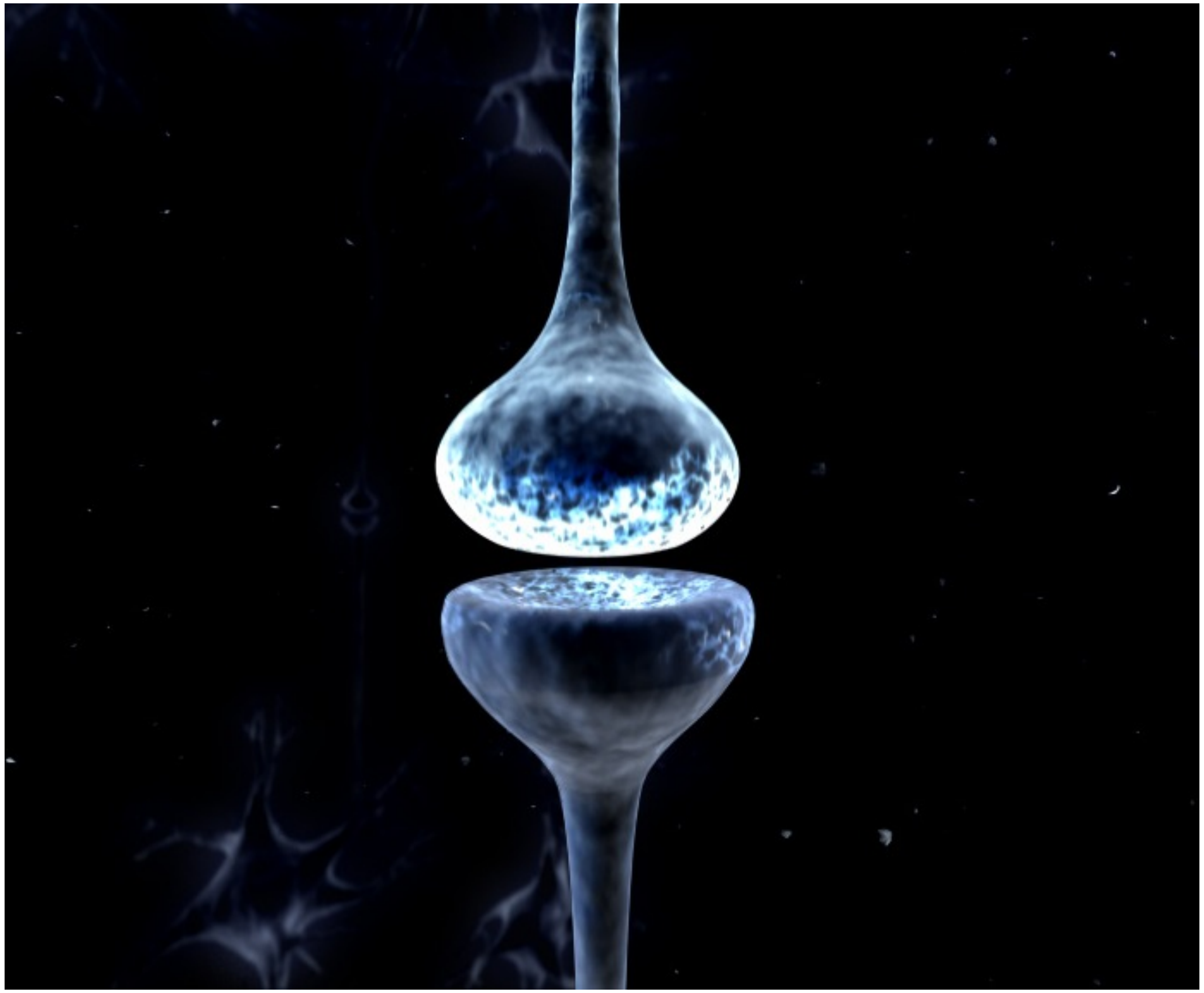
Learning and Plasticity



Benjamin F. Grewe
Introduction to Neuroinformatics,
November 14th, HS 2019

ETH Zürich

University of Zurich UZH

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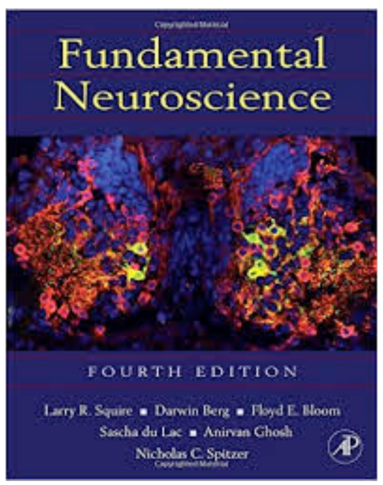

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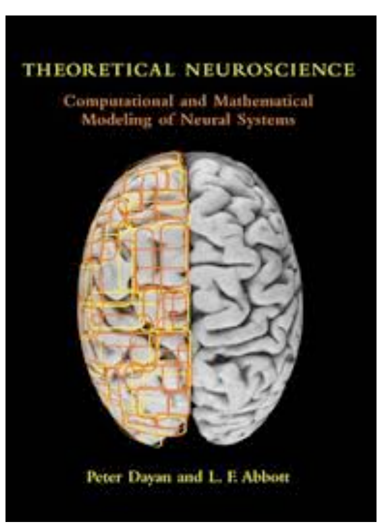

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1. Plasticity in Neuronal Networks
   - <u>Why do we need plasticity/learning?</u>
   - Defining plasticity/learning.
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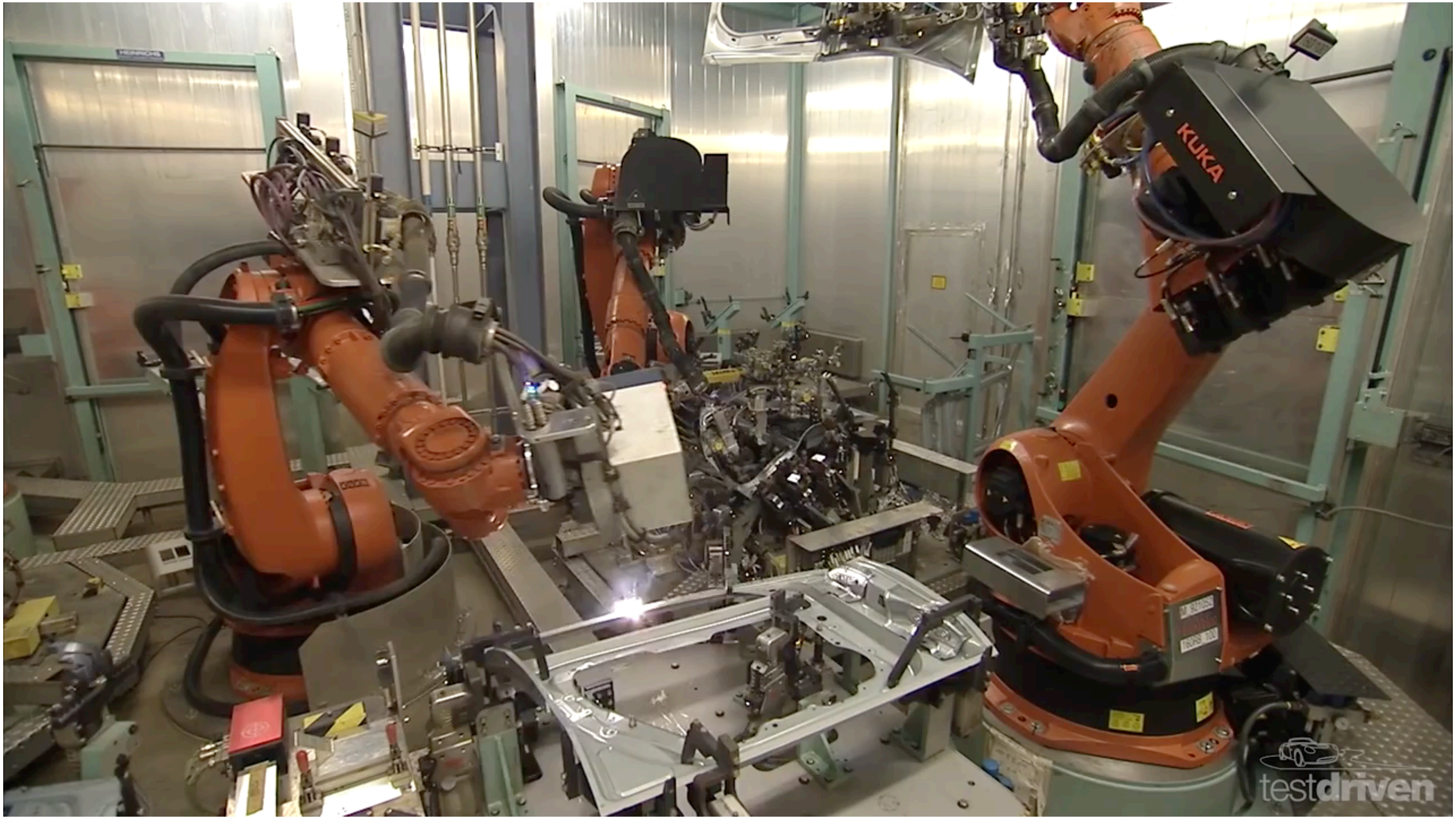
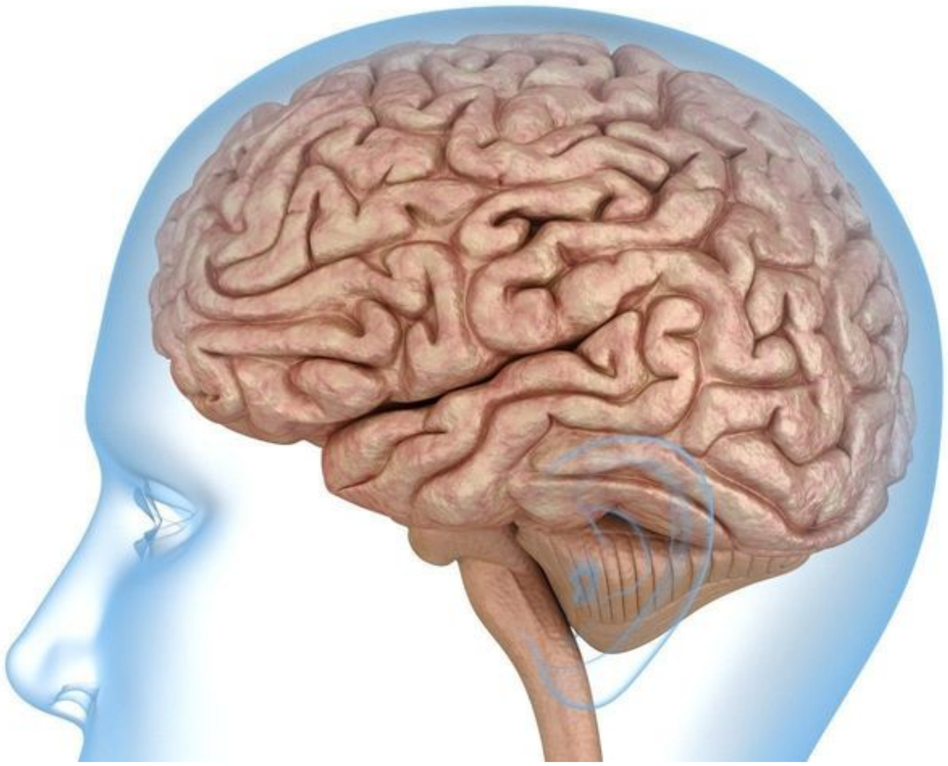
Why do we need learning!



https://www.youtube.com/watch?v=VreG1iC65Lc

Why do we need learning!

Connections in the mammalian Brain are mostly learned.



The human brain has about 10^{11} neurons, and more than 10^3 synapses per neuron. Specifying a connection target requires about $\log_2 10^{11} = 35$ bits/synapse. Thus it would take about 3.5×10^{15} bits (~400 TB) to specify all 10^{14} connections in the brain.

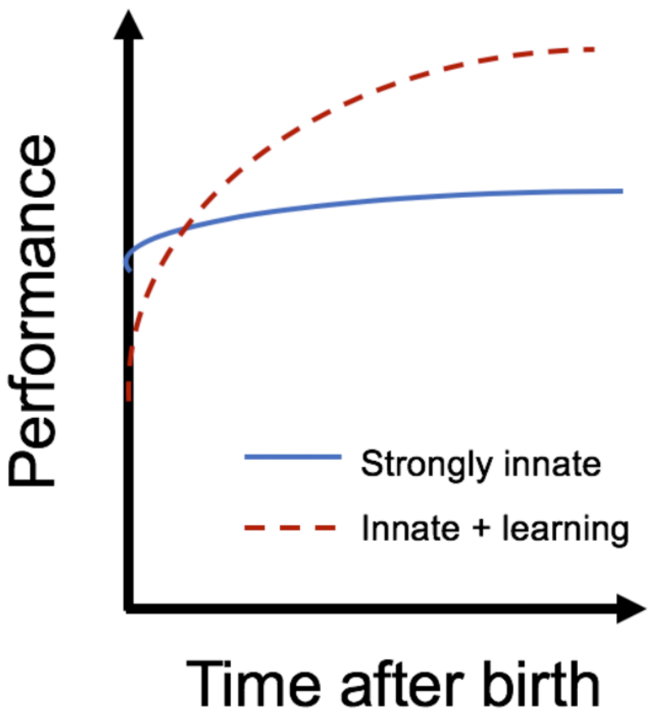
The C.Elegans genome stores all synaptic connections.

The simple worm C. Elegans, for example, has 302 neurons and about 7000 synapses and in each individual of an inbred strain, the wiring pattern is exactly the same (Chen et al., 2006).

Learning as evolutionary survival strategy.

Is the brain a Universal Learning Machine?

A species using the mixed strategy may thrive if that strategy achieves a higher asymptotic level of performance.



A CRITIQUE OF PURE LEARNING: WHAT ARTIFICIAL NEURAL NETWORKS CAN LEARN FROM ANIMAL BRAINS

dx.doi.org/10.1101/582643.

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Cold Spring Harbor Laboratory
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Intelligent Behavior Emerges with Learning!

Intelligent Behavior Emerges with Learning!

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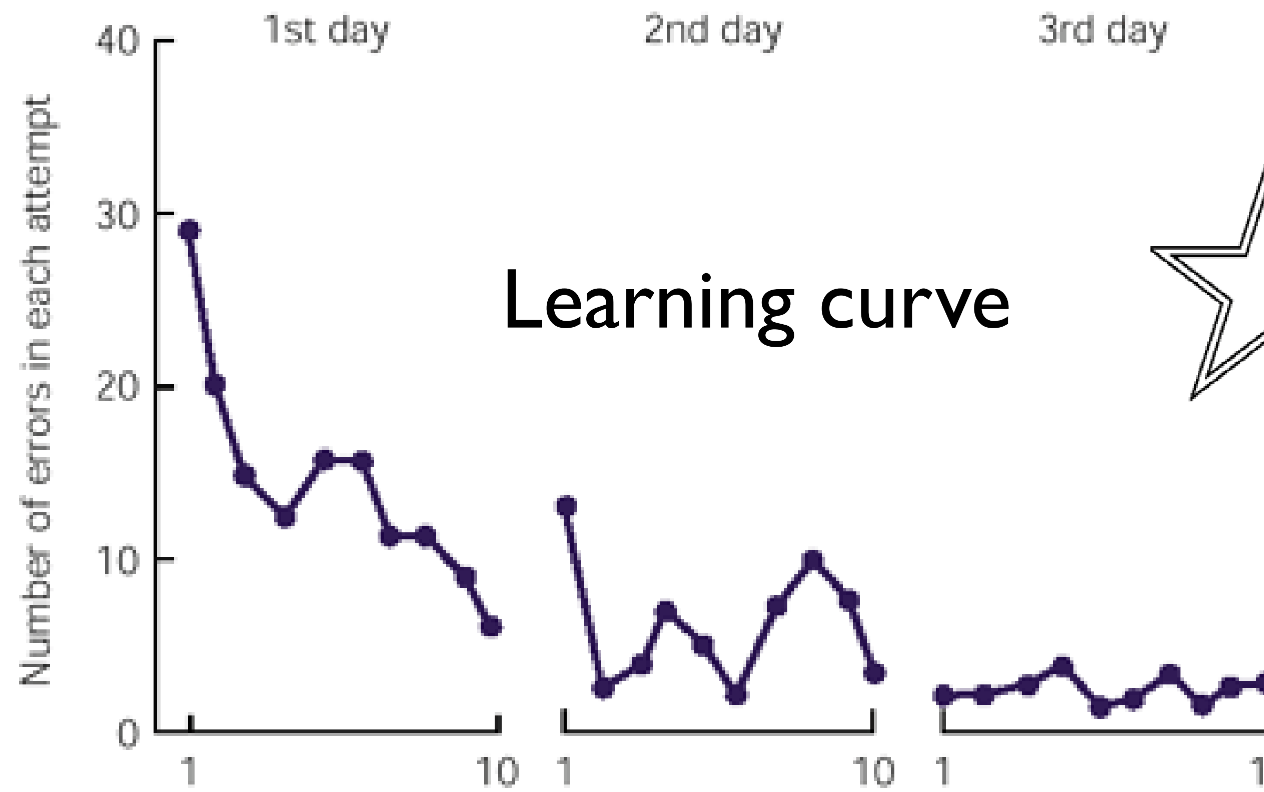
Learning&Memory vs. Plasticity

Learning - The acquisition/storage of knowledge/information or the formation of a memory through experience.

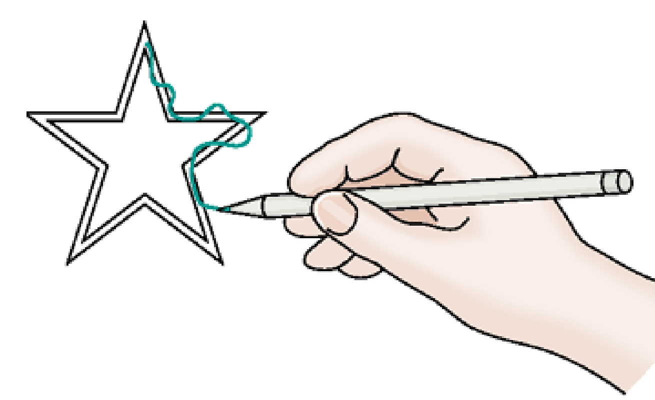
Memory – Stored information that can be recalled at a later stage in time.

- Learning results in memory - which itself has a further outcome - a change in future behaviour.
- Learning does not always imply a conscious attempt to learn. Simple observation can lead to the creation of a new memory.

Plasticity - The biological implementation of learning. Plasticity allows us to form a memory.

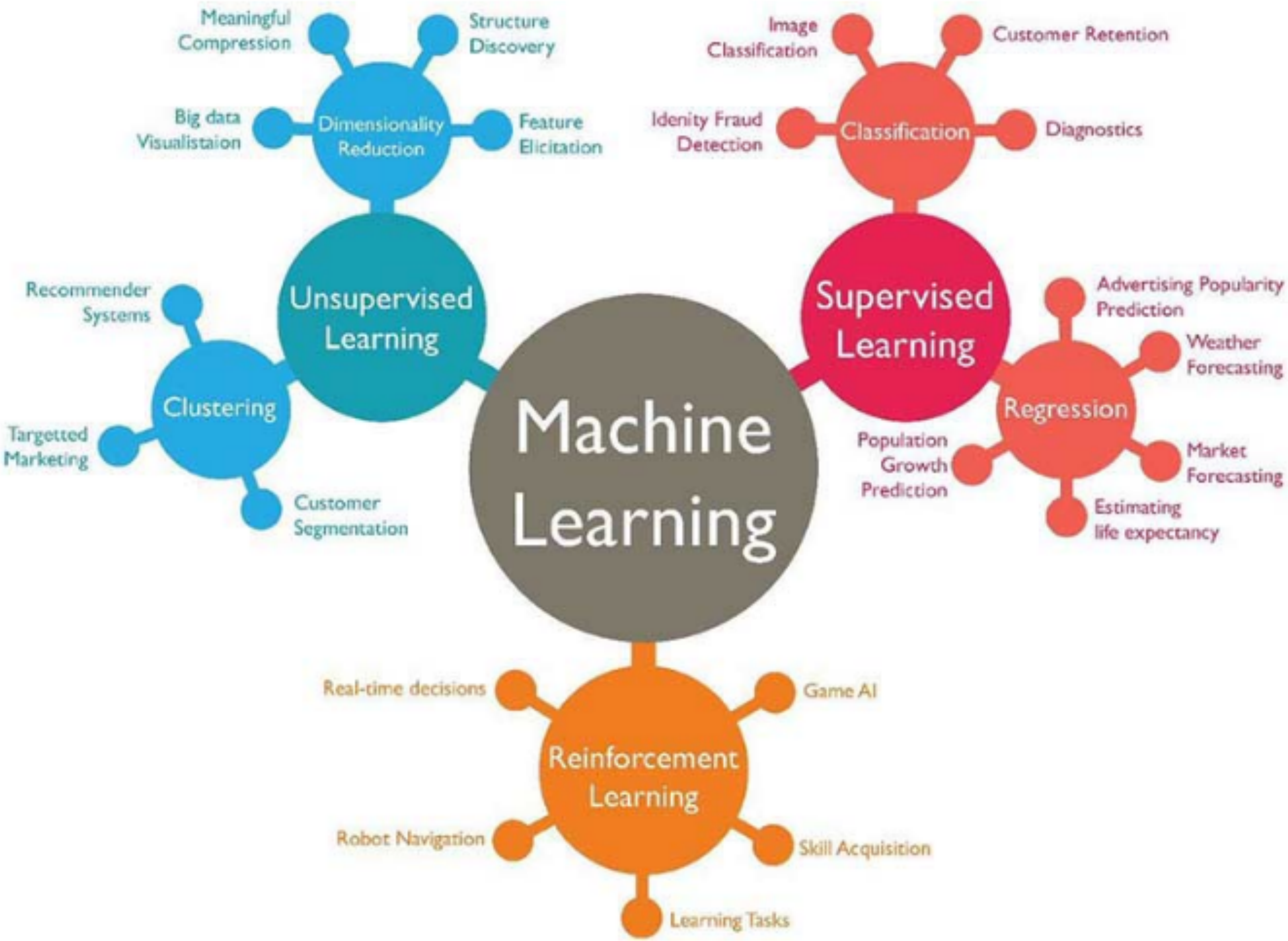


Learning curve



Kandel, *Principles of neural science*, 2001

Learning in Computer Science

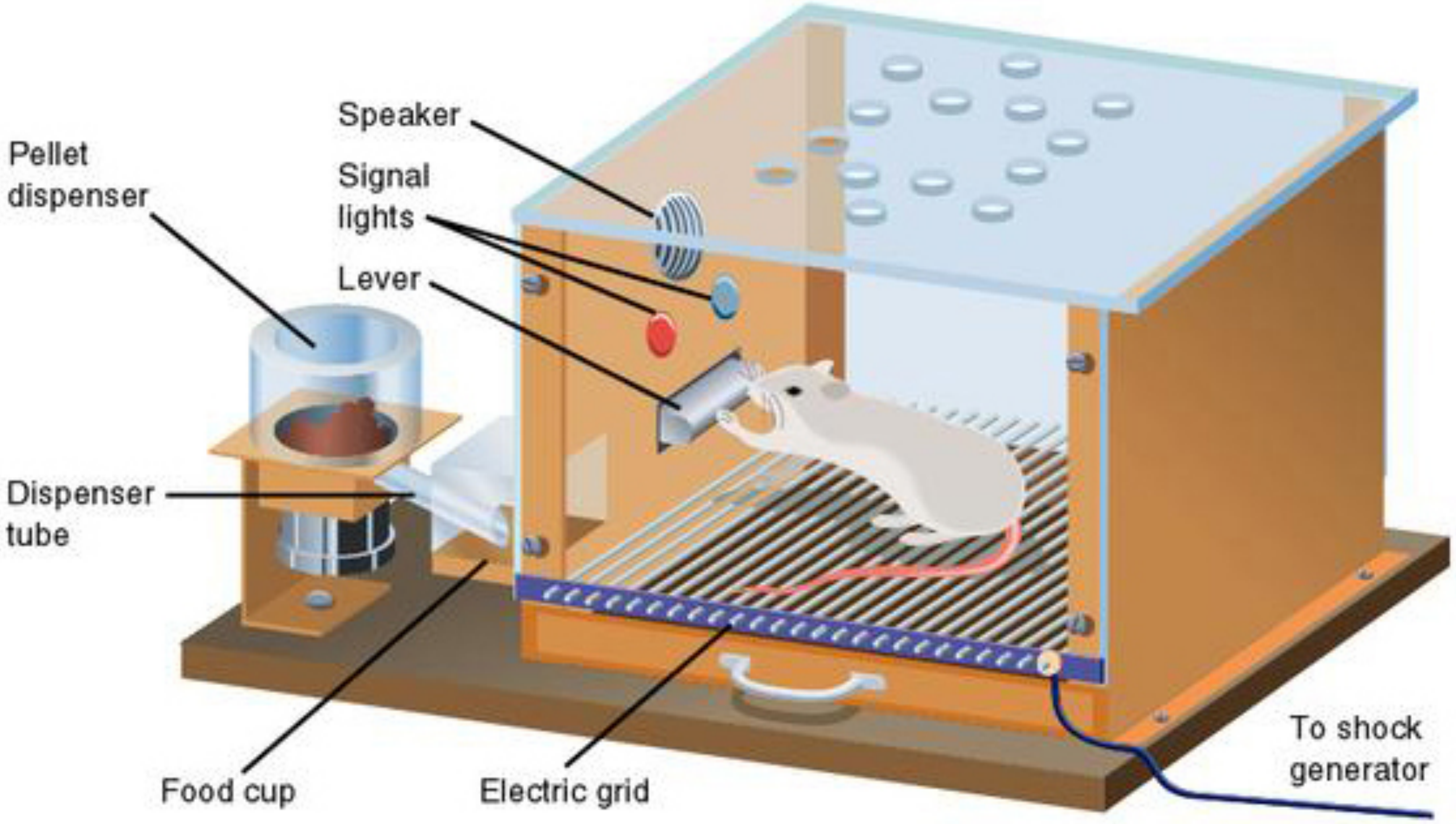


Learning in Neuro-Science

- Pavlovian Conditioning
- Instrumental Conditioning
- Reward/Aversive Learning
- Social Learning
- Perceptual Learning
- Motor Learning

Pav. Fear Cond.

Instrumental Cond.



Types of Biological Memory.

Memory is fundamental to the discipline of psychiatry and neuroscience.

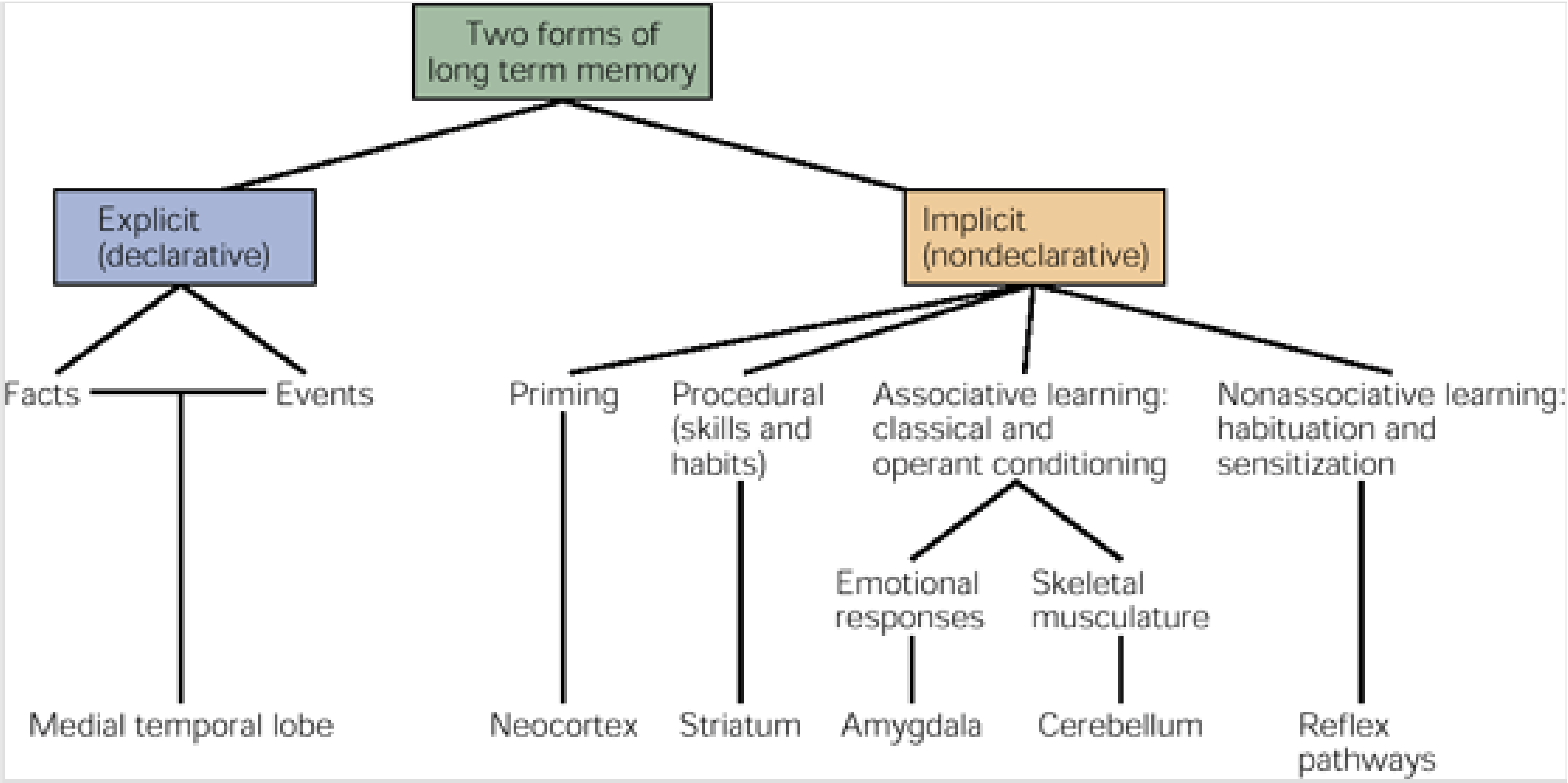
Our memory stores:

- Our personal experiences
- Emotions
- Preferences/dislikes
- Motor skills
- World knowledge
- Language
- Cognitive Memories
- Spatial Memories

Fundamentally, we are derived from ‘learning’ experiences that have been stored in our nervous system.

Kandel, *Principles of neural science*, 2001

Psychological Categorization of Memory



Kandel, *Principles of neural science*, 2001

Further examples of each form of memory

Events

Facts

$$\pi = 3.1415\ldots$$

Priming

presented words during training

during recall

ABSENT

INCOME

FILLY

DISCUSS

CHEESE

ELEMENT

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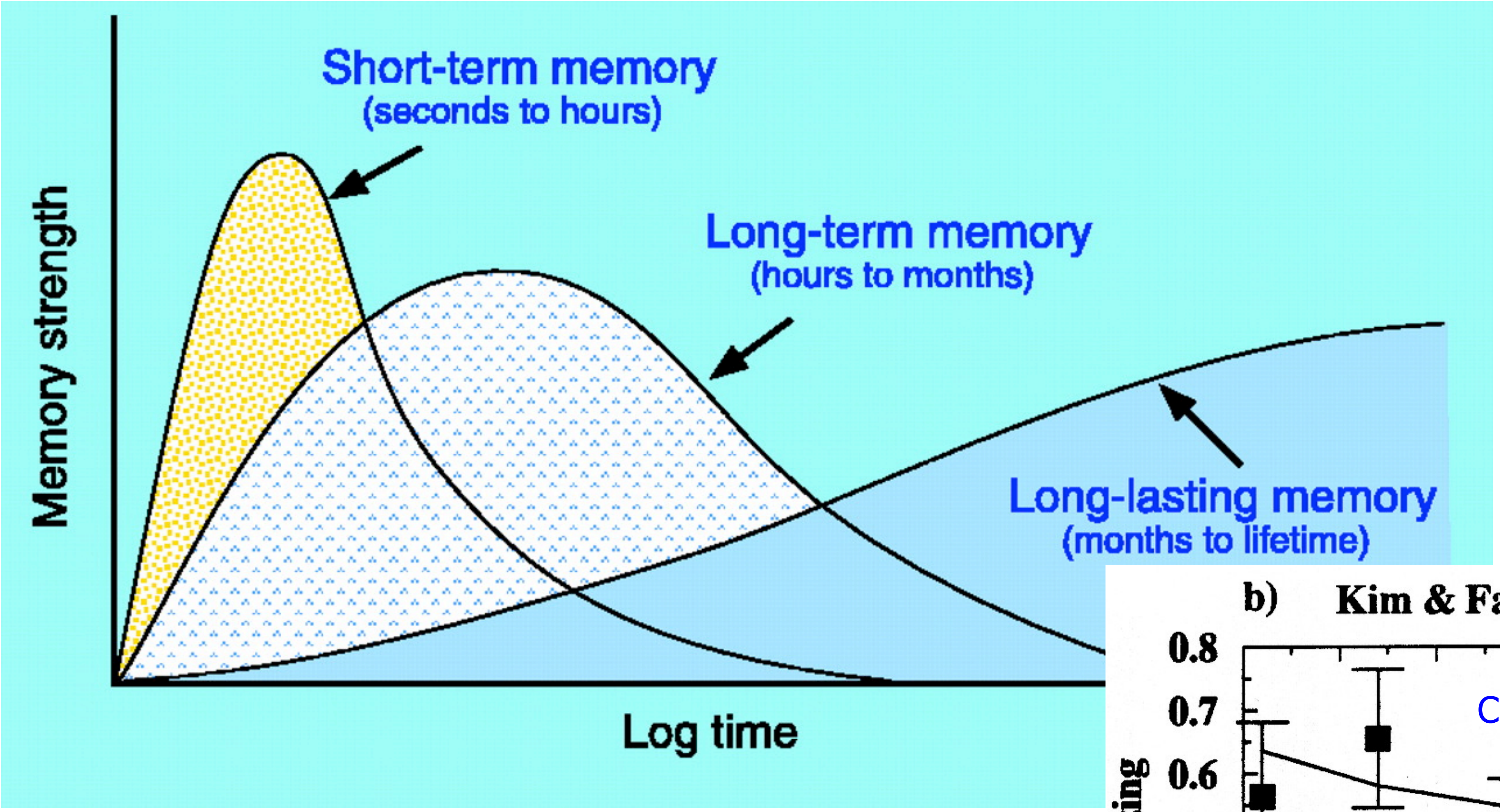
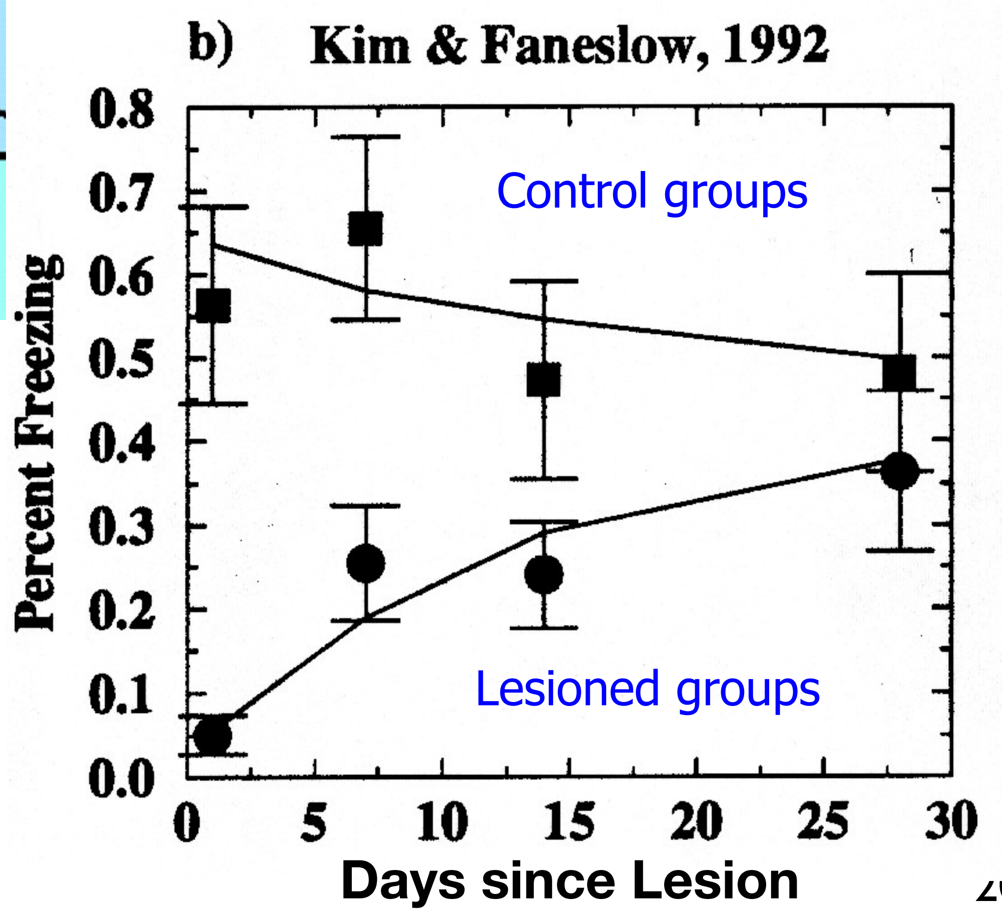
The Concept of Short- and Long-term Memory





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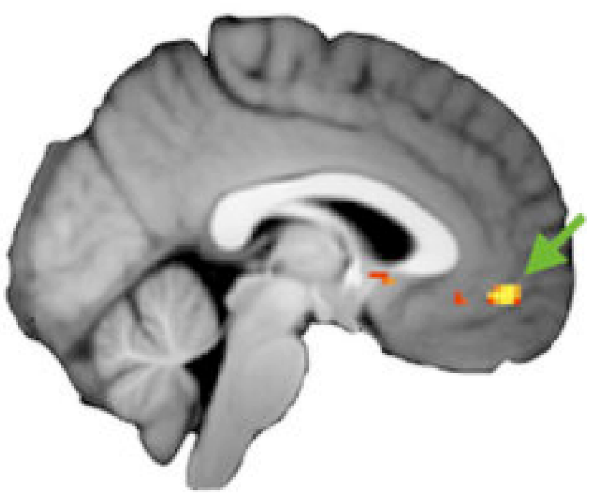
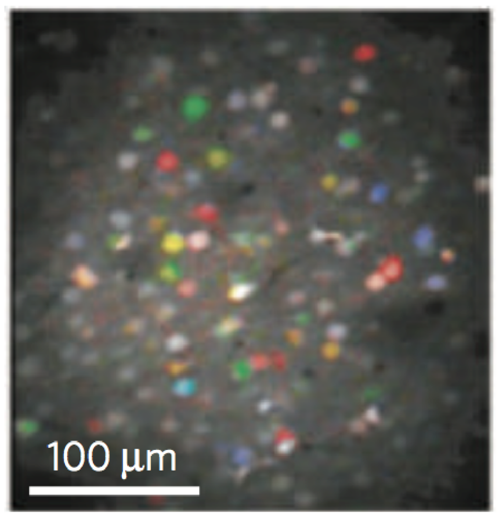
Neural Substrates of Plasticity.

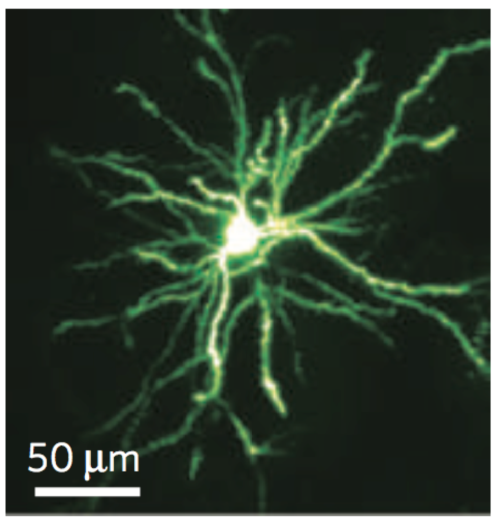
Brain Area



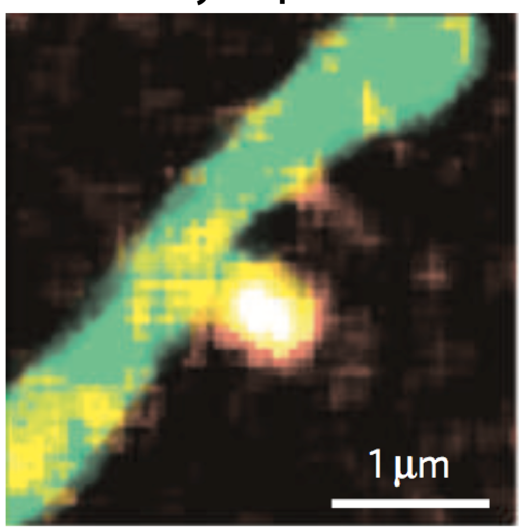
Local Brain Circuit



Neuron

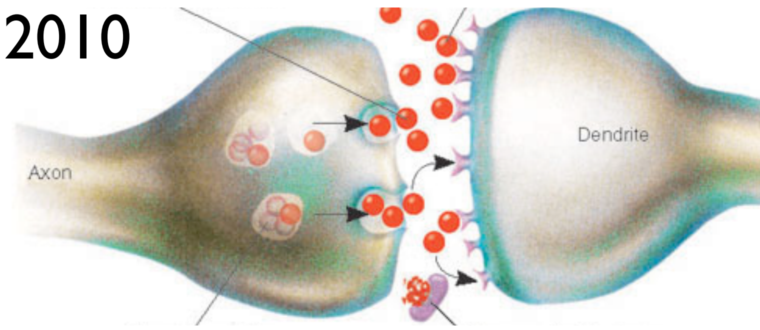


Synapse



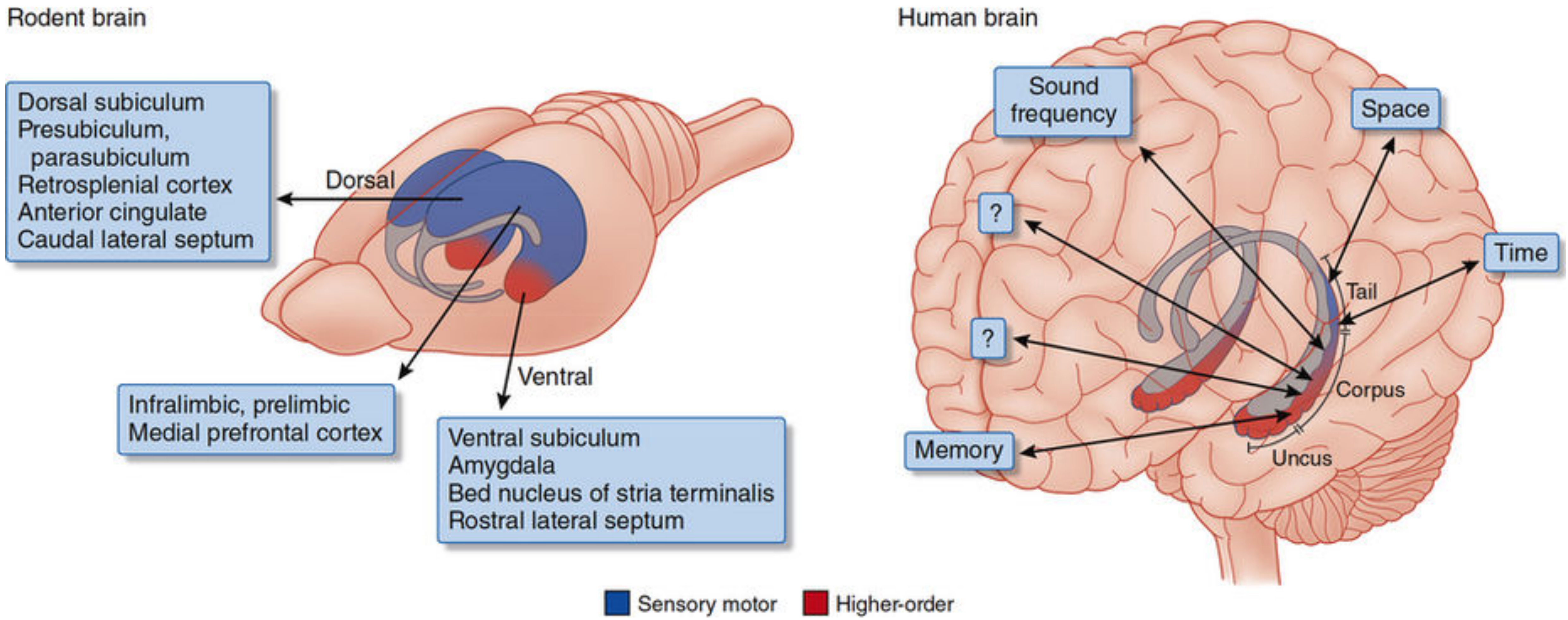
Scale | centimeter | millimeter | hundreds of micrometers | micrometer | nanometer

Mozzachoidi, 2010

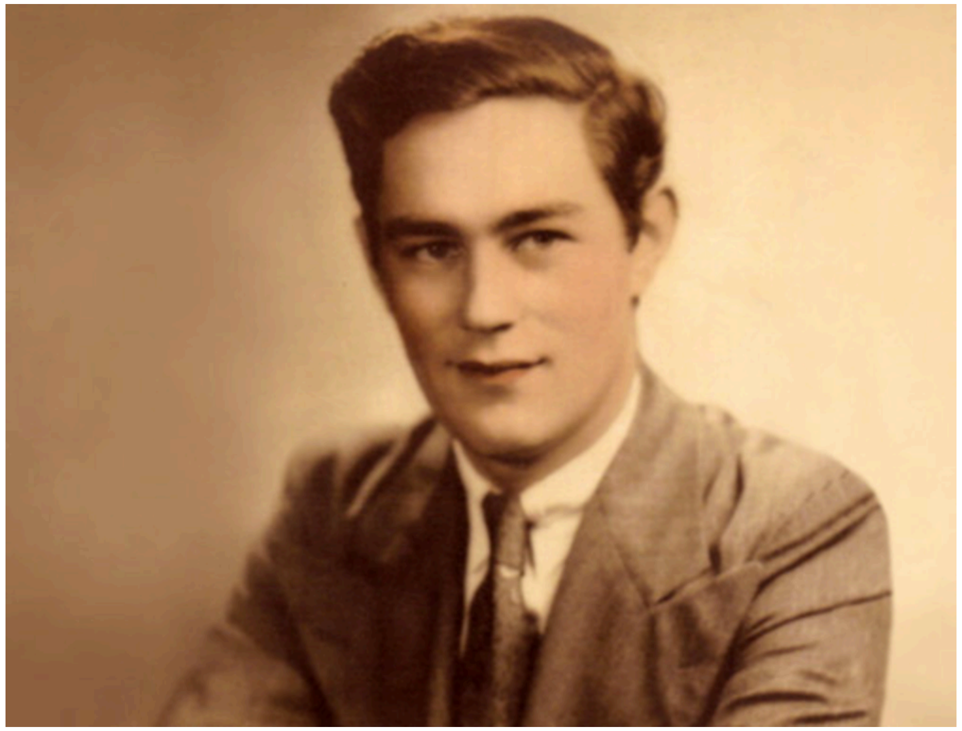


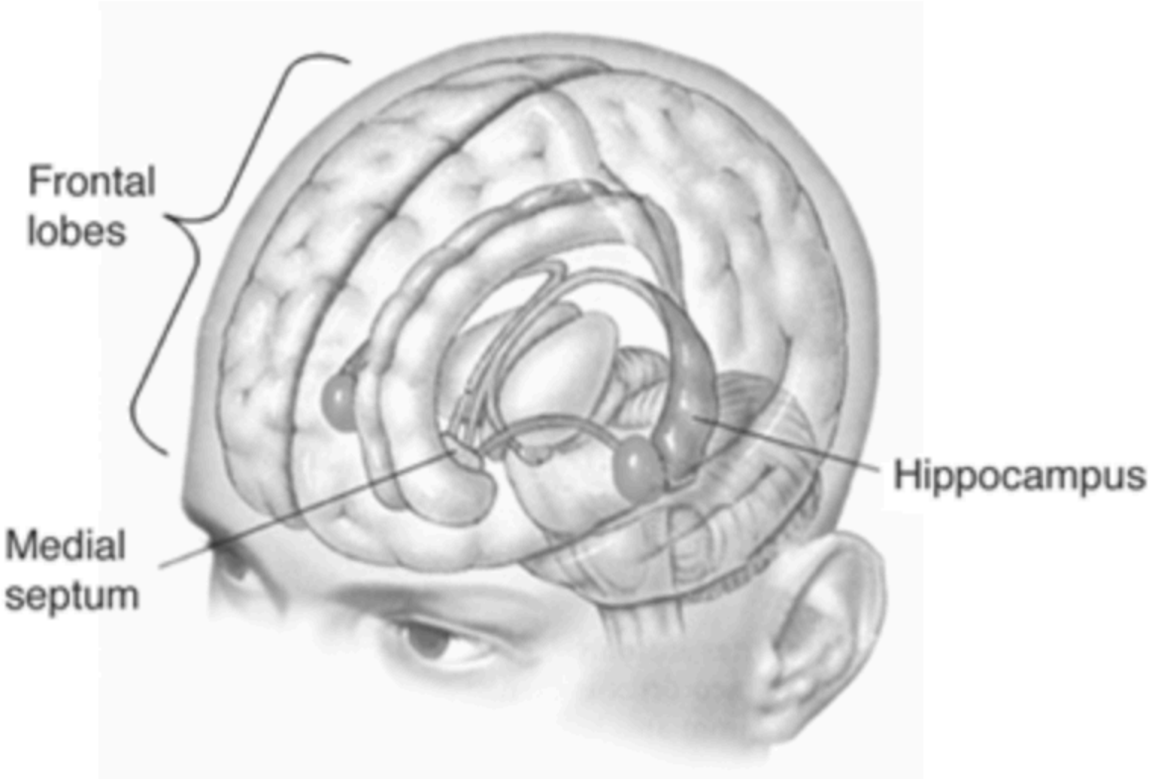
Molecules

The Hippocampus as a Model System to Study Learning and Memory



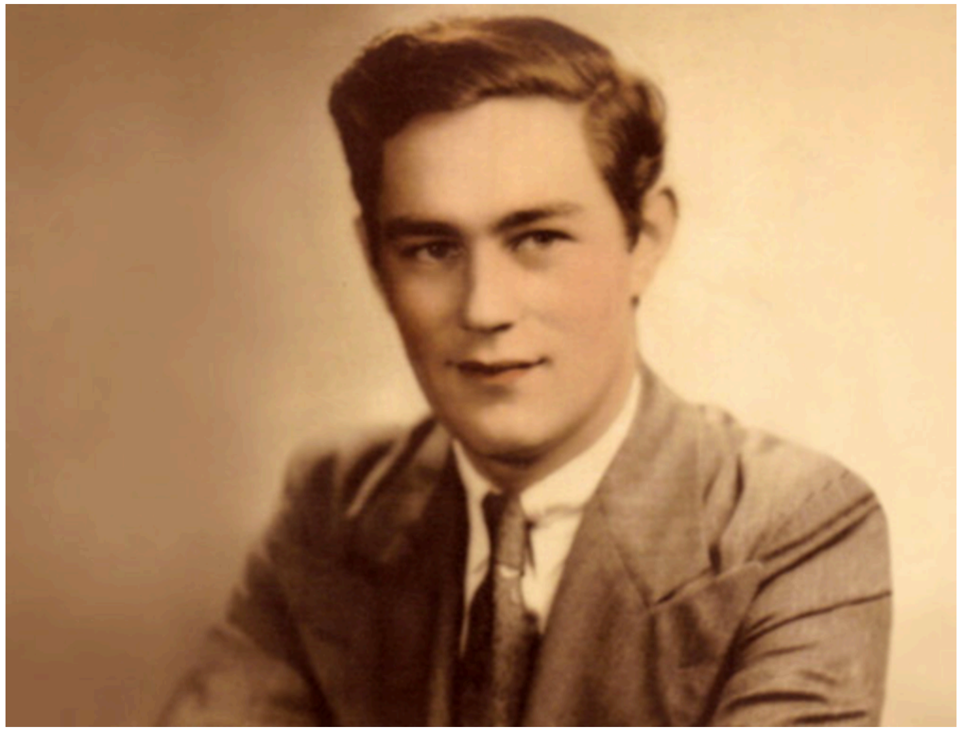
Henry Gustav Mollison (H.M.) 1926-2008





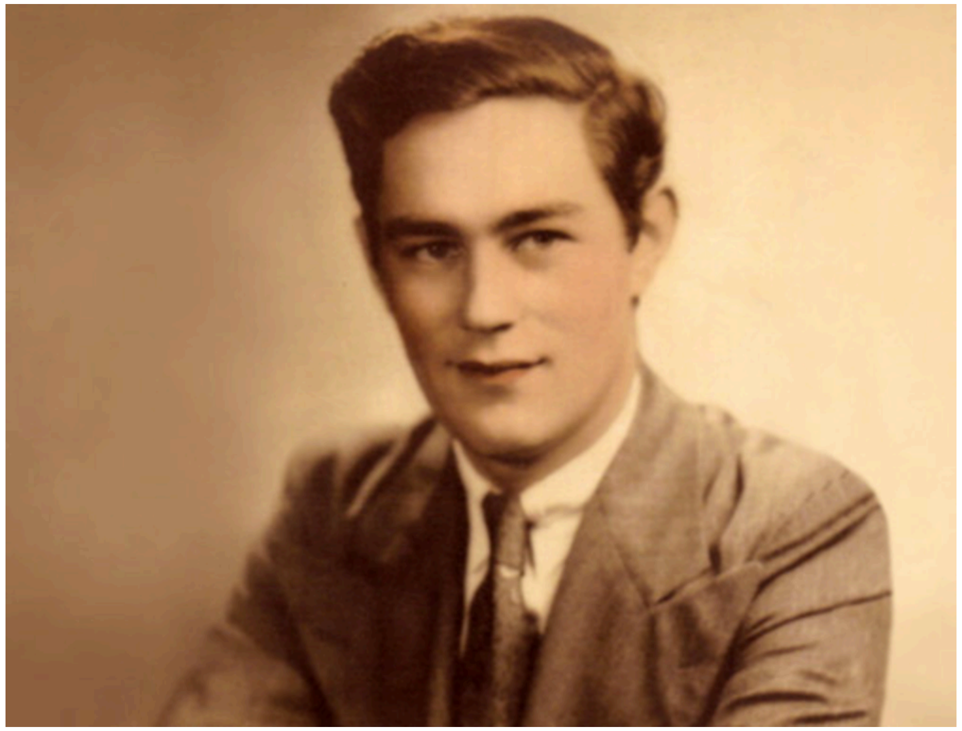
Amygdala, hippocampal
gyrus, and anterior two thirds of the
hippocampus were removed.

Henry Gustav Mollison (H.M.) 1926-2008



Diagnosis: Severe anterograde amnesia
• normal STM
• Normal LTM (for events prior to surgery)
• Problem: transfer from STM to LTM
• Could not consolidate new declarative knowledge
• Capable of acquiring implicit knowledge

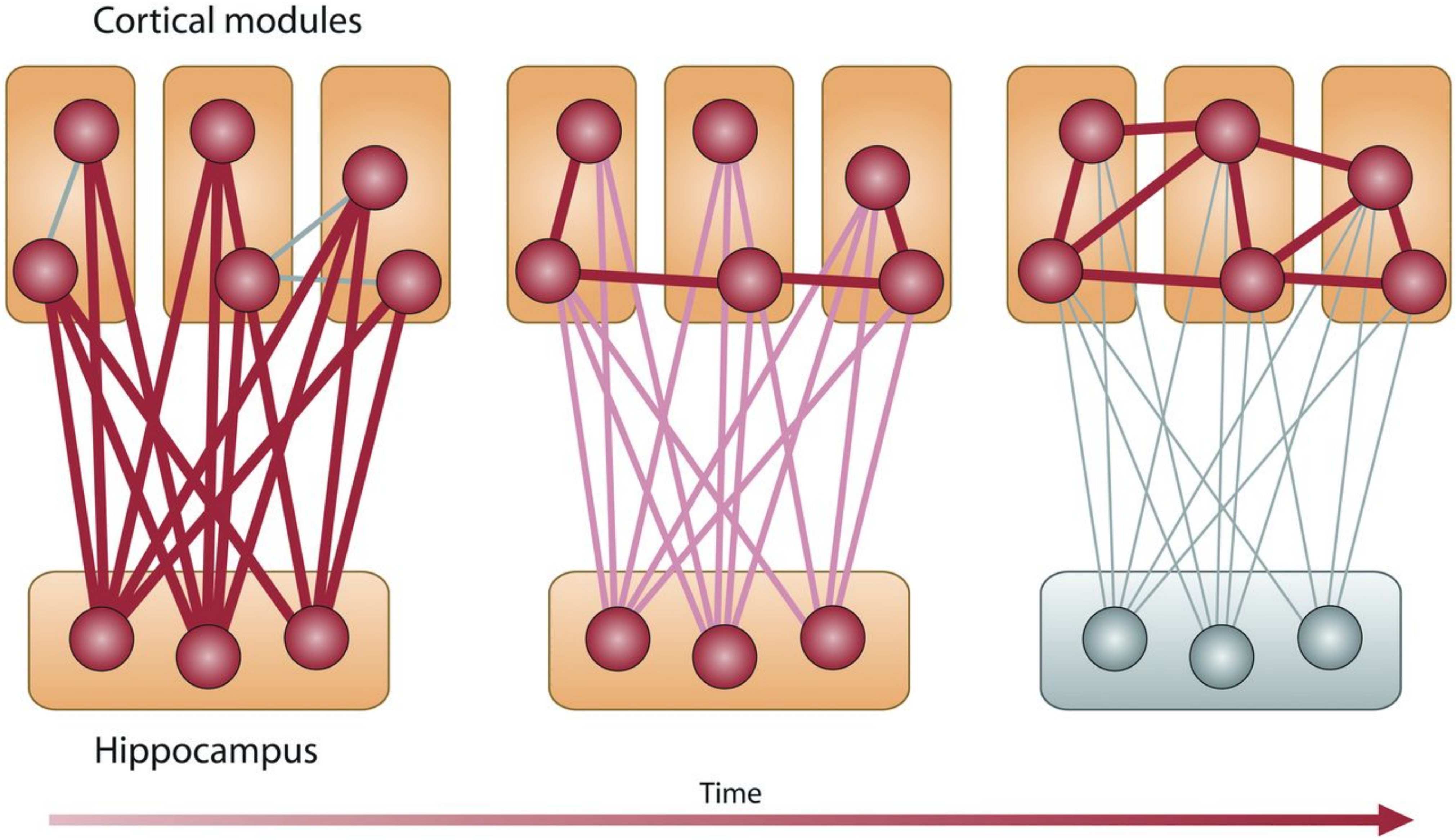
Henry Gustav Mollison (H.M.) 1926-2008



Conclusions:

- The Hippocampus is not a permanent storage area for explicit knowledge.
- The hippocampus is involved [with other cortical areas] in consolidation, a longer term process taking months to years (note retrograde amnesia in hippocampus lesion patients for up to 3 yrs).
- Consolidation is understood to involve biological changes taking place in those other areas of cortex,
- Once this has fully taken place, the hippocampus is not required for retrieval.

Henry Gustav Mollison (H.M.) 1926-2008



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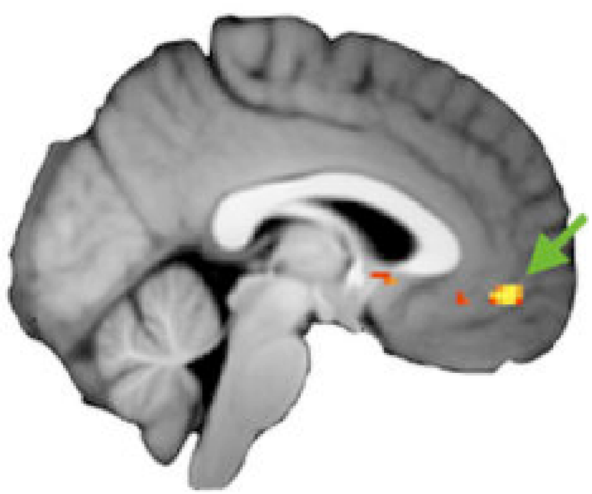
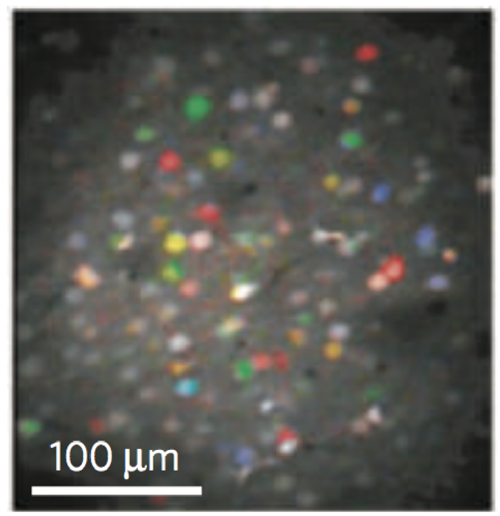
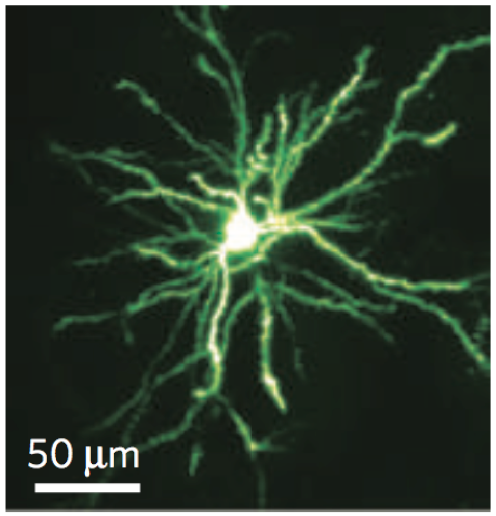


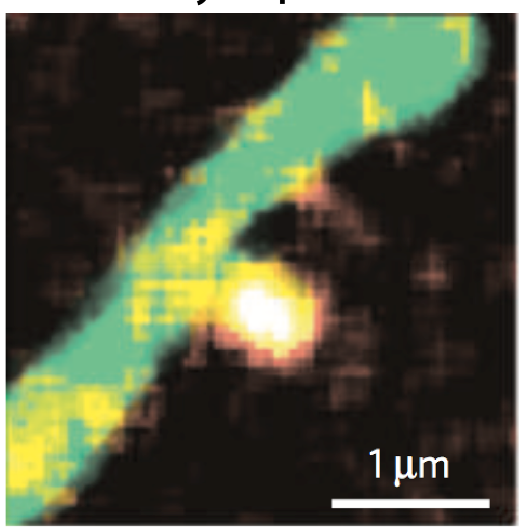
Local Brain Circuit



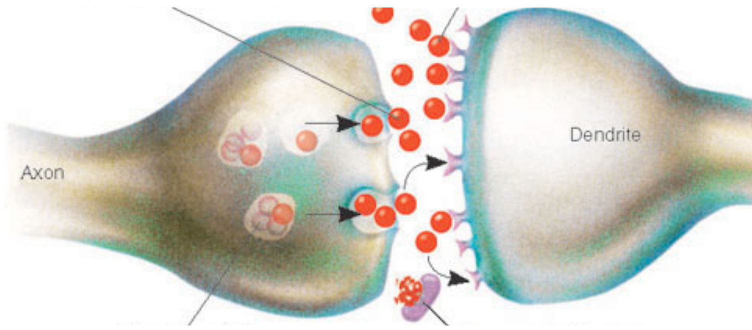
Neuron



Synapse



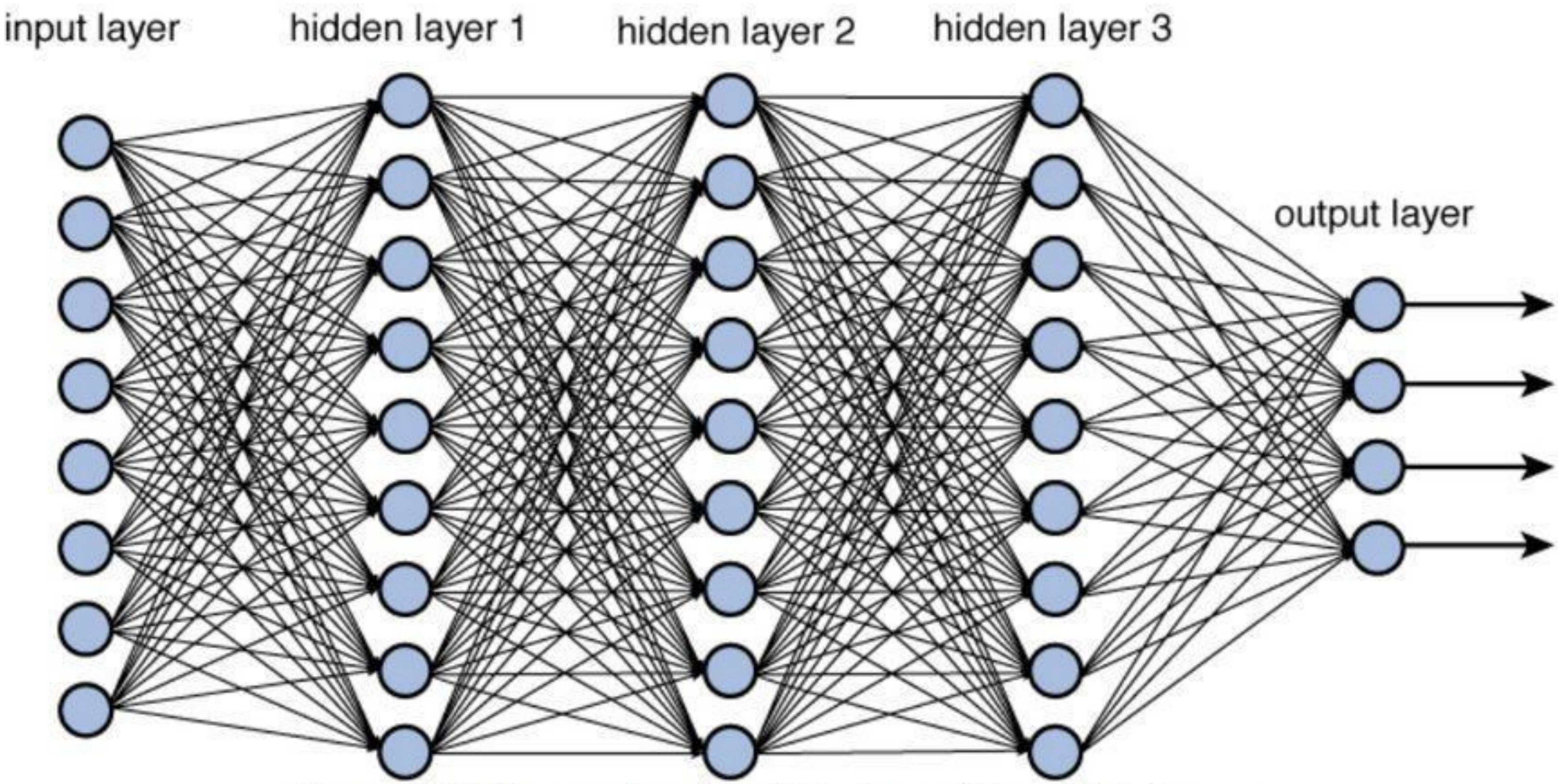
Scale — centimeter — millimeter — hundreds of micrometers — micrometer — nanometer



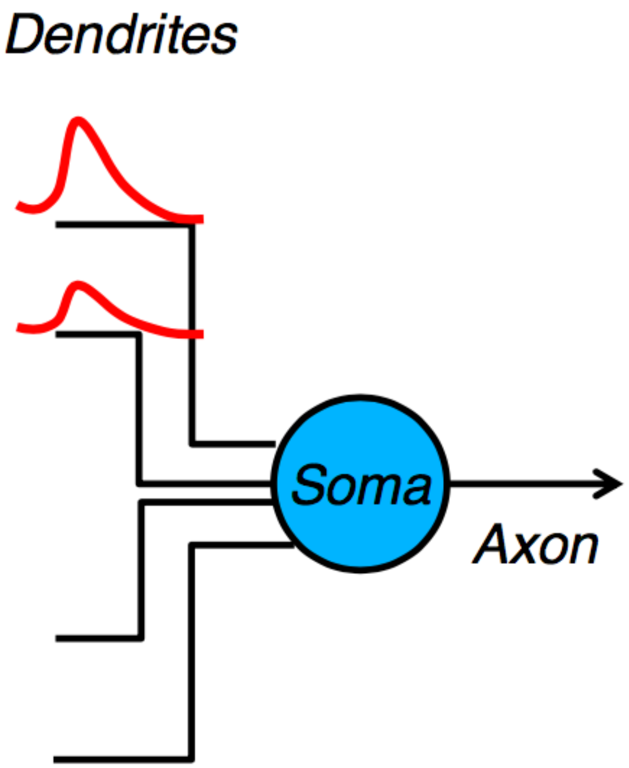
Molecules

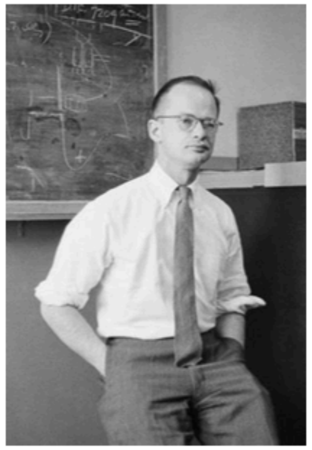
Mozzachoidi, 2010

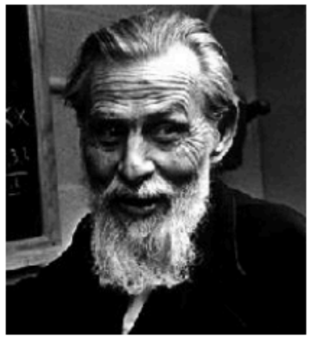
Training the weights of a deep neuronal network.

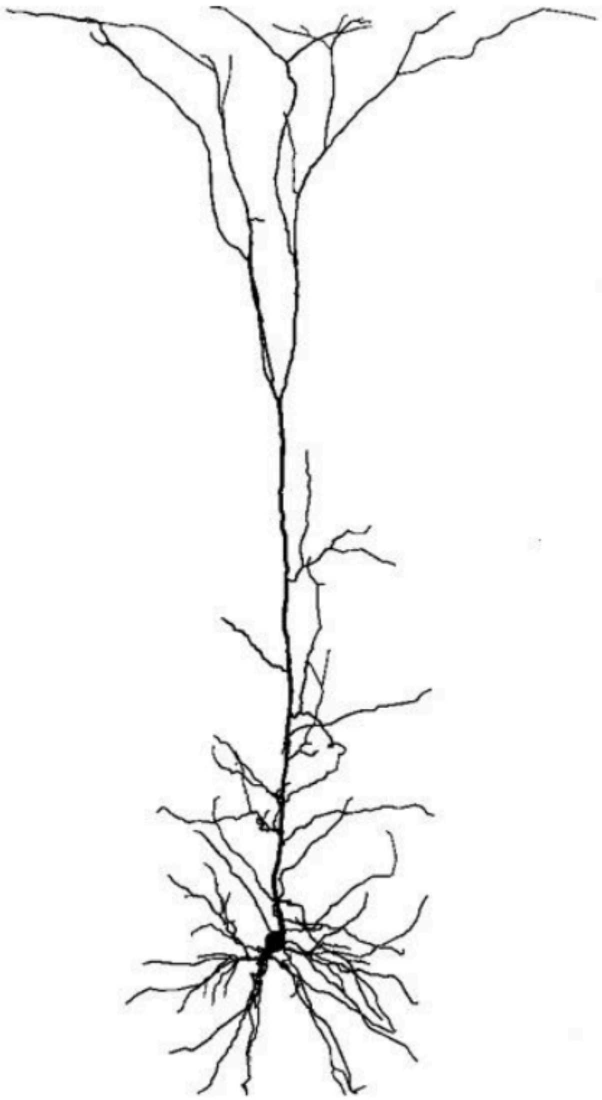


What can we learn form the Brain?



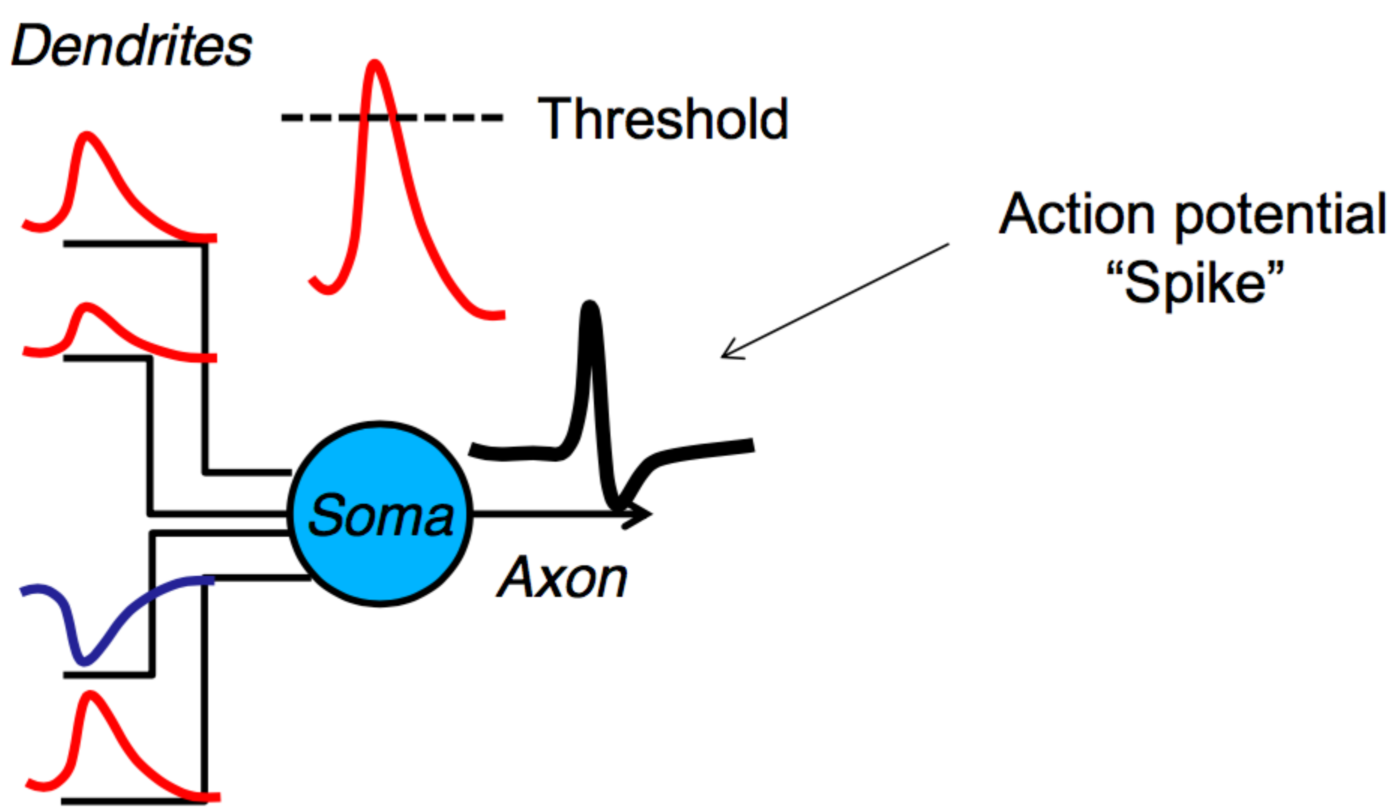






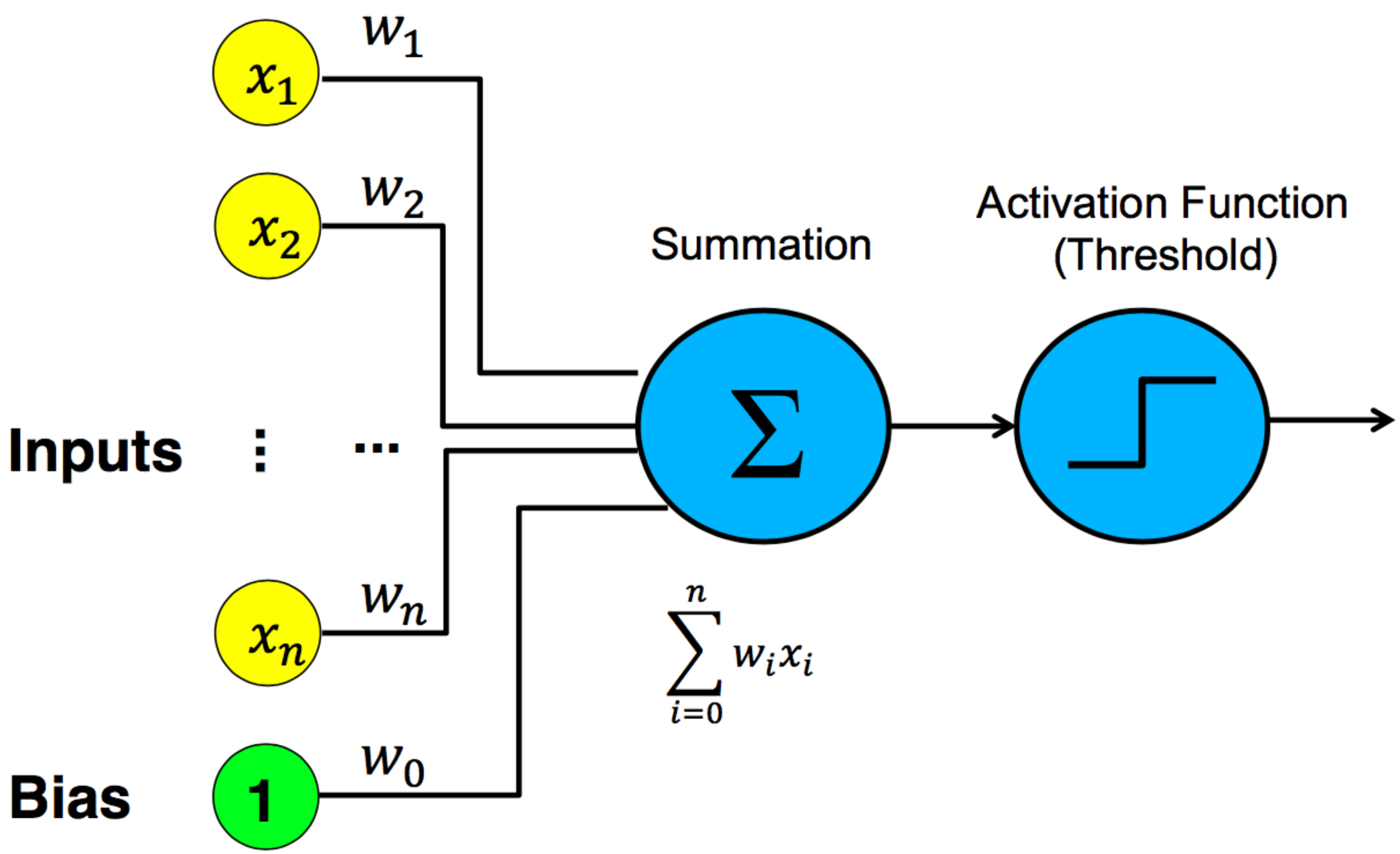
McCulloch & Pitts, 1943

What can we learn form the Brain?

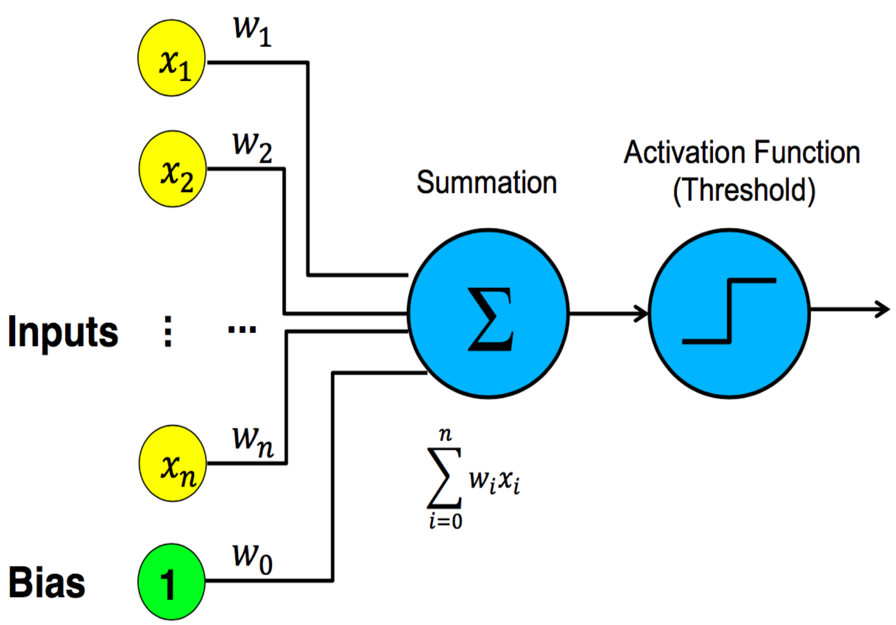


McCulloch & Pitts, 1943

The McCulloch & Pitts Neuron AKA The Perceptron



The Perceptron

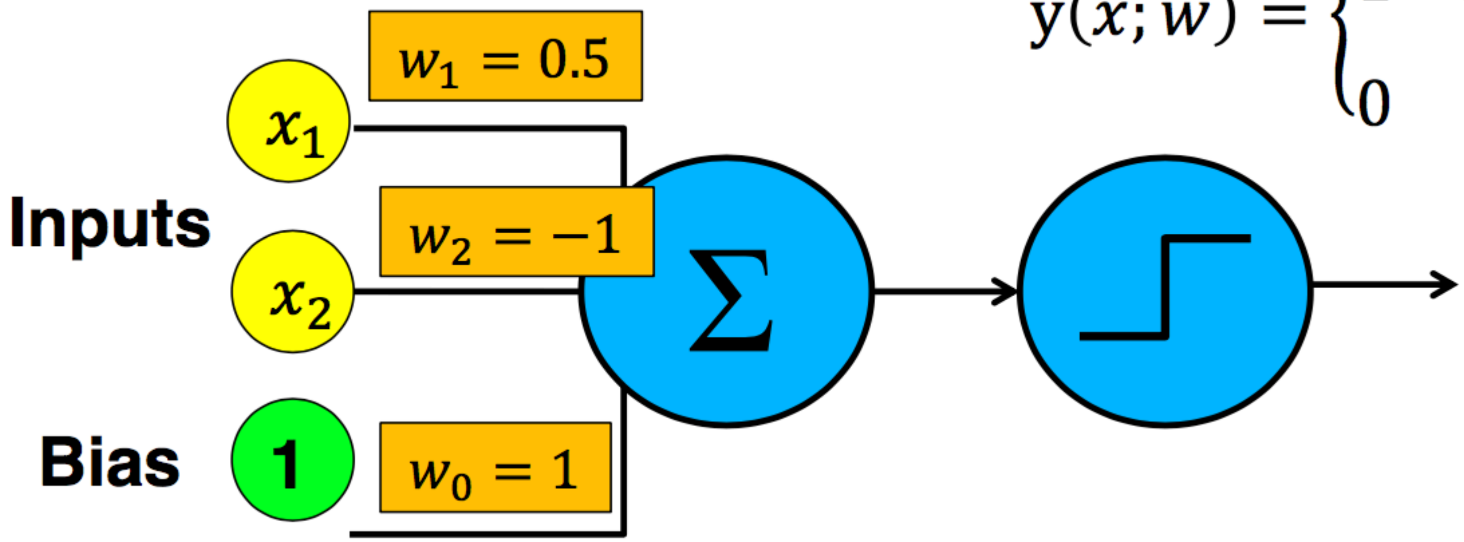


$$\text{output} = \begin{cases} 0 & \text{if } \sum_j w_j x_j \leq \text{ threshold} \\ 1 & \text{if } \sum_j w_j x_j > \text{ threshold} \end{cases} \tag{1}$$

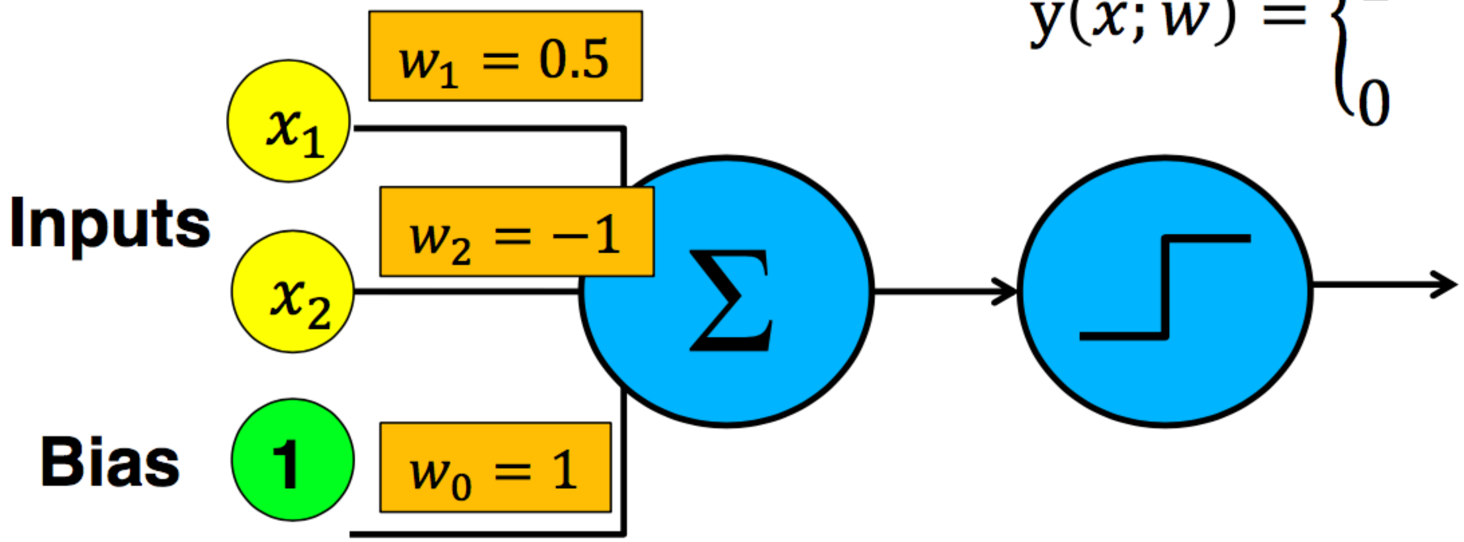
$$\text{output} = \begin{cases} 0 & \text{if } w \cdot x + b \leq 0 \\ 1 & \text{if } w \cdot x + b > 0 \end{cases} \tag{2}$$

The Perceptron

$$y(\vec{x};\vec{w}) = \begin{cases} 1 & \text{if } \sum_{i=0}^{n} w_i x_i > 0 \\ 0 & \text{otherwise} \end{cases}$$



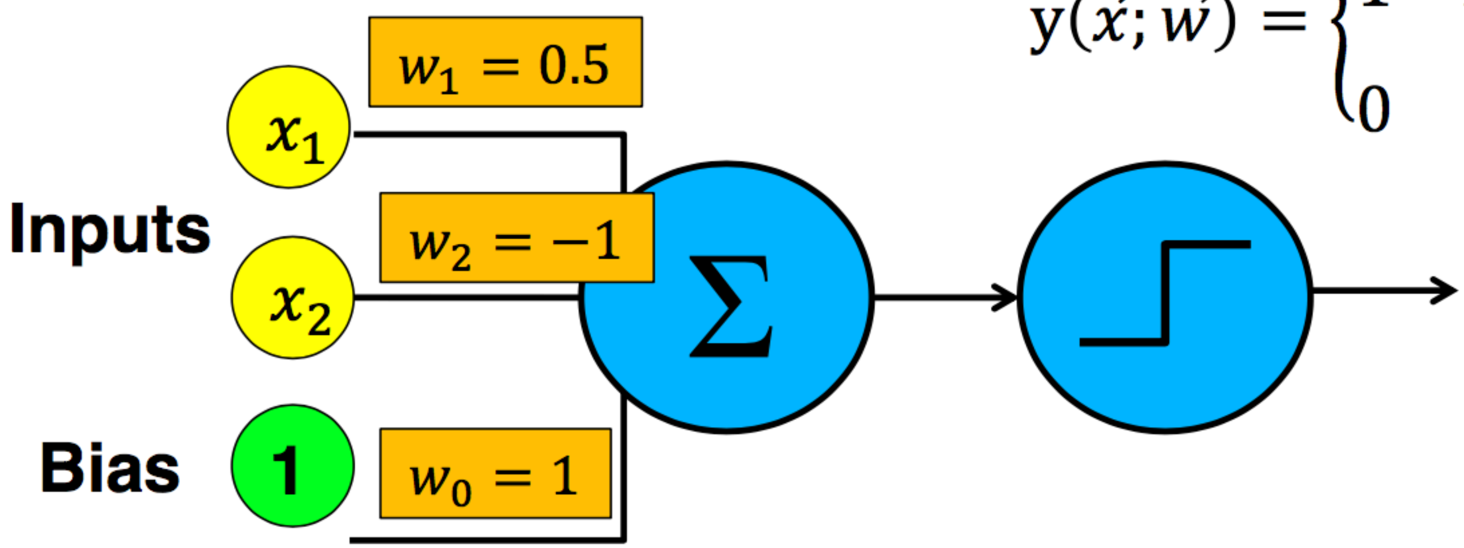
The Perceptron



$$y(\vec{x};\vec{w}) = \begin{cases} 1 & \text{if } \sum_{i=0}^{n} w_i x_i > 0 \\ 0 & \text{otherwise} \end{cases}$$

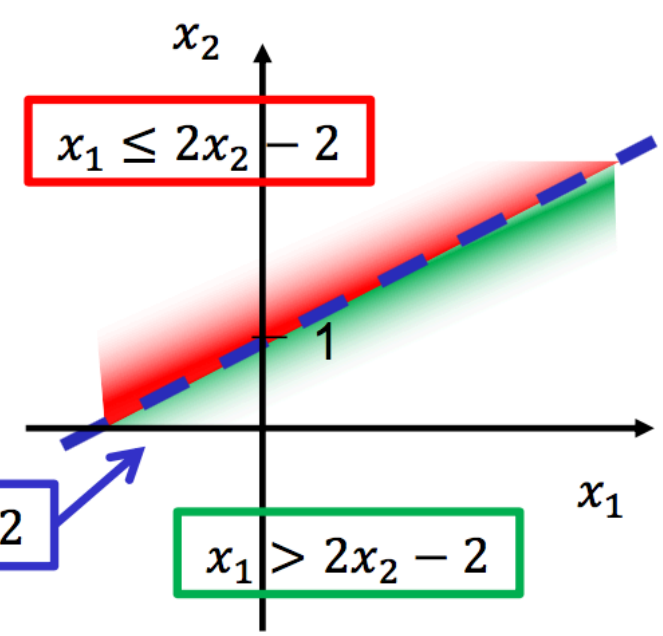
$$\begin{aligned} y(\vec{x};\vec{w}) = 1 &\Leftrightarrow w_1 x_1 + w_2 x_2 + w_0 \\ &= 0.5\, x_1 - x_2 + 1 > 0 \Leftrightarrow x_1 > 2x_2 - 2 \end{aligned}$$

The Perceptron



$$y(\vec{x};\vec{w}) = \begin{cases} 1 & \text{if } \sum_{i=0}^{n} w_i x_i > 0 \\ 0 & \text{otherwise} \end{cases}$$

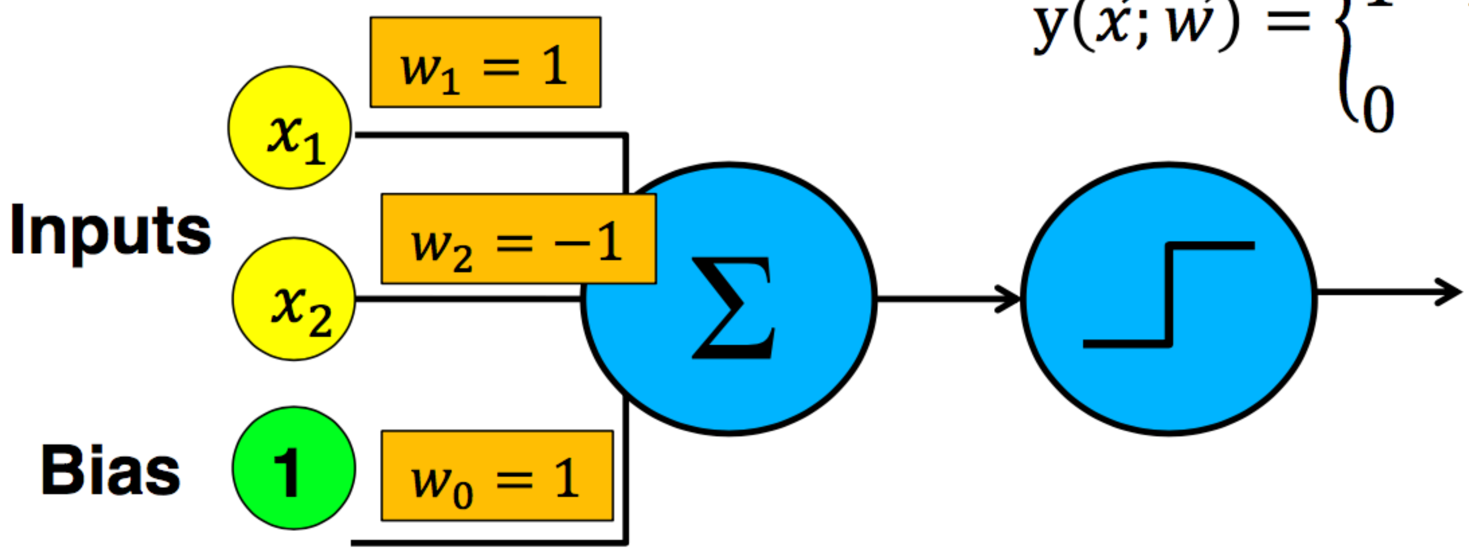
$$y(\vec{x};\vec{w}) = 1 \Leftrightarrow w_1 x_1 + w_2 x_2 + w_0$$
$$= 0.5\, x_1 - x_2 + 1 > 0 \Leftrightarrow x_1 > 2x_2 - 2$$



<u>Decision Boundary:</u> $x_1 = 2x_2 - 2$

What can this neuron do?

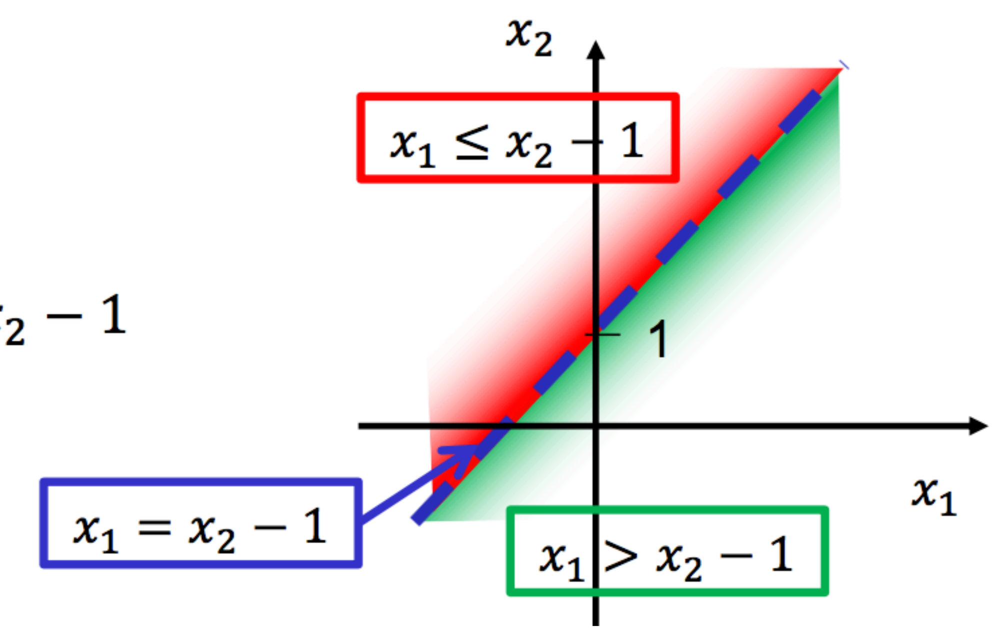
The Perceptron



$$y(\vec{x};\vec{w}) = \begin{cases} 1 & \text{if } \sum_{i=0}^{n} w_i x_i > 0 \\ 0 & \text{otherwise} \end{cases}$$

$$y(\vec{x};\vec{w}) = 1 \Leftrightarrow w_1 x_1 + w_2 x_2 + w_0$$
$$= x_1 - x_2 + 1 > 0 \Leftrightarrow x_1 > x_2 - 1$$

Decision Boundary:



The Perceptron Learning Algorithm

Algorithm: Perceptron Learning Algorithm

$P \leftarrow inputs \quad with \quad label \quad 1;$
$N \leftarrow inputs \quad with \quad label \quad 0;$
Initialize $\mathbf{w}$ randomly;
while !*convergence* **do**
    Pick random $\mathbf{x} \in P \cup N$;
    if $\mathbf{x} \in P \quad and \quad \mathbf{w}.\mathbf{x} < 0$ **then**
        $\mathbf{w} = \mathbf{w} + \mathbf{x}$;
    end
    if $\mathbf{x} \in N \quad and \quad \mathbf{w}.\mathbf{x} \geq 0$ **then**
        $\mathbf{w} = \mathbf{w} - \mathbf{x}$;
    end
end
//the algorithm converges when all the inputs are classified correctly

The Perceptron

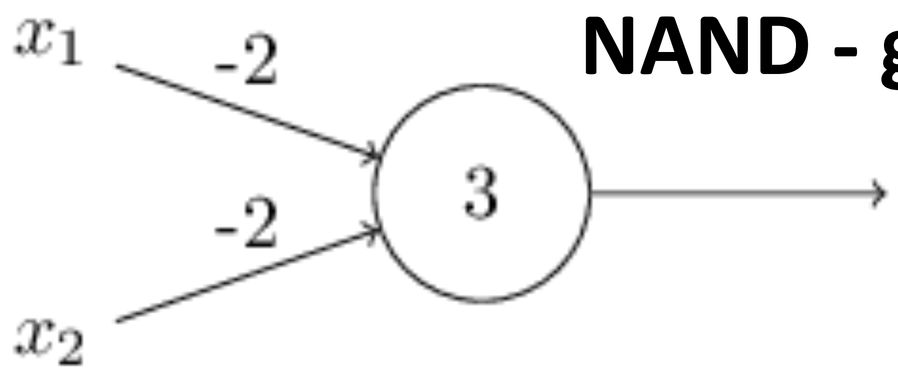
x_1	x_2	x_1 *AND* x_2
0	0	0
0	1	0
1	0	0
1	1	1

Can a McCulloch-Pitts neuron implement this function?

How should the weights be set?

The Perceptron

Which Logical Function does this Perceptron realize?



NAND - gate

Check 00 produces output 1, since $(-2)*0+(-2)*0+3=3$ is positive
01 and 10 produce output 1
11 produces output 0, since $(-2)*1+(-2)*1+3=-1$ is negative

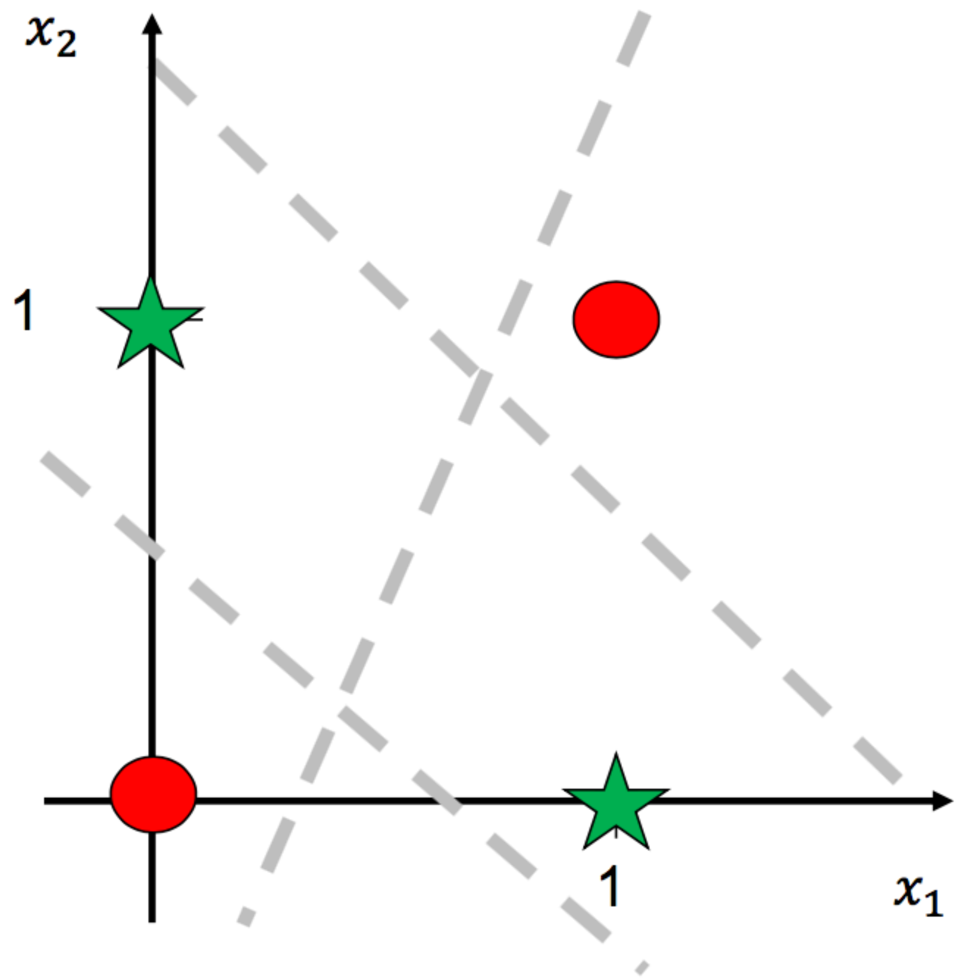
The Perceptron

- OR gate: $w_1 = 1, w_2 = 1, w_0 = -0.5$
- NOT gate: $w_1 = -1, w_0 = 0.5$

Can all logical operations be implemented by a McCulloch-Pitts neuron?

The Perceptron

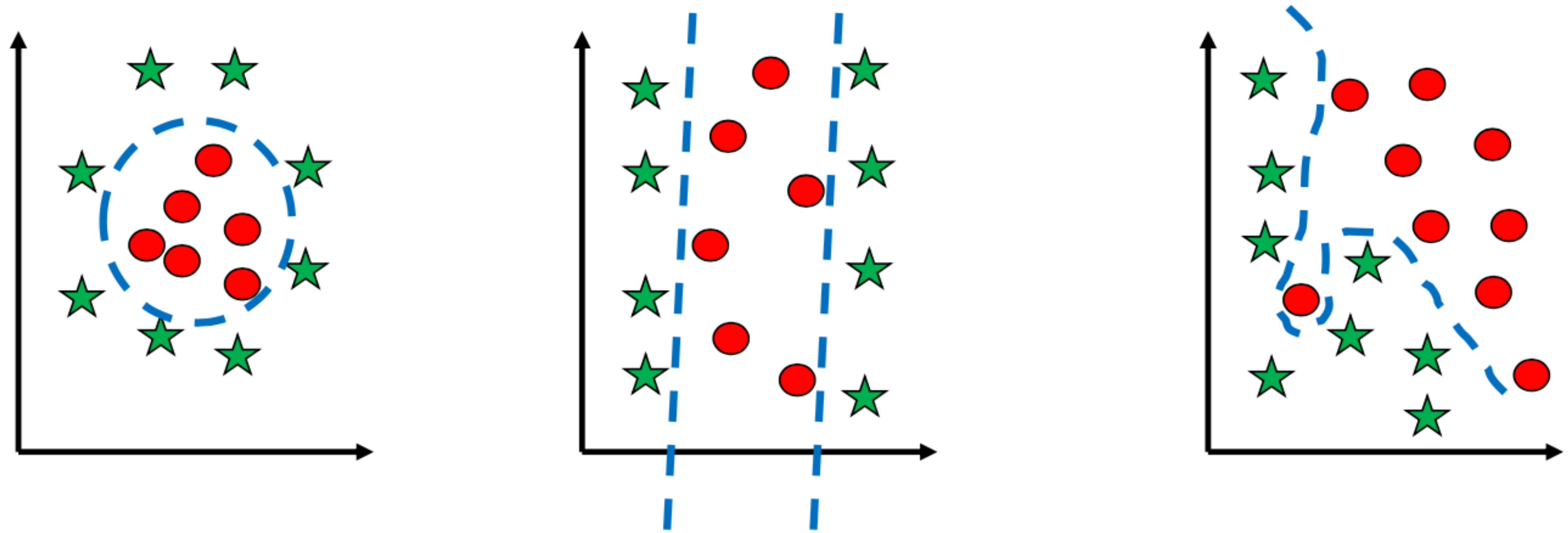
x_1	x_2	x_1 XOR x_2
0	0	0
0	1	1
1	0	1
1	1	0



There is no line which perfectly separates the two classes in the XOR problem

XOR cannot be solved by a single McCulloch-Pitts Neuron

The Perceptron - Unsolvable Problems!



The Perceptron - Summary

- McCulloch-Pitts neurons implement a linear decision boundary (separating hyperplane)
- The weights and bias define the decision boundary
- They can implement many logical operations (AND, OR, NOT)
- They cannot implement XOR (not linearly separable)
- They can be trained on labeled datasets (supervised learning)

Algorithm: Perceptron Learning Algorithm

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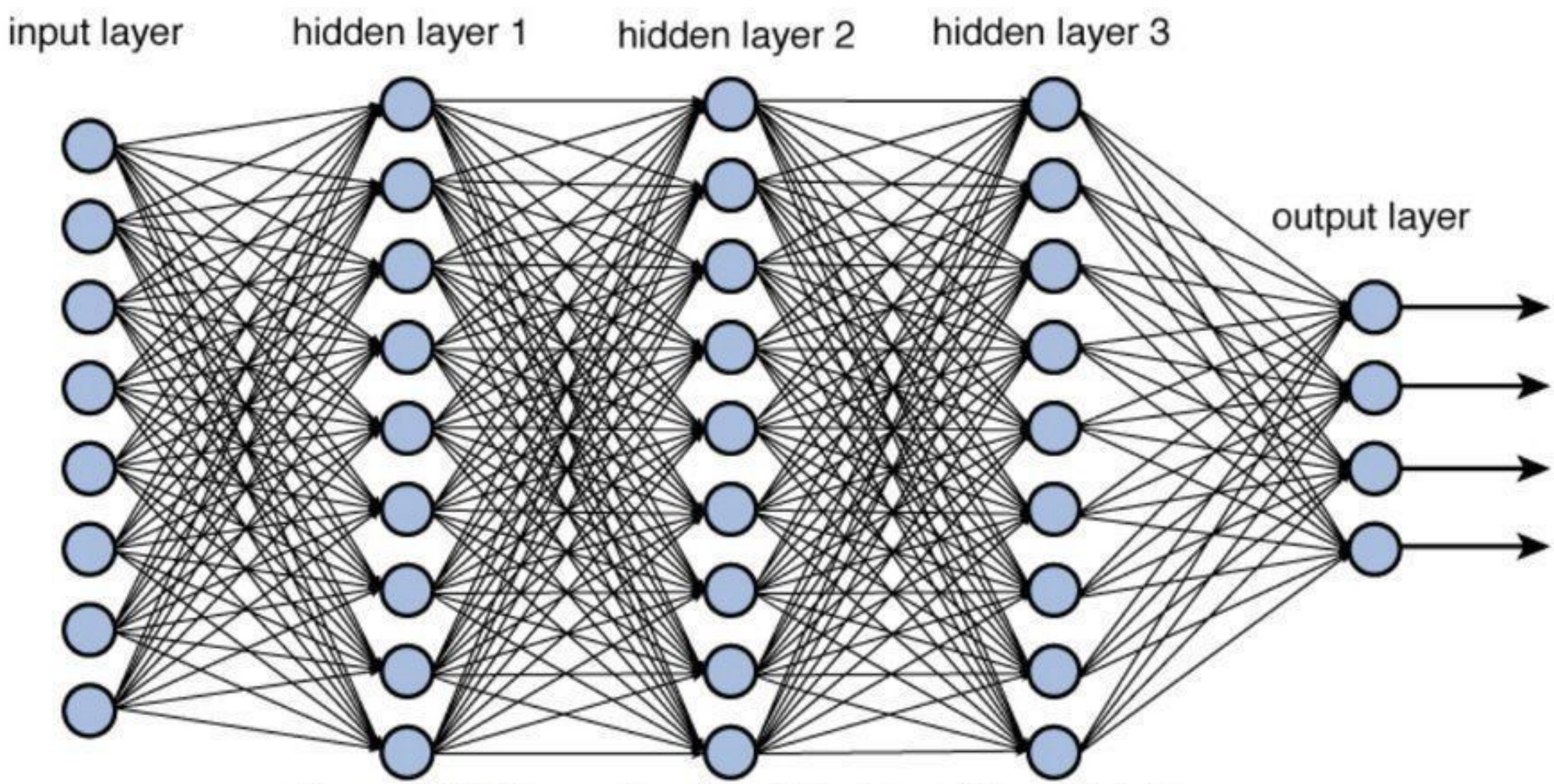
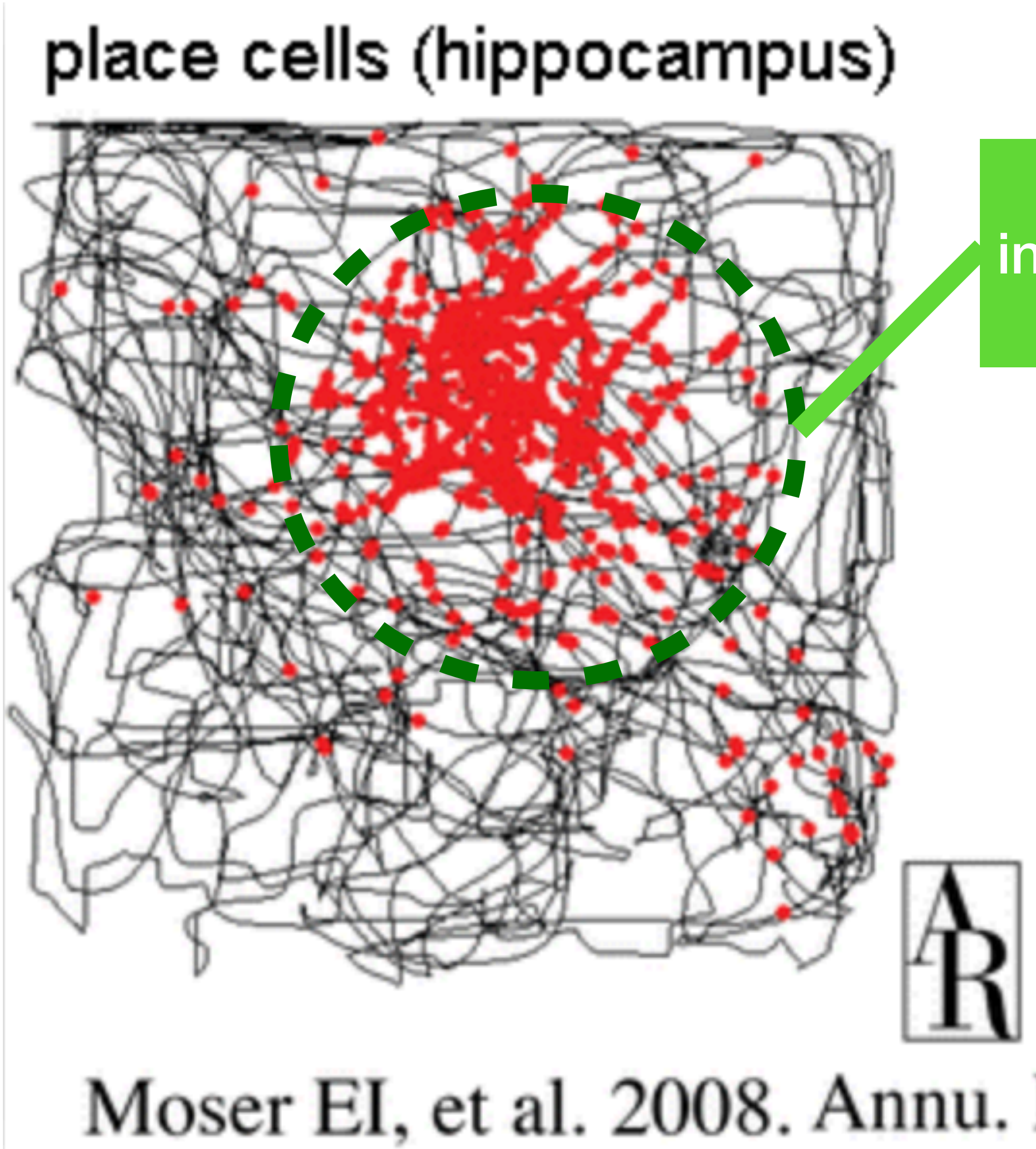
while $!convergence$ **do**
  Pick random $\mathbf{x} \in P \cup N$;
  if $\mathbf{x} \in P \quad and \quad \mathbf{w.x} < 0$ **then**
    $\mathbf{w} = \mathbf{w} + \mathbf{x}$;
  end
  if $\mathbf{x} \in N \quad and \quad \mathbf{w.x} \geq 0$ **then**
    $\mathbf{w} = \mathbf{w} - \mathbf{x}$;
  end
end
//the algorithm converges when all the inputs are classified correctly

Training the weights of a deep neuronal network.



Break.

The Hippocampus and Spatial Memory



At this place input features x_1-x_6 *are present.*

John O'Keefe

Neural Coding in Rodent Hippocampus.

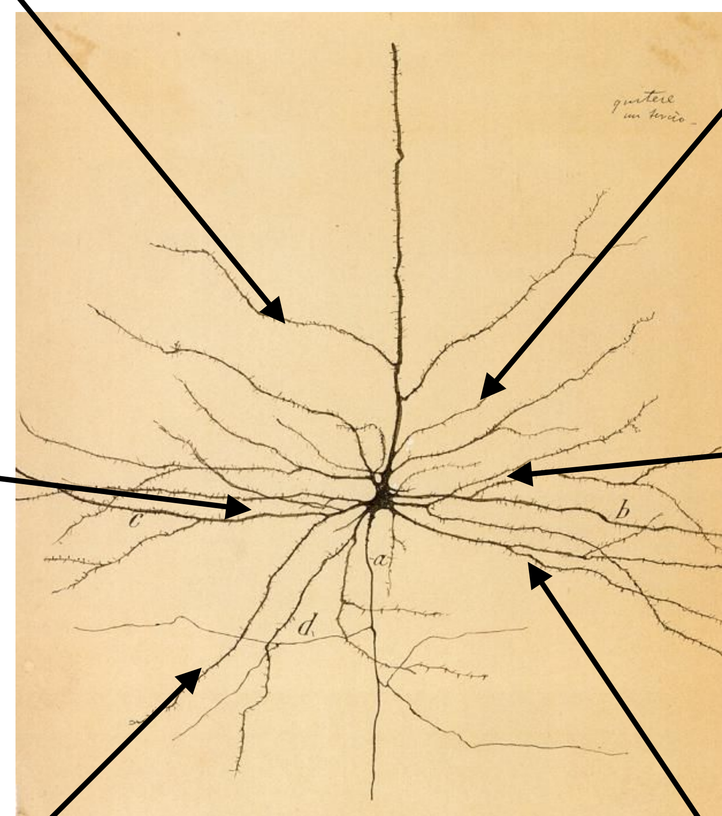
Features x_1-x_6

Somato Sensory.

Smell

Windy?

Background Noise

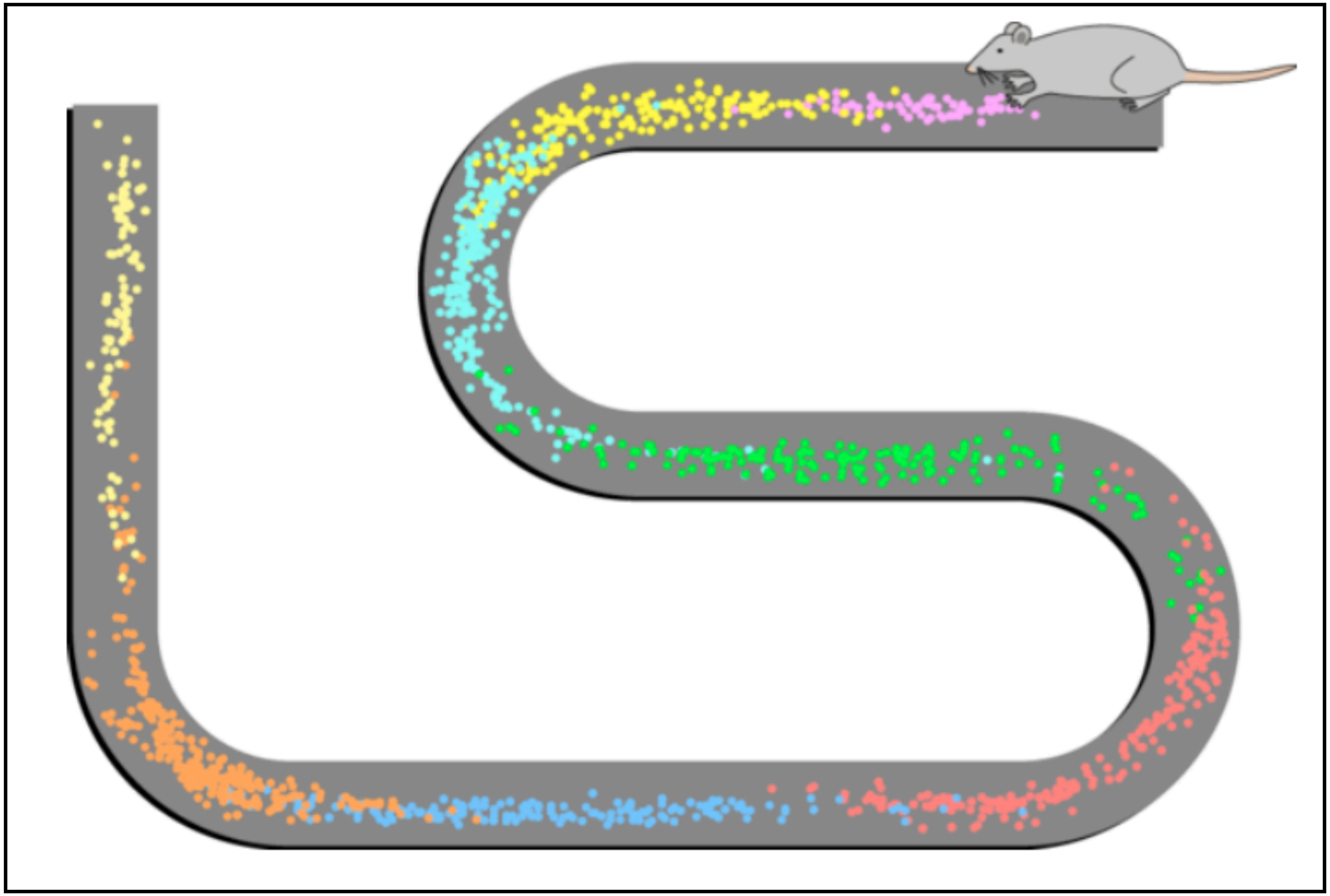


Ramón y Cajal (1852-1934)

Texture of the Floor.

Visual image of a corner.

The Hippocampus and Spatial Memory



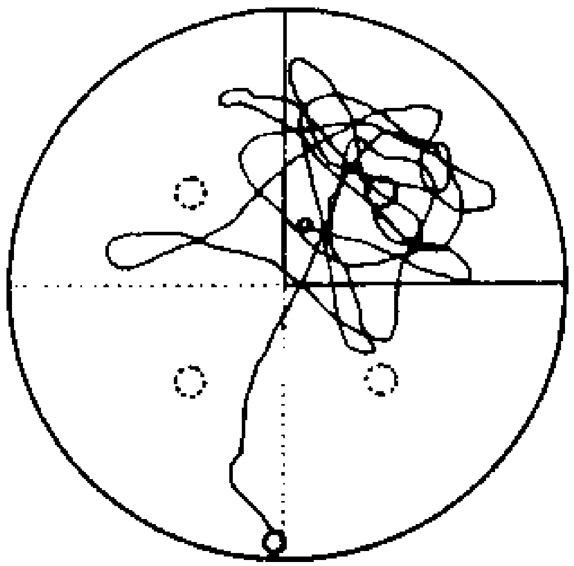
Morris Water Maze

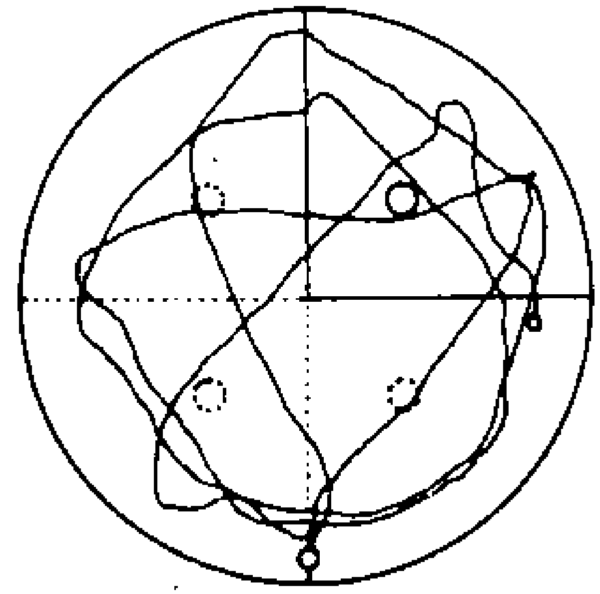
Morris et al. *Nature* 1986

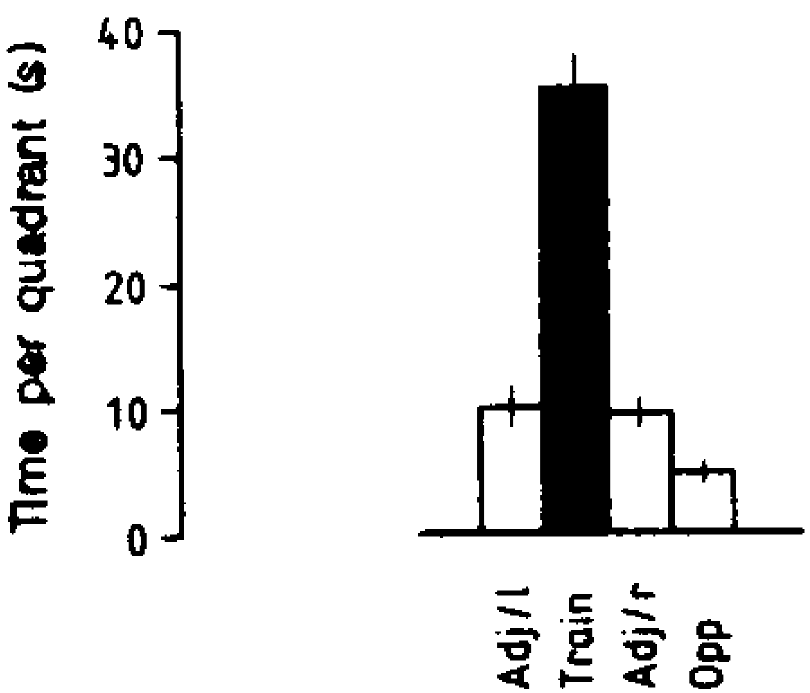
Morris Water Maze

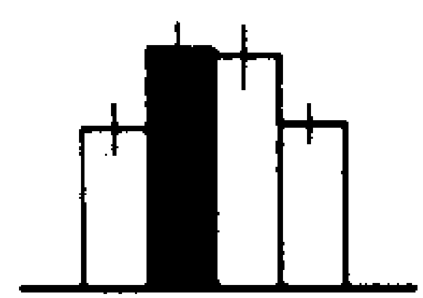
Control

NMDA receptors blocked in HC



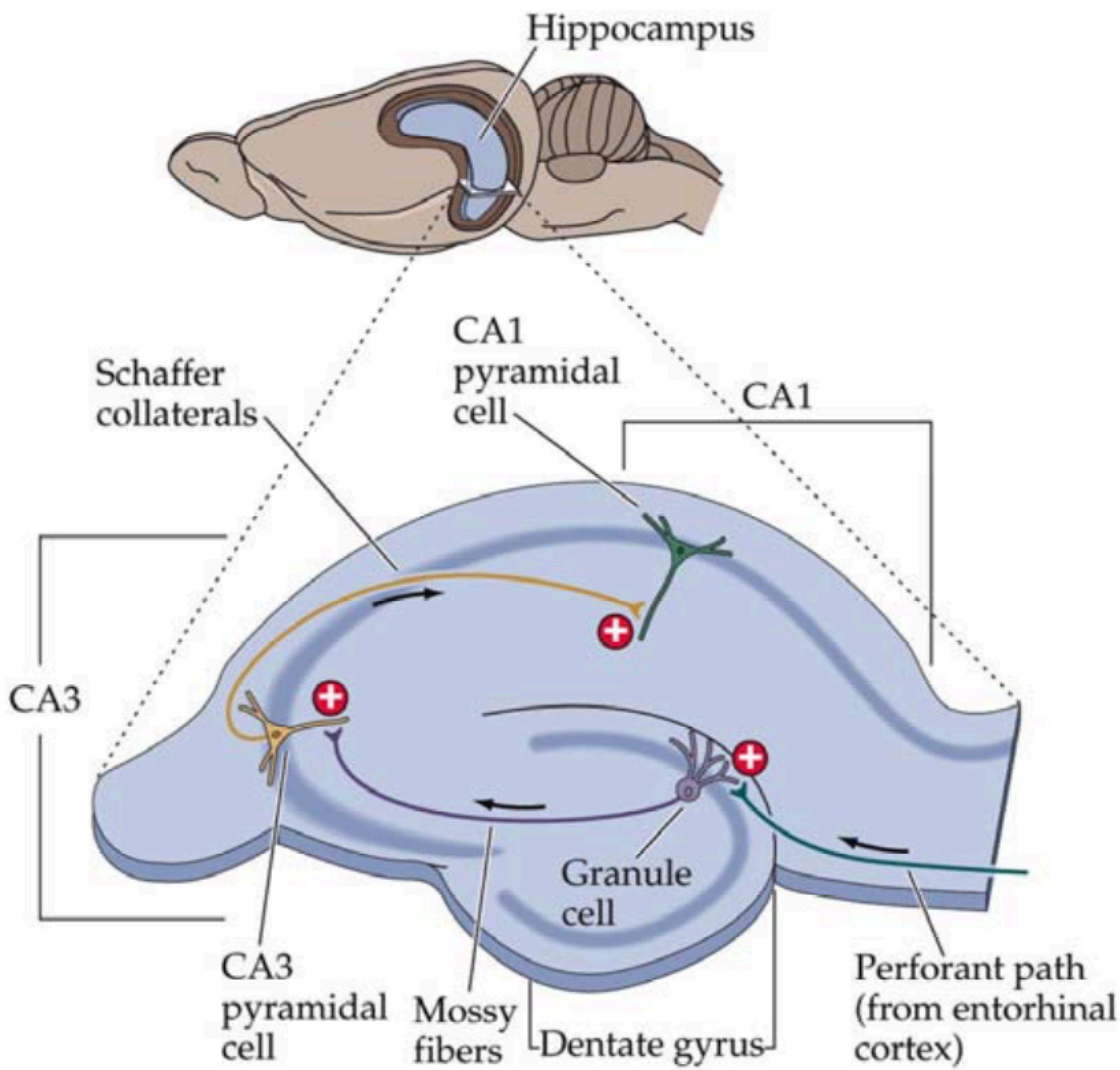




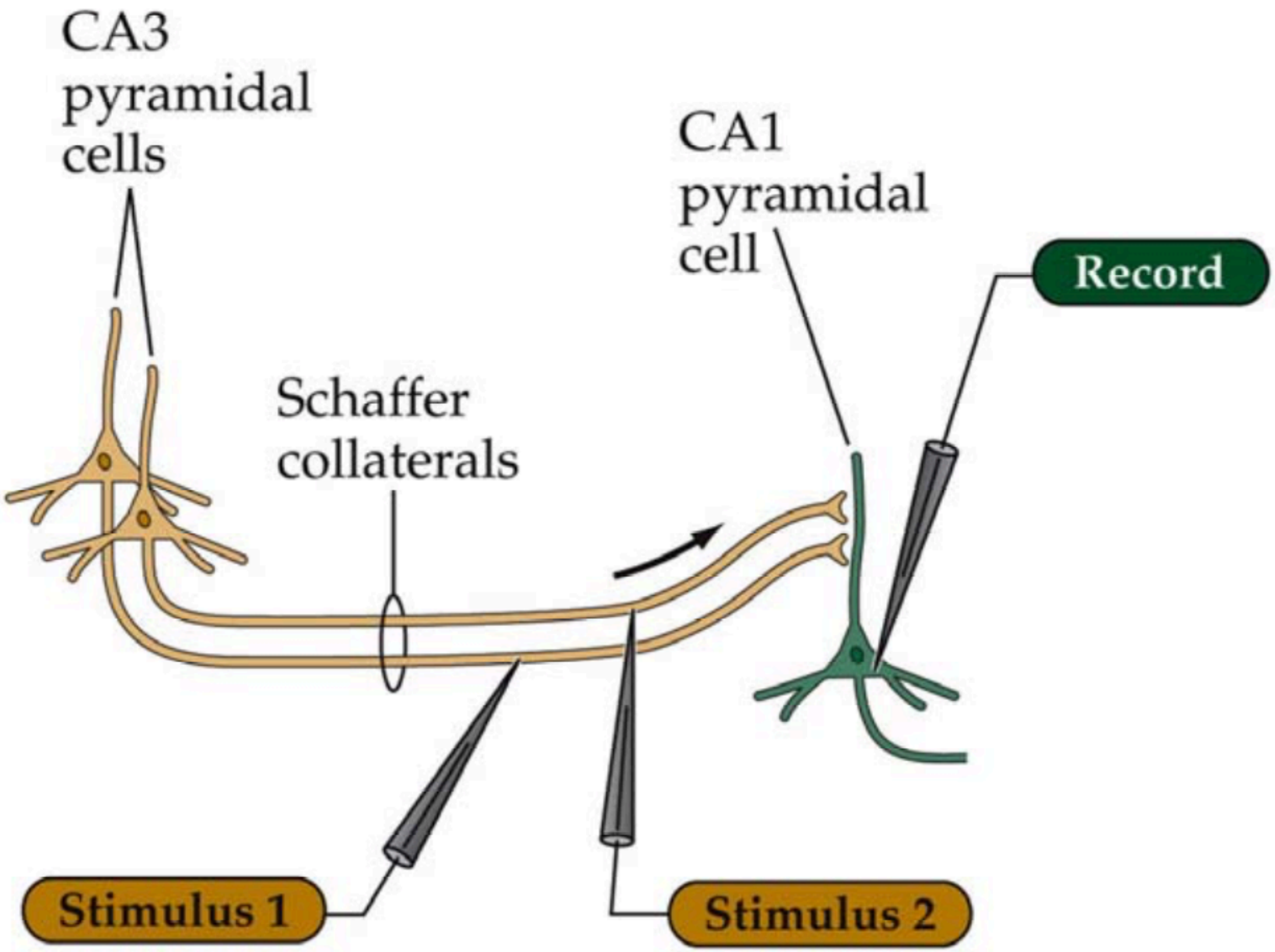


Morris et al. *Nature* 1986

How can we measure neuronal plasticity in the Hippocampus?

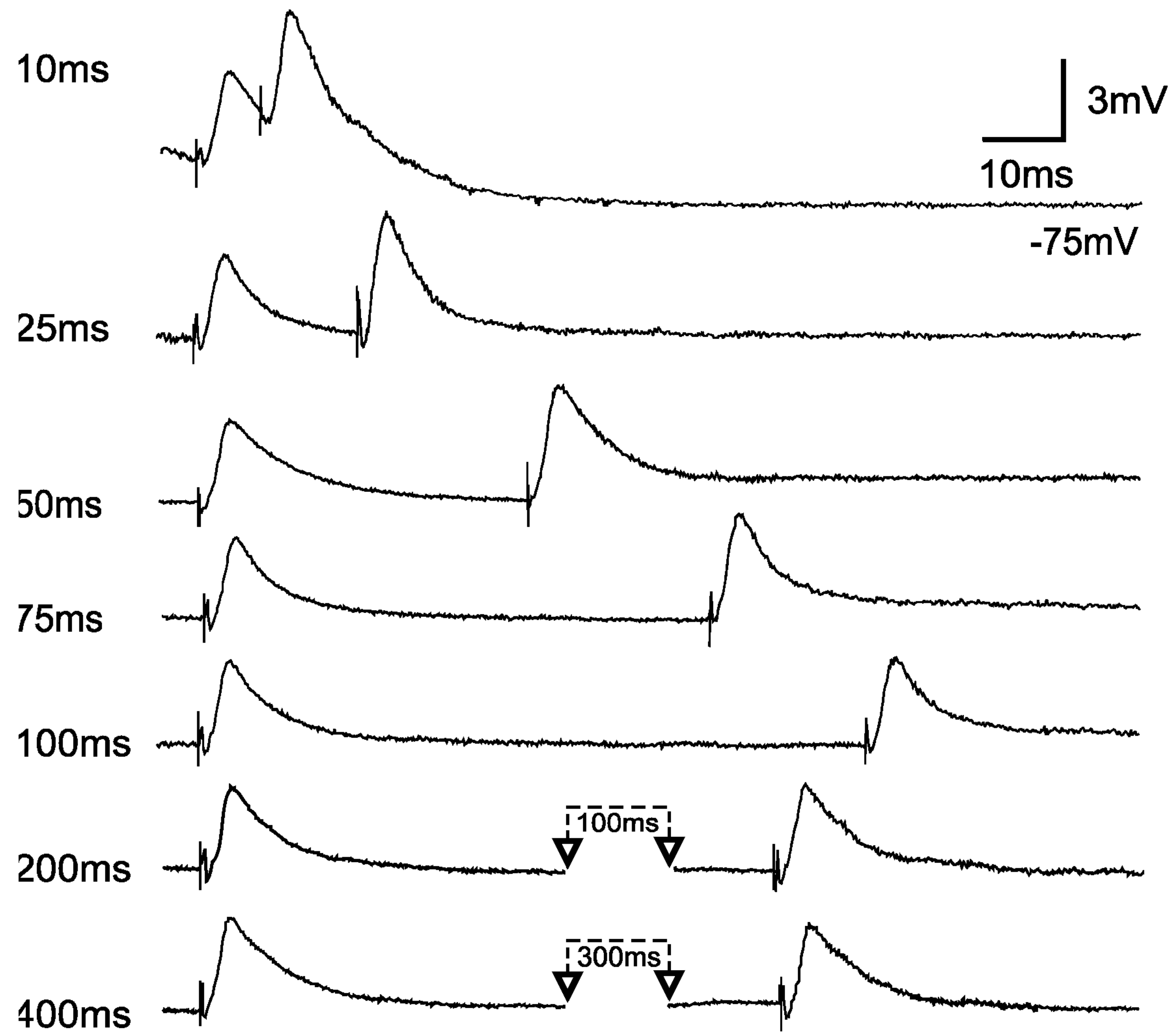


Most studied synapses: CA3->CA1



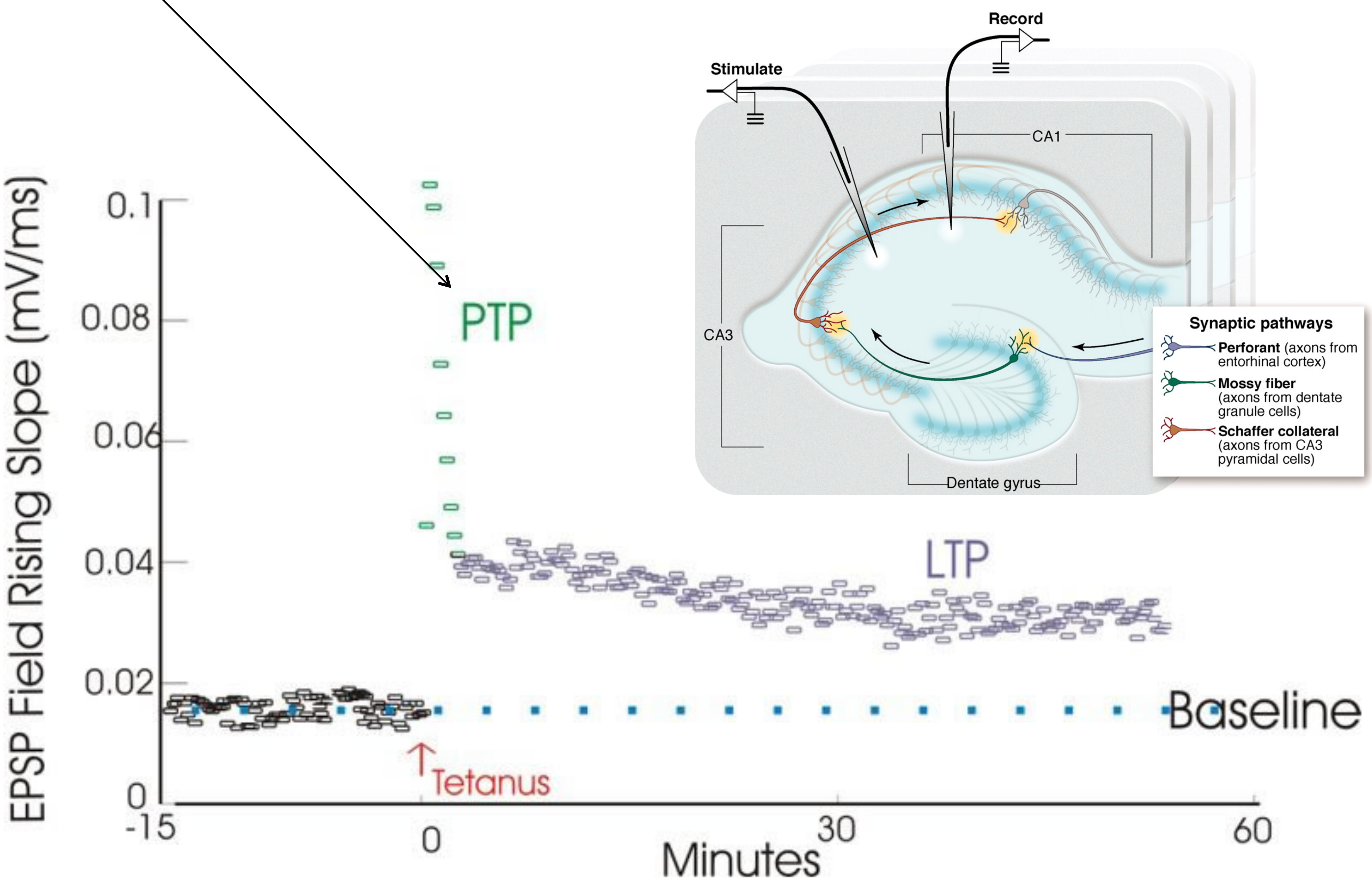
Squire 2013, p1017

Short-term Plasticity: Paired Pulse Facilitation



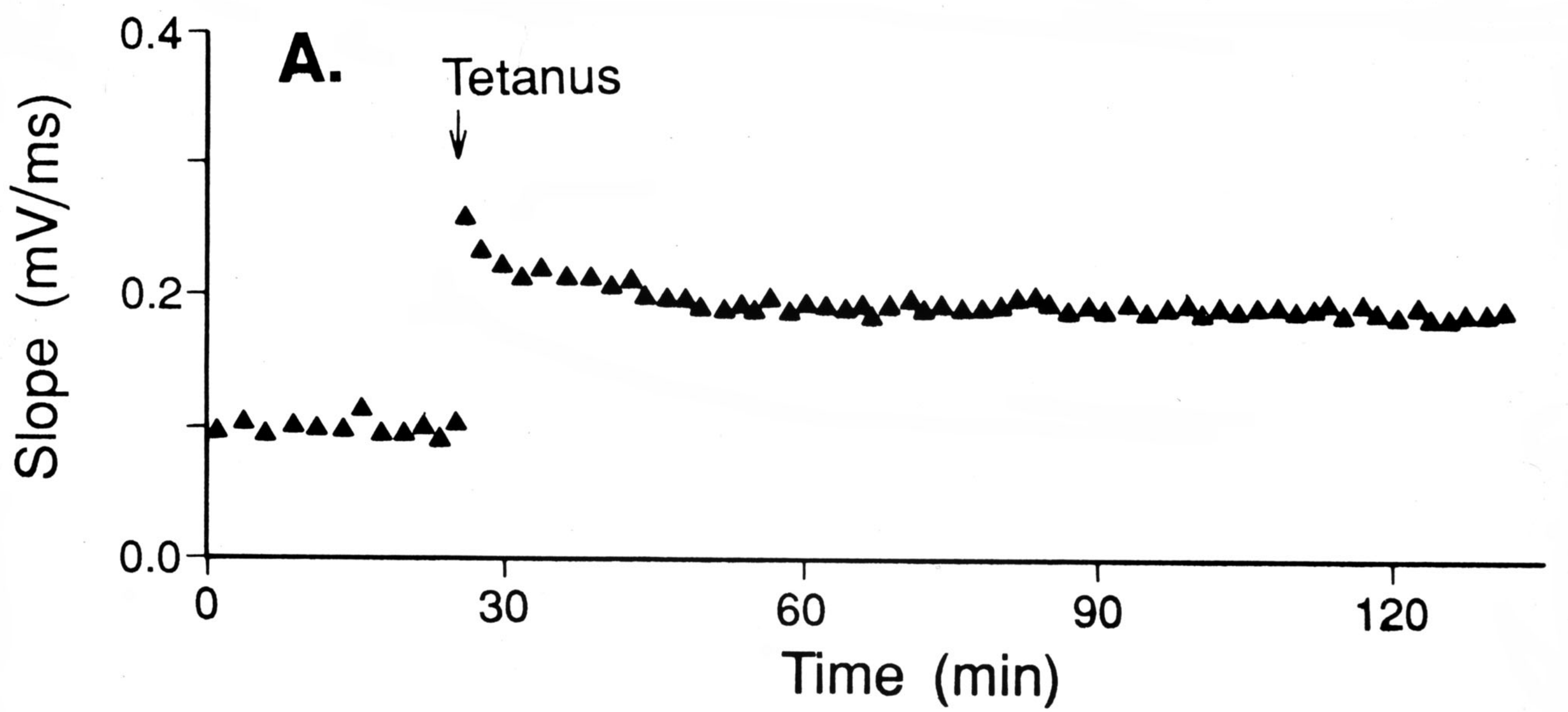
Paired activations of a synapse onto a CA 1 neuron. “Residual Ca^{2+}” in terminal for 10 to 100 ms after first stimulus increases probability of release.

Post Tetanic Potentiation and Long Term Potentiation



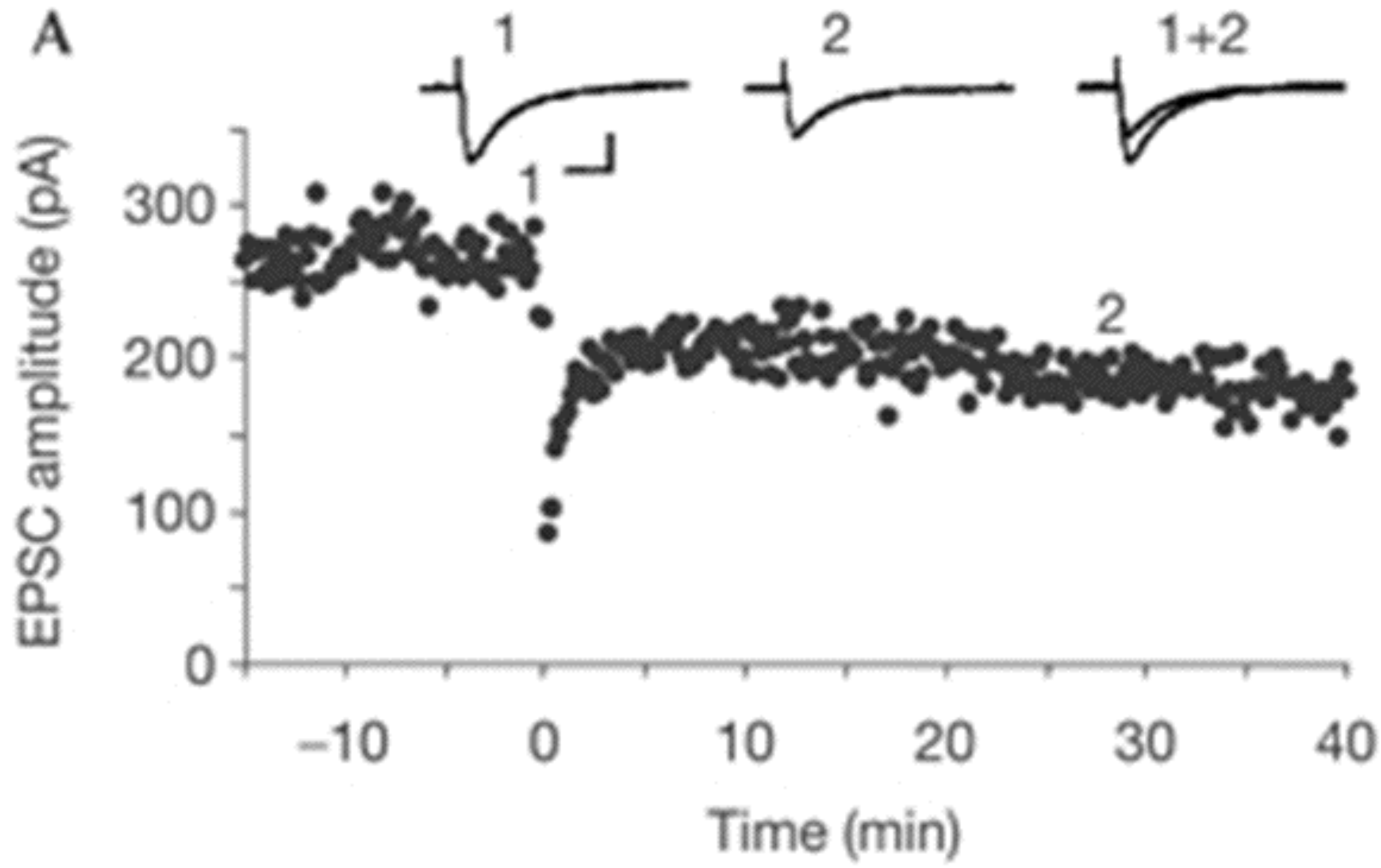
PTP believed to be caused by a large accumulation of Ca^{2+} in the terminal caused by a high frequency tetanic stimulation.

Recording of LTP in a Hippocampal Slice



Stimulation frequencies that produce LTP usually range from ~50 to 200 Hz.

Recording of LTD in the Hippocampus



Stimulation frequencies usually range from 1 to 10 Hz.

Summary of Cellular LTP and LTD

I. Frequency-dependent Long-term Potentiation (LTP)
   A. This term involves many mechanisms, all of which result in strengthening of the synapse for varying periods of time following tetanic stimulation.
   B. The mechanisms for LTP lasting 30 min to a few hours do not require new protein synthesis
   C. The mechanisms for LTP lasting longer than a few hours do require protein synthesis.

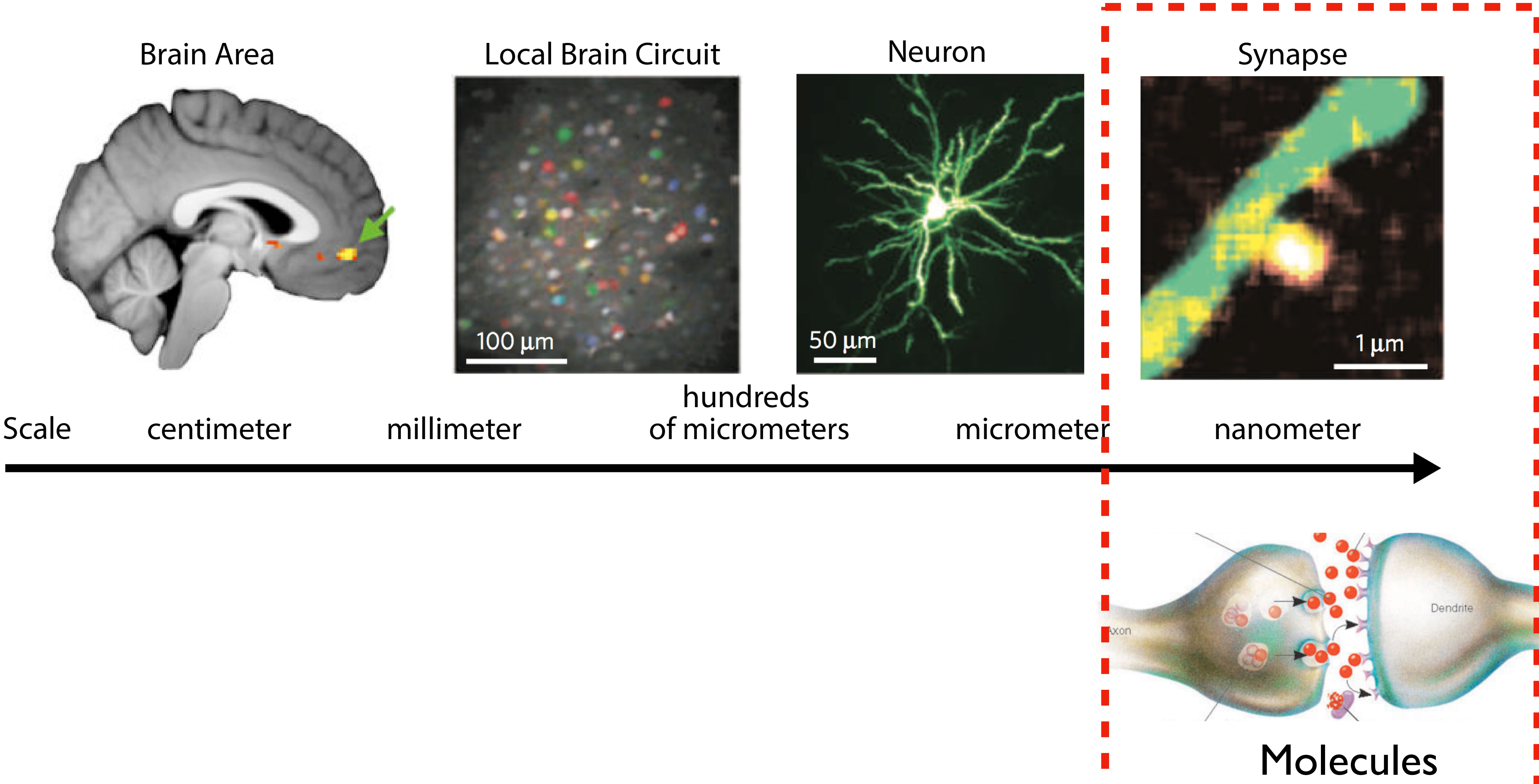
II. Frequency-dependent Long-term Depression (LTD)
   A. This term also involves many mechanisms
   B. LTD, like LTP is thought to be used for sculpting circuits to store information.

III. Spike-timing dependent synaptic plasticity (STDP) is thought to arise from the same set of mechanisms as LTP and LTD.

Content of this Lecture

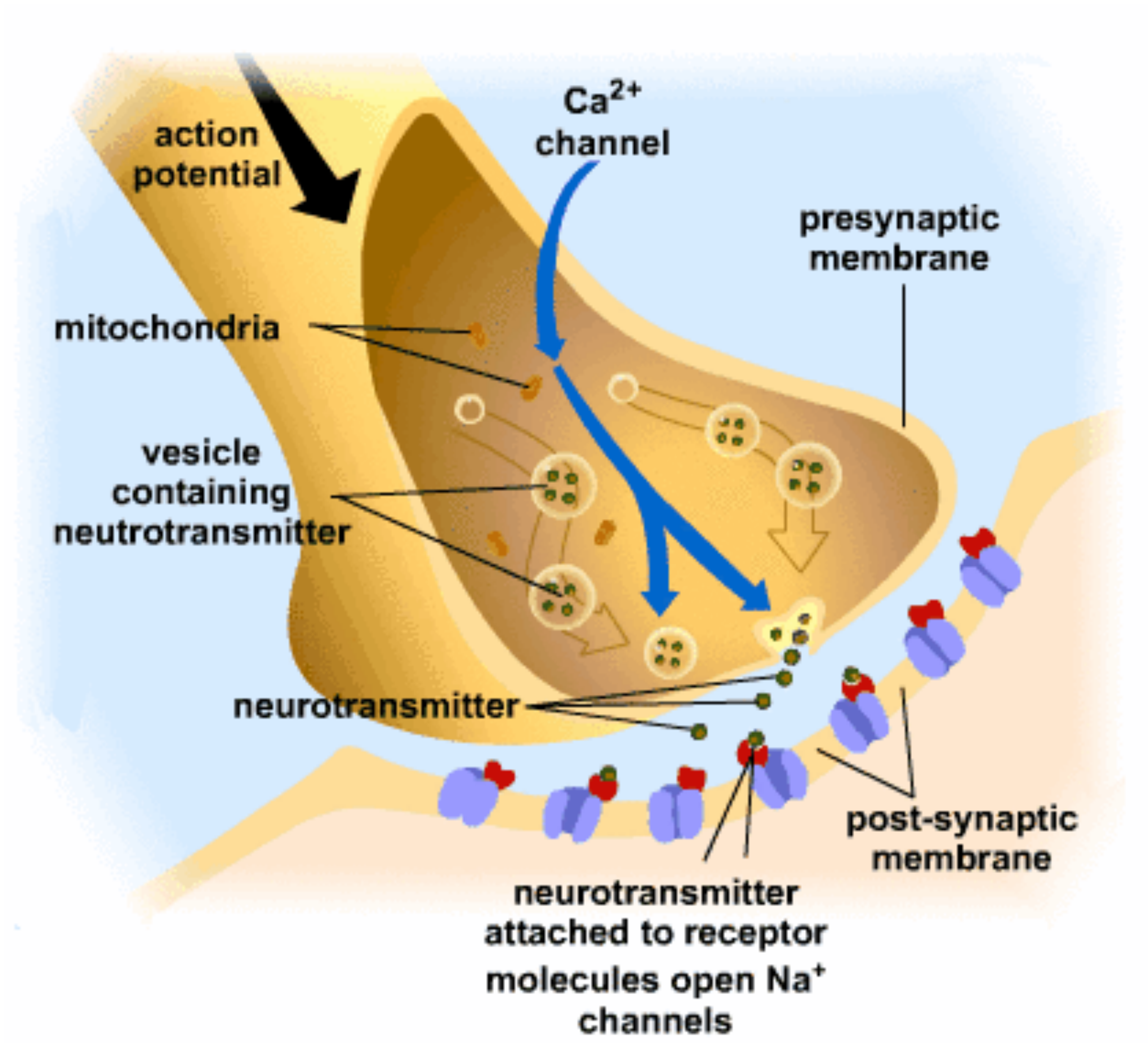
1. Plasticity in Neuronal Networks
   - Why do we need plasticity/learning?
   - Defining Plasticity/Learning.
   - Relevant temporal scales for learning.
2. Substrates of neural plasticity
   - Network and Systems Plasticity
   - Cellular Plasticity, the Perceptron
   - <u>Synaptic plasticity, the Hebbian Synapse</u>

Neural Substrates of Plasticity.



Mozzachoidi, 2010

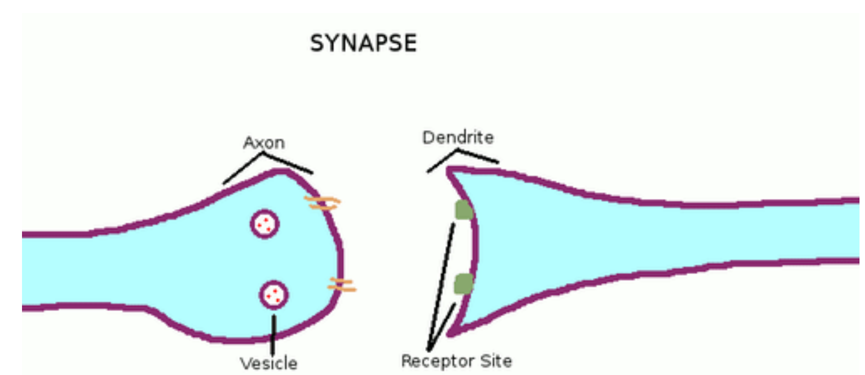
Synaptic Plasticity - A Short Recap of Synaptic Function.



1. AP comes in
2. AP triggers Ca^{2+} influx via voltage dependent Ca^{2+} channels
3. Ca^{2+} induces NT release
4. NTs pass the synaptic cleft.
5. NTs bind to post-synaptic receptors

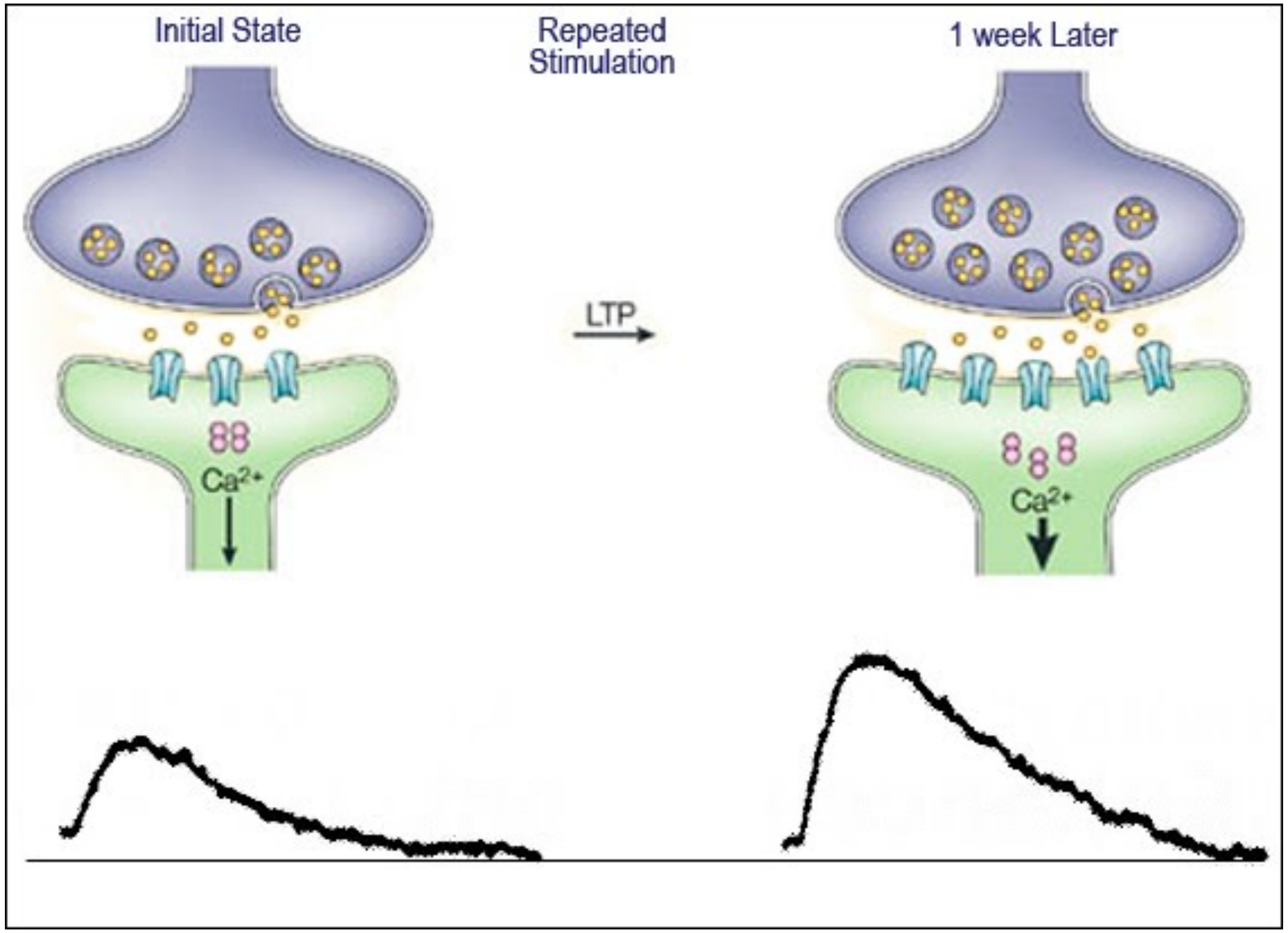
Neurotransmitters:

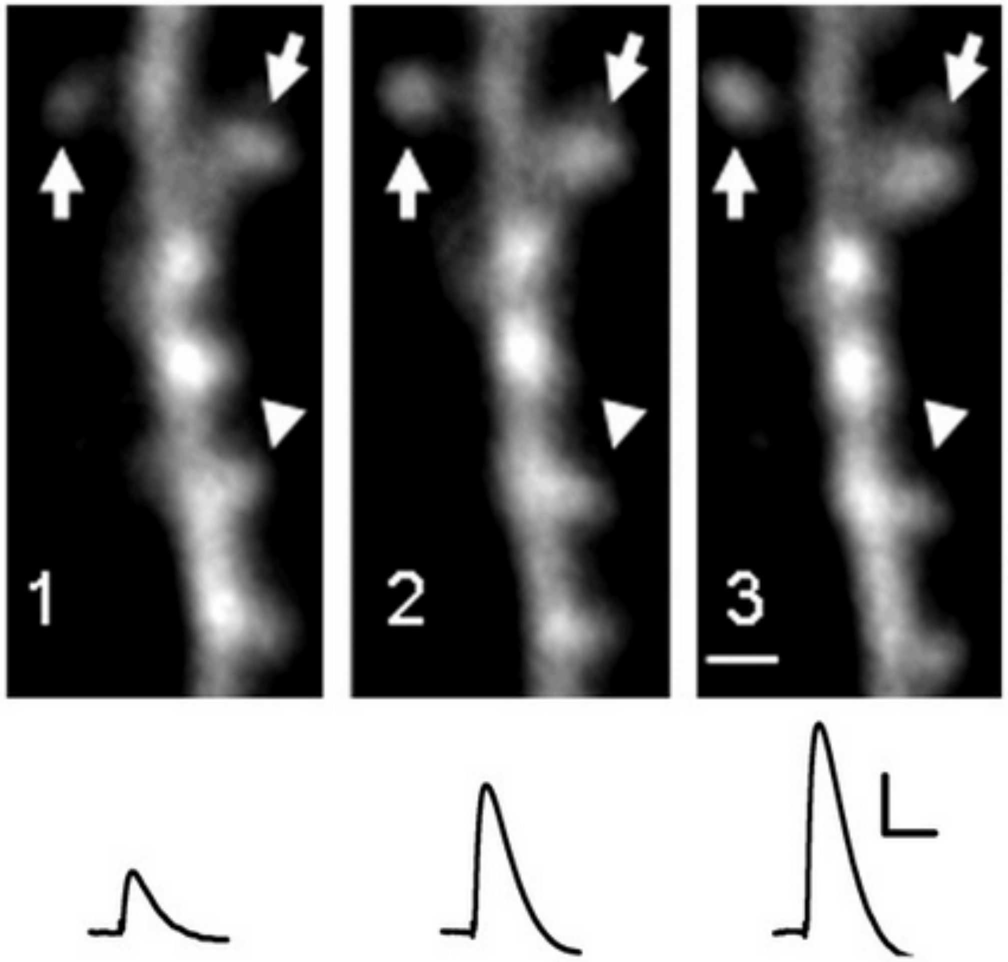
- Amino Acids …Glutamate, GABA
- Biogenic Amines … Dopamine, Histamine
- Neuropeptides … LHRH, Proctolin



….what factors determine the synaptic strength?

Plasticity (LTP) at the Synapse

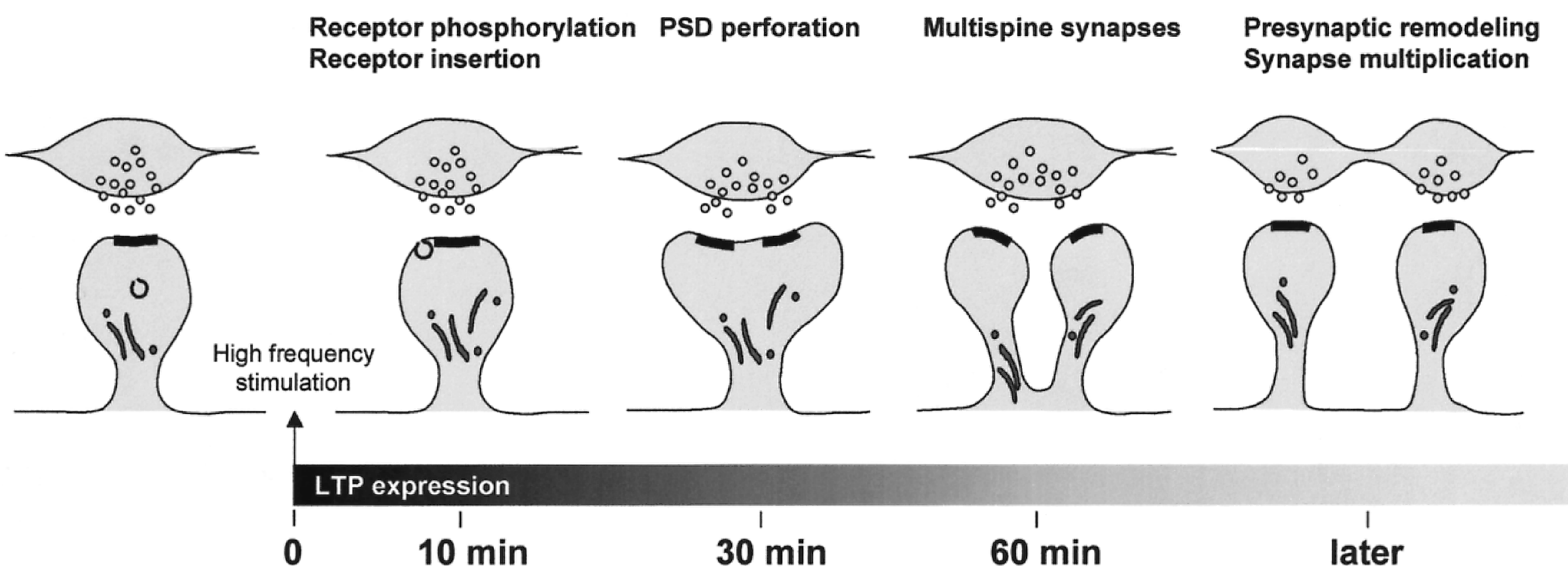




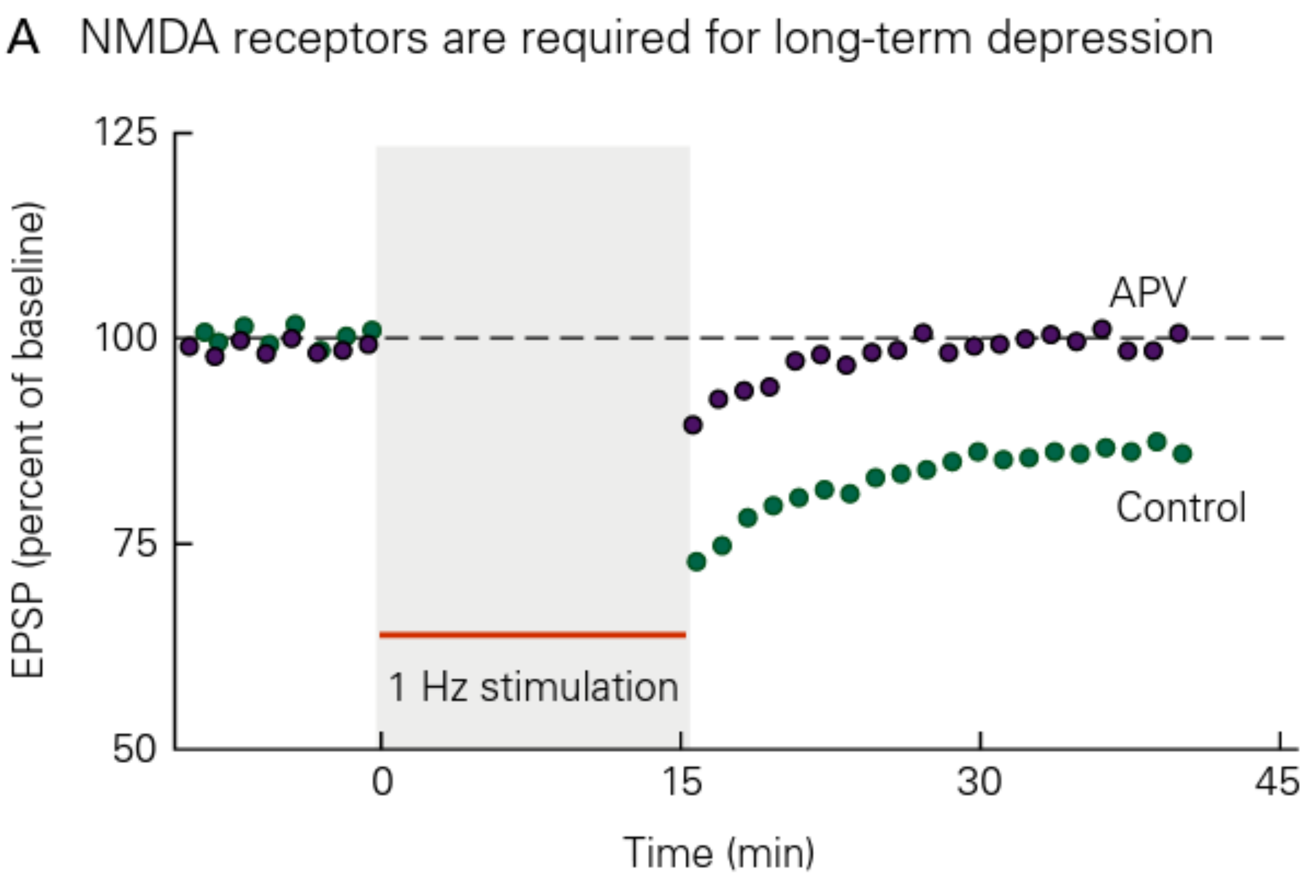
1. Synapse size changes
2. AMPA/NMDA ratio changes / More vesicles
3. Number of spines changes.

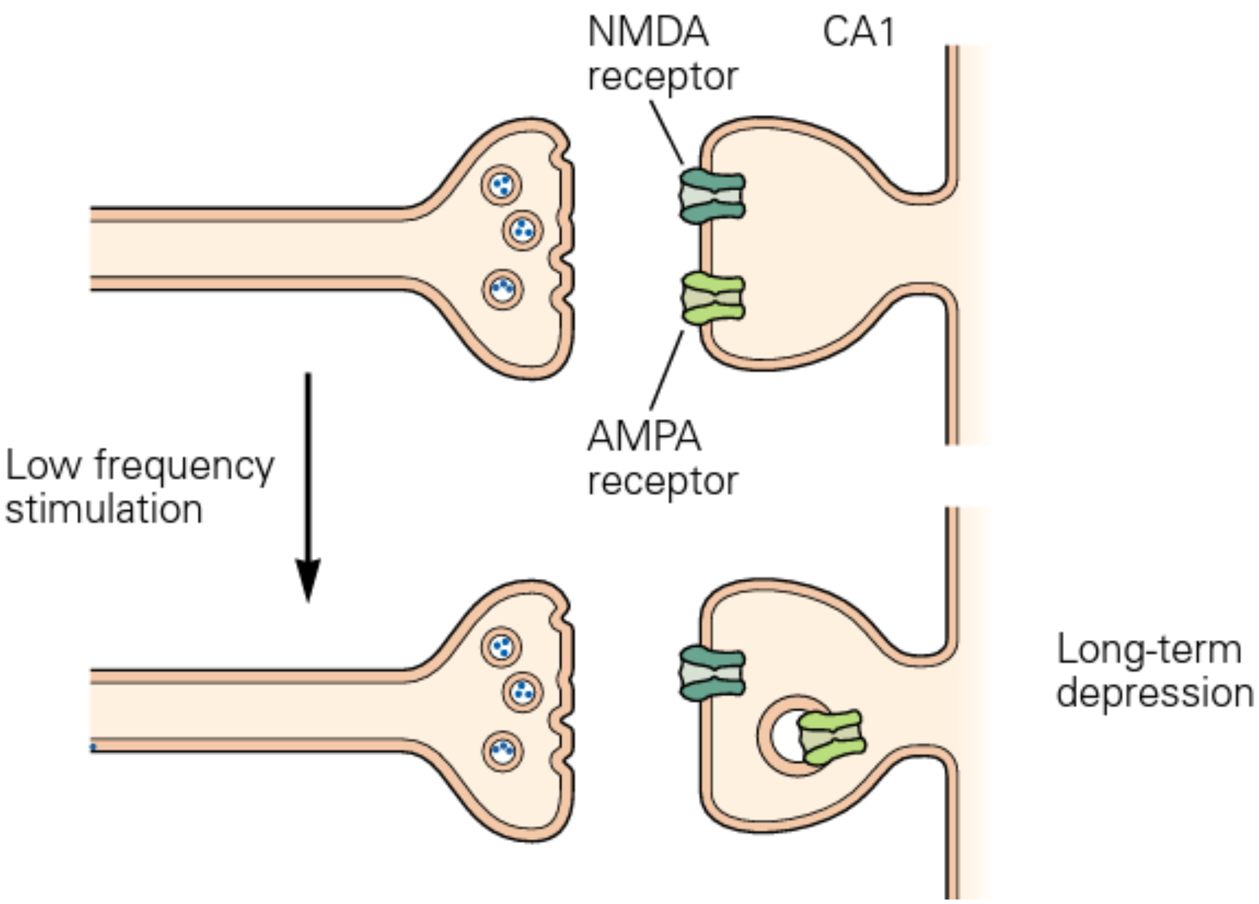
Time Scales of Synaptic Plasticity.

1. Synaptic density size changes (short term).
2. AMPA/NMDA ratio changes (short term).
3. Number of spines changes (long term).



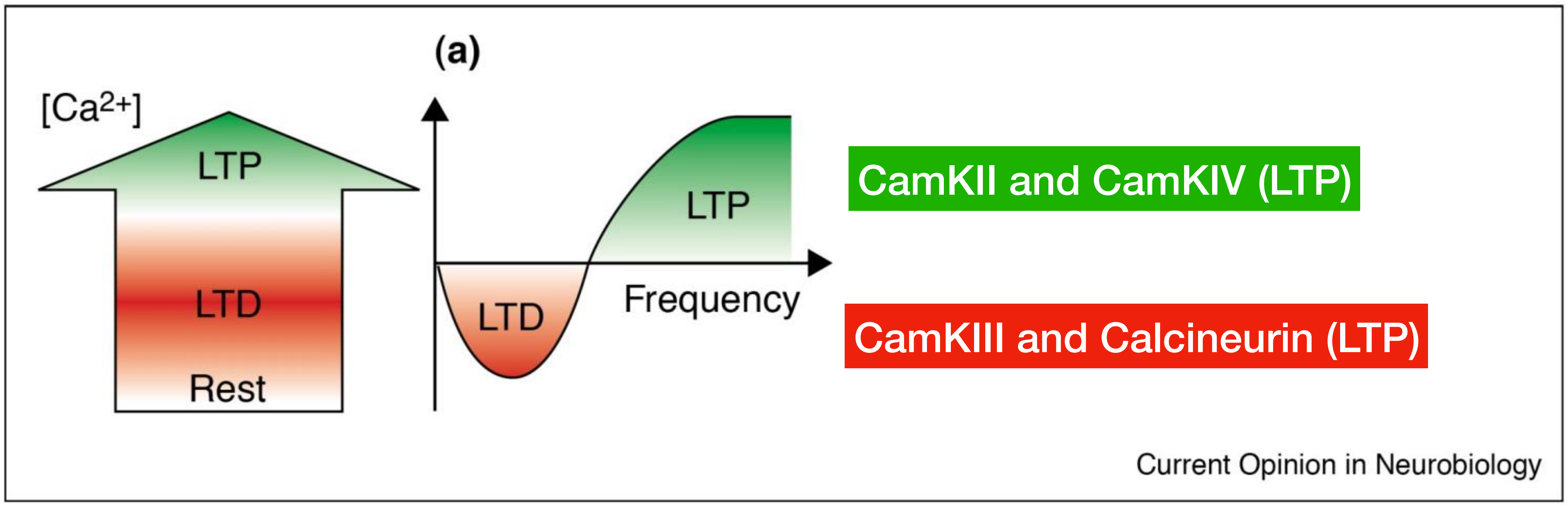
Long Term Depression (LTD)





The Role of Calcium in LTP/LTD.

1. Calcium ions flow through the activated NMDA receptor.
2. One of its targets is calcium/calmodulin-regulated Protein Kinase.

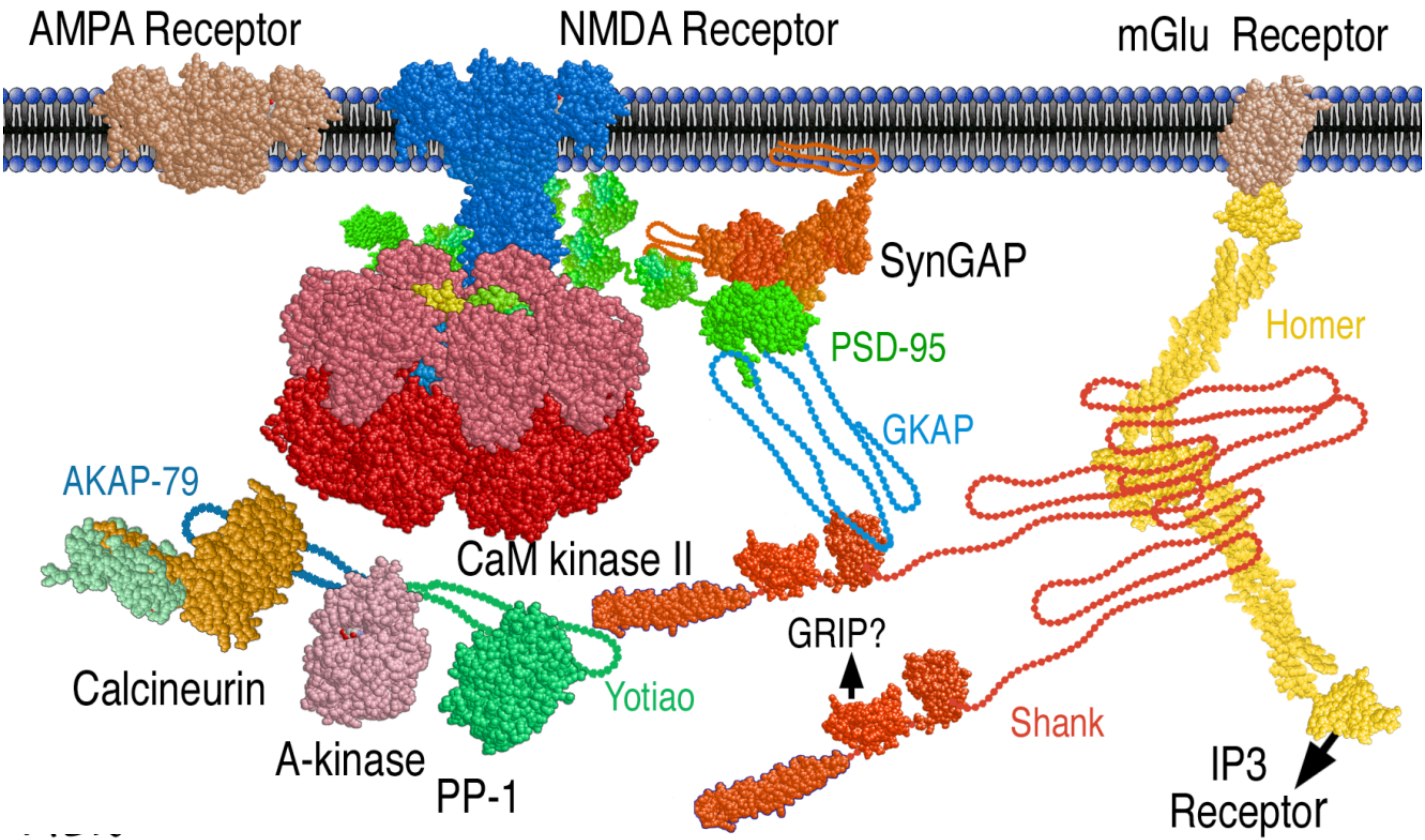


3. Level and timing of Ca^{2+} rise in spine determines LTD or LTP.

4. Low frequency synaptic firing (~5 Hz) produces LTD;
high frequency synaptic firing (~50 to 100 Hz) produces LTP.

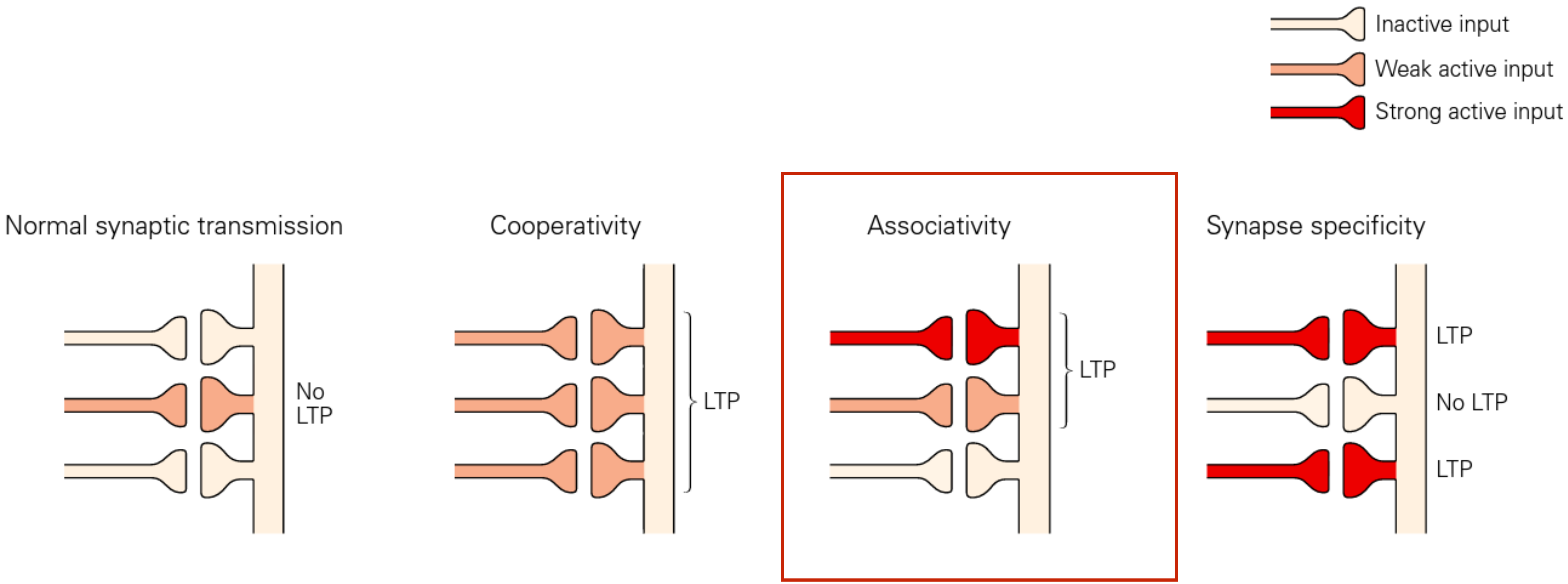
5. The same Ca^{2+} rules may underlie
"spike-timing-dependent synaptic plasticity (STDP).

Molecular Signalling and Plasticity in the PSD



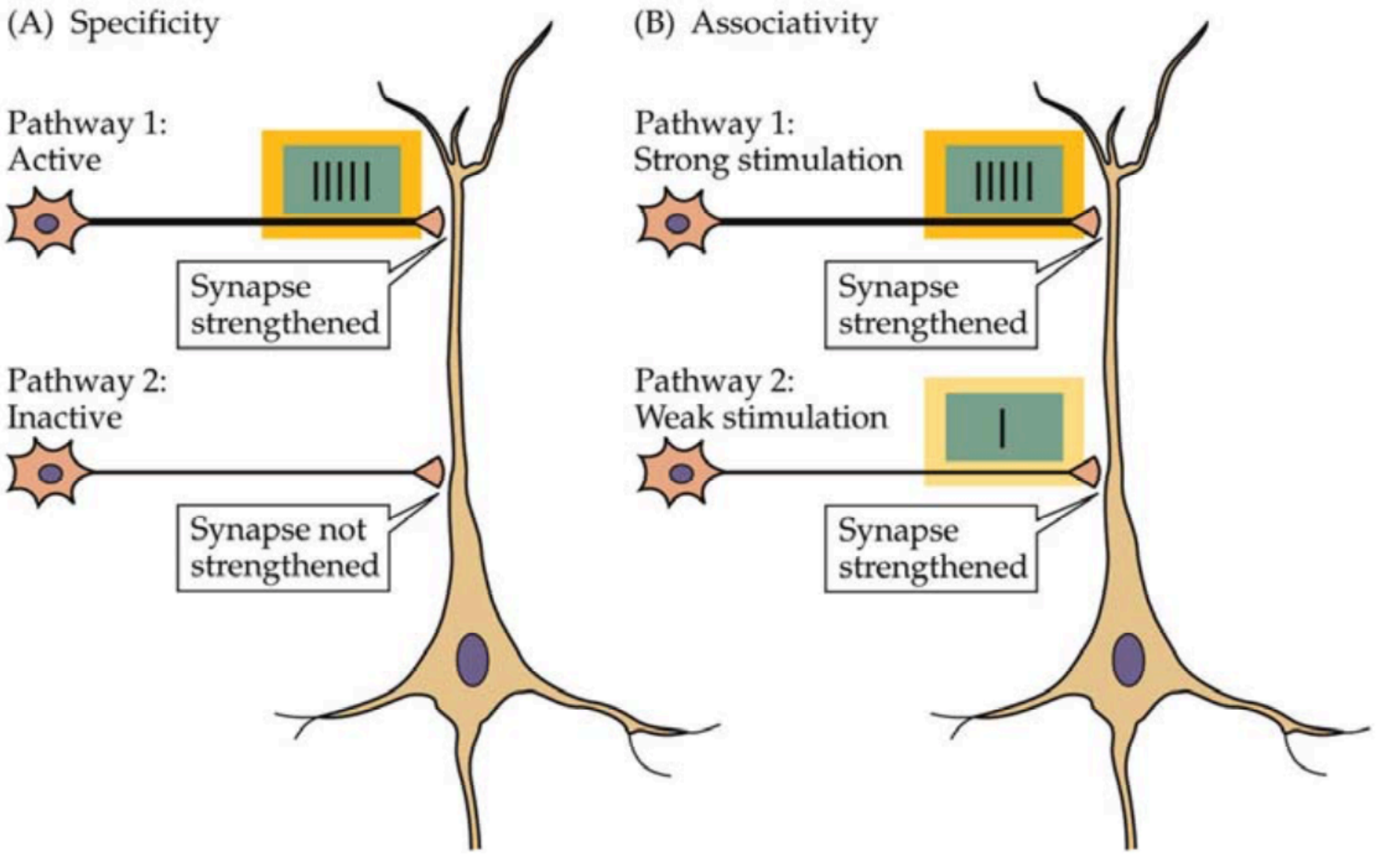
http://psych.lf1.cuni.cz/bpen/neurochemistry.htm

LTP and LTD are 'input synapse specific'

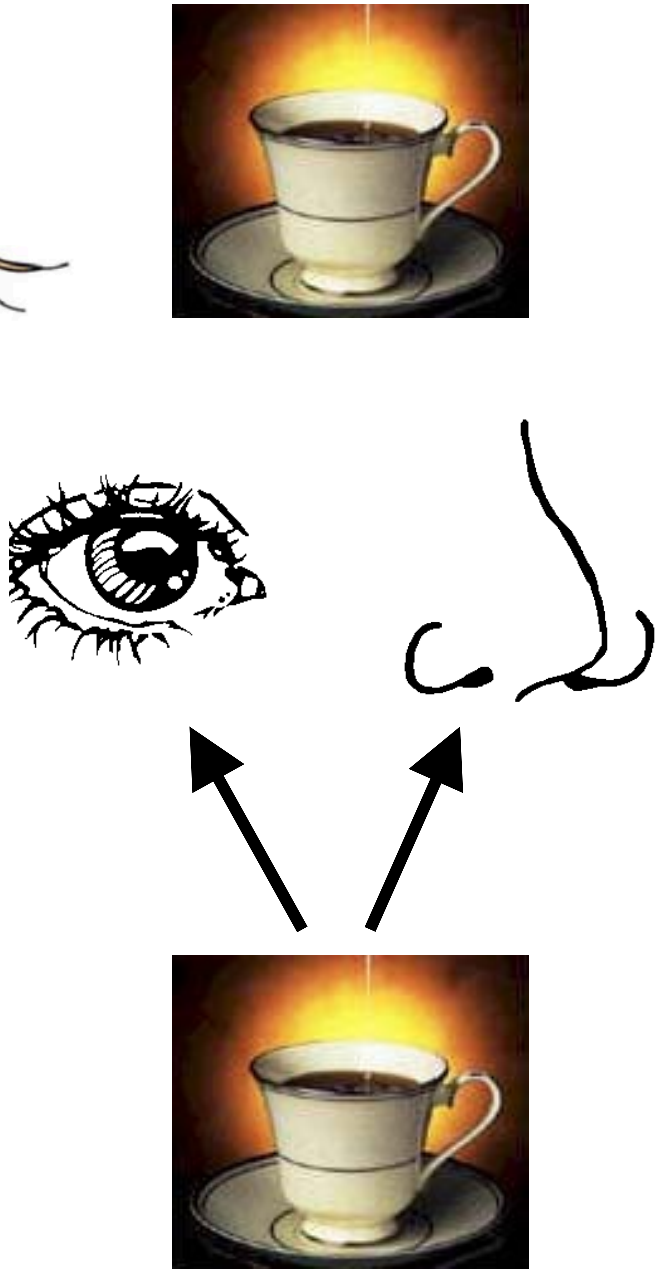


1. Cooperativity (induction threshold)
2. Input/synapse specificity
3. Enables associative learning

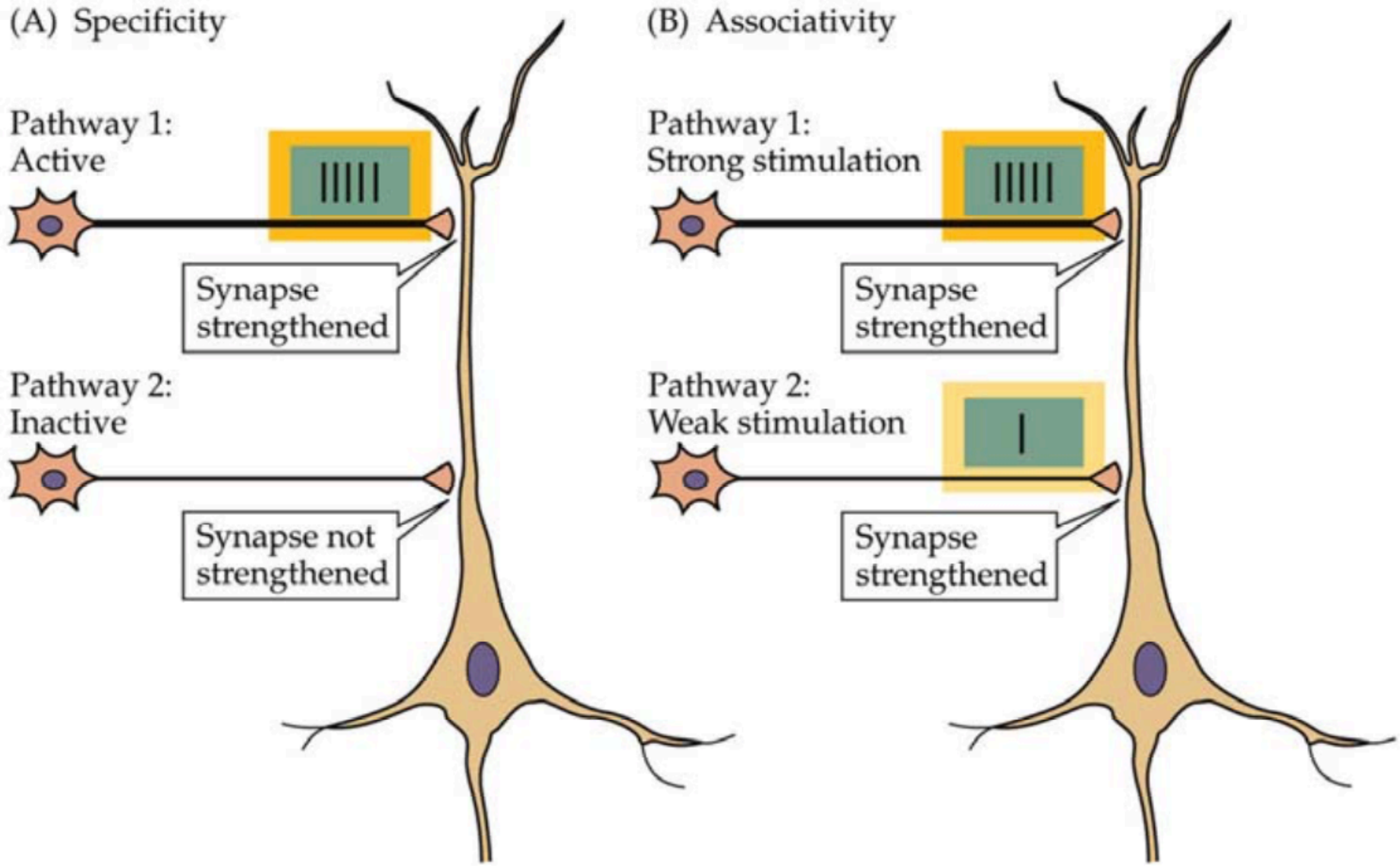
Hebb's Idea



Donald O. Hebb (1904-1985)



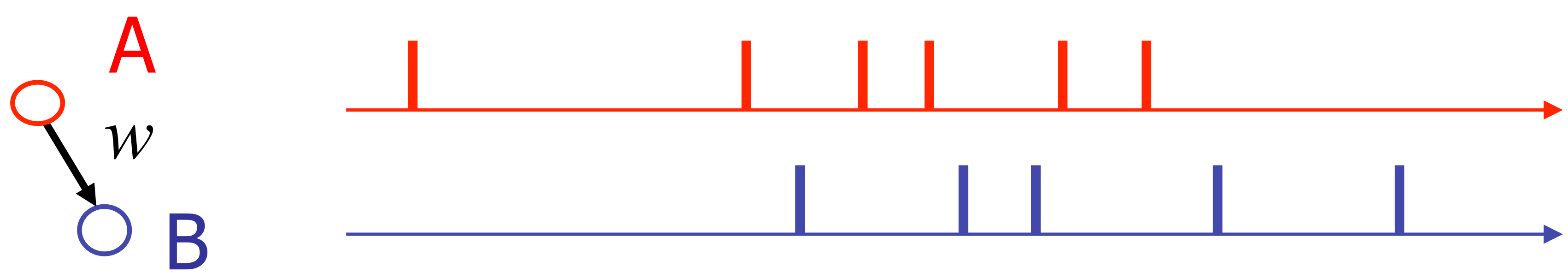
Hebb's Idea



(A) Specificity
Pathway 1:
Active
Synapse
strengthened
Pathway 2:
Inactive
Synapse not
strengthened
(B) Associativity
Pathway 1:
Strong stimulation
Synapse
strengthened
Pathway 2:
Weak stimulation
Synapse
strengthened

Hebb’s Postulate

$$\Delta w = r_A \cdot r_B$$



*When an axon of cell **A** repeatedly or persistently takes part in firing cell **B**, then A’s efficiency as one of the cells firing B is increased*

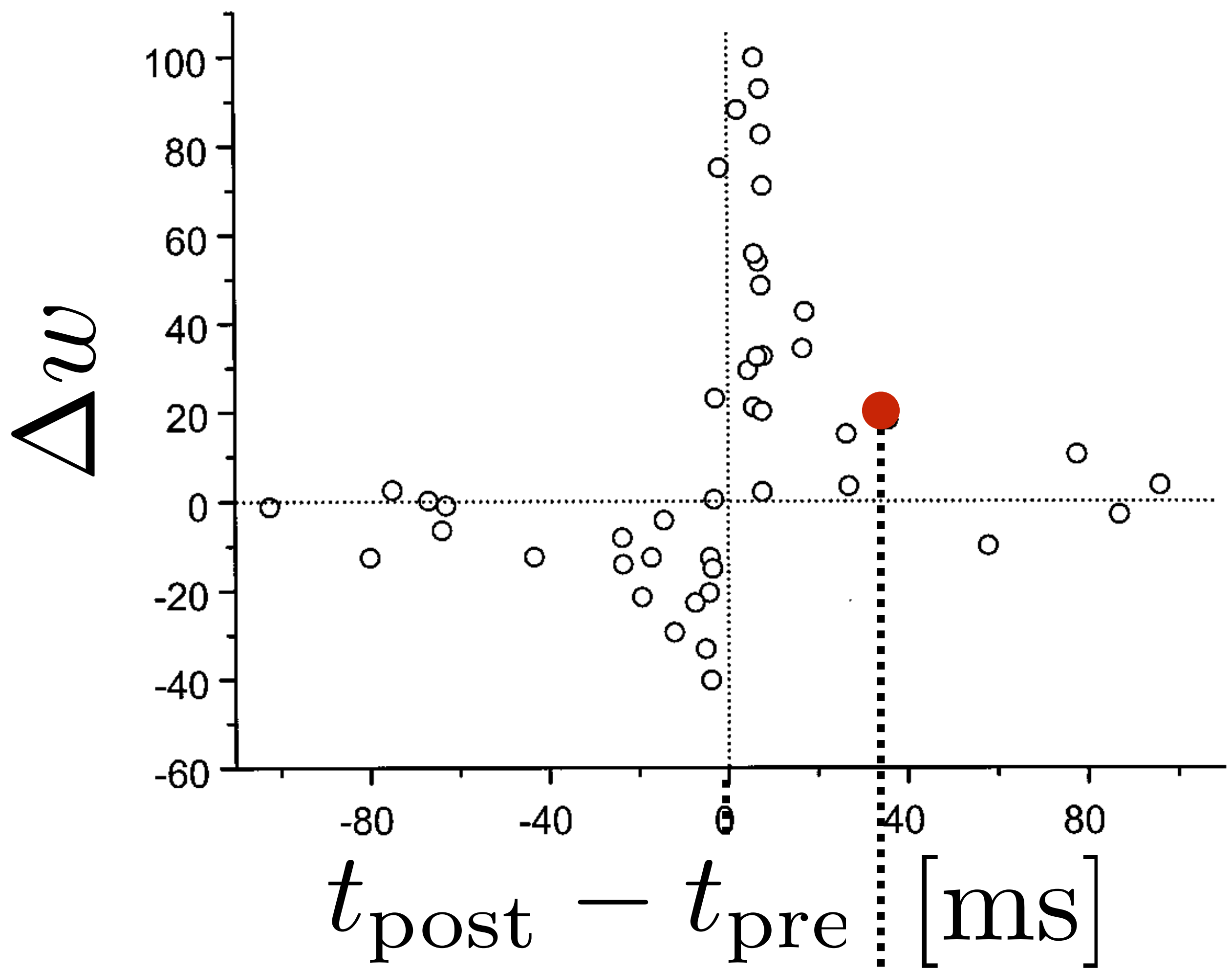
D.O. Hebb, The organization of Behavior, 1949

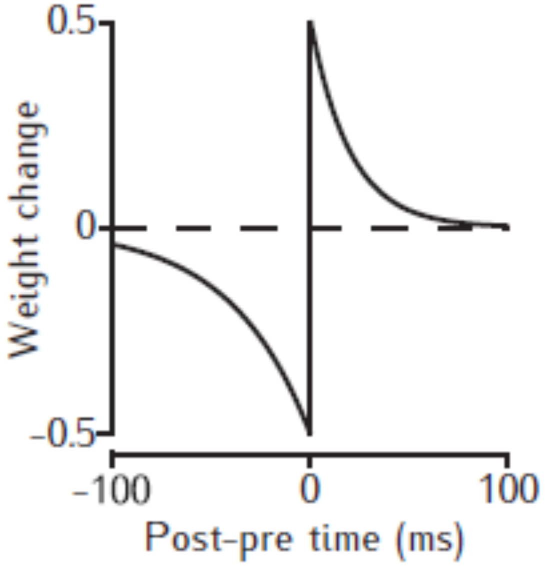
A, B simultaneously active => w ↑

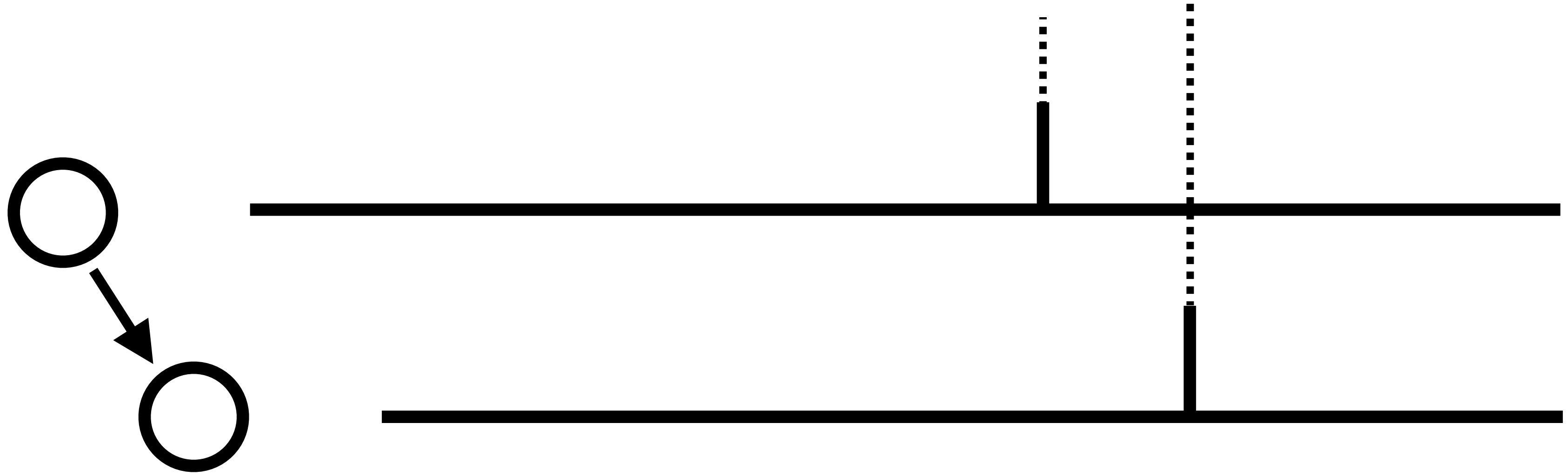
rule { local (time, space)
causal

Spike-Timing Dependent Plasticity

Data



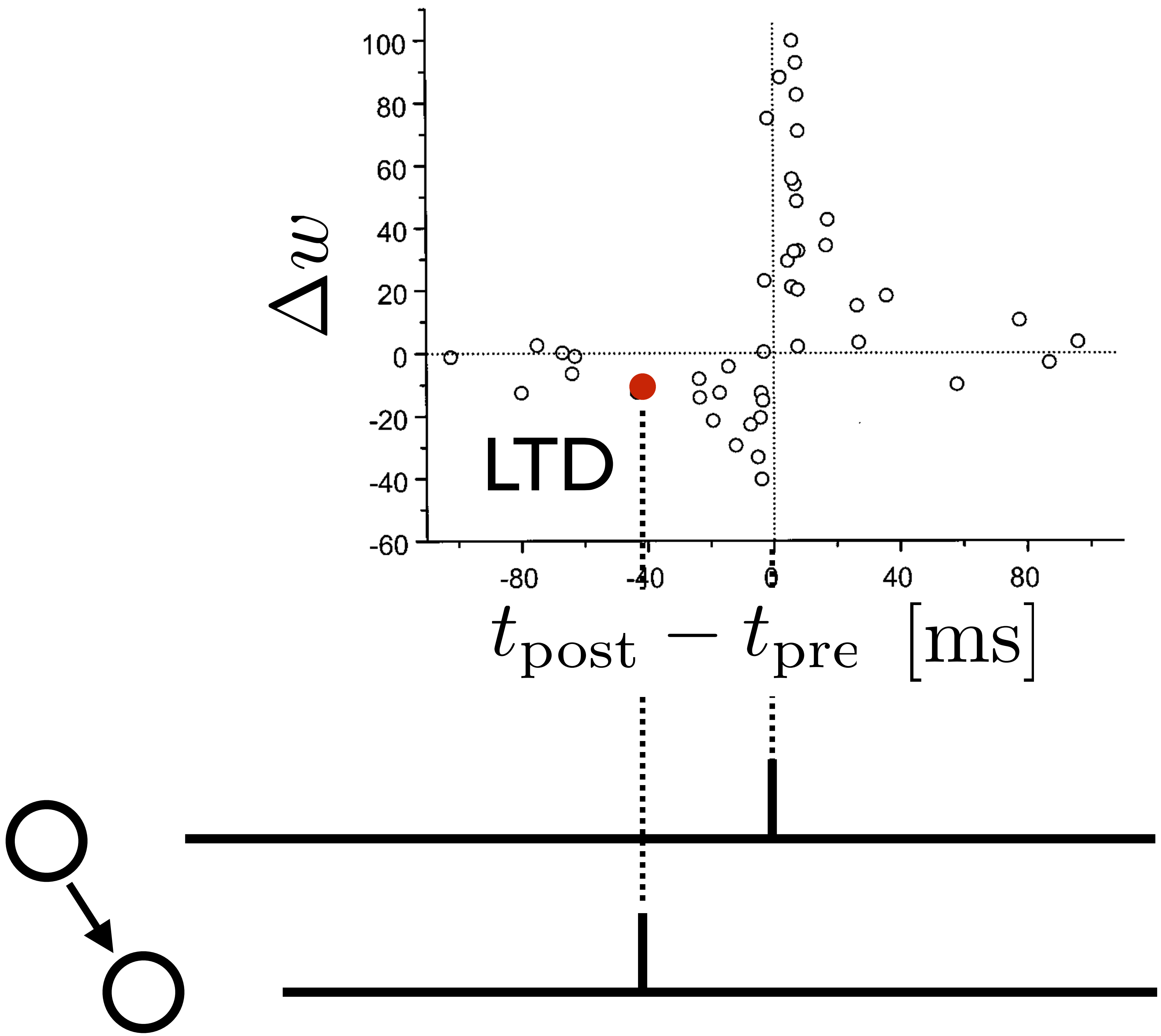


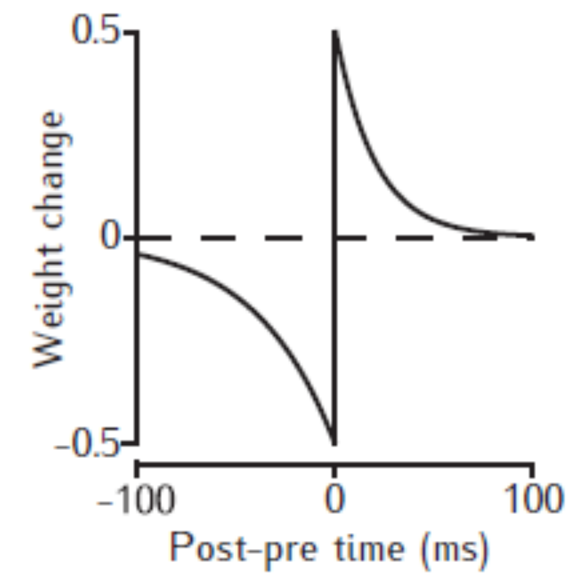


Bi and Poo, 1998

Spike-Timing Dependent Plasticity

Data





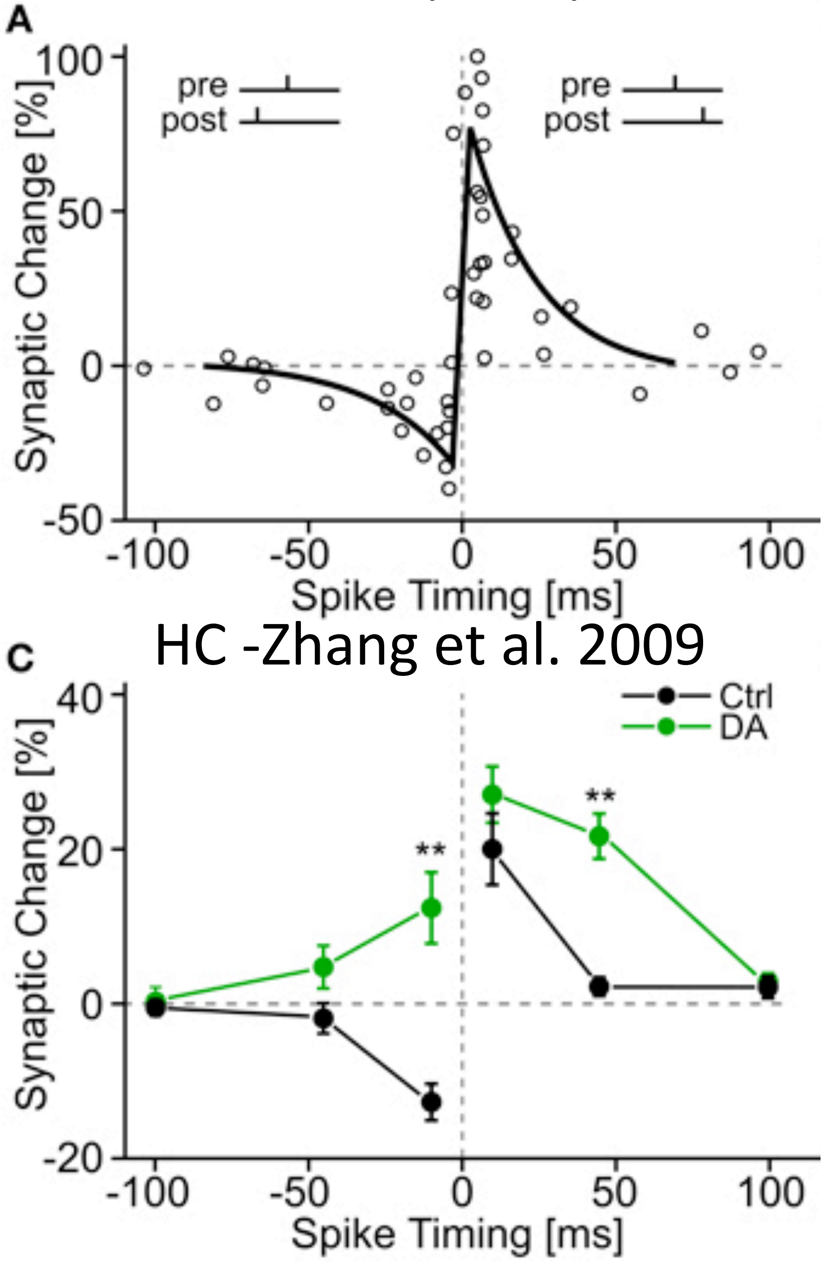
Bi and Poo, 1998

Neuromodulatory effects on STDP

HC-control

Bi and Poo (1998)

HC -Zhang et al. 2009



The effect of the presence of neuromodulators *after* the pairing is not known.

Thank you for your Attention!