Neural Computation: Learning and memory

Table of contents:

- Various types of memory
- How to measure types of memory
- Biophysics of LTP and LTD
- Computational models
  (of unsupervised learning)

Testing animal memory

(Classical) conditioning

- Pavlov's dog
- Aplysia gill reflex

Mazes and environments for rodents

- water maze
- place avoidance
- fear
- food location

More reading

Reviews of experimental LTP:
- Kandel and Schwartz book
- Hippocampus book

Theory of Hopfield networks and Backpropagation
- Herz, Krogh and Palmer

Neural computation theory
- Dayan & Abbott
- Trappenberg

Priming

Think of a zoo...

Priming

Think of a zoo….

Now think of words starting with ‘T’

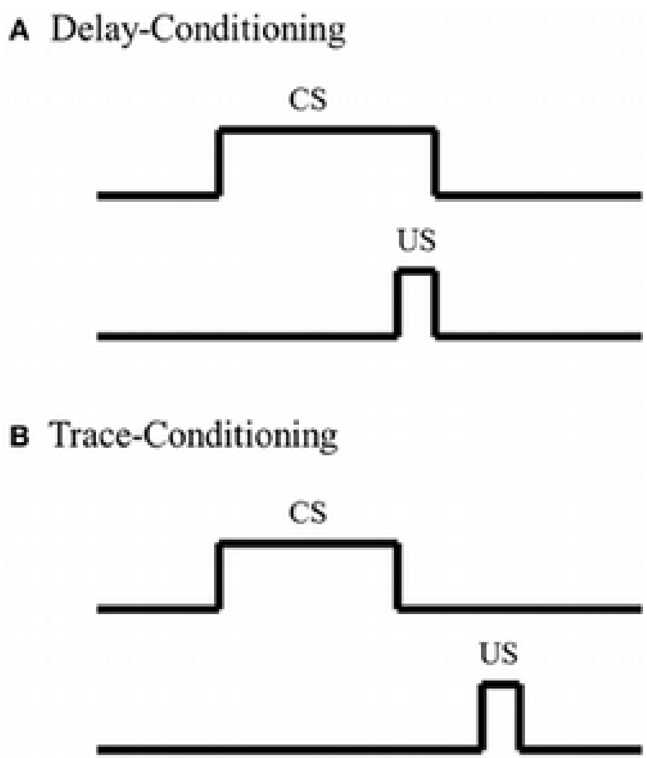
Priming

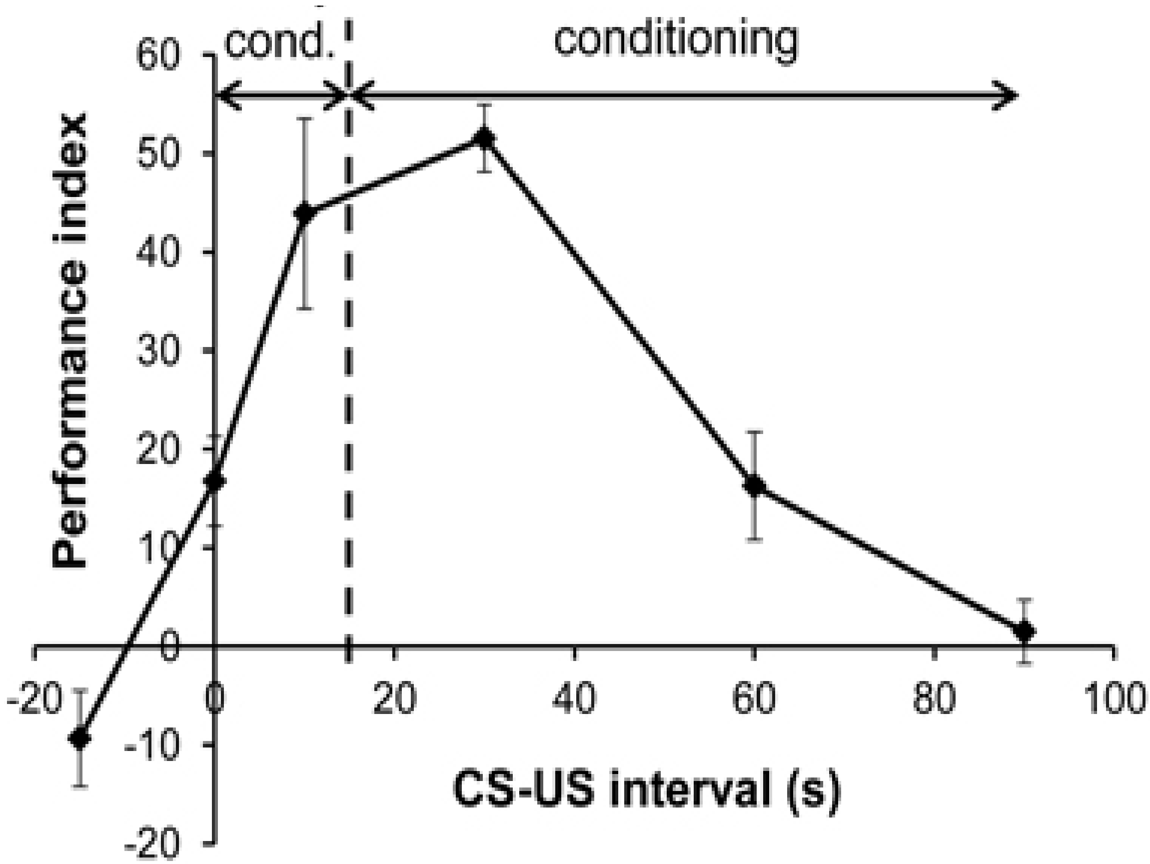
Think of a hospital….

Now think of words starting with ‘T’

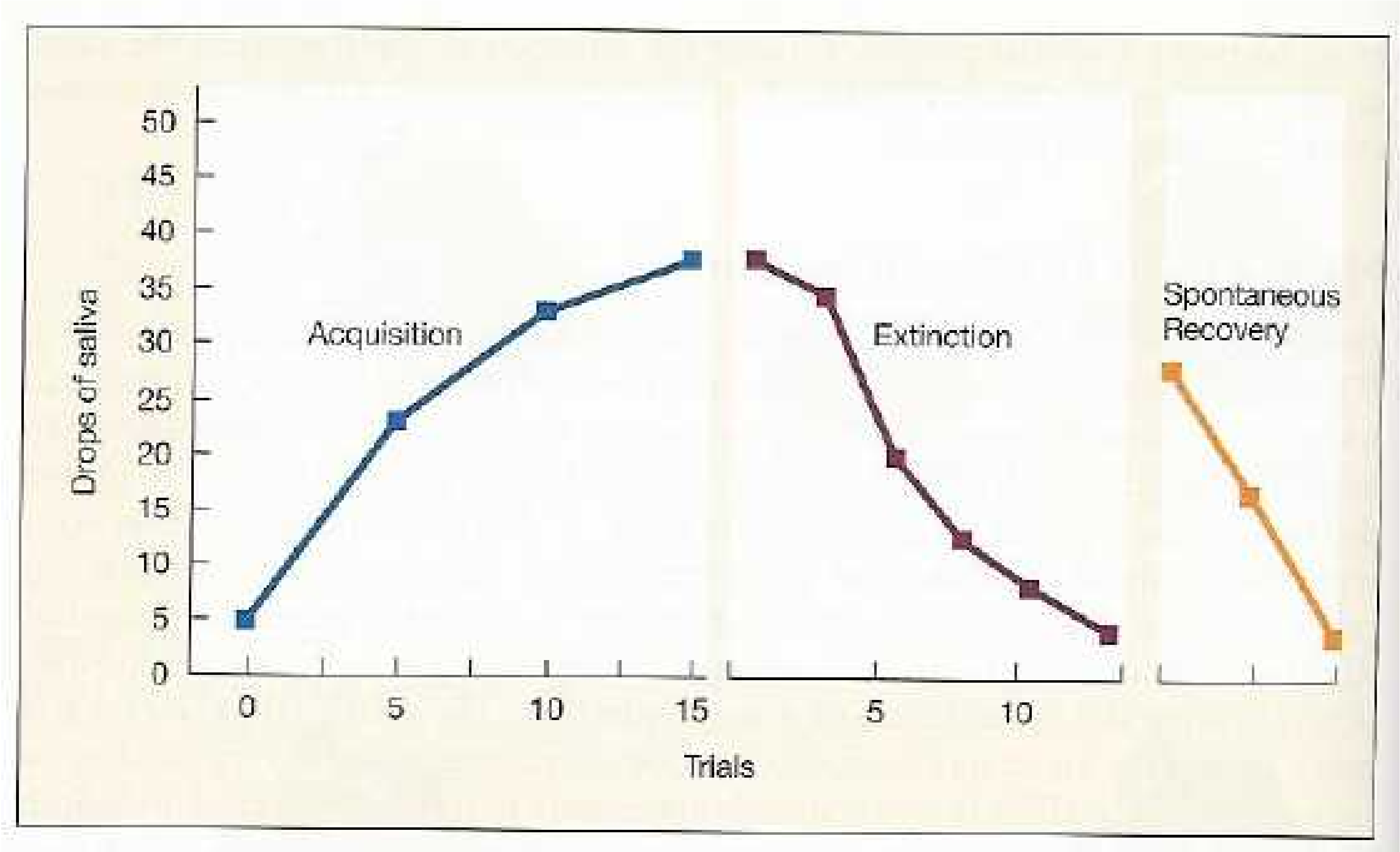
Measuring memory: Classical conditioning

Measuring memory: Classical conditioning



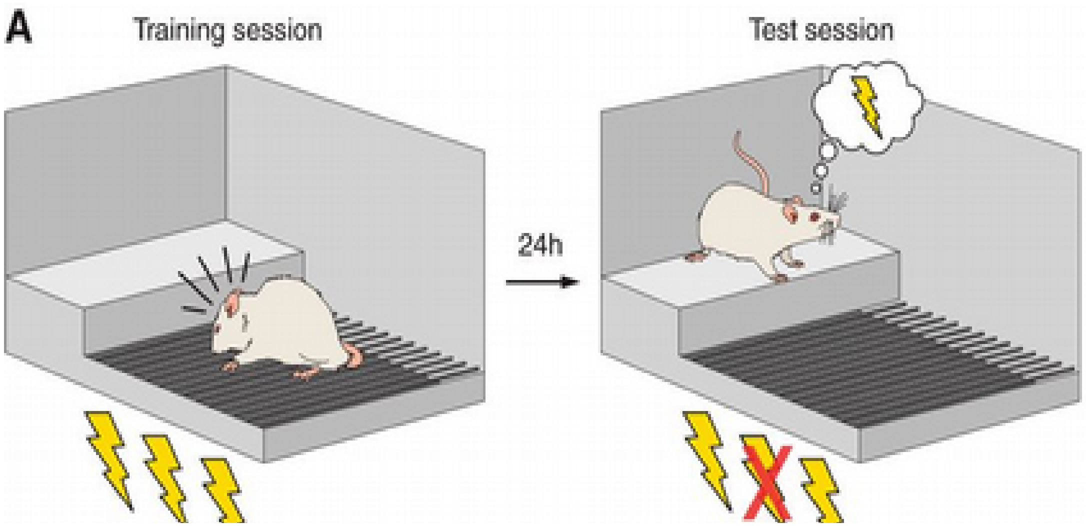


Measuring memory: Classical conditioning

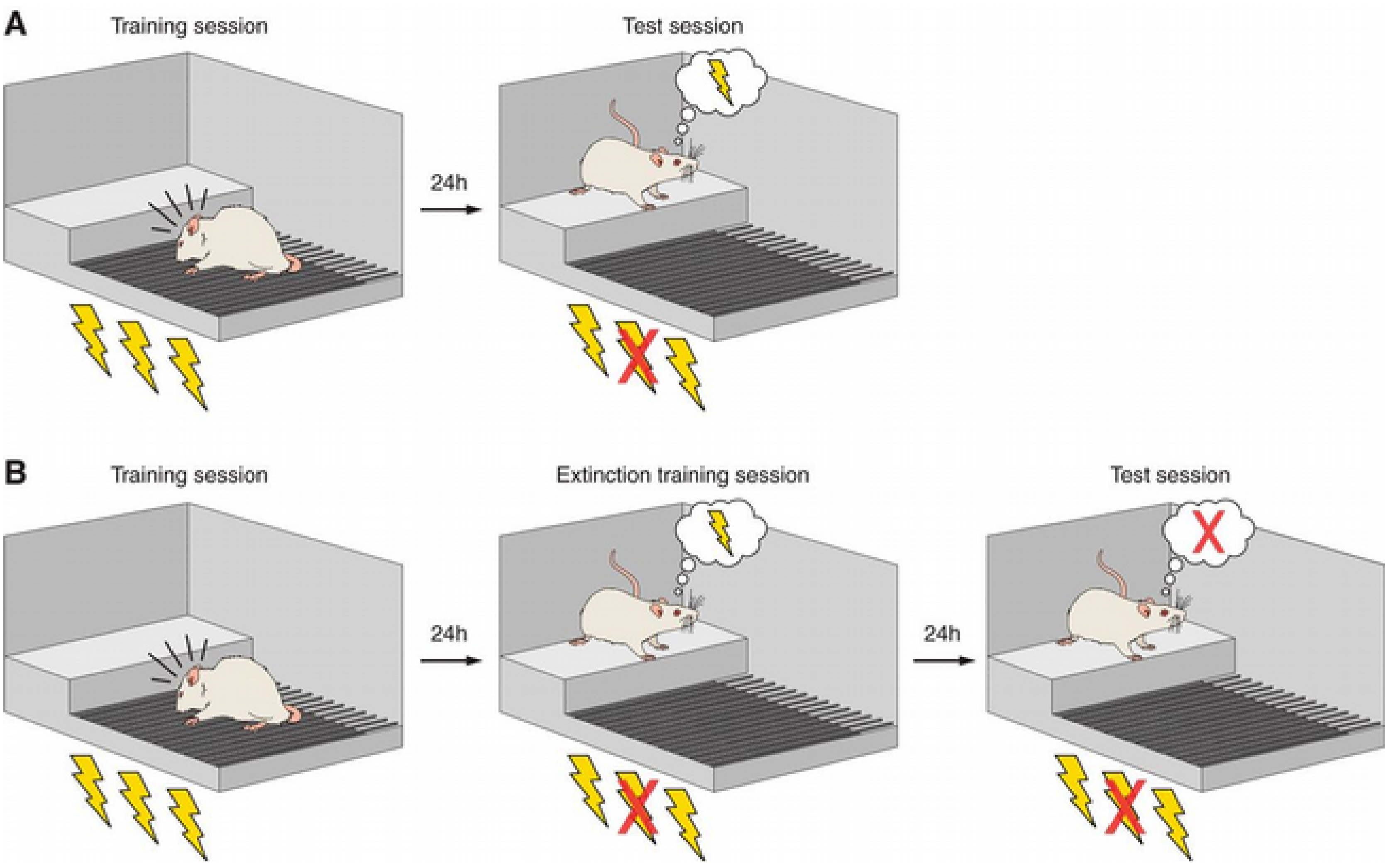


Functional perspective

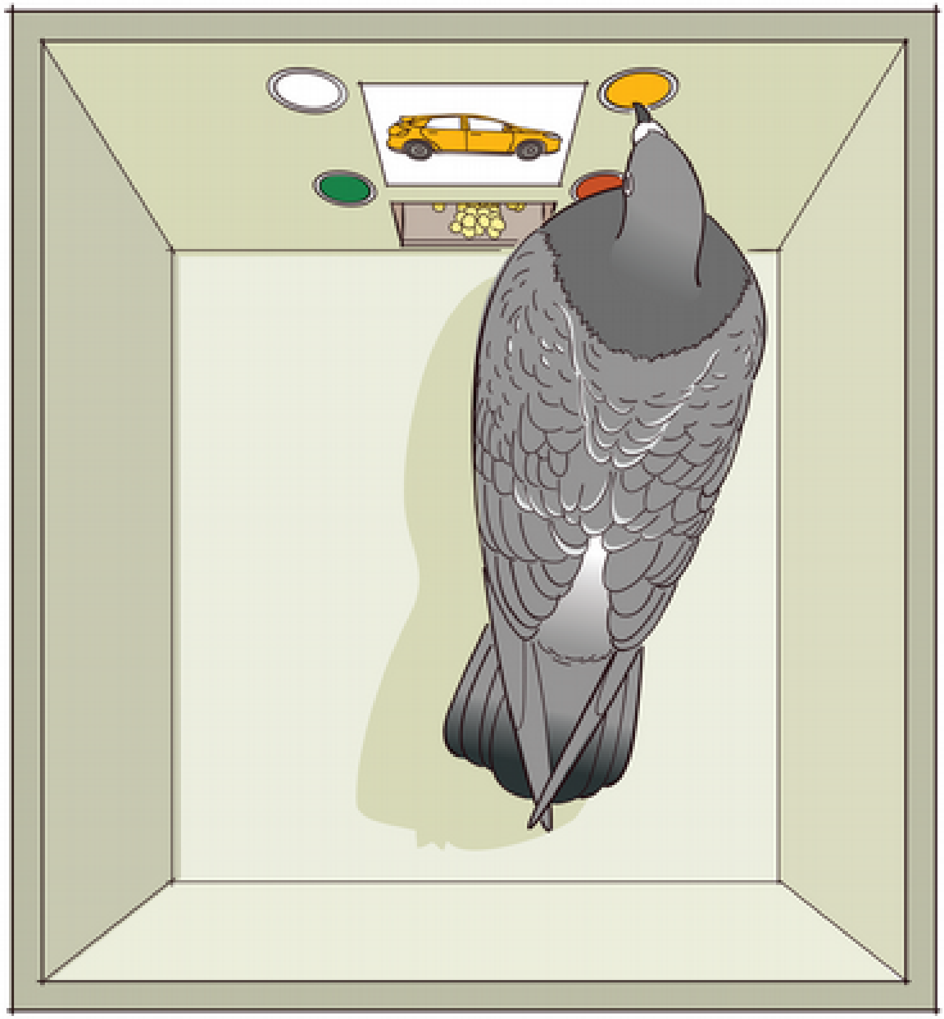
Measuring memory: Inhibitory avoidance



Measuring memory: Inhibitory avoidance



Measuring memory: Instrumental conditioning



Reward dependent on action.
Which action?

Human memory systems

Psychologists (e.g. Tulvin 1972) have split up memory in:

Working memory (likely activity based)

Non-declarative memory

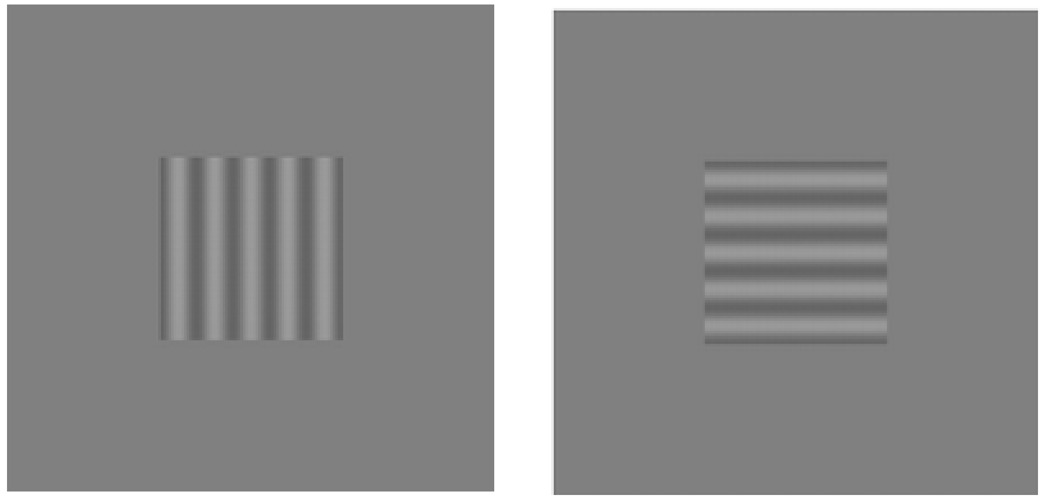
Motor skills, sensory, priming, emotional, procedural...

Declarative memory

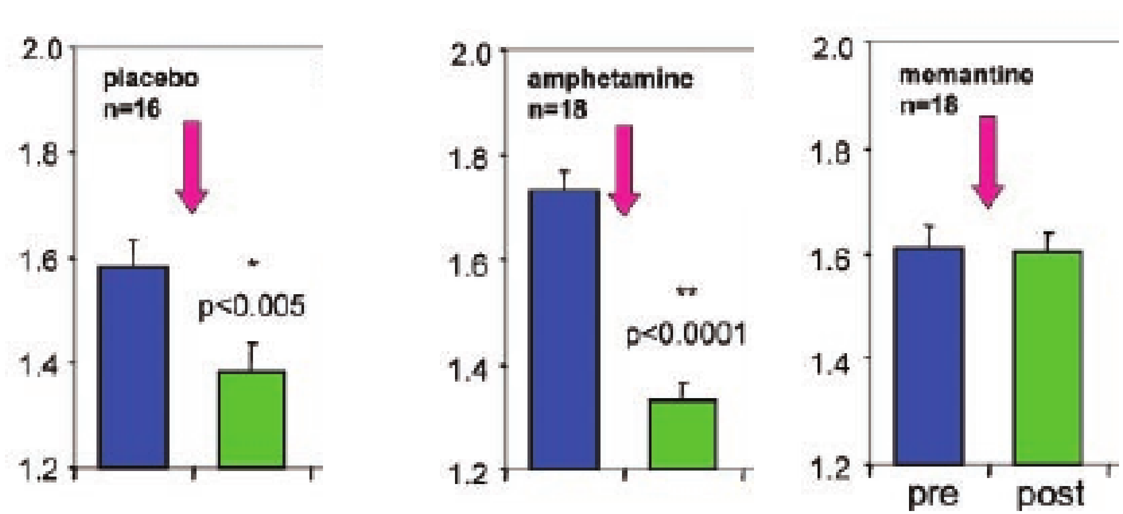
* Episodic memory
    - recollection memory/familiarity
* Semantic memory: General facts about the world

Are there specific brain regions for each?

Measuring memory: perceptual learning



Finger sensitivity

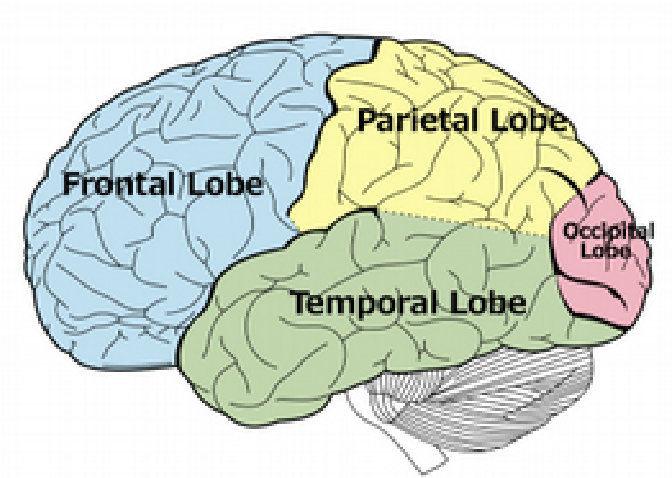


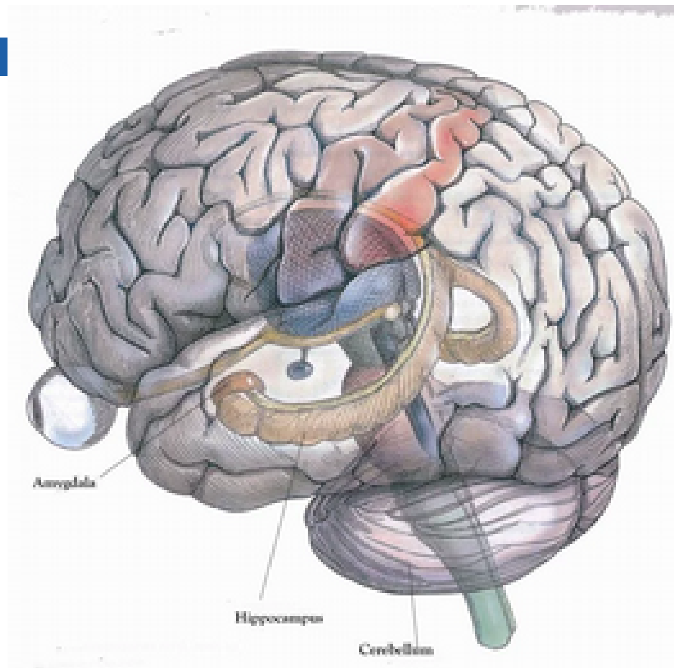
Humans [Dinse ‘03]

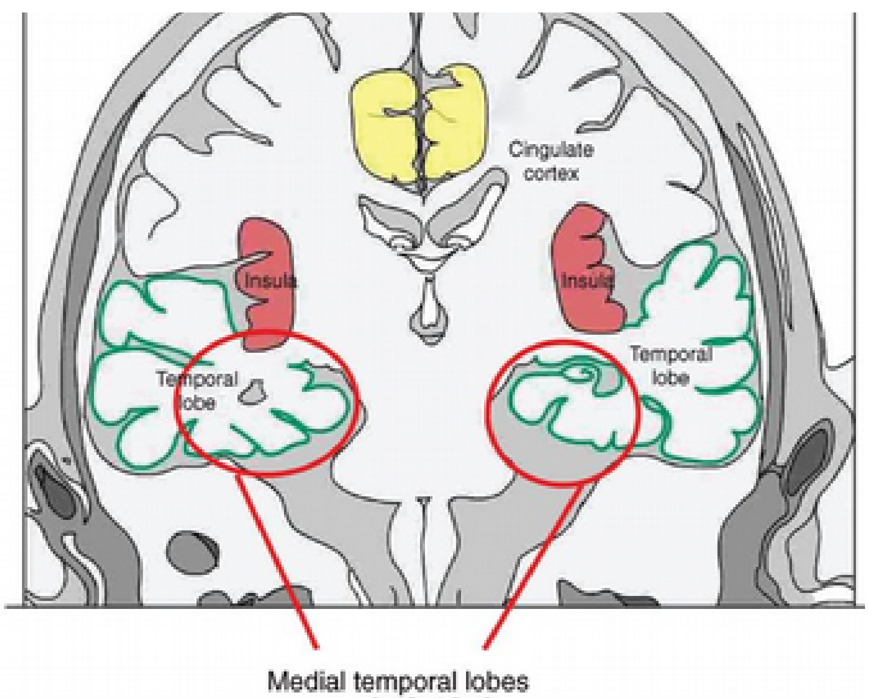
Episodic memory

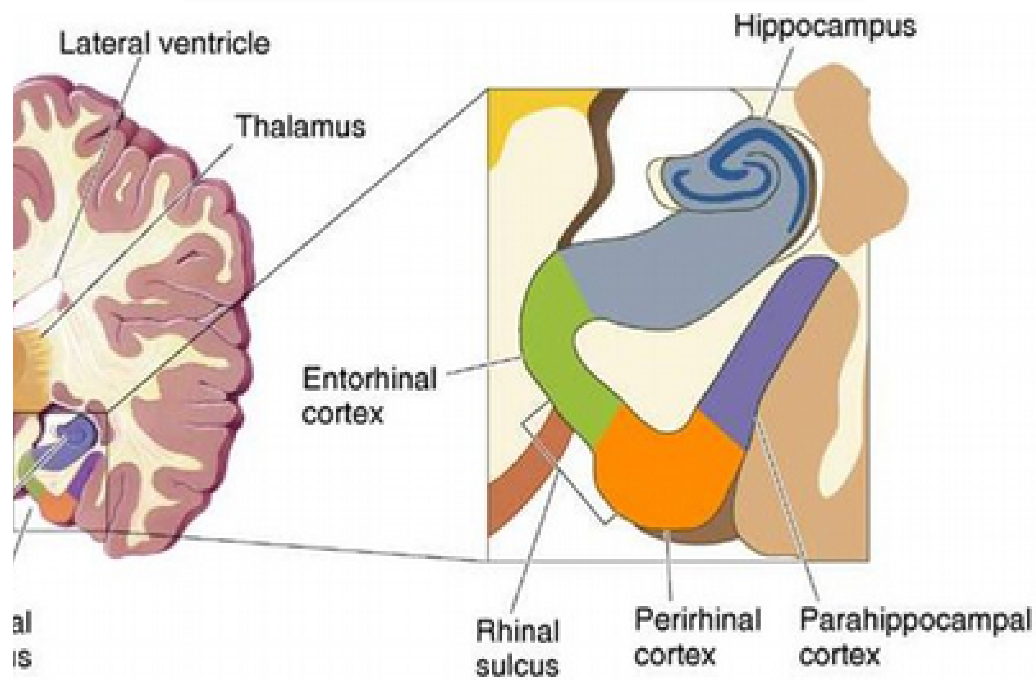
- Episodic memory: what, where, when?
- Can link things that are not naturally linked
- Hippocampus (or Medial Temporal Lobe) based.
- Has been modeled as Hopfield network
- Patient H.M.

Medial temporal lobe



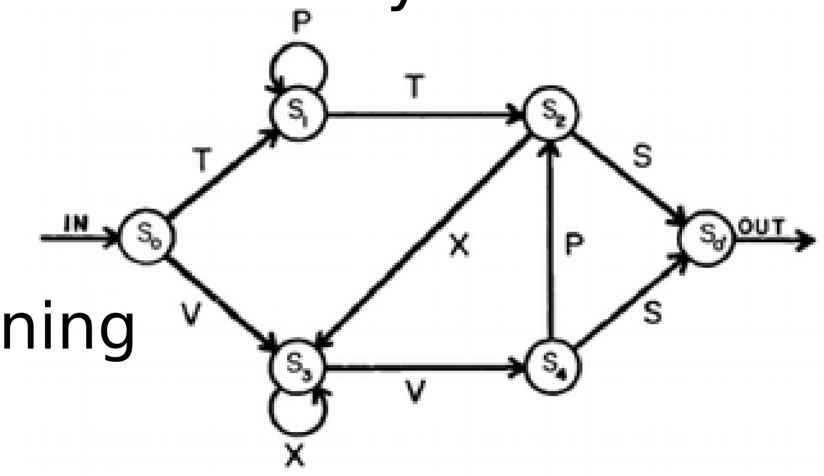






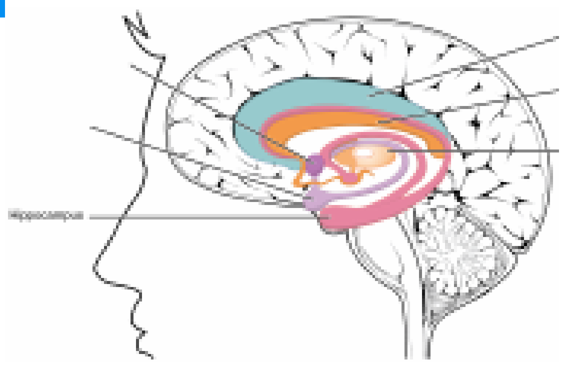
Semantic memory

- Statistical information about the world.
- Stored in neocortex
- Localized cortical lesions can lead to limited dysfunction
  (e.g. speech, faces,...)
- H.M. showed
  -normal priming,
  -skill, grammar and motor learning
  -liked doing cross-words(!)

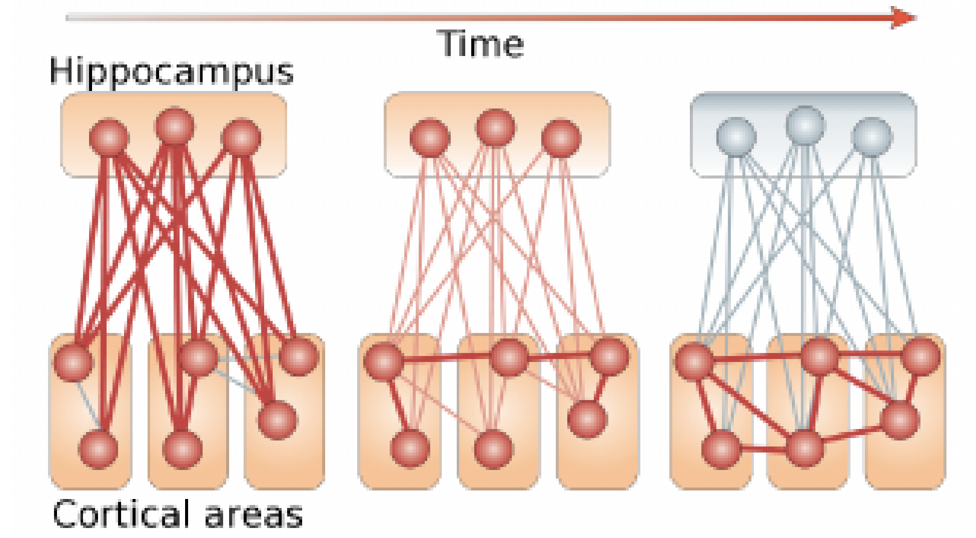


- What is Hippocampus (or MTL) responsible for:
  explicit (vs implicit) memory?
  episodic (vs semantic) memory?
  relational memory?
  relational processing [Eichenbaum]?

Semantic memory



[Wikipedia]



[Frankland, Bontempi - Nature Review Neuroscience, 2005]

- HM did have remote memories. How can that be?
- During systems consolidation, memory is transferred/copied from hippocampus to cortex. During sleep?
- Is long-term memory only cortical, or is there still a hippocampal component?
- It is possible to store information in cortex without HPC, but typically more slowly.

Episodic memory
Recollection vs. Familiarity

Recollection

Example: remember where, when..

Low capacity

Hippocampus dependent

Asymmetric ROC (binary)

Long lasting

Familiarity memory

Example: faces, pictures

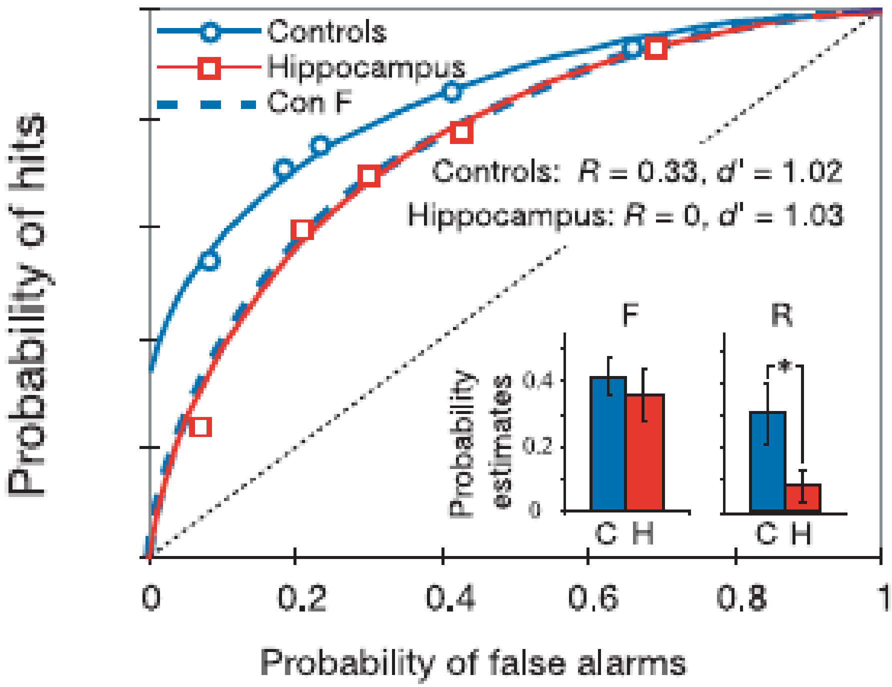
High capacity

Spared with HC-lesions

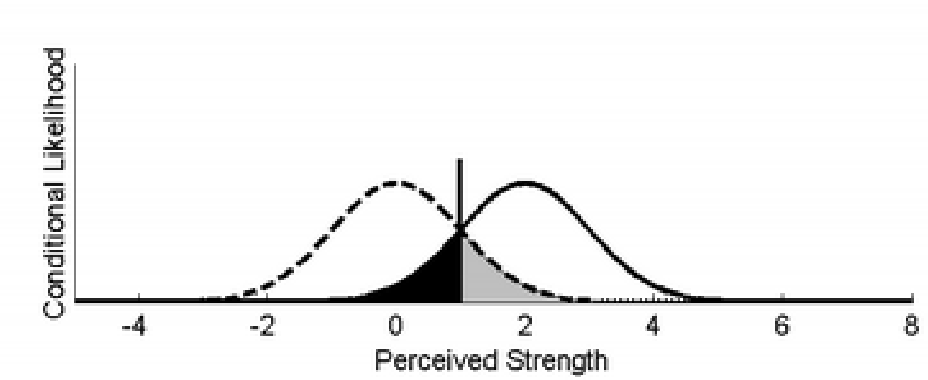
Symmetric ROC (confidence)

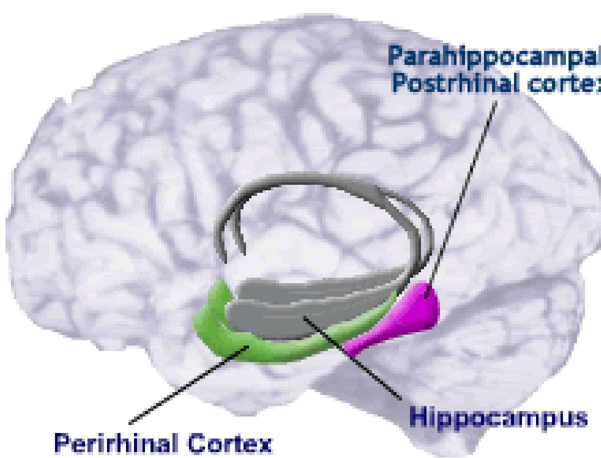
Short lasting

Episodic memory
Recollection vs. Familiarity



[Fortin & Eichenbaum]





Familiarity memory appears located in
Peri-rhinal cortex

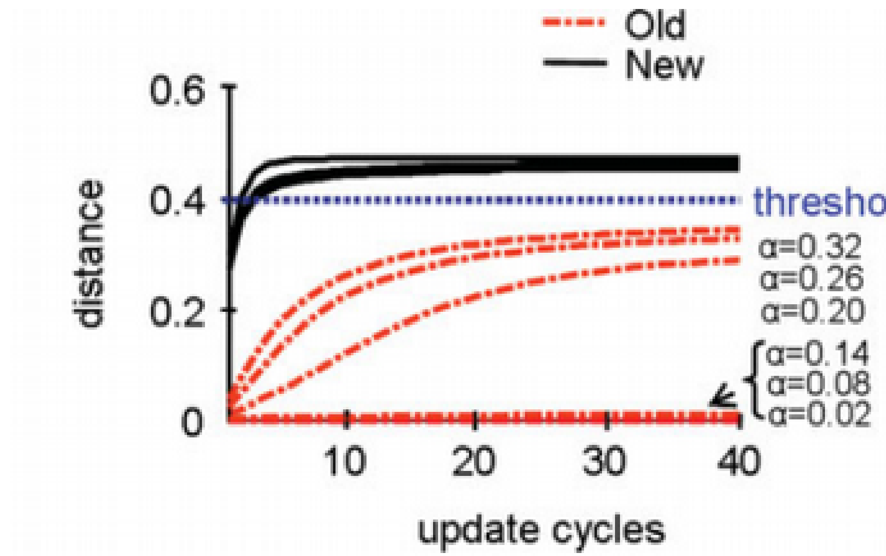
Familiarity memory

- High capacity (~N²) [Bogazc],
  cf Hopfield (~N)

- Use scenario 1:
  If something is not familiar,
  don't even bother remembering.

- Use scenario 2:
  Search for novelty (exploitation)

- Bloom-filter in software (cache system)



Combined model
[Greve &MvR 09]

Memory systems

Declarative memory

* Episodic memory
  - recollection
  - familiarity
  - hippocampus (patient HM)

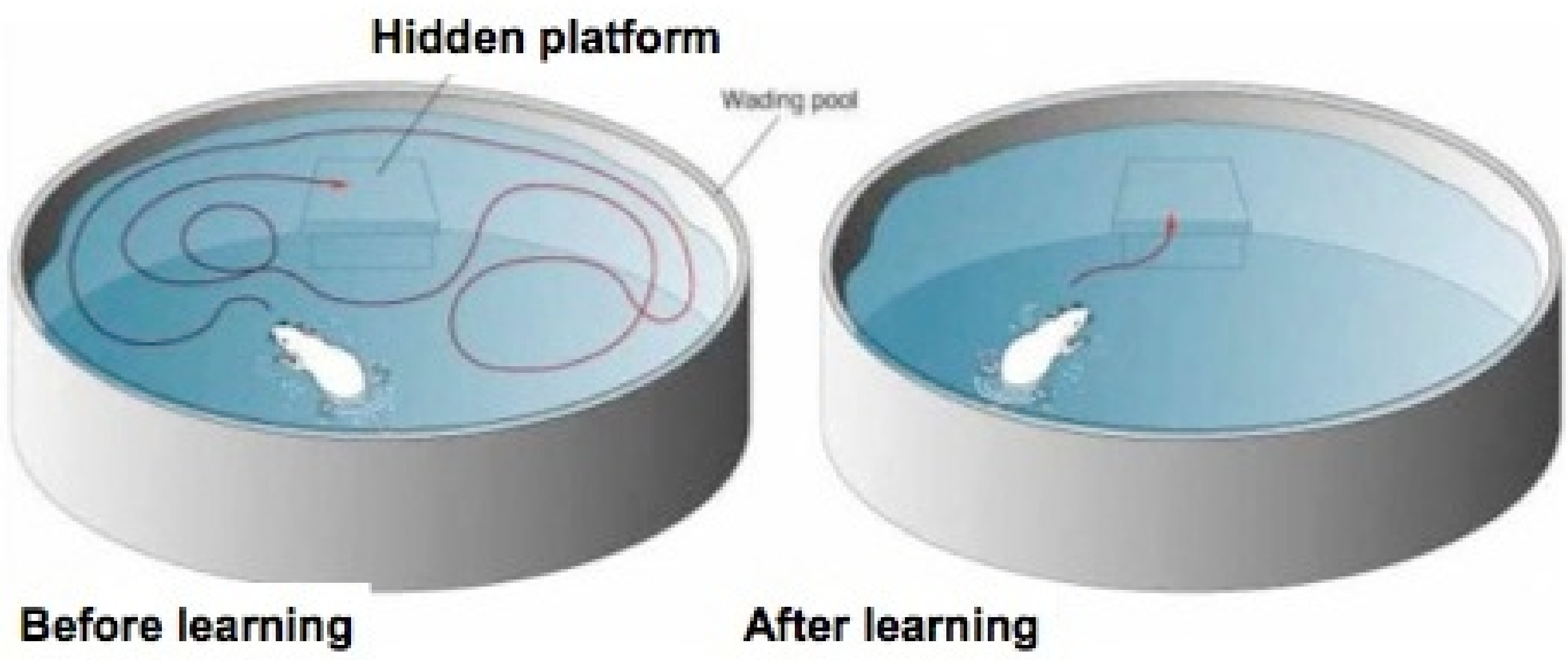
* Semantic memory: General facts

Non-declarative memory

Motor skills, sensory processing, ...

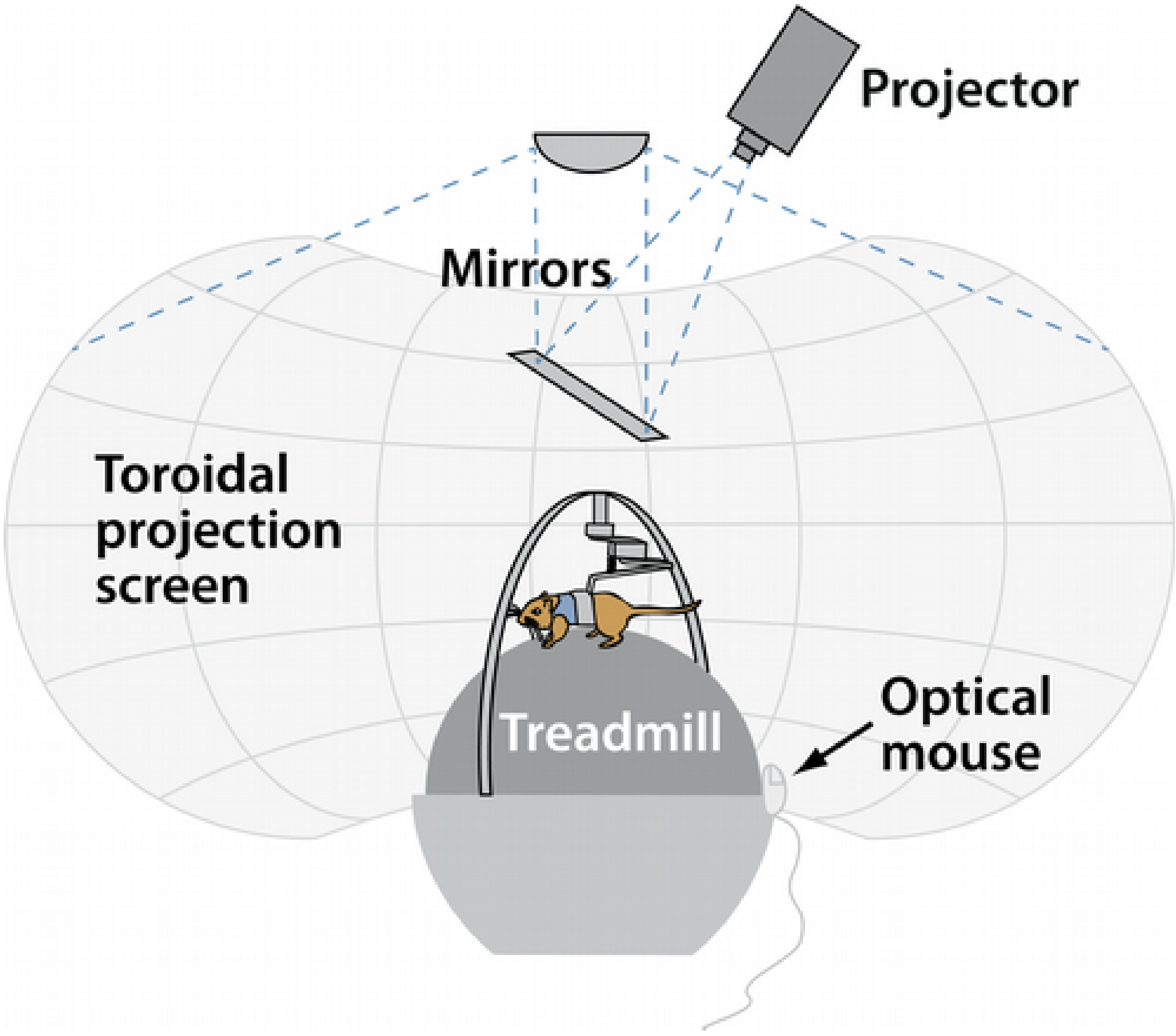
All done with Synaptic plasticity ?

Measuring Episodic and Semantic memory: Mazes

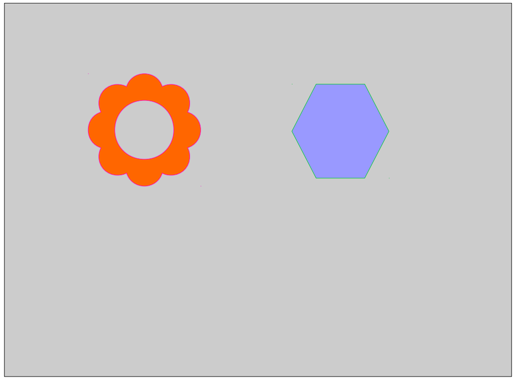


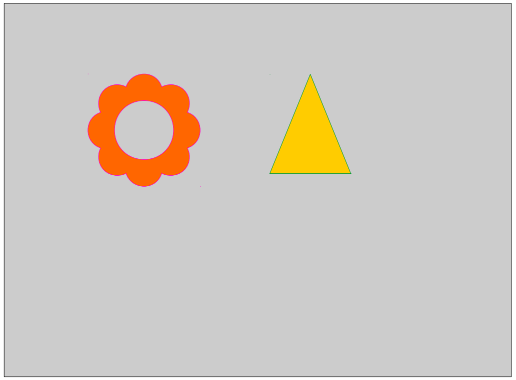
If start point is not varied,
can be learned with procedural learning (without HPC)

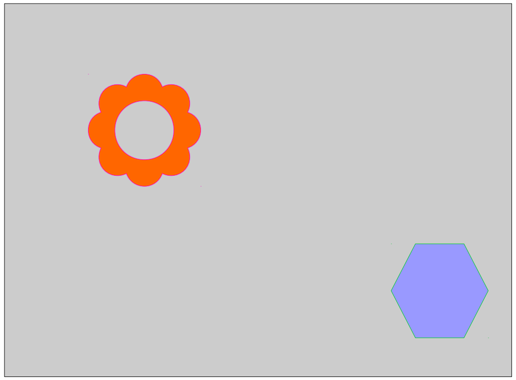
Measuring memory: Mazes



Measuring memory: Object-place tasks







Models of memory

Correlation-based learning

• [James 1898] Objects once experienced together tend to become associated in the imagination, so that when any one of them is thought of, the others are likely to be thought of also, in the same order of sequence or coexistence as before.

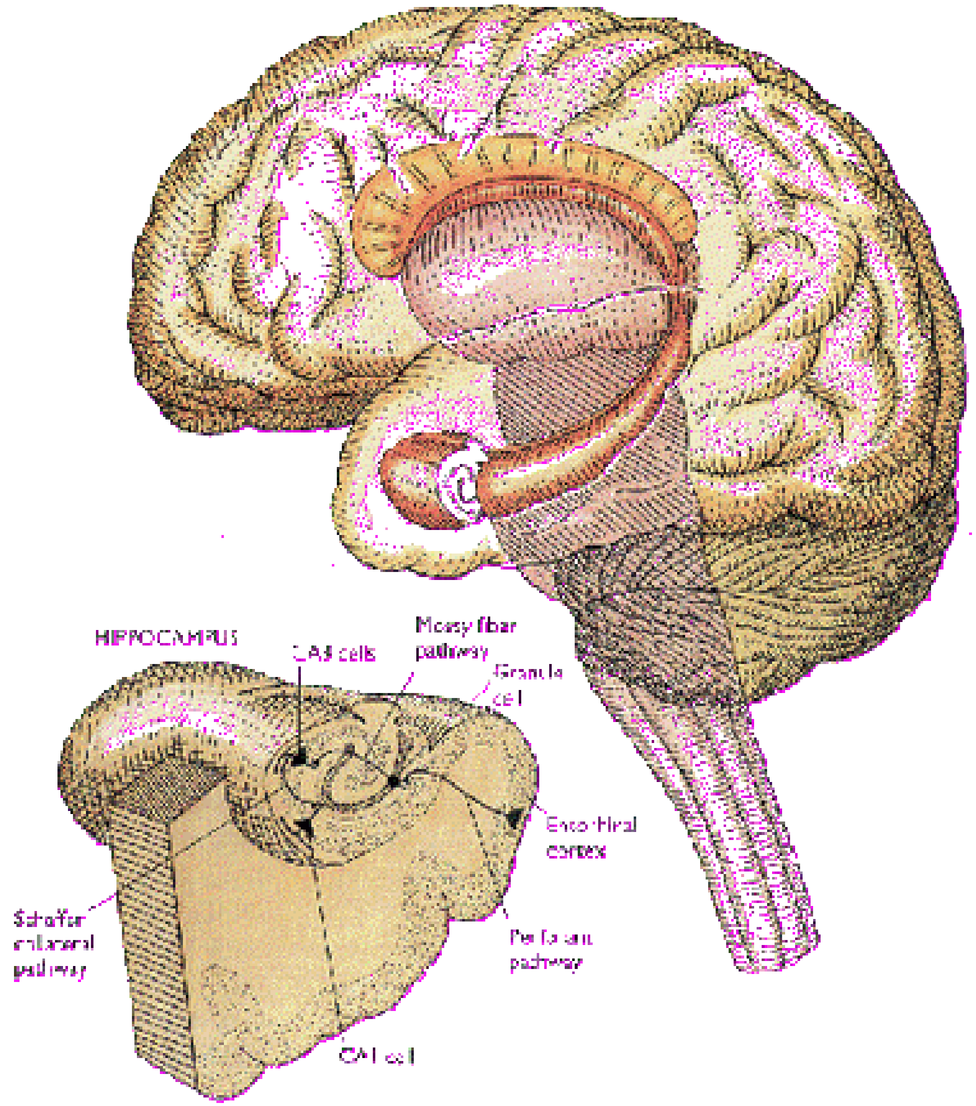
• [Hebb 1949] Let us assume that the persistence or repetition of a reverberatory activity (or ‘trace’) tends to induce lasting cellular changes that add to its stability … When an axon of cell A is near enough to excite A cell B and repeatedly or persistently takes part in firing it, some growth Process or metabolic change takes place in one or both cells such that A’s efficacy, as one of the cells firing B is increased.

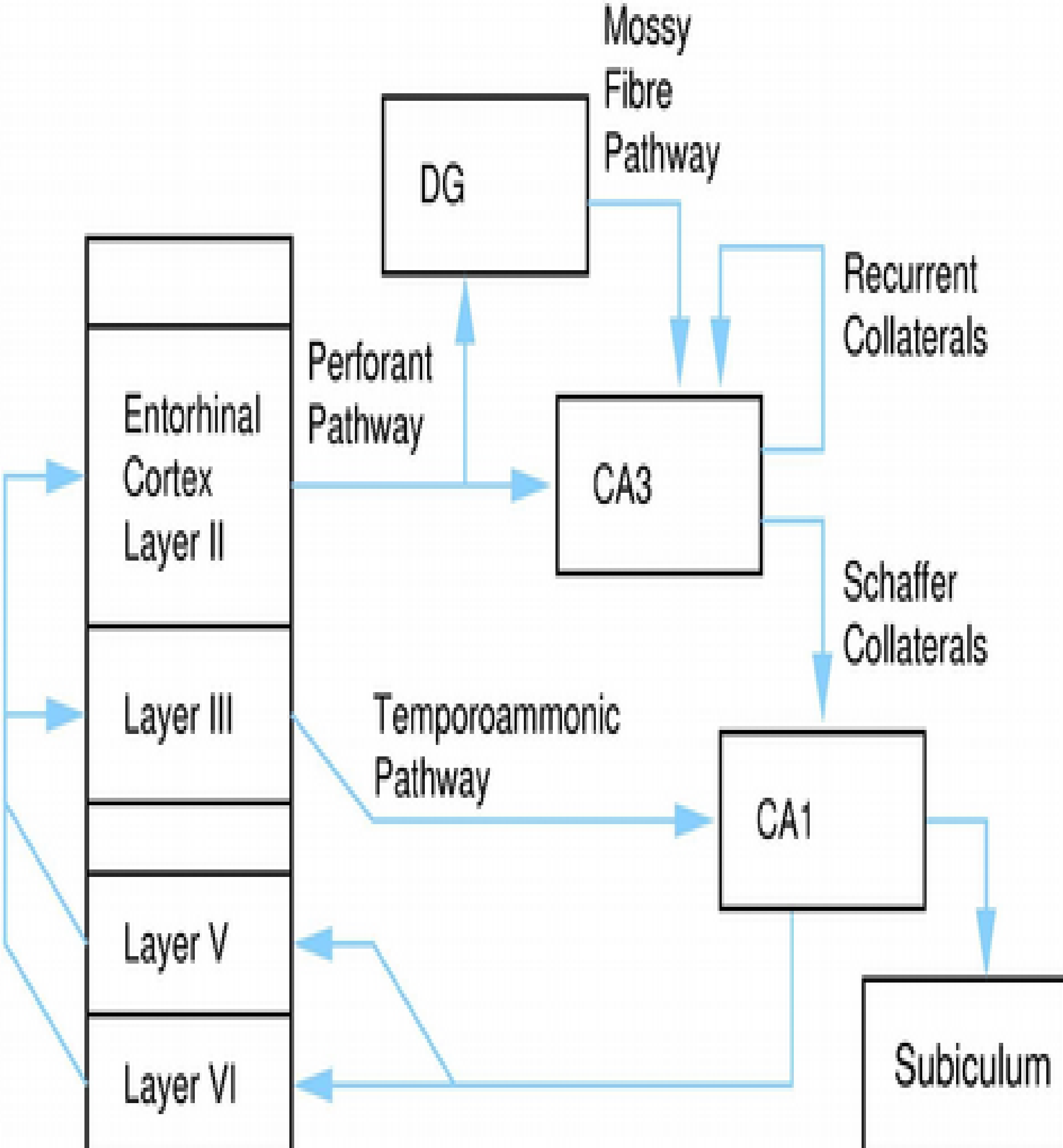
• [Schatz] What fires together, wires together.

Phenomenology of synaptic plasticity

Hippocampus

- Essential for declarative memory
- cylindrical structure
- longitudinal axis surrounds thalamus





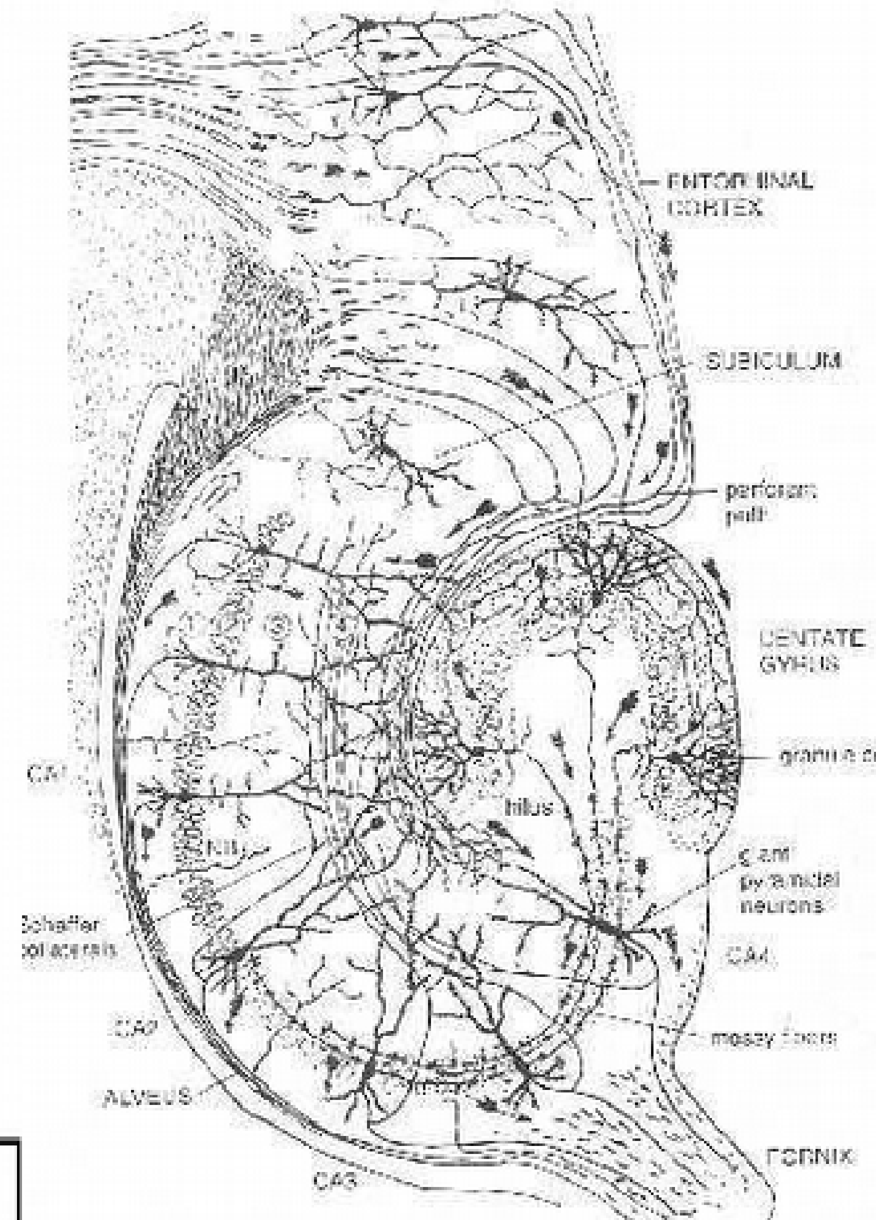
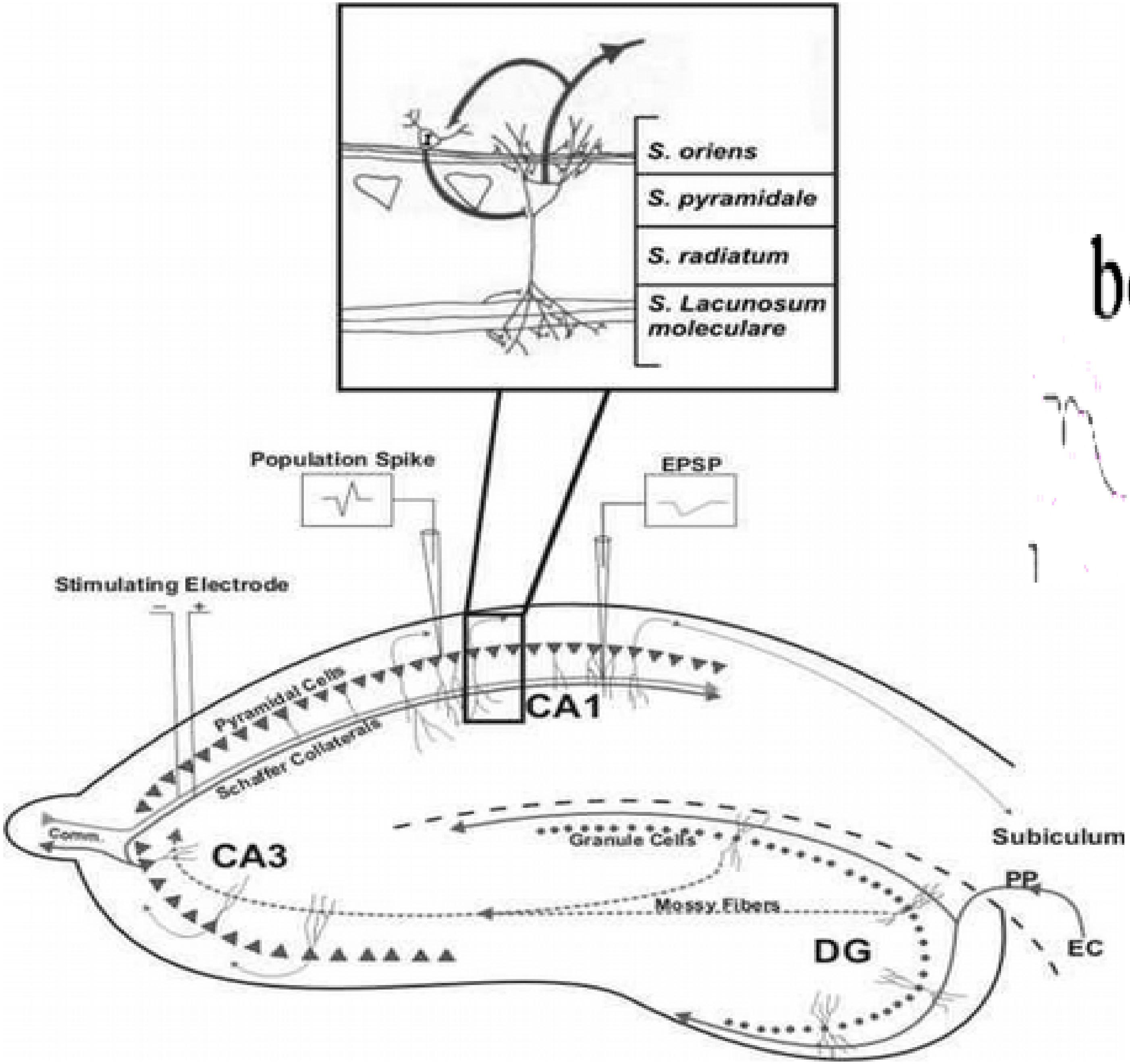
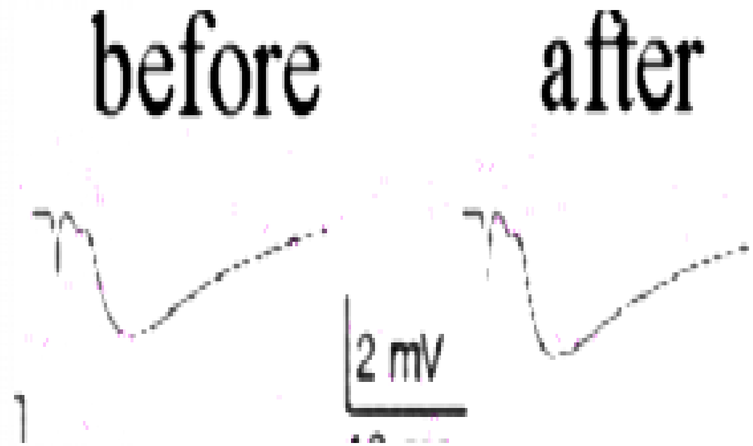
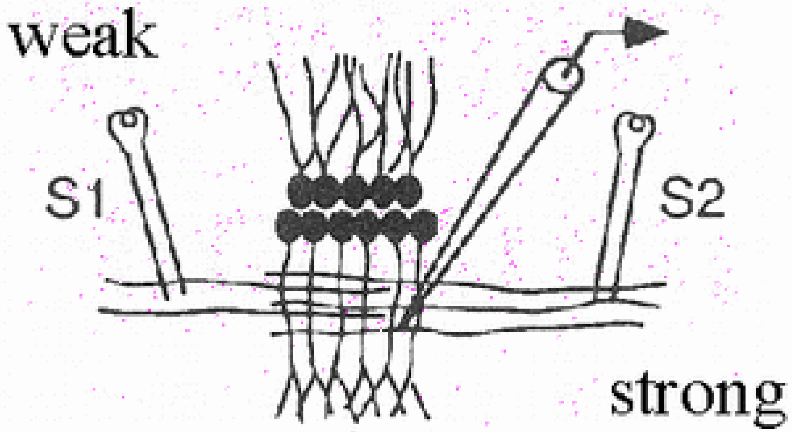


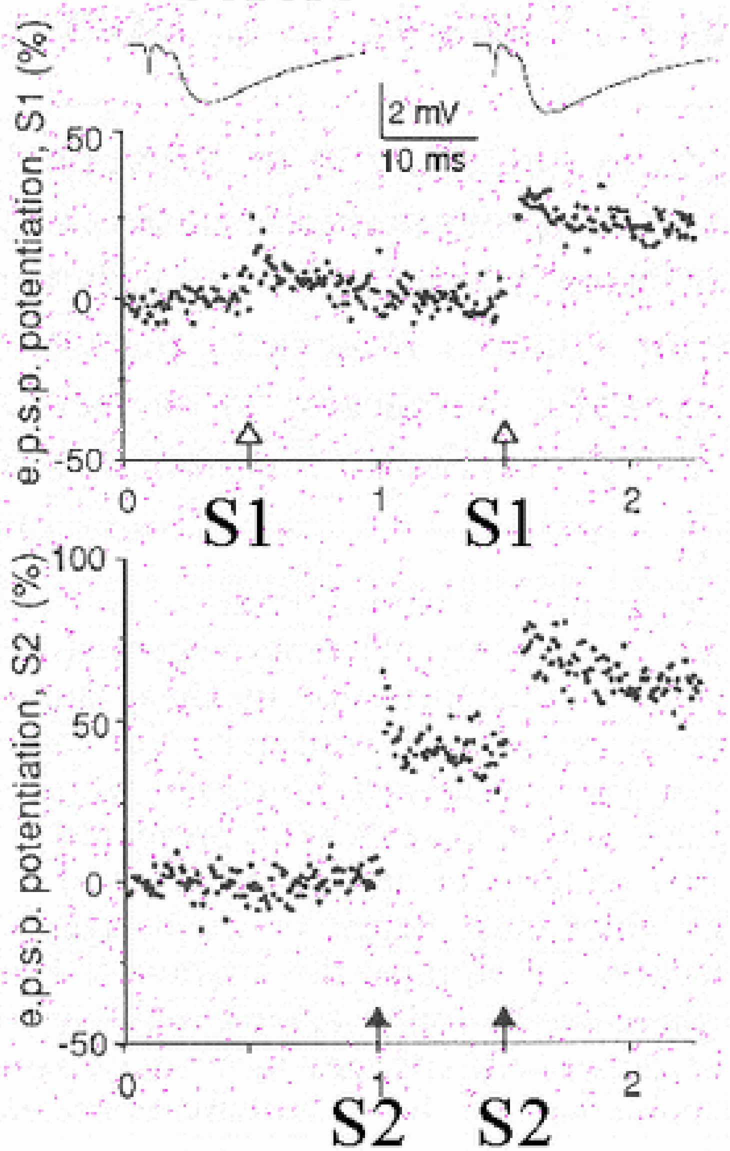
Diagram: Kit Longden


S. oriens
S. pyramidale
S. radiatum
S. Lacunosum moleculare
Population Spike
EPSP
Stimulating Electrode
Pyramidal Cells
Schaffer Collaterals
CA1
CA3
Comm.
Granule Cells
Mossy Fibers
DG
Subiculum
PP
EC


before
after
2 mV

Schaffer collateral LTP (in vitro)





alternate at 15 sec intervals

tetanic stimulation

S1: cooperative

S2: input-specific

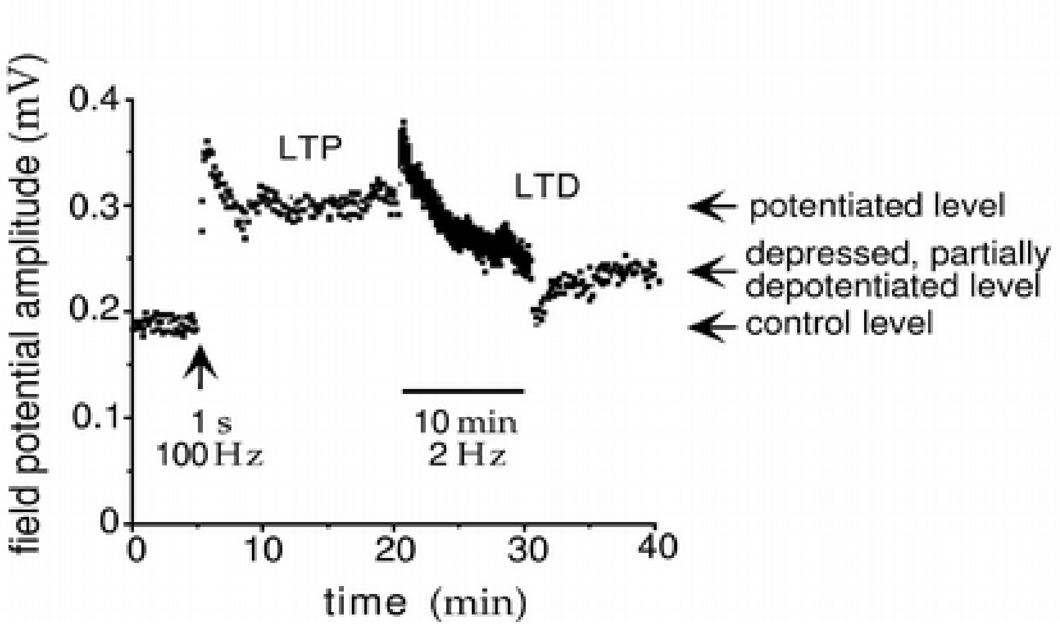
S1+S2: associative

Long term synaptic plasticity

What is (activity dependent, long term) synaptic plasticity?

Long term, semi-permanent changes in the synaptic efficacy, induced by neural activity.

In contrast to:
- development
- short term changes
- excitability changes



Biophysics of LTP

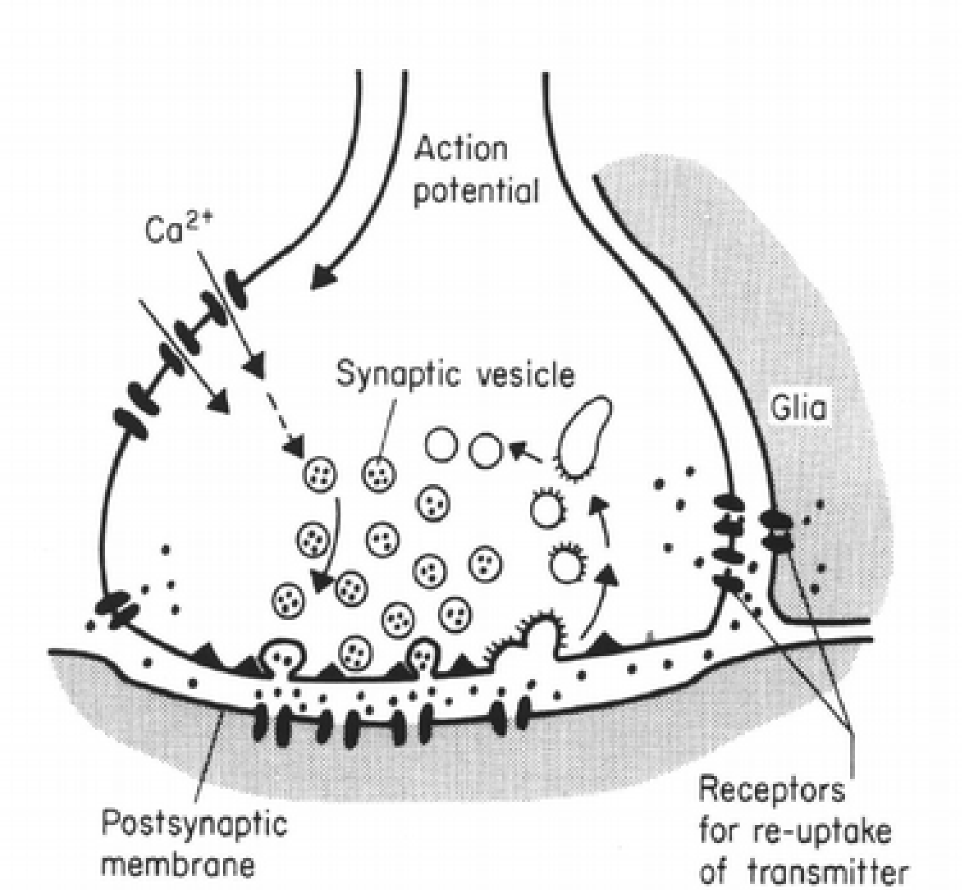
LTP stages

Induction:

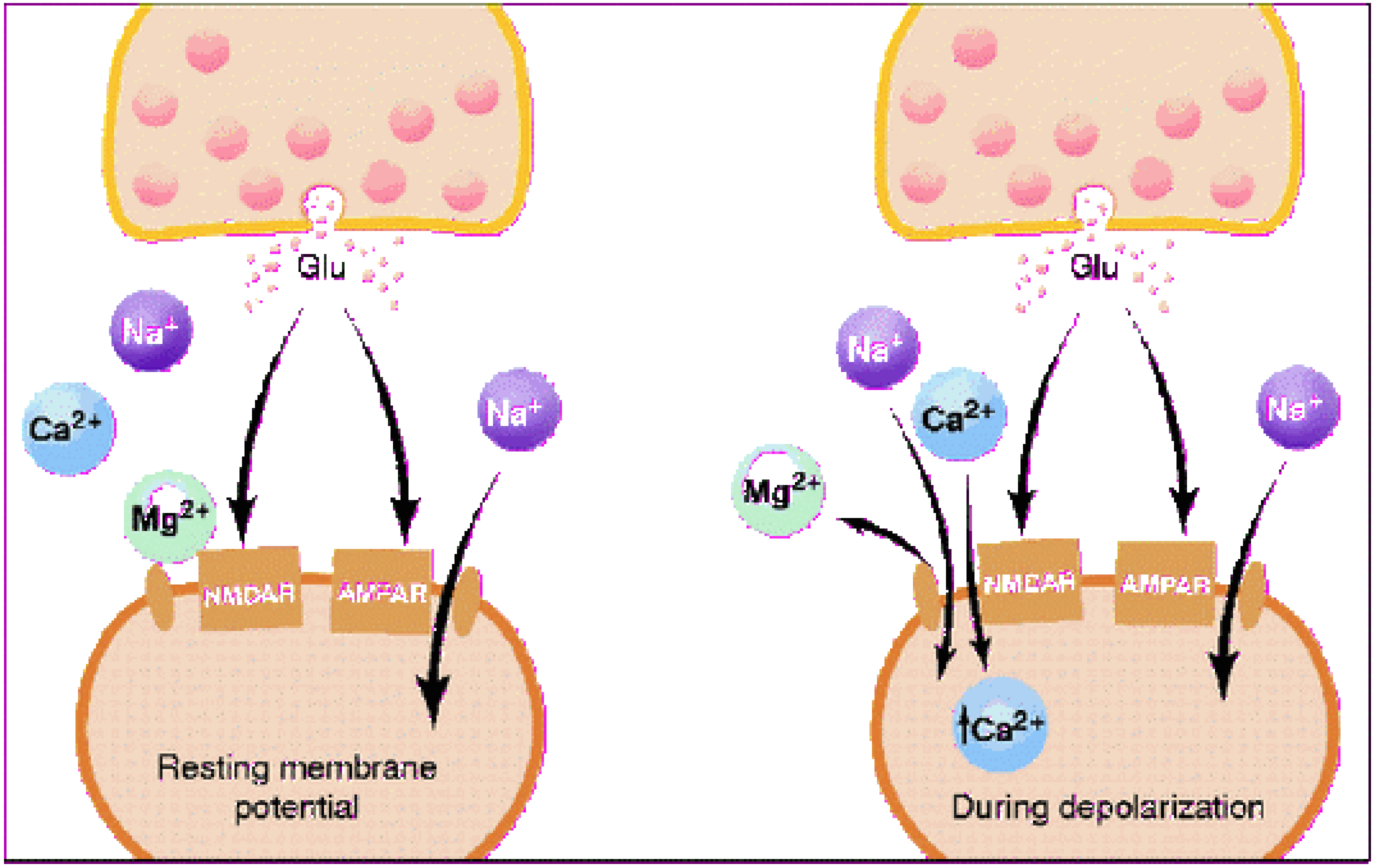
- Requires pre- and post synaptic activity.
- Mechanism: NMDA and Ca influx

Expression / maintenance phases:

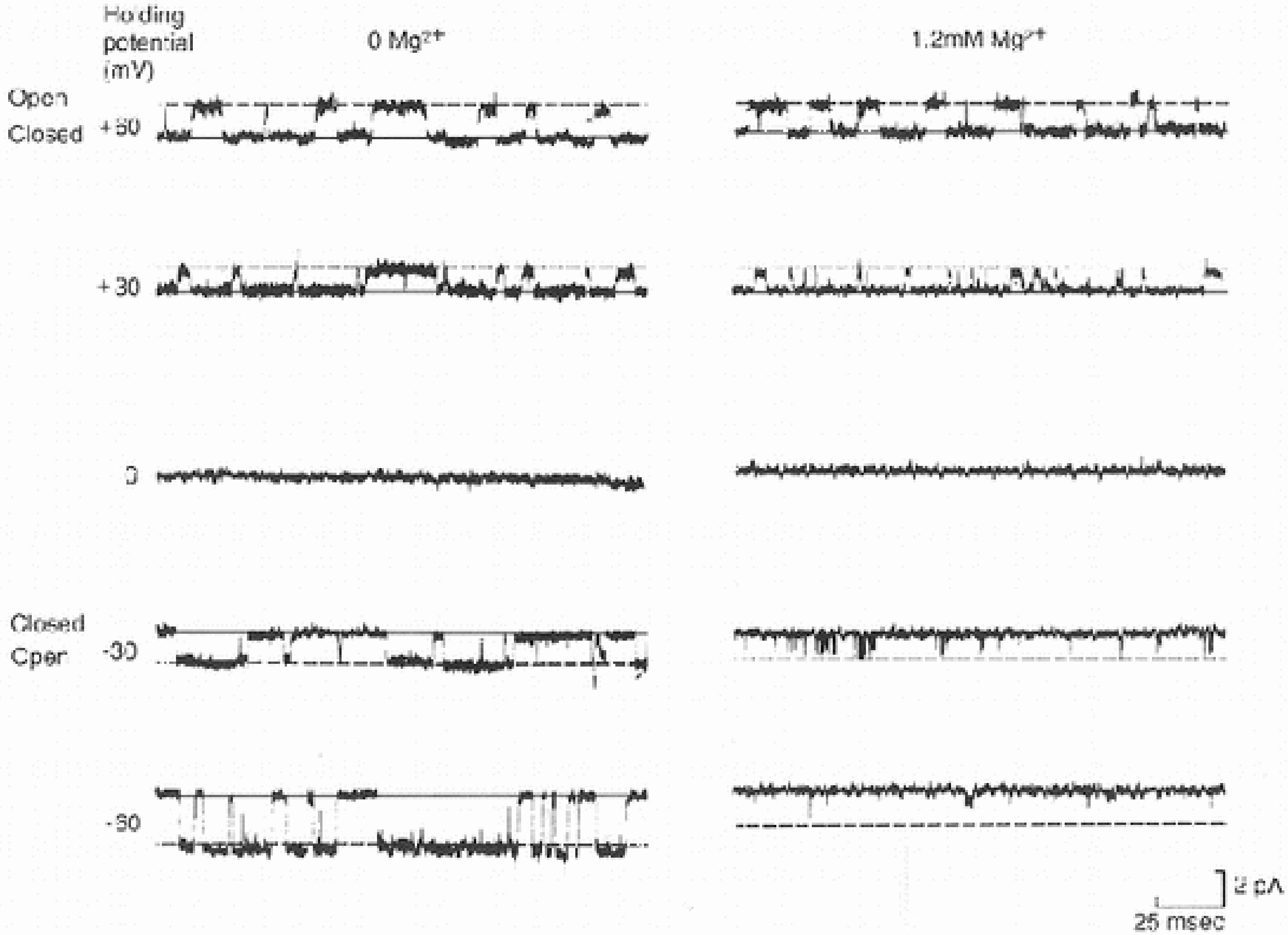
- Early LTP
- Late LTP



Model for LTP induction

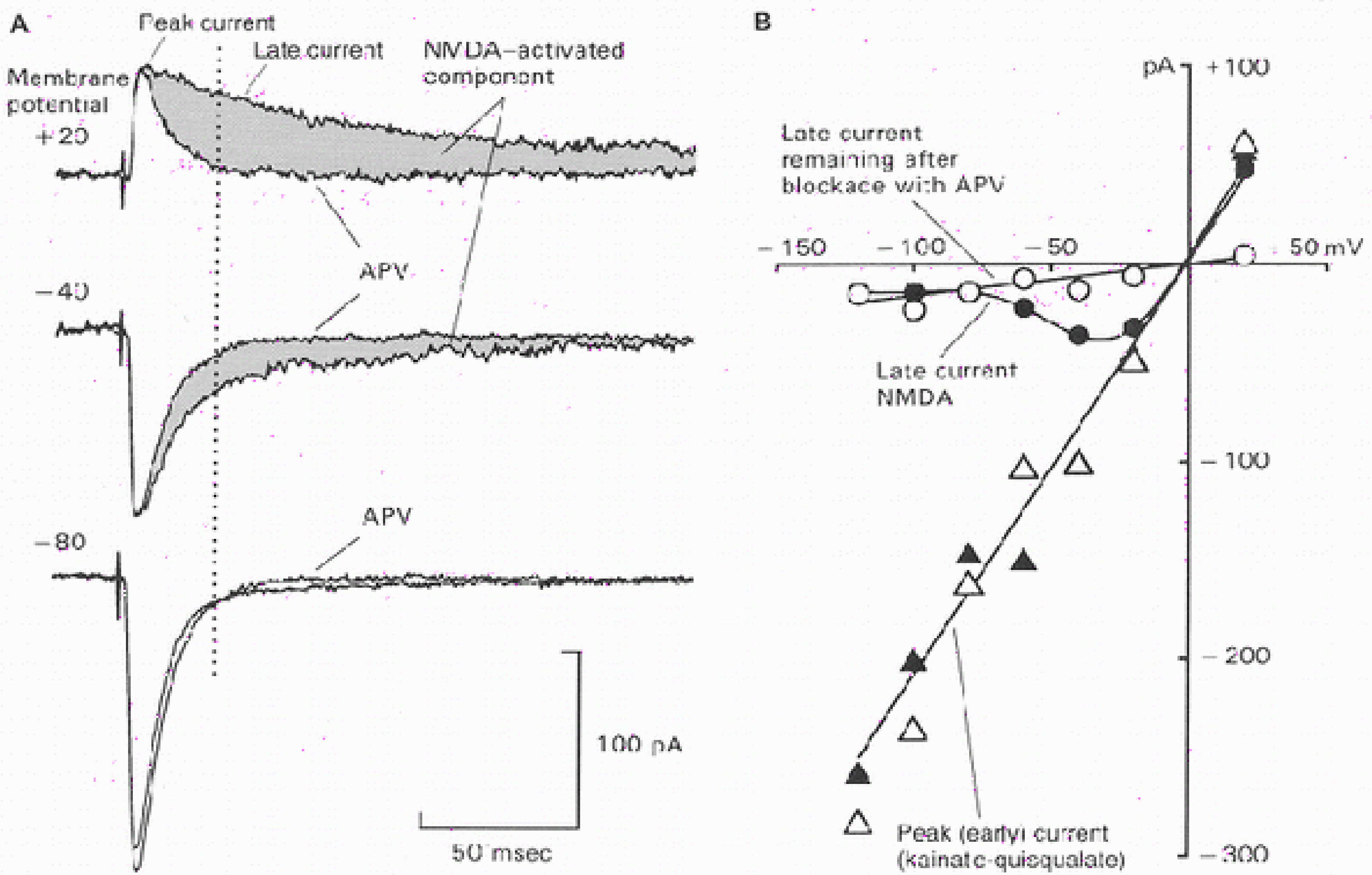


Magnesium block

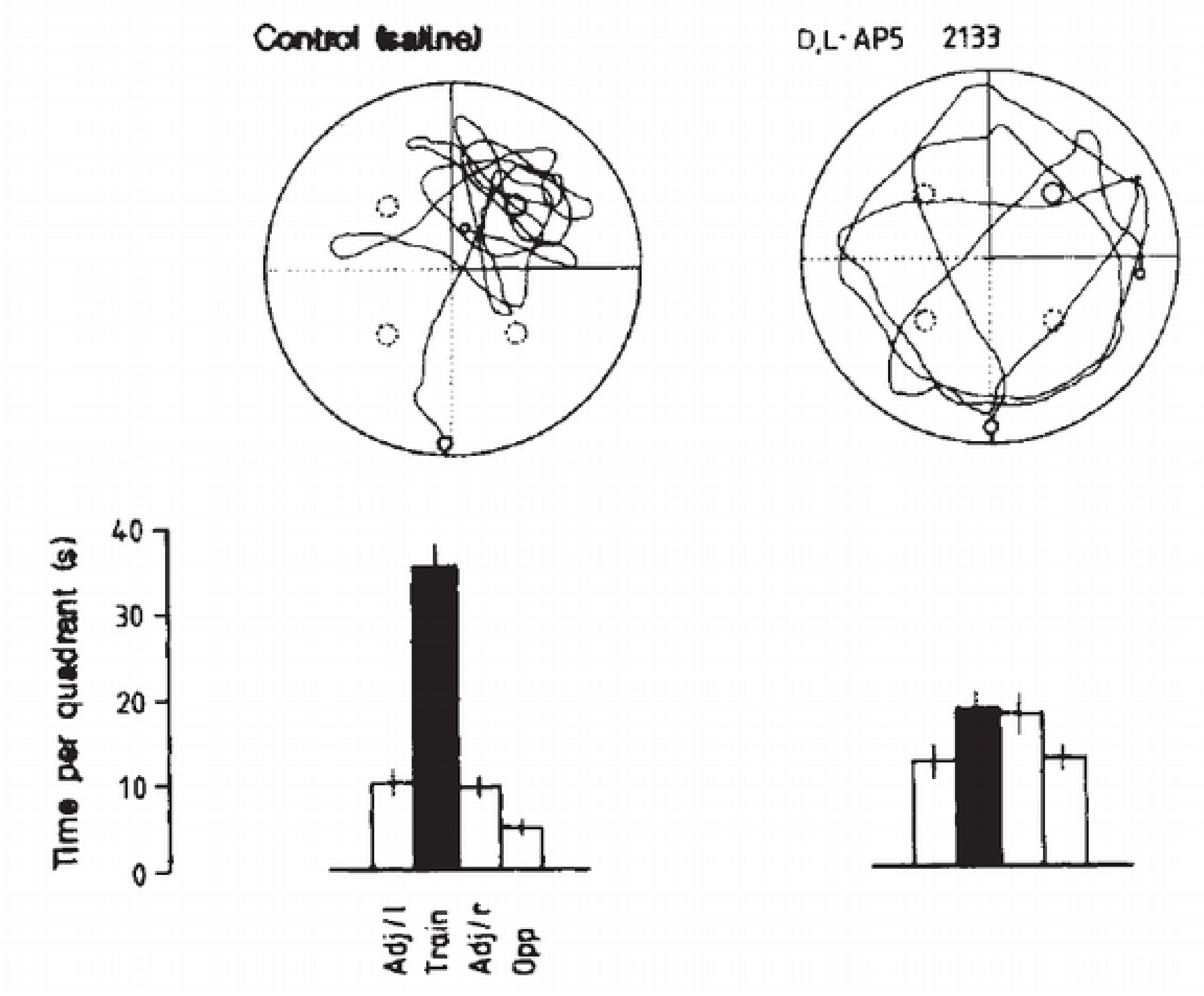


cultured hippocampal cells, outside-out patch (Jen and Stevens)

AP5 is a selective blocker

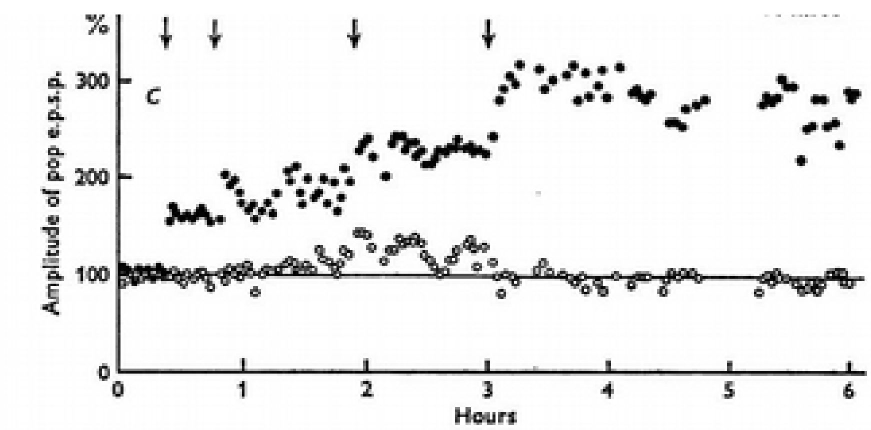


AP5 blocks learning



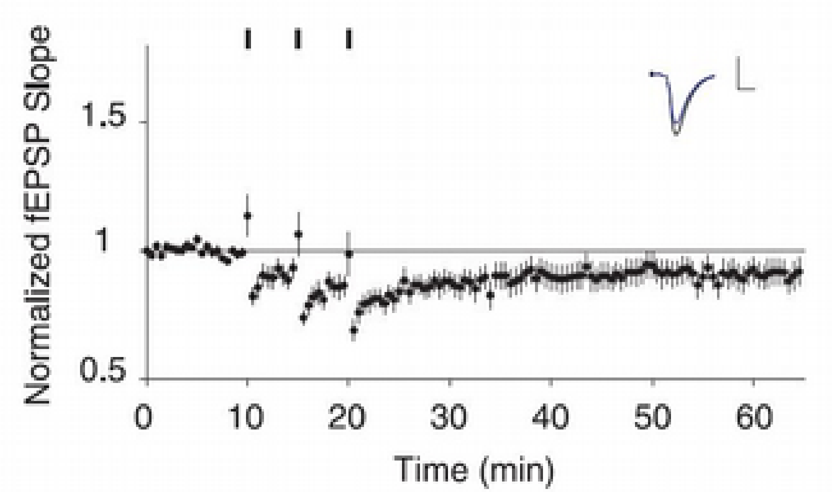
Ca hypothesis

LTP

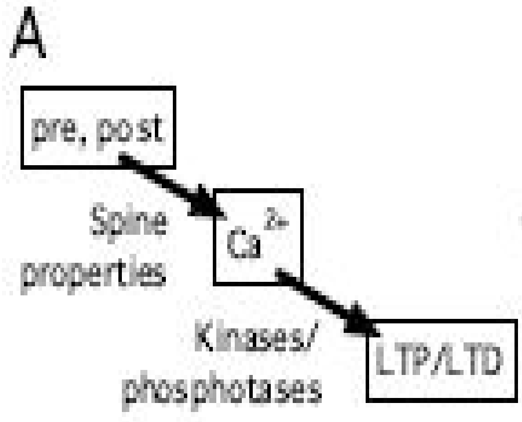


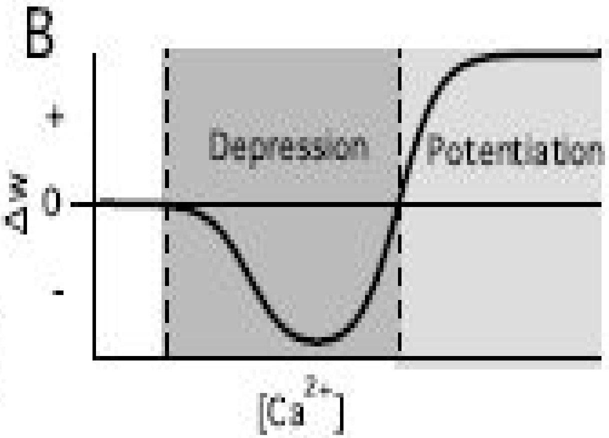
[Bliss & Lomo '73]

LTD



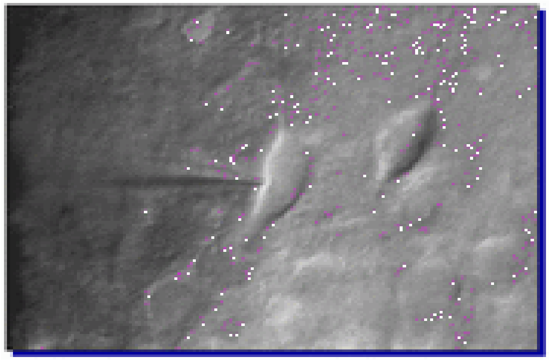
[O'Connor & Wang '05]

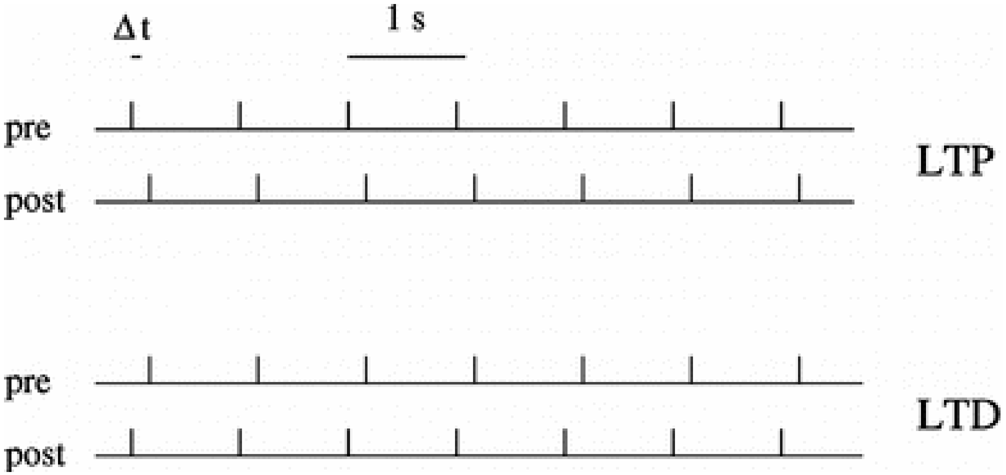


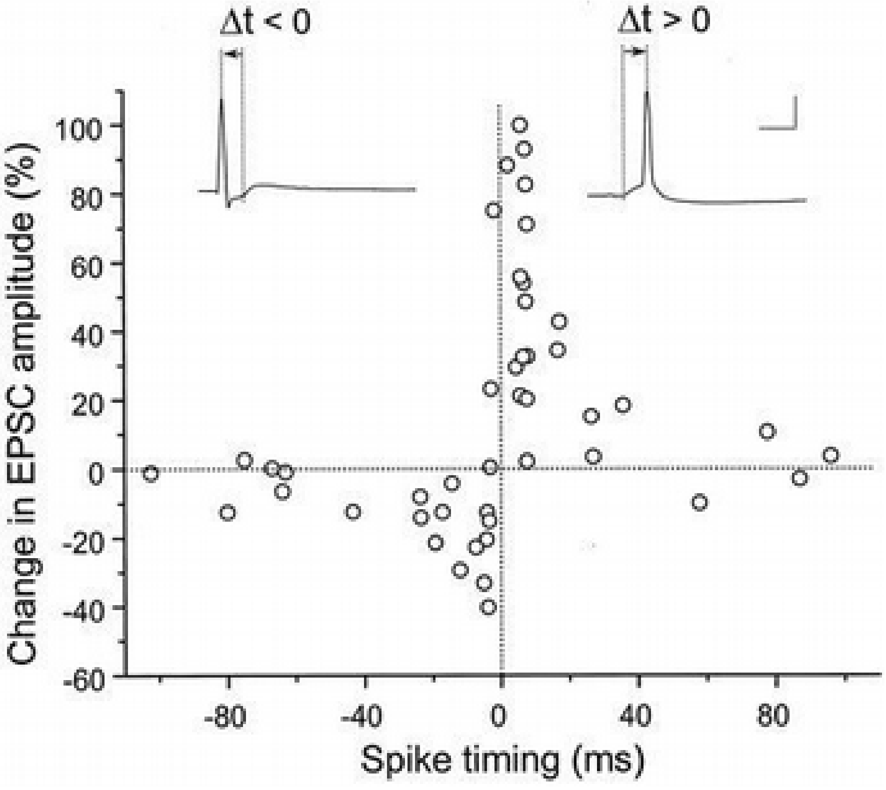


Pairing high pre- and post synaptic activity => LTP
Pairing with low activity => Long term depression

Spike Timing Dependent Plasticity: Experimental data







[Bi & Poo 1998]

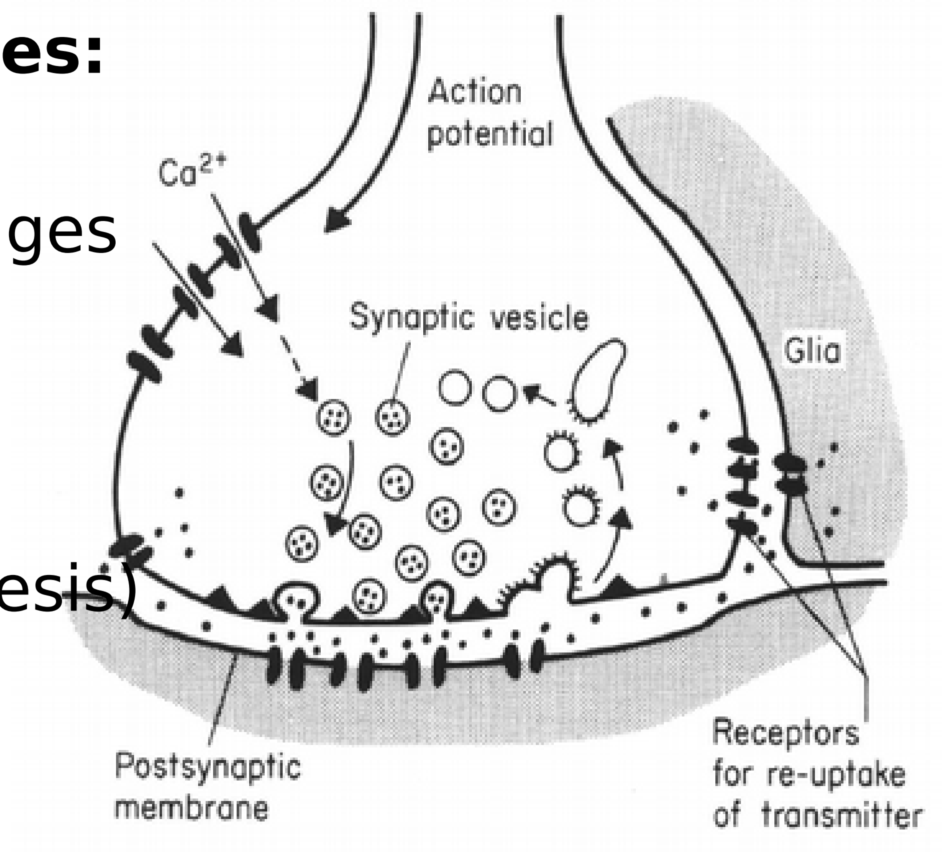
LTP stages

Induction:

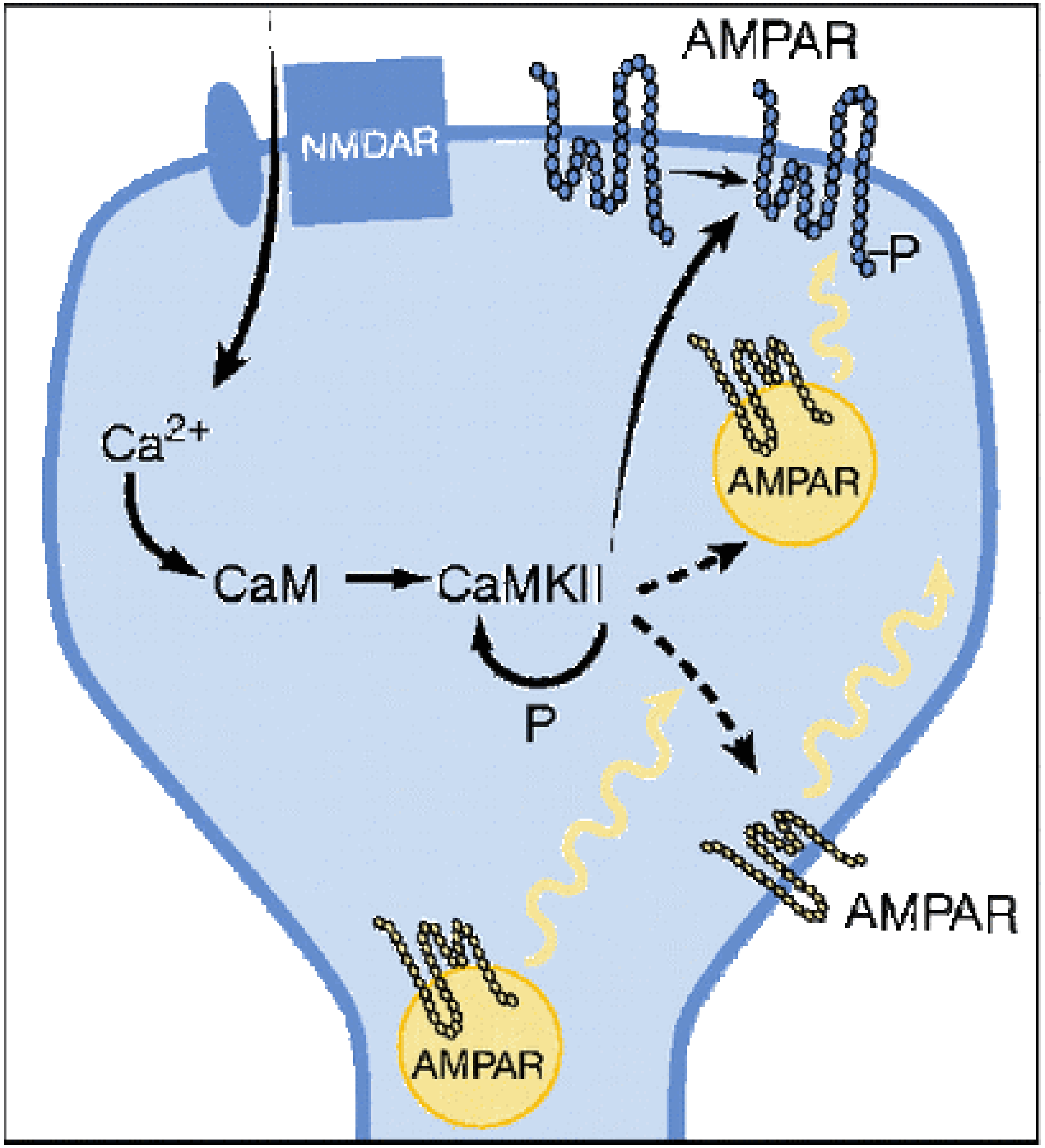
- Requires pre- and postsynaptic activity.
- Mechanism: NMDA and Ca influx

Expression / maintenance phases:

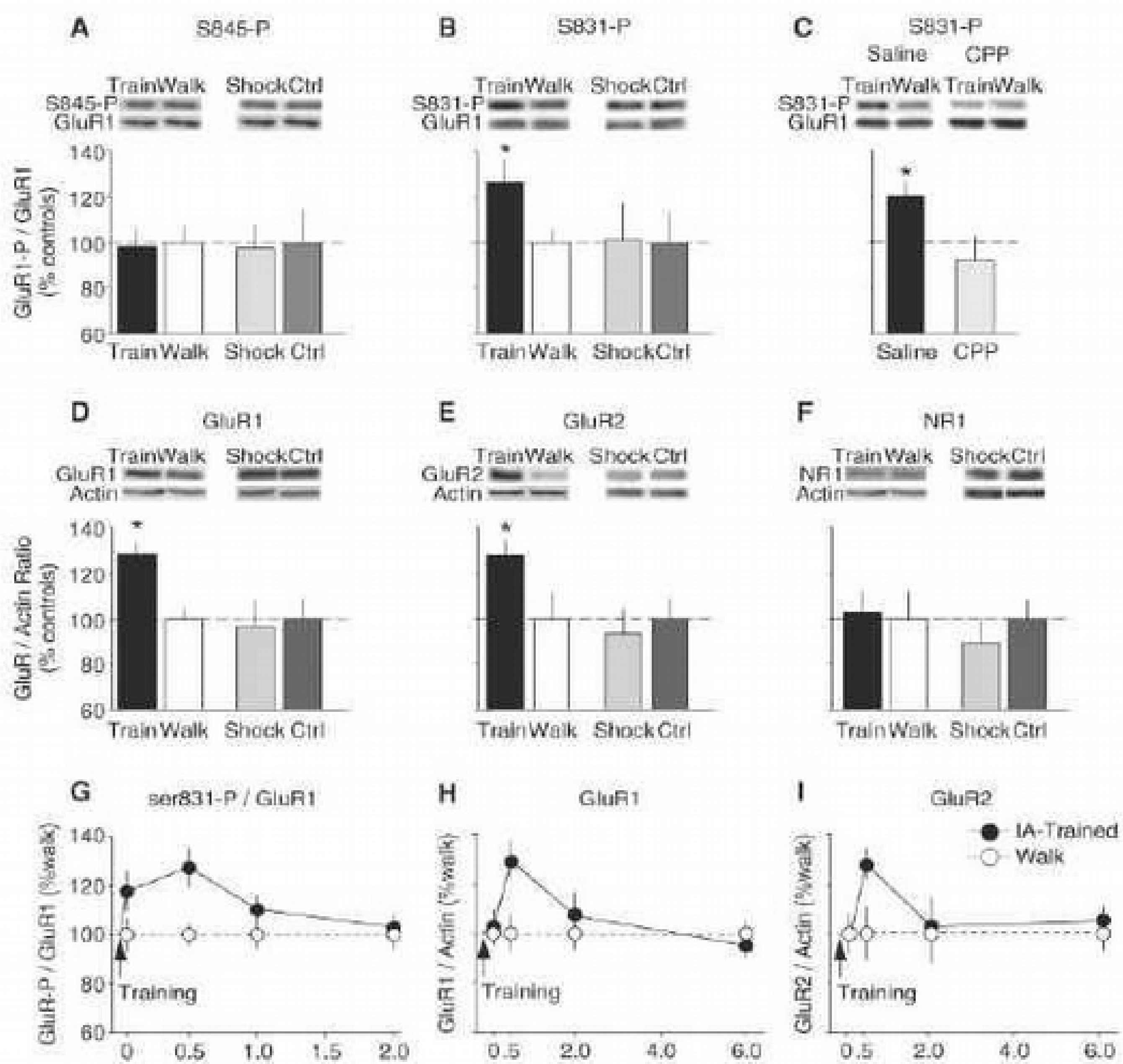
- Early LTP (1 hr):
  - partly pre-synaptic changes
  - AMPAR phosphorylation
  - AMPAR insertion
- Late LTP
  - ? (requires protein synthesis)



"Post-" model for expression

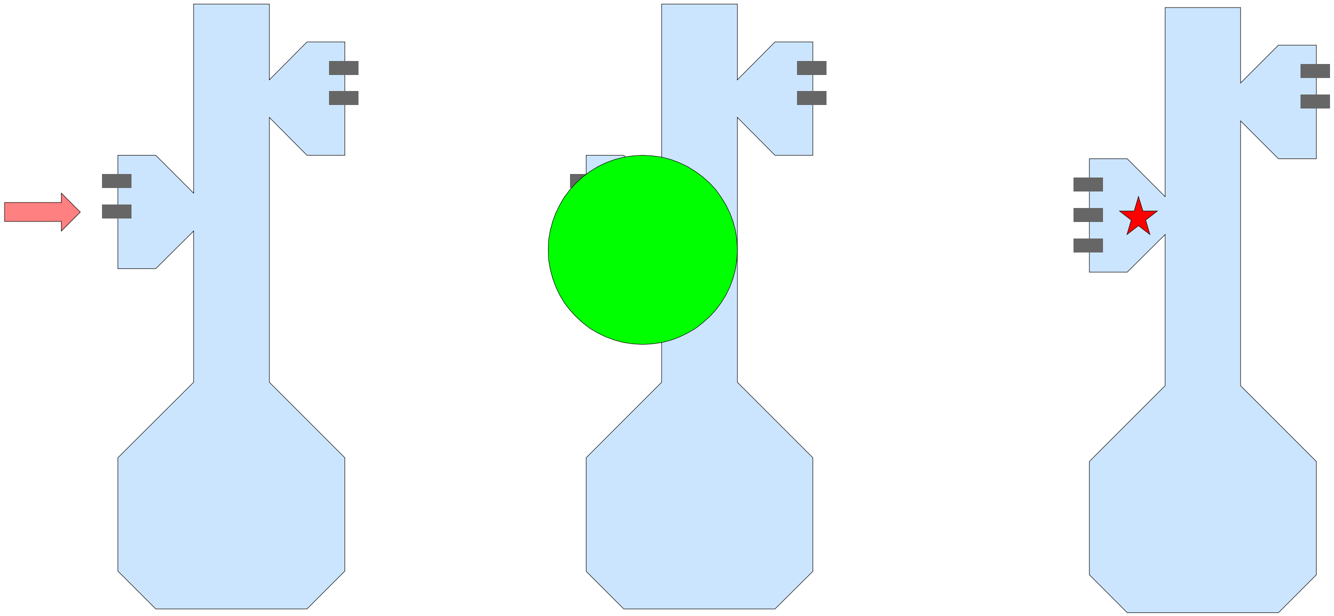


Changes in AMPA receptor phosphorilation

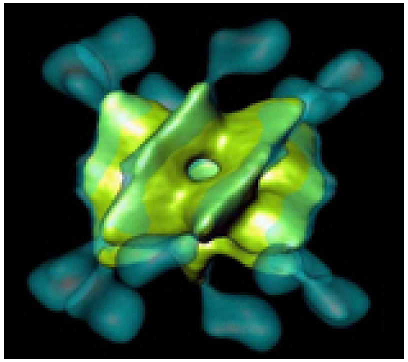


[Whitlock,
.. and Bear '06]

Early phase LTP



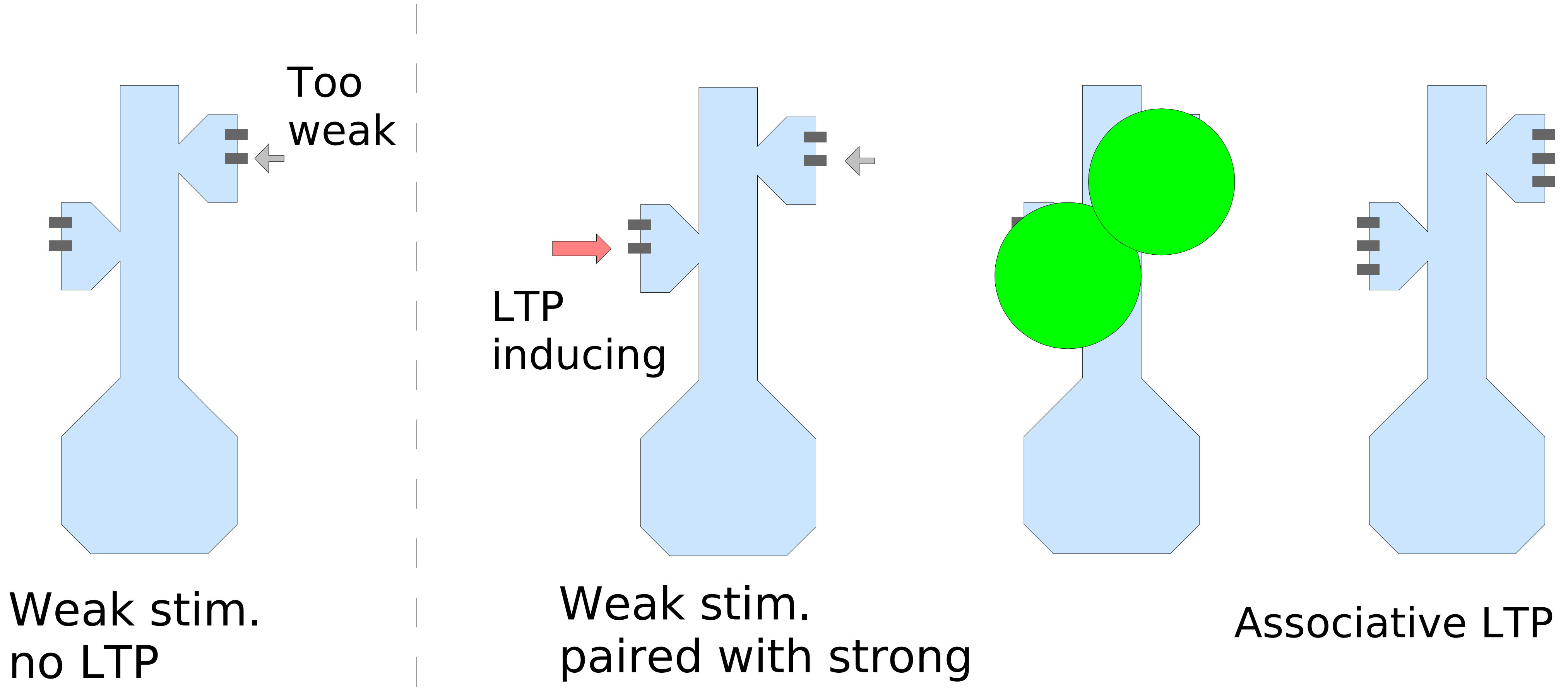
★ CaMKII



Stim.:
1 s @ 100Hz

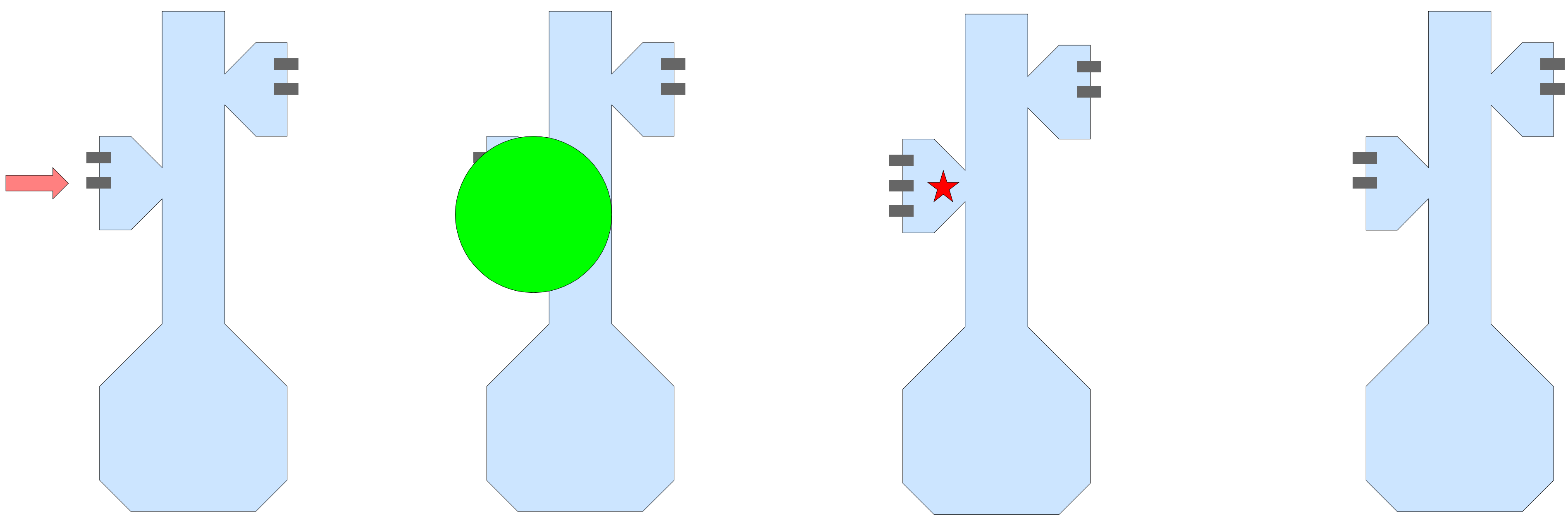
Rapid and local
change

Associativity



- Can be explained with voltage dependence of NMDA
- Associative learning such as Classical conditioning (Pavlov)

Early phase LTP

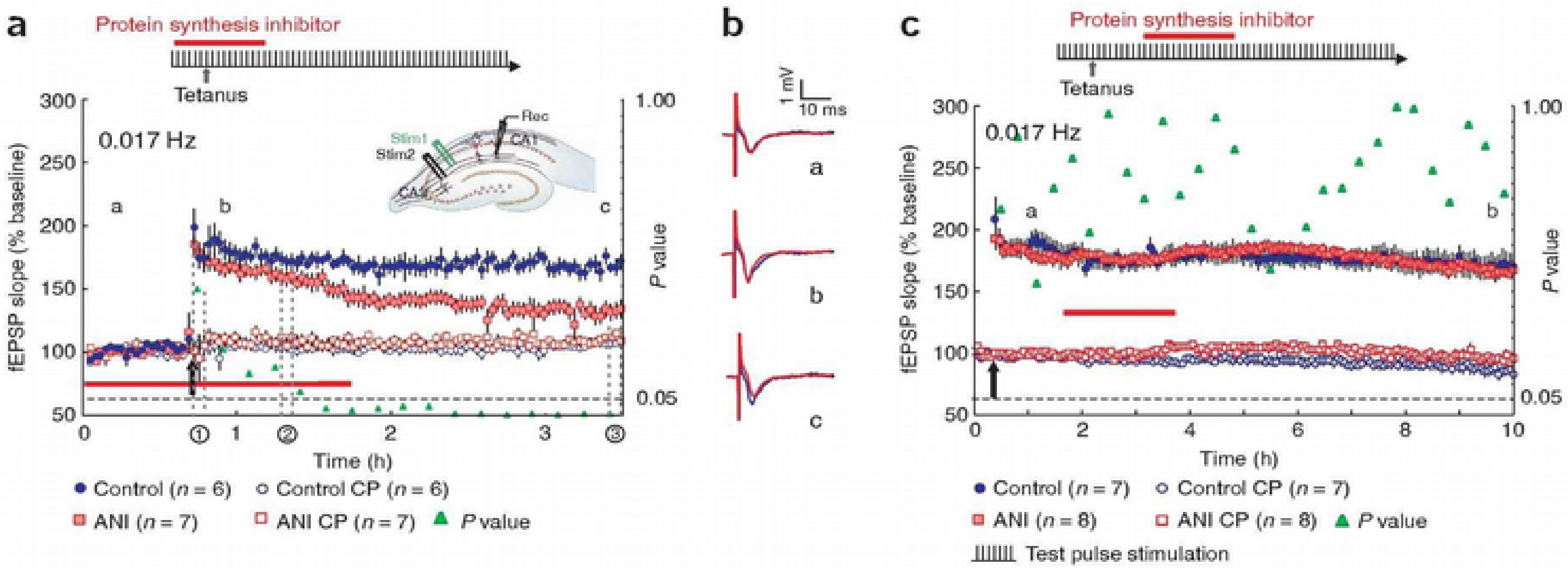


Stim.:
1 s @ 100Hz

Rapid and local
change

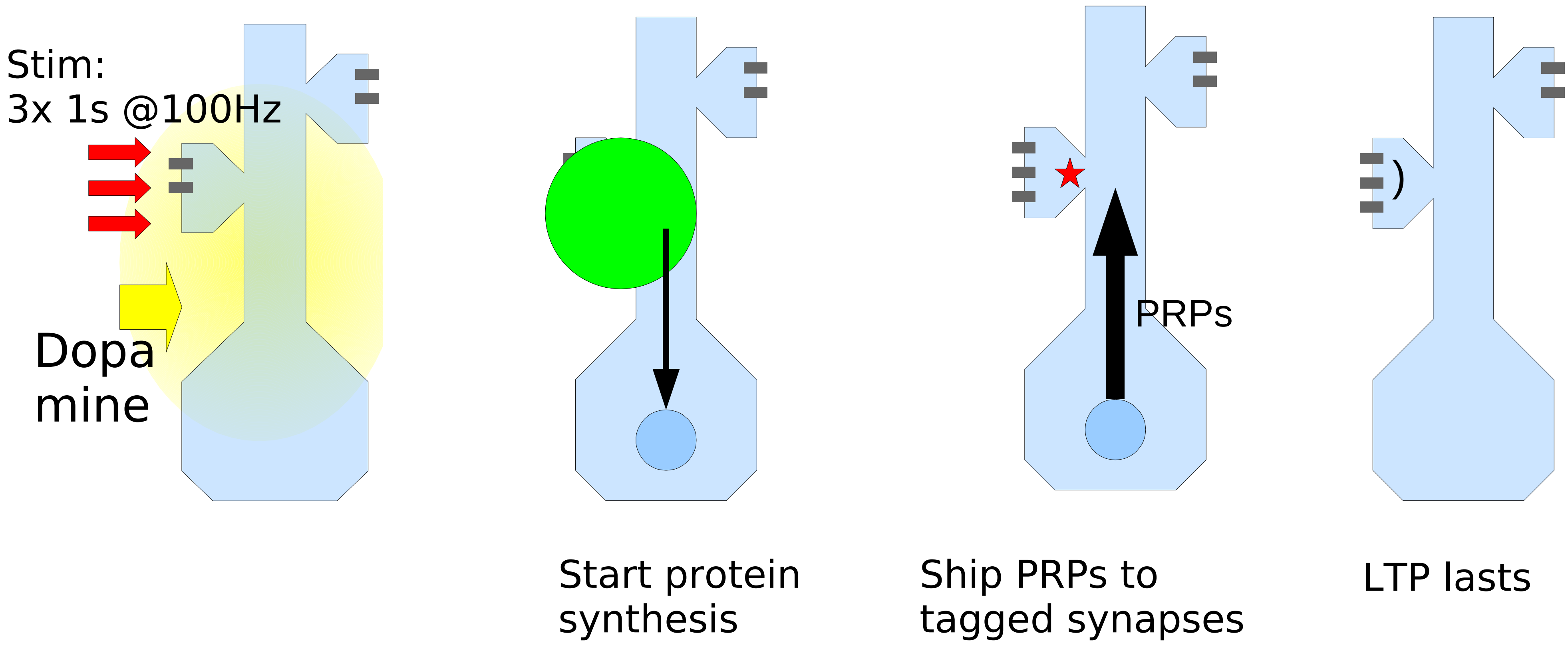
But gone
after few hours

Late LTP requires protein synthesis



[Fonseca et al 06]

Late phase LTP



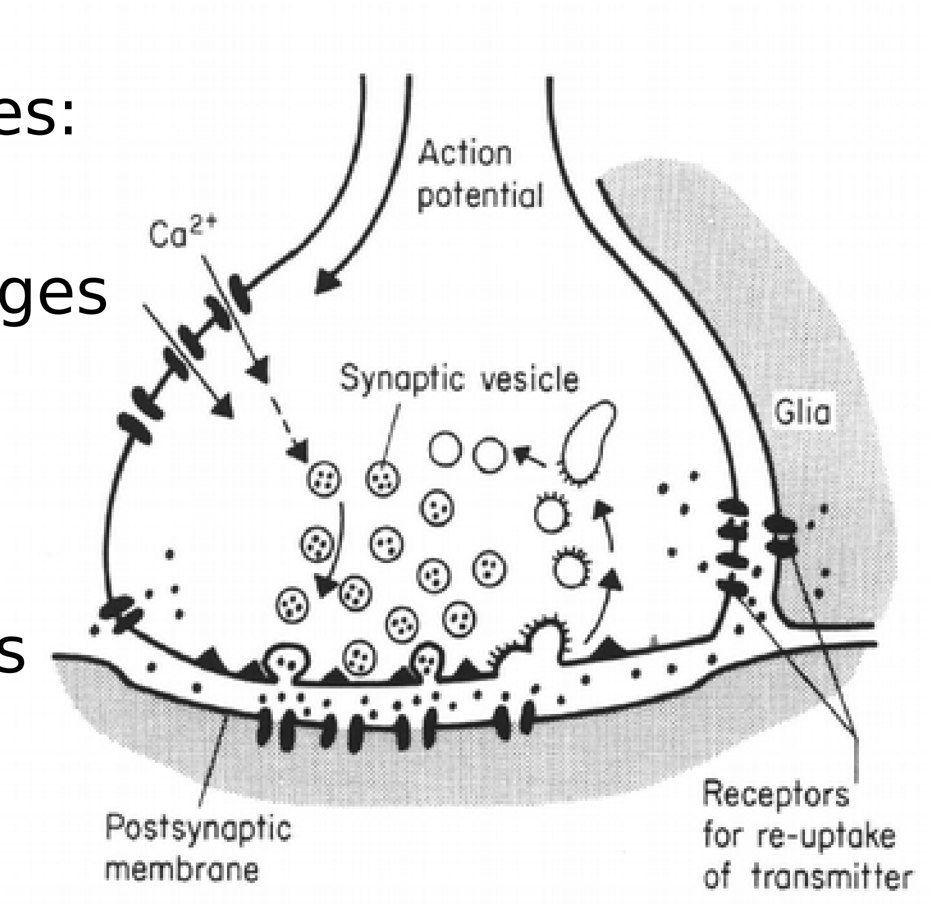
LTP stages

Induction:

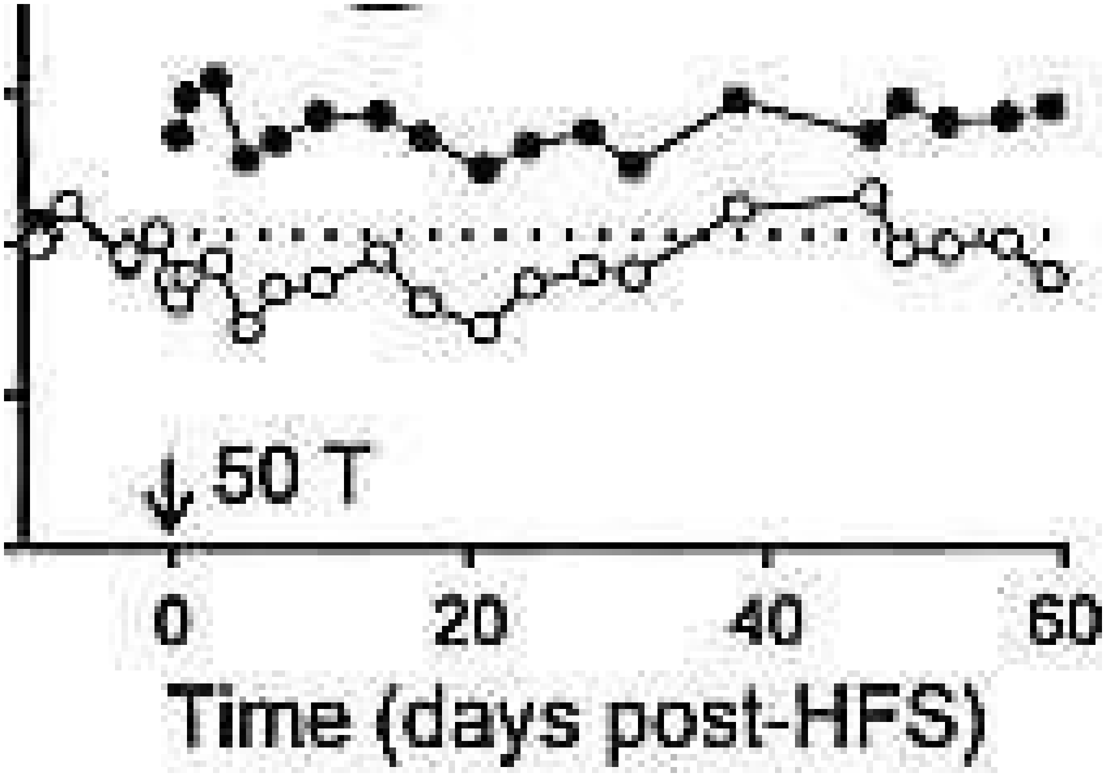
- Requires pre- and post synaptic activity.
- Mechanism: NMDA and Ca influx

Expression and Maintenance phases:

- Early LTP (1 hr):
    - partly pre-synaptic changes
    - AMPAR phosphorylation
    - AMPAR insertion
- **Late phase LTP**
    - requires protein synthesis



Longevity: In vivo physiology

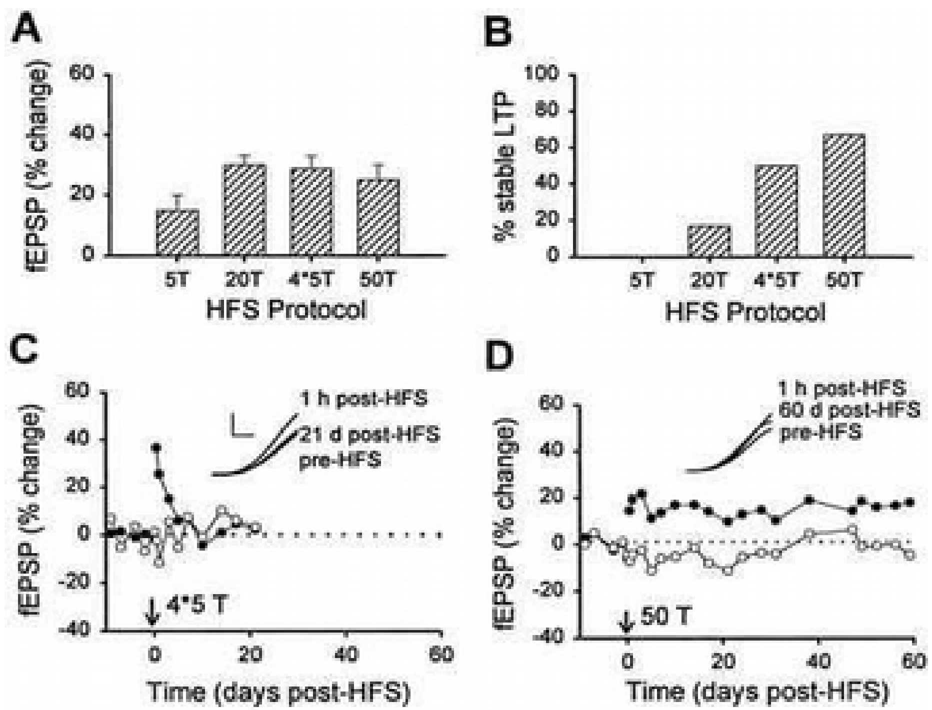


[Abraham '00]

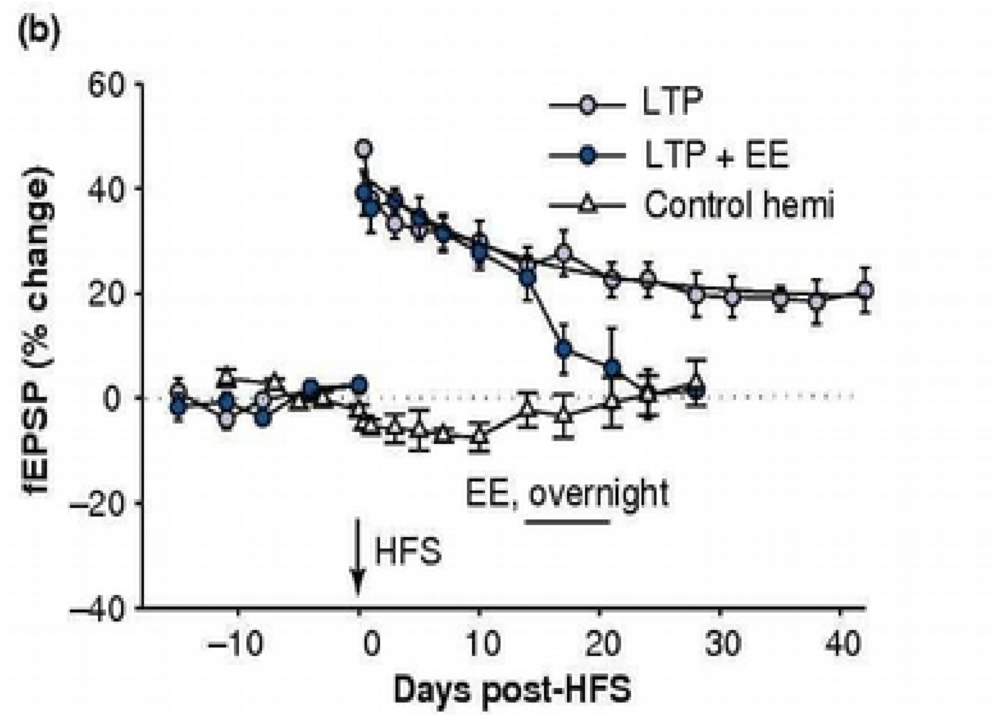
• Strong extracellular stimulation, leads to long lasting strengthening of synapse [Bliss and Lomo '73]

What determines if LTP lasts?

Stimulus protocol



Environment

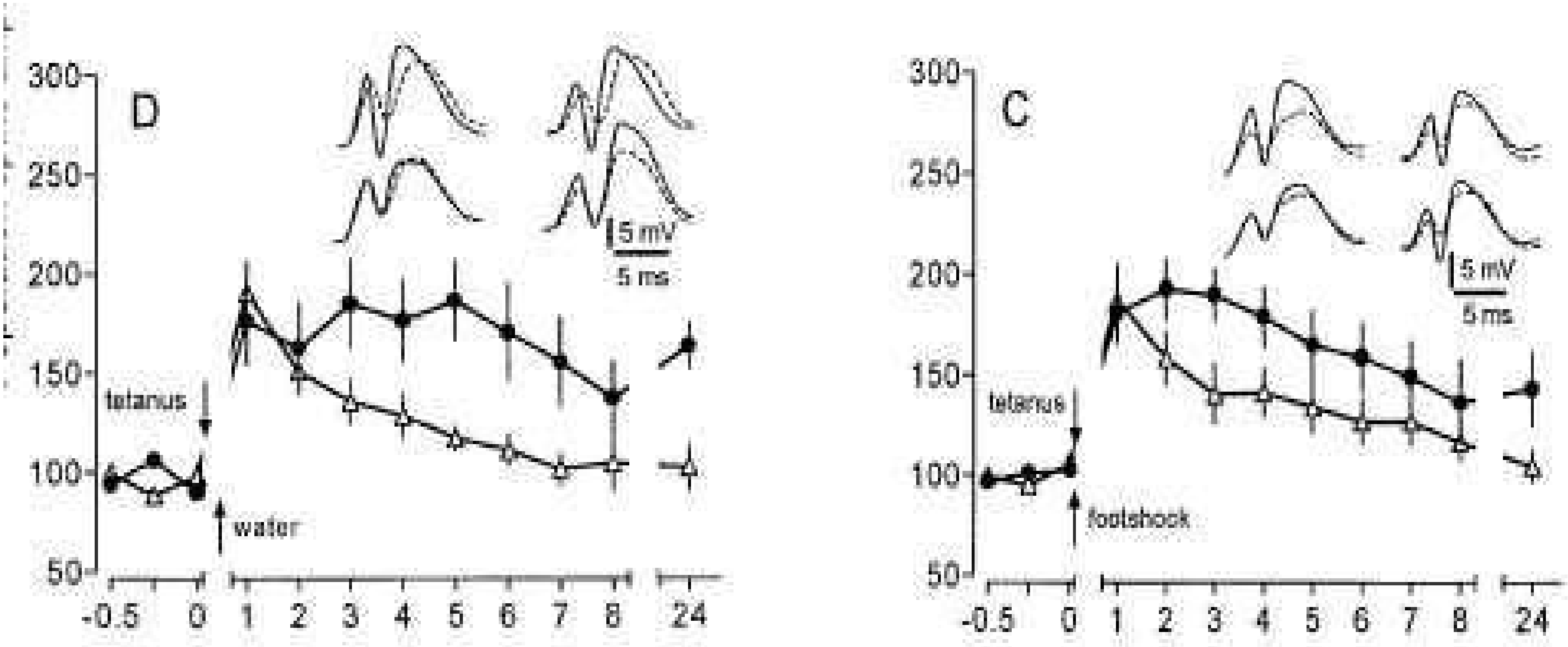


[Abraham '00]

[Abraham '02, Li & Rowan '00]
(Dopamine mediated)
Does a novel environment 'reset' hippocampal learning?

What determines if LTP lasts?

Reward and punishment

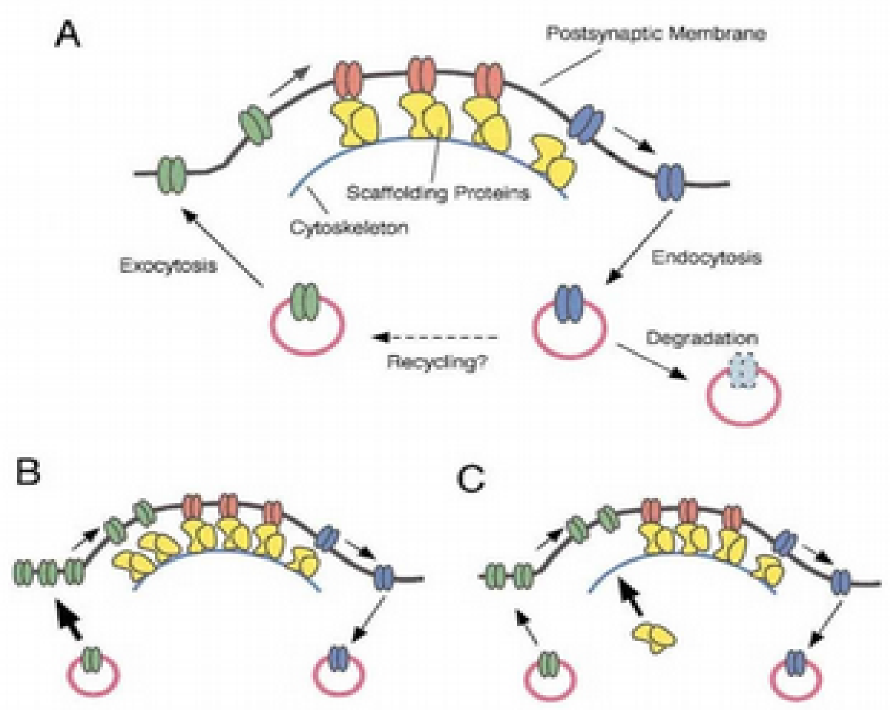


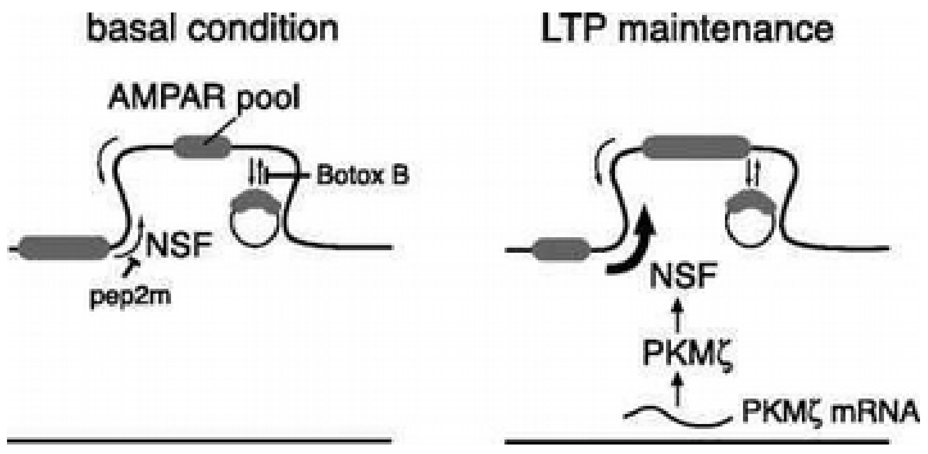
[Seidenbecher '95]

Hypotheses for long term stability

Slots for AMPA receptors

GluR2 trafficking

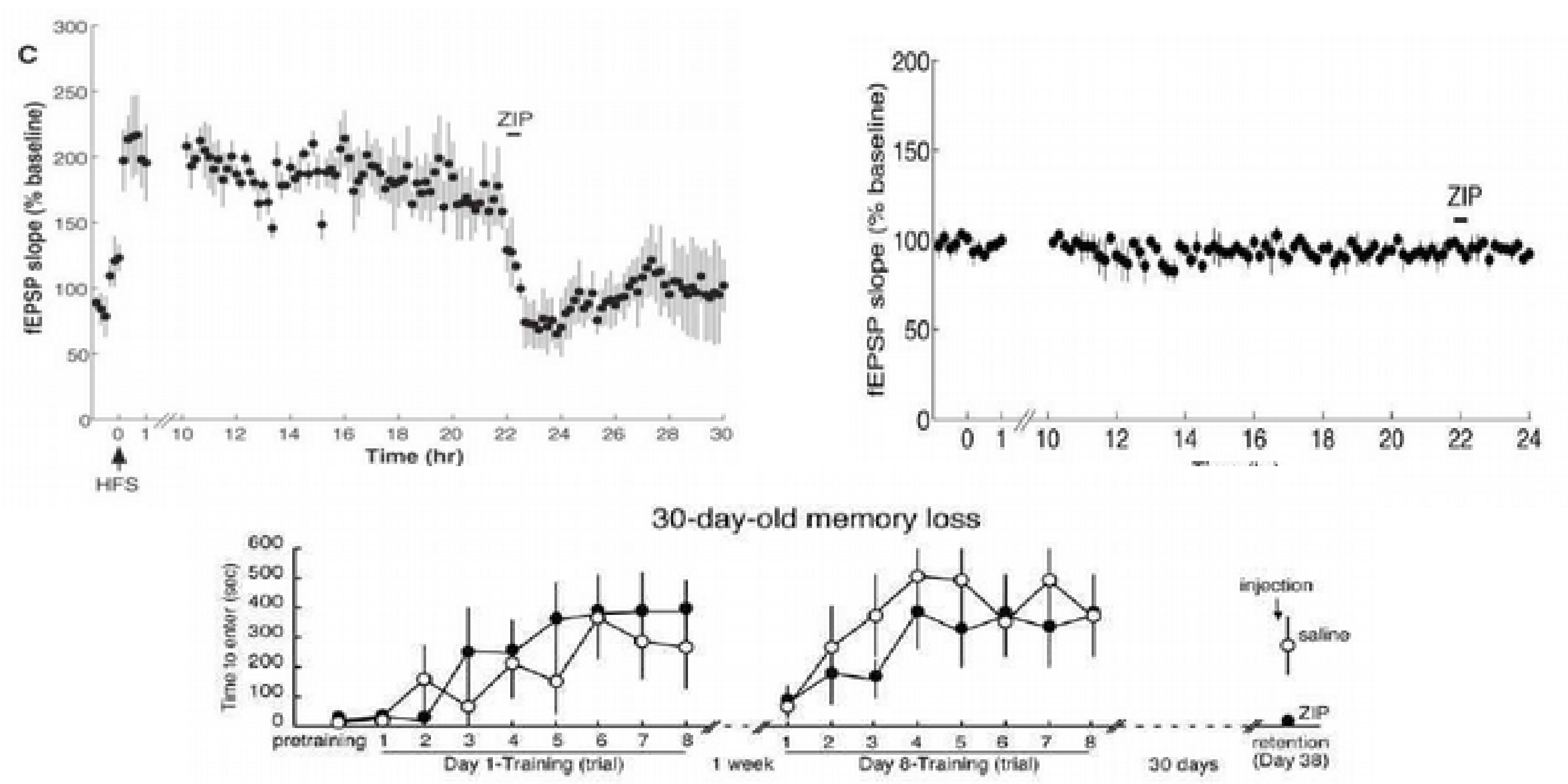




[Turrigiano '02]

[Yao & Sacktor '08]

Late LTP maintenance as an active process



ZIP disrupts one month old memory

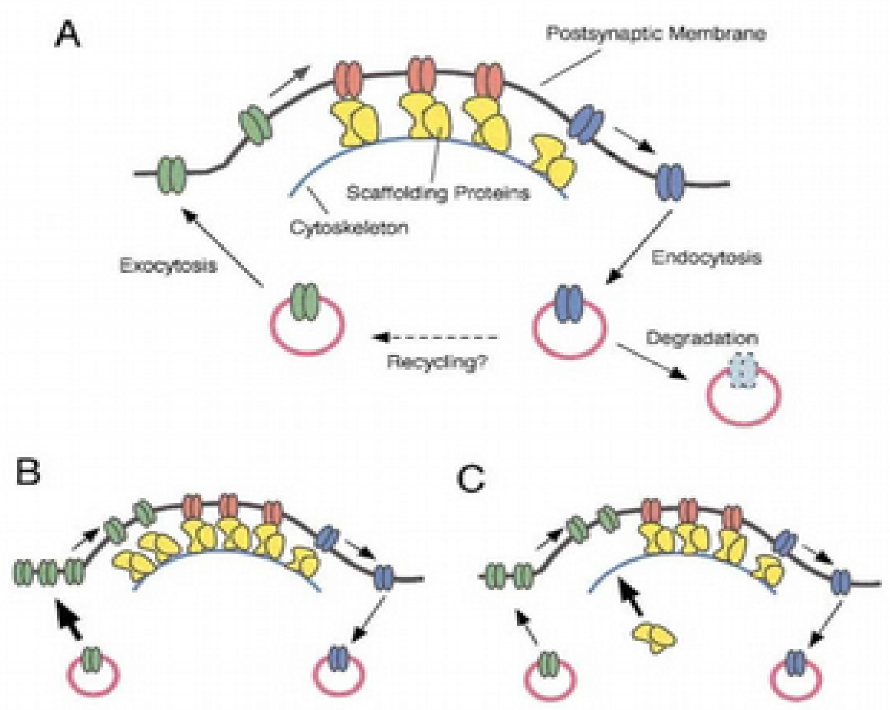
[Pastalkova et al '06]

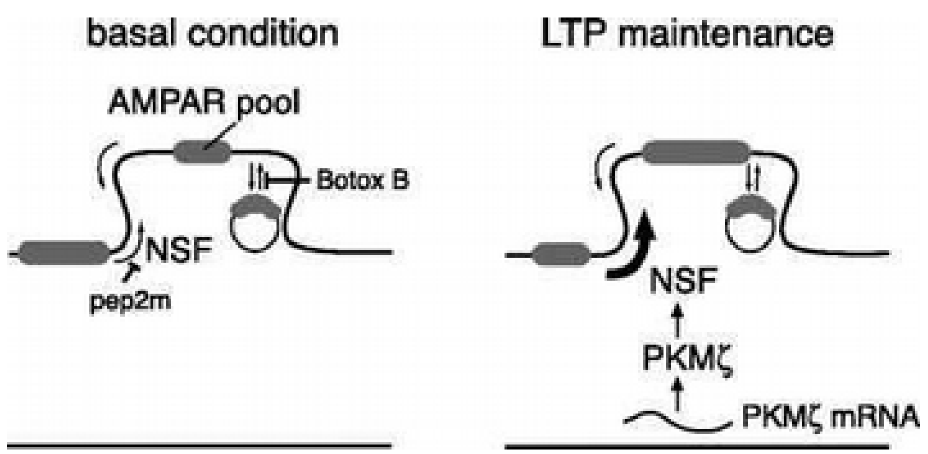
[movie demo]

Hypotheses for maintaince / long term stability

Slots for AMPA receptors

GluR2 trafficking





[Turrigiano '02]

[Yao & Sacktor '08]

Stable memory despite changes

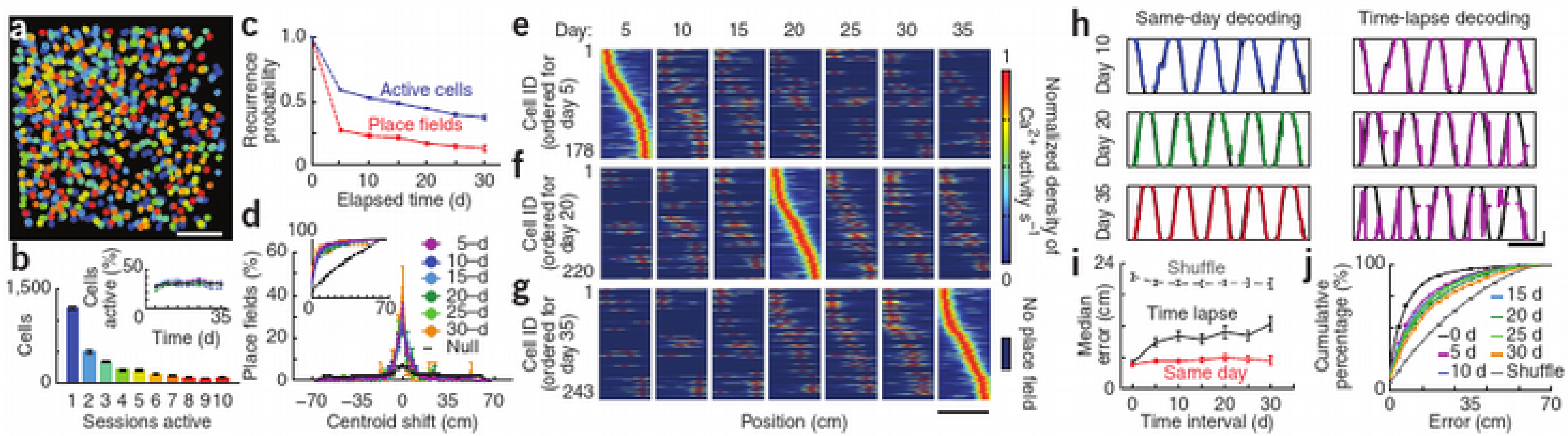


Figure 3 Place fields are spatially invariant and temporally stochastic while preserving a stable representation at the ensemble level. (a) We found Ca^{2+} activity in 826 cells in one mouse over 45 d. Color as in b. (b) Histogram of the number of sessions in which each of 2,960 cells from four mice

[Ziv et al 2013]

Synaptic plasticity = memory?

- Detectability
  changes in behaviour and synaptic efficacy should be correlated
  Yes

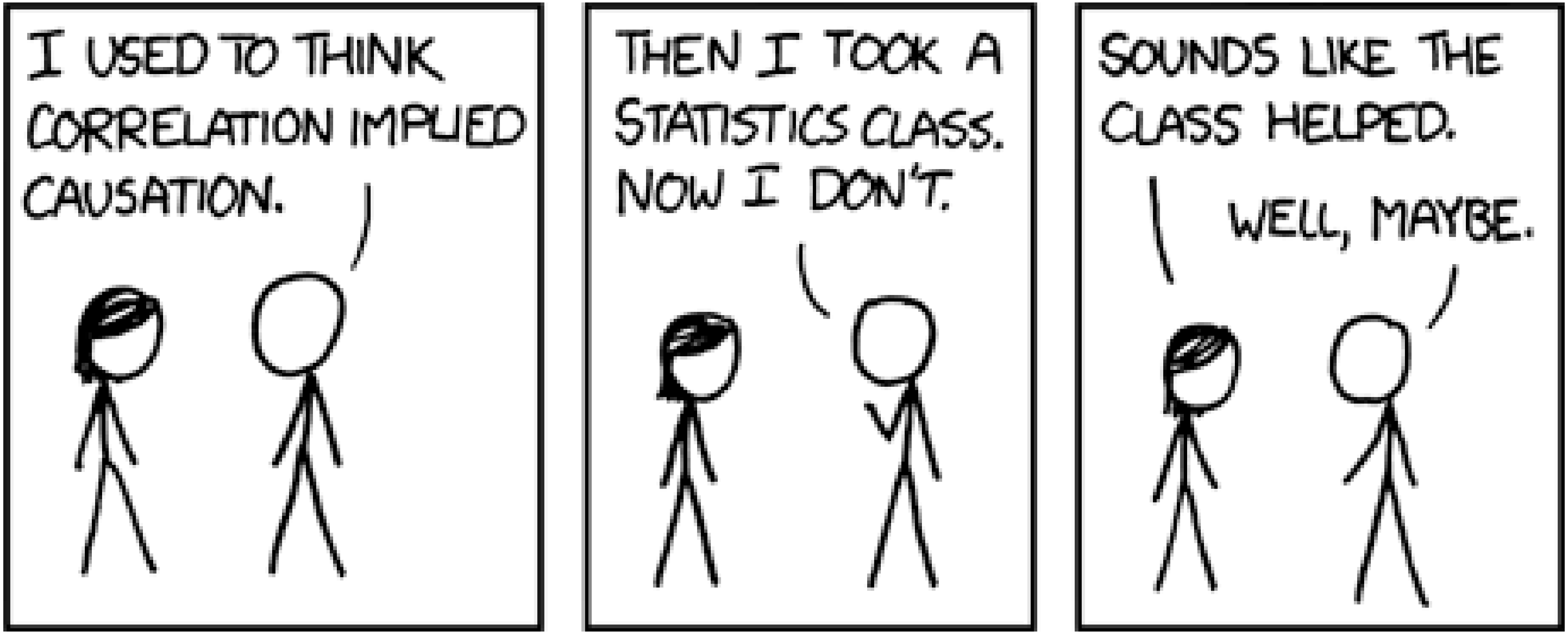
- Mimicry
  change synaptic efficacies → new ‘apparent’ memory
  Not quite yet...

- Anterograde alteration
  prevent synaptic plasticity → anterograde amnesia
  Yes (e.g. NMDA block)

- Retrograde alteration
  alter synaptic efficacies → retrograde amnesia
  Yes, but...

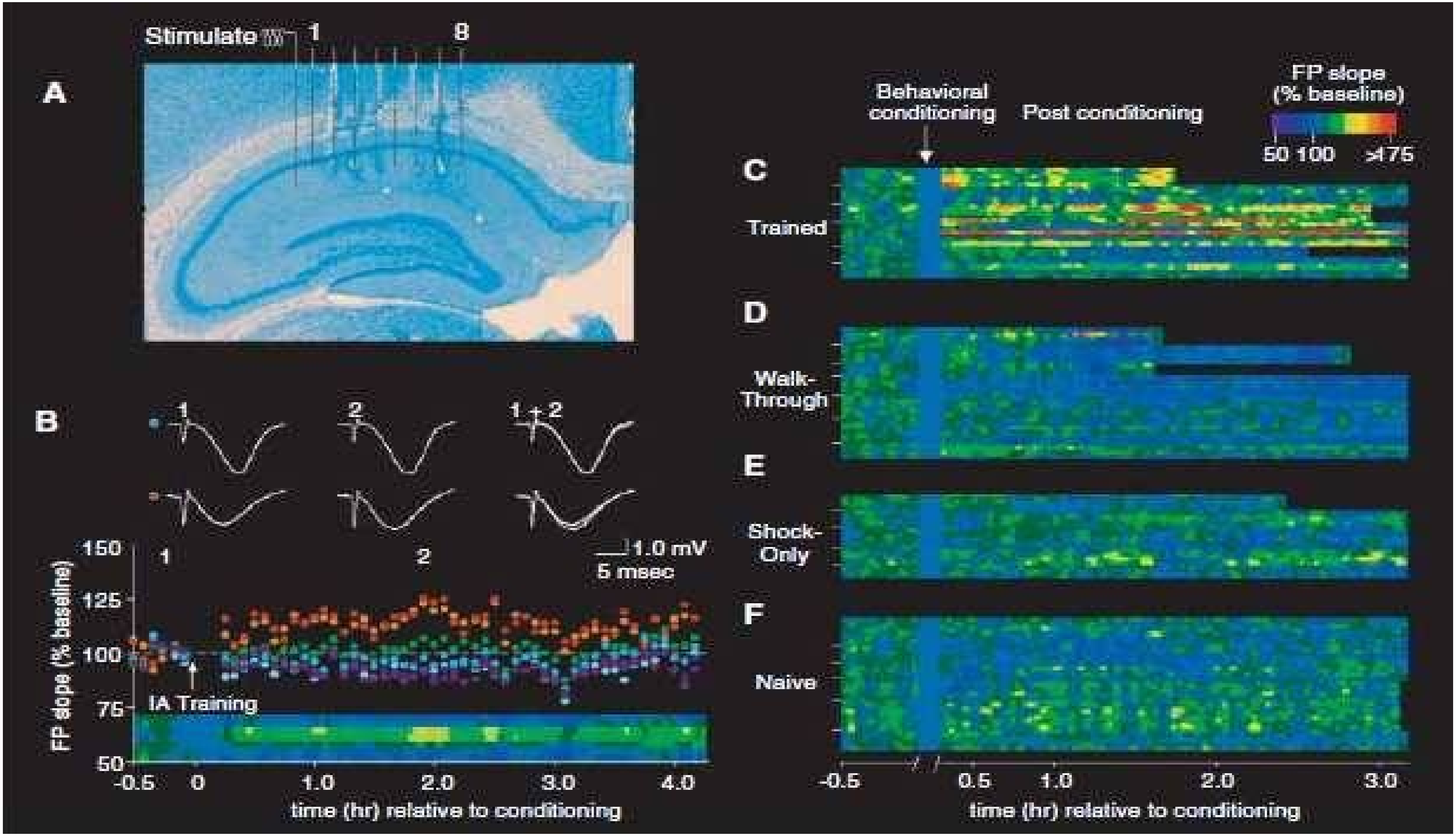
[Martin, Greenwood, Morris]

Synaptic plasticity = memory?



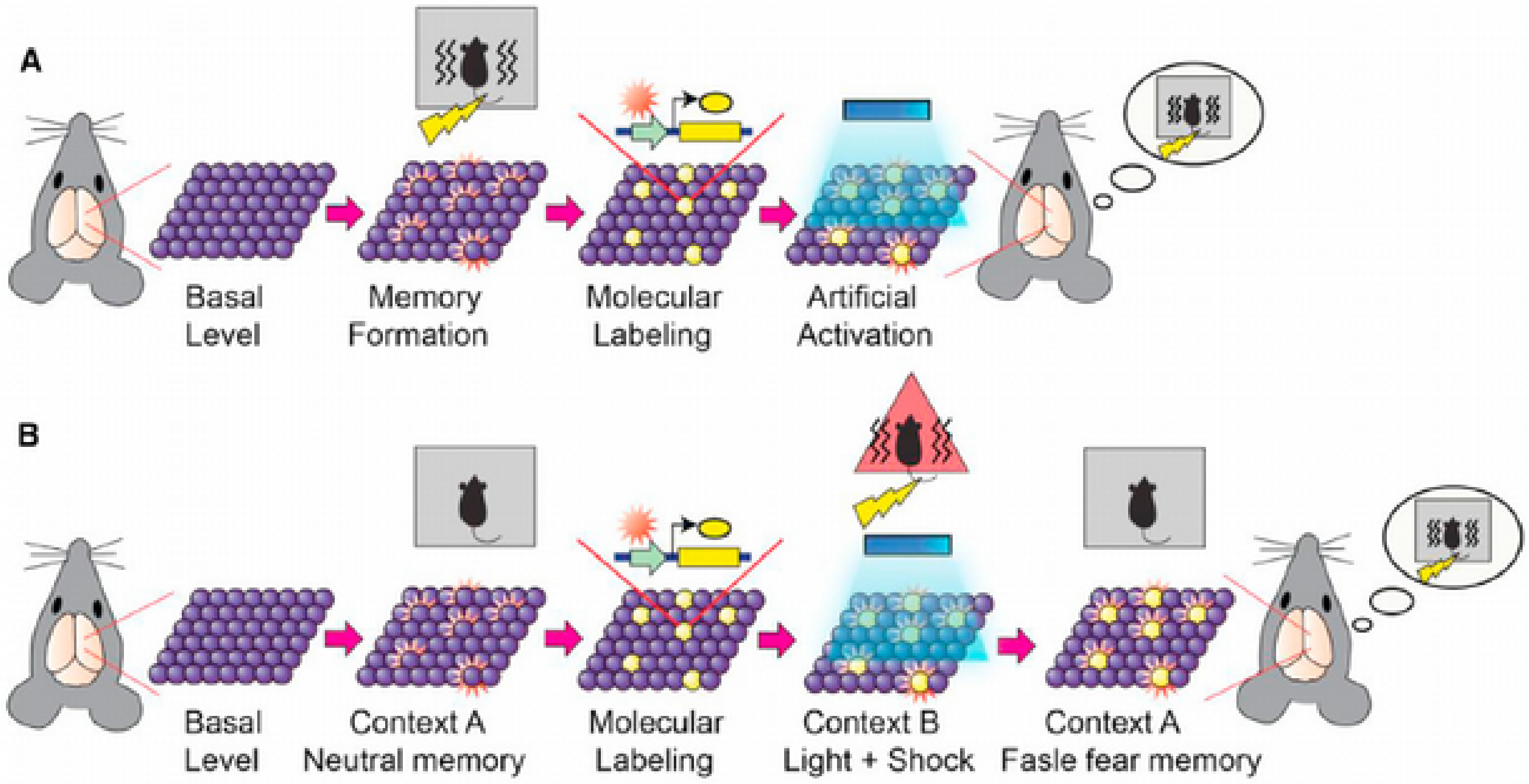
[Martin, Greenwood, Morris]

Synaptic plasticity=memory?



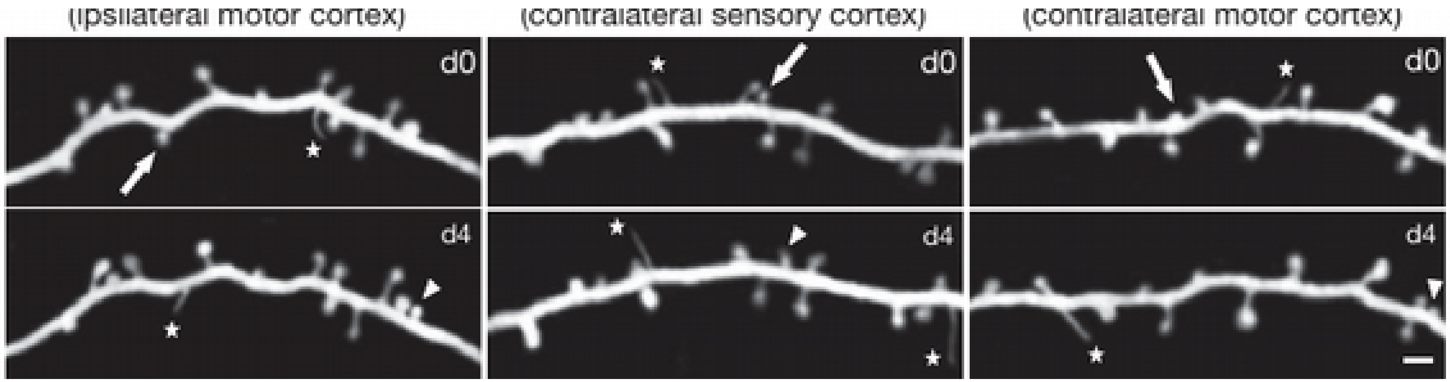
[Whitlock,.. and Bear '06]

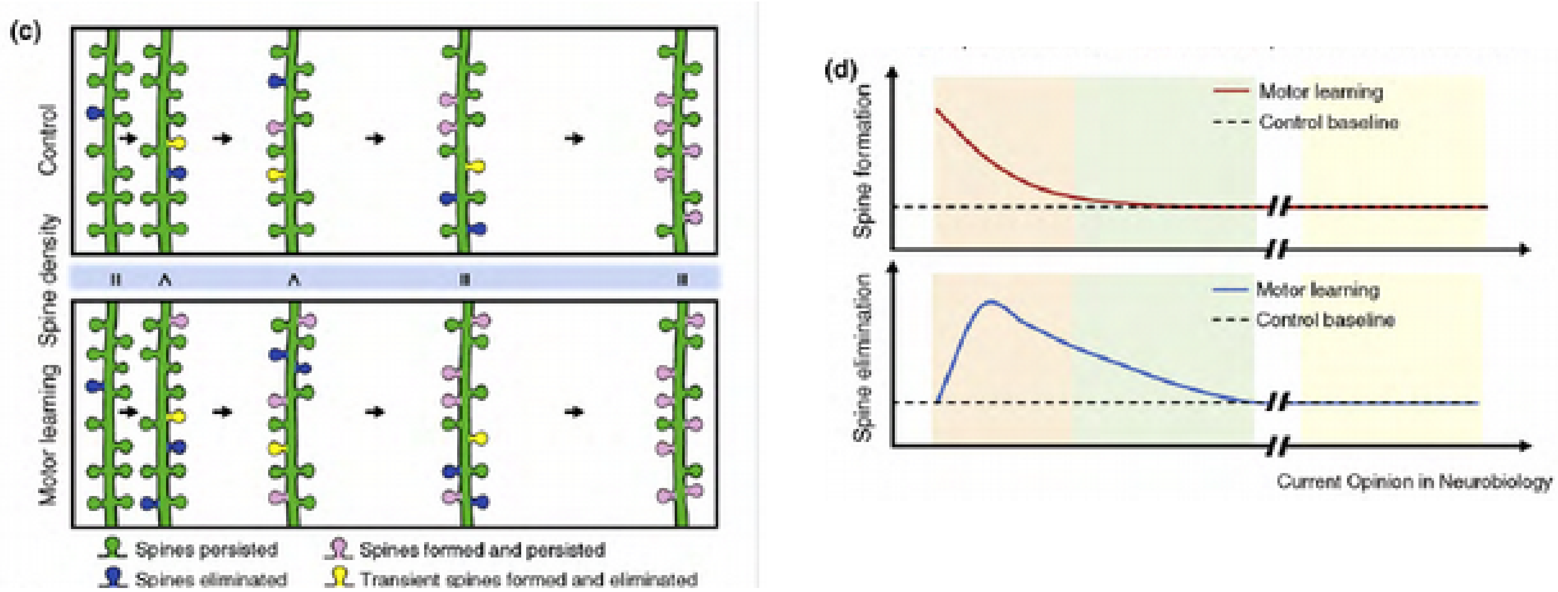
False memories



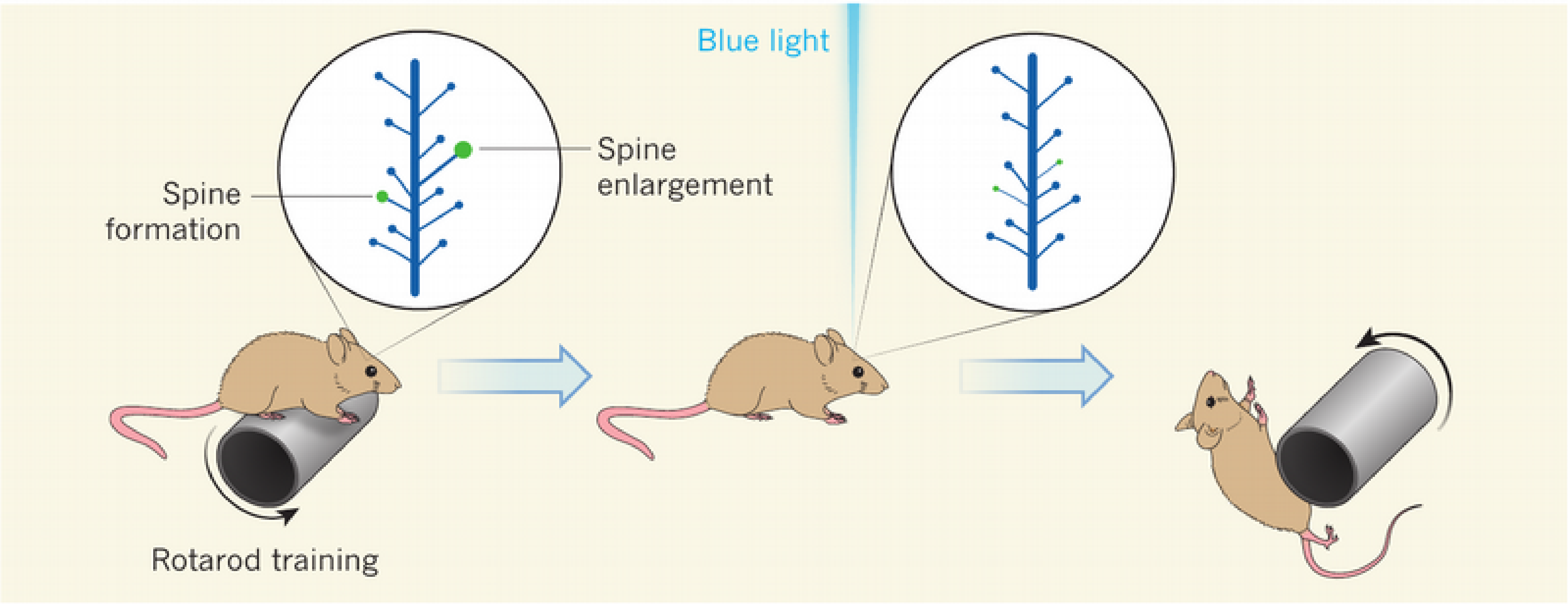
[Tonegawa review 2010]

Spine plasticity





Yu Zuo Curr Opin Neurobiol (2010)



[Hayashi-Takagi et al., 2015]

Learning models

Why modelling plasticity

Why modeling plasticity: 2 cross-fertilizing approaches

1) Artificial neural networks, engineering approach

- make a network do something
- now somewhat superseded by more formal machine learning

2) Insight in biology

- extrapolate single neuron plasticity to network level
- how can organisms adapt?

Models of plasticity and memory

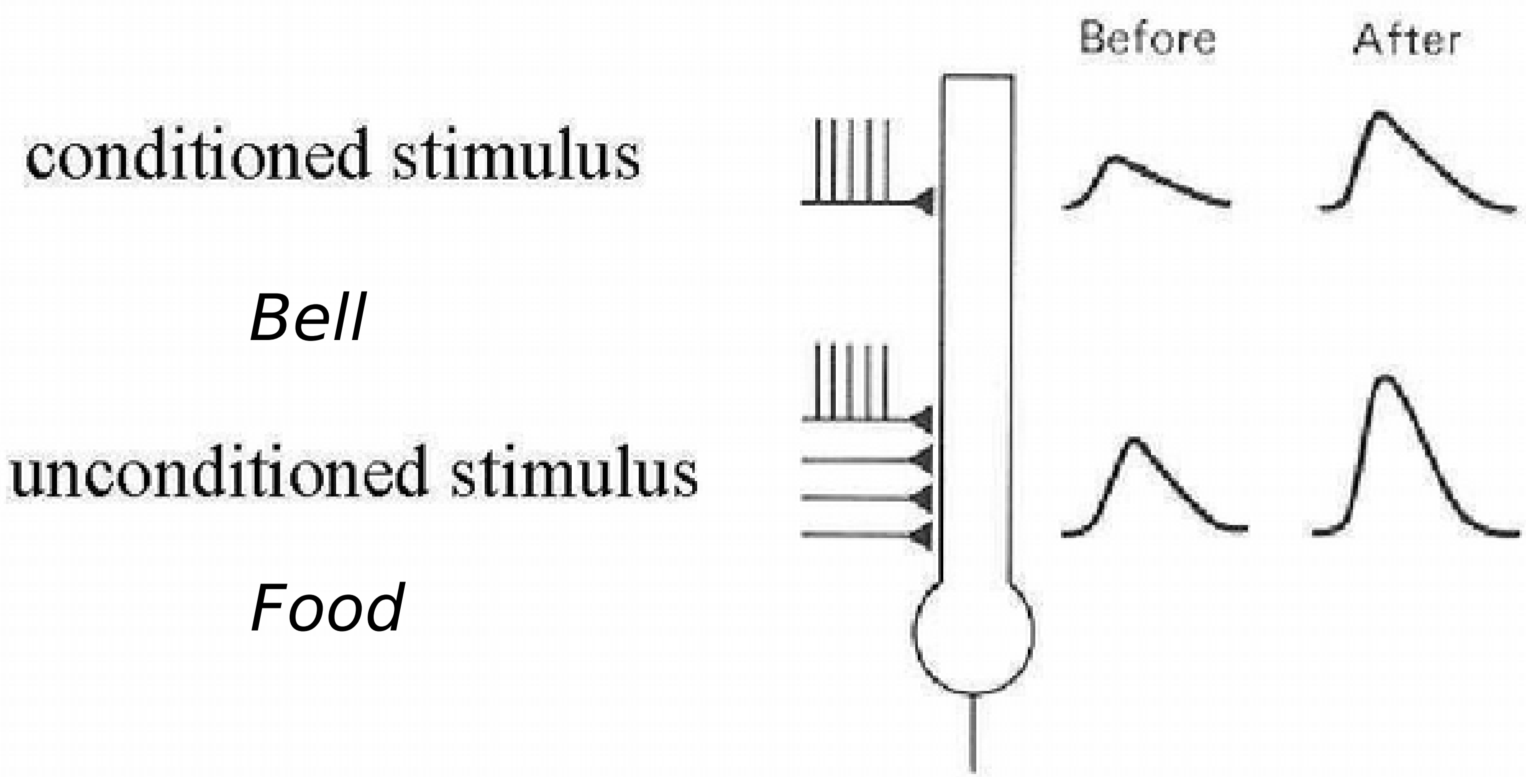
Supervised learning
- tell network exactly what desired output is
- train network by changing the weights

Reinforcement learning
- Only give reward/punishment

Unsupervised learning
- Let the network discover things (statistics) about the input, e.g. Create representations that are useful for further processing (V1)

Animals can do all three presumably

Modeling classical conditioning



‘Saliva’-neuron

NB: just a cartoon!

Modeling classical conditioning

Rescorla-Wagner (delta-rule)

Reward prediction model:

$$\Delta w_i = \epsilon x_i \delta$$

$$\delta = r - y$$

Learn until r=y.

Modeling classical conditioning

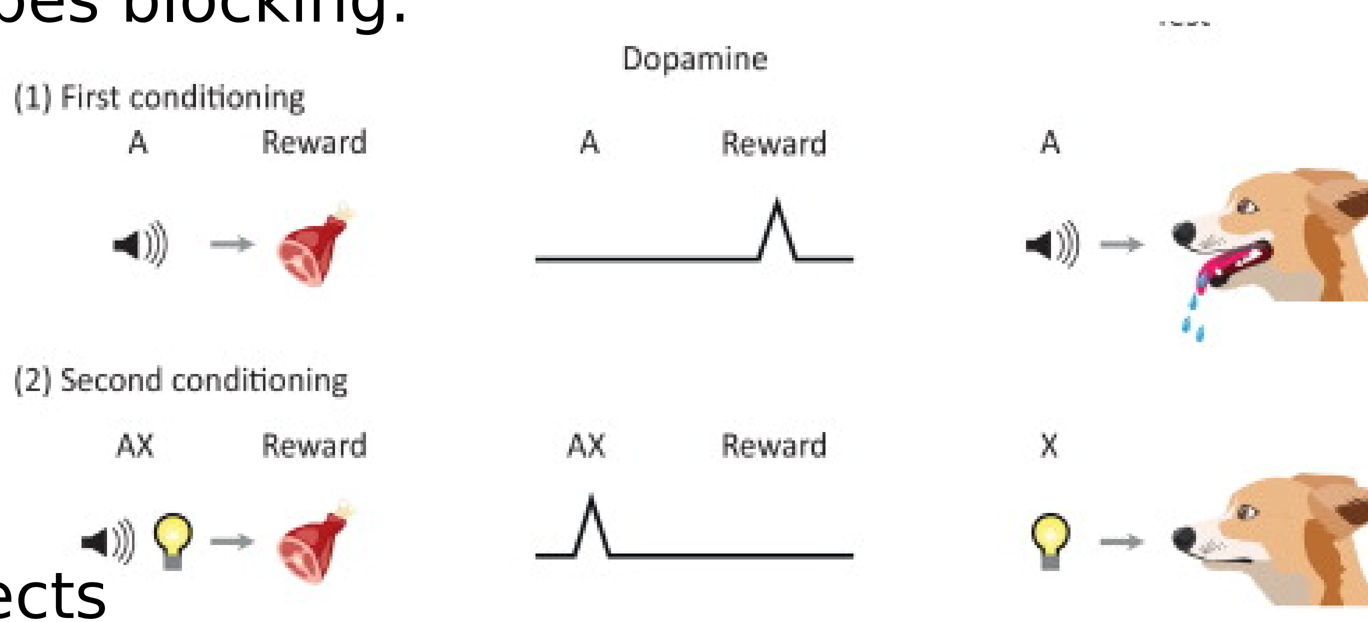
Rescorla-Wagner (delta-rule)

Reward prediction model:

$$\Delta w_i = \epsilon x_i \delta$$

$$\delta = r - y$$

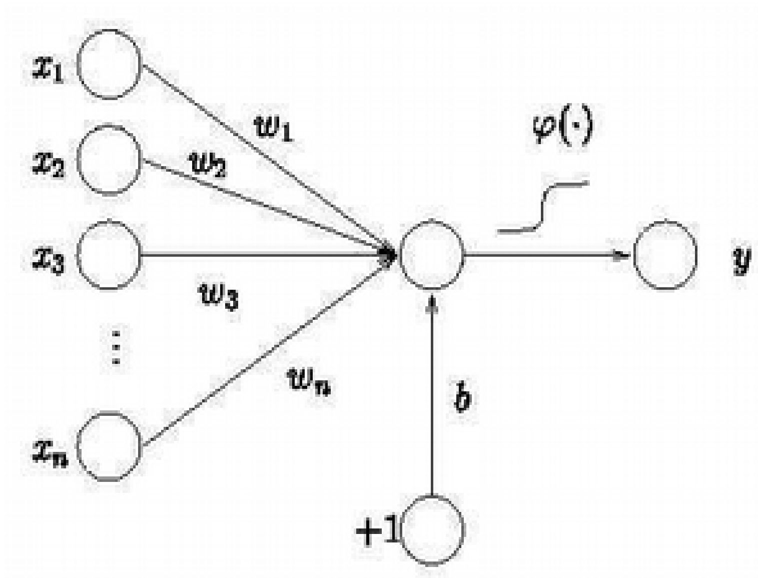
For instance describes blocking:

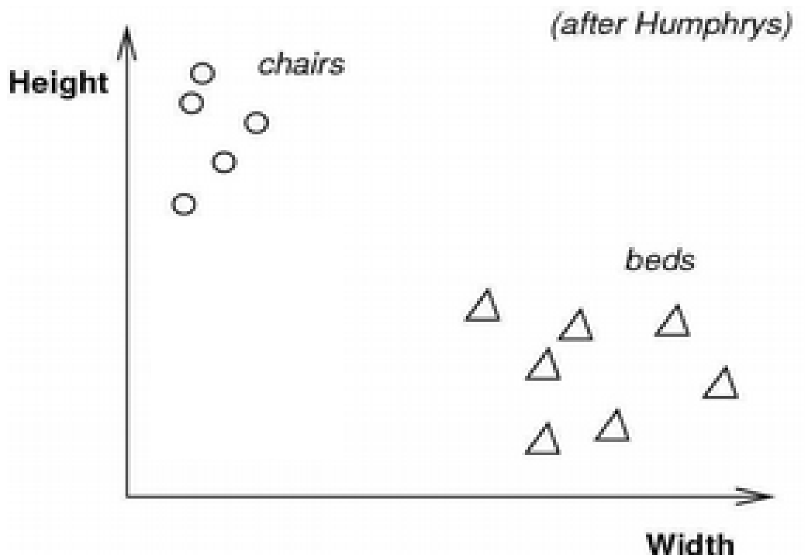


Lacks temporal effects
[Dayan and Abbott book]

Supervised: Perceptron

Categorize inputs into two classes

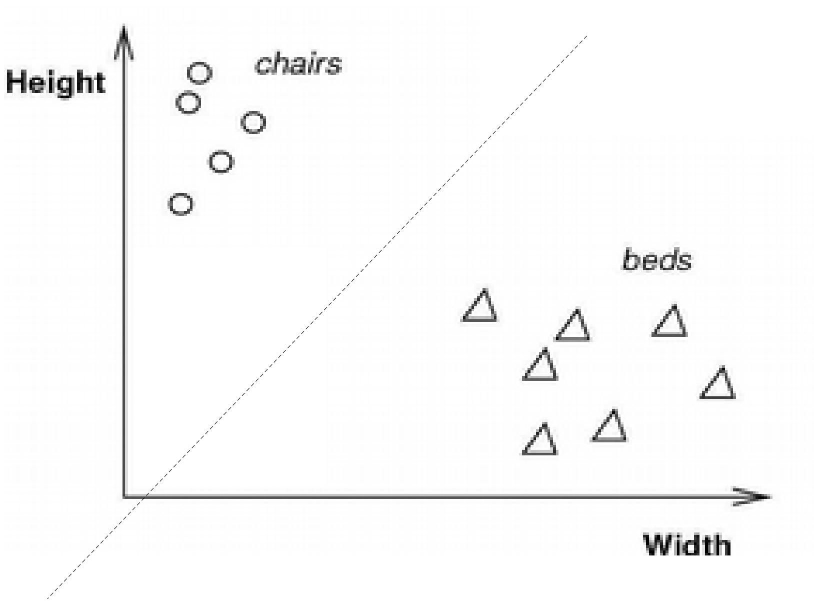




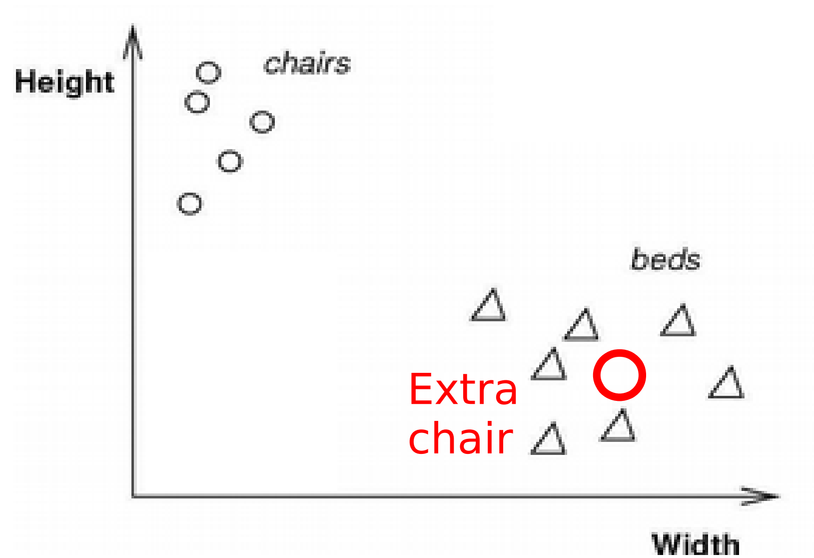
$$y = \phi(\Sigma w_i . x_i)$$

Perceptron learning rule [Rosenblatt 1952]
- If it can be learned, the rule converges
- Not all classification problems can be learned

Linear separability



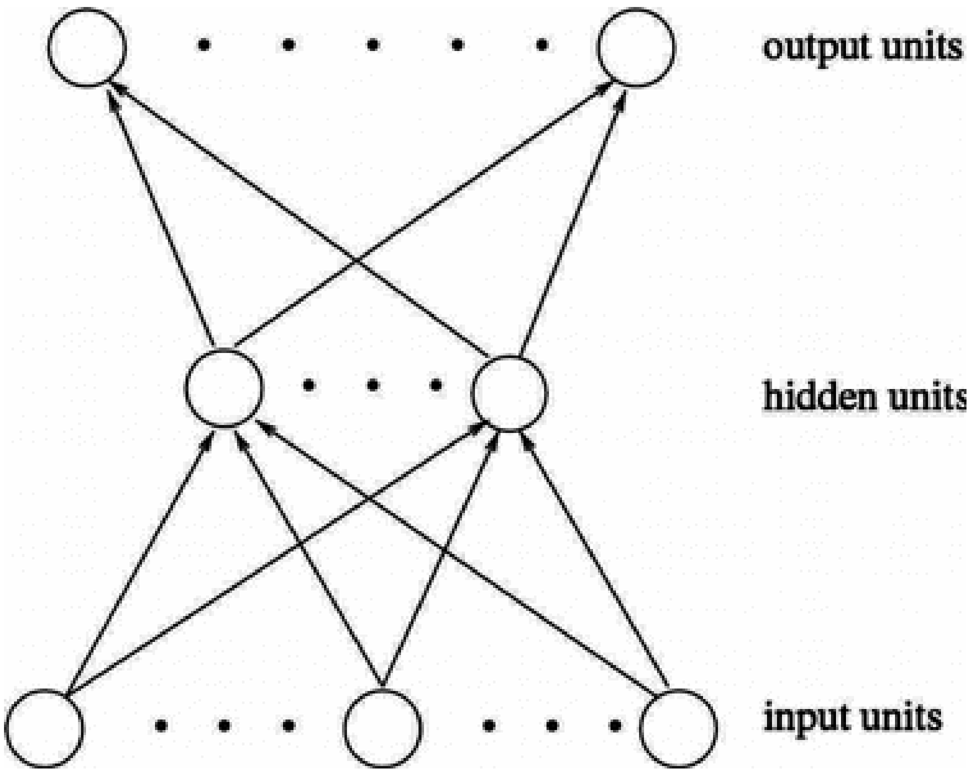
Separable
Perceptron can classify



Non-separable
Perceptron can't classify
Need multiple layers

Multi-layer perceptron

Network to approximate any function with arbitrary number of inputs and outputs



Back propagation

$$E = \sum_{pattern} \left(out_{actual} - out_{desired} \right)^2$$

$$E\left(in, out \middle| w_1, w_2, \ldots \right)$$

$$\Delta w_i = -\epsilon \frac{\partial E}{\partial w_i}$$

Back propagation

General approach:

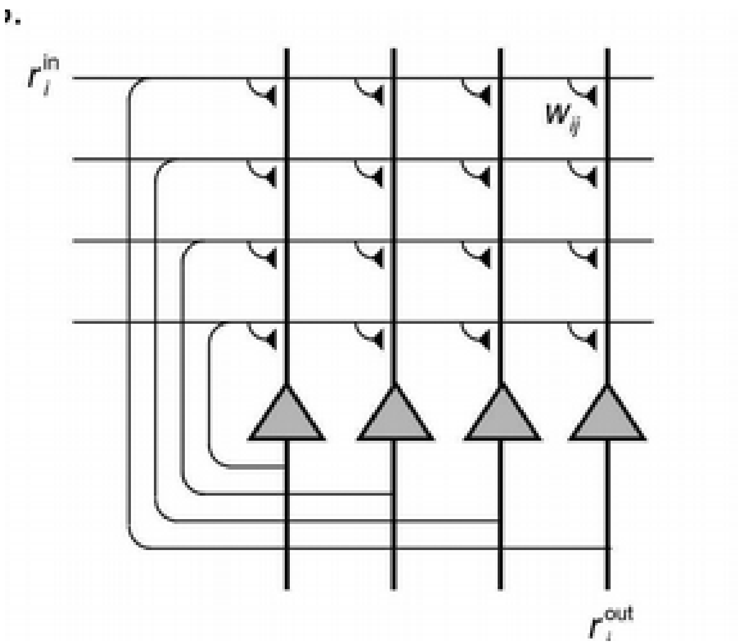
- Come up with cost function, (objective function)
  Examples: #errors, sparseness, invariances

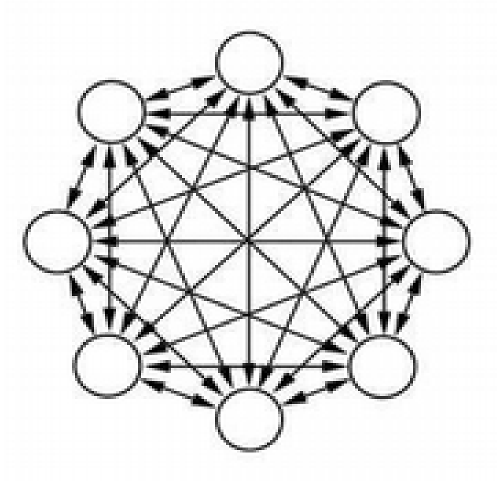
- Take the derivative wrt synaptic weights.

- You have created a learning rule

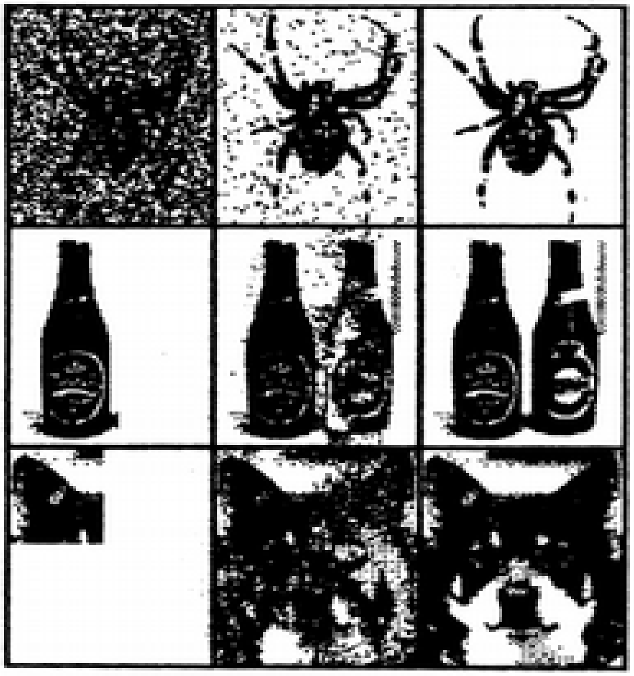
Hopfield network

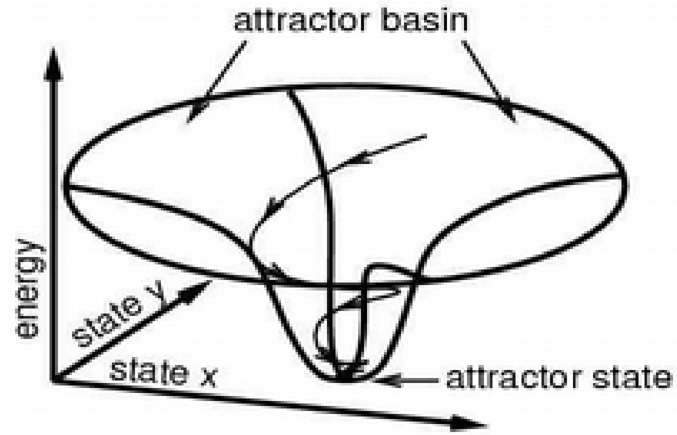
- Model for CA3
- Recurrent network
- Auto-associator (i.e. Pattern completion)

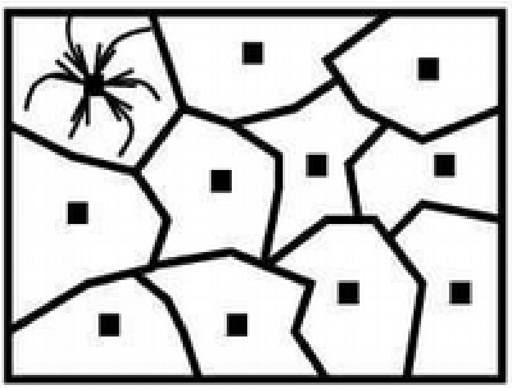




Hopfield network





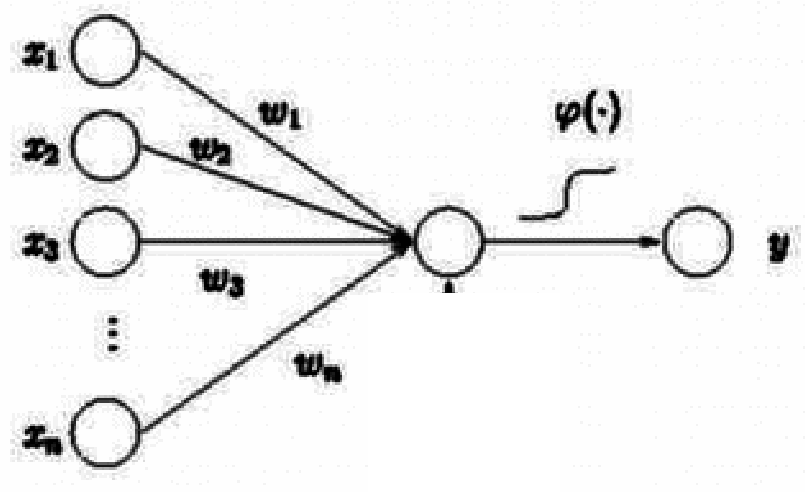


One shot learning: $w_{ij} = \sum_{patterns} x_i^{\mu} x_j^{\mu}$

Phenomenological models of plasticity (unsupervised)

Vanilla model: $\Delta w_i = \epsilon x_i y$

Covariance rule: $\Delta w_i = \epsilon \left(x_i - \langle x_i \rangle \right) . \left(y - \langle y \rangle \right)$



Assumptions made:
- w can change sign
- w is unbounded
- dw independent of w
- linear
- dw independent of other synapses
- changes are gradual and small

Unsupervised learning

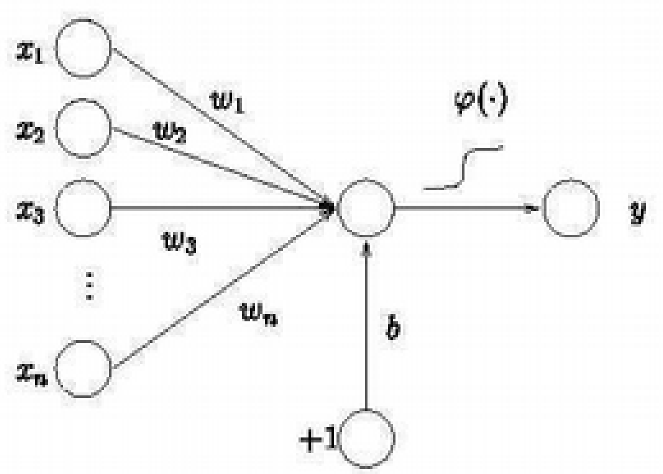
$$\Delta w_i = \langle \epsilon x_i y \rangle$$

$$\Delta w_i = \epsilon \langle x_i \sum_j w_j x_j \rangle (slow, linear)$$

$$\Delta w_i = \epsilon \sum_j \langle x_i x_j \rangle w_j$$

$$\Delta w_i = \epsilon Q_{ij} w_j$$

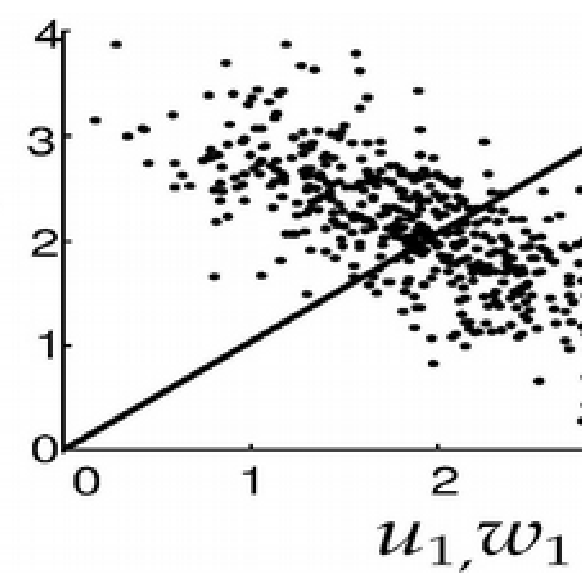
$$\frac{\partial \vec{w}(t)}{\partial t} = Q . \vec{w}(t)$$



PCA

$$\vec{w}(t) = \sum_i c_i \vec{w}_i e^{\lambda_i t}$$

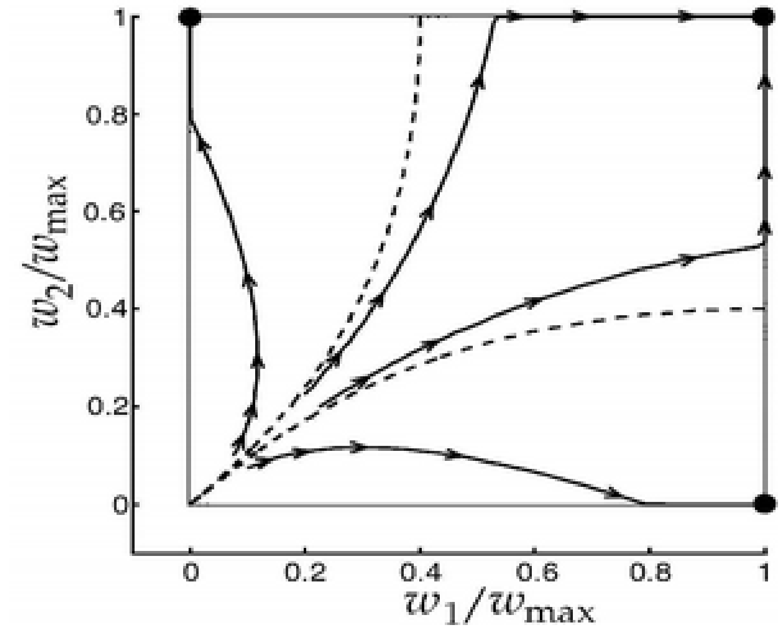
Diverges
OOPS...



Constraints and competition

Constraints

Keep each weight within bounds



Normalization

Make sure that $\sum_i w_i$ is constant

This leads to competition

- Divisive normalization (weak competition)
- Subtractive normalization (strong competition)

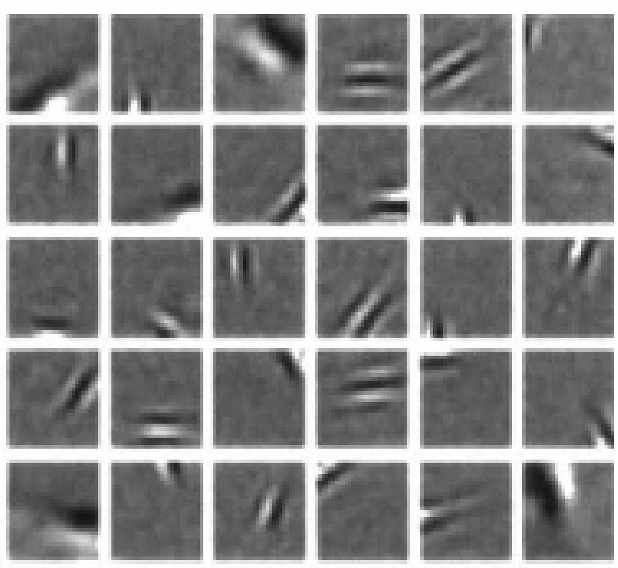
Constraints and competition

The outcome of the learning is strongly determined by the constraints [Miller & Mackay]
(Alternatives: BCM, Oja's rule)

Practical tip:

Use subtractive normalization

Formation of V1 receptive fields



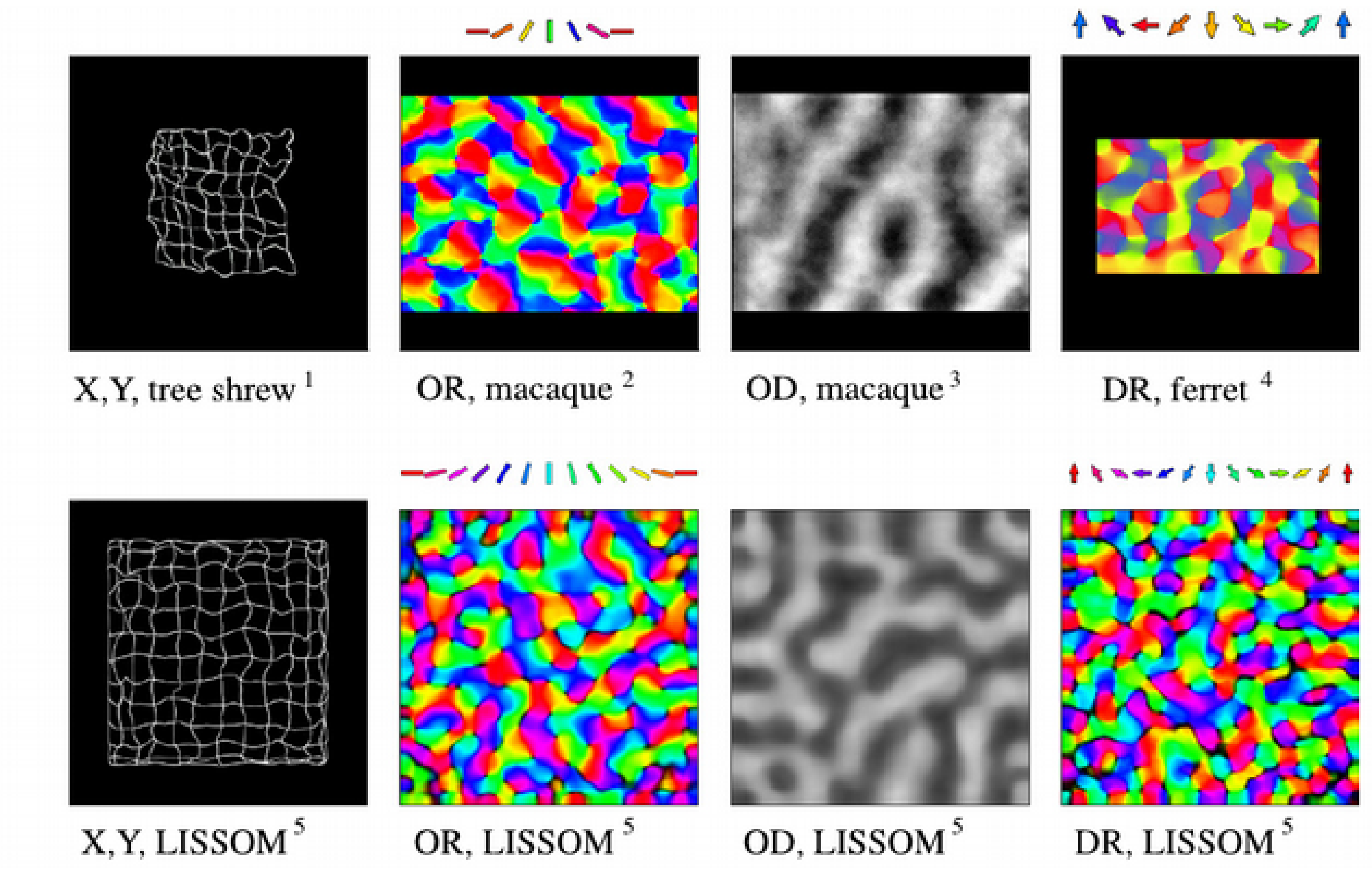
Sparse coding [Olshausen &Field]
ICA [Bell & Sejnowski]

- A wide class of learning rules lead to V1 like receptive fields [Britto & Gerstner '16]
- Lateral inhibition ensures complimentary RFs [Dayan and Abbott book]
- Unless lateral interaction, there will be no map.

Map formation

Data

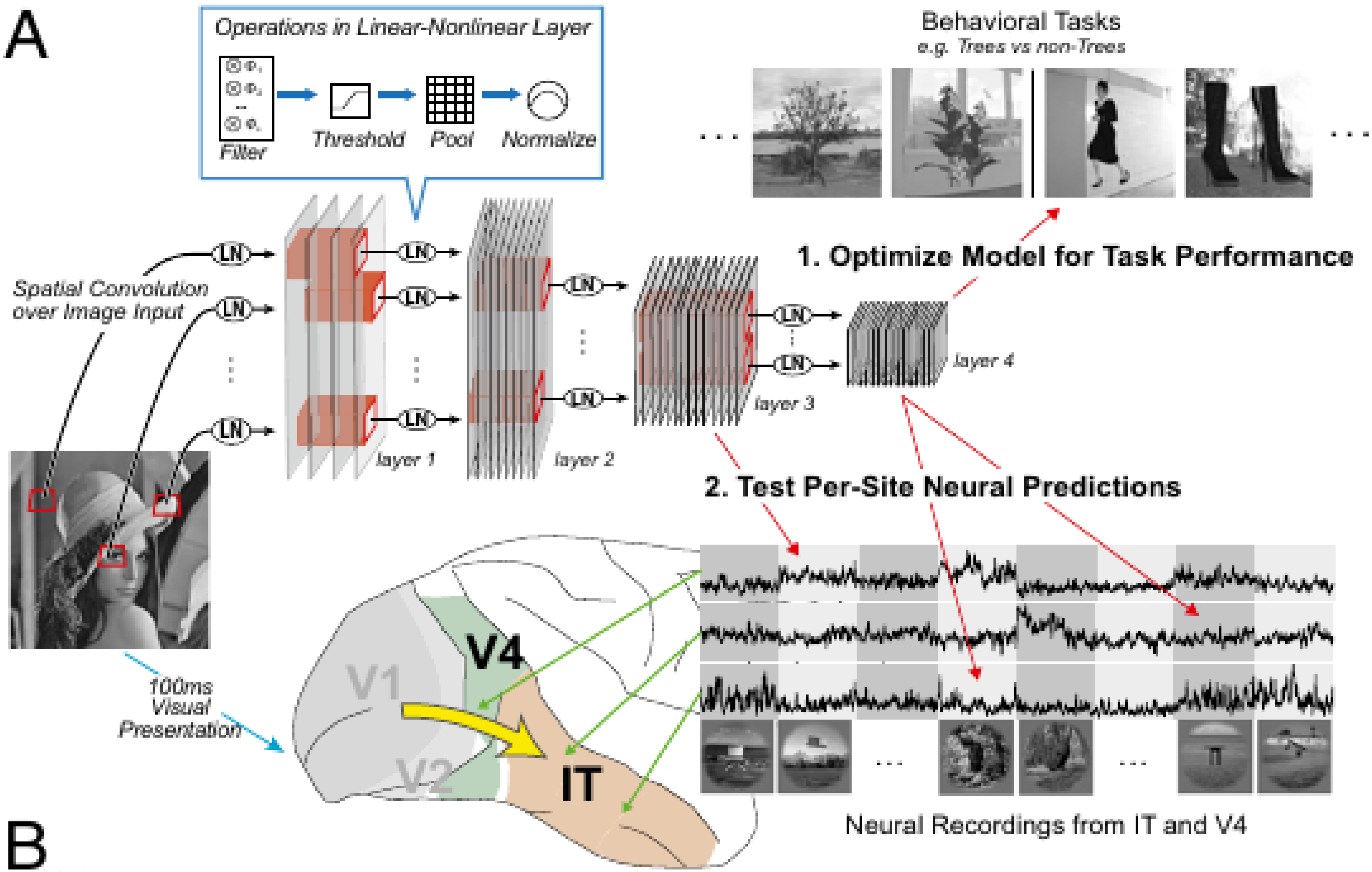
Model



[Bednar, 2012]

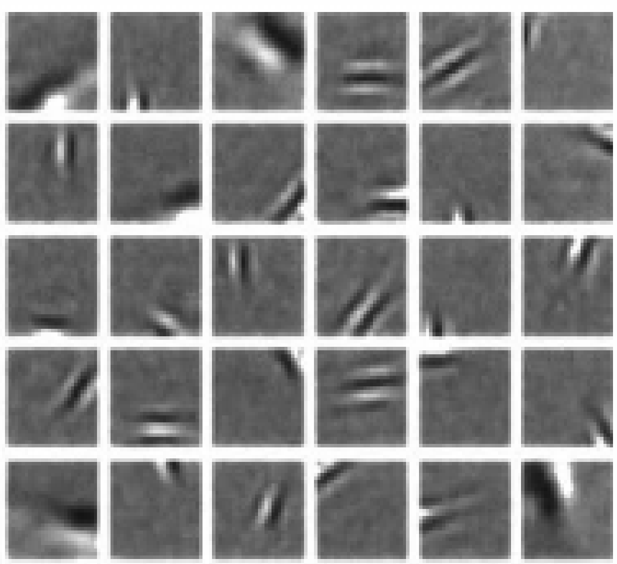
Rate-based Hebbian learning, subtractive normalization
Simple learning rules, can lead to realistic maps.

Higher visual areas

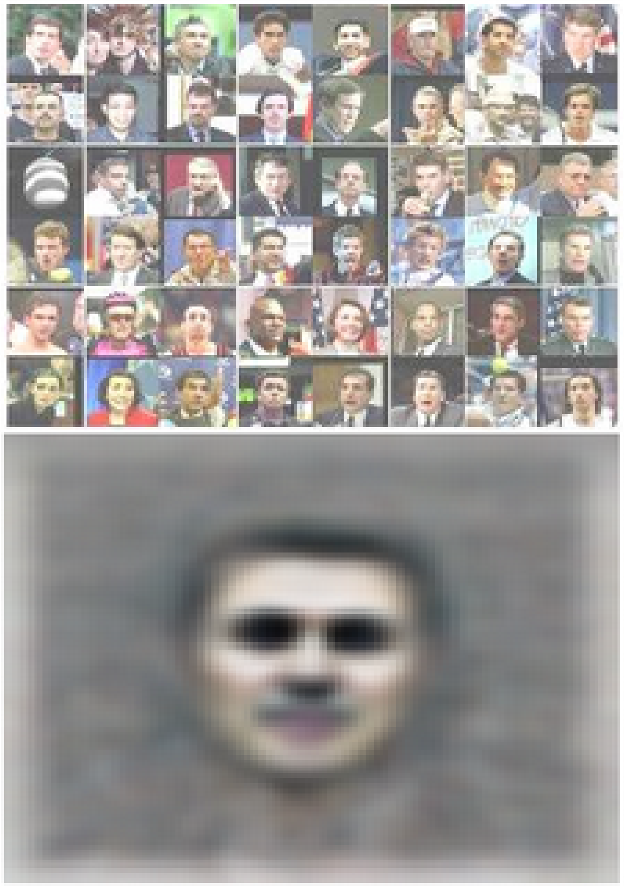


V4 and IT “match” machine learning [Yamins 2014]

Unsupervised learning



V1 (1997)



IT [Le … Ng, 2012]

Development of realistic receptive fields
using generative models.