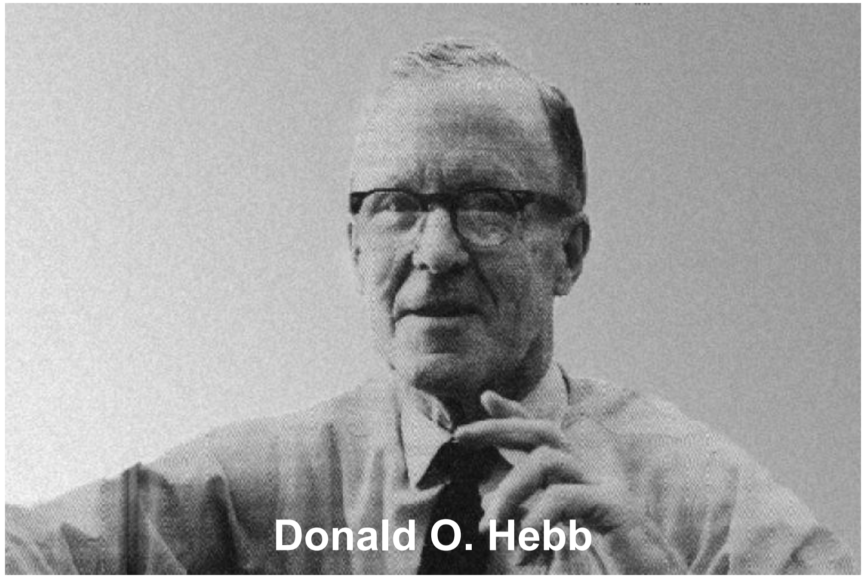
Hebb‘s ‚Cell Assemblies‘

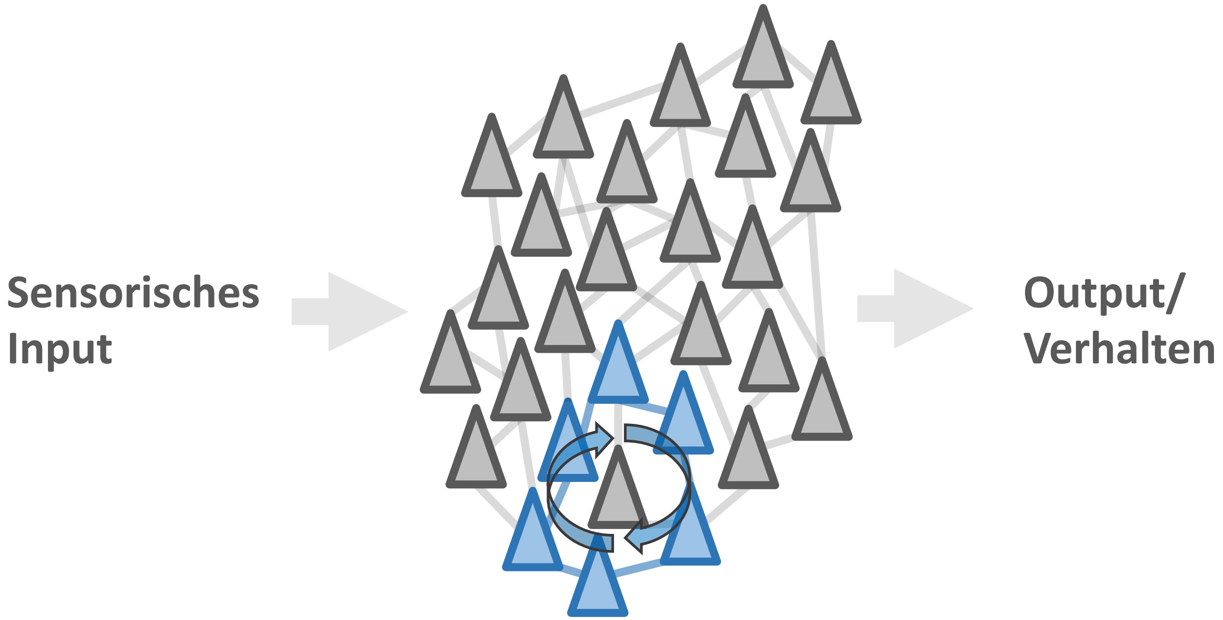




- decentralised *cell assemblies* code information (engrams)
- *Short-term memory* is reverberating activity in distributed closed-loop circuits
- Persisting activation in these circuits triggers structural changes at the synapses, which mediates the transfer of memories from short- into long-term memory within the same pathways

Hebb‘s ‚Cell Assemblies‘





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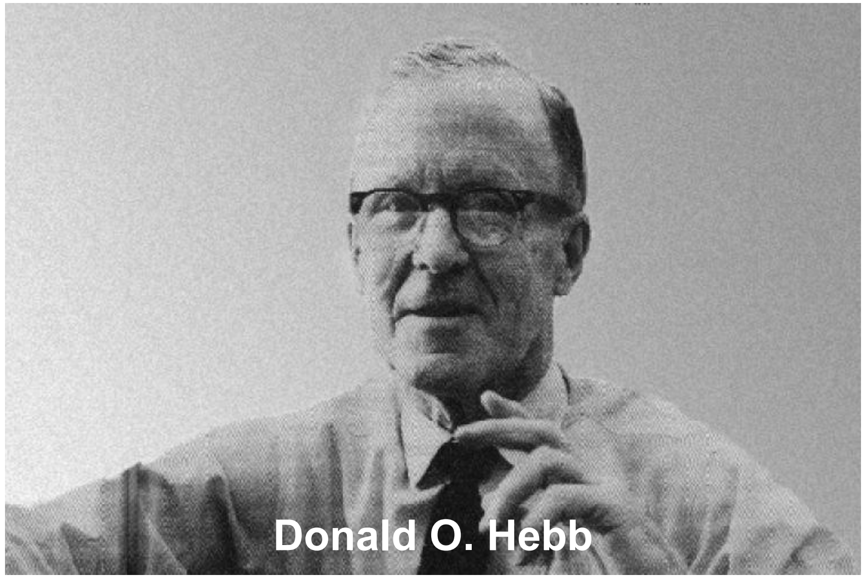
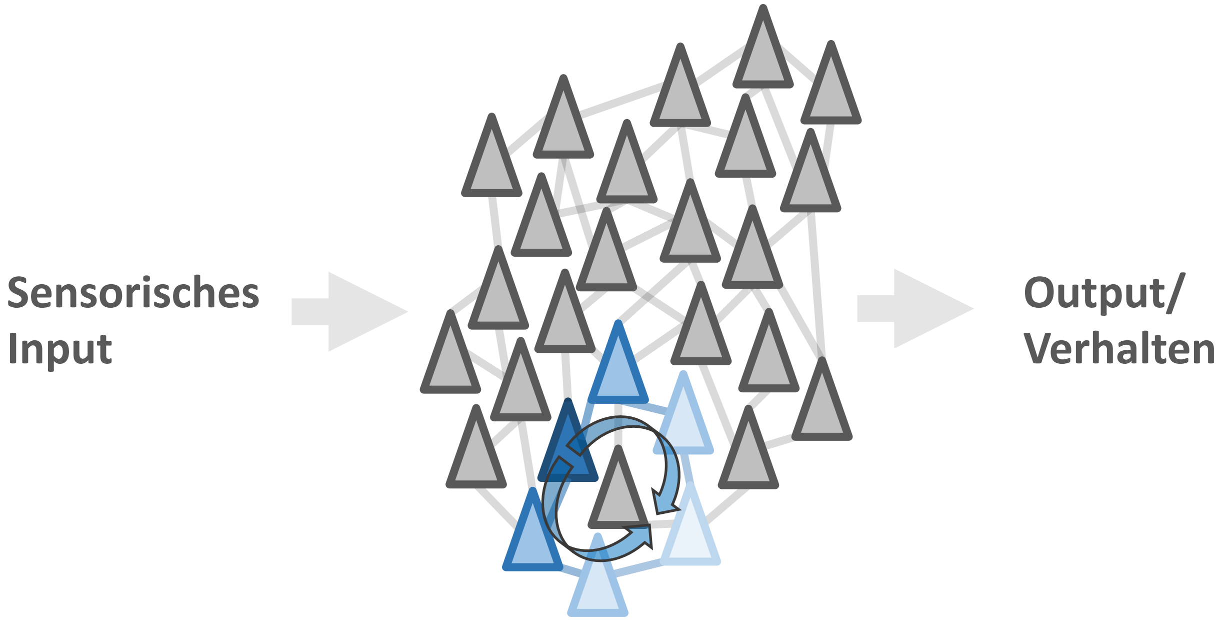
Hebb's ,Cell Assemblies'





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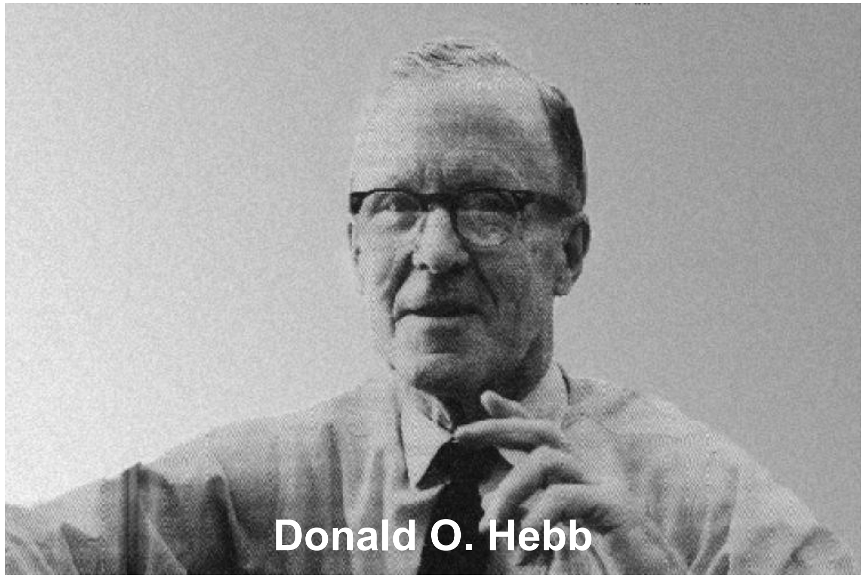
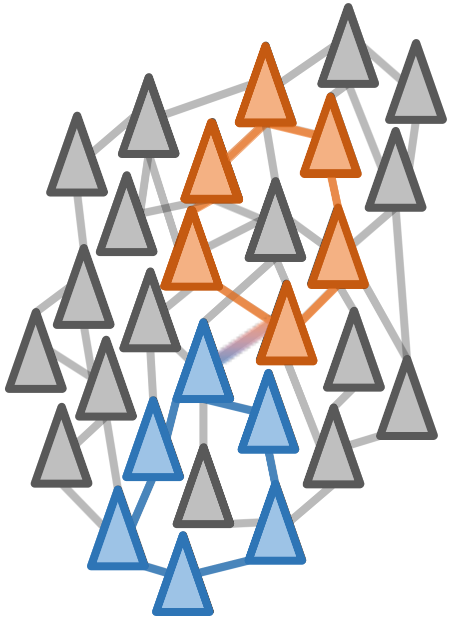
Hebb‘s Theory of Consolidation

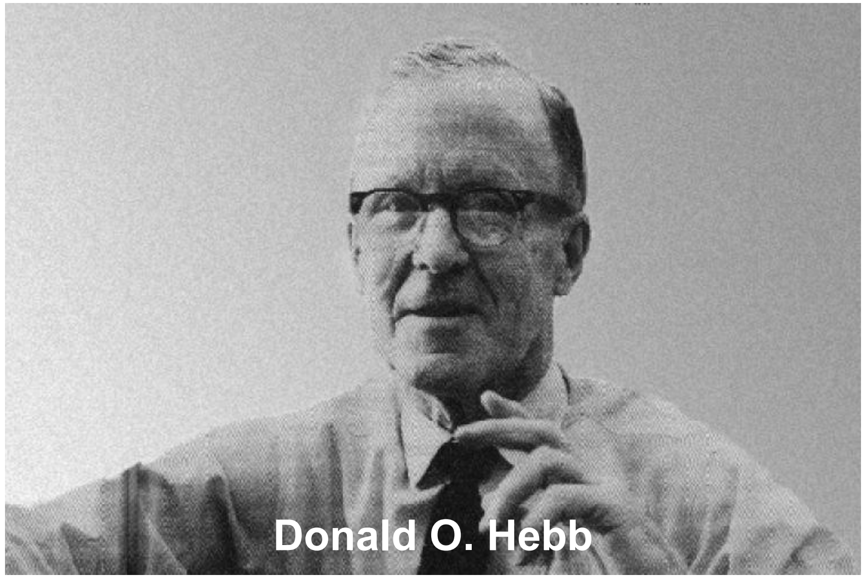


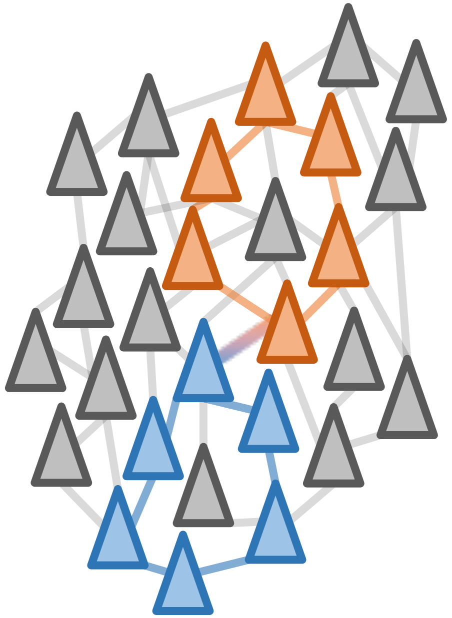


Let us assume that the persistence or repetition of a reverberatory activity (or "trace") tends to induce lasting cellular changes that add to its stability.[…] When an axon of cell A is near enough to excite a cell B and repeatedly or persistently takes part in firing it, some growth process or metabolic change takes place in one or both cells such that A's efficiency, as one of the cells firing B, is increased.

The Organization of Behavior, 1949

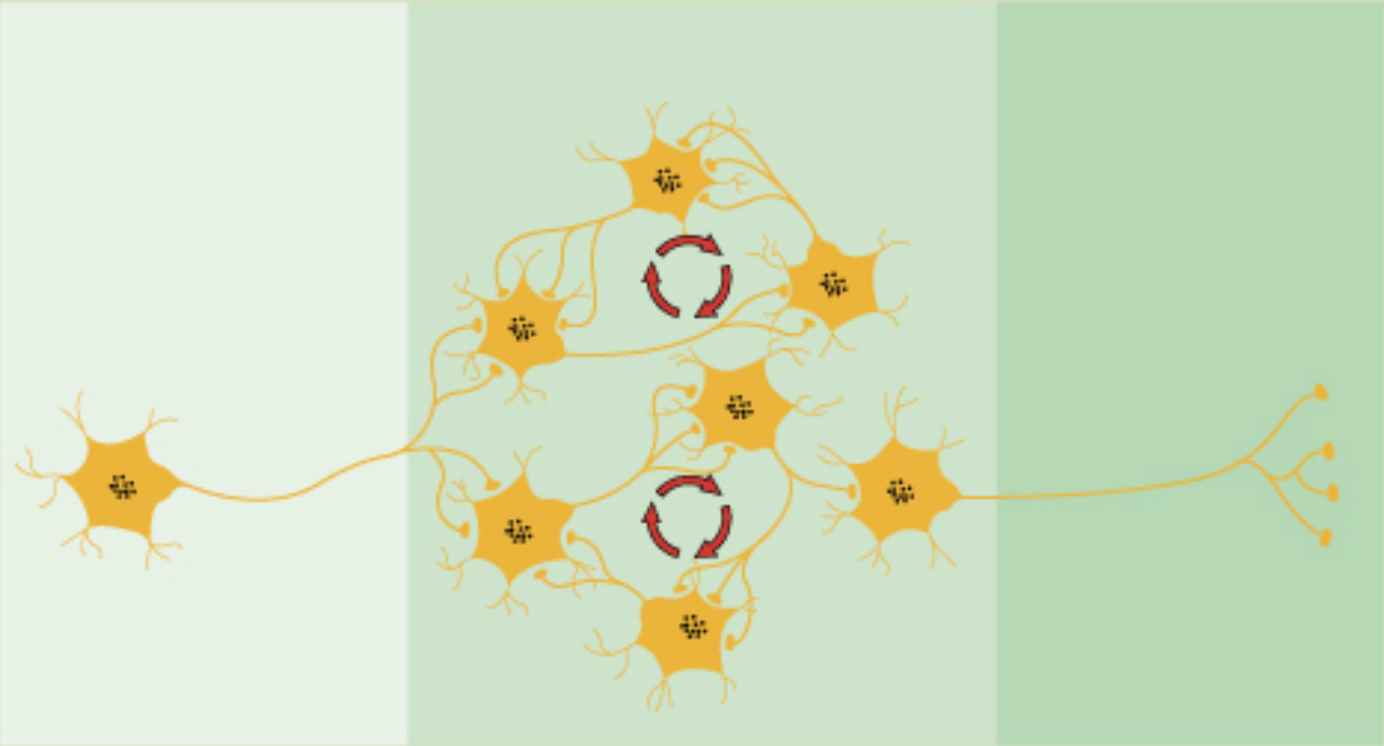
Hebbs Theorie der Konsolidierung





„What fires together, wires together.“

Hebb's (1949) Theory of Consolidation



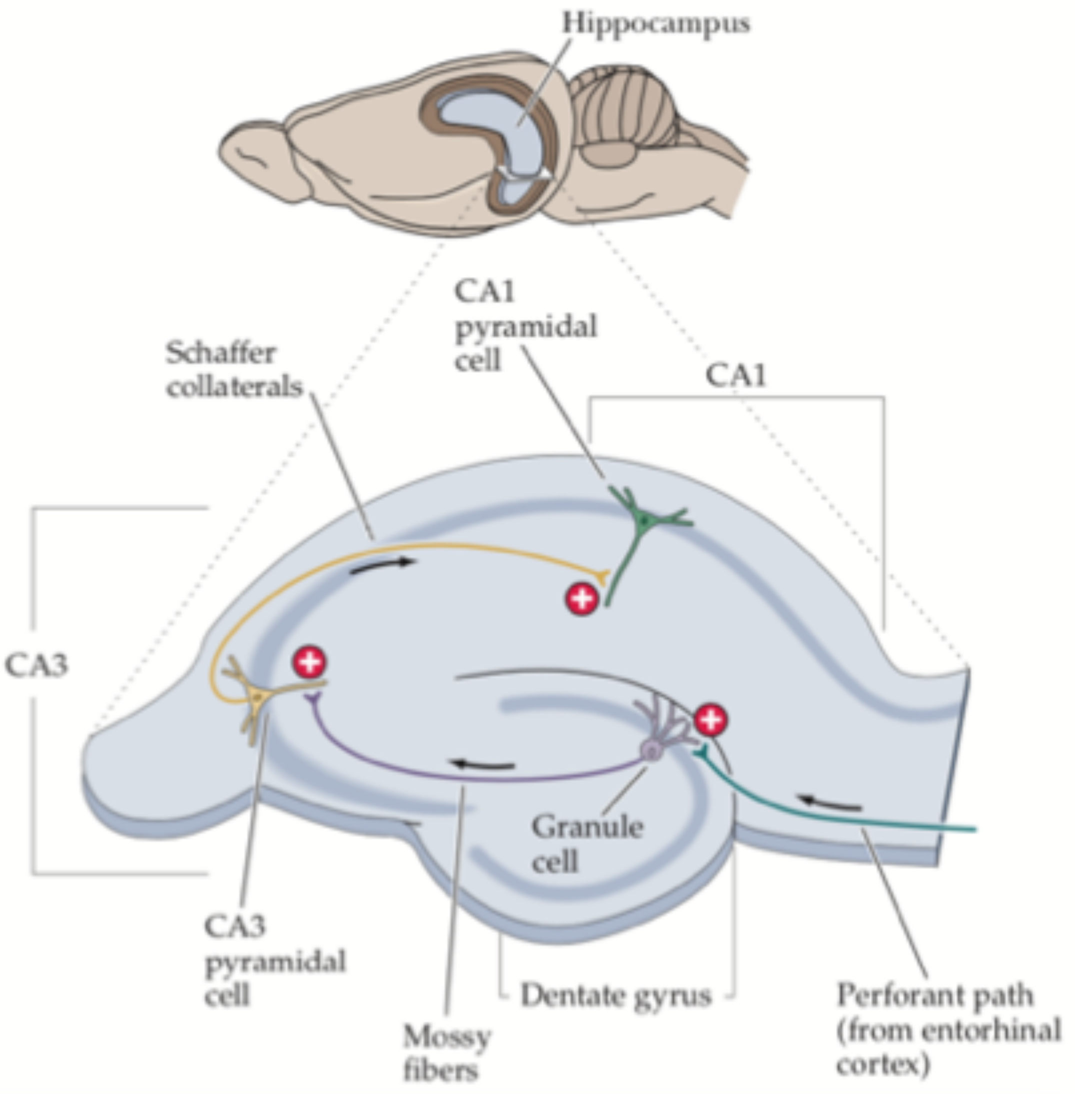
1 Experience activates sensory pathways, which conduct neural impulses to the CNS.

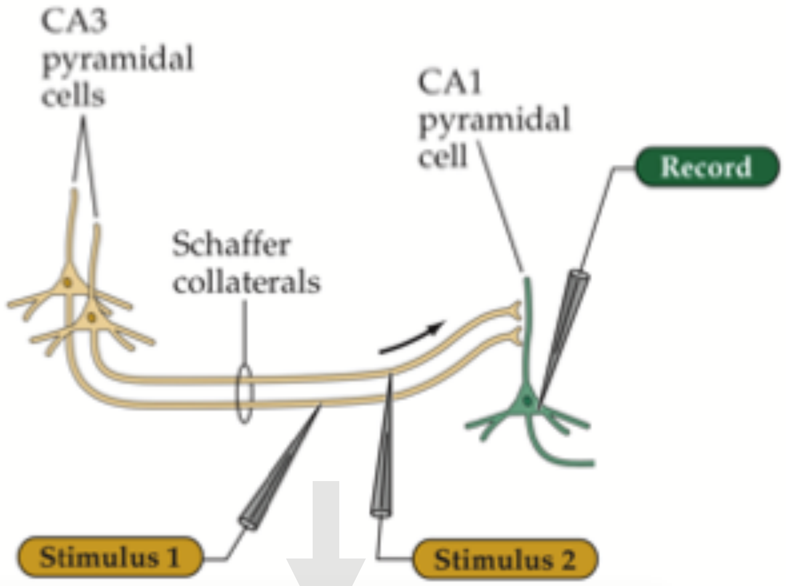
2 **Short-Term Memory**: Hebb hypothesized that the short-term memory of each experience is stored by neural activity reverberating in closed-loop CNS circuits.

Long-Term Memory: Hebb hypothesized that reverberating activity, if maintained for a sufficiently long time, produces structural changes in synapses and that these changes facilitate subsequent transmission over the same pathways.

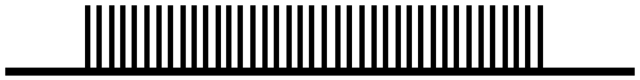
3 The changed pathways of transmission produced by synaptic facilitation can influence motor output and thus behavior.

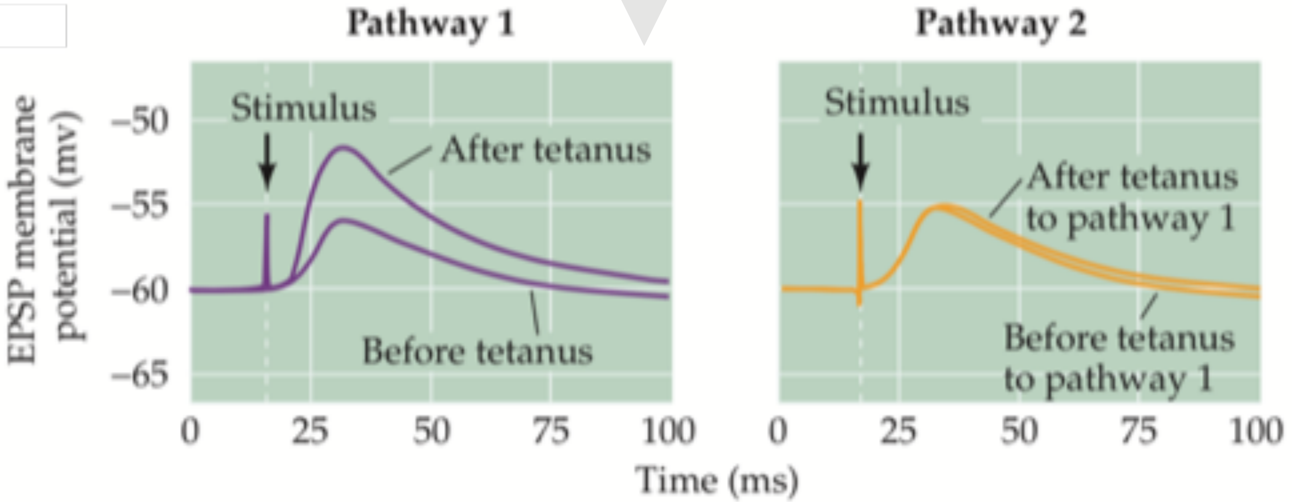
Long-term Potentiation (LTP)





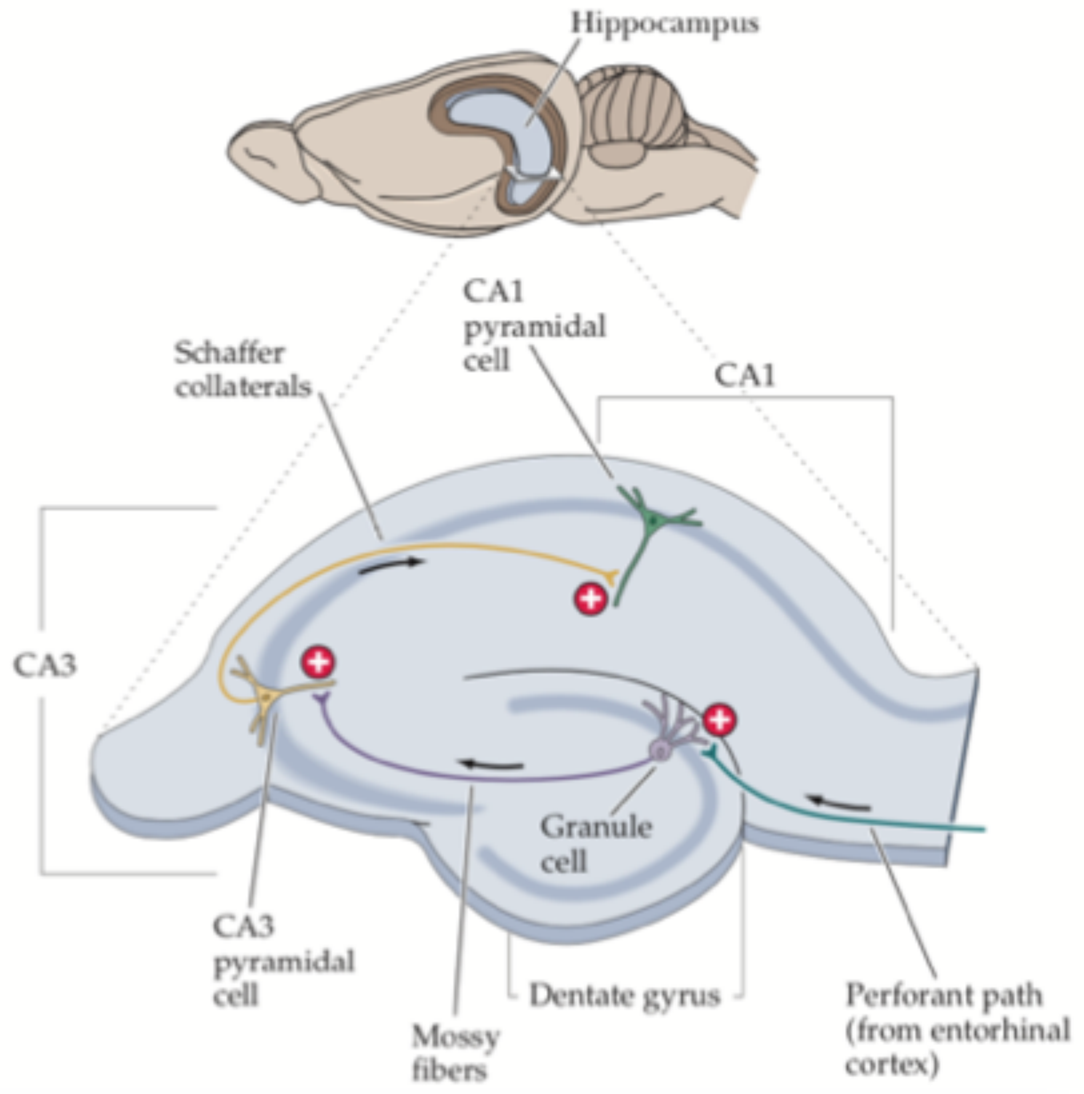
‘Tetanus’ of action potentials

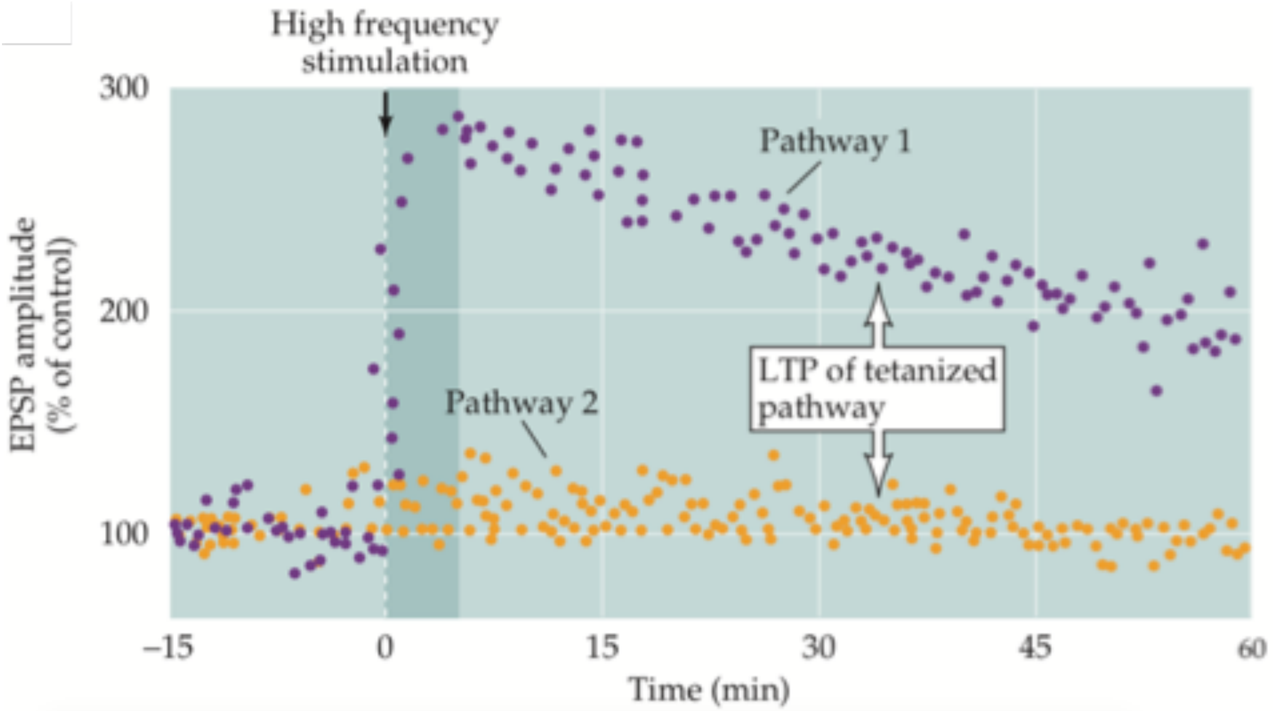


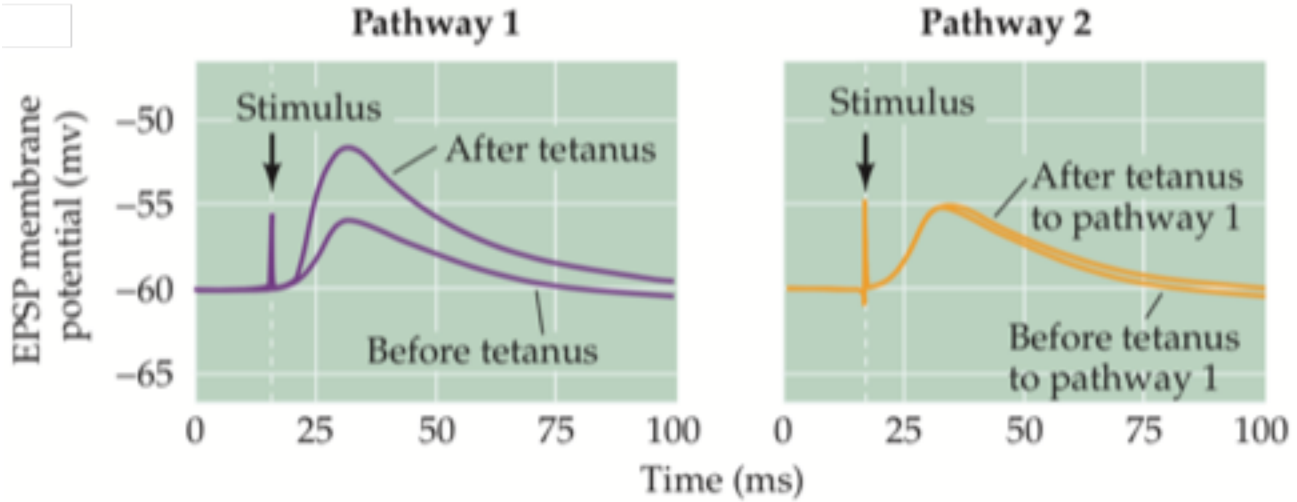


‘Purves’ Bliss, Lomo, 1973

Long-term Potentiation (LTP)

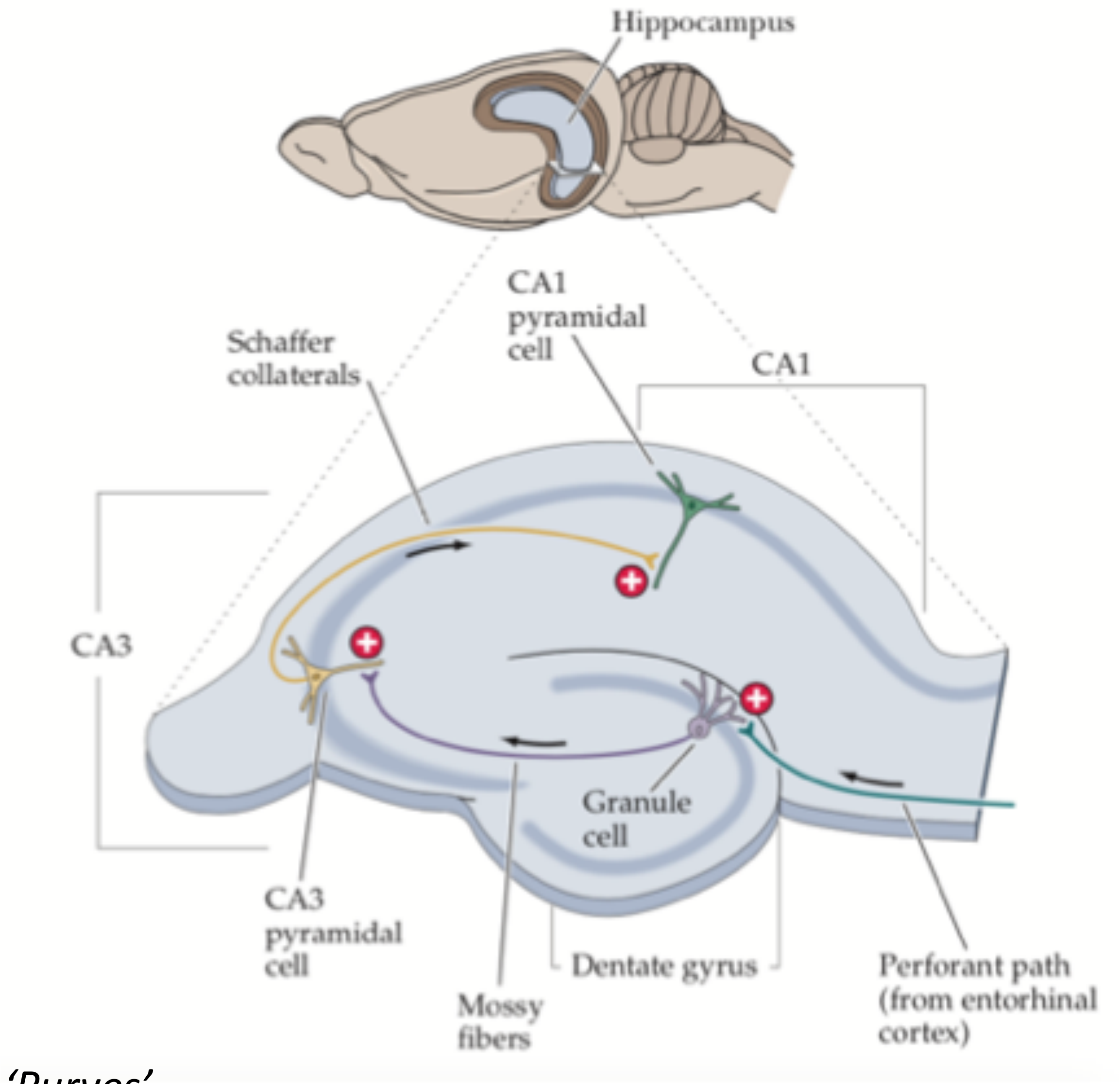


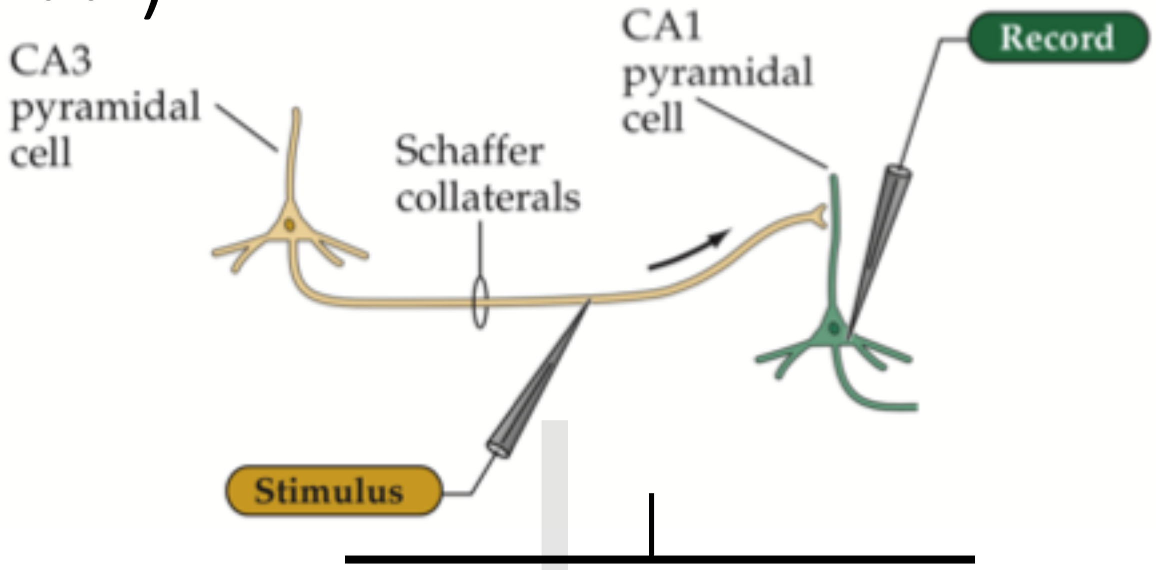




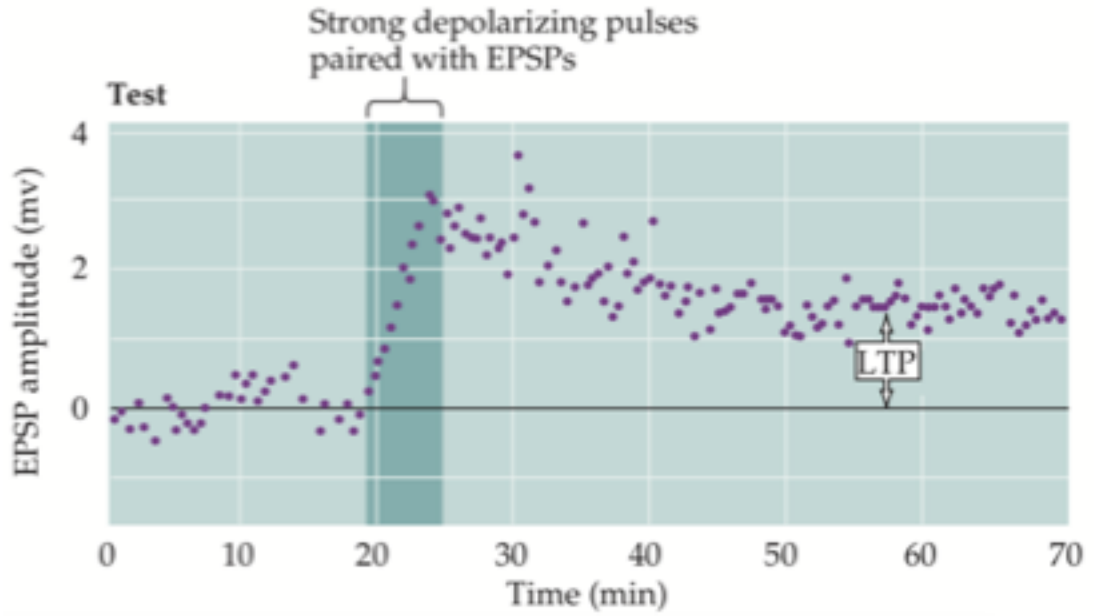
'Purves'

Long-term Potentiation (LTP)



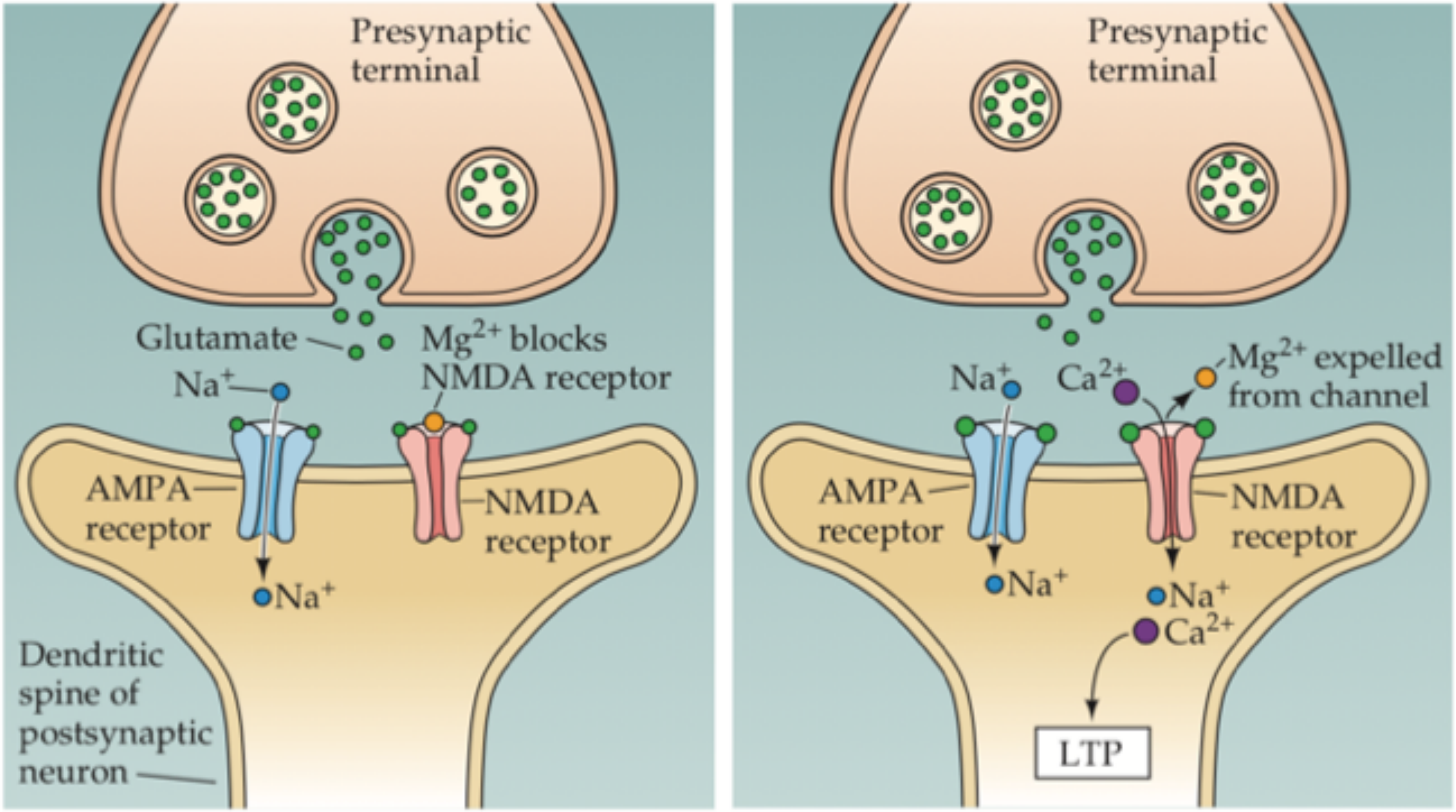


Single action potential



'Purves'

NMDA receptors are coincidence detectors



'Purves'

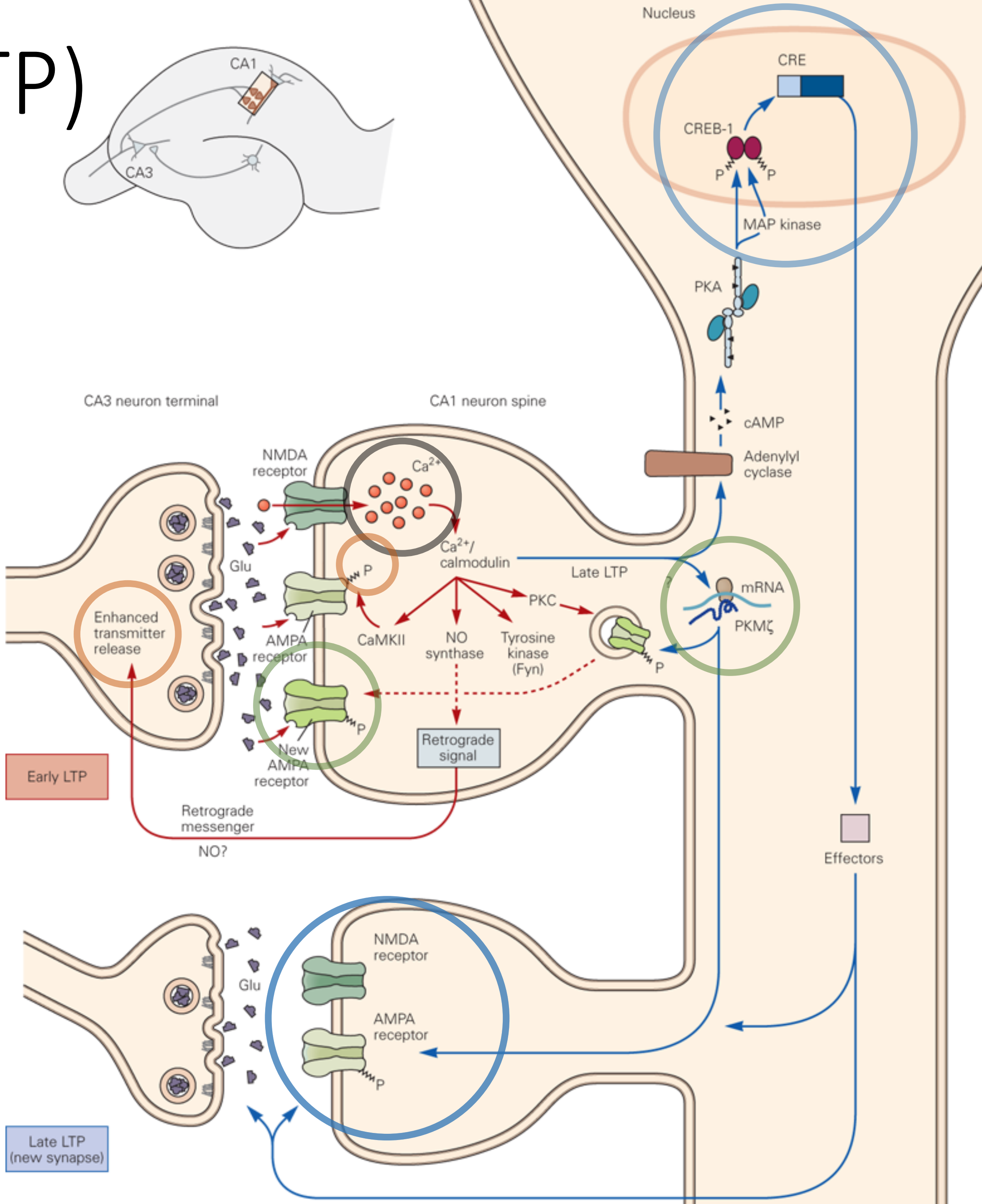
Long-term Potentiation (LTP)

- NMDA-R -> Ca^{2+} als sekundärer Botenstoff

- Phosphorylierung von AMPA-R
- Signal an präsynaptische Zelle

- Translation von lokaler mRNA
- Einbau von neuen AMPA-R

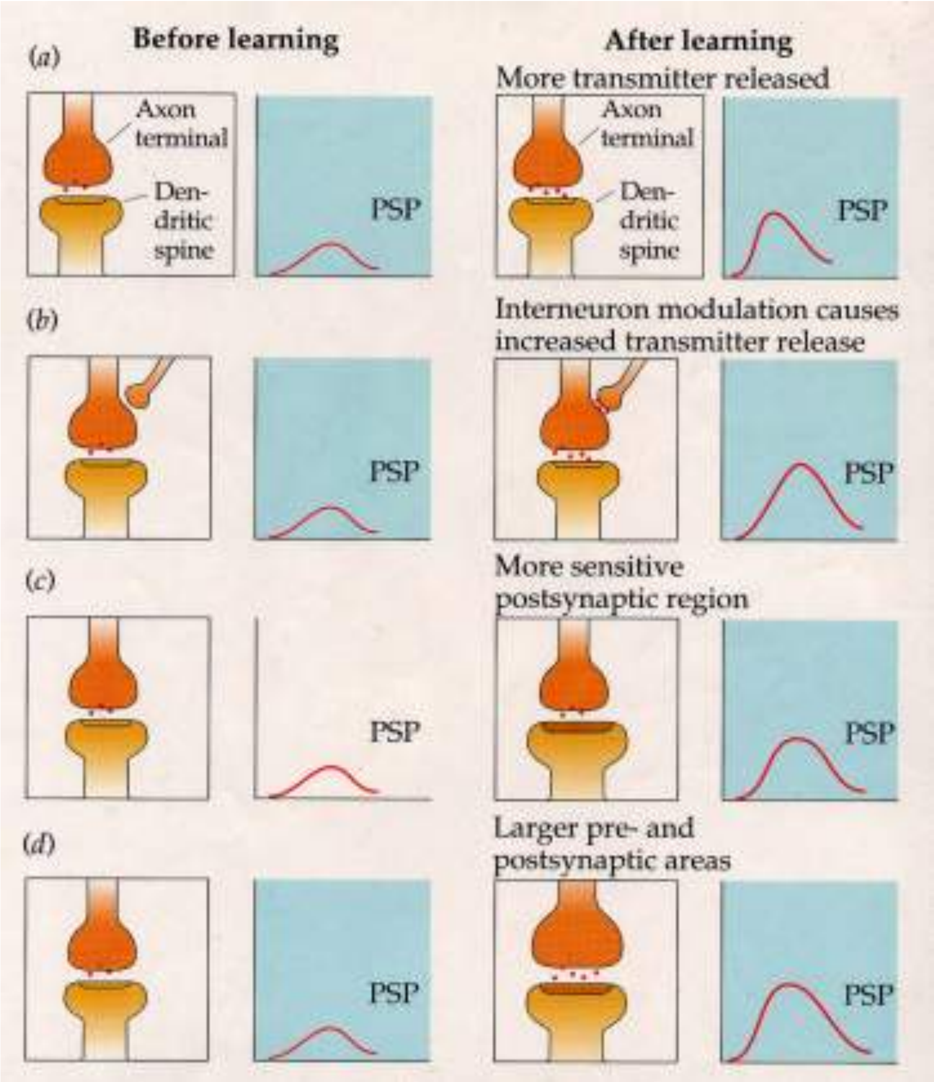
- Komplexe Signalwege mit Zellkern
- Transkription von DNA
- Einbau von neuen AMPA-R
- Bildung neuer Synapsen

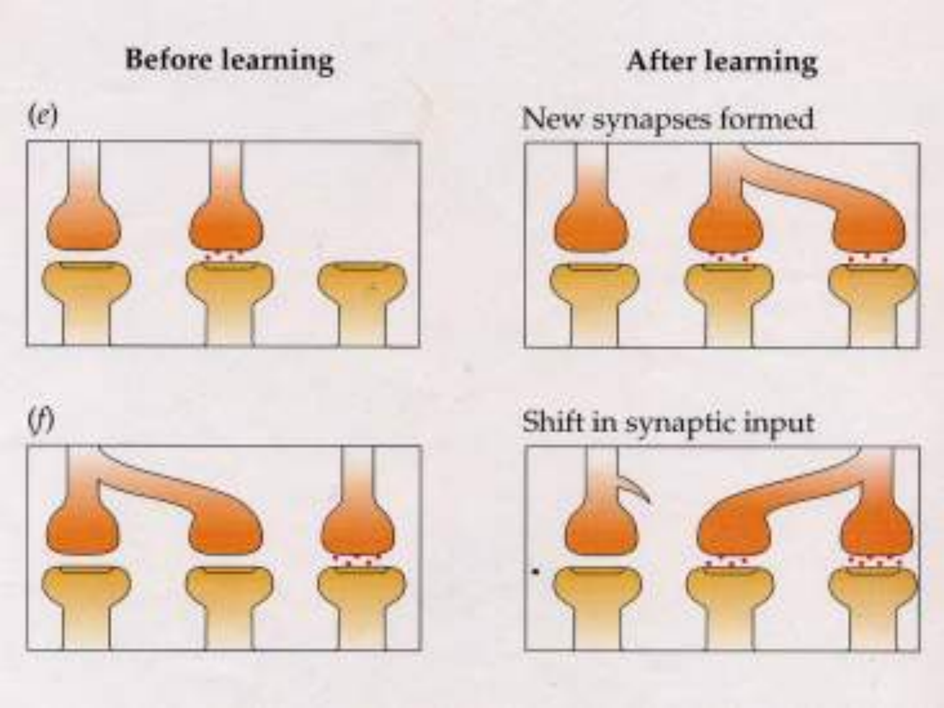


LTP Phasen	
Early	(sec – min)
Medium	(min – h)
Late	(h – d)

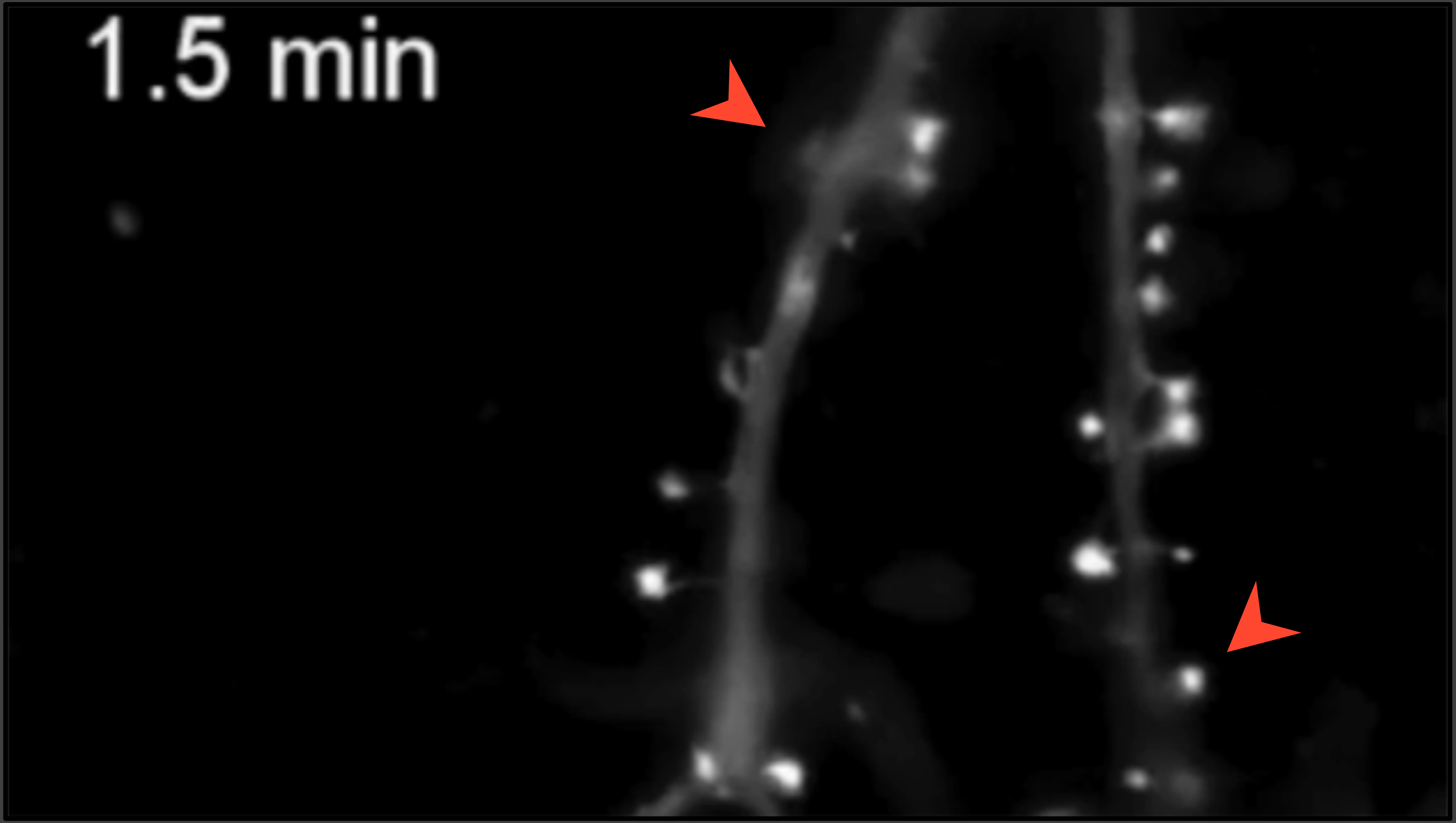
'Kandel'

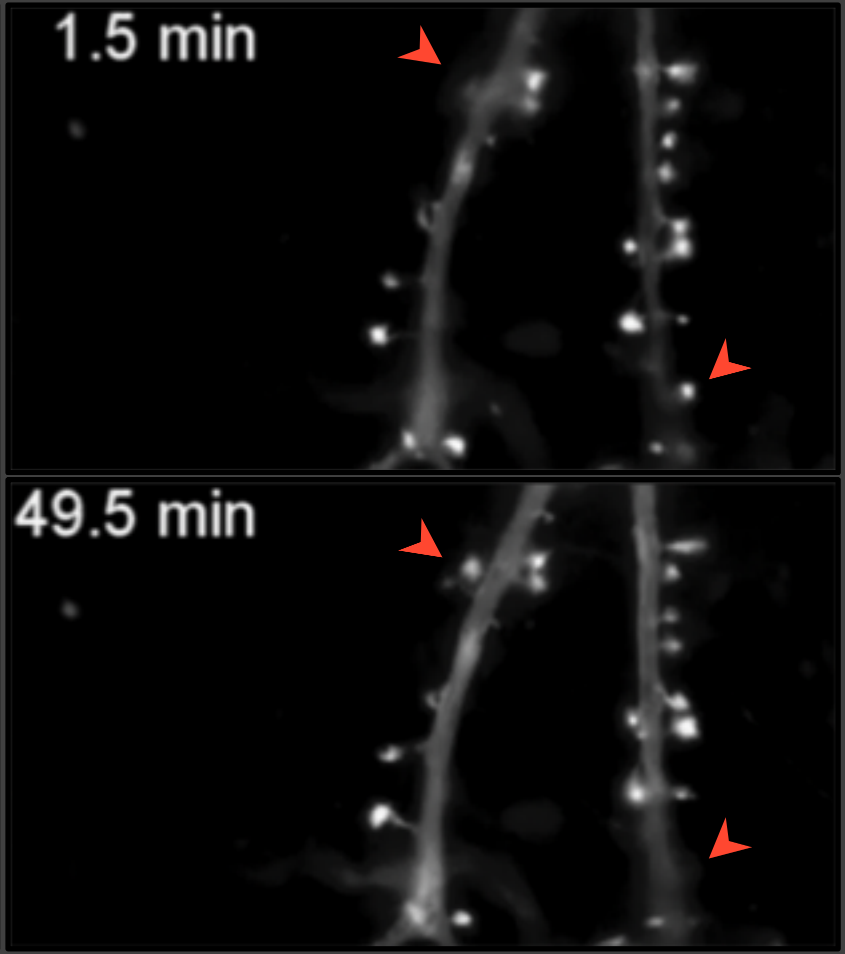
Synaptic Changes that Could Support Memory





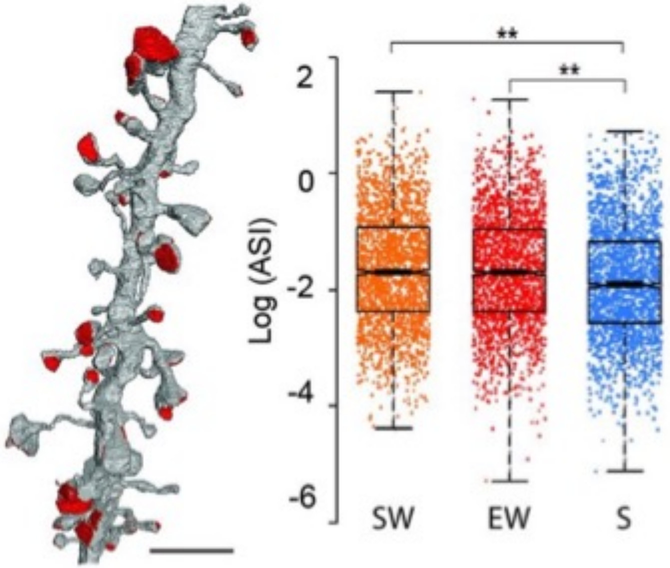
Formation and pruning of dendritic spines

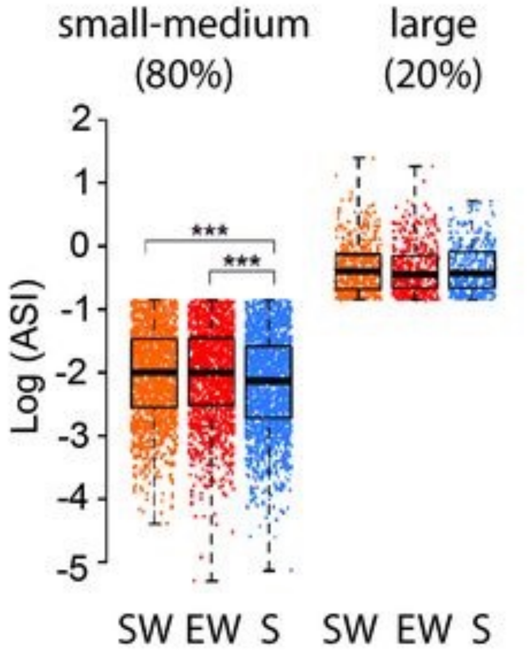


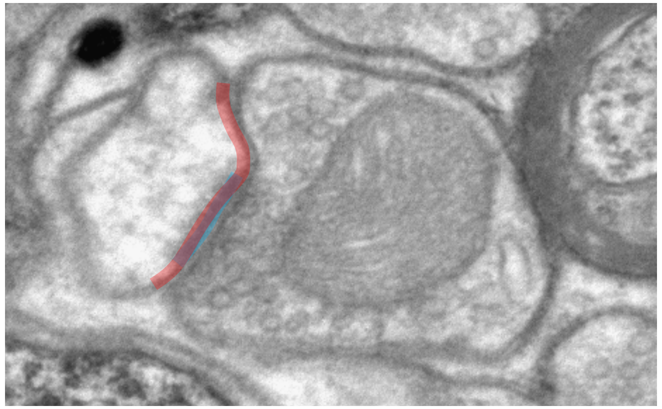


Michael J Schell, YouTube

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



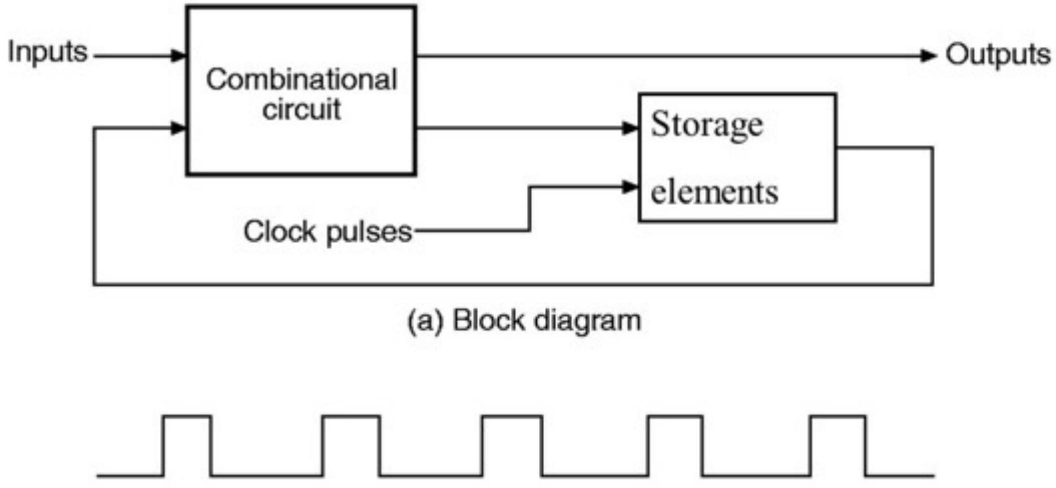




500nm

De Vivo et al., Science, 2017

Biological vs. computer memory



(a) Block diagram

(b) Timing diagram of clock pulses

- Fully digital
- Memory distant to computation
- Memory collected in registers
- Bit-perfect, deterministic
- clocked (>1GHz)

- Analog and digital
- Synaptic Memory at computation
- Memory distributed across network and across neurons
- Synapses are stochastic
- Self-timed, data-driven (1-100Hz)

Artificial neural networks