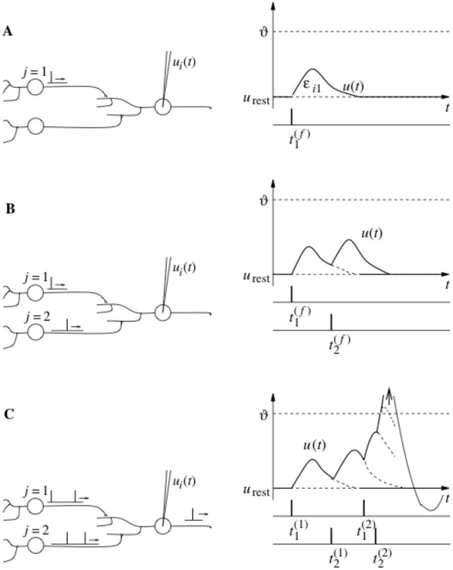
Neuroinformatics 2013

March 19, 2014

Lecture 4: Associators and synaptic plasticity

PSP and AP - Supplement of lec4:LIF-neuron noise simulation II

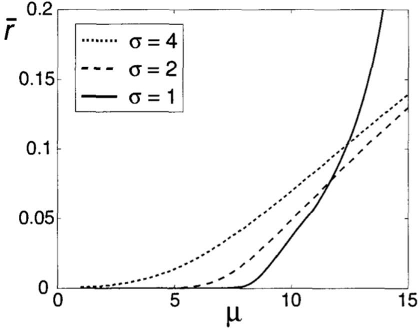


From Buracas et al. 1998

Activation function

- IF neuron driven by I_{ext} with normal pdf $\rightarrow$ stochastic differential equation
- t^f is random variable
- average firing rate

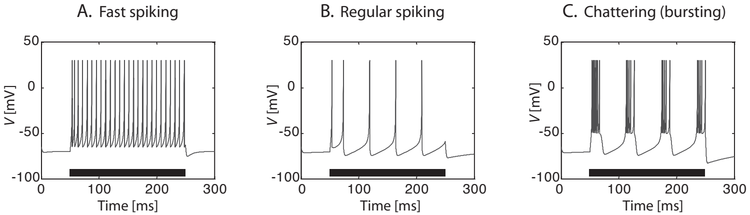
$$\bar{r} = (t^{ref} + \tau_m \int_{\mathrm{v_{res}} - \mathrm{RI_{ext}}/\sigma}^{\vartheta - RI_{ext}/\sigma}) \sqrt{(}\pi) e^{v^2} [1 + erf(v)dv])^{-1}$$



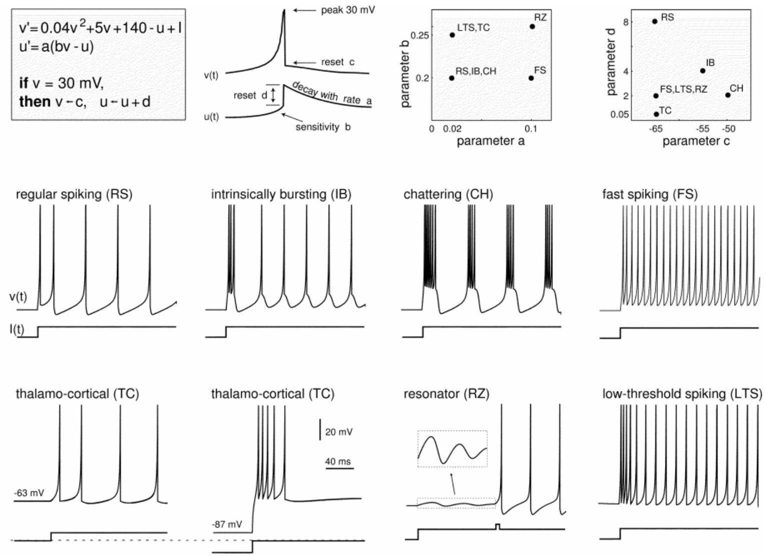
The Izhikevich neuron I

$$\frac{\mathrm{d}v(t)}{\mathrm{d}t} = 0.04v^2 + 5v + 140 - u + I(t)$$
$$\frac{\mathrm{d}u(t)}{\mathrm{d}t} = a(bv - u)$$

$$v(v > 30) = c \;\text{ and }\; u(v > 30) = u + d$$



The Izhikevich neuron II



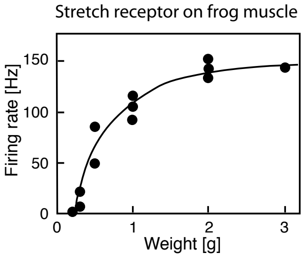
McCulloch-Pitts neuron

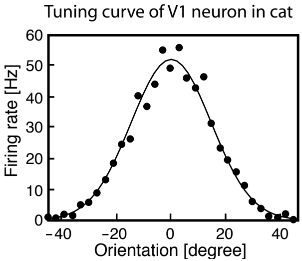
- first model of neuron, A logical calculus of the ideas immanent in nervous activity, Bulletin of Mathematical Biophysics 5:115-133, 1943
- 1958 - percepton by Rosenblatt
- heavy side function as transfer (activation) function, simple logical OR, AND

$$h = \sum_i x_i^{\text{in}}$$

$$x^{\text{out}} = \begin{cases} 1 & \text{if } h > \Theta \\ 0 & \text{otherwise} \end{cases}$$

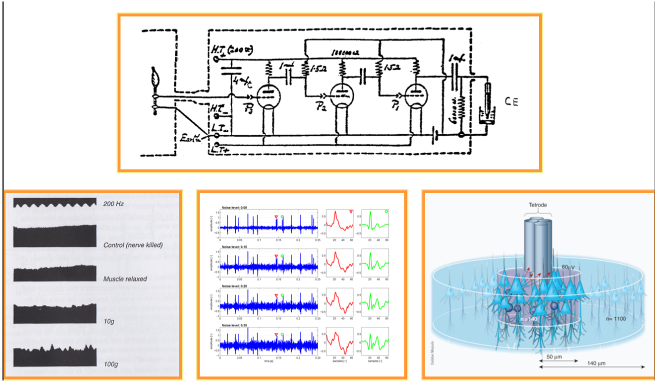
The firing rate hypothesis





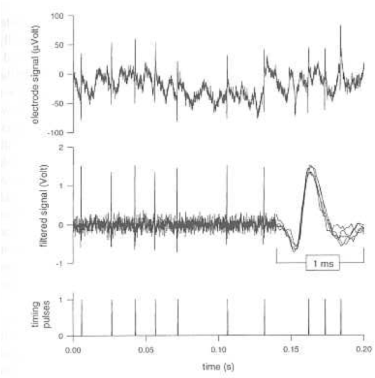
History: Adrian

- Sir Edgarda Adriana (Nobel price for medicine - 1932) `http://nobelprize.org/nobel_prizes/medicine/laureates/1932/adrian-bio.html`

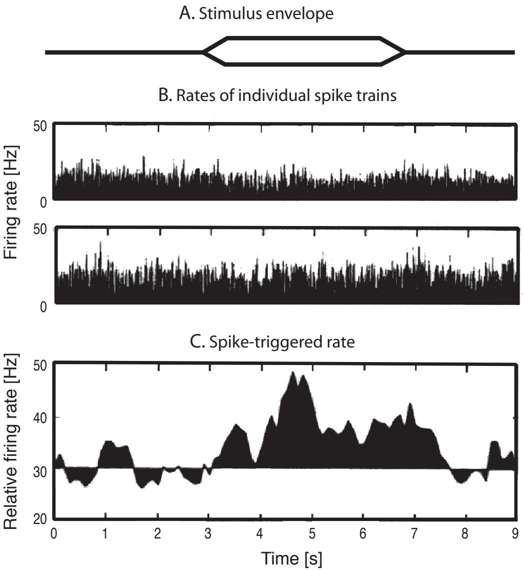


All or none coding

- top:tungsten electrode in fly's brain, middle: low frequency removal, bottom: spikes

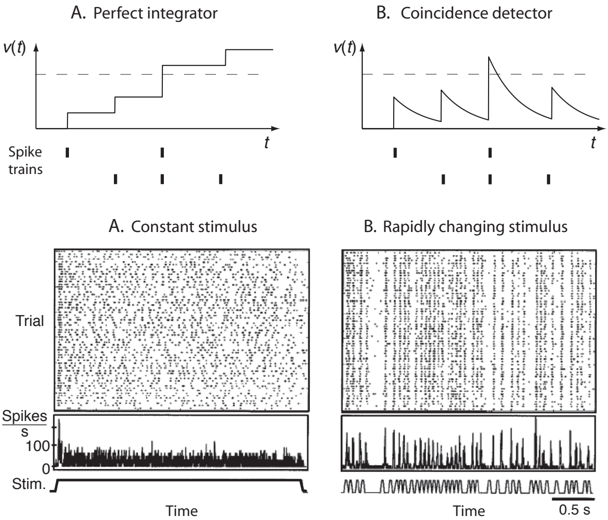


Correlation coding



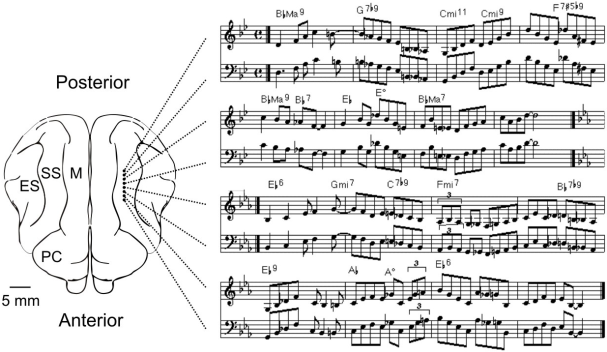
From DeCharms and Merzenich 1996

Integrator or coincidence detector?



From Buracas et al. 1998

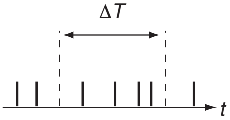
Neuronal music

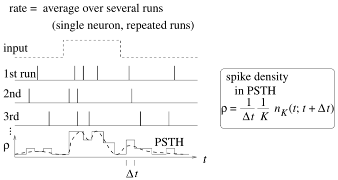


http://cns.iaf.cnrs-gif.fr/alain_music.html

Rate codes

- Spike count - average over time
- Spike density - average over several trial: peri-stimulus-timehistogram (PSTH)
- Population activity - organization of many neurons in columns cells. Idealized situations - neurons with the same properties.



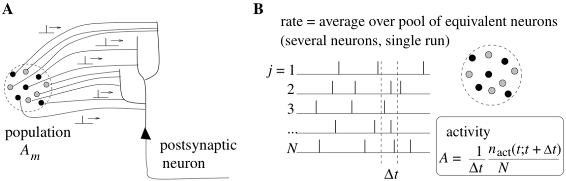


Population model

$$a(t) = \frac{numberofspikesin\Delta T}{\Delta T} = \frac{1}{\Delta T}\int_{t-\Delta T/2}^{t+\Delta T/2} \delta(t^{'} - t^{f})dt^{'}$$

$$A(t) = \lim_{\Delta T \to 0} \frac{numberofspikesinpopulationofsizeN}{N}$$

$$= \lim_{\Delta T \to 0} \frac{1}{\Delta T}\int_{t-\Delta T/2}^{t+\Delta T/2} \frac{1}{N}\sum_{i=1}^{N} \delta(t^{'} - t^{f})dt^{'}$$



Population dynamics

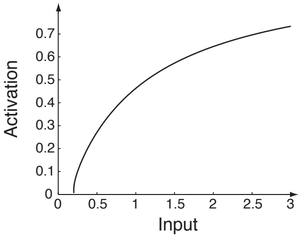
For slow varying input (adiabatic limit), when all nodes do practically the same, same input, etc (Wilson and Cowan, 1972):

$$\tau \frac{\mathrm{d}A(t)}{\mathrm{d}t} = -A(t) + g(RI^{\mathrm{ext}}(t)). \tag{1}$$

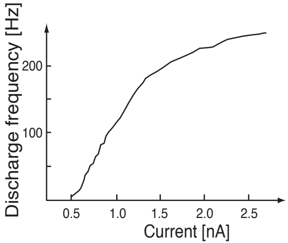
Gain function:

$$g(x) = \frac{1}{t^{\mathrm{ref}} - \tau \log(1 - \frac{1}{\tau x})}, \tag{2}$$

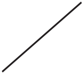
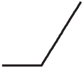
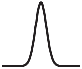
A. Activation function for population average in adiabatic limit



B. Activation function of hippocampal pyramidal neuron

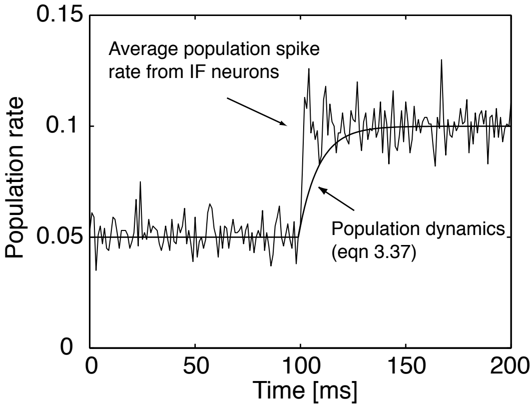


Other gain functions

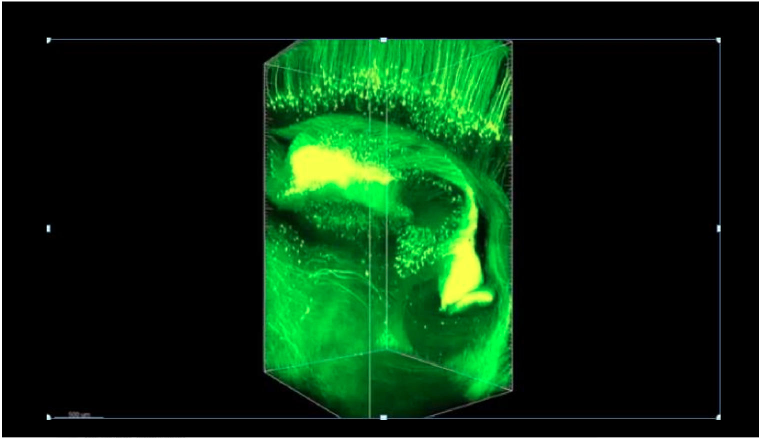
Type of function	Graphical represent.	Mathematical formula	MATLAB implementation
Linear		$g^{\text{lin}}(x) = x$	`x`
Step		$g^{\text{step}}(x) = \begin{cases} 1 & \text{if } x > 0 \\ 0 & \text{elsewhere} \end{cases}$	`floor(0.5*(1+sign(x)))`
Threshold-linear		$g^{\text{theta}}(x) = x\,\Theta(x)$	`x.*floor(0.5*(1+sign(x)))`
Sigmoid		$g^{\text{sig}}(x) = \frac{1}{1+\exp(-x)}$	`1./(1+exp(-x))`
Radial-basis		$g^{\text{gauss}}(x) = \exp(-x^2)$	`exp(-x.^2)`

SIMULATION - Fast population response

- Simulation with 1000 independent (NOT CONNECTED) IF neurons:$I_{ext} = I_{ext} + \eta, \eta \in N(0,1)$, $\tau_m = 10$ ms,$\vartheta = 10$ mV
- Switching from $RI_{ext} = 11$ mV at $t = 100$ ms to $RI_{ext} = 16$ mV

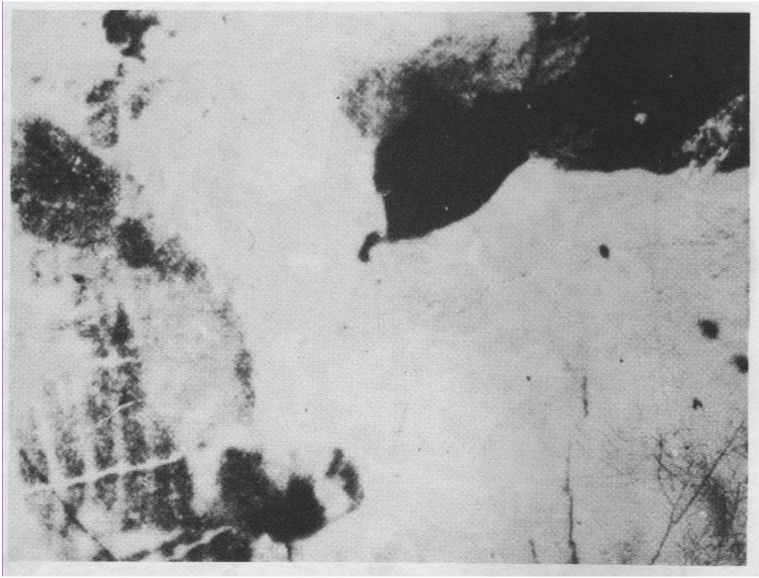


New imaging method - Clarity - Nature April 2013

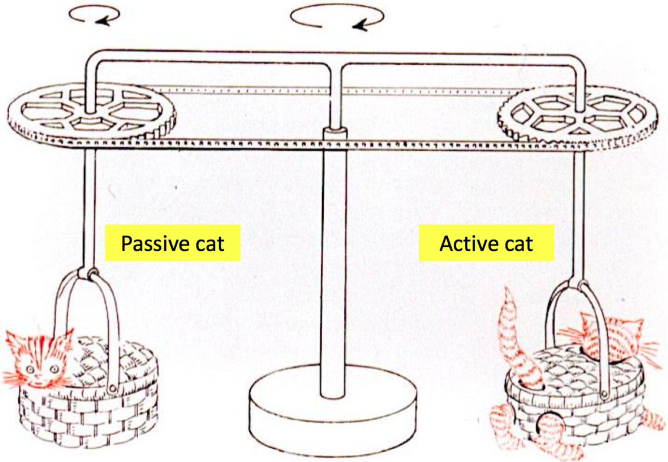


Learning what is is?

Learning what is is?



Action-perception loop



Held R, Hein A (1963)

Types of plasticity

- **Structural plasticity** is the mechanism describing the generation of new connections and thereby redefining the topology of the network.
- **Functional plasticity** is the mechanism of changing the strength values of existing connections.

Hebbian plasticity

”When an axon of a cell A is near enough to excite cell B or repeatedly or persistently takes part in firing it, some growth or metabolic change takes place in both cells such that A’s efficiency, as one of the cells firing B, is increased.”

Donald O. Hebb, **The organization of behavior**, 1949
See also Sigmund Freud, **Law of association by simultaneity**, 1888
Santiago Ramn y Cajal - memories might instead be formed by strengthening the connections between existing neurons to improve the effectiveness of their communication, 1894

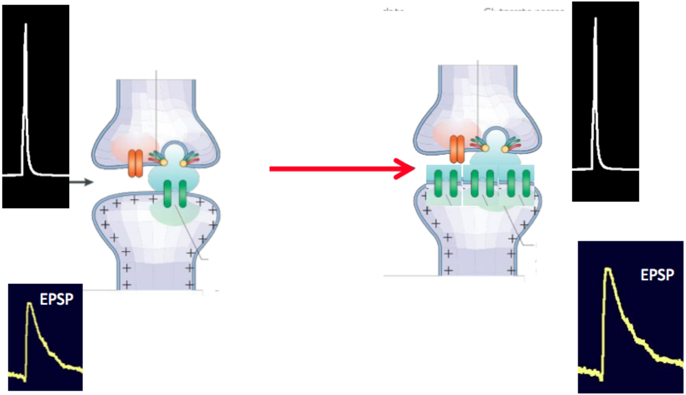
Possible neuronal mechanisms sub-serving learning and memory

New nerve cells grow - new functional neural networks are formed .1
for exhibiting new learned items- structural plasticity

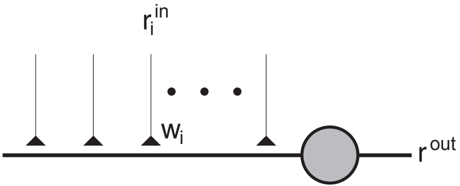
New synaptic connections (new functional neural networks) are .2
formed - structural plasticity - (*Ramon Y. Cajal)*

Strength of existing (synaptic) connections change - (new functional .3
neural networks) - functional plasticity (Donald Hebb)

Synaptic mechanism



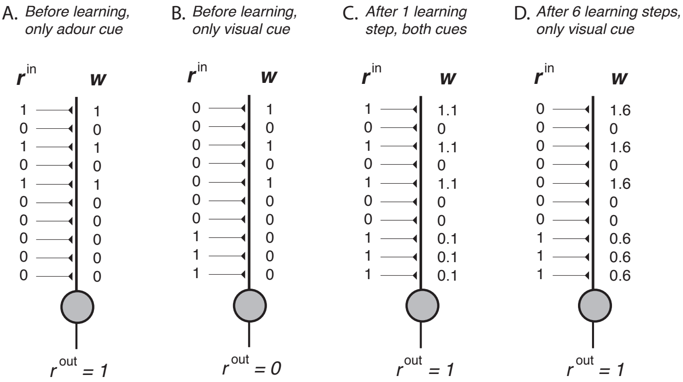
Association



Neuron model: In each time step the model neurons fires if $\sum_i w_i r_i^{\text{in}} > 1.5$

Learning rule: Increase the strength of the synapses by a value $\Delta w = 0.1$ if a presynaptic firing is paired with a postsynaptic firing.

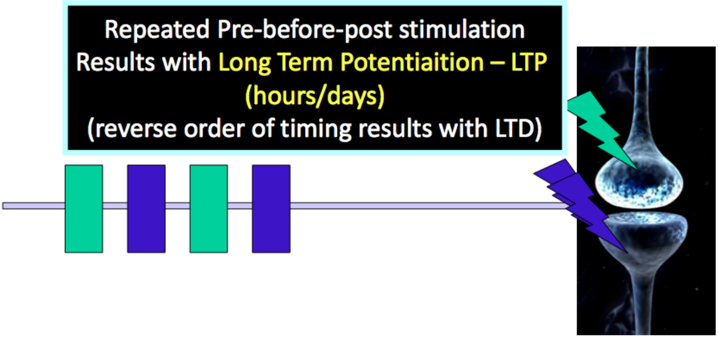
Associative learning



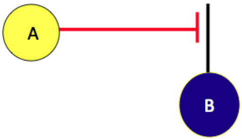
Features of associators and Hebbian learning

- Pattern completion and generalization, recall from partial input, overlap between input and trained pattern (recognition of noisy numbers)
- Prototypes and extraction of central tendencies, training on many similar but not equivalent examples (individual face, many common features in all faces)
- Graceful degradation and fault tolerance (loss of synapses or whole neurons)

Long term potentiaition

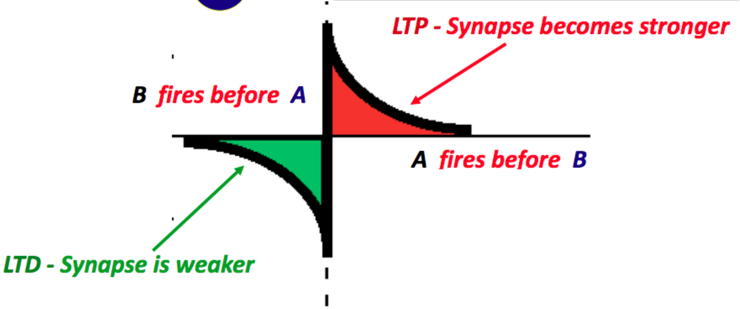


Hebbian model



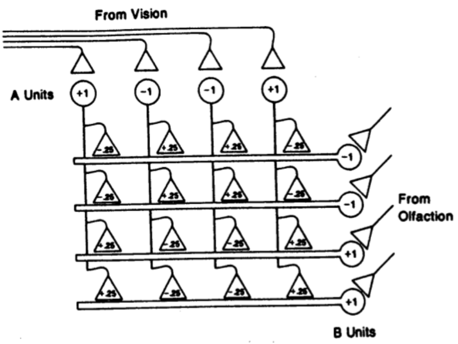
$$\Delta w_+ = A_+ e^{\frac{-(t_{post}-t_{pre})}{\tau_+}} \quad when\left(t_{post} > t_{pre}\right)$$

$$\Delta w_- = A_- e^{\frac{-(t_{post}-t_{pre})}{\tau_-}} \quad when\left(t_{pre} > t_{post}\right)$$



How memory is stored?

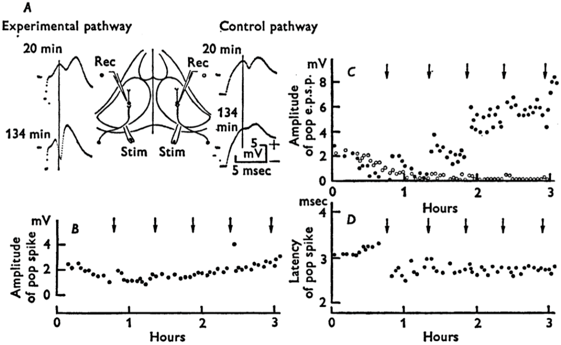
- Connectionist modeling of memory, one neural network (associator) for visual and olfactory system!
- machine learning theory of neural networks -e.g. back propagation principle



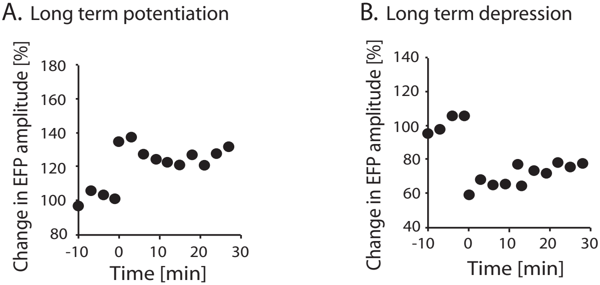
$$\begin{bmatrix} - & + & + & - \\ - & + & + & - \\ + & - & - & + \\ + & - & - & + \end{bmatrix} + \begin{bmatrix} + & - & + & - \\ - & + & - & + \\ - & + & - & + \\ + & - & + & - \end{bmatrix} = \begin{bmatrix} & & ++ & -- \\ -- & ++ & & \\ & & -- & ++ \\ ++ & -- & & \end{bmatrix}$$

Original LTP by Bliss and Lomo, 1973

- Long-lasting changes of synaptic response characteristics
- High frequency-stimulus is applied (plasticity-induced tetanus) $\rightarrow$ long-term potentiation(to strengthen, make more potent) (LTP) average amplitude of EPSP increased
- Long frequency stimulus $\rightarrow$ long-term depression (LTD)

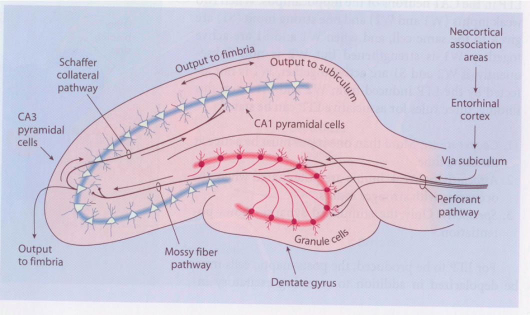


Classical LTP and LTD



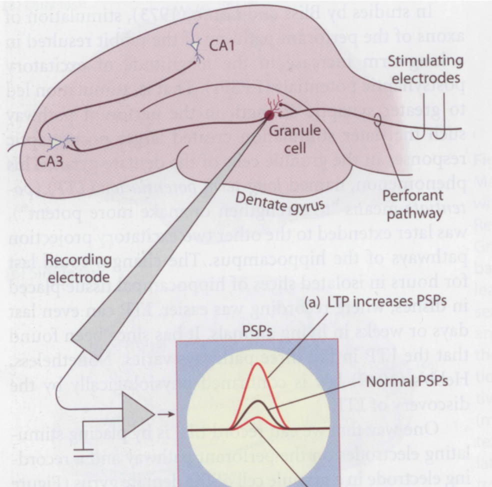
Hippocampus

- Hippocampus: centre of memory storage, The dentate gyrus is thought to contribute to the formation of new memories. It is notable as being one of a select few brainstructures currently known to have high rates of neurogenesis in adult rats
- Neurons must be plastic
- Experiment: isolated slices of hippocampal tissue placed in dishes



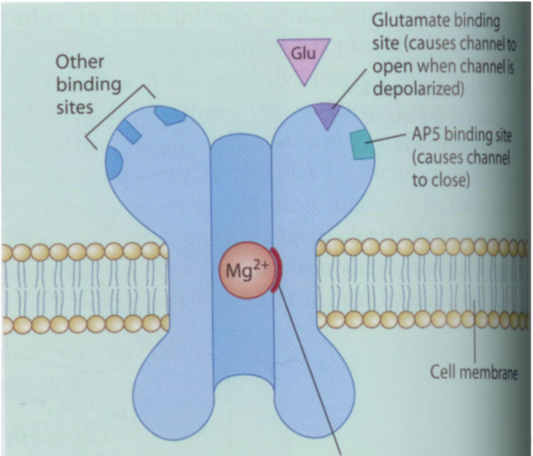
LTP experiment

- EXPERIMENTAL confirmation of Hebb's rule (1949)
- i) single pulse is presented ii) stimulation with burst of pulses: 100 pulses/sec ii) After LTP induced, single pulse stimulation
- Postsynaptic cells must be depolarized to LTP be produced AND receiving excitatory input - see Associative learning slide.



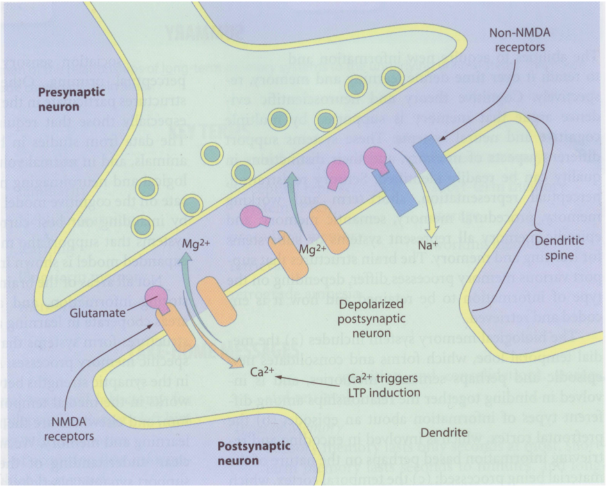
NMDA receptors

- N-methyl-D-aspartarte receptor lacated on dendrytic spines of postsynaptic neurons showing LTP
- i) NMDA receptors are blocked by Mg^{2+} ii) Channel unblocking after glutamate binding (glucamate is major excitatory transmitter in hippocampus) AND membrane depolarized (NMDA are voltage gated) $\rightarrow$ Mg^{2+} ejection, Ca^{2+} influx



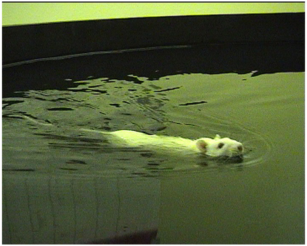
Ca^{2+} role

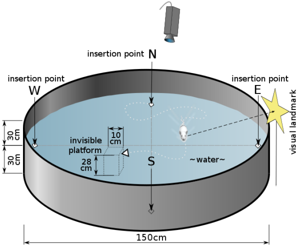
- Ca^{2+} changes enzyme activities that influence synaptic strength
- LTP raises sensitivity of non-NMDA glucamate receptors prompting release of more glucamate



Morris Water Maze - spatial memory

- i) mice training ii) Chemical blocking of LTP by AP5 impair spatial learning, keep control group iii) AP5-treated mice significantly impaired
- i) slices of the hippocampus were taken from both groups ii) LTP was easily induced in controls, but could not be induced in the brains of APV-treated rats
- Alzheimer's disease $\rightarrow$ cognitive decline seen in individuals with AD may result from impaired LTP ??

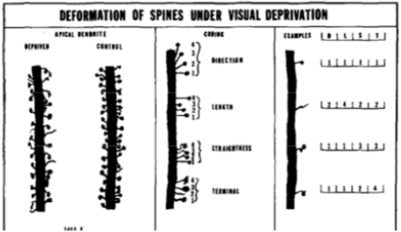




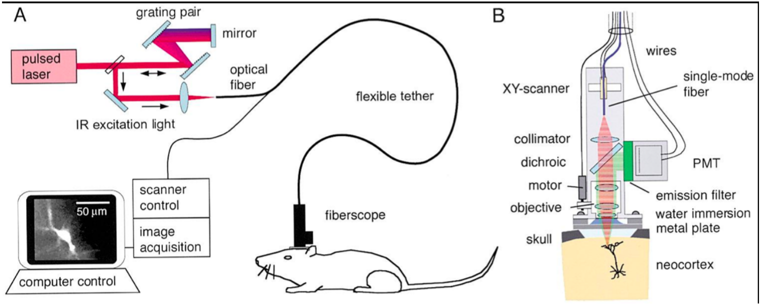
New spines - after , before learning experiment

1967 – Globus & Scheibel

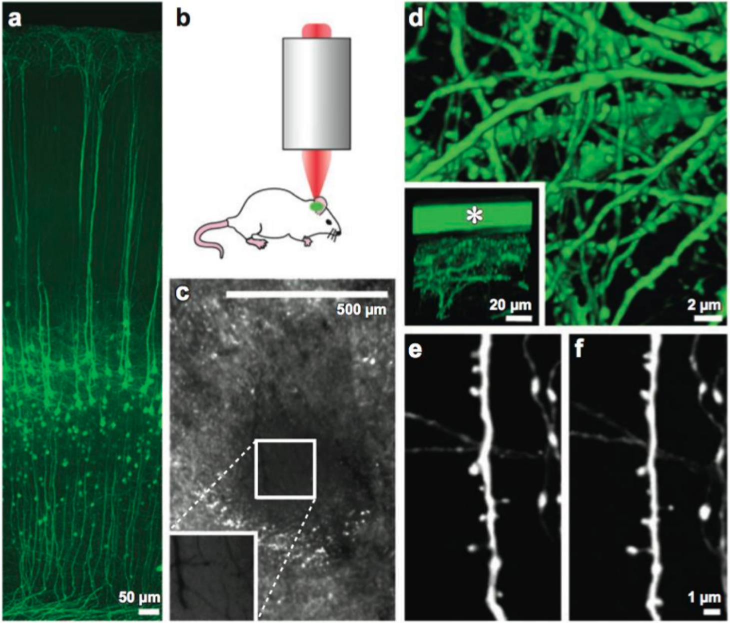
Sensory experience (visual deprivation) affects spine variation in rabbits



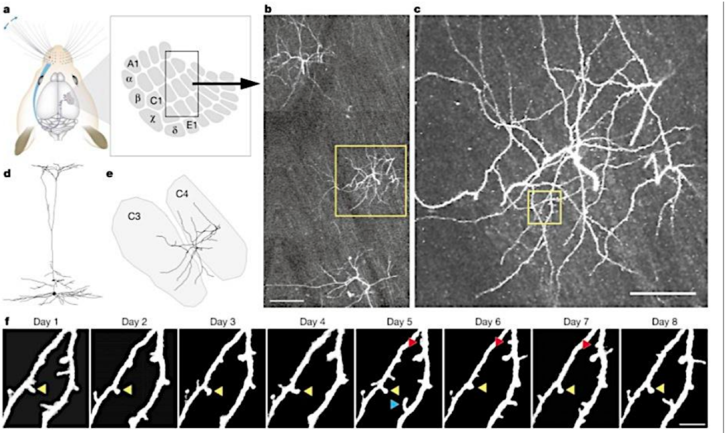
the 2-photons microscope enable viewing spines in living brain tissue



Imaging dendritic spines in the living brain



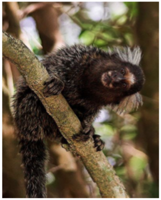
Spines appear and disapper frequently



(Trachtenberg et al. 2002)

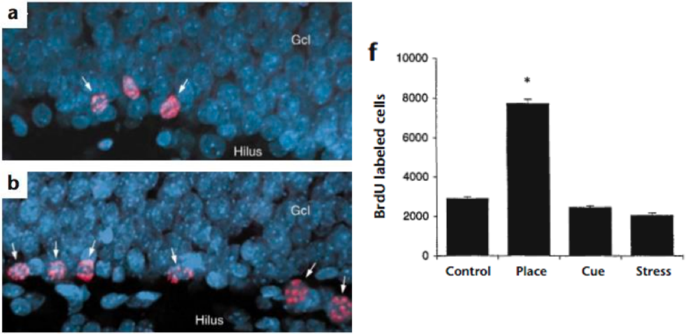
Neurogenesis

1997 –Elizabeth Gould, assistant professor of neuroscience at Princeton, and colleagues, showed neurogenesis in tree shrews



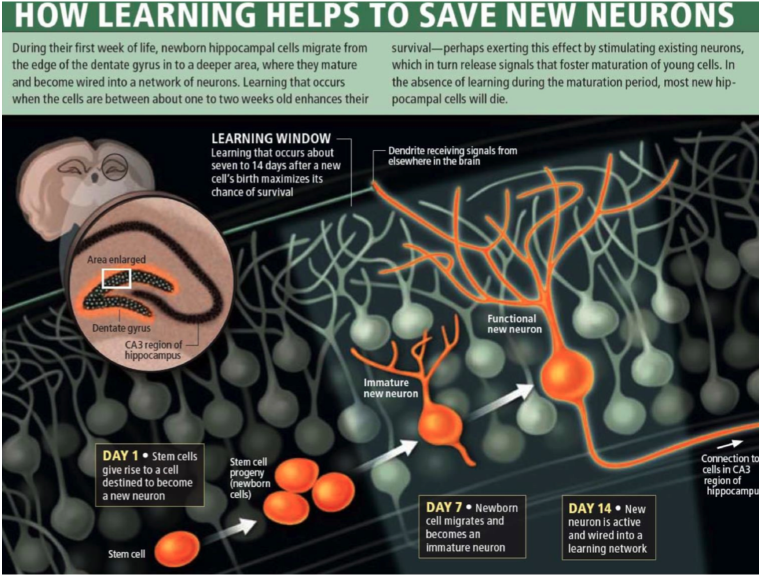
1998 – neurogenesis in marmoset monkeys (primate)

New cells in Morris Water Maze experiment

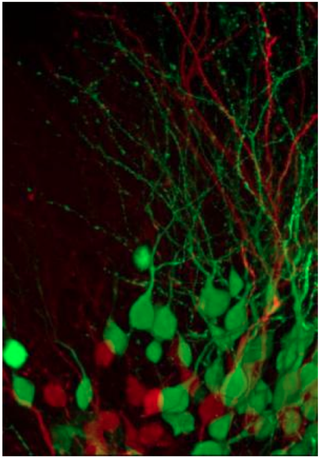


(Gould et al. 1999)

Human Brain - Hippocampus



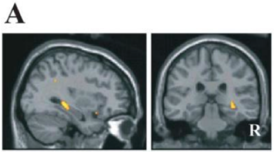
Implications - desease

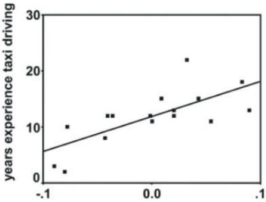


Neurogenesis: provides hope for therapies for neurodegenerative diseases such as Parkinson's and Alzheimer's... as well as for rehabilitation from stroke and brain injury

London Taxi Drivers

Hippocampus of London Taxi Drivers





Further Readings

Laurence F. Abbott and Sacha B. Nelson (2000), **Synaptic plasticity: taming the beast**, in **Nature Neurosci. (suppl.)**, 3: 1178–83.

Alain Artola and Wolf Singer (1993), **Long-term depression of excitatory synaptic transmission and its relationship to long-term potentiation**, in **Trends in Neuroscience** 16: 480–487.

Mark C. W. van Rossum, Guo-chiang Bi, and Gina G. Turrigiano (2000) **Stable Hebbian learning from spike timing-dependent plasticity**, in **J. Neuroscience** 20(23): 8812–21