BIOSYSTEMS II: NEUROSCIENCES

2015 Spring Semester

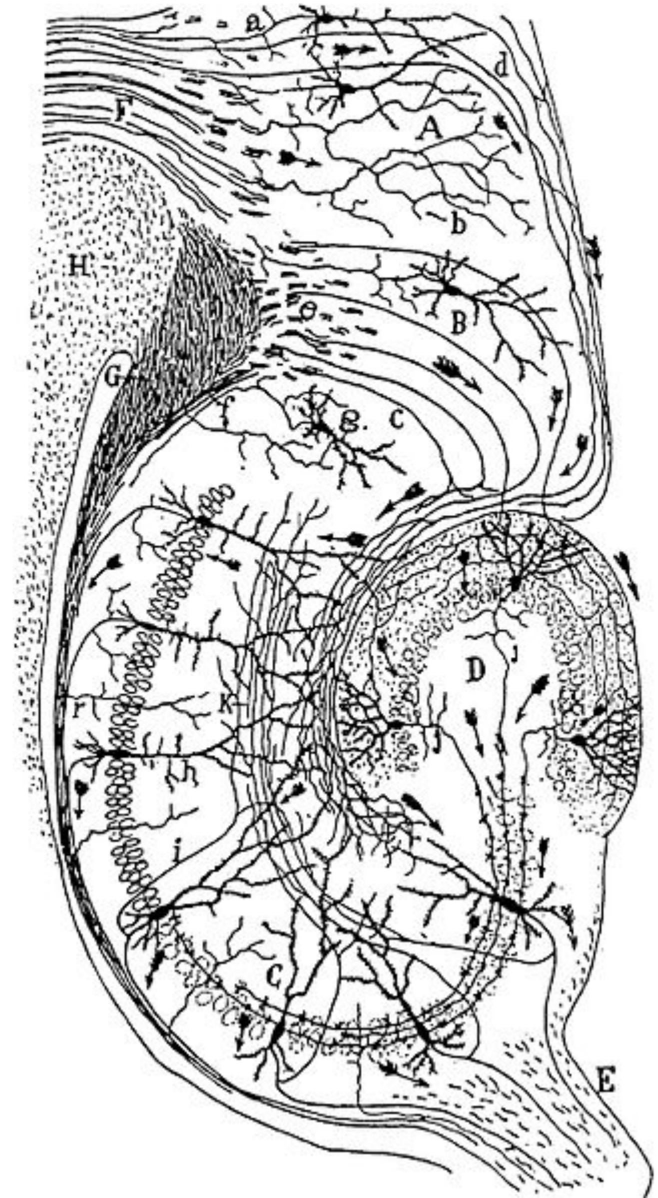
Lecture 34

Kechen Zhang

4/20/2015

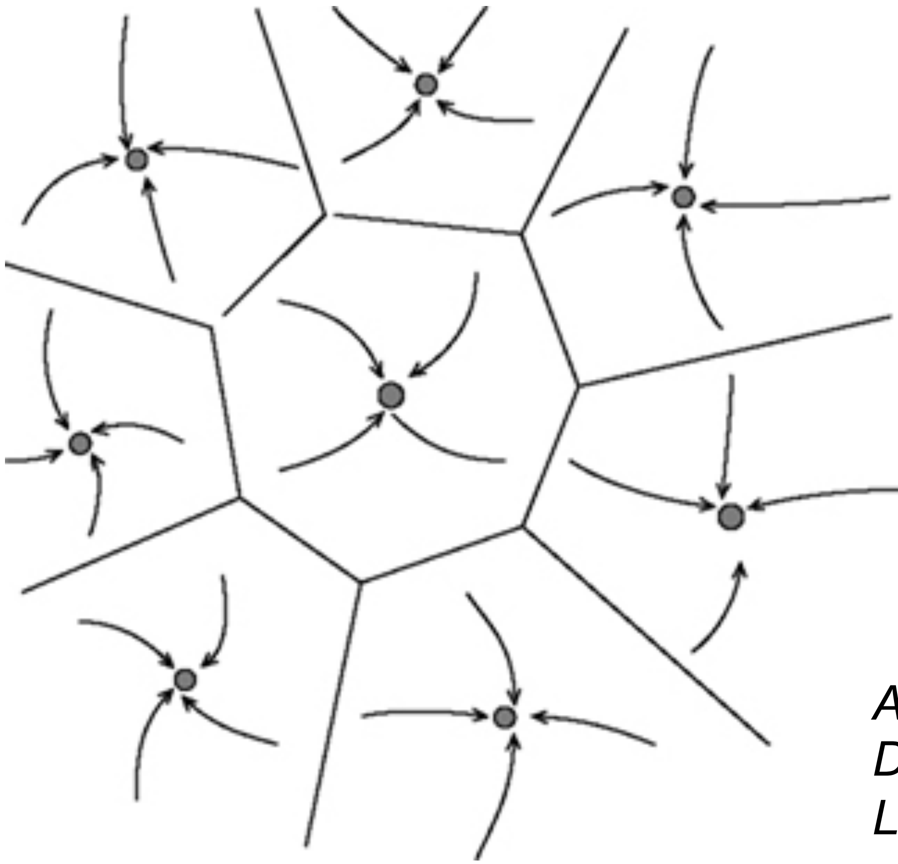
How can the brain remember things?

- Sustained activity in a recurrent network
- Sustained activity in a single neuron
- Change in synaptic connections



(Hippocampus: Cajal)

Memory as stable states (point attractors) in a recurrent network



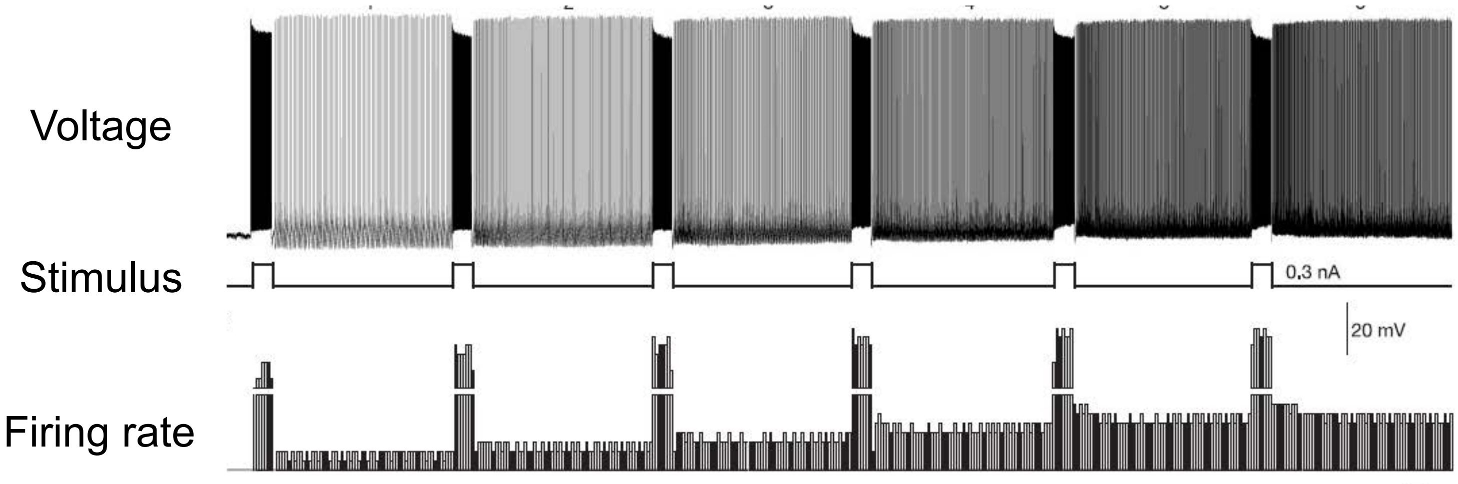
The state of activity can used to store information.

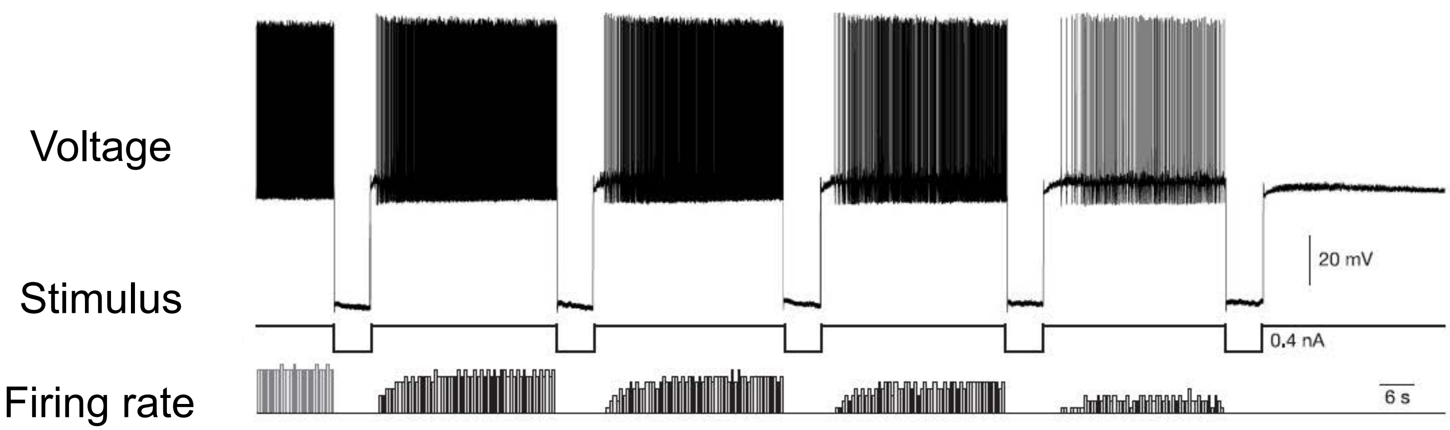
The synaptic weights of the network stay constant.

Arrows: state trajectory
Dots: point attractors
Lines: boundaries of basins of attraction

(Brunel)

Persistent firing in a single neuron (entorhinal cortex)

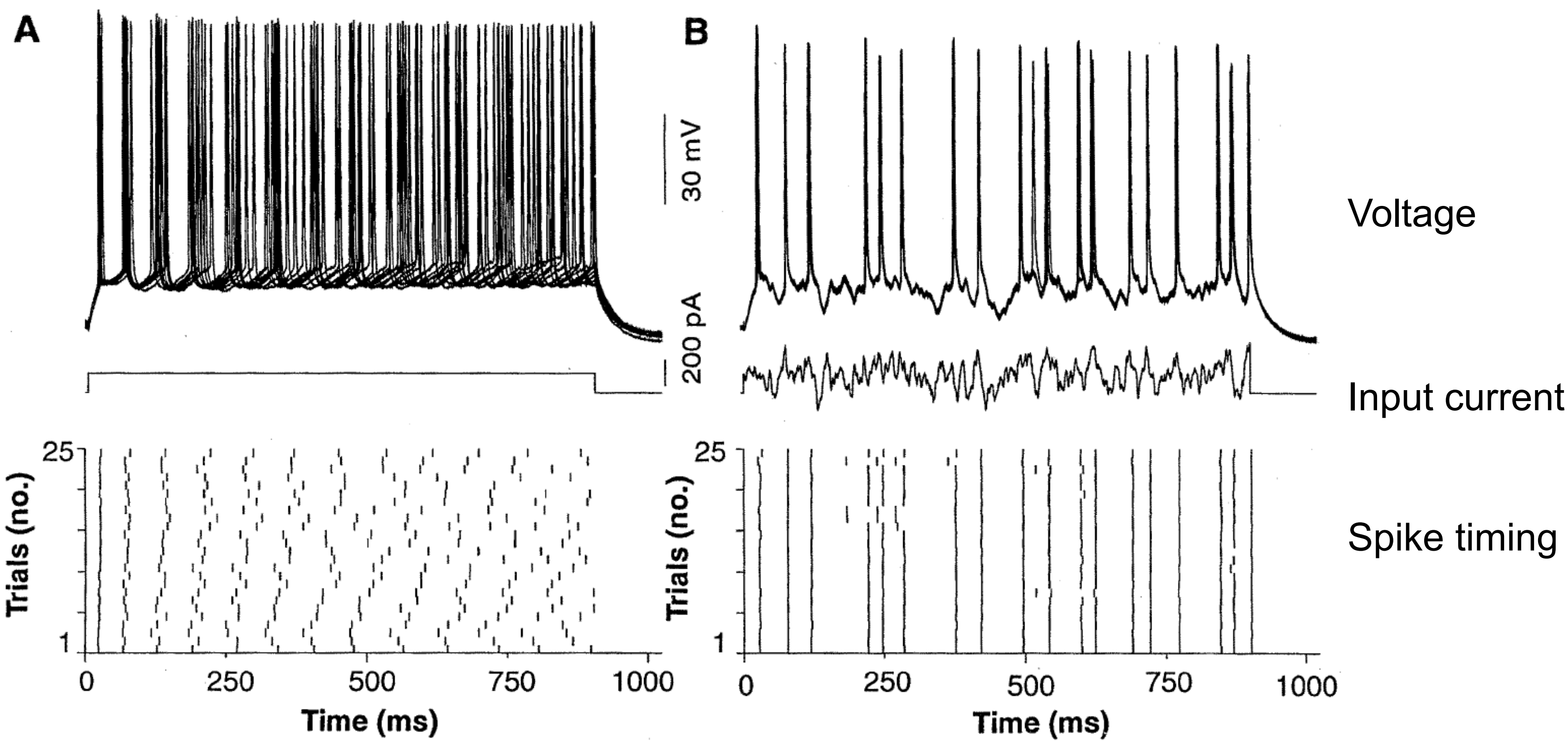




Firing rate depends on stimulus history (memory) and has many stable levels.

(Egorov)

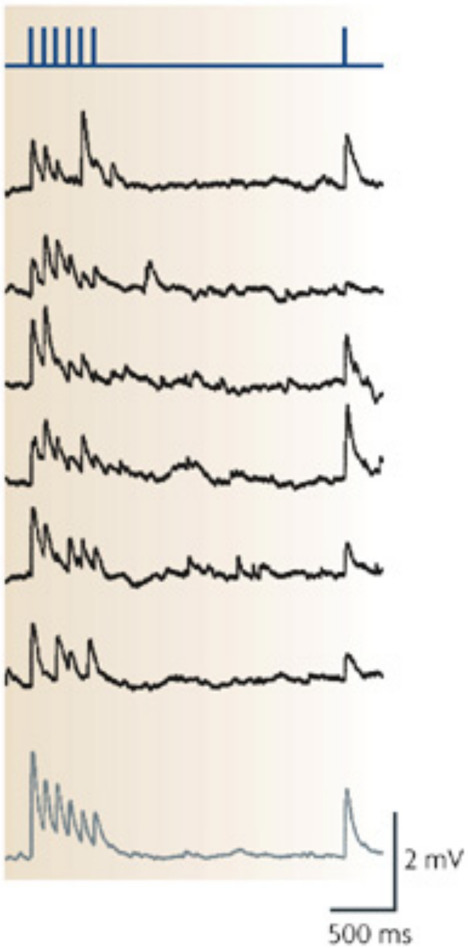
Deterministic mechanism of spike generation



A cortical neuron responds reliably to fluctuating current inputs which mimic the effect of typical synaptic bombardments.

(Mainen)

Stochastic nature of synaptic transmission



Pre-synaptic spikes

Response 1

Response 2

…

Average response

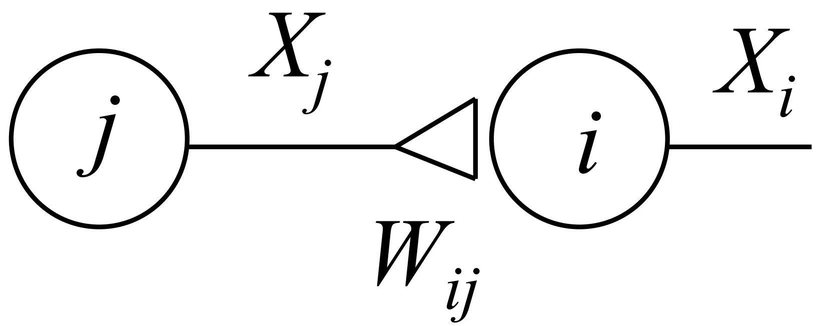
Synaptic transmission in the central nervous system is random and prune to failure because the release of each vesicle is an all-or-none event.

Left: The synaptic response of a neuron in the somatosensory cortex to repeated presynaptic stimulation varies from trial to trial.

(Steriade)

Review: Simple Hebb rule for synaptic learning

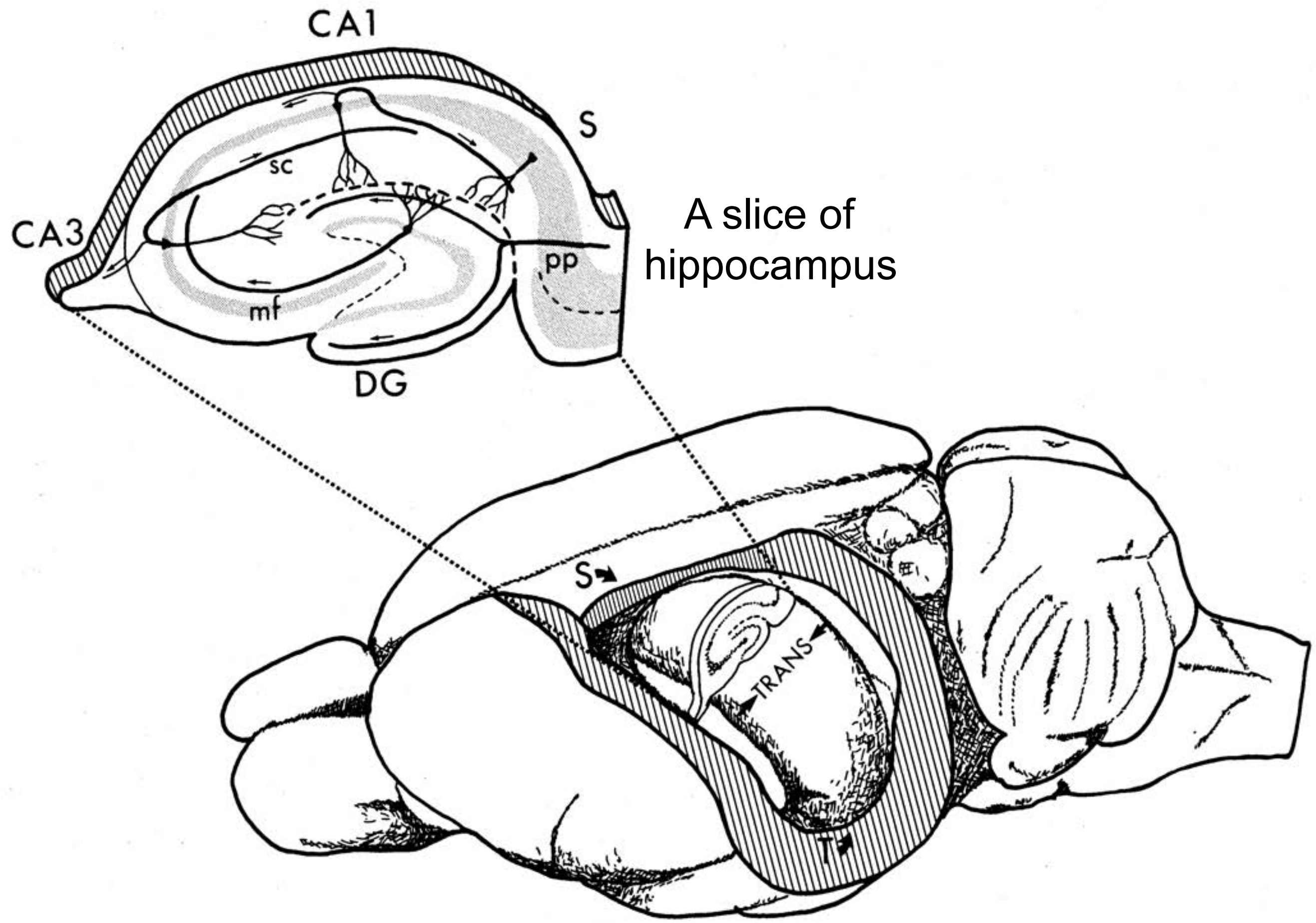
Simultaneous pre-synaptic and post-synaptic activities lead to strengthened synapse.



$$\Delta W_{ij} = k\ X_i\ X_j$$

where X_j and X_i are presynaptic and postsynaptic activities, respectively, and $k > 0$ is learning rate.

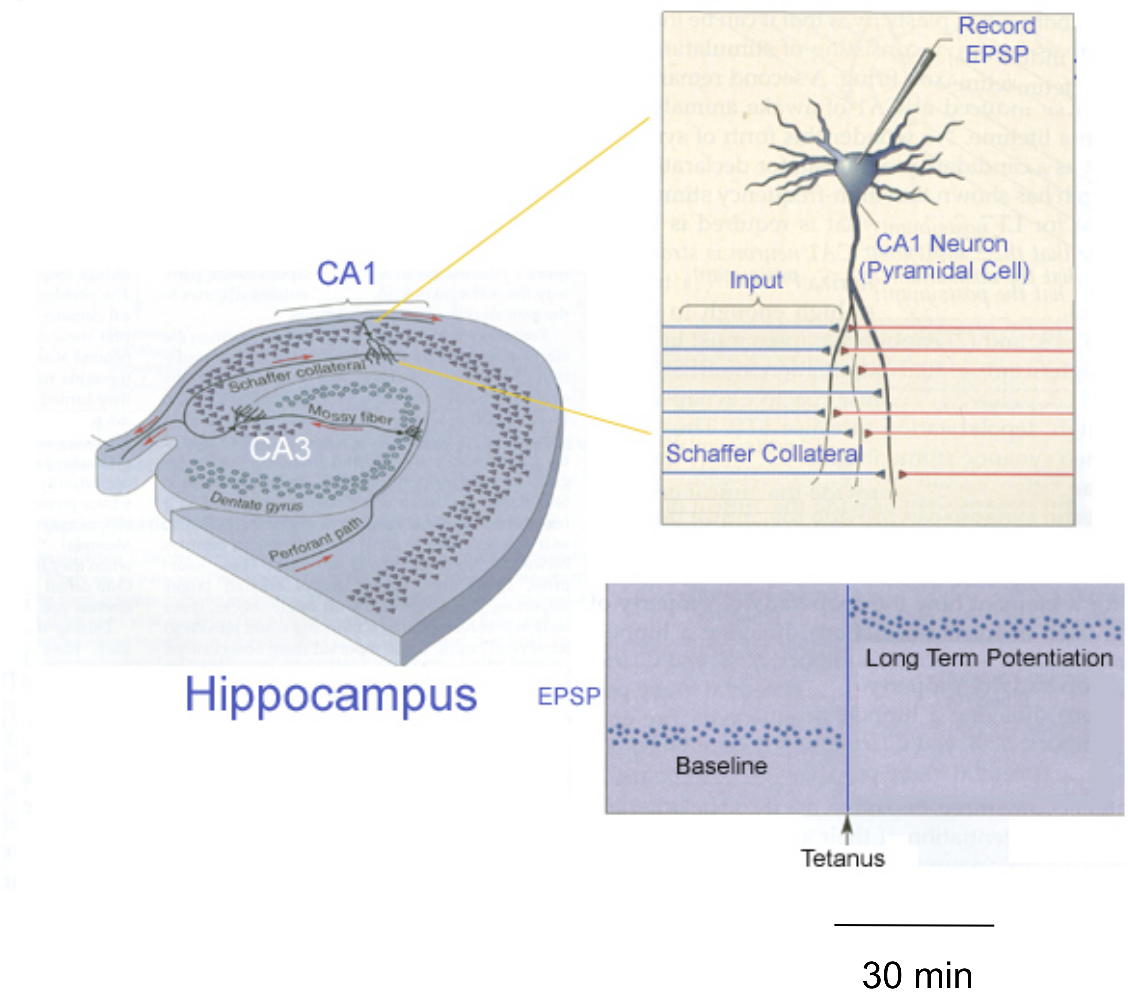
Hippocampus in Rat Brain



A slice of hippocampus

Cortex is cut out to reveal the left hippocampus

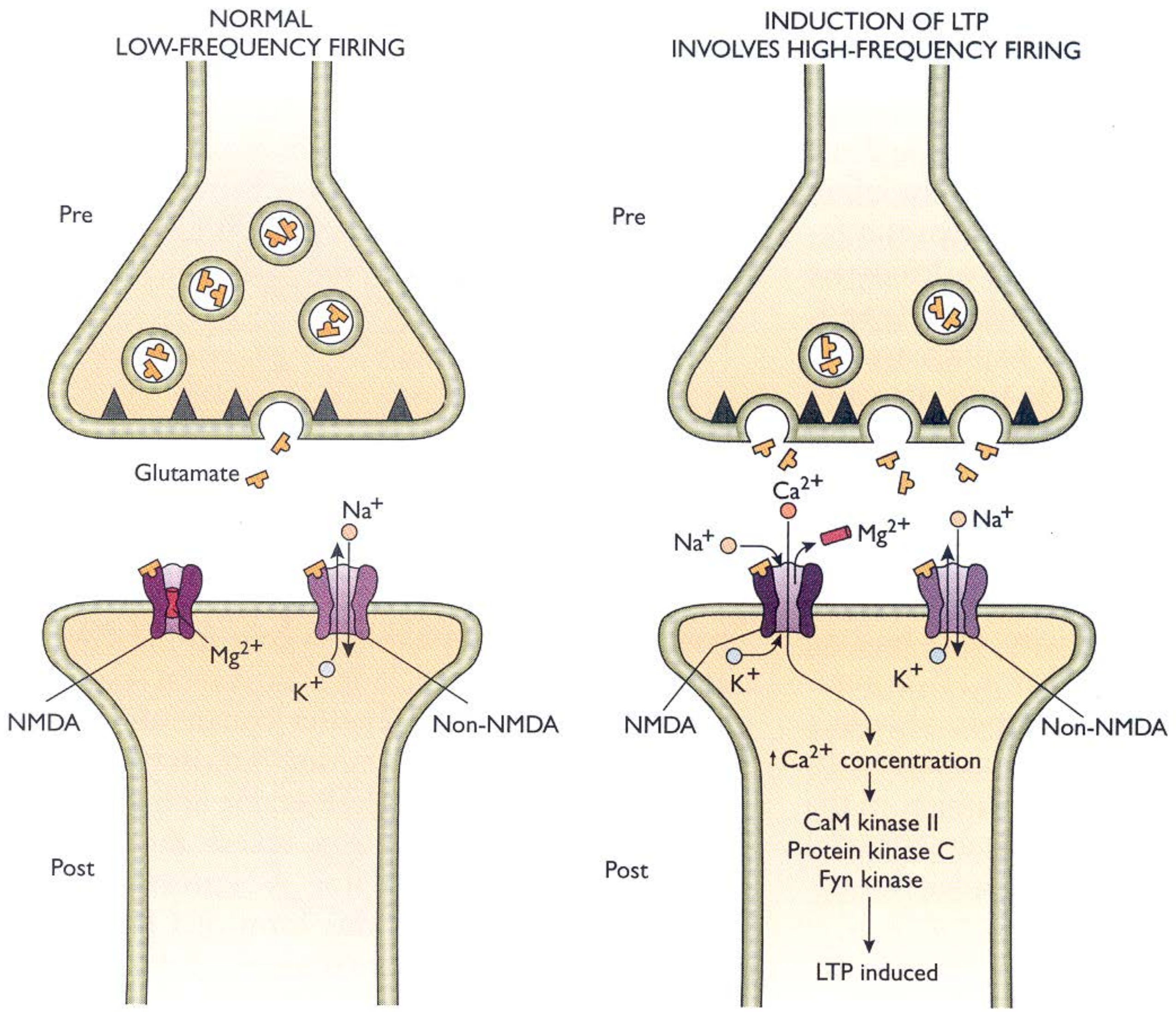
Long-Term Potentiation (LTP)



The synapses from the CA3 neurons to a CA1 neuron were enhanced, as measured by the excitatory postsynaptic potential (EPSP), after brief (~1 sec) and strong stimulation (tetanus).

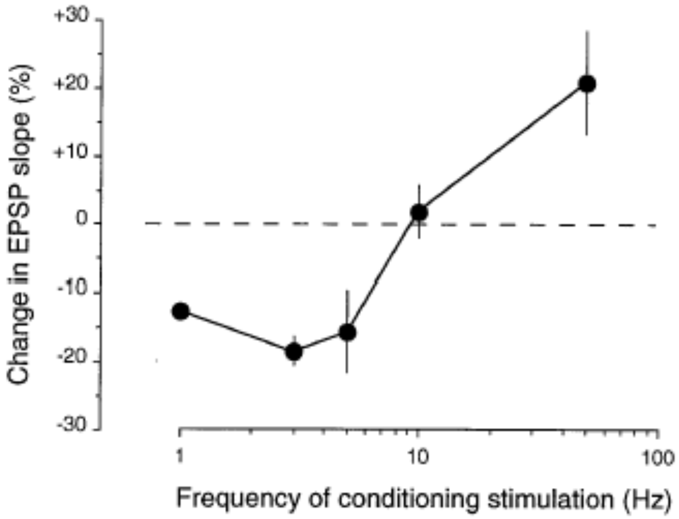
Strong stimulation can fire the postsynaptic cell while weak stimulation cannot.

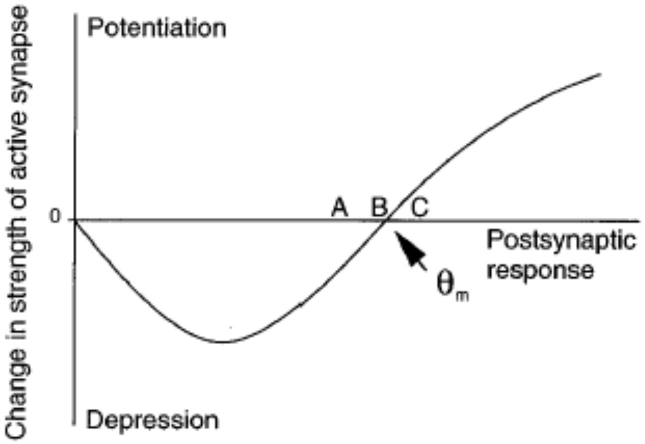
LTP and NMDA channels



The N-methyl-D-aspartate (NMDA) channels require both glutamate and post-synaptic deplorization to open up, which conditions normally imply simultaneous activation of both the pre- and the post-synaptic neurons. Ca2+ influx through open NMDA channels eventually leads to a strengthened synapse.

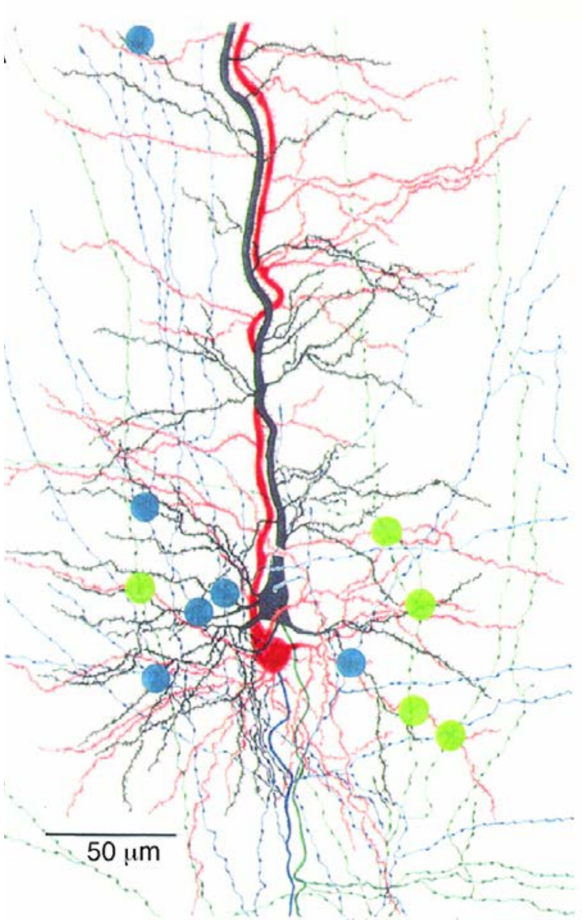
Long-Term Depression (LTD)

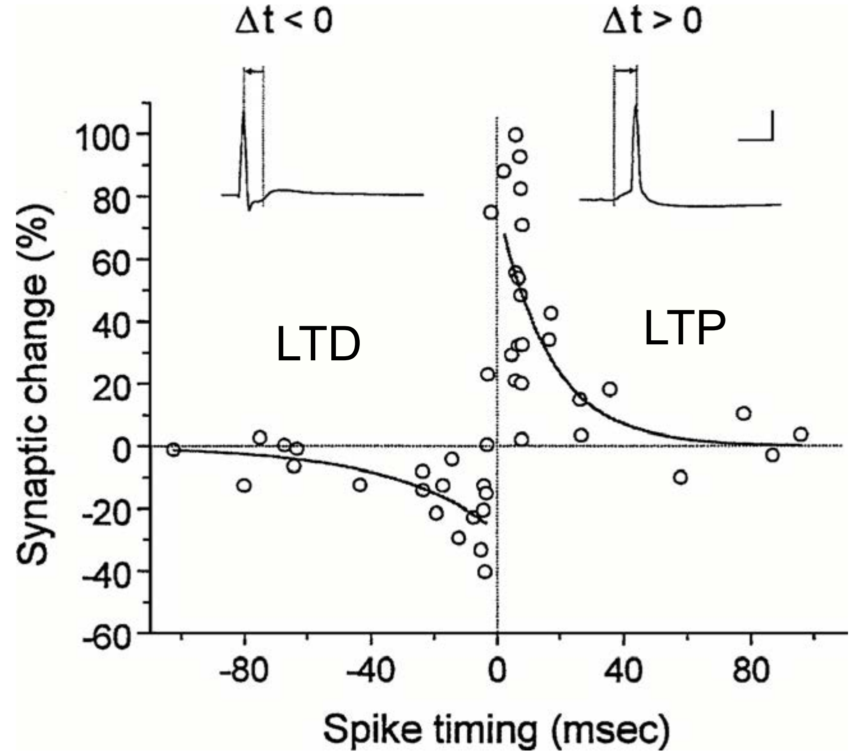




Strong stimuli can lead to enhanced synapse or long-term potentiation (LTP) as described above, whereas weak stimuli can lead to weakened synapse or long-term depression (LTD). LTD was first found in the cerebellar parallel-fiber to purkinje cell synapse. The example shown at the left comes from the hippocampal CA3 to CA1 synapse.

Spike-timing-dependent plasticity





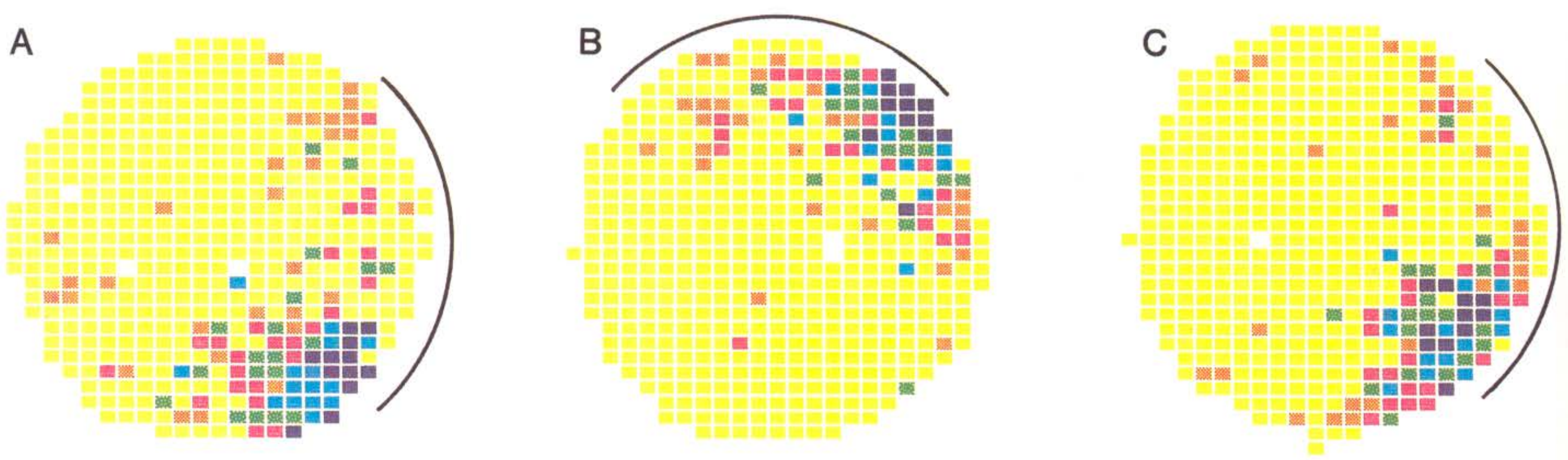
LTP (strengthened synapse) if presynaptic input precedes postsynaptic spike.

LTD (weakened synapse) if presynaptic input follows postsynaptic spike.

Temporal Hebb rule has been found in tectum, cerebellum, hippocampus, and neocortex.

(Poo)

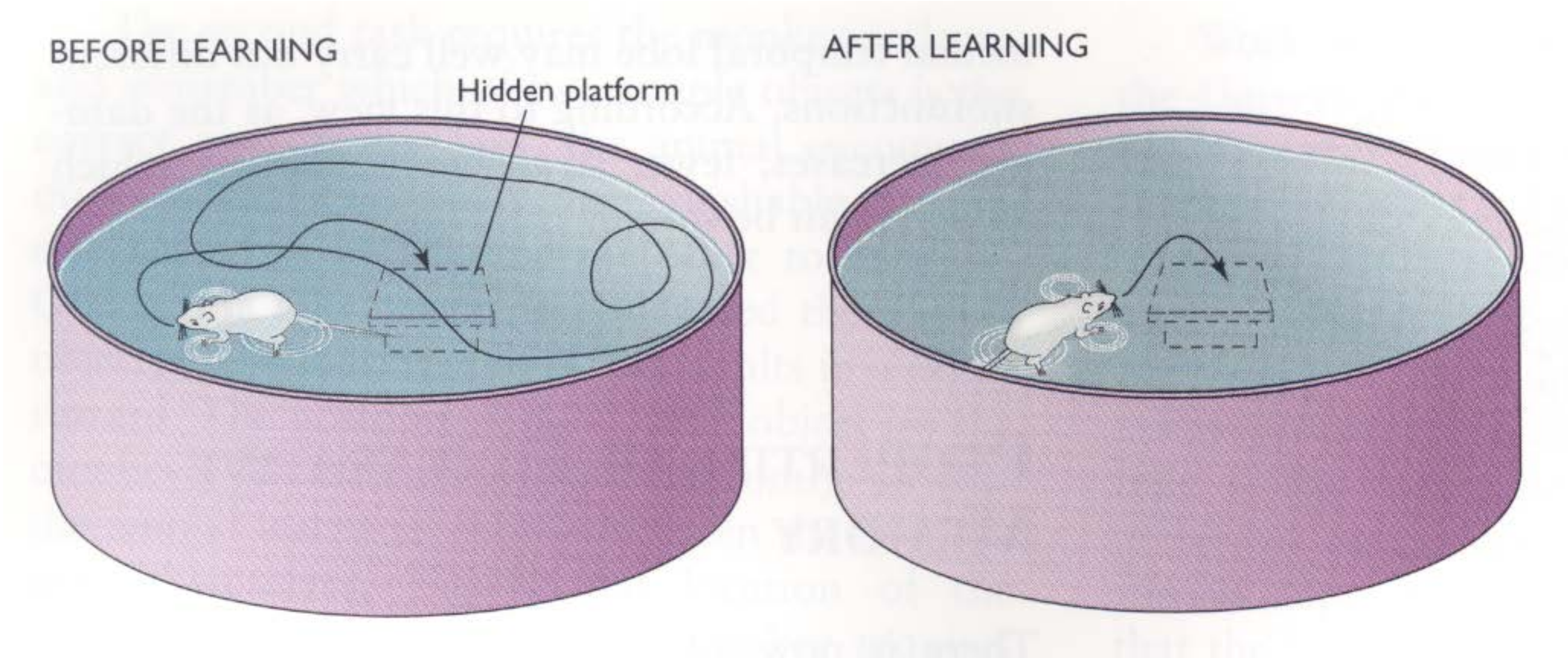
Place Field Follows Learned Visual Landmark



Basic properties of place cells:

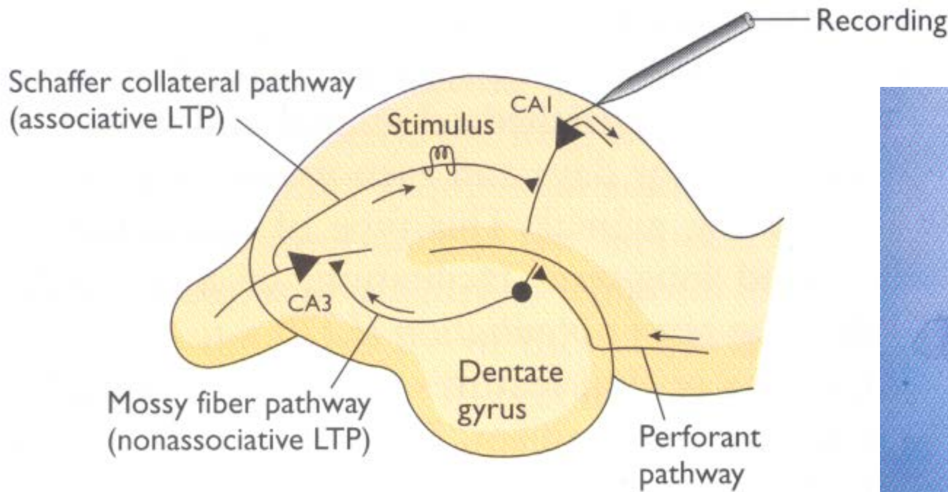
- Place cell firing is determined primarily by spatial location
- Cues for spatial location come from multiple sensory modalities and self-motion
- Rapid learning of landmarks within a few minutes

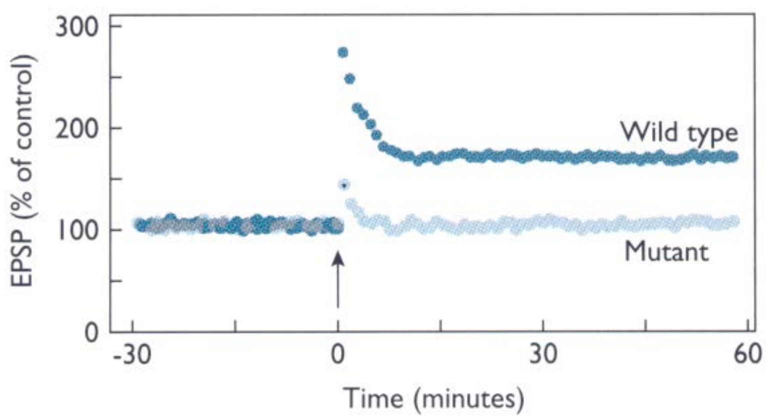
Morris water maze: Remembering a good place



- Learning the location of a platform hidden under opaque water requires intact hippocampus. The spatial information come from sensory cues outside of the maze and from self-motion
- Drugs that block synaptic plasticity (long-term potentiation mediated by NMDA channels) impair behavioral learning.

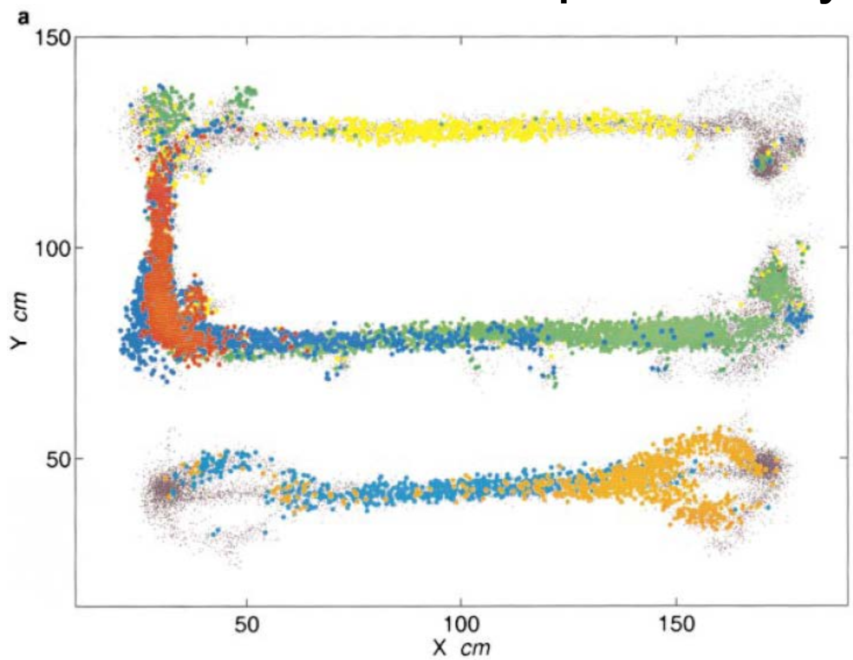
Long Term Potentiation (LTP) and NMDA Receptor Gene Knockout



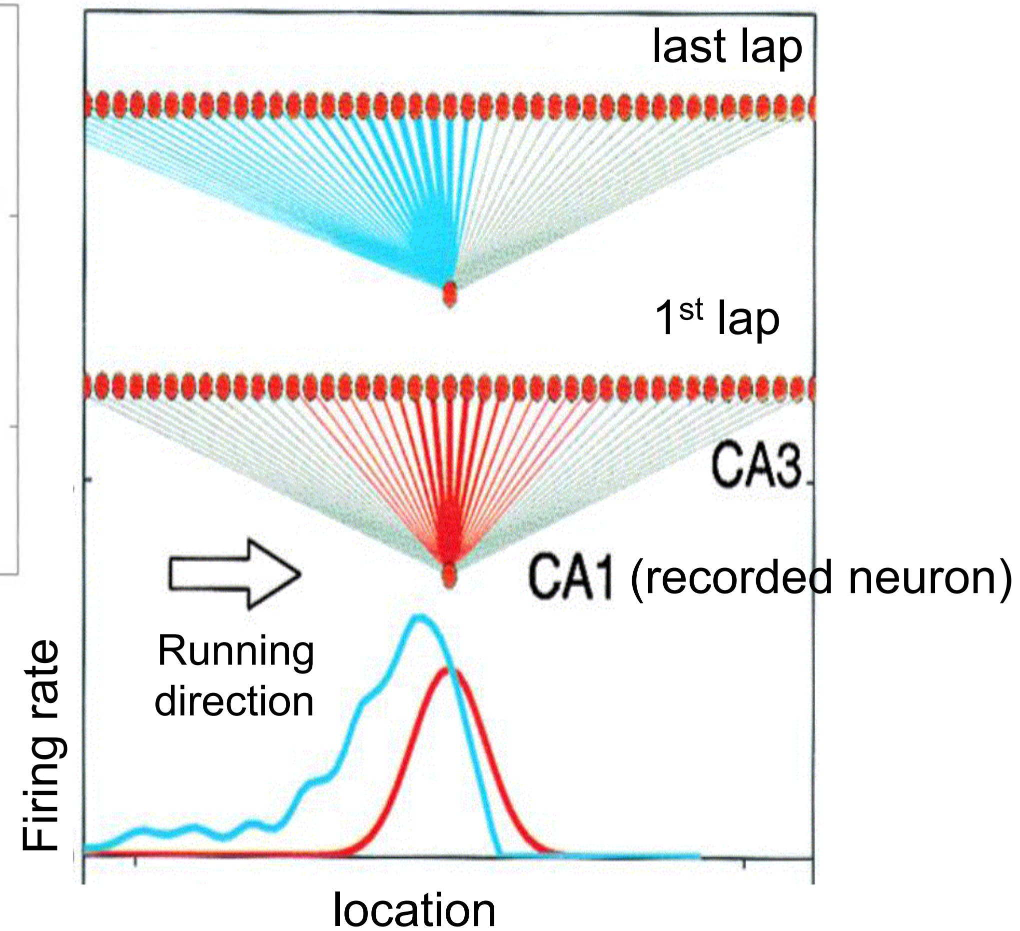


NMDA receptor is responsible for the associative LTP in CA3 to CA1 synapses. The synaptic strength, as measured by the excitatory postsynaptic potential (EPSP), can stay increased over 1 hour after only 1 second of strong stimuli. Knockout mice that lack one subunit of NMDA receptor in CA1 (dark band in the slice above) have defective LTP (left), unstable place fields, and cannot learn Morris water maze.

Place cell plasticity: Asymmetric expansion effect explained by Hebbian learning



Hippocampal place fields on a track with a rat running continuously back and forth



CA1 place field expands and shifts backwards.
Red curve: 1st lap
Blue curve: last lap

(Mehta)

Review: supervised learning in a perceptron

Output: $$y = \sum_i w_i x_i$$

where

input pattern: $x_1, x_2, x_3, \ldots$

weights: $w_1, w_2, w_3, \ldots$

Each input pattern is classified into one of two classes depending on whether $y > 0$ or $y < 0$.

Learning rule: $$\Delta w_i = k(\tilde{y} - y)x_i$$

where

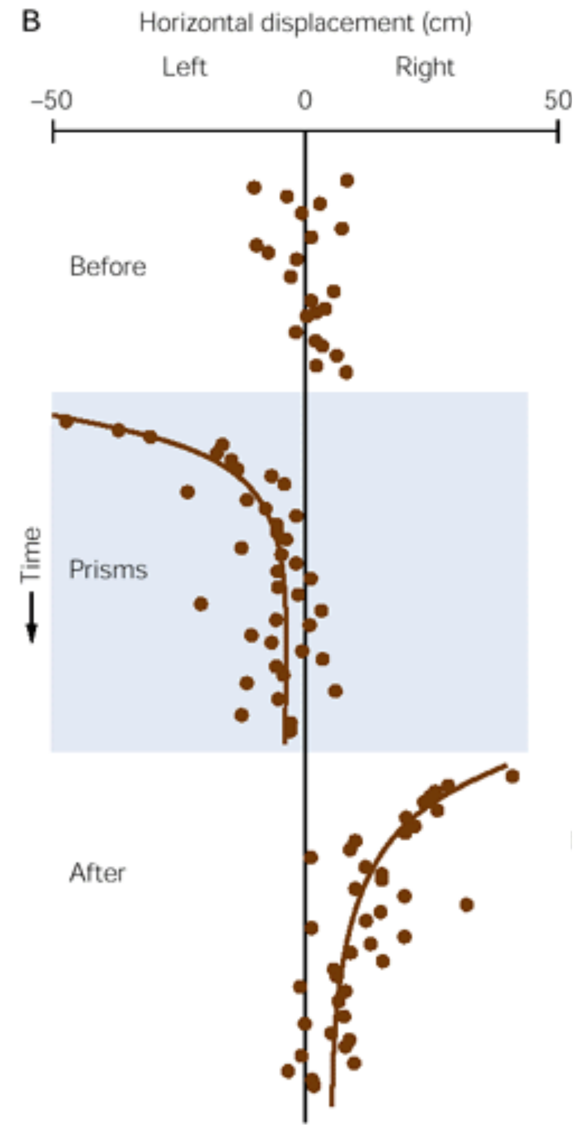
desired output: $\tilde{y}$

learning rate: $k > 0$

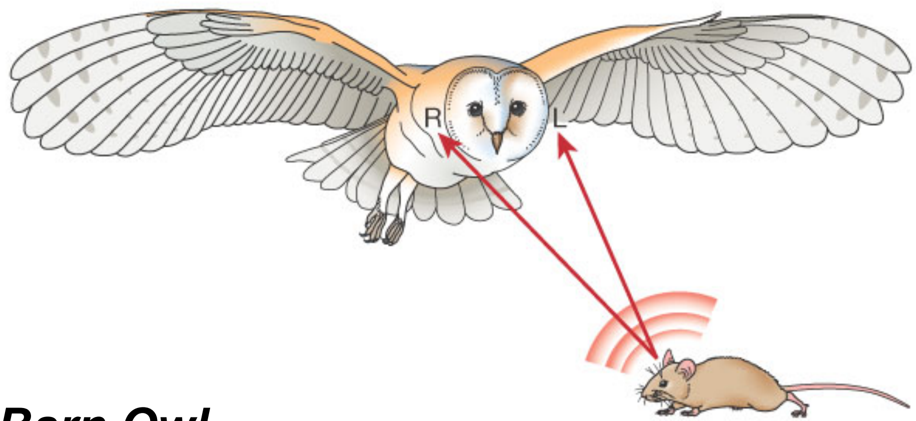
Example of supervised learning

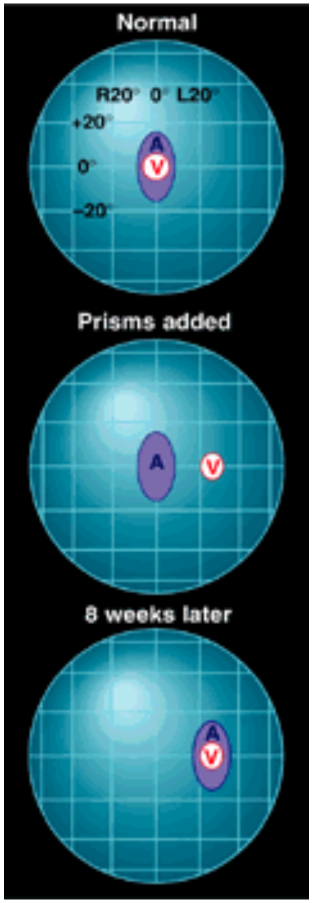
Eye-hand coordination
during adaptation to prism glasses

A



Example of supervised learning



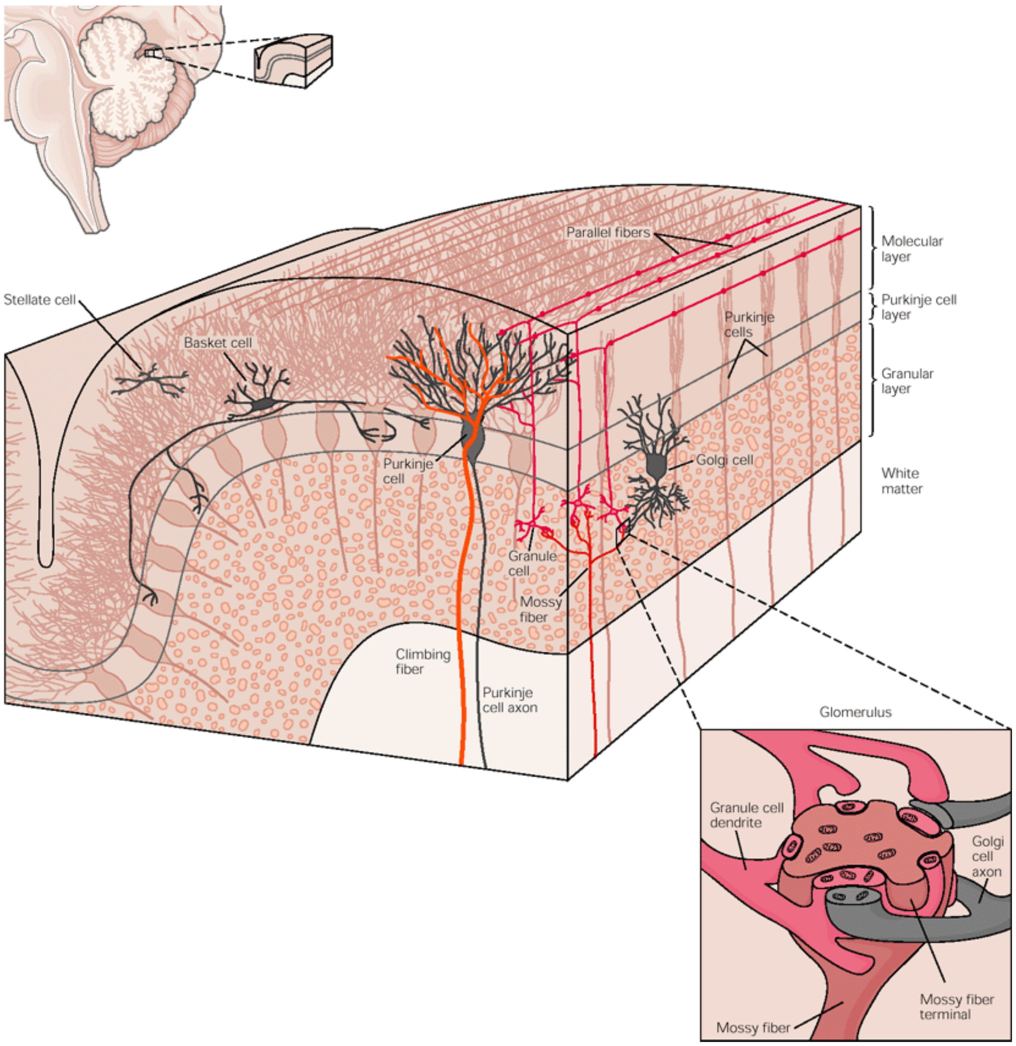


Barn Owl

Behavior: Visual input serves as a teacher for learning to orient towards an auditory target.

Neurophysiology: Some neurons in the optic tectum have both a visual receptive field (V) and an auditory receptive field (A). Prisms shift the location of visual space, making it misaligned with the auditory space. After training, the auditory receptive field is shifted to realign with the visual receptive field.

Supervised learning: Purkinje cell in cerebellum



Purkinje cells are the output of cerebellum

Teaching signal (excitatory): climbing fiber from inferior olive

Long-term depression (LTD): parallel fiber synapses (excitatory) are weakened by co-activation of climbing fiber and parallel fiber.

Supervised learning:
Relation to optimal linear mapping

Optimal linear mapping $\mathbf{y} = \mathbf{W}\mathbf{x}$ finds the weight matrix $\mathbf{W}$ that minimizes

$E = \sum_{m=1}^{M} \left| \tilde{\mathbf{y}}^{(m)} - \mathbf{W}\mathbf{x}^{(m)} \right|^2$ where $\left[\mathbf{x}^{(1)}, \cdots, \mathbf{x}^{(M)} \right] = \mathbf{X}$ are the input vectors, and

$\left[\tilde{\mathbf{y}}^{(1)}, \cdots, \tilde{\mathbf{y}}^{(M)} \right] = \tilde{\mathbf{Y}}$ are the desired output vectors. The result is $\mathbf{W} = \tilde{\mathbf{Y}}\mathbf{X}^{\dagger}$

where $\mathbf{X}^{\dagger}$ is the pseudoinverse of $\mathbf{X}$.

Perceptron learning rule for $\mathbf{y} = \mathbf{W}\mathbf{x}$ is $\Delta\mathbf{W} = k(\tilde{\mathbf{y}} - \mathbf{y})\mathbf{x}^{\mathrm{T}}$ ("online learning").

For "batch learning" with all the data included, the learning rule becomes:

$\Delta\mathbf{W} = k\sum_{m=1}^{M} (\tilde{\mathbf{y}}^{(m)} - \mathbf{y}^{(m)})\mathbf{x}^{(m)\mathrm{T}}$ where $\mathbf{y}^{(m)} = \mathbf{W}\mathbf{x}^{(m)}$ is the output vector.

When learning stops $(\Delta\mathbf{W} = \mathbf{0})$, we have $\tilde{\mathbf{Y}}\mathbf{X}^{\mathrm{T}} = \mathbf{W}\mathbf{X}\mathbf{X}^{\mathrm{T}}$ (normal equation).

Thus $\mathbf{W} = \tilde{\mathbf{Y}}\mathbf{X}^{\mathrm{T}}(\mathbf{X}\mathbf{X}^{\mathrm{T}})^{-1} = \tilde{\mathbf{Y}}\mathbf{X}^{\dagger}$ if the matrix inverse exists.

Computational theories of learning

- Supervised learning:
  A teaching signal knows the exact value of the desired output and helps to correct the error of the actual output.
  Examples: perceptrons

- Unsupervised learning:
  No explicit teaching signal.
  Examples: Hebb rule, self-organizing maps

- Reinforcement learning:
  Maximize reward in a stochastic environment.

Dopamine neuron in VTA (ventral tegmental area) signals reward prediction error (= actual reward – predicted reward)