Synaptic plasticity

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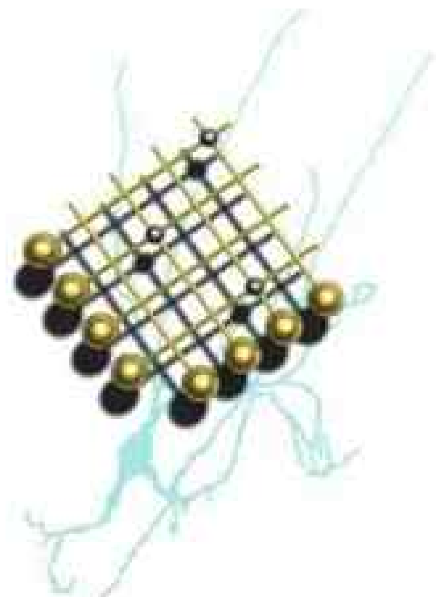

Acknowledgements

Guy Billings

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HFSP

Human memory systems

Psychologists have split up memory in:

Declarative memory

* Episodic memory (personal what, when, where memories)

  - recollection
  - familiarity
  - hippocampus (patient HM)

* Semantic memory: General facts about the world (cortex)

Non-declarative memory (cortex, cerebellum,..)

Motor skills, sensory processing, ...

Working memory (prefrontal, not discussed here)

Testing animal memory

(Classical) conditioning

Pavlov's dog

Aplysia gill reflex

Mazes and environments for rodents

- water maze
- place avoidance
- fear
- food location

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:

- some aspects of development
- short term changes
- excitability changes

Memory systems

Declarative memory

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

* Semantic memory: General facts

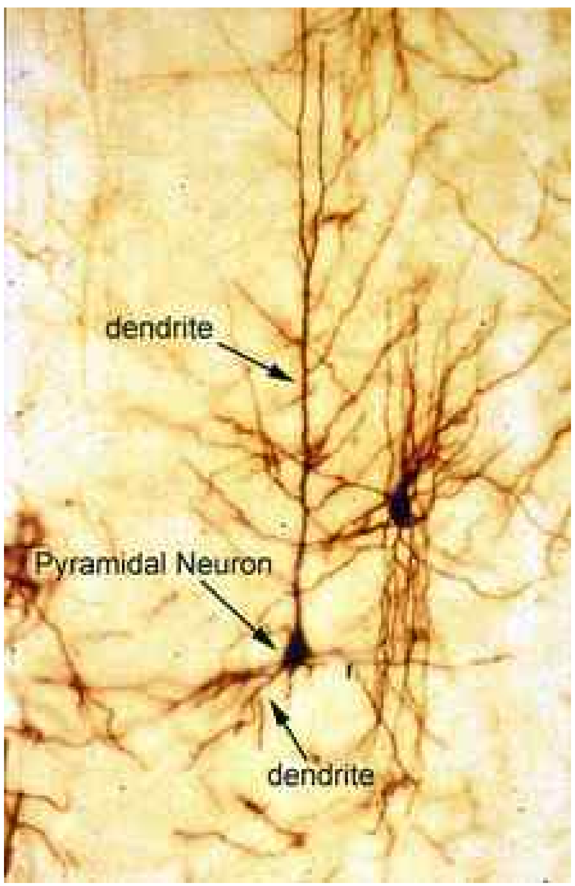
Non-declarative memory

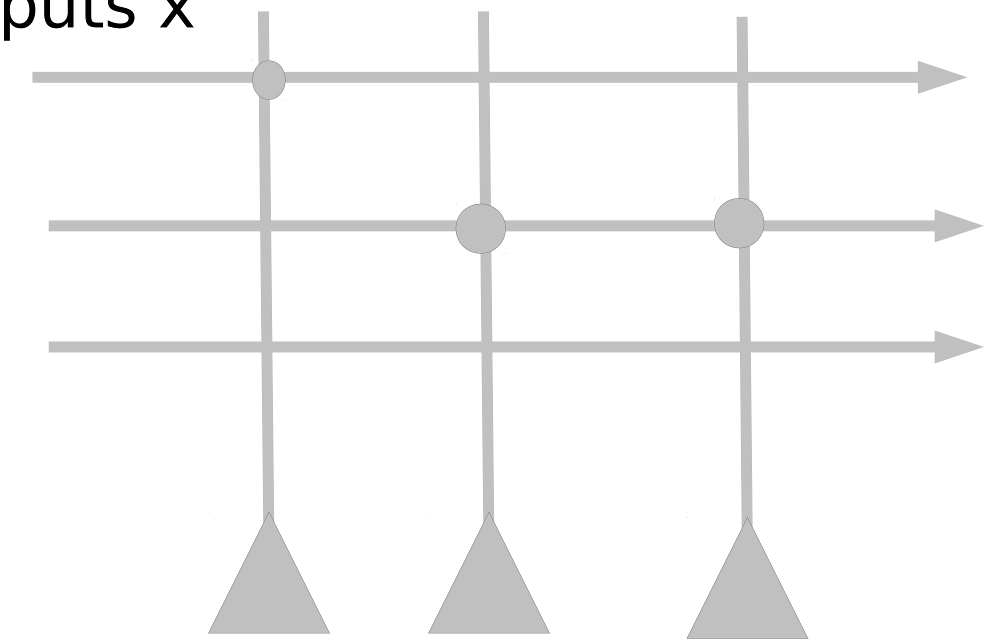
Motor skills, sensory processing, ...

Synaptic plasticity

Long term synaptic plasticity

Inputs x

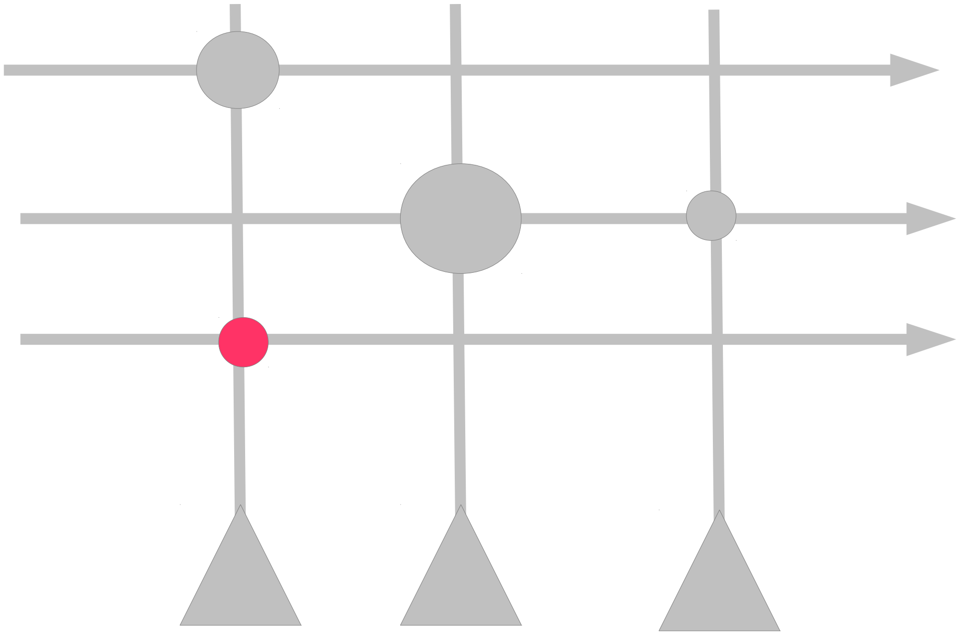




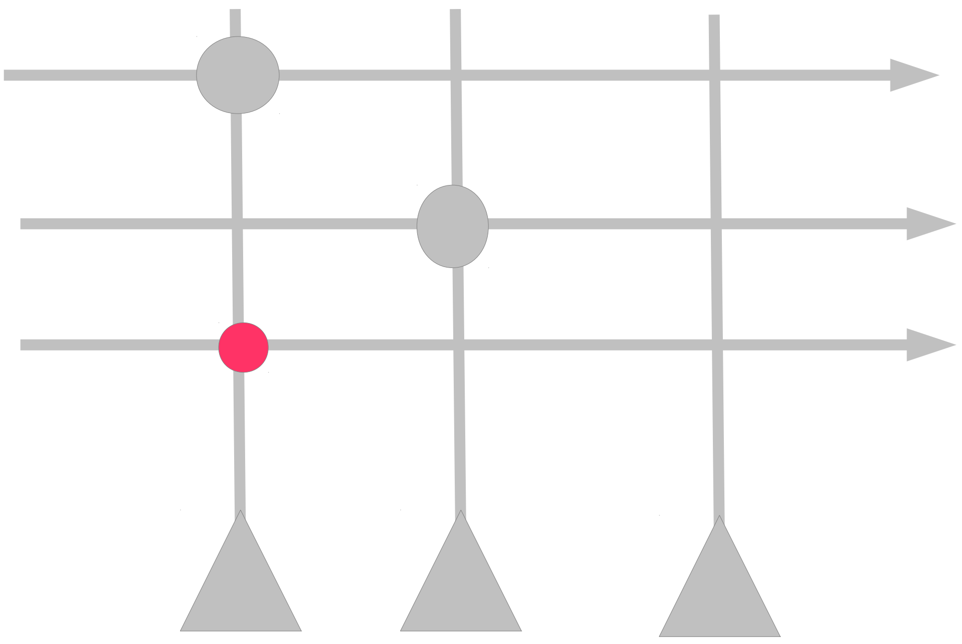
Outputs y

$$y_j = \Phi\left(\sum_i w_{ji} x_i\right)$$

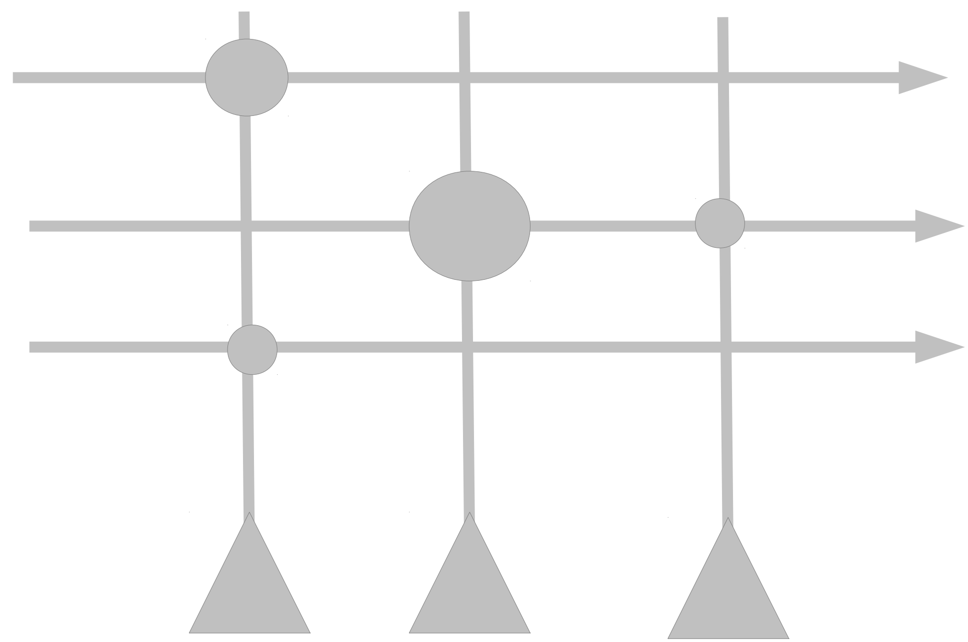
Long term synaptic plasticity



Long term synaptic plasticity



Long term synaptic plasticity



Why plasticity

Why should a neuron selectively change it inputs?

- Adapt to environment and other neurons
- Store explicit information (episodic and semantic memory)
- Implicit information (sensory statistics, motor learning

- Note, computation and memory share the substrate in neural networks.

Why plasticity

Why modelling plasticity

- extrapolate single neuron plasticity to network level
- so we don't need to specify all connections in
  a model (smarter networks)

Outline

- Some new and old data
    - neurobiology of LTP
    - relation of LTP to memory
    - long term stability and forgetting

- Recent own work

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

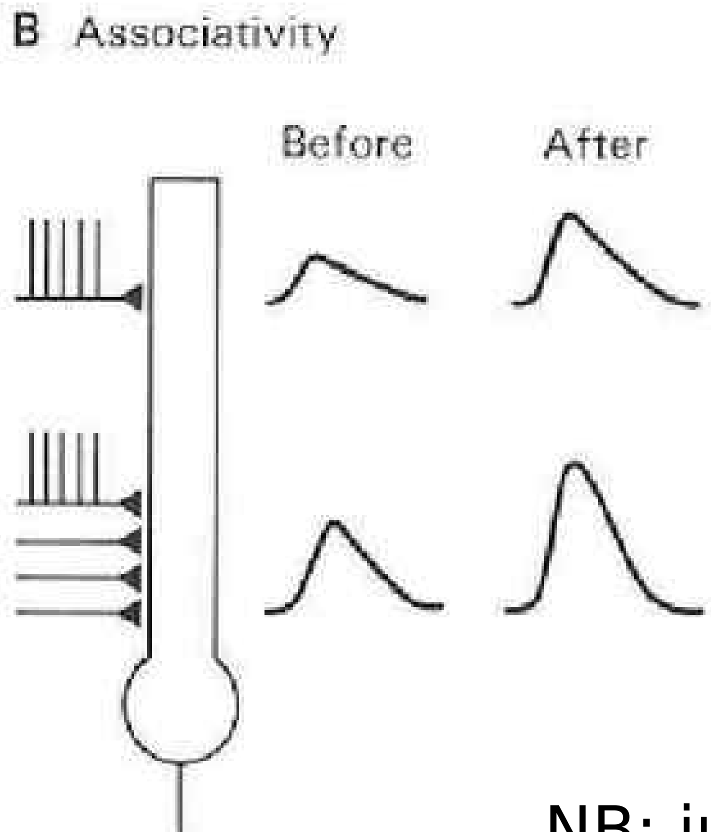
Basis of classical conditioning?

conditioned stimulus

Bell

unconditioned stimulus

Food



Saliva

NB: just a cartoon!

For Aplysia see Kandel book

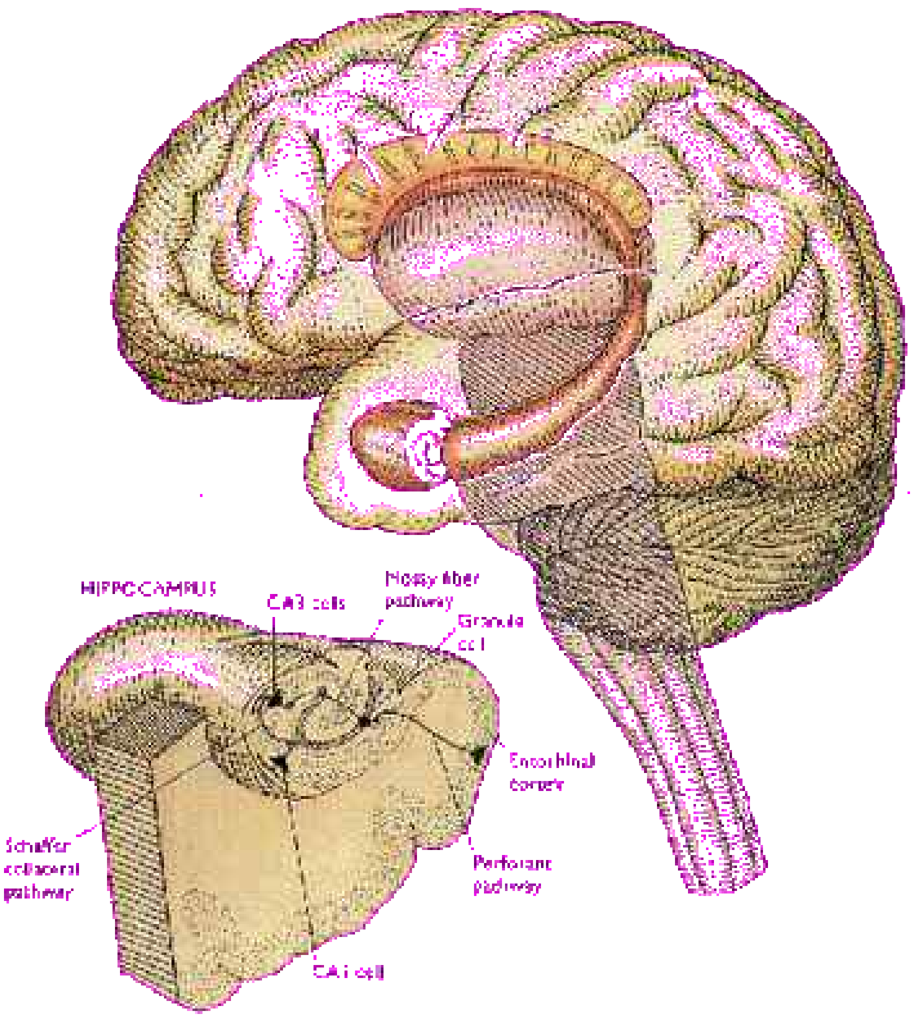
Donald Hebb (1949)

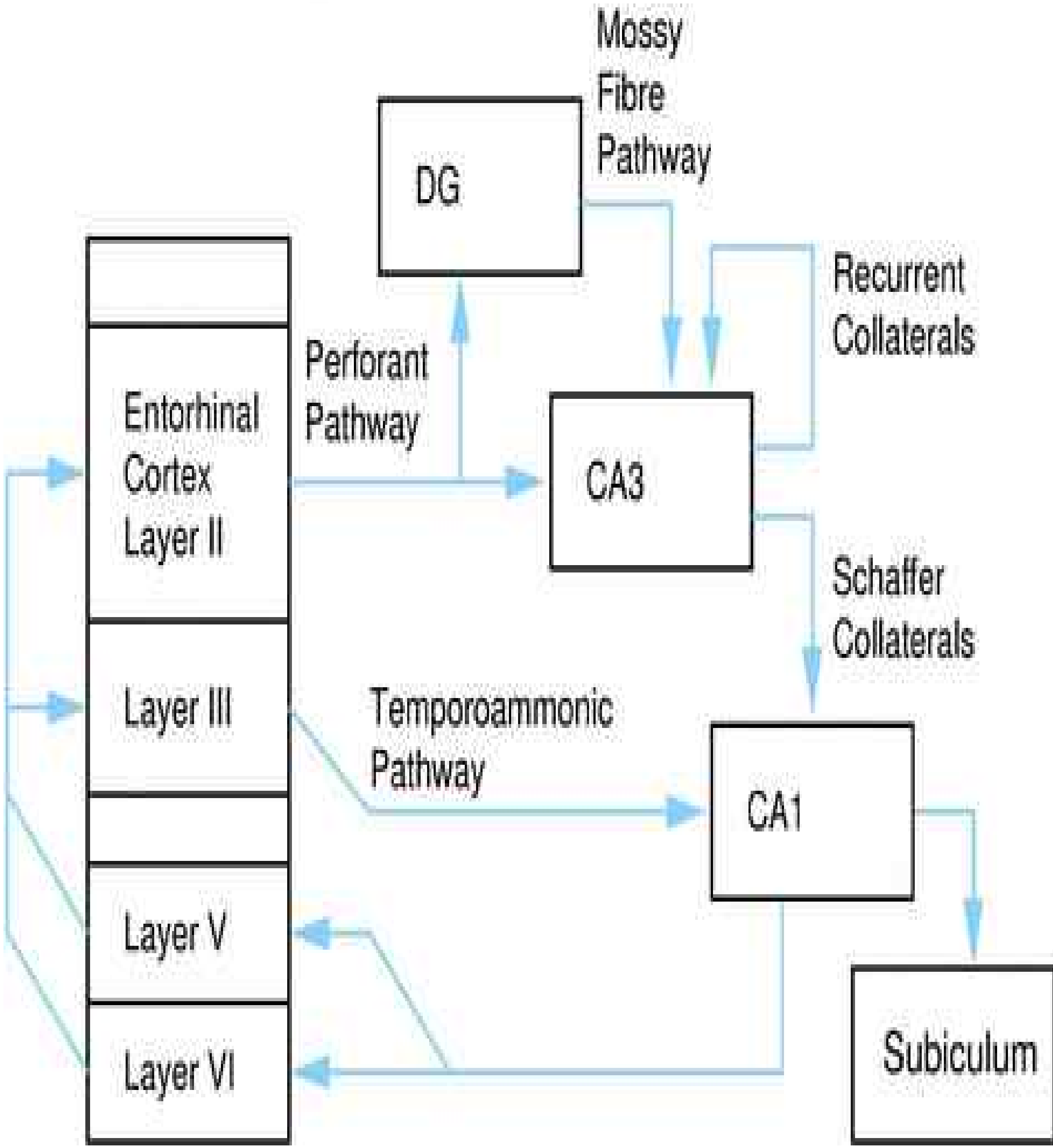
Let us assume that the persistence or repetition of a reverberatory activity (or "trace") tends to induce lasting cellular changes that add to its stability. . . . When an axon of cell A is near enough to excite a cell B and repeatedly or persistently takes part in firing it, some growth process or metabolic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

"What fires together, wires together"

Hippocampus

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





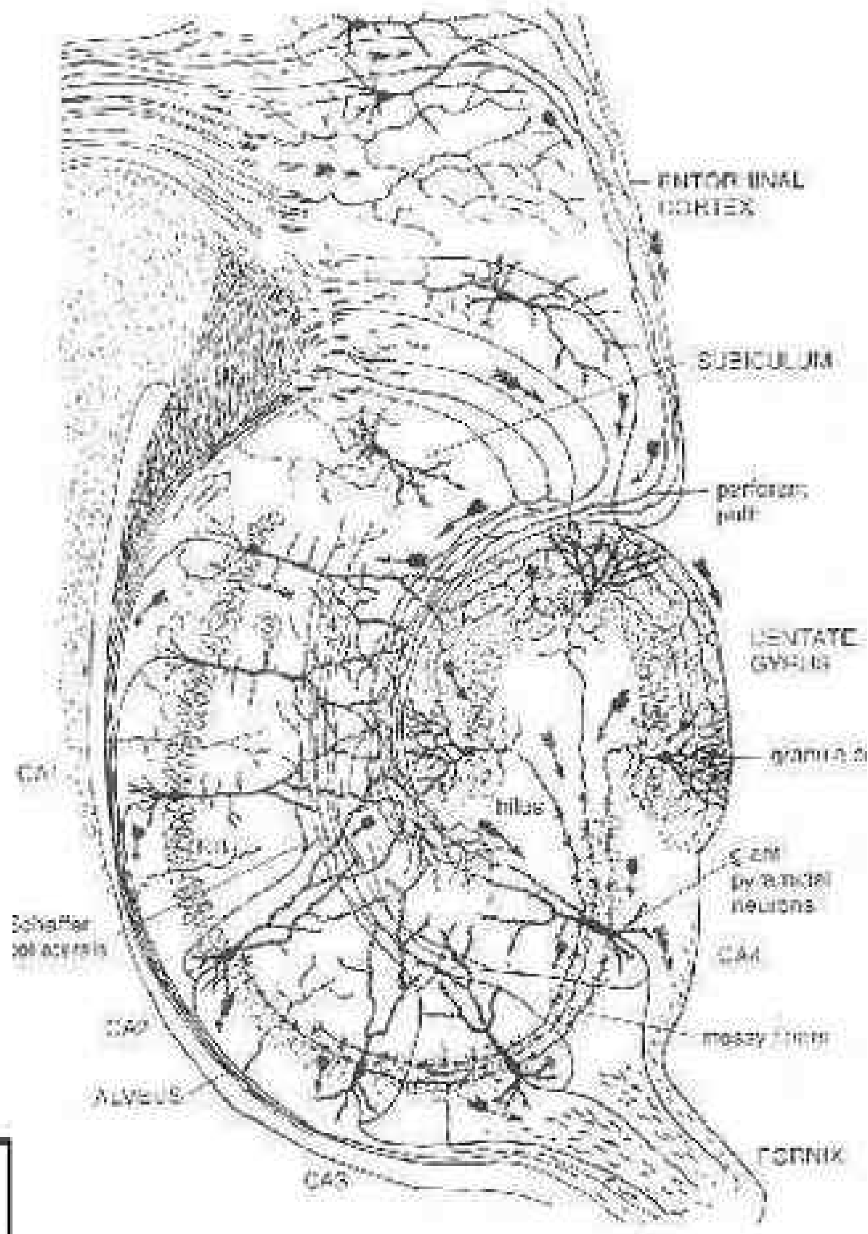
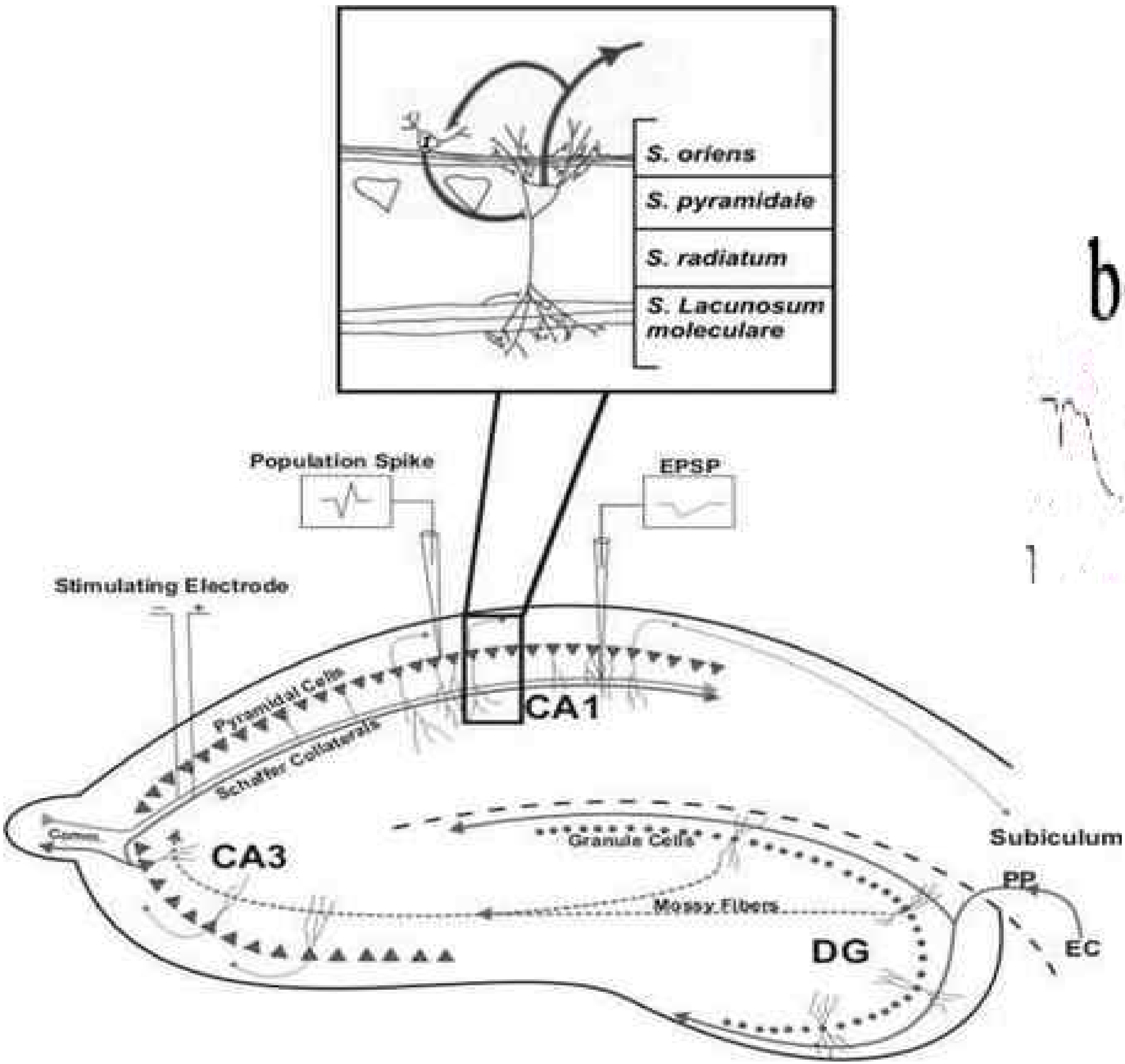
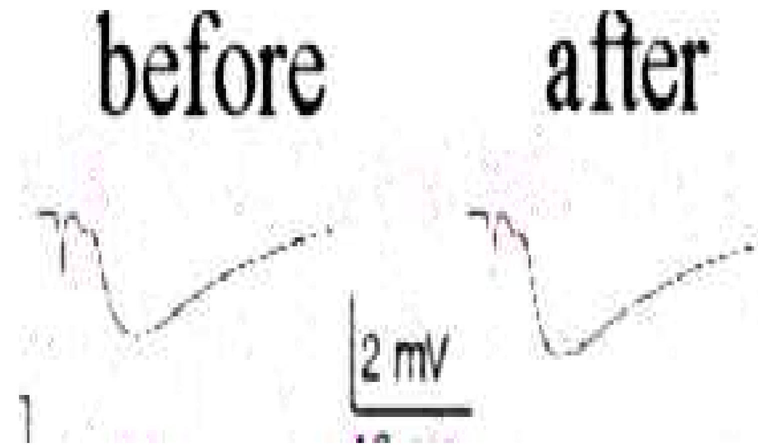
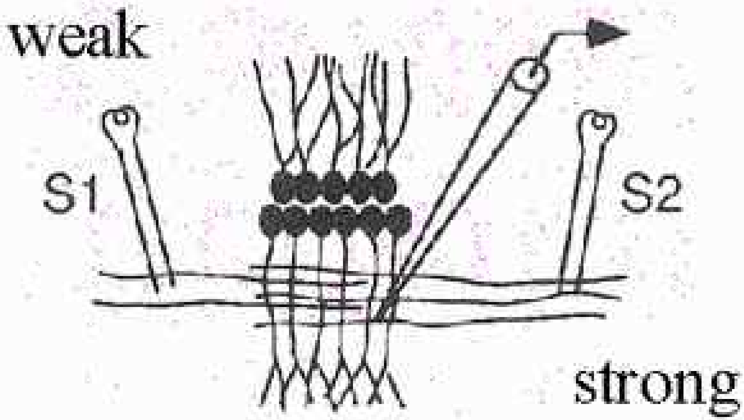


Diagram: Kit Longden


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

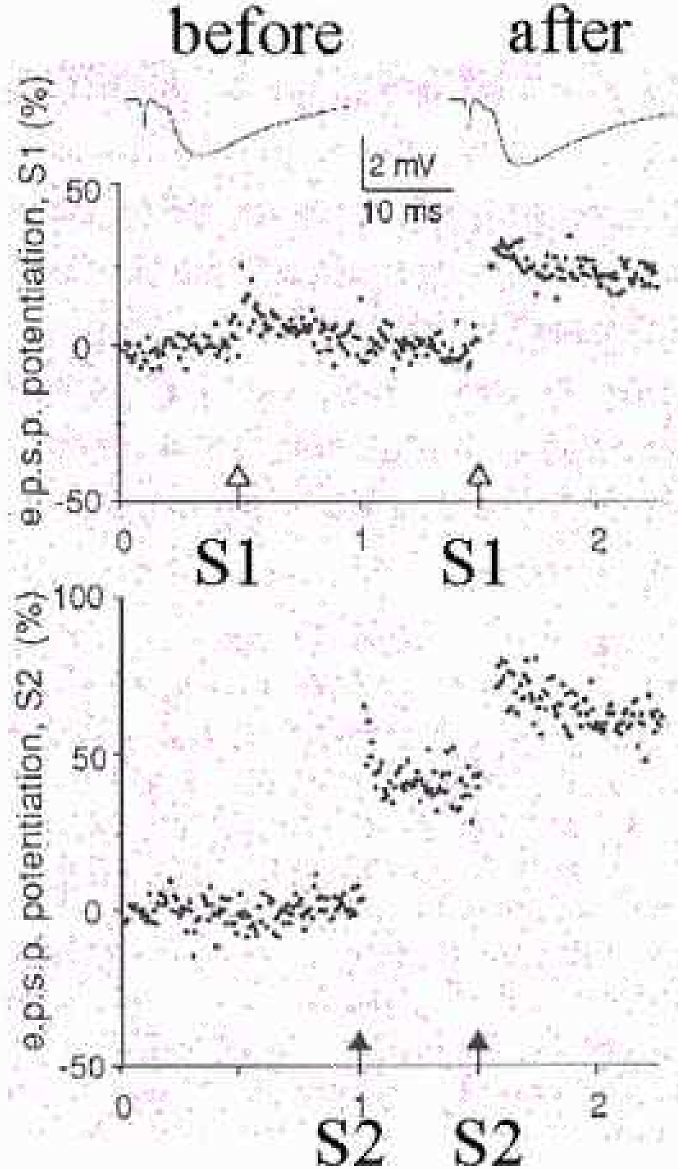

before
after
2 mV

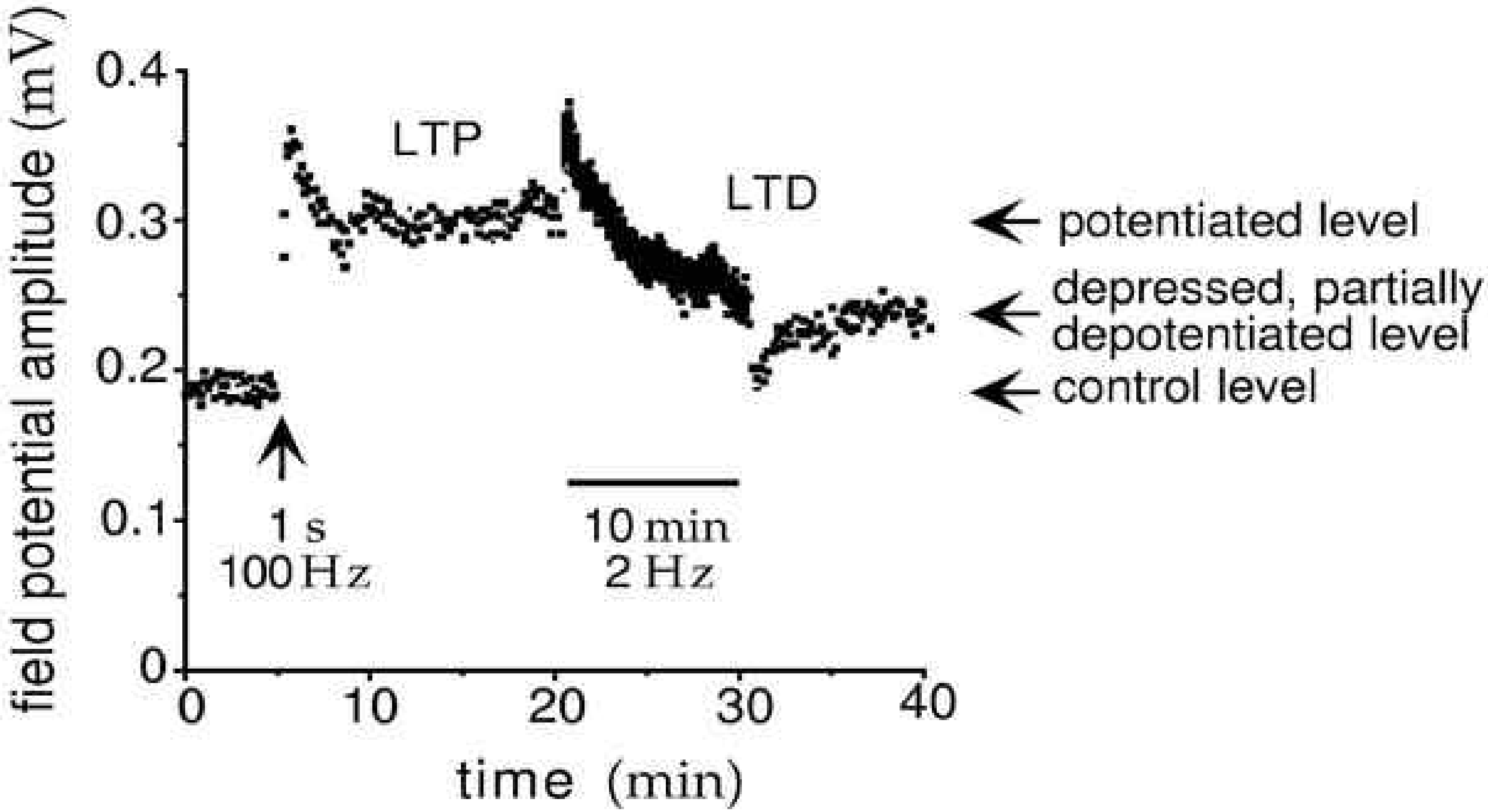
Schaffer collateral LTP (in vitro)



alternate at 15 sec intervals

tetanic stimulation
S1: cooperative
S2: input-specific
S1+S2: associative





field potential amplitude (mV)
0.4
0.3
0.2
0.1
0
LTP
LTD
1 s
100 Hz
10 min
2 Hz
0
10
20
30
40
time (min)
potentiated level
depressed, partially
depotentiated level
control level

Synaptic plasticity = memory? Criteria

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

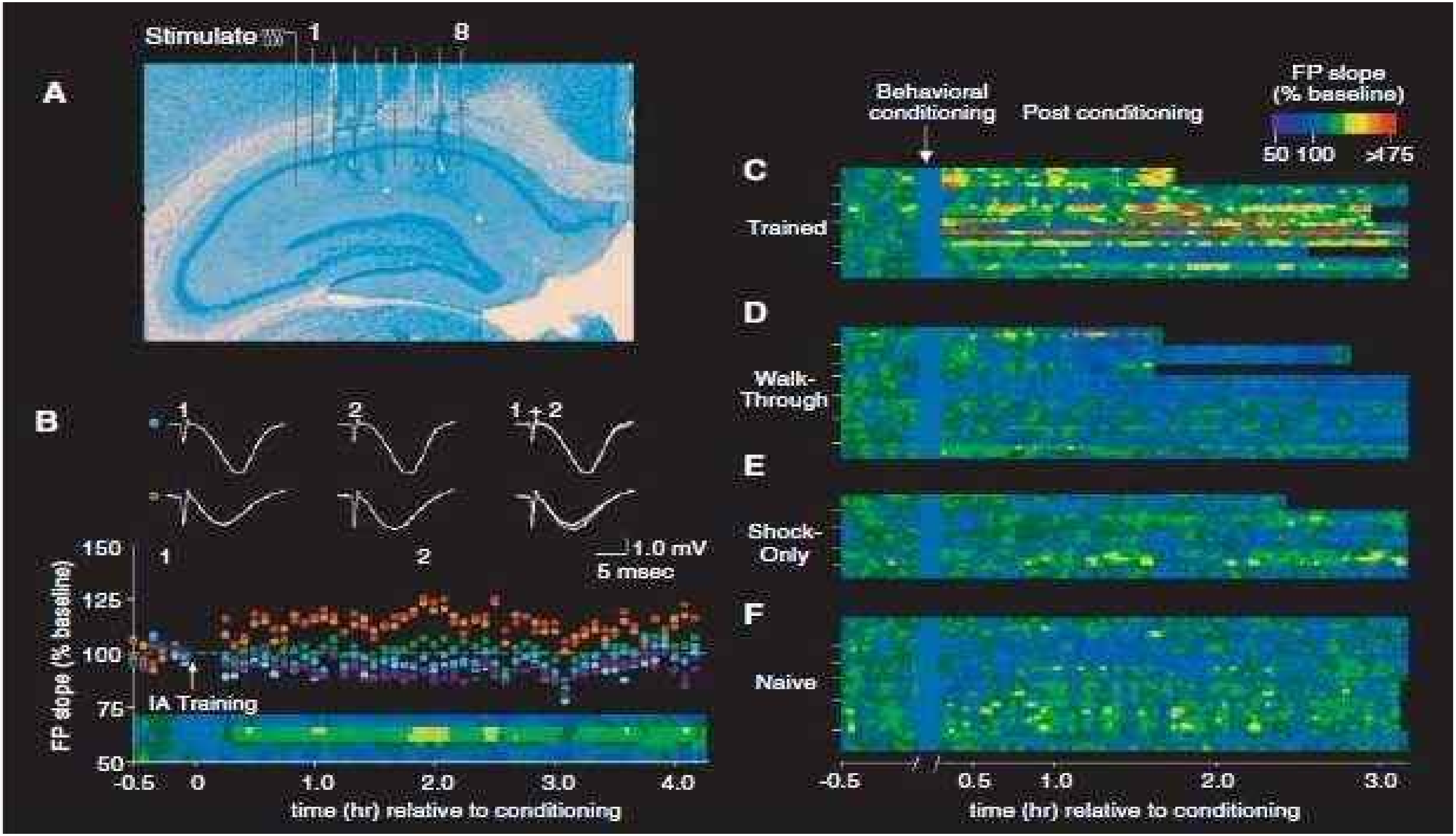
- Mimicry
  - change synaptic efficacies → new ‘apparent’ memory
  - **Rudimentary**

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

- Retrograde alteration
  - alter synaptic efficacies → retrograde amnesia
  - **Yes (e.g. PKMz), but...**

[Martin, Greenwood, Morris '04]

Synaptic plasticity=memory?



[Whitlock,.. and Bear '06]

LTP stages

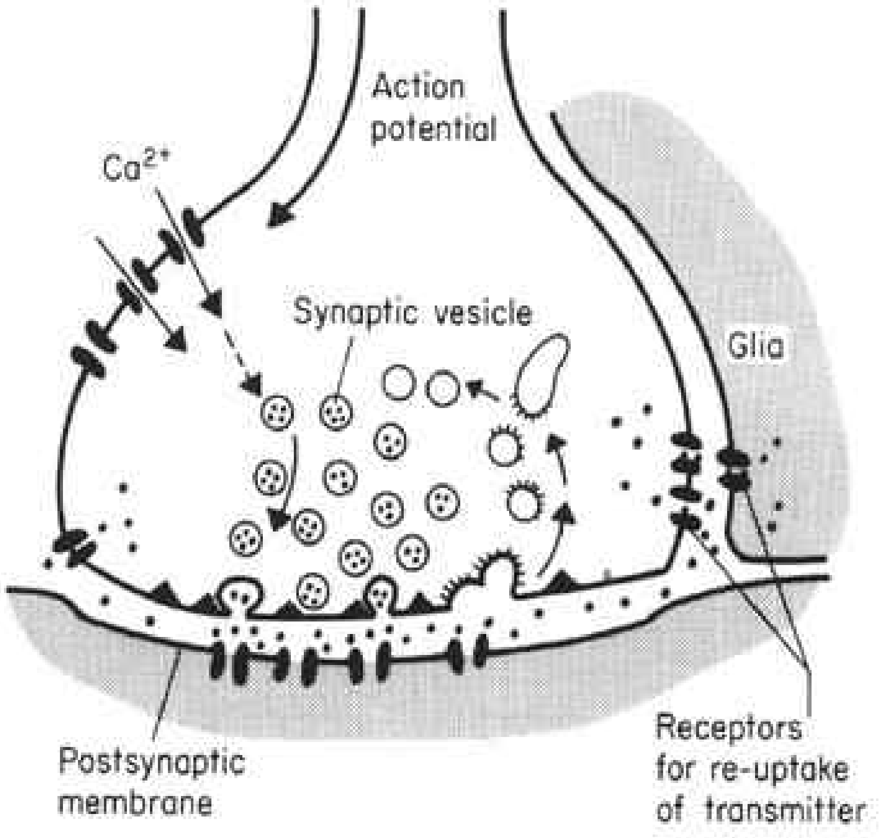
Induction:

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

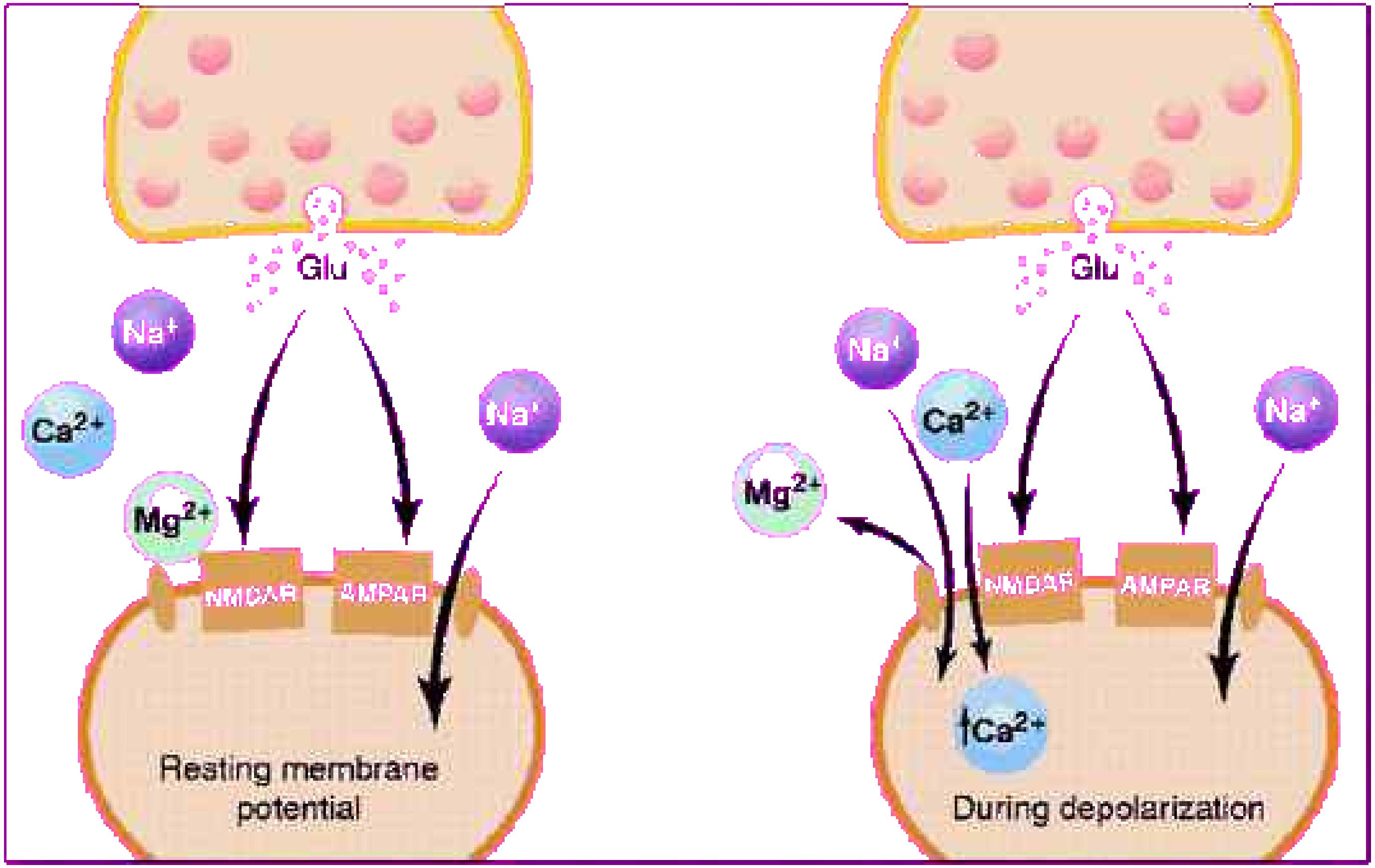
Expression

- Early LTP
- Late LTP

Maintainance

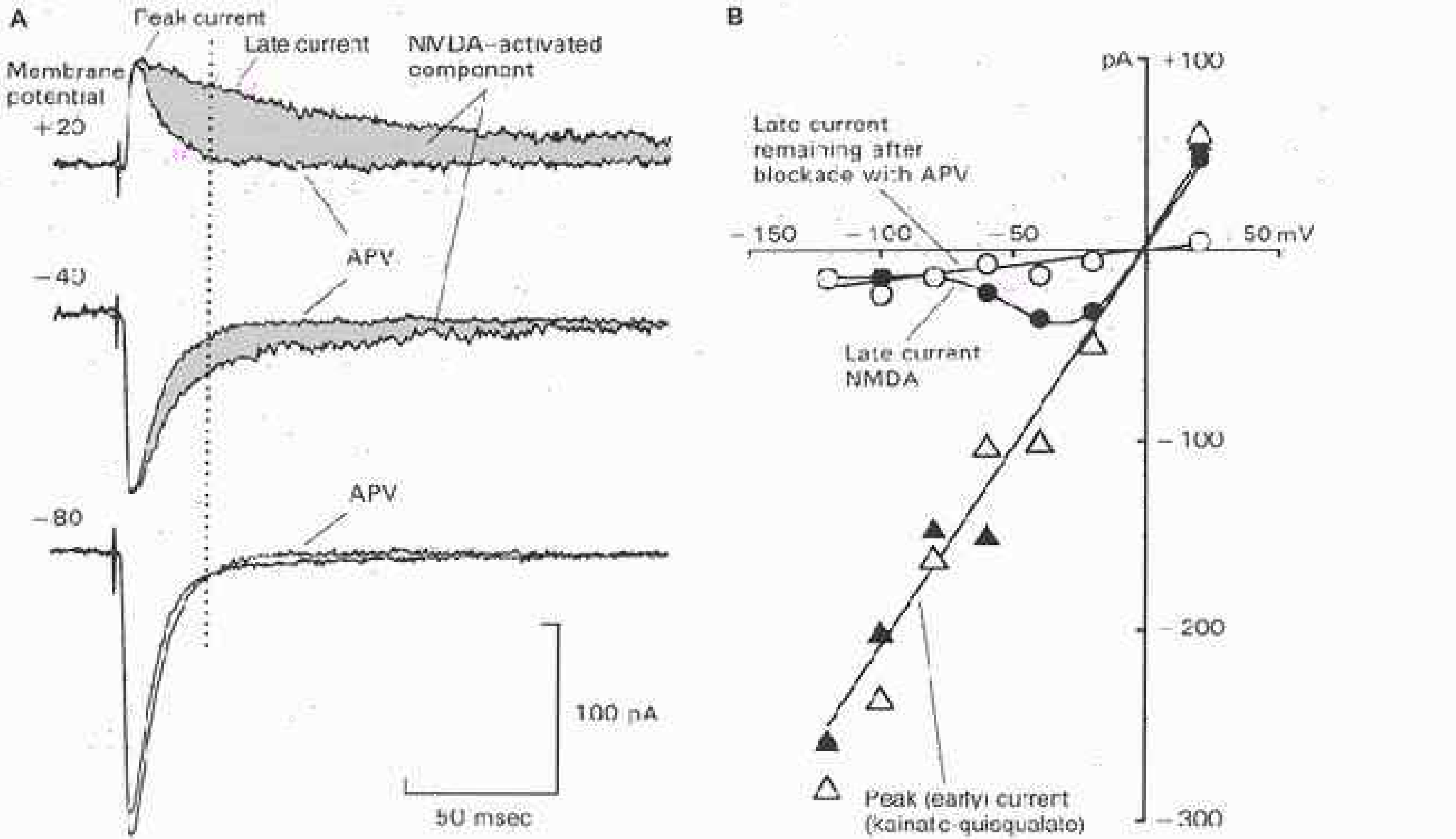


Model for LTP induction

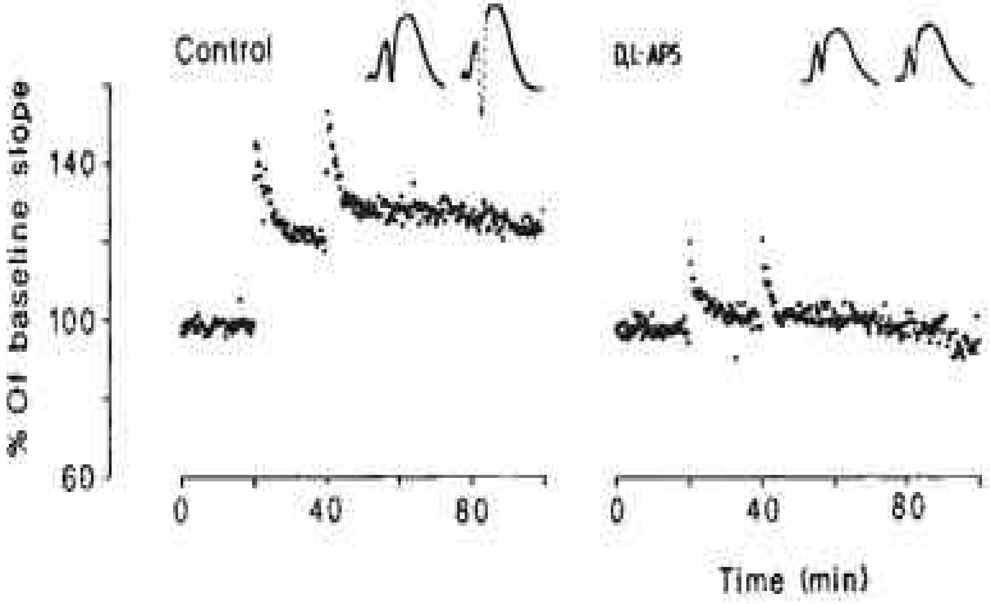


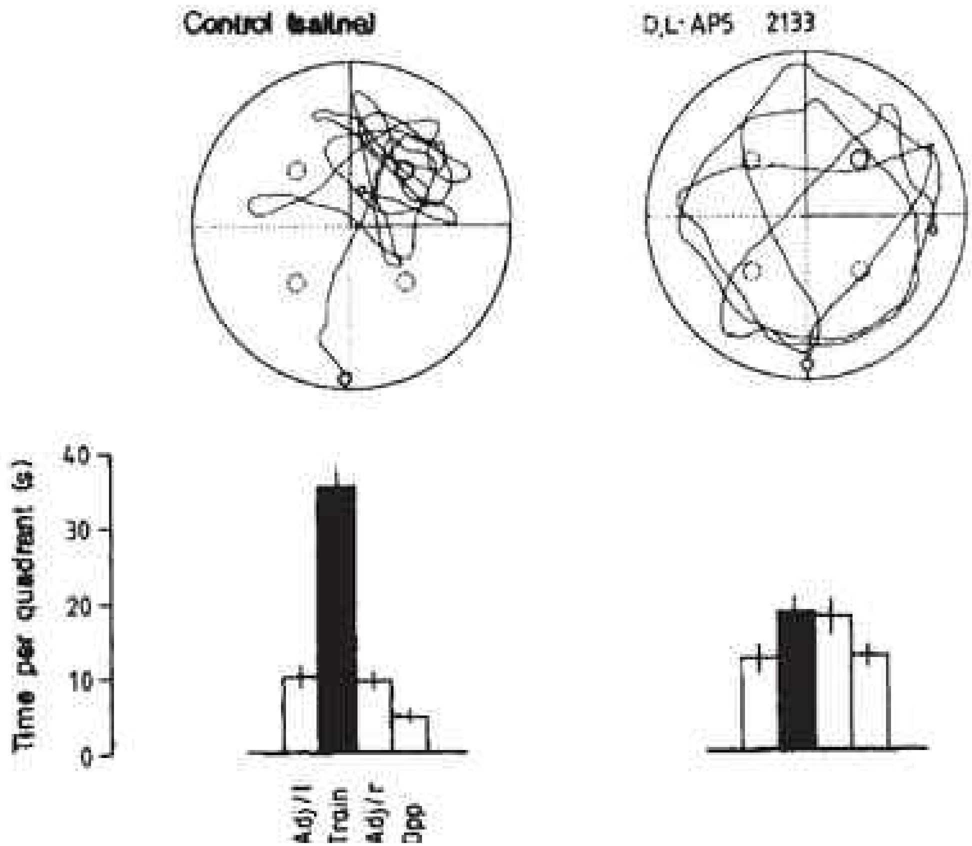
NMDA requires pre and post activity, hence ideal for Hebbian Learning

AP5 is a selective blocker



AP5 blocks learning





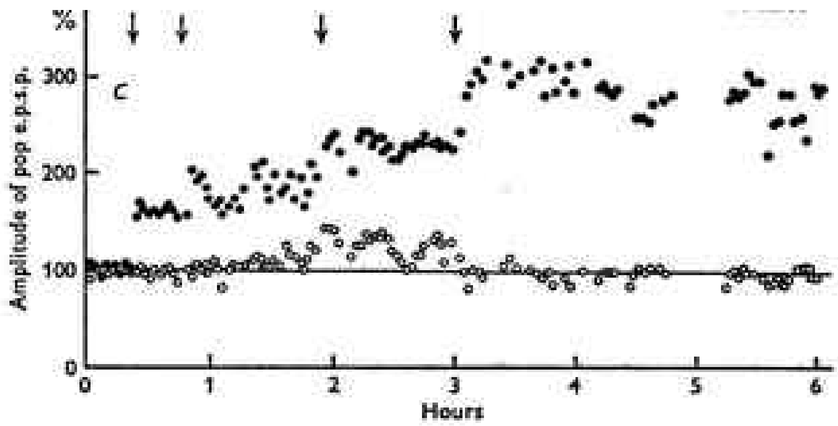
NMDA- block

NMDA- block

[Morris et al 86]

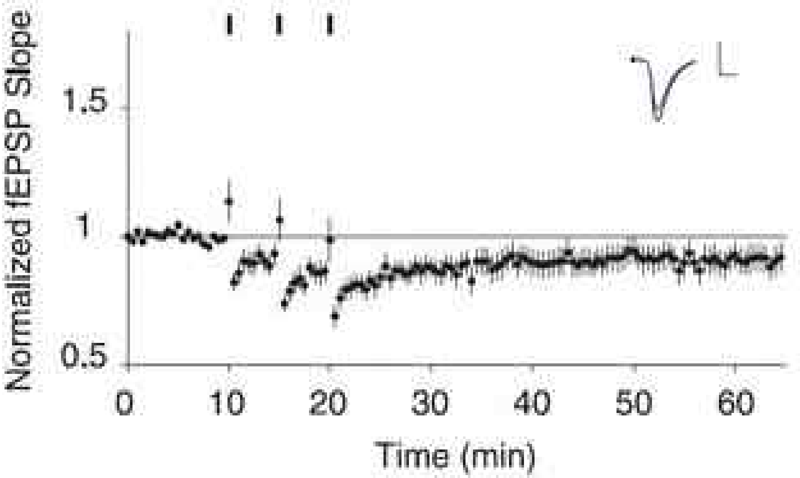
Ca hypothesis

LTP

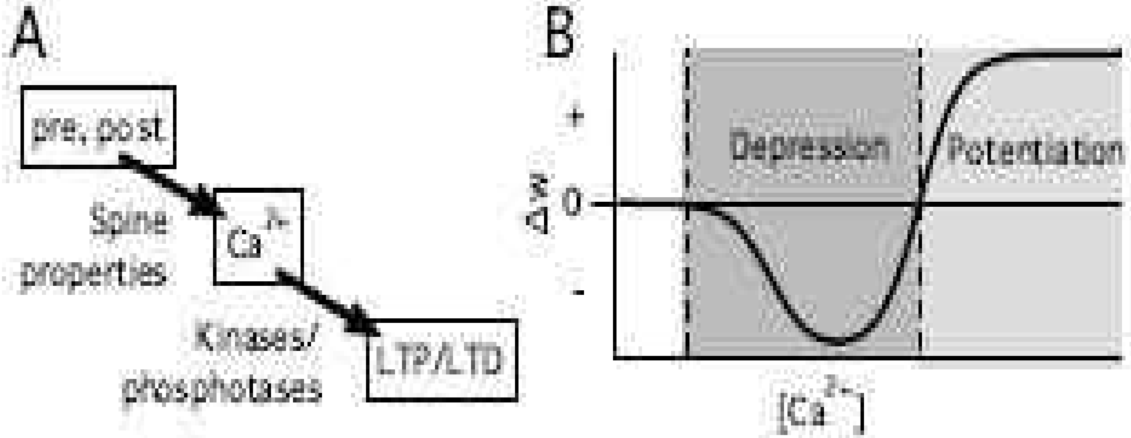


[Bliss & Lomo '73]

LTD



[O'Connor & Wang '05]



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

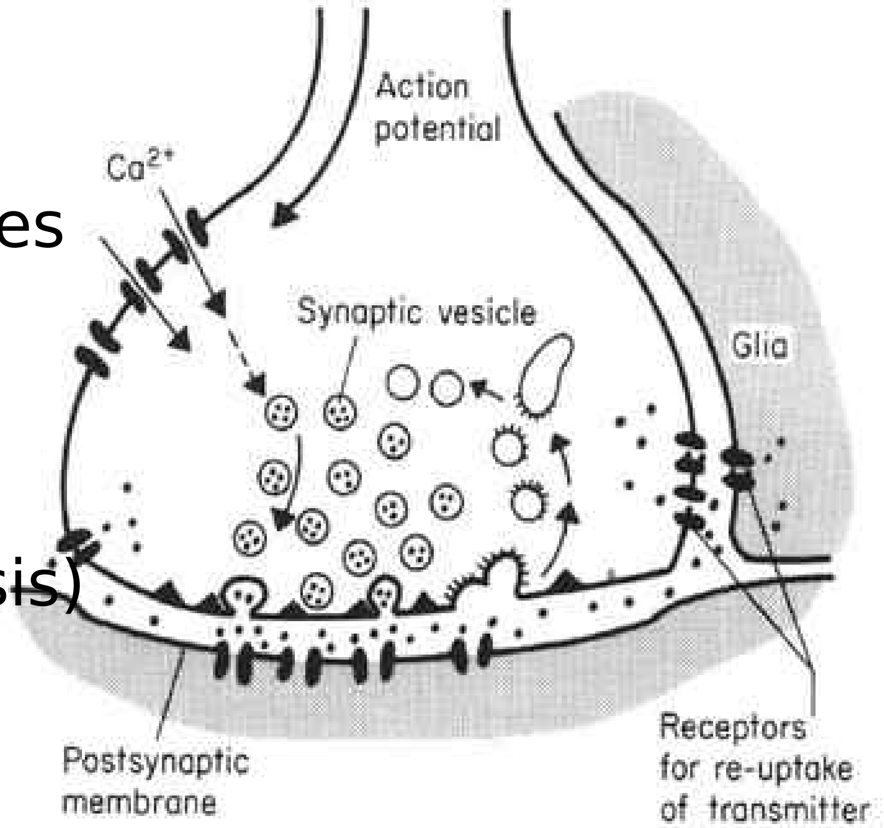
LTP stages

Induction:

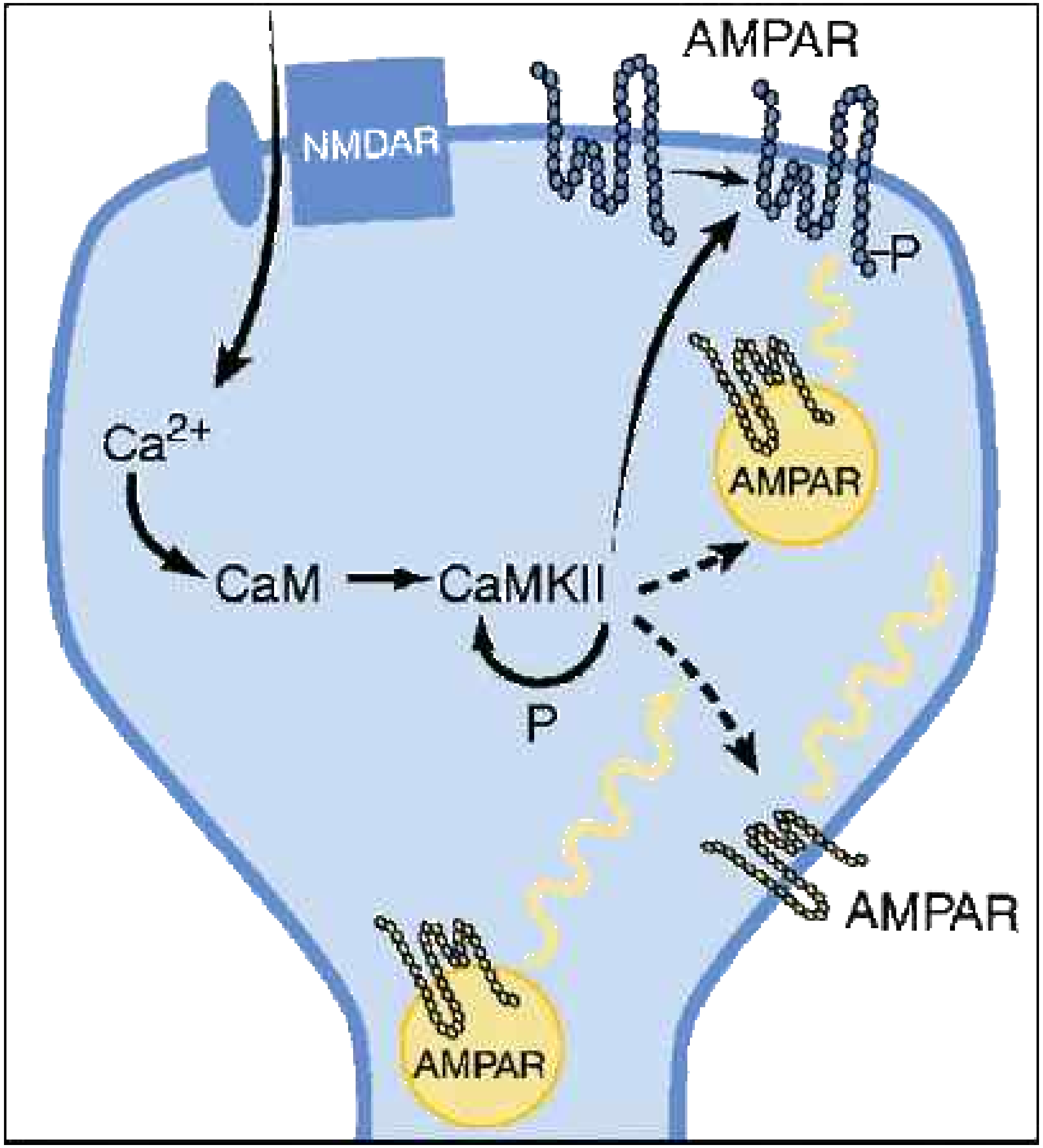
- Requires pre- and postsynaptic activity.
- Mechanism: NMDA and Ca influx

Expression:

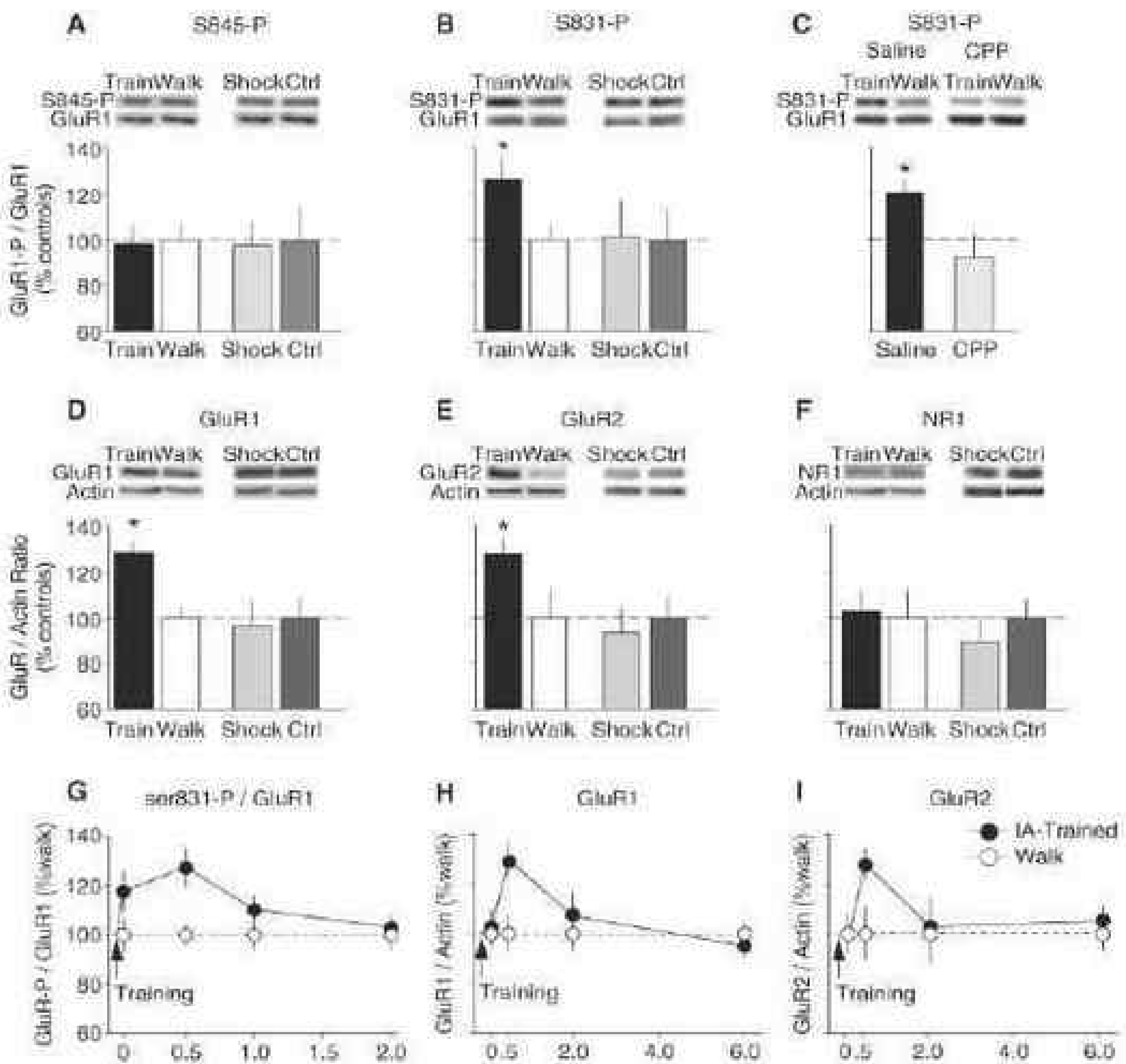
- Early LTP (1 hr):
    - partly pre-synaptic changes
    - AMPAR phosphorylation
    - AMPAR insertion
- Late LTP
    - ? (requires protein synthesis)



“Post-” model for expression

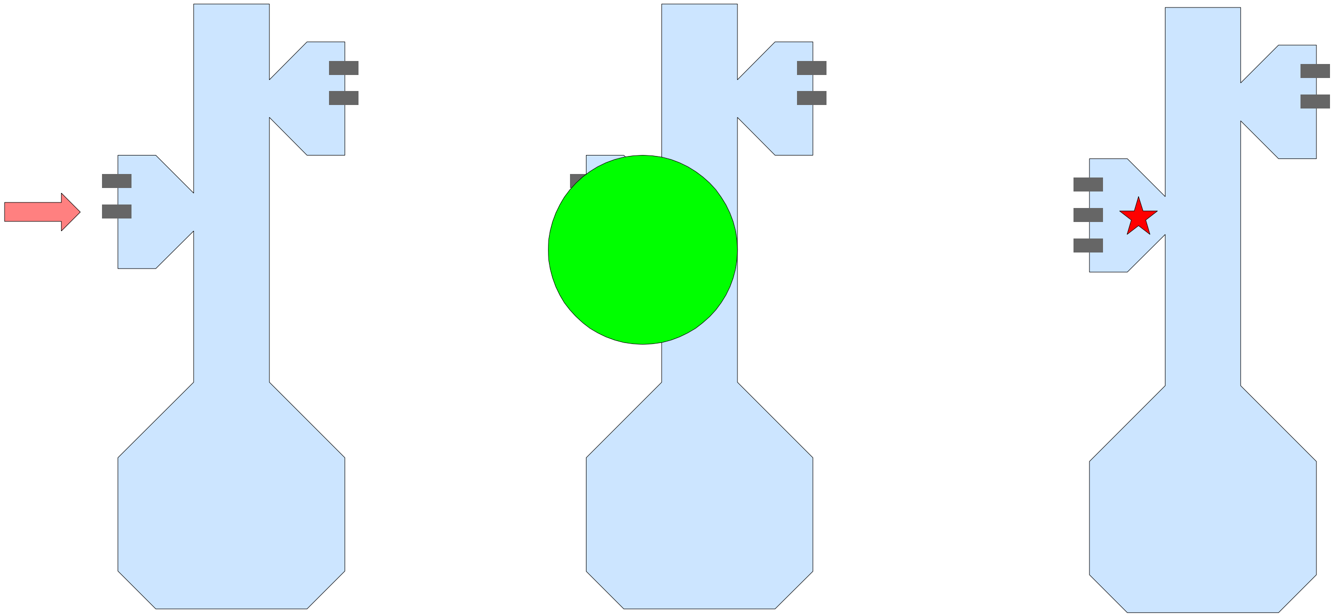


Changes in AMPA receptor phosphorilation

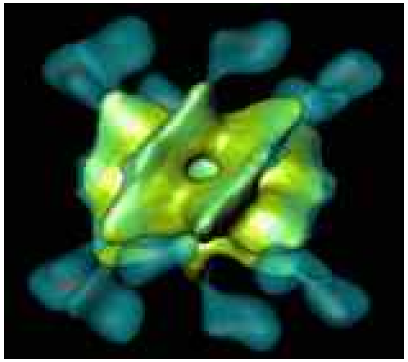


[Whitlock, .. and Bear '06]

Early phase LTP



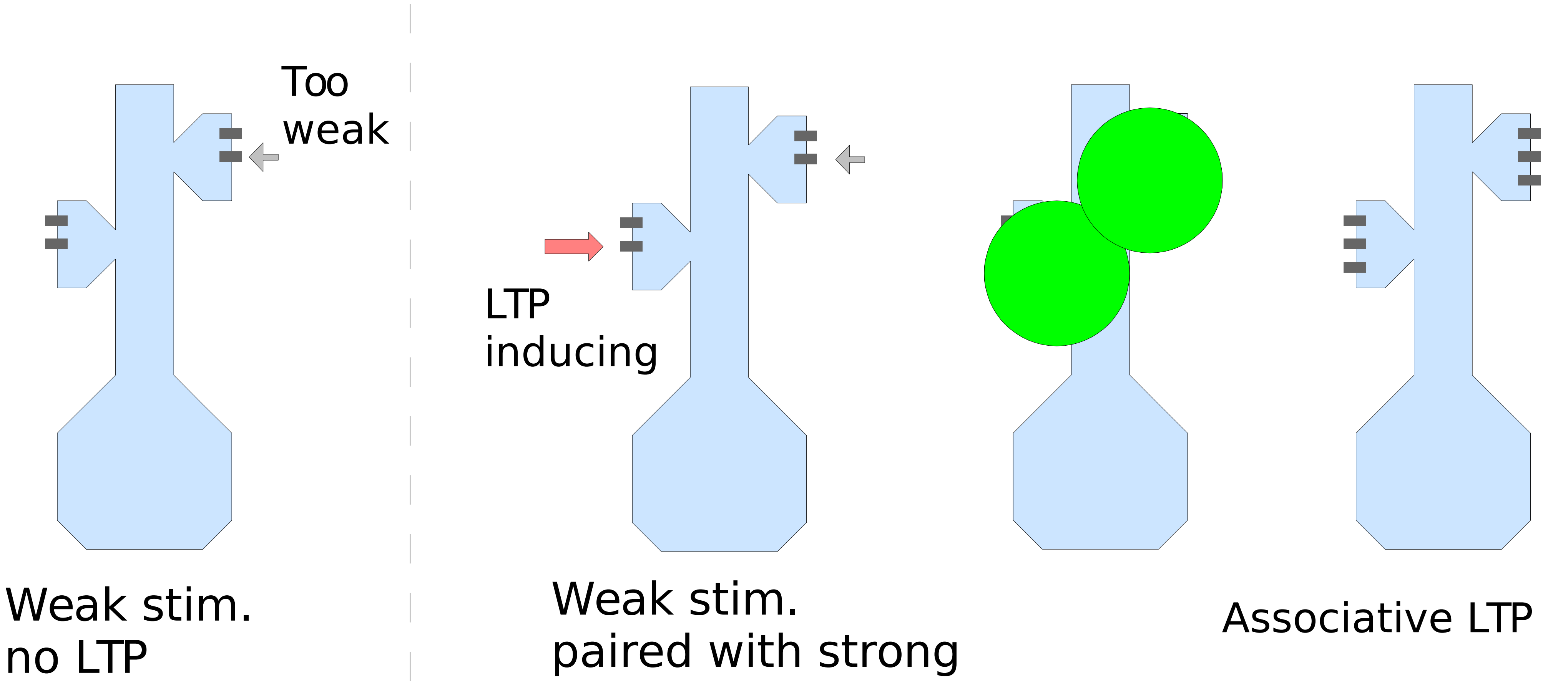
★ CaMKII



Stim.:
1 s @ 100Hz

Rapid and local
change

Associativity



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

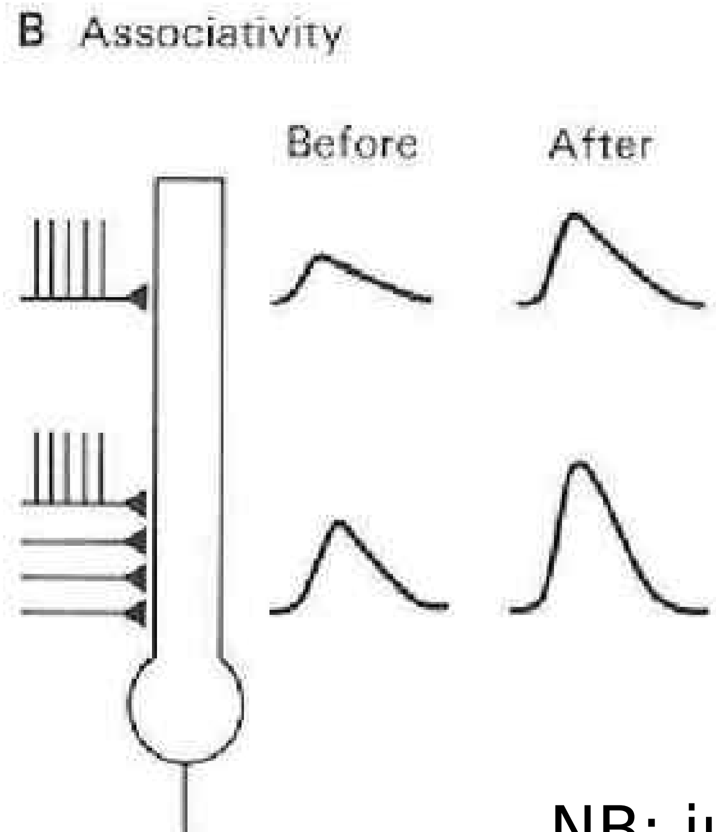
Basis of classical conditioning?

conditioned stimulus

Bell

unconditioned stimulus

Food

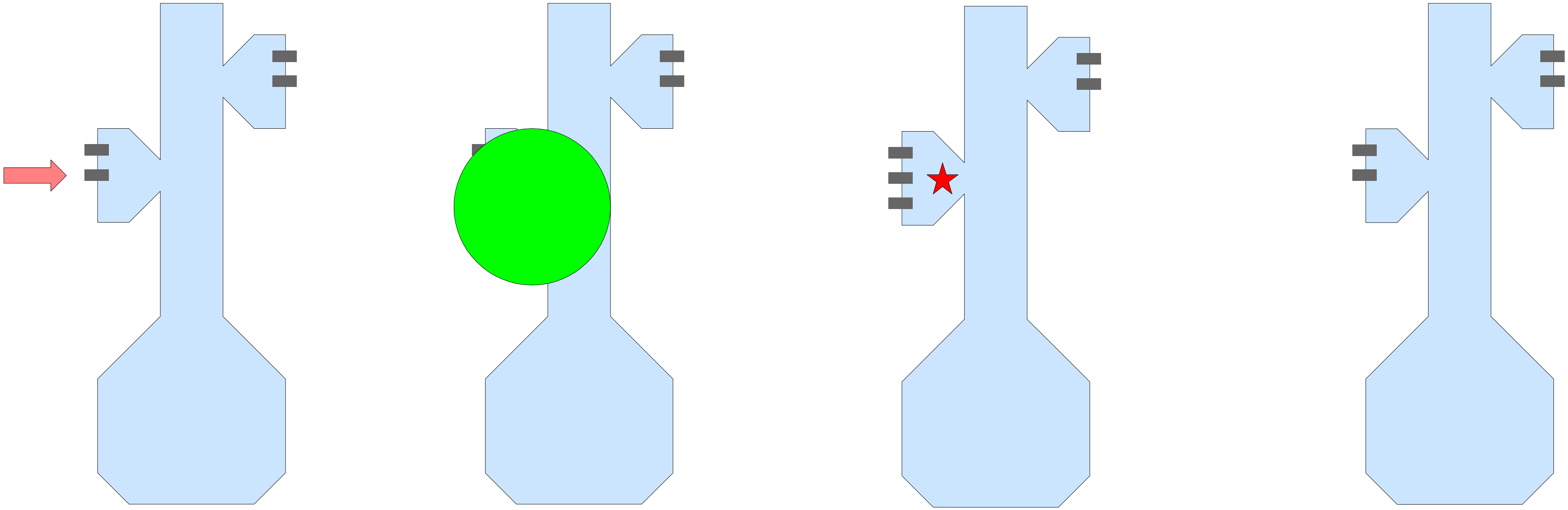


Saliva

NB: just a cartoon!

For Aplysia see Kandel book

Early phase LTP

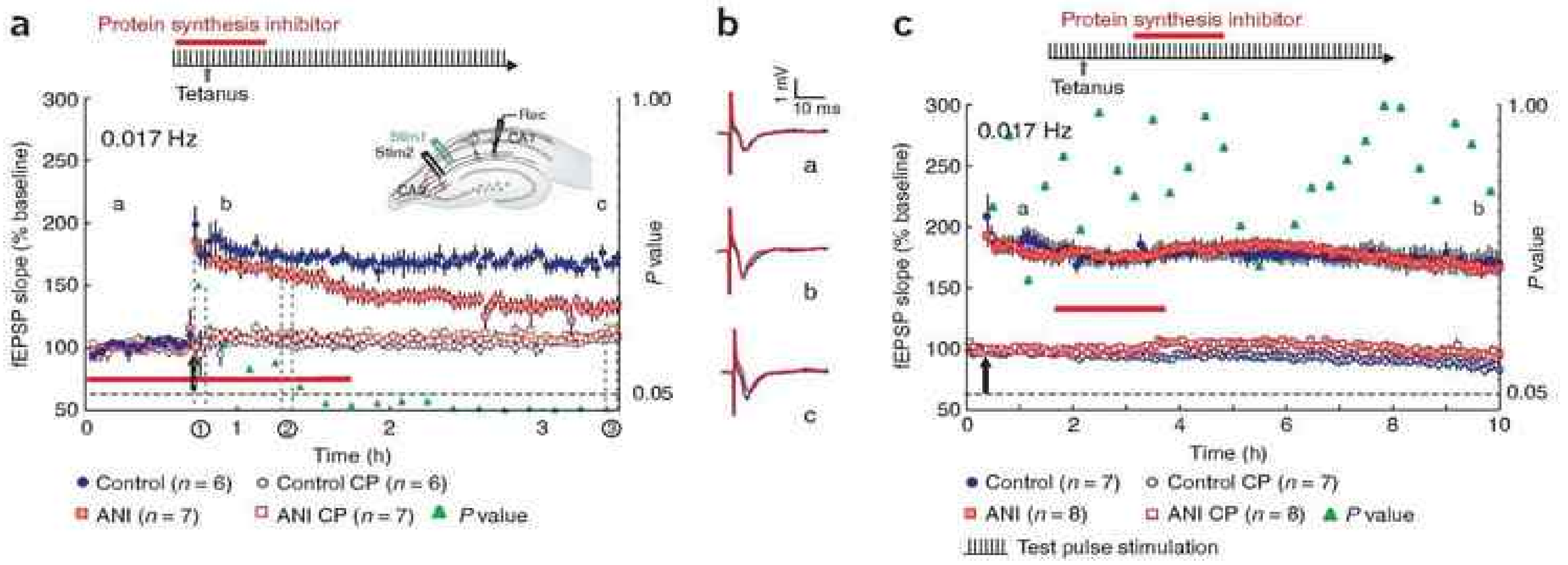


Stim.:
1 s @ 100Hz

Rapid and local
change

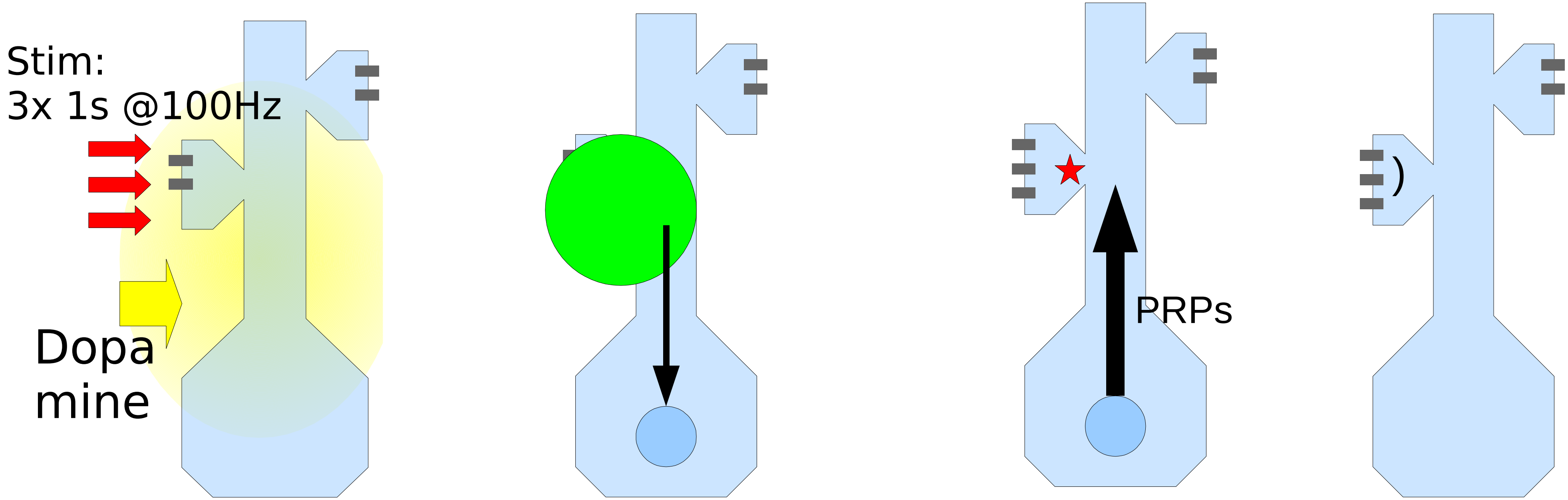
But gone
after few hours

Late LTP requires protein synthesis



[Fonseca et al 06]

Late phase LTP



Start protein synthesis

Ship PRPs to tagged synapses

LTP lasts

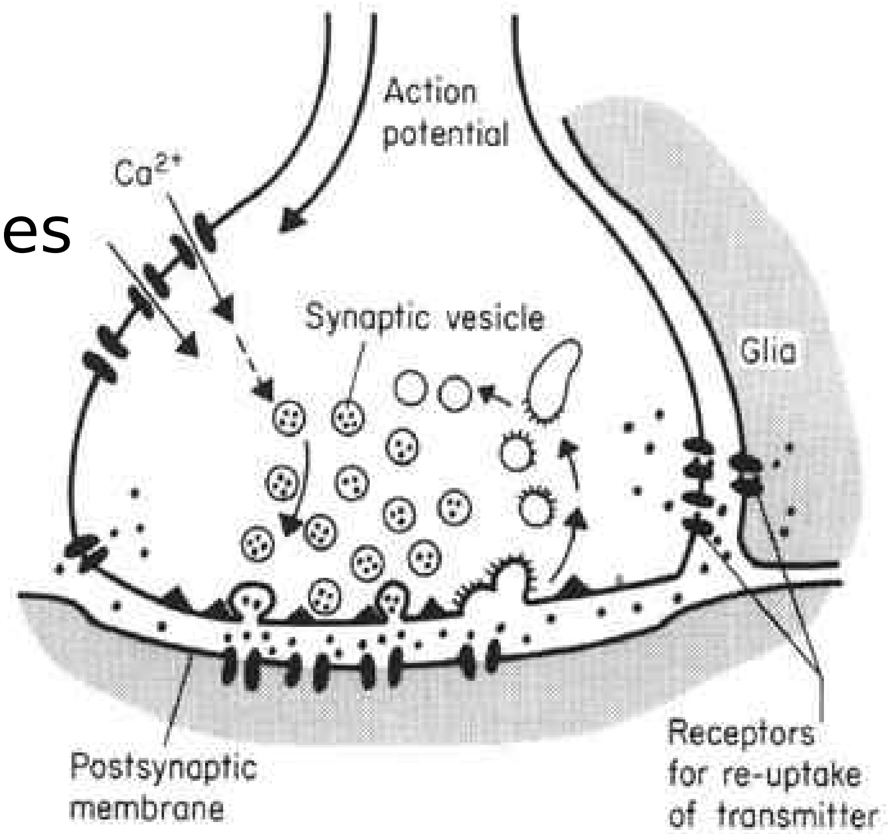
LTP stages

Induction:

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

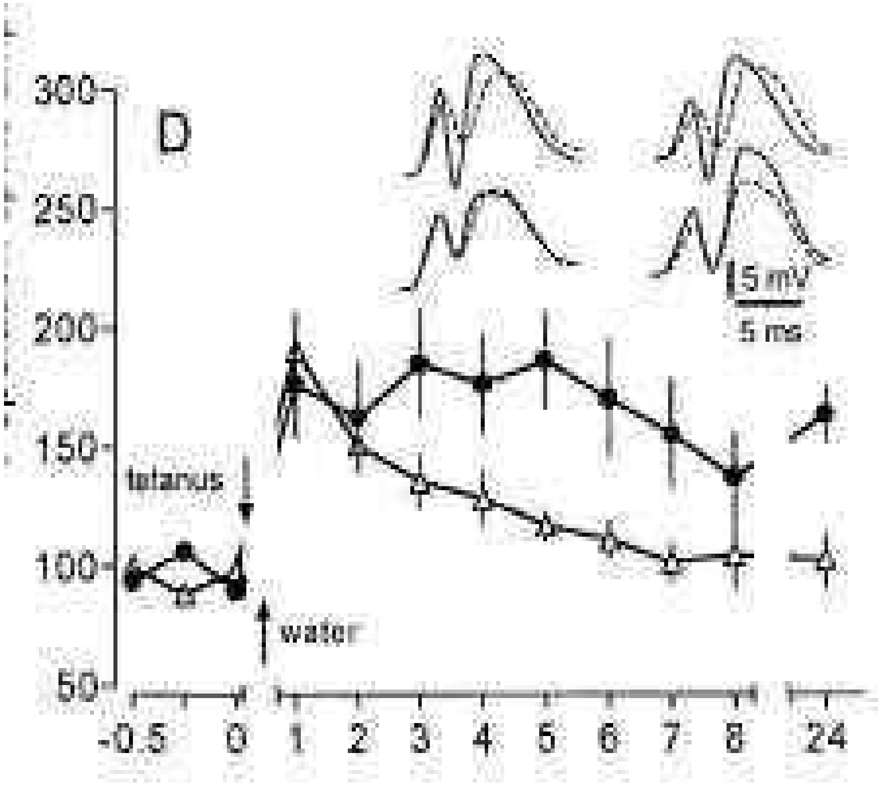
Expression:

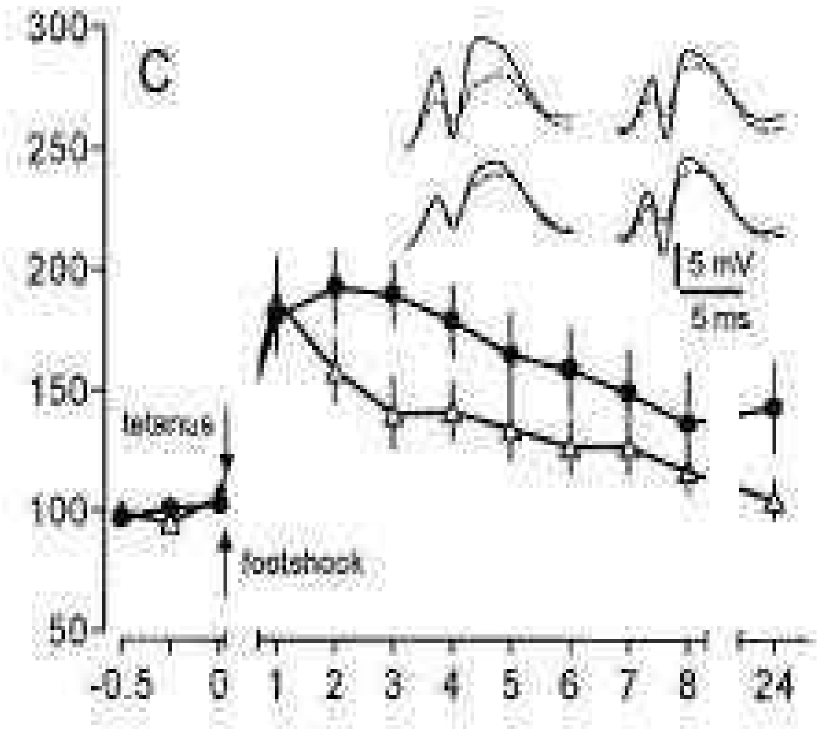
- Early LTP (1 hr):
    - partly pre-synaptic changes
    - AMPAR phosphorylation
    - AMPAR insertion
- **Late phase LTP**
    - requires protein synthesis



What determines if LTP lasts?

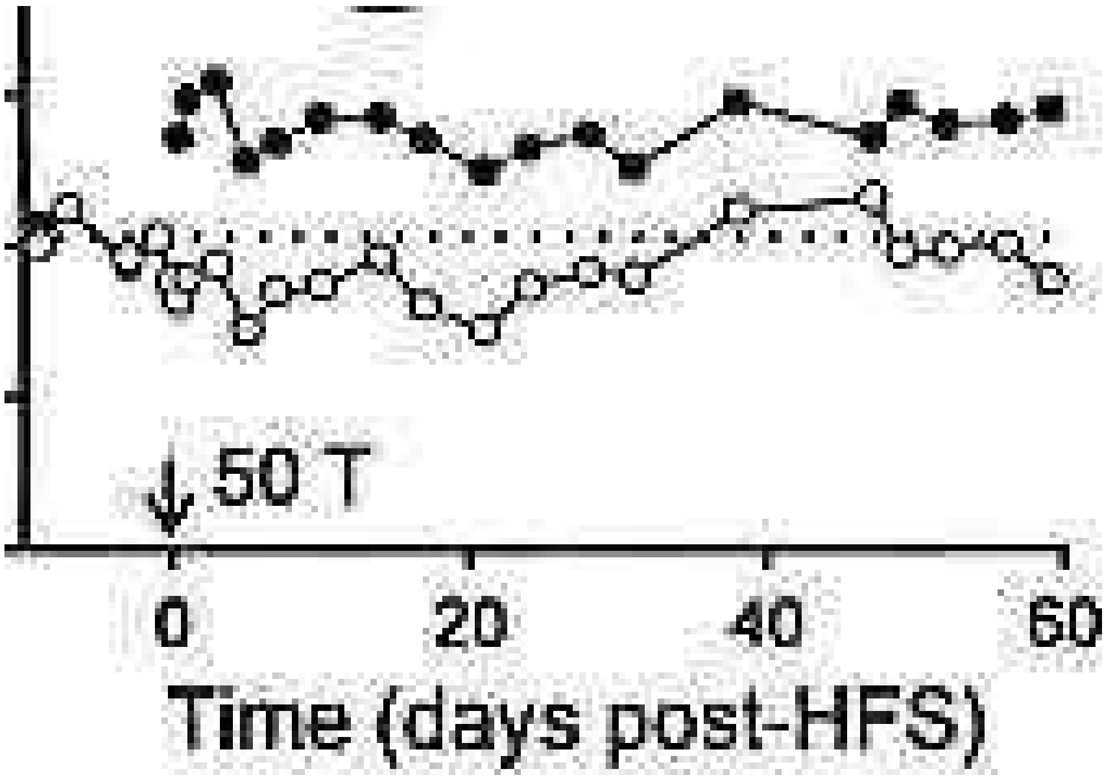
Reward and punishment





[Seidenbecher '95]

Longevity: In vivo physiology

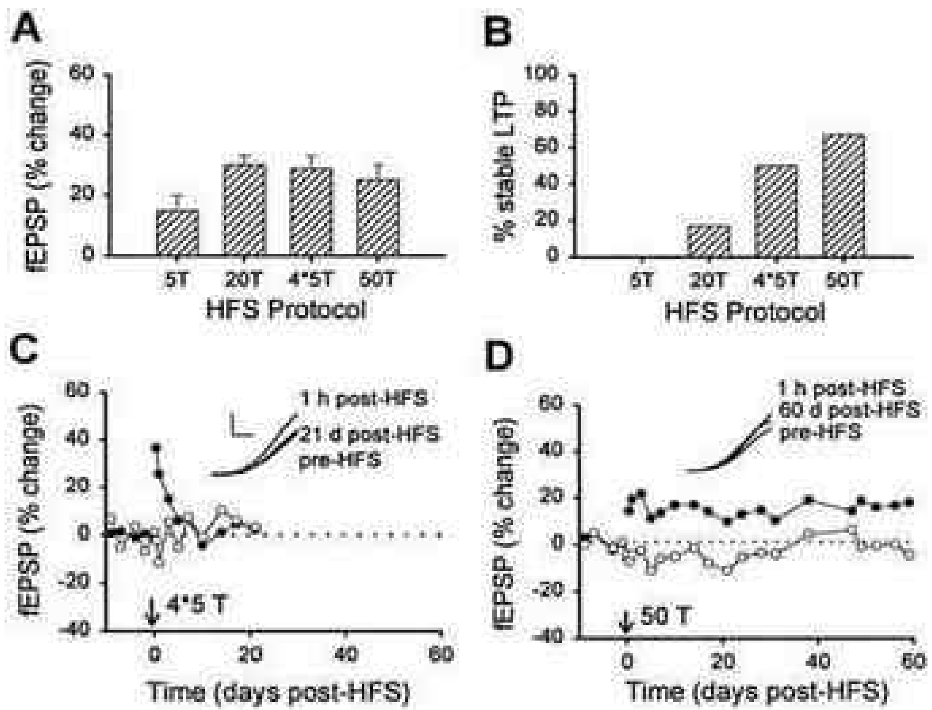


[Abraham '00]

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

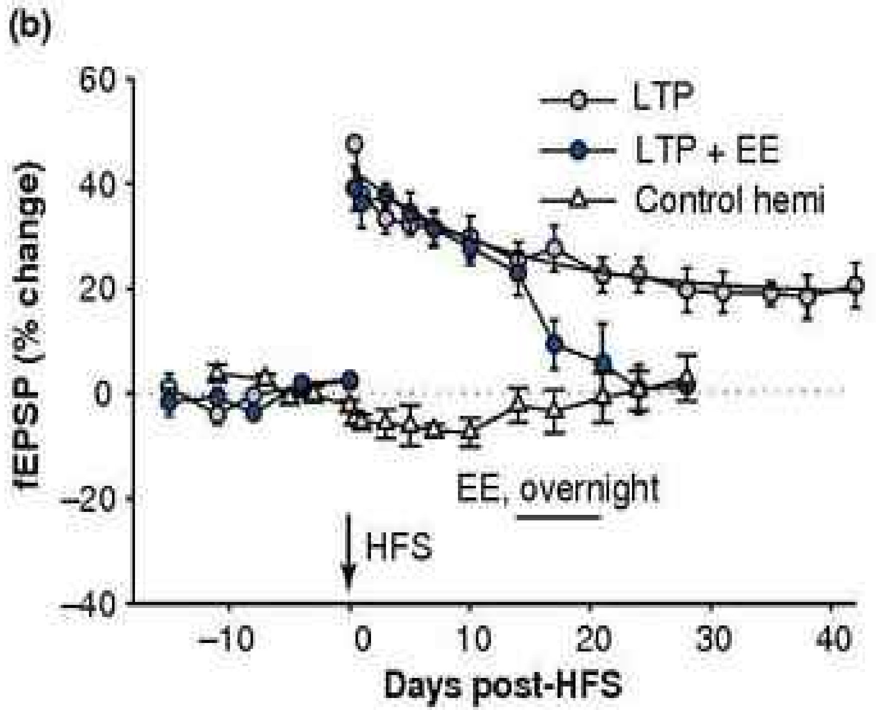
What determines if LTP lasts?

Stimulus protocol



[Abraham '00]

Environment



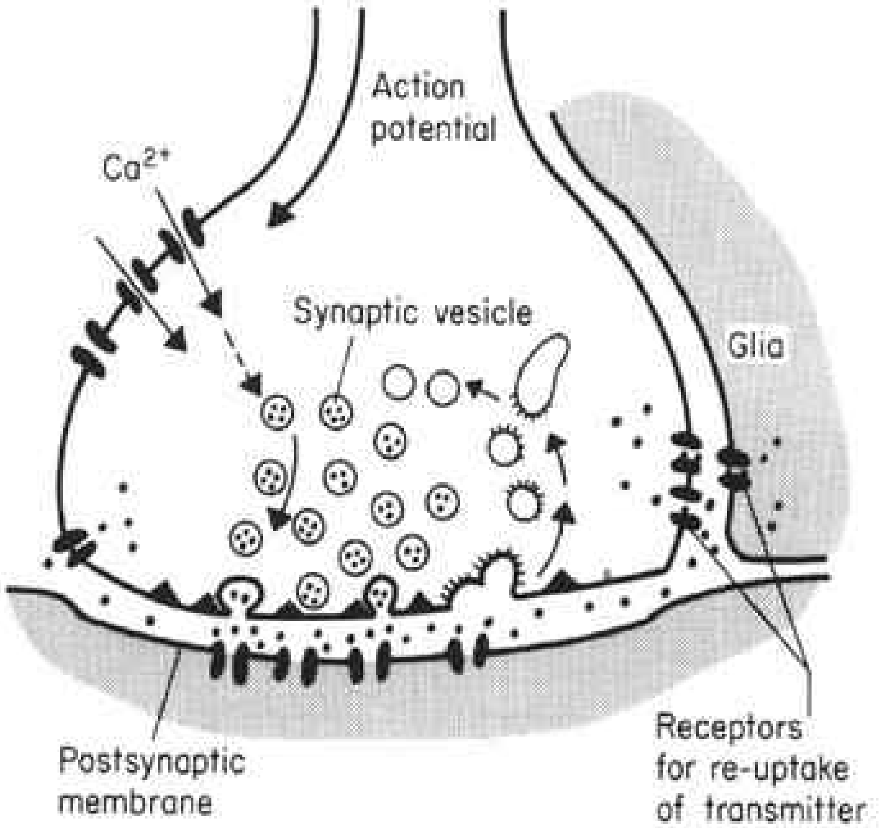
[Abraham '02, Li & Rowan '00]
(Dopamine mediated)
Does a novel environment 'reset' hippocampal learning?

LTP stages

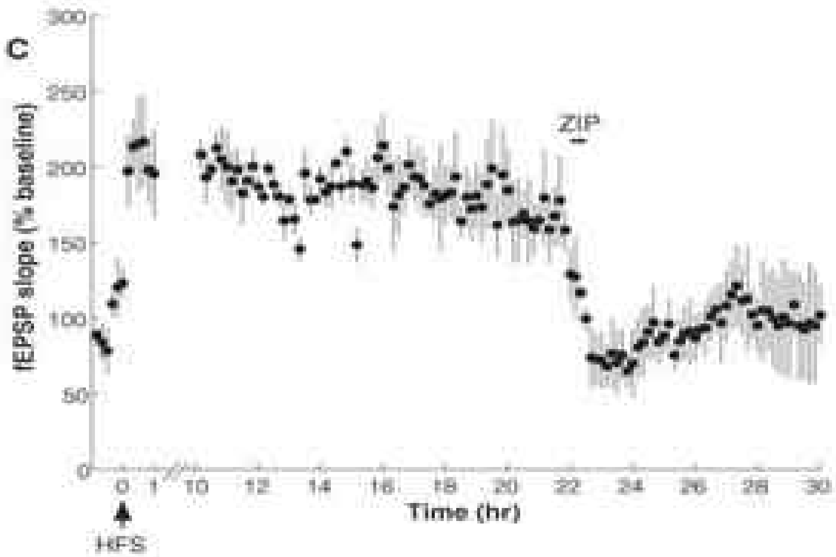
Induction

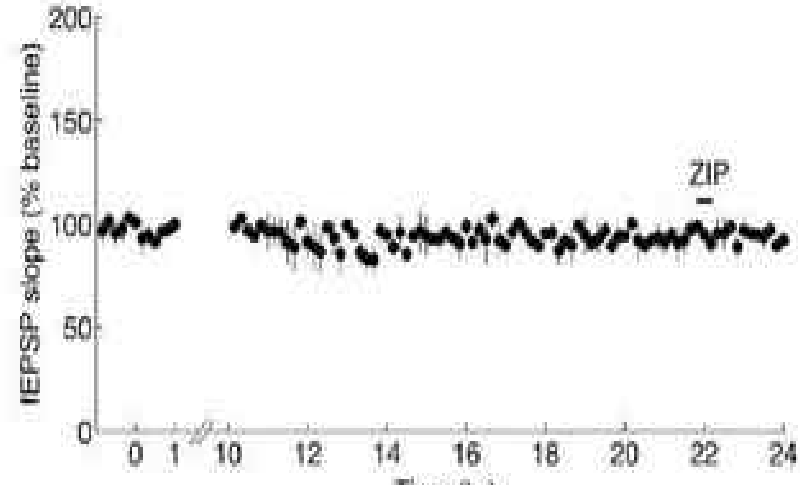
Expression

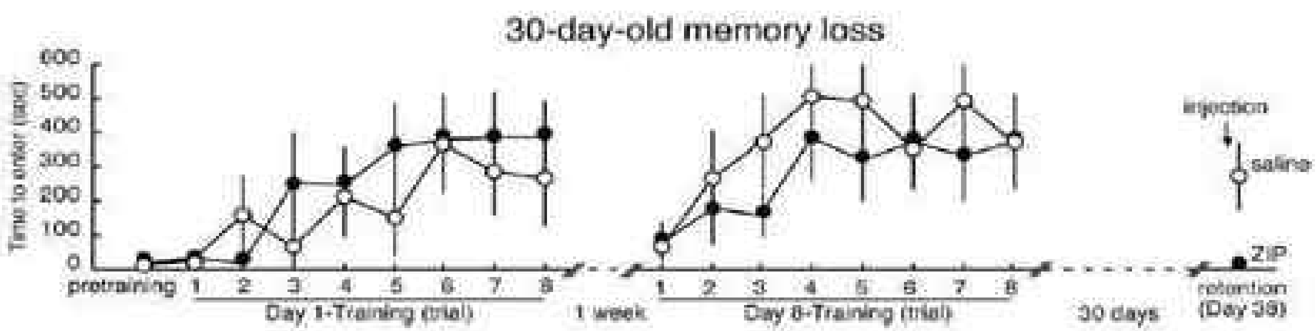
Maintainance



LTP maintenance as an active process







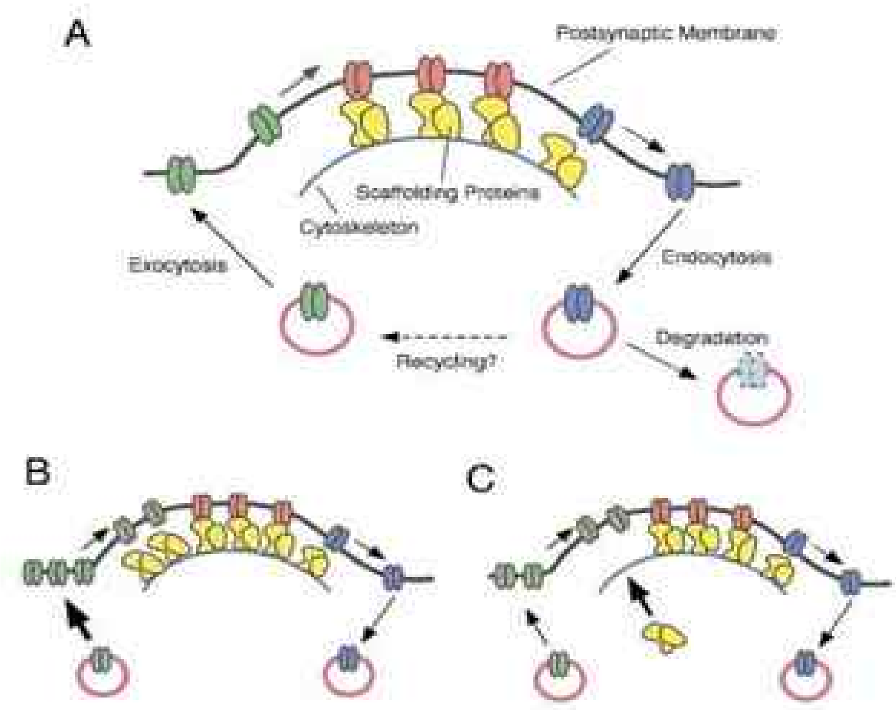
ZIP disrupts one month old memory

[Pastalkova et al '06]

[movie demo]

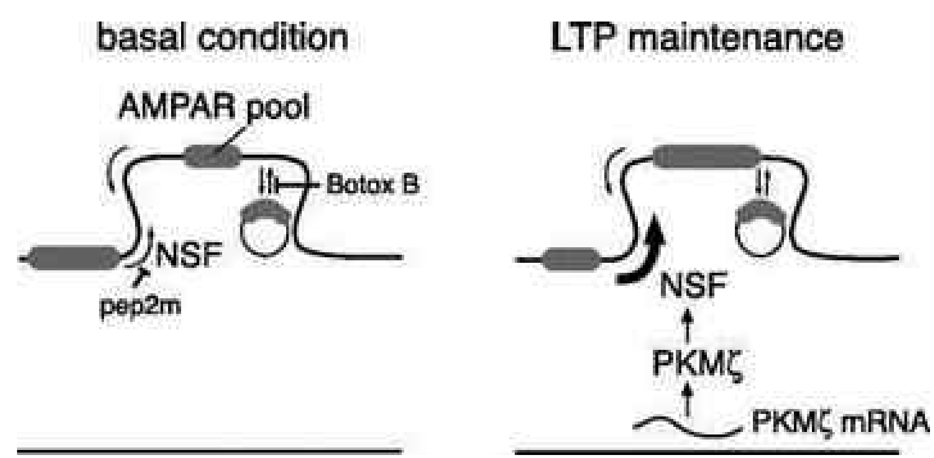
Hypotheses for maintaince / long term stability

Slots for AMPA receptors



[Turrigiano '02]

GluR2 trafficking



[Yao & Sacktor '08]

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

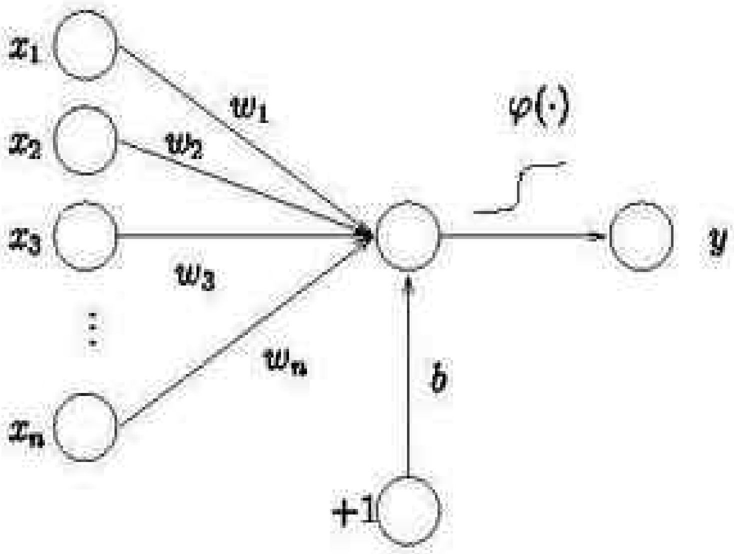
Reinforcement learning
- Only give reward/punishment

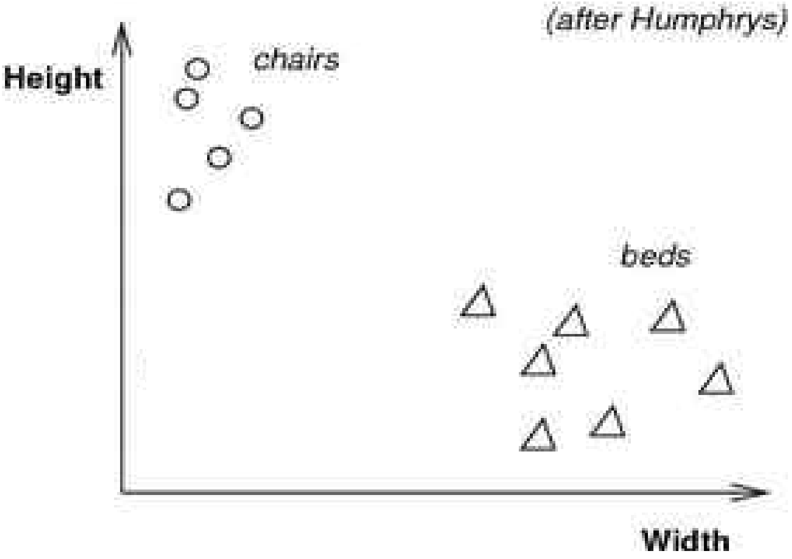
Unsupervised learning
- Let the network discover things (statistics) about the input, e.g. Create representations that are useful for further processing (V1)

Animals/humans can do all three presumably

Supervised: Perceptron

Categorize inputs into two classes

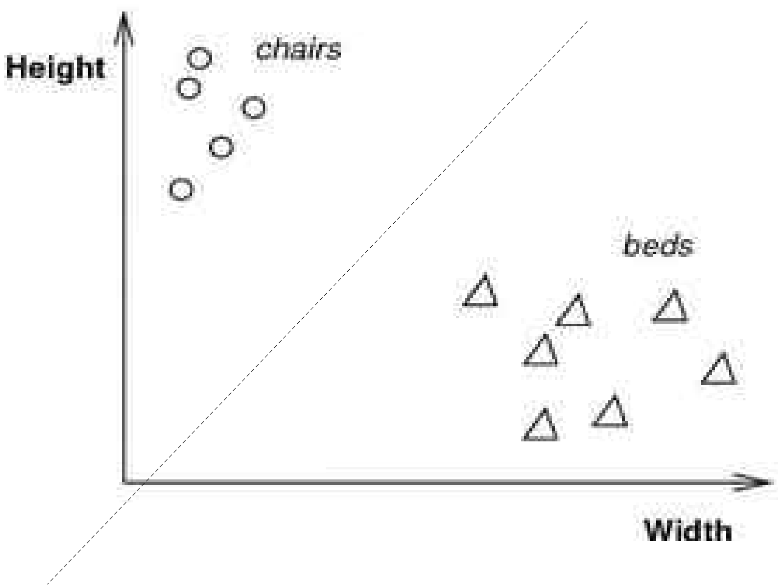




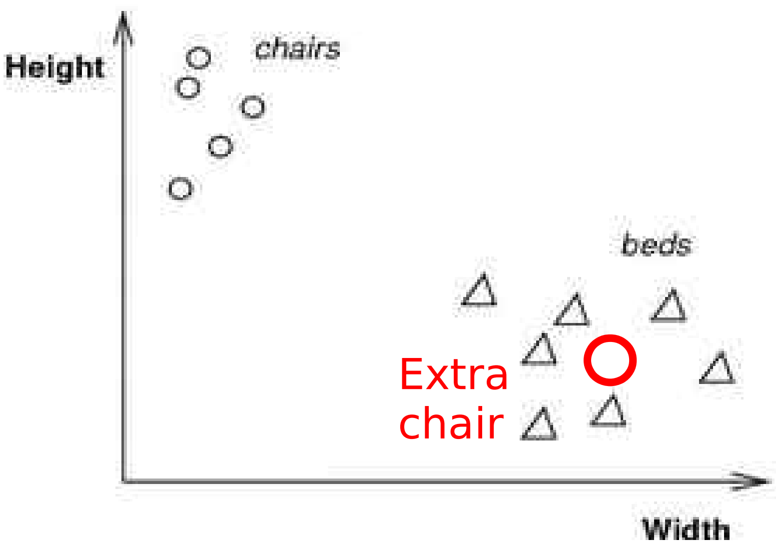
$$y = \phi(\Sigma w_i . x_i)$$

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

Linear separability



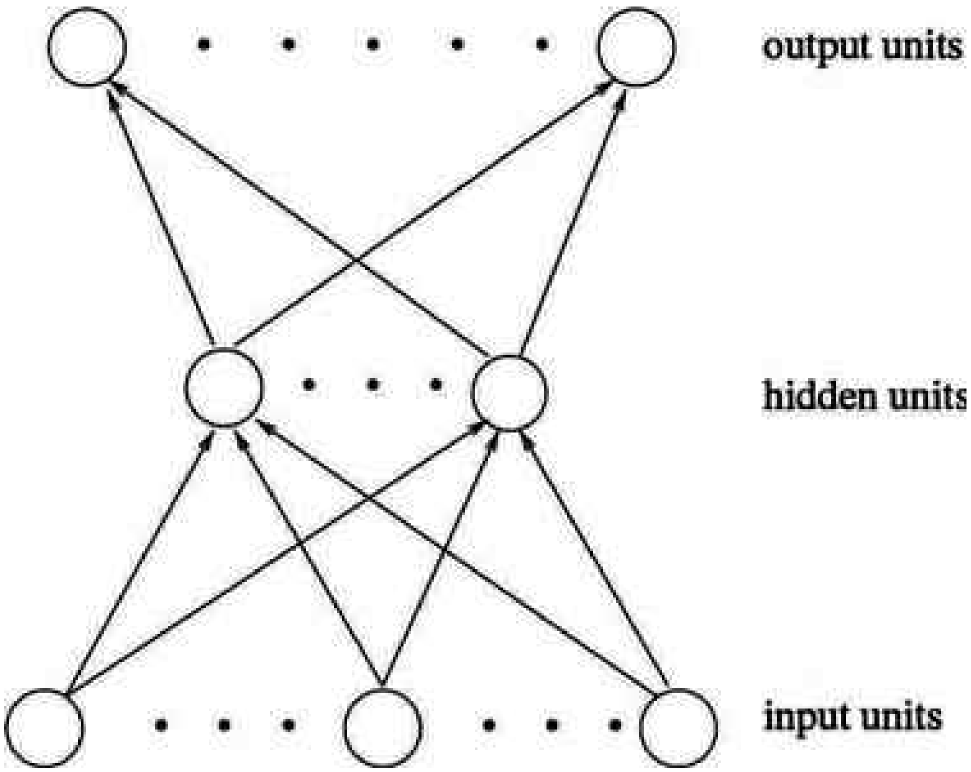
Separable
Perceptron can classify



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

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

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

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

Back propagation

General approach:

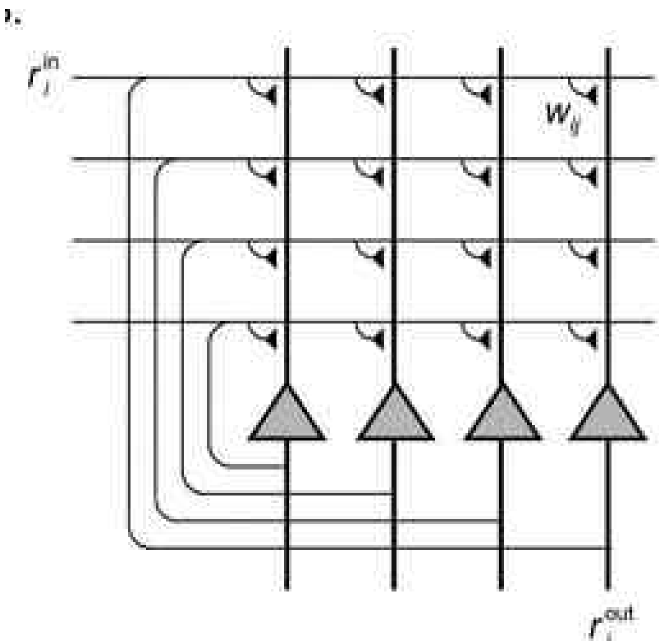
- Come up with cost function, (objective function)
  Examples: #errors, sparseness, invariances

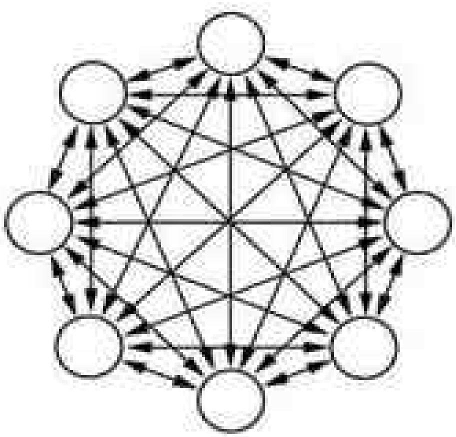
- Take the derivative wrt synaptic weights.

- You have created a learning rule

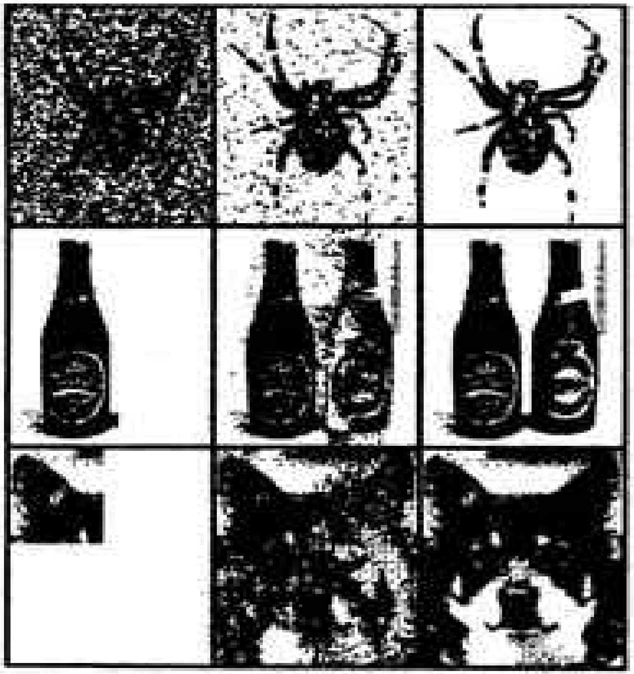
Hopfield network

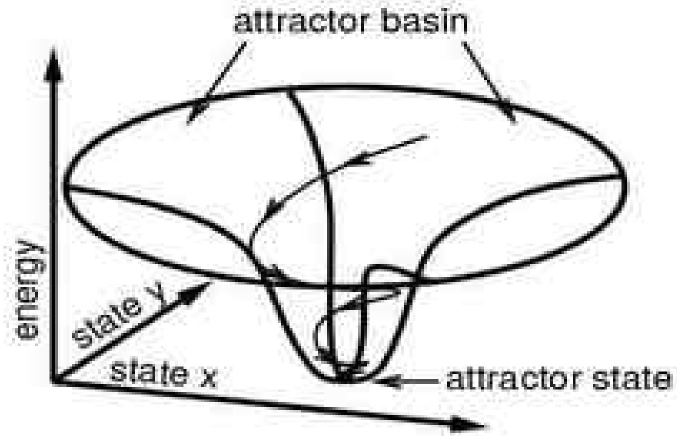
- Model for CA3
- Recurrent network
- Auto-associator (i.e. Pattern completion)

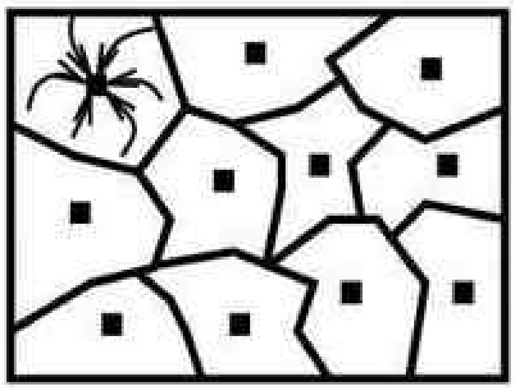




Hopfield network





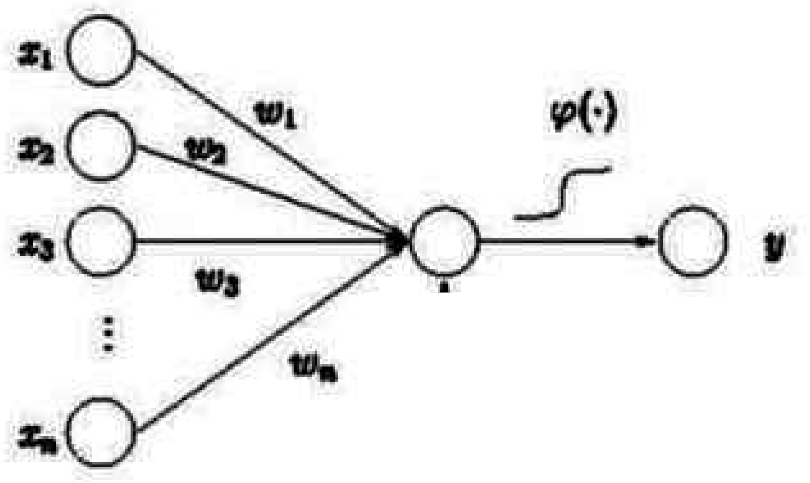


One shot learning: $w_{ij} = \sum_{patterns} x_i^{\mu} x_j^{\mu}$

Unsupervised plasticity

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

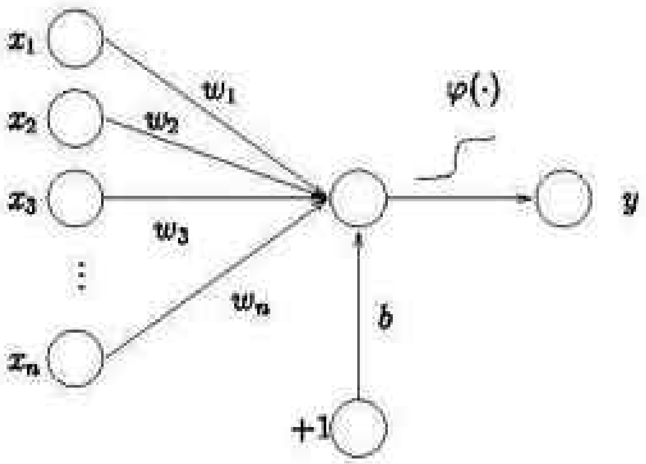
$$\Delta w_i = \langle \epsilon x_i y \rangle$$

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

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

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

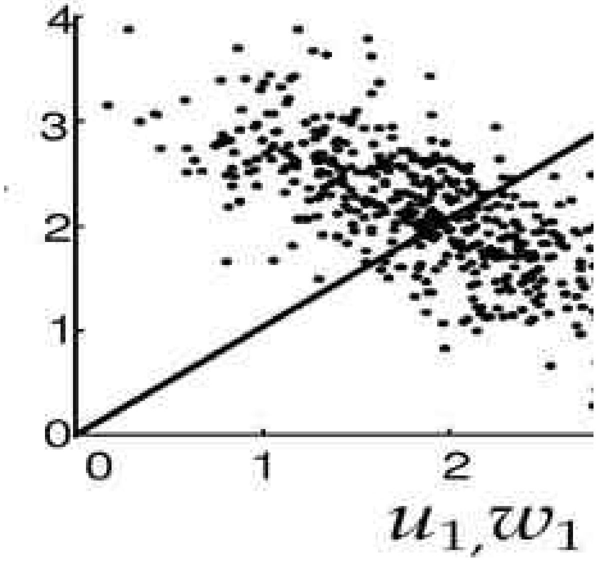
$$\frac{\partial \vec{w}(t)}{\partial t} = Q . \vec{w}(t)$$



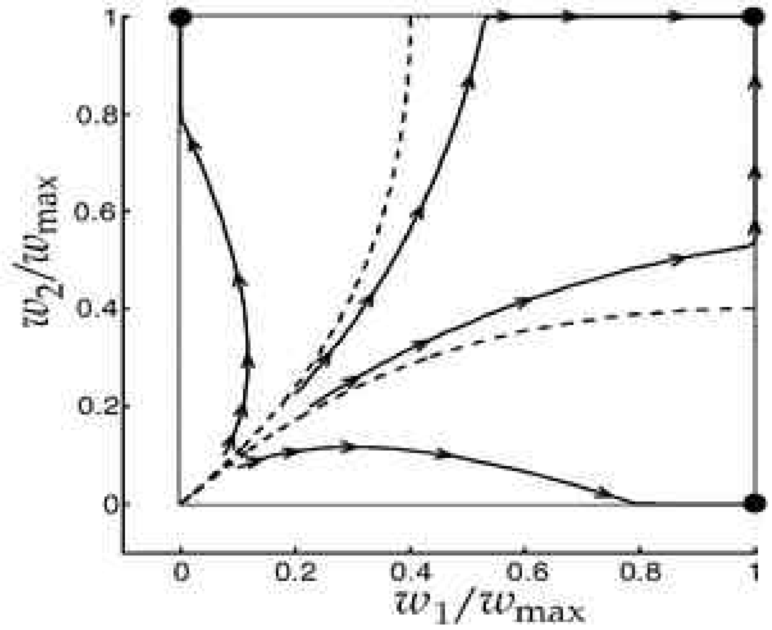
PCA

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

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

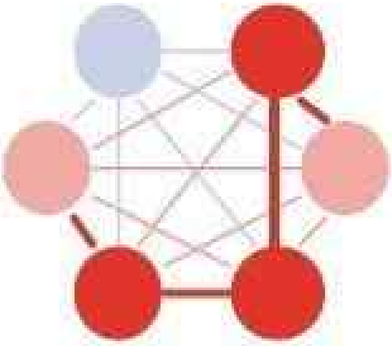
Own Work

Computational modelling of synaptic plasticity

Ultimate goal:
Quantitative, accurate models in health and disease

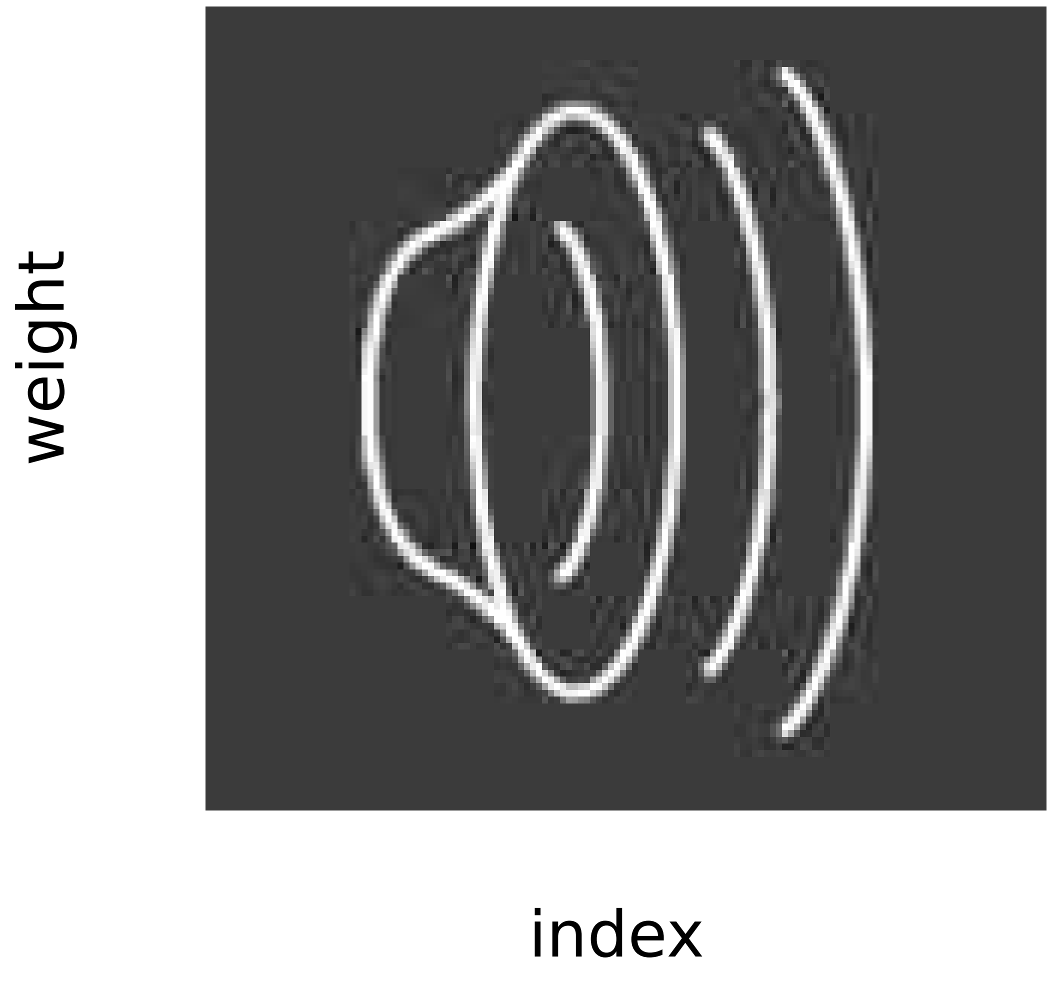
Most models are oversimplified

Plasticity is complicated and depends on, for instance:
- pre and post activity,
- reward, modulation, history, other synapses, homoeostasis..
- **synaptic weight itself**

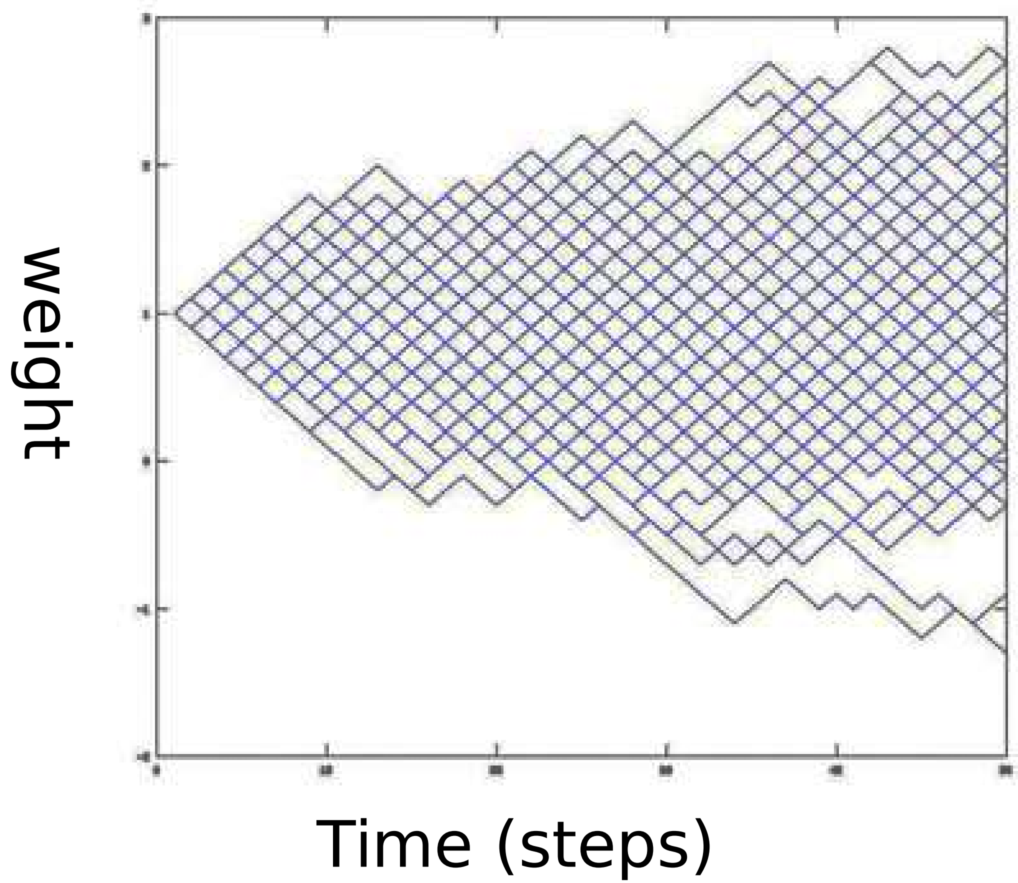


Plasticity due to random patterns: random walk

Random, independent sequence of LTP and LTD



Synaptic weights divergence



- Diffusion of weights, hence unlimited (Sejnowski '77)

Dealing with synaptic weights divergence

<u>Some possible solutions:</u>

- Hard bounds
- BCM (*)
- Normalization/homoeostasis (*)

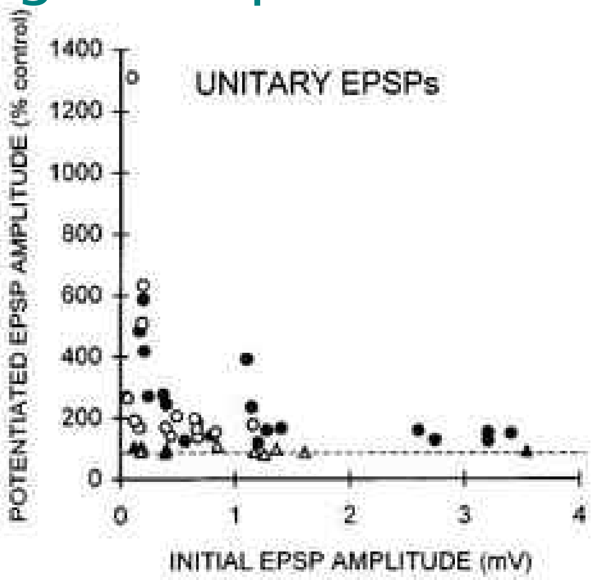
$$\sum_i w_i = 1$$
$$\sum_i w_i^2 = 1$$

- The outcome of the rules depends strongly on the chosen solution...
- Which is consistent with biology ?

(*) Competitive

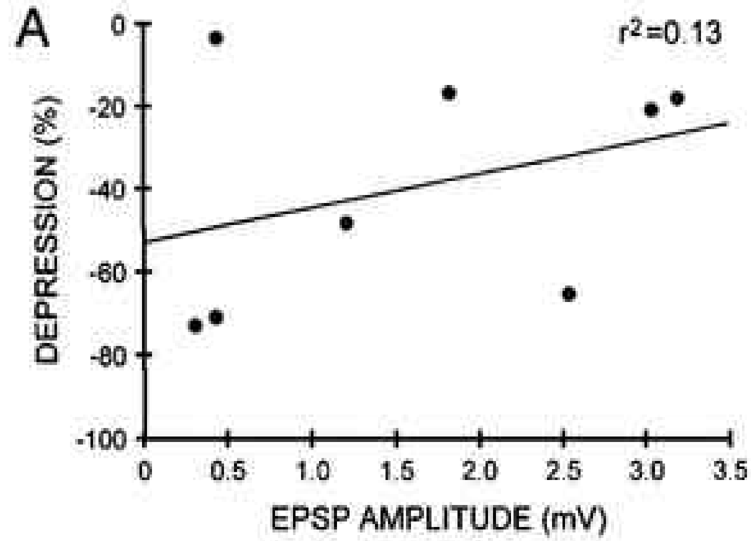
LTP/LTD is weight dependent

Long term potentiation

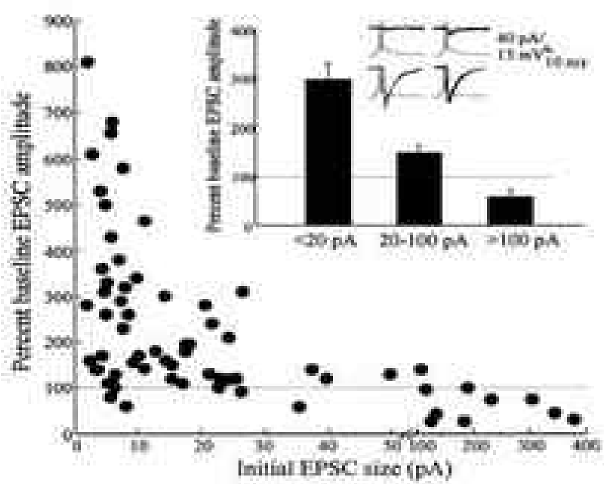


[Debanne '99]

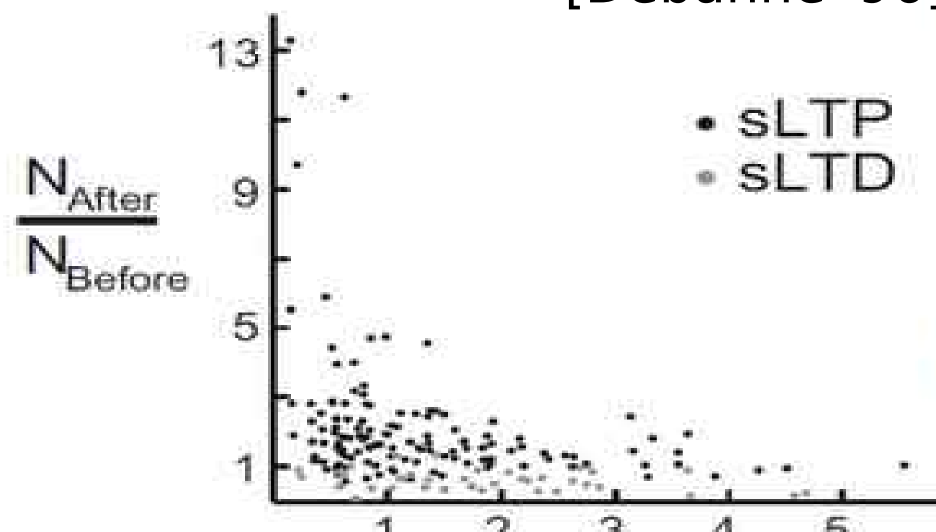
Long term depression



[Debanne '96]



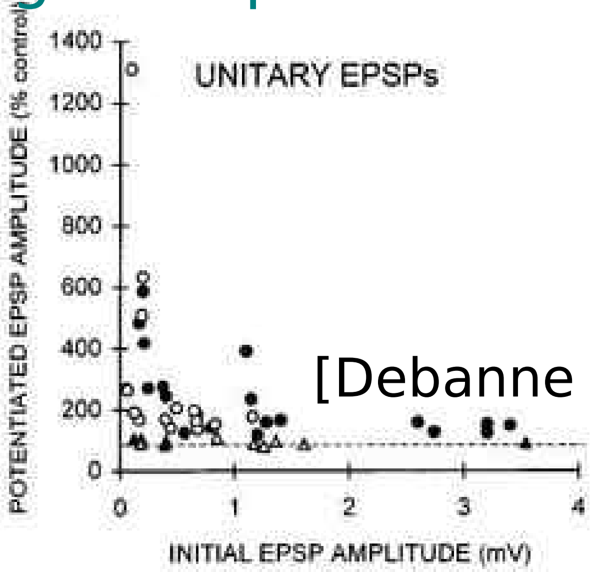
[Montgomery '01]



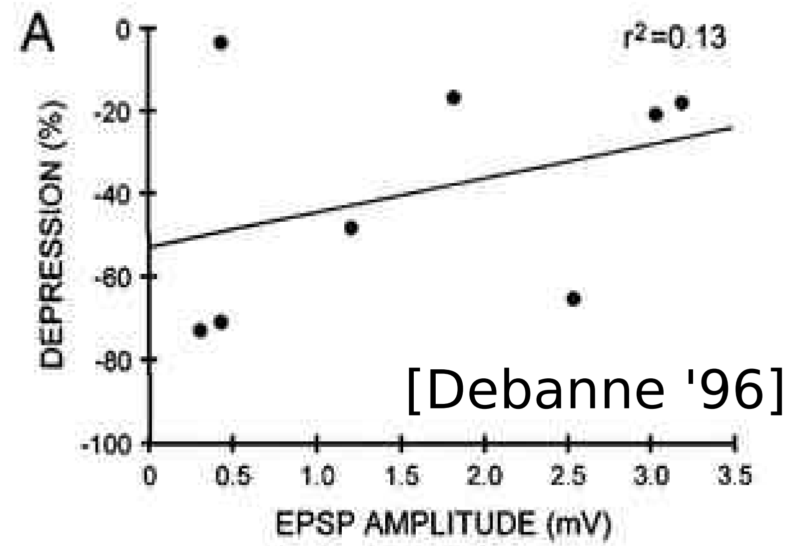
[Loebel '13]

Simple model

Long term potentiation



Long term depression



Simple description

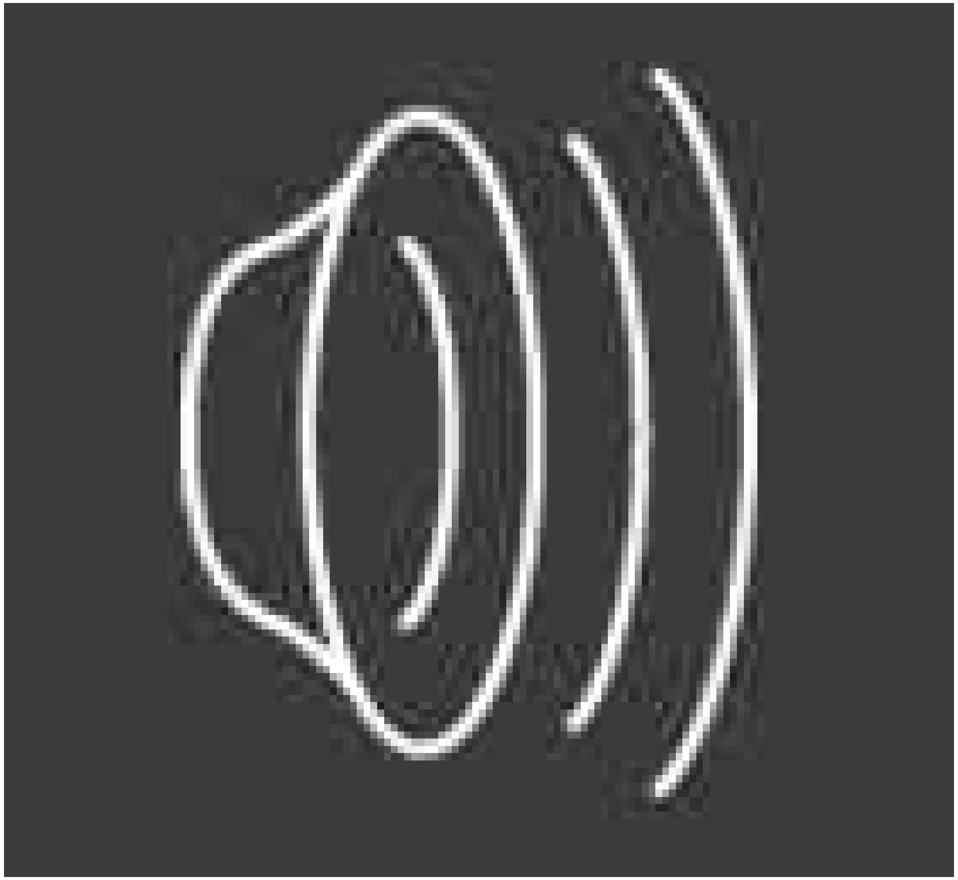
Relative change:

$$\frac{\Delta W^-}{W} = -c_1; \quad \frac{\Delta W^+}{W} = \frac{c_2}{W}$$

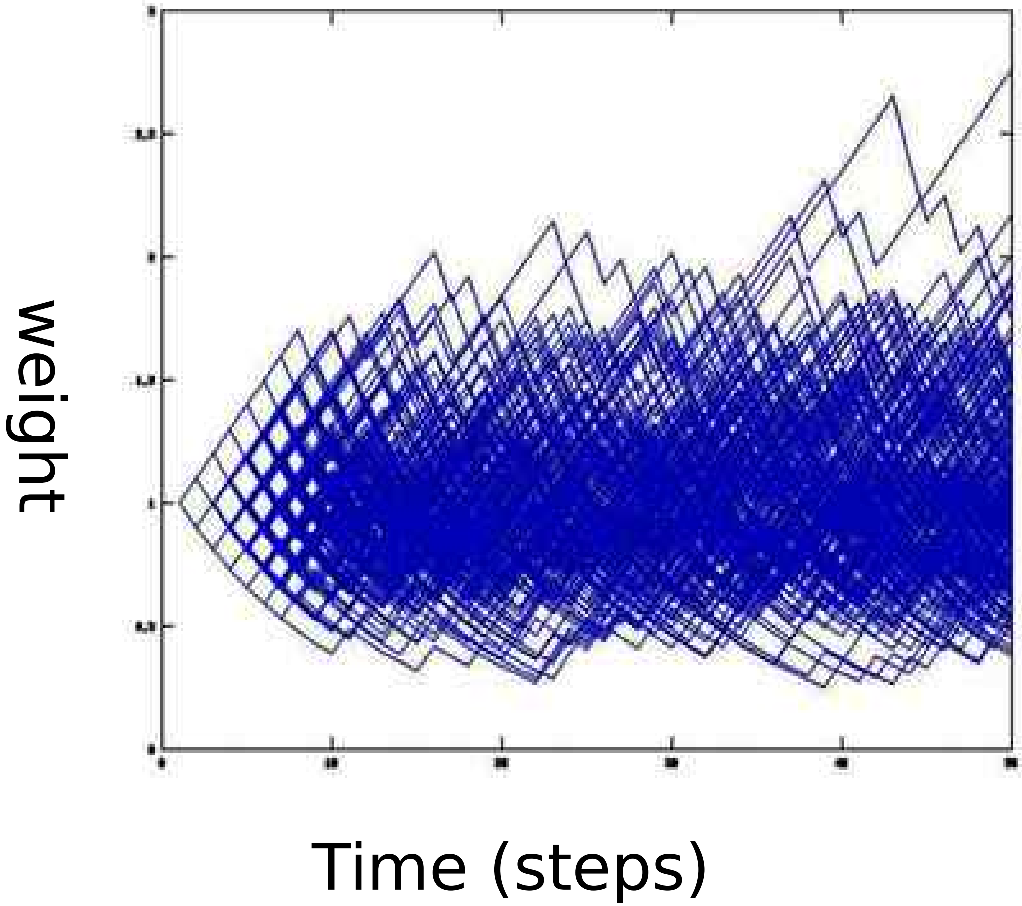
Absolute change:

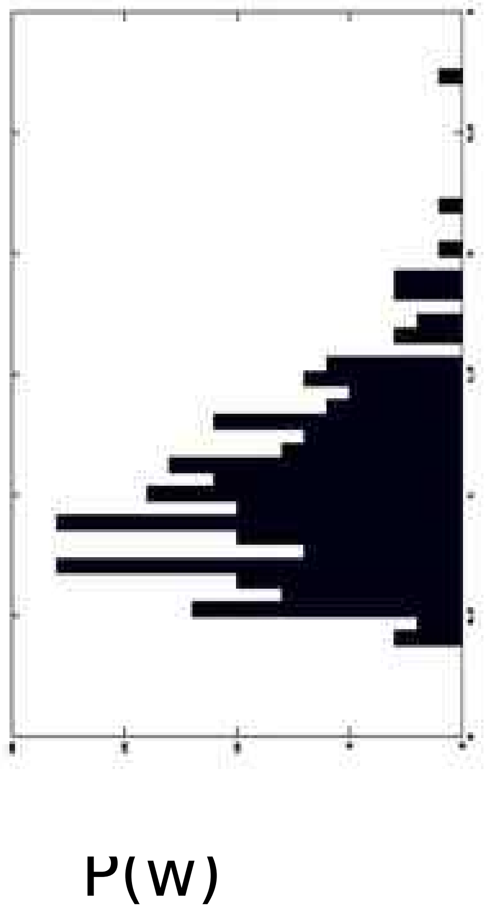
$$\Delta W^- = -c_1 W; \quad \Delta W^+ = c_2$$

Weight dependent random walk



Weight dependent learning rules





- Weight dependent plasticity prevents run away
- Leads to realistic weights distributions

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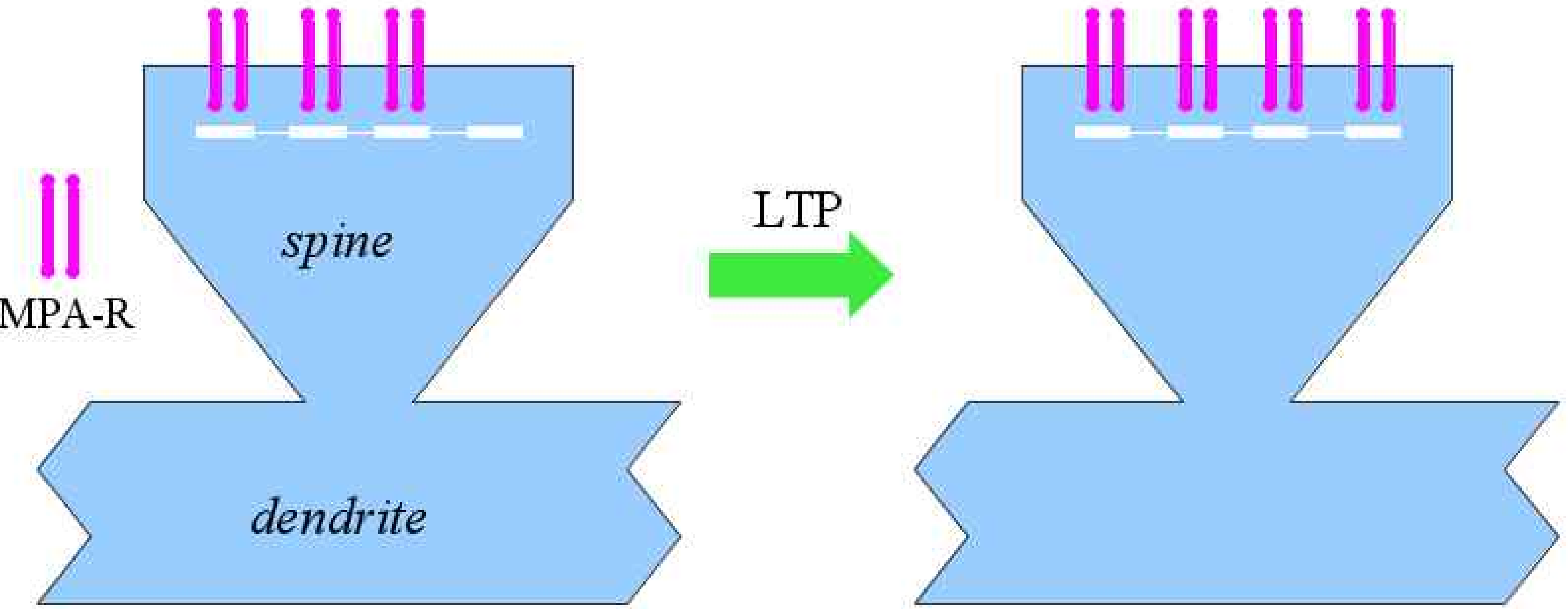
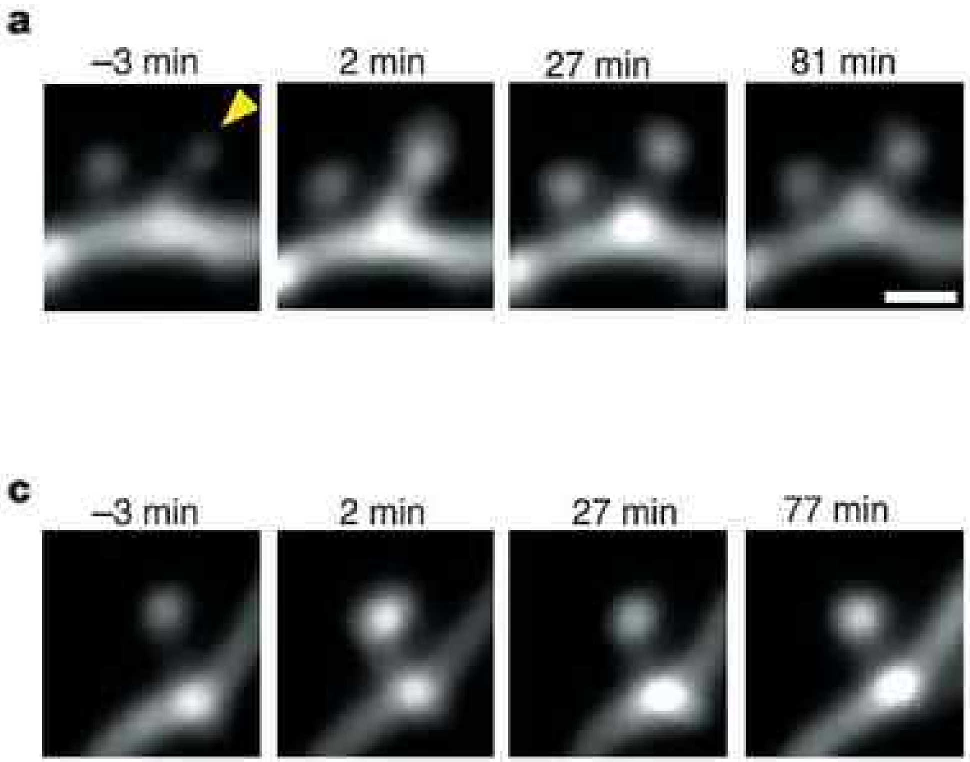
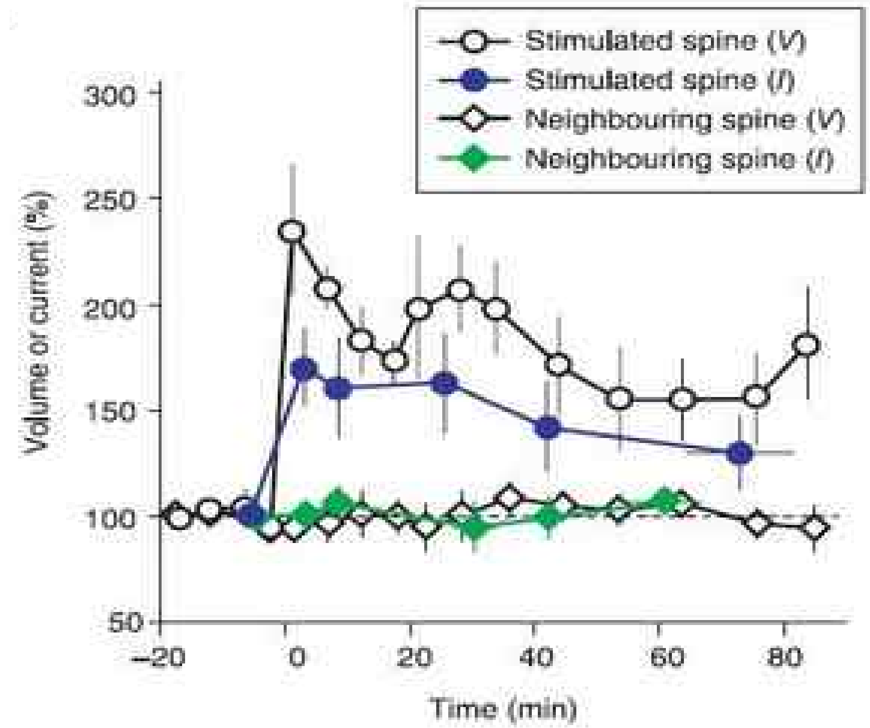
Biophysics of LTP saturation?

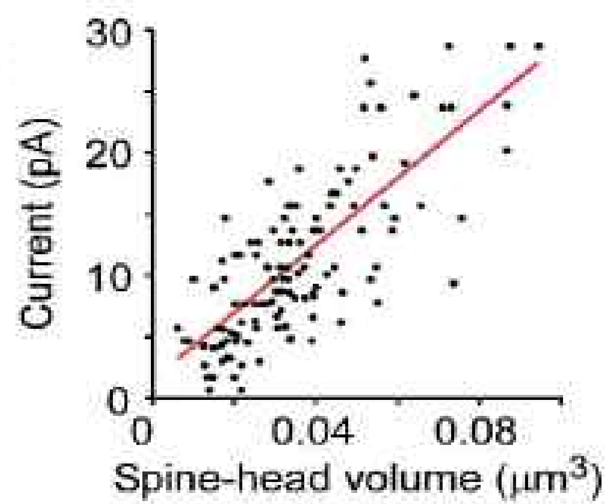


Simple model for weight dependence: biophysical saturation

Spine morphology is very plastic

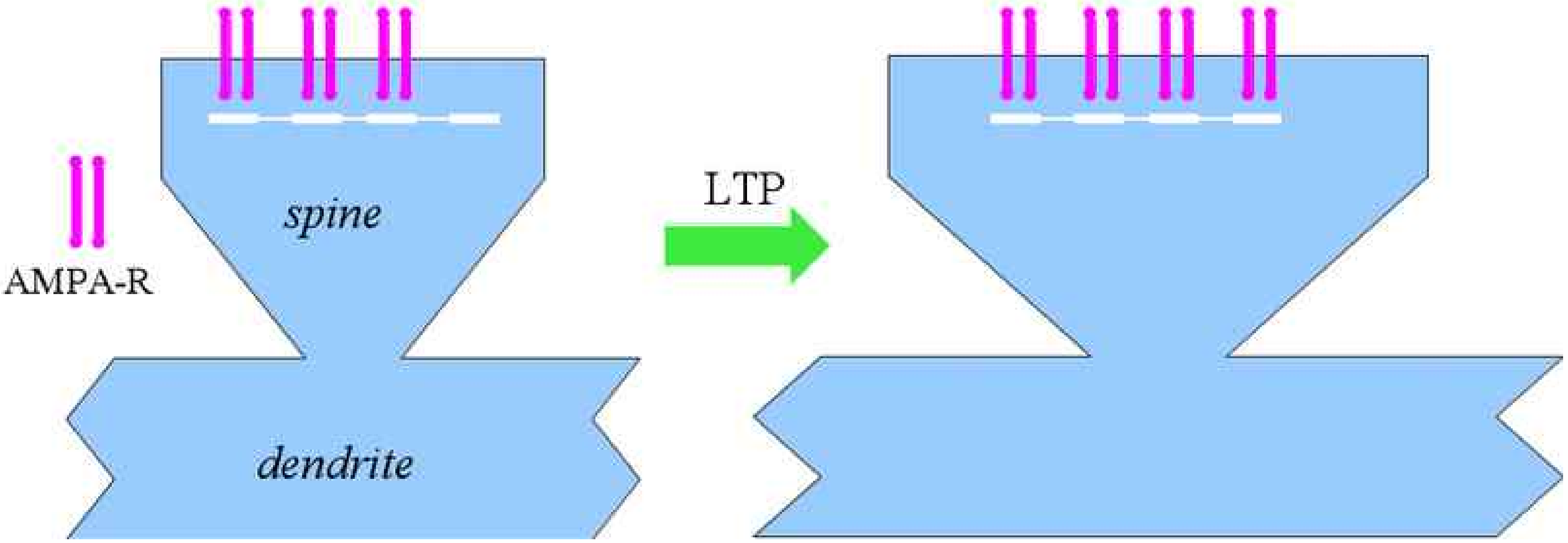




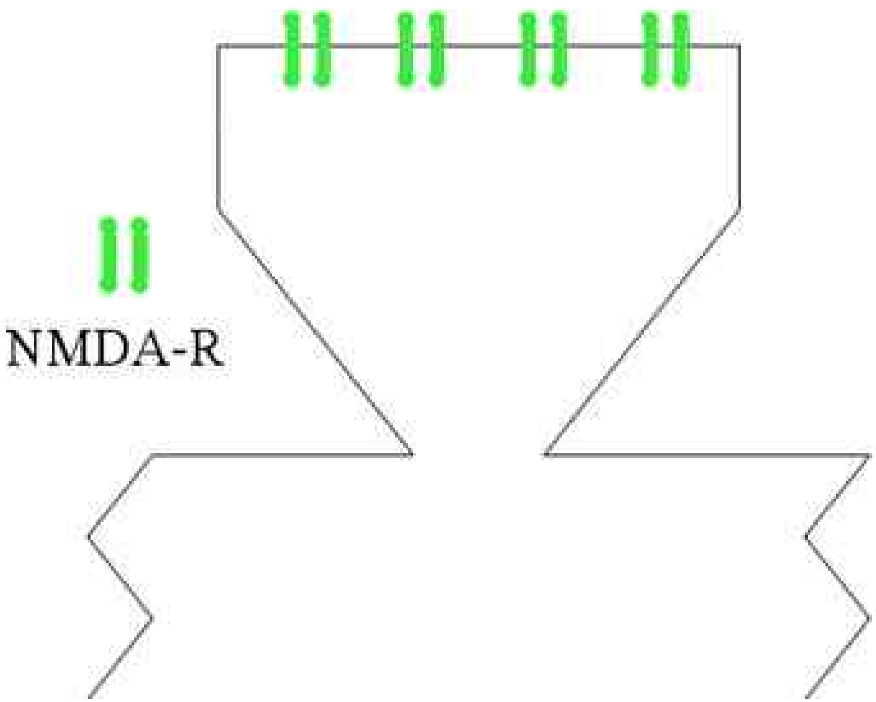


[Matsuzaki '04, Glu uncaging]

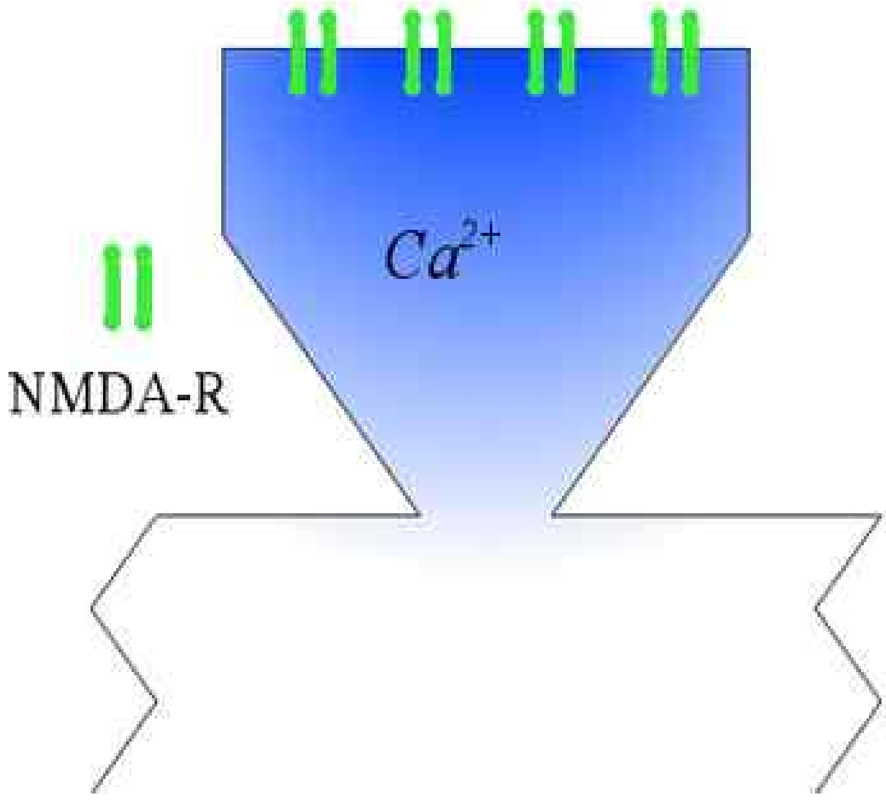
Synapse growth



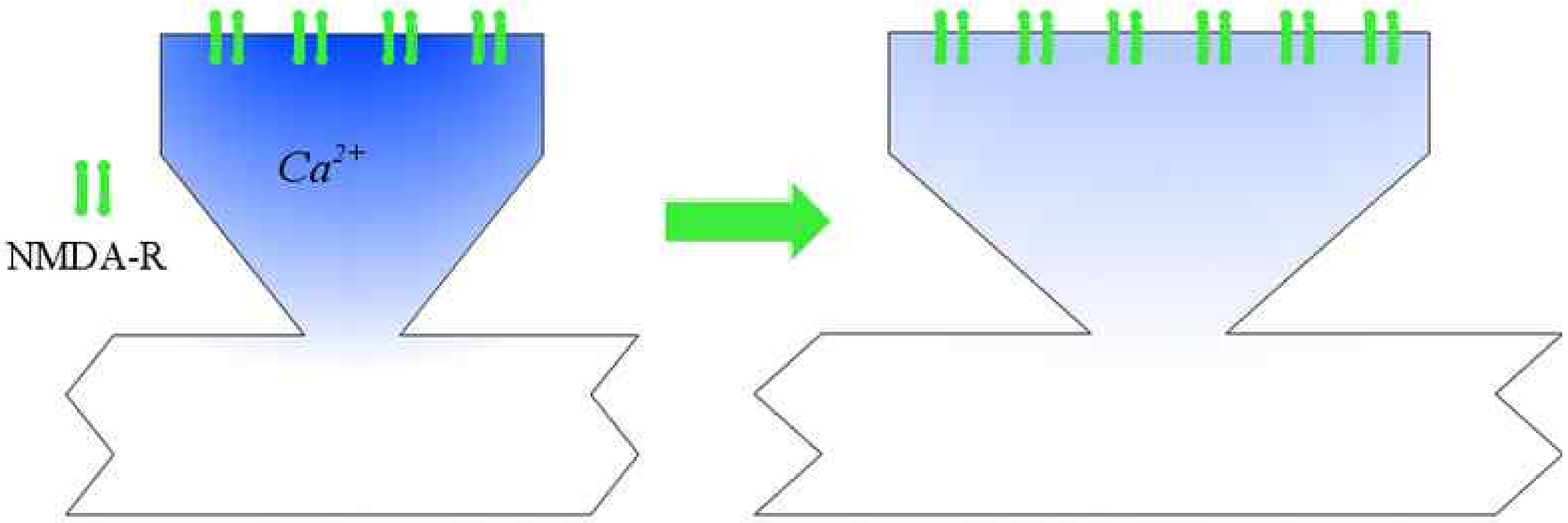
Synapse growth: effect on Calcium



Synapse growth: effect on Calcium

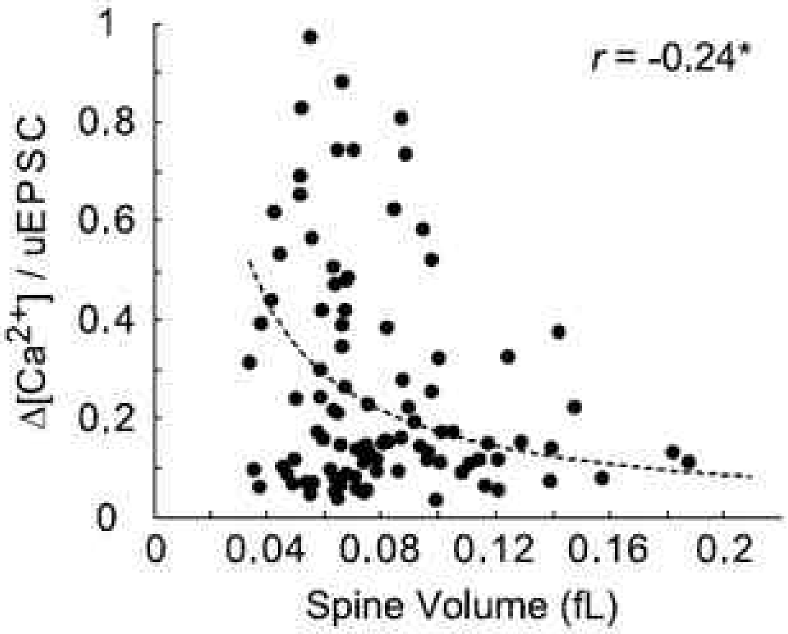


Synapse growth: effect on Calcium

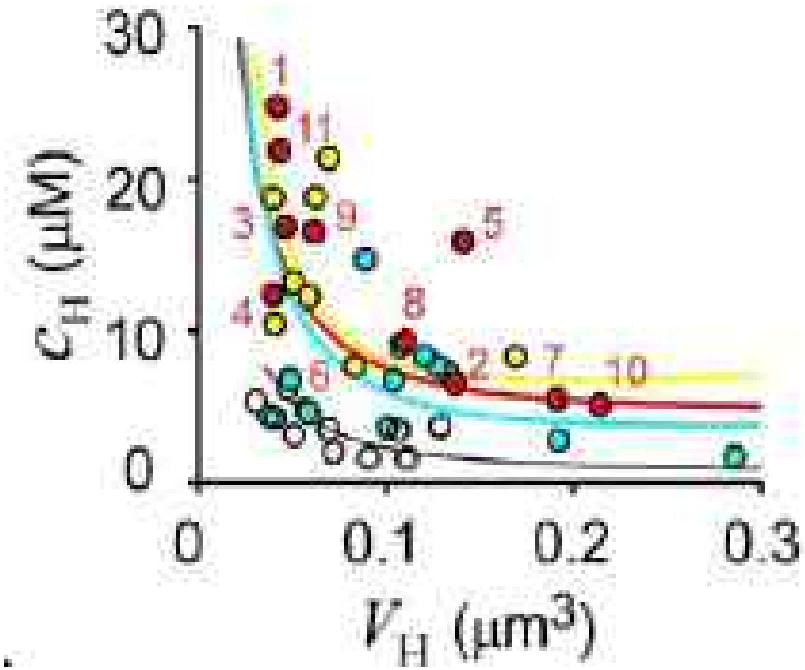


Ca only invariant if: $\rho_{NMDA} \propto r^{(3/2)}$

Spine [Ca] after uncaging

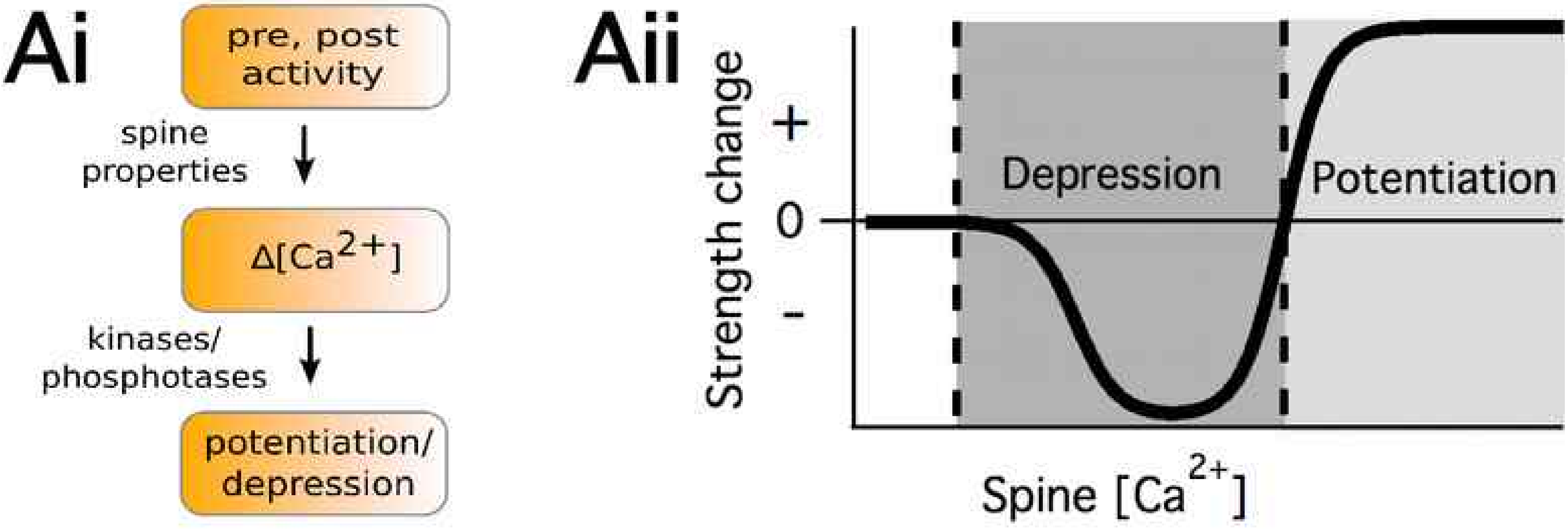


[Sobczyk '05]



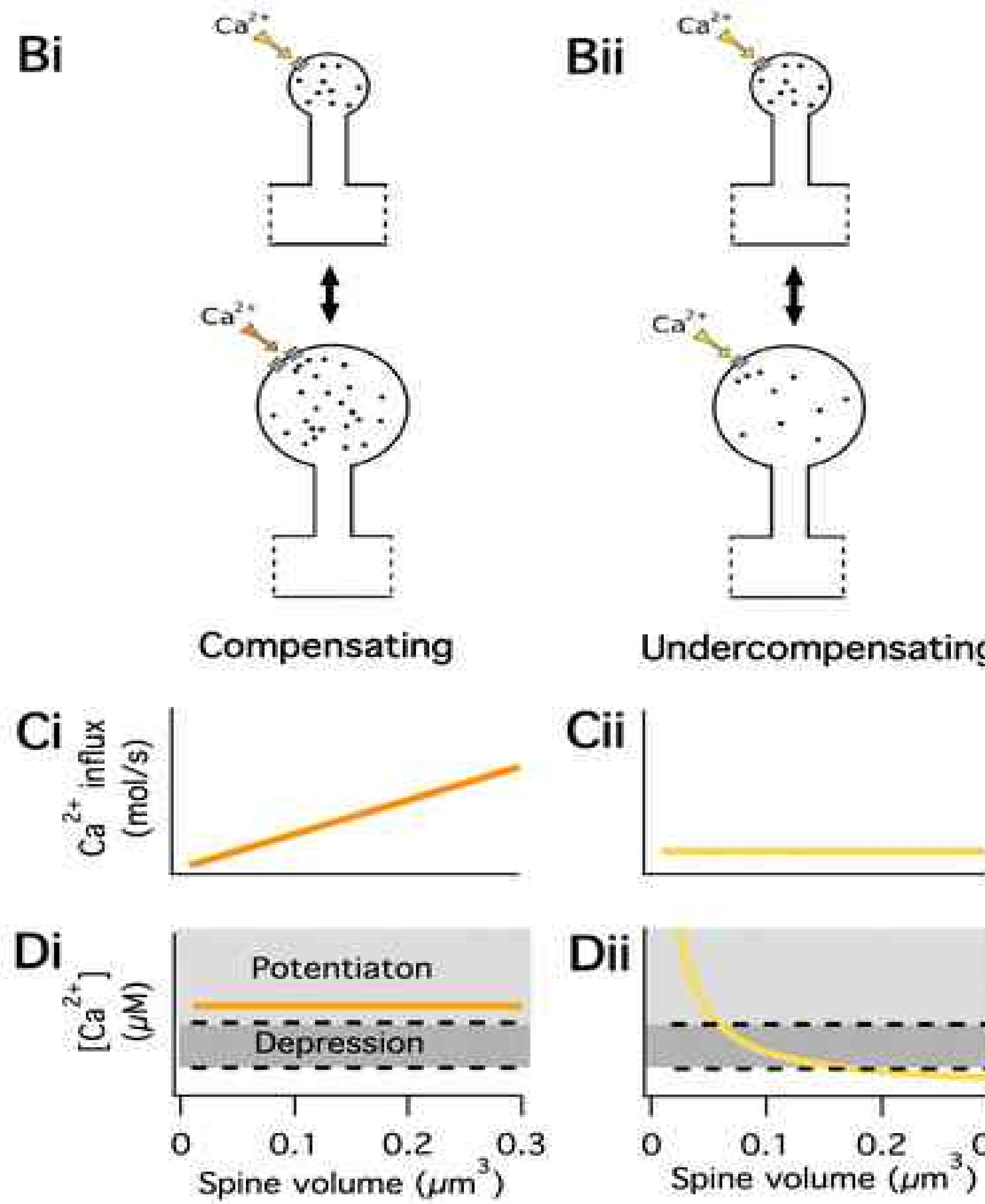
[Noguchi'05]

Modelling plasticity



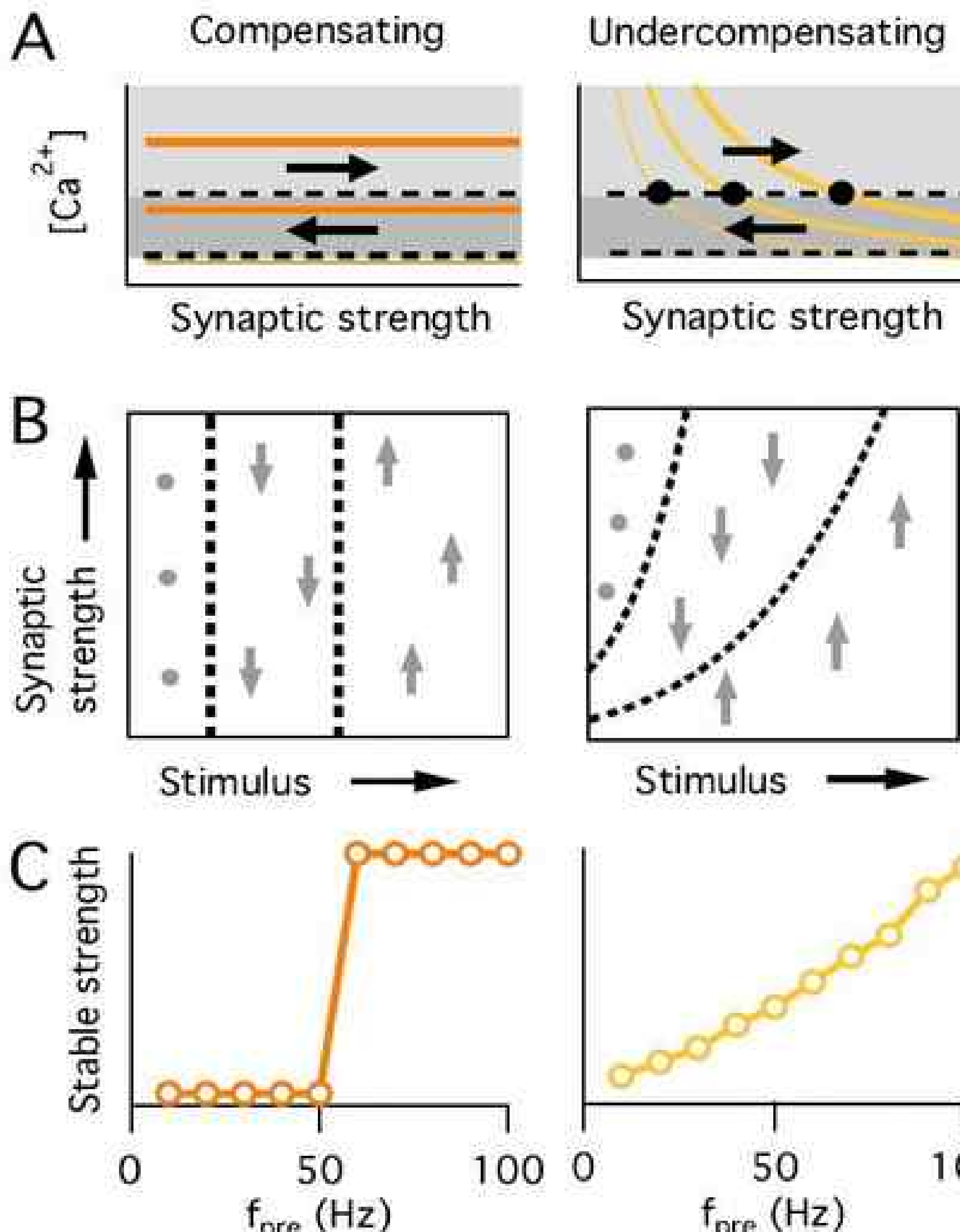
[e.g. Shouval et al '02]

Ca-volume scenarios

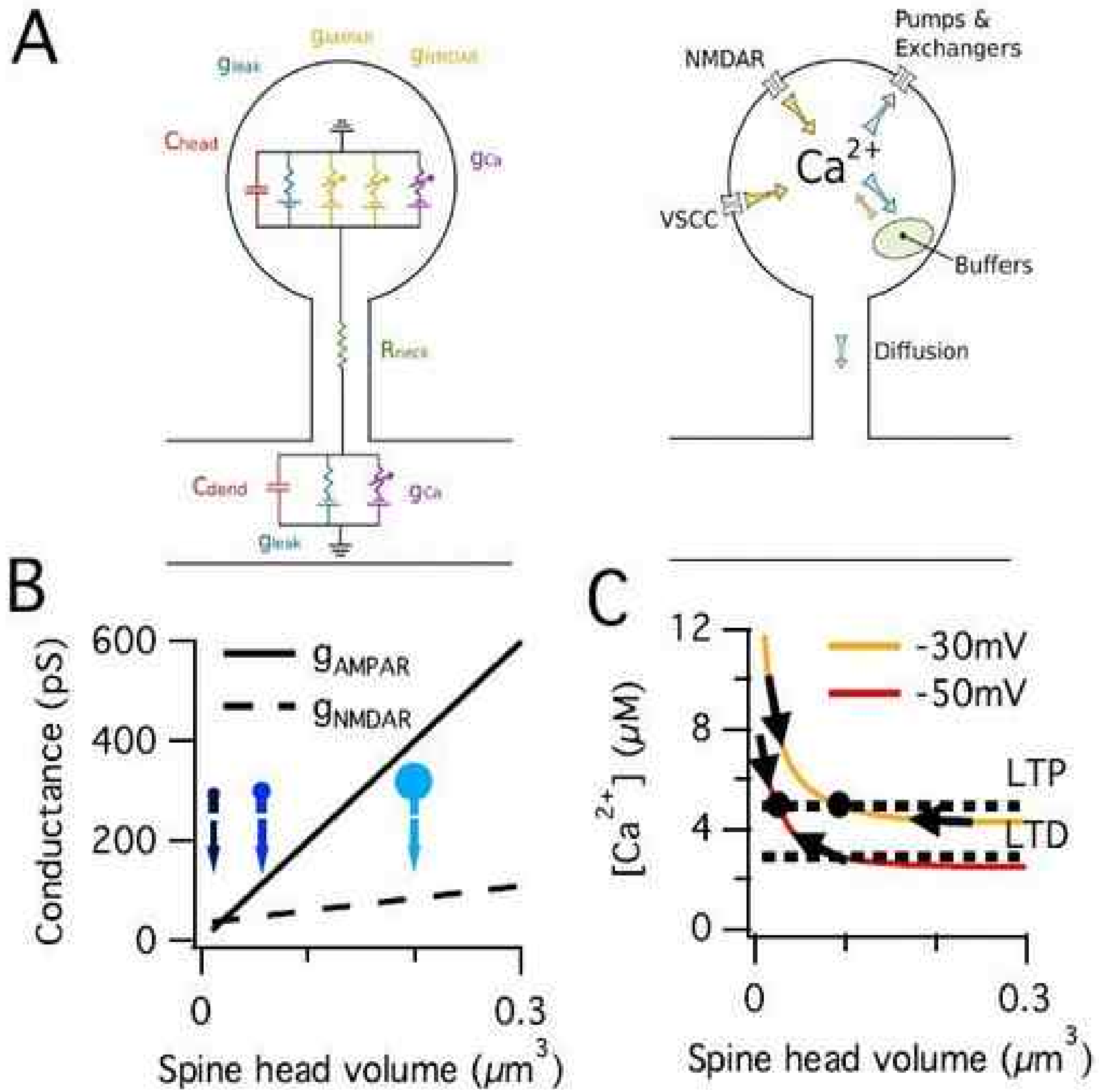


[O'Donnell, Nolan & MvR, 2011]

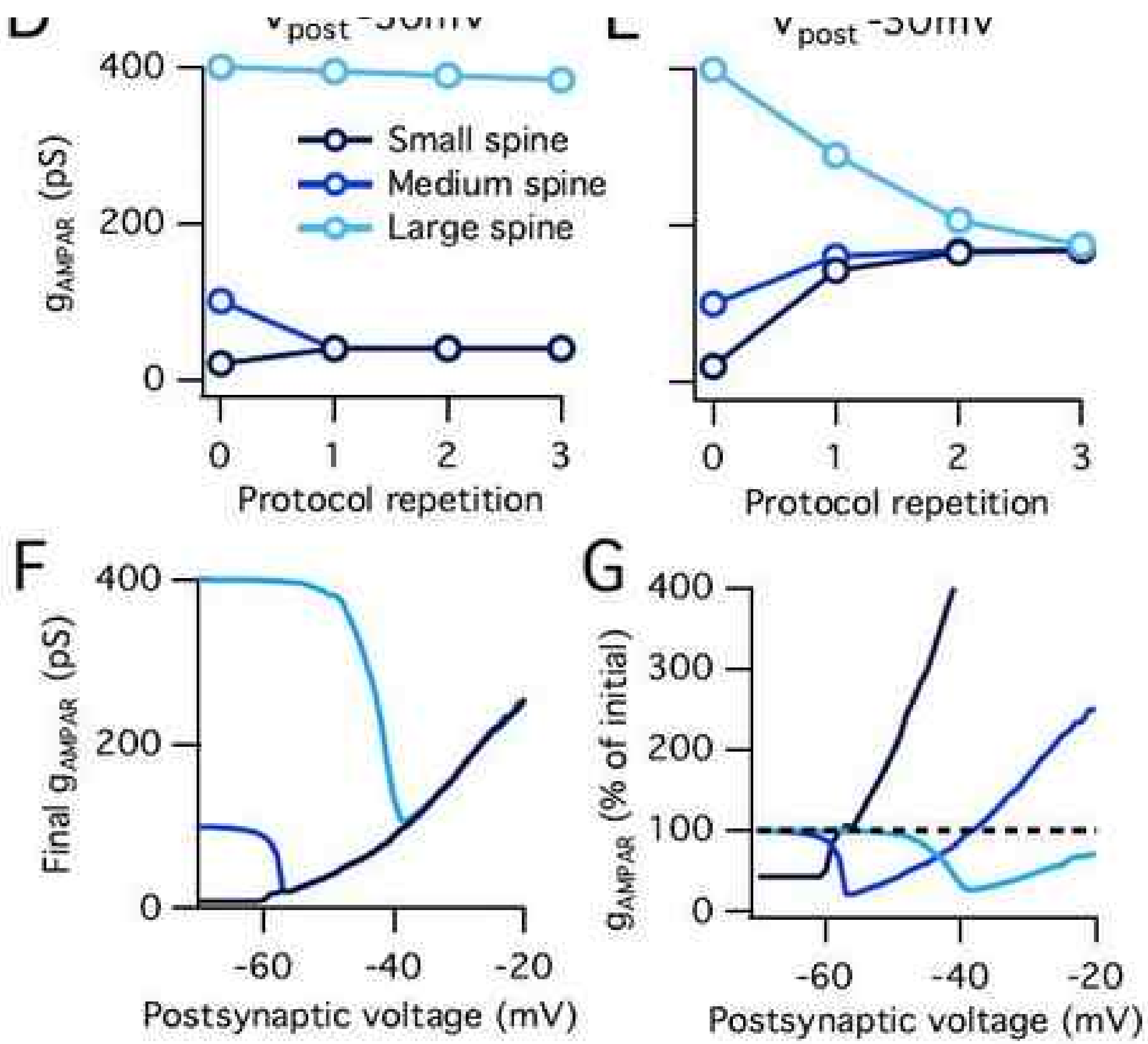
Calcium scenarios



Biophysical implementation

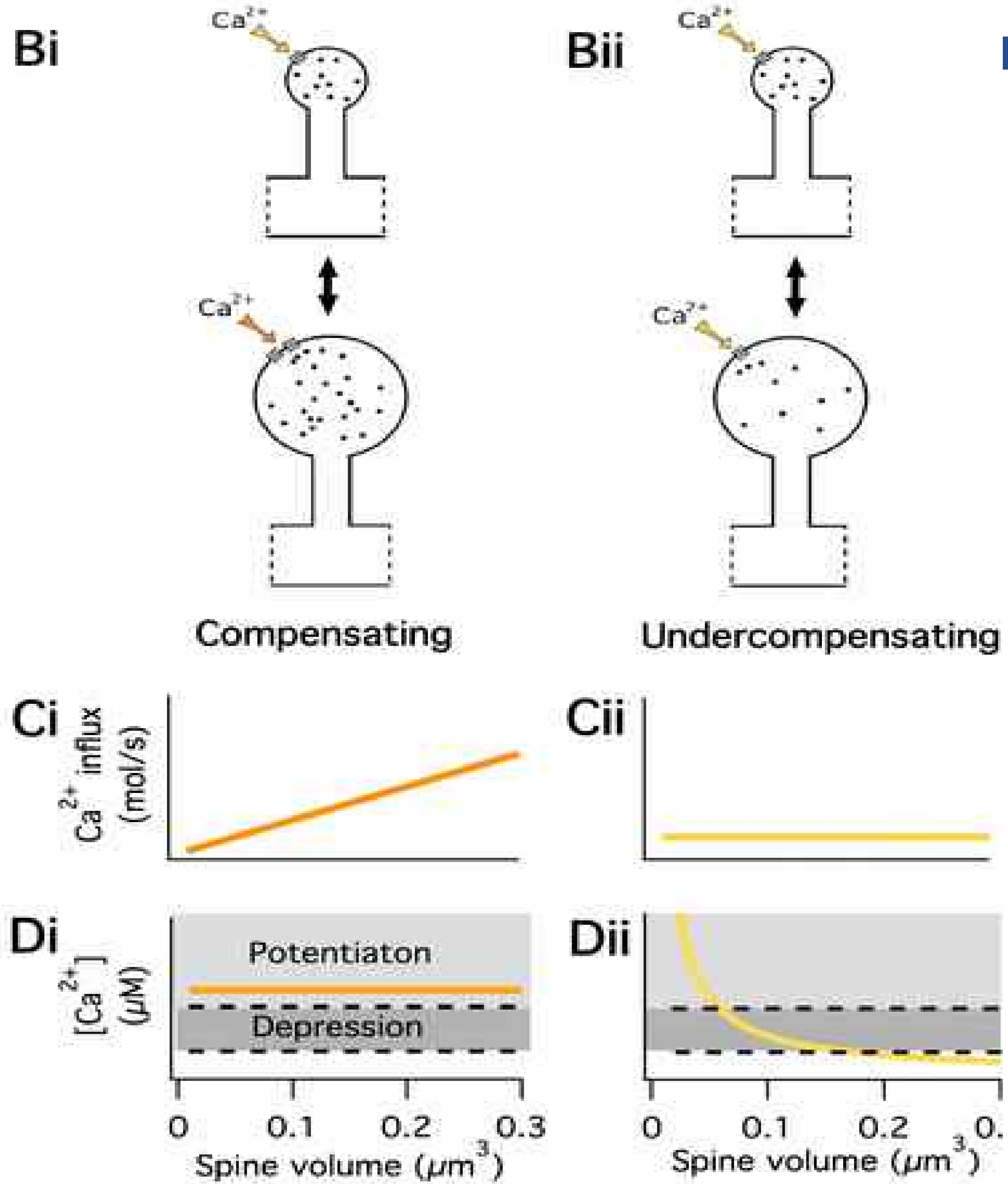


Weight dependent plasticity curves

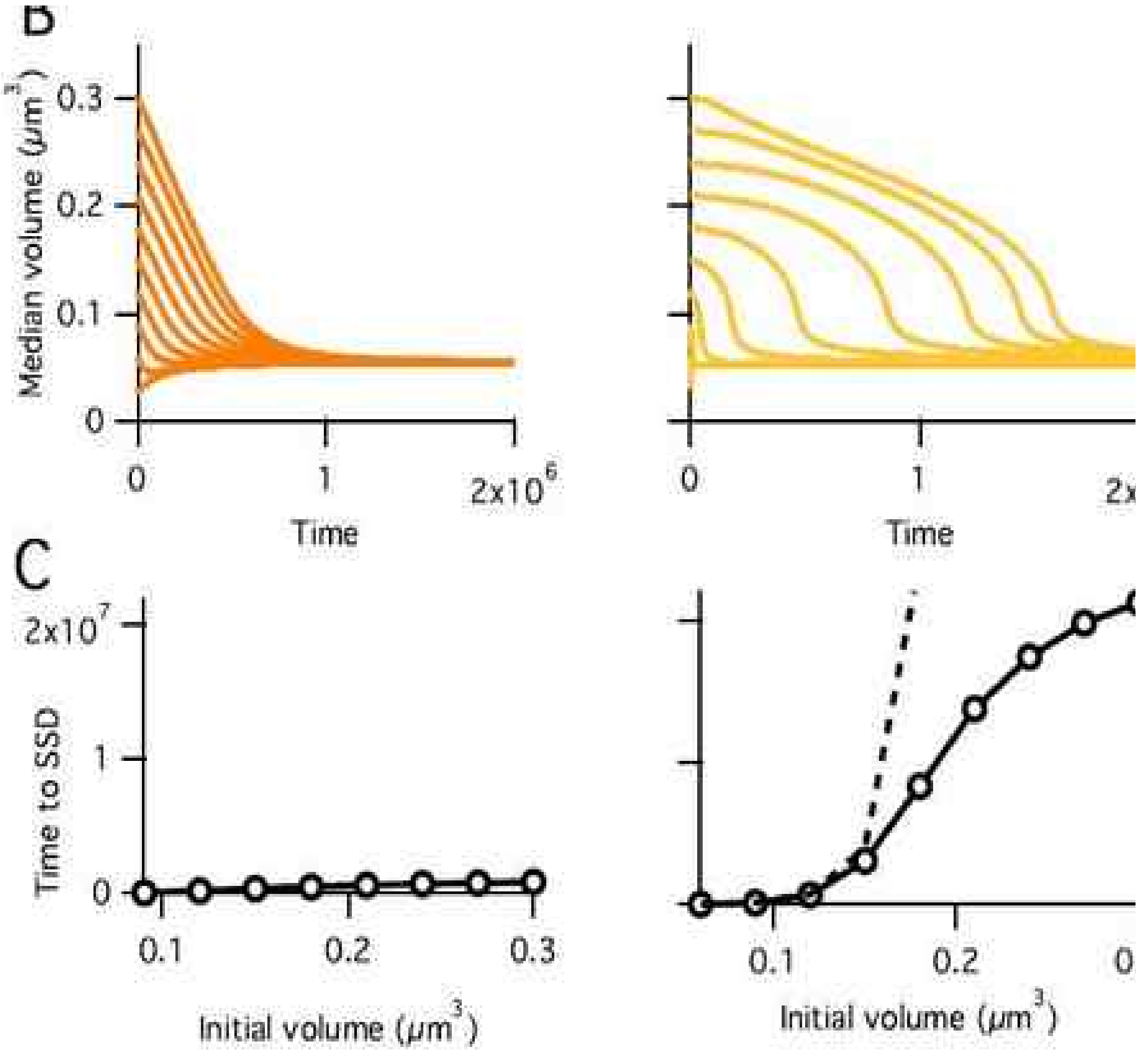


- see also [Kalantzis & Shouval '09]
- Might help to explain experimental variability

Meta-stability of large synapses

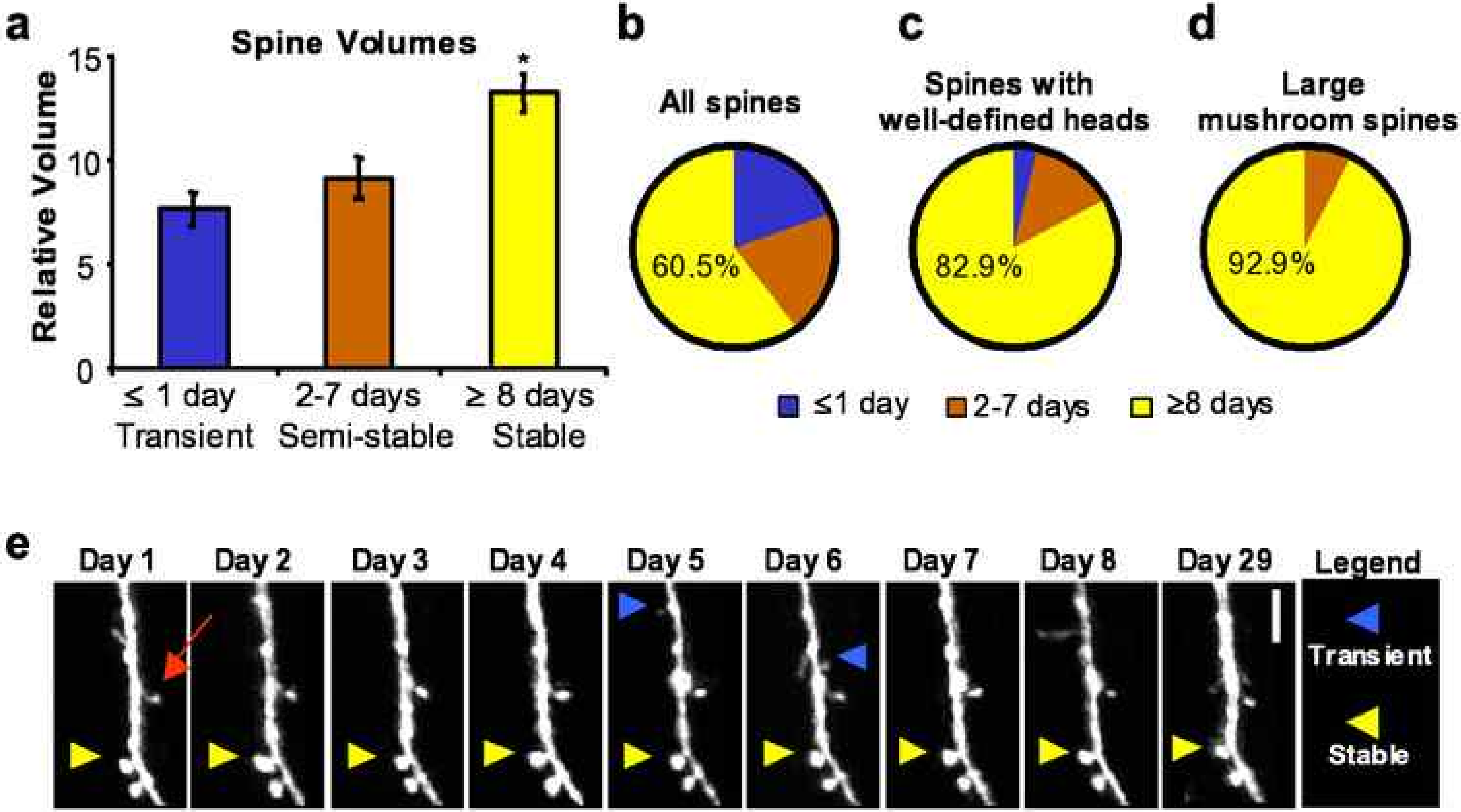


Under-compensation freezes large weights



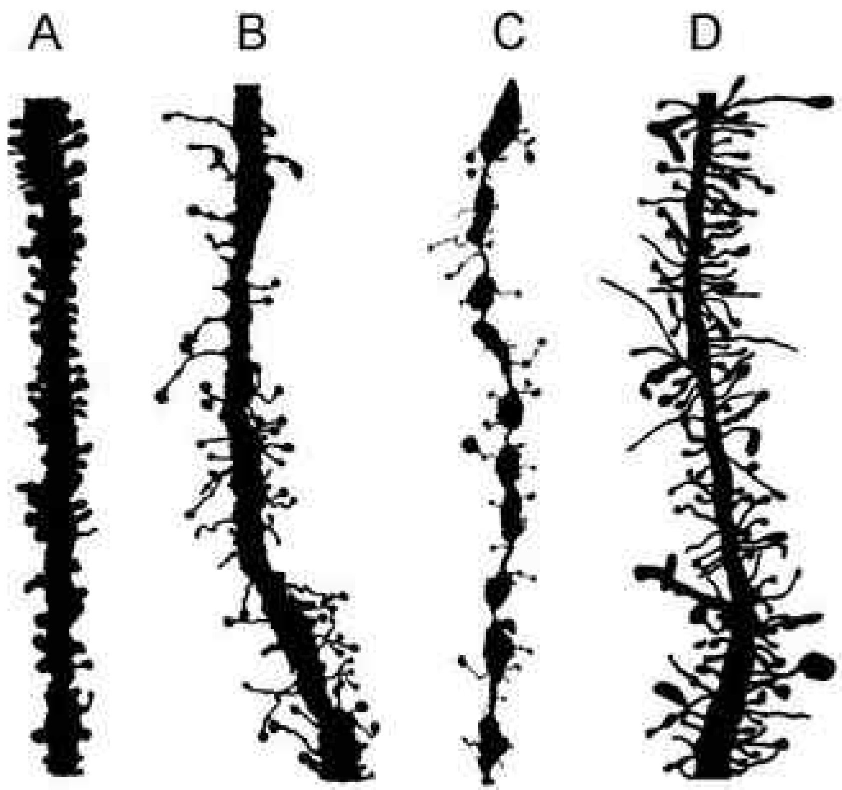
Note, contrasts with most softbound rules.

Large spines are more stable

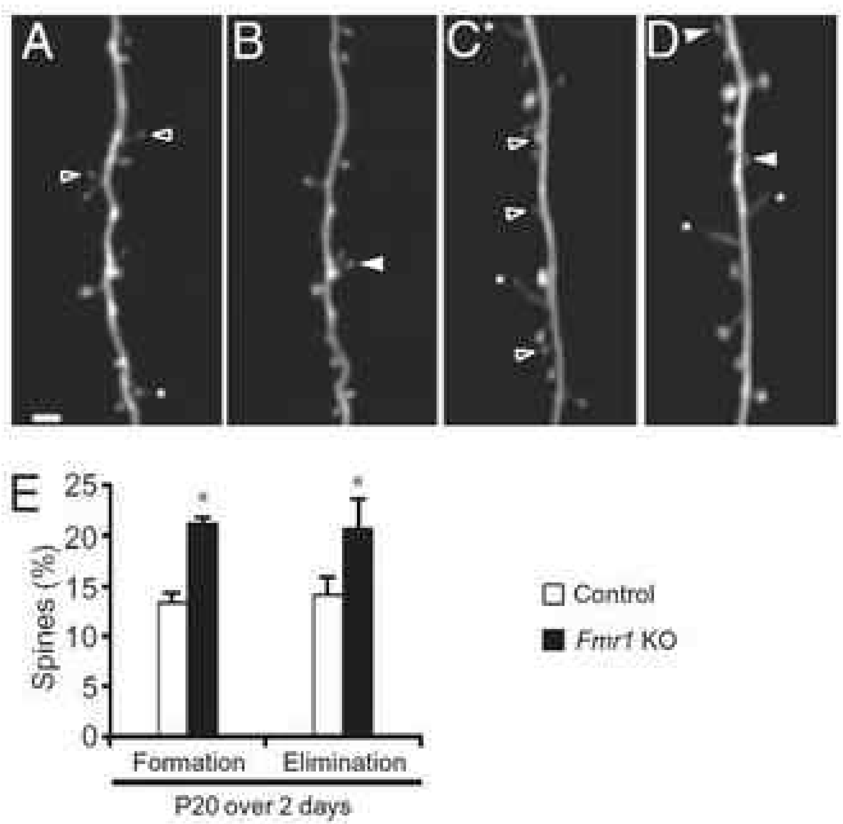


[from Trachtenberg '02 Supp Info]

Relation to disease?



[Fiala et al. '02]



[Pan et al. '10]

Spine plasticity

- Spine volume dynamics has strong effect on plasticity dynamics
- Can explain a number of plasticity phenomena
- Leads to meta-stable states

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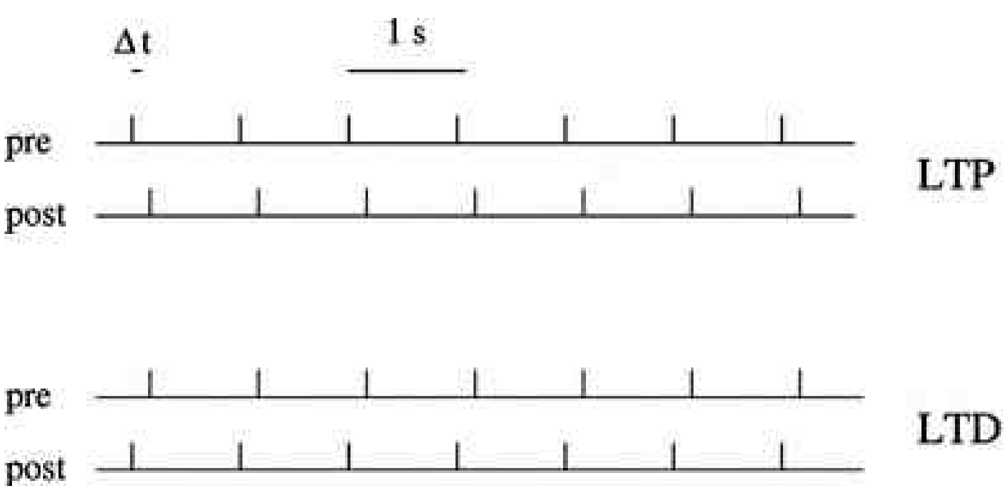
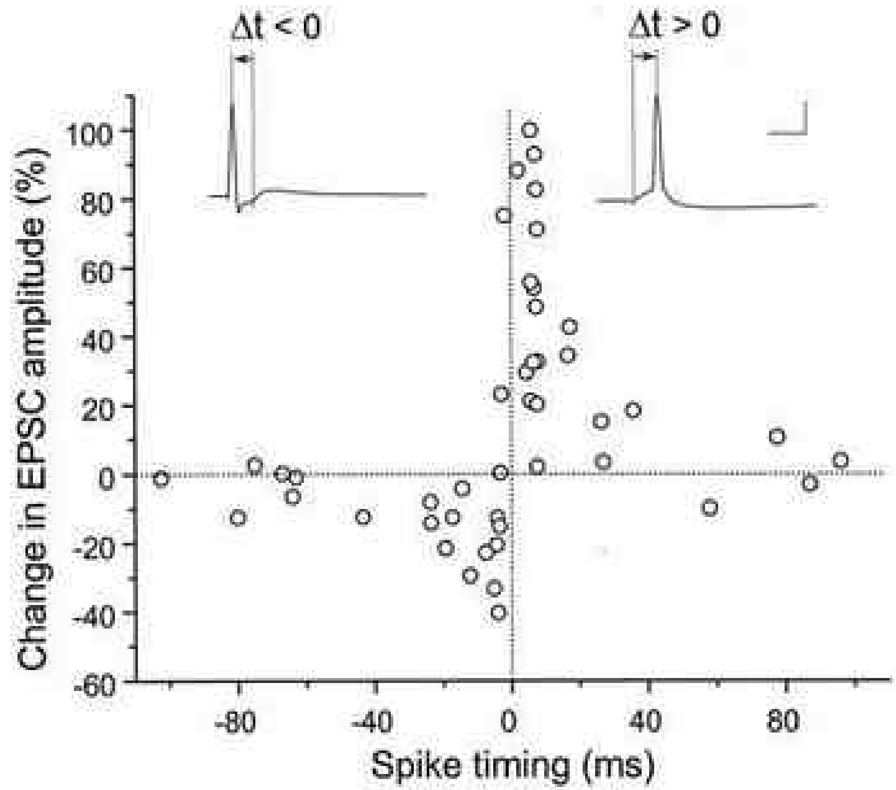
Spike Timing Dependent Plasticity: Experimental data



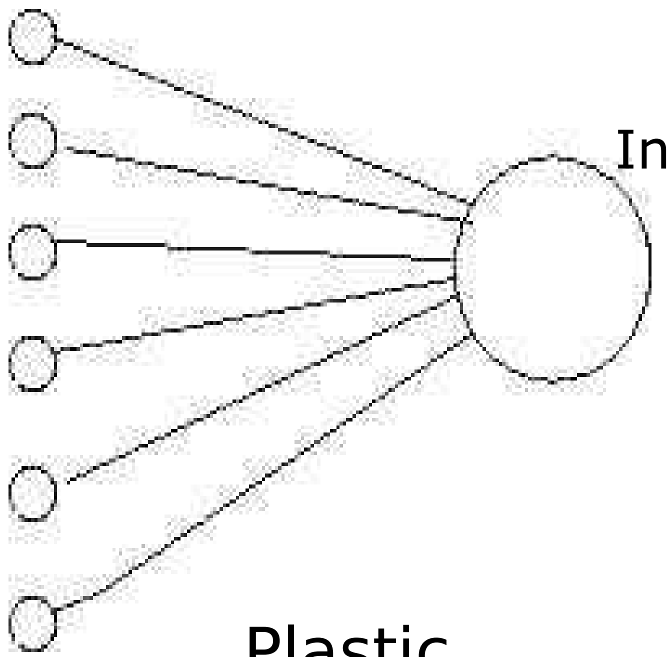


[Bi & Poo 1998]

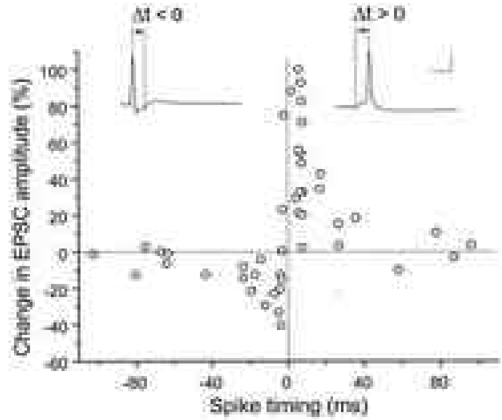
Modelling STDP

Poisson trains

Integrate & fire



Plastic

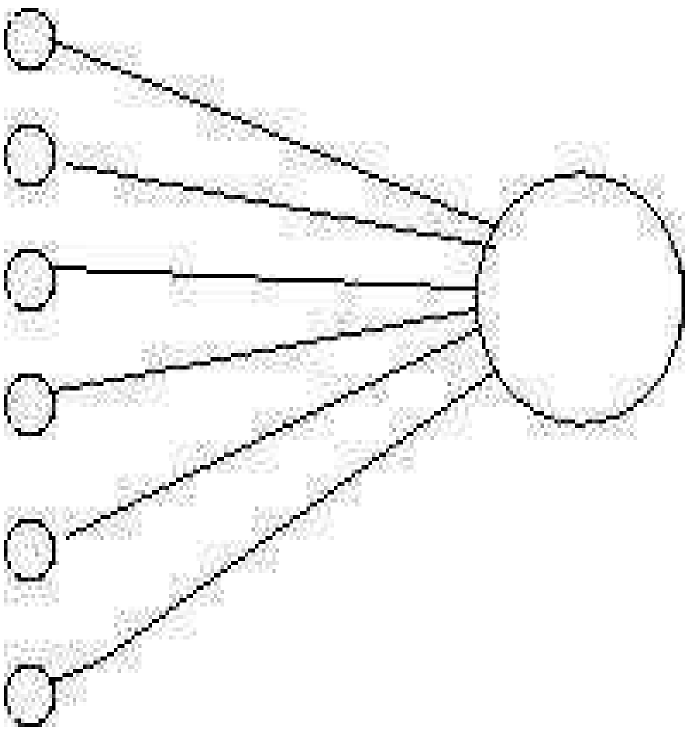


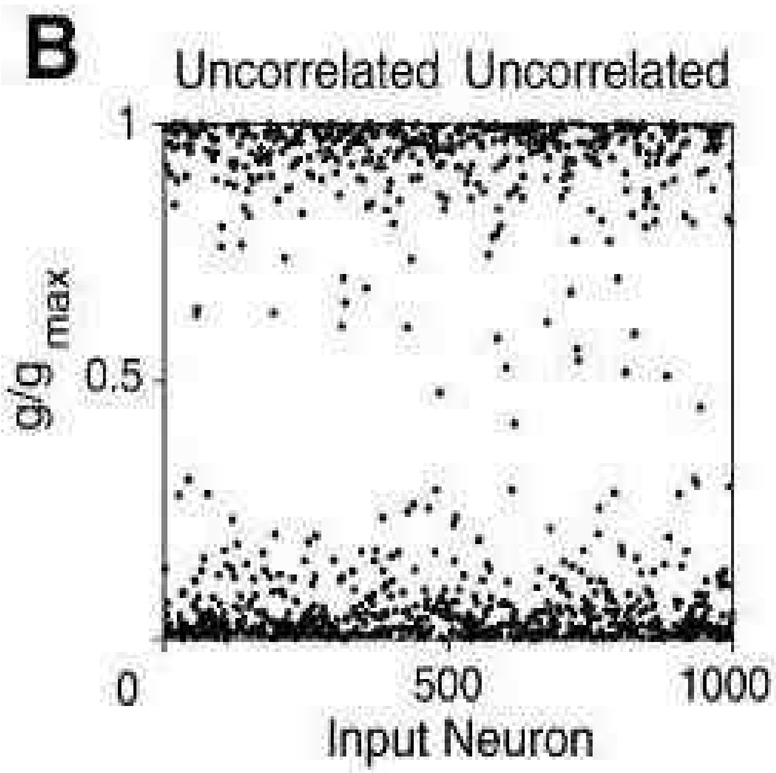
$$\Delta w = -A_{-} e^{-(t_{post} - t_{pre})/\tau_{-}}$$

$$\Delta w = A_{+} e^{-(t_{pre} - t_{post})/\tau_{+}}$$

Modelling STDP

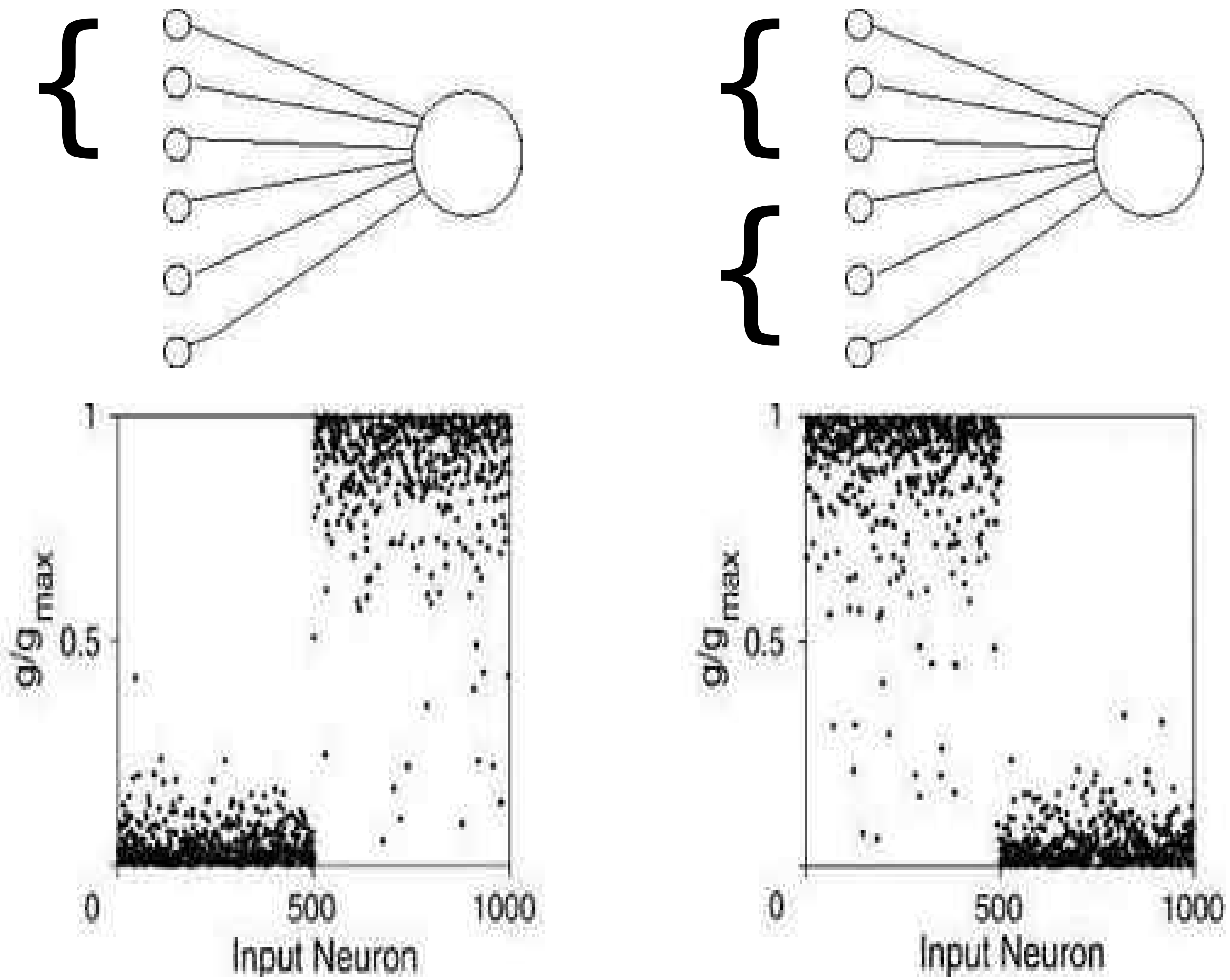
Poisson trains





Modelling STDP

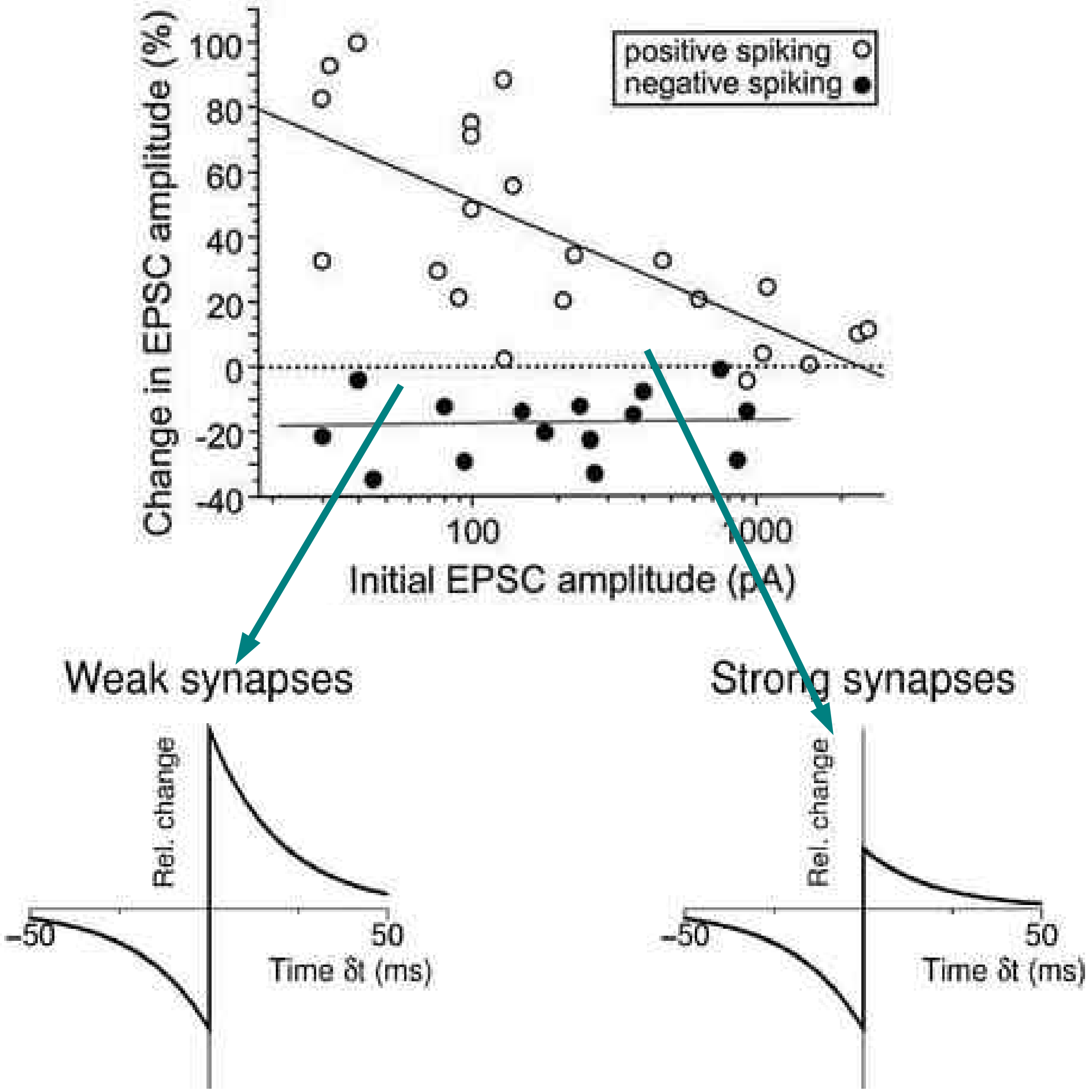
Correlated Poisson trains



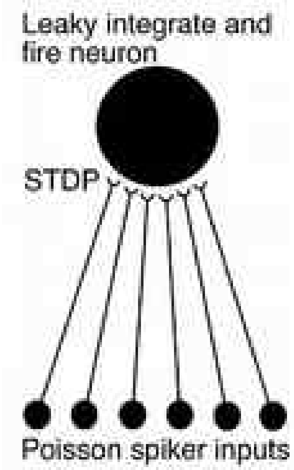
- Require hard bounds on weights
- Competitive

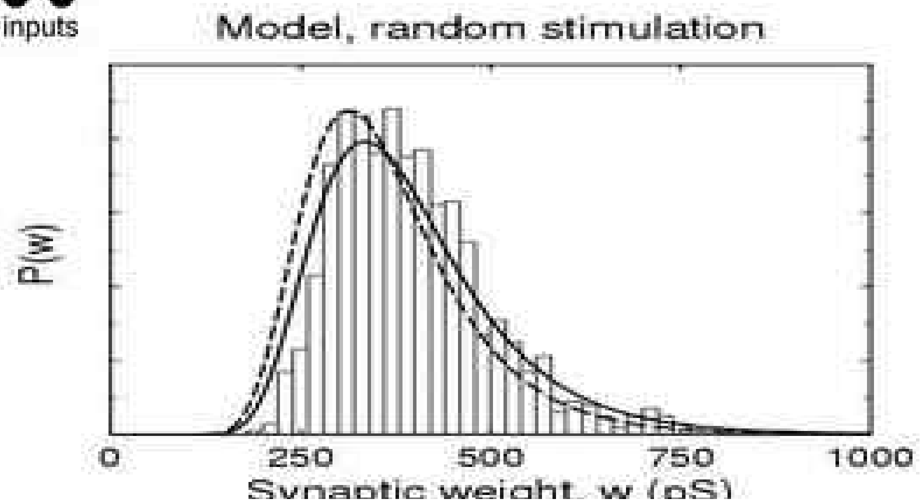
[Song & Abbott '01]

But STDP is weight dependent ('soft bounds')



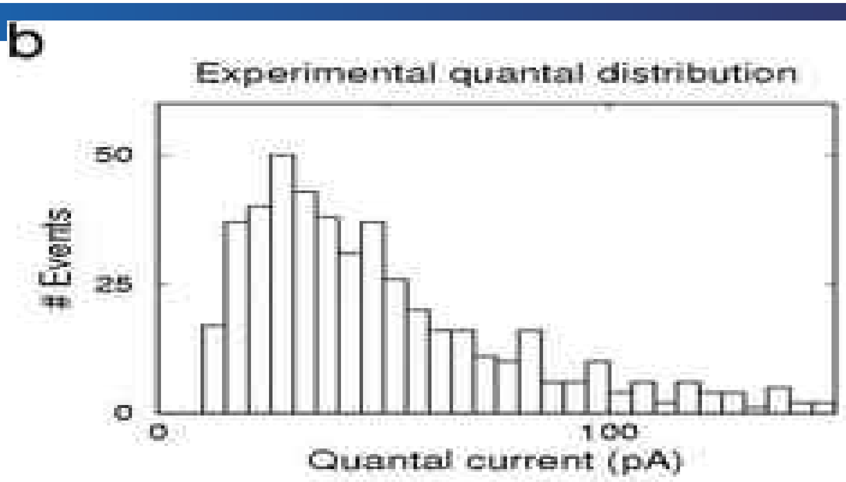
Weight dependence leads to observed weight distribution

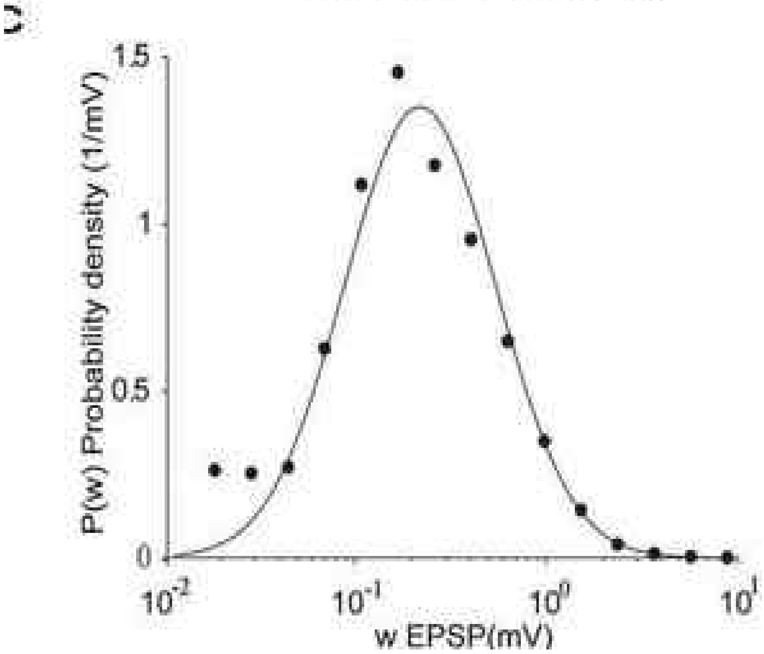




$$P(w) \propto \frac{e^{\operatorname{atan} w}}{\sqrt{1+w^2}}$$

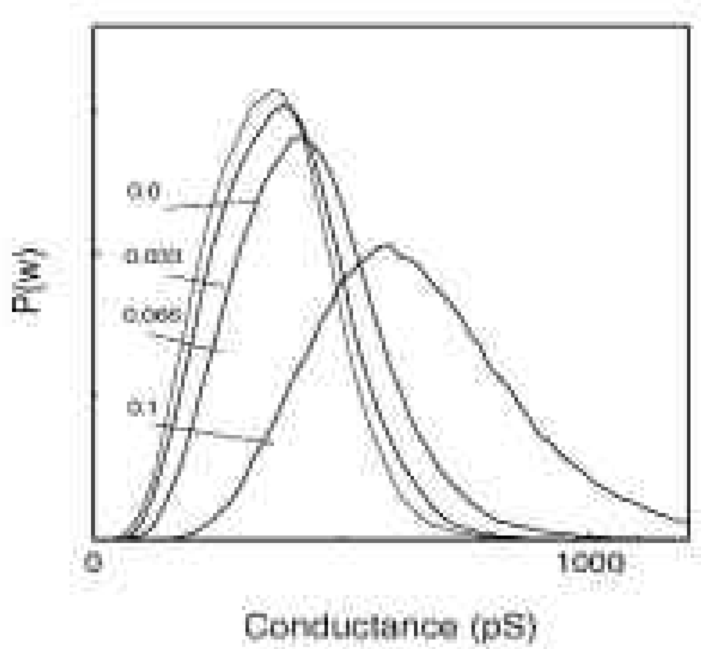
[MvR, Bi, Turrigiano '00]

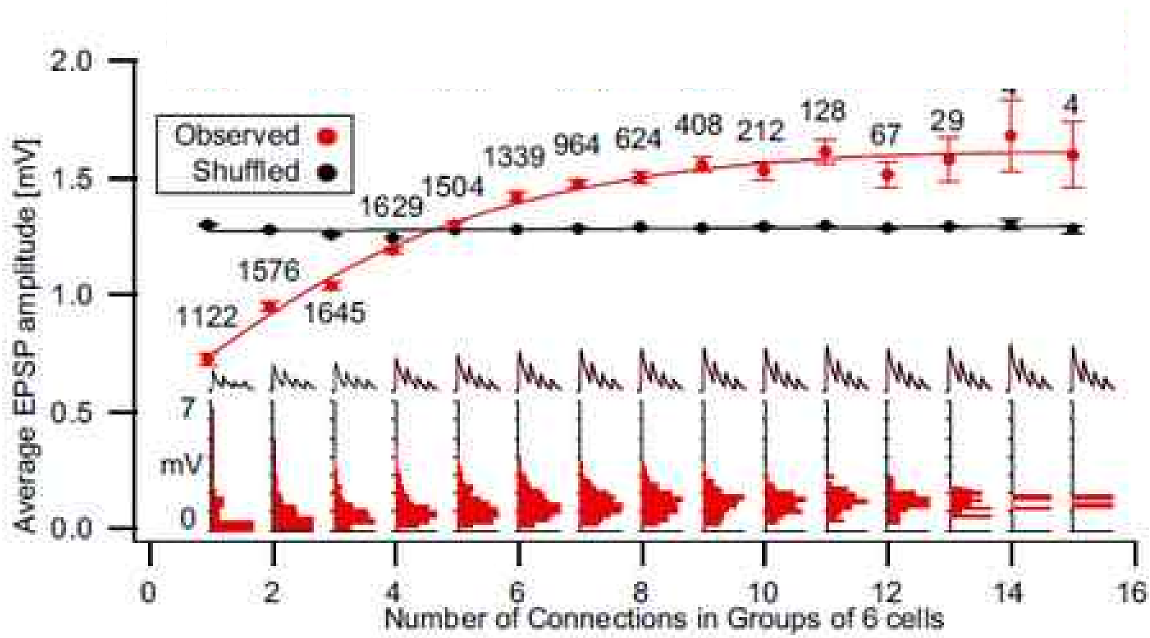




[Song et al '05]

Weight vs correlation

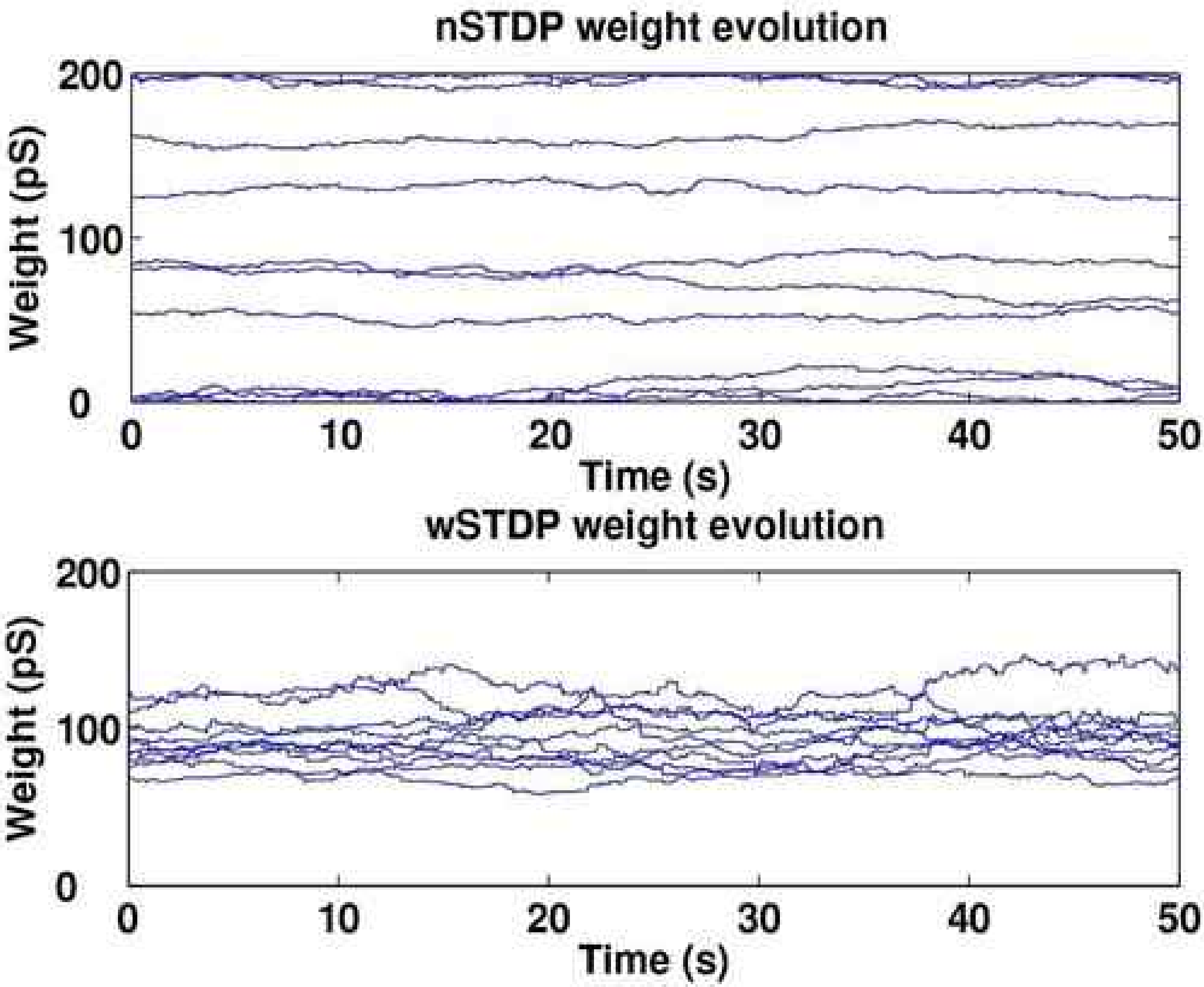


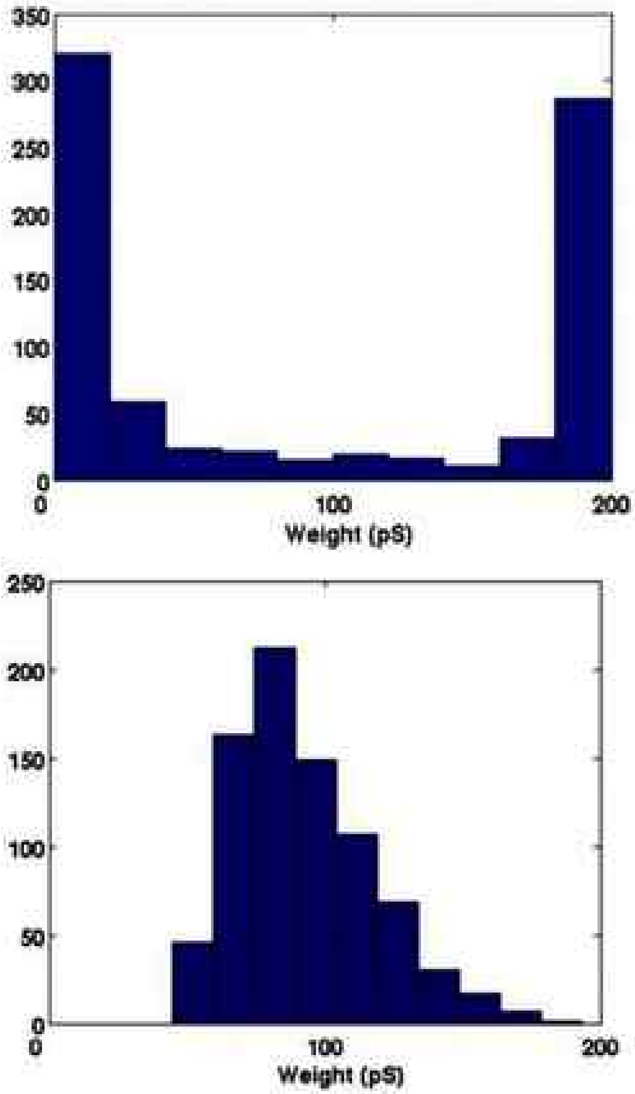


[MvR Turrigiano '01]

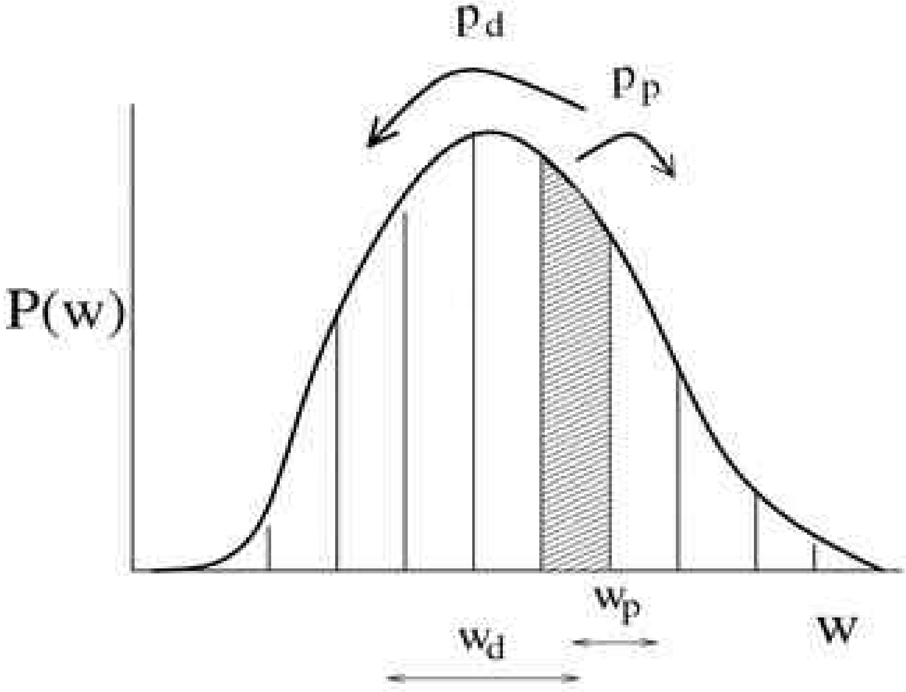
[Perin & Markram'11]

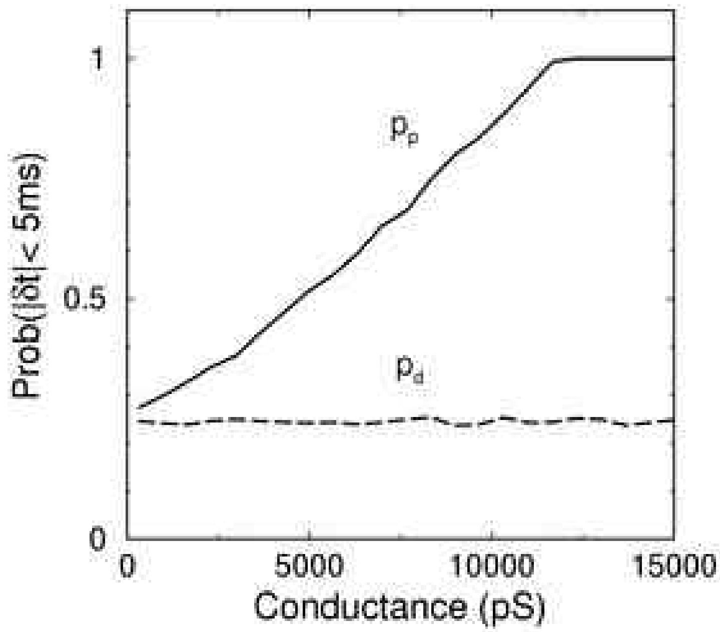
Ongoing background activity leads to weight fluctuations





Fokker-Planck approach





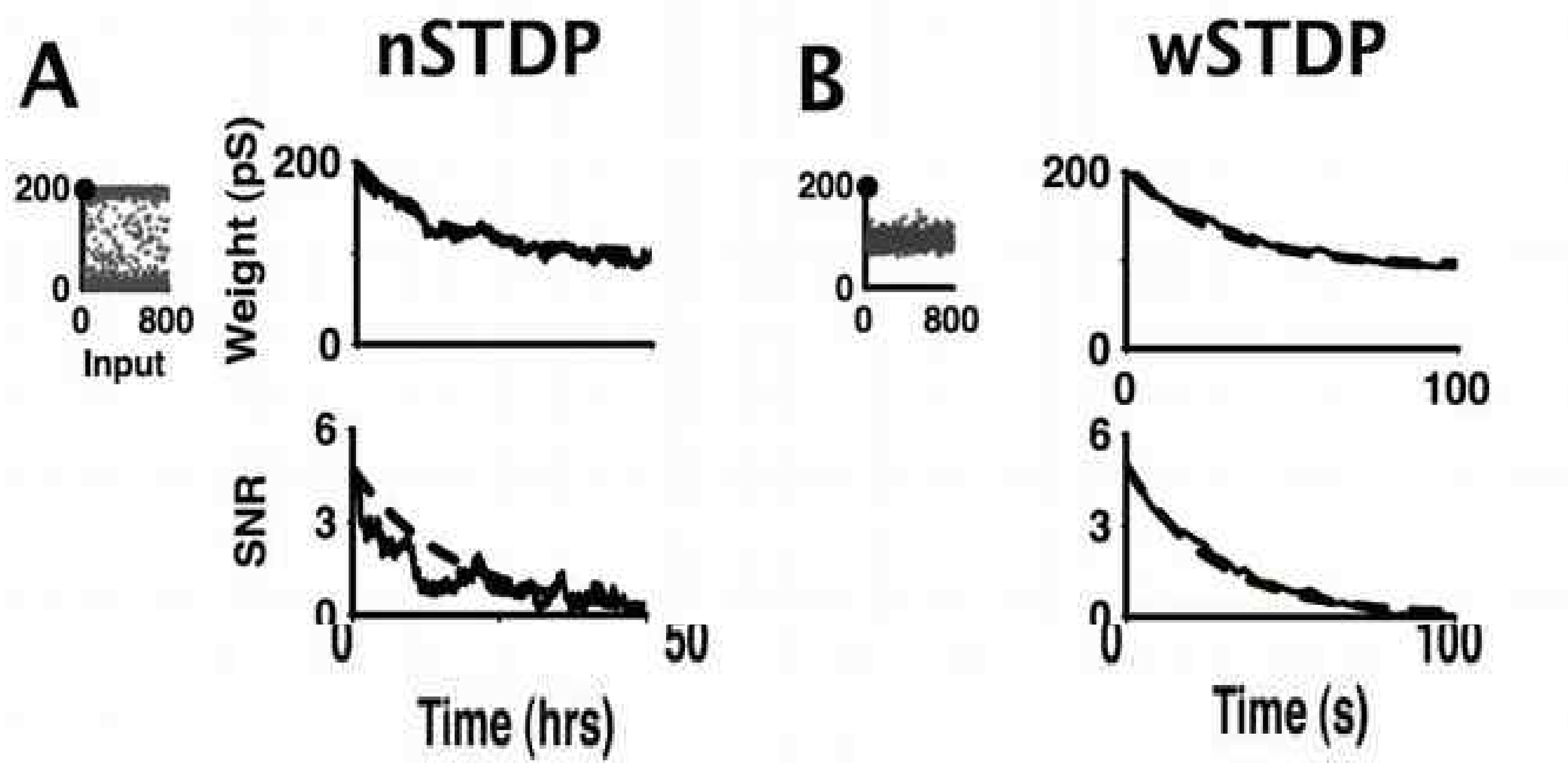
$$p_p = p_d (1 + w / \Sigma w)$$

drift diffusion

$$\frac{\partial P(w,t)}{\partial t} = \frac{-\partial}{\partial w}[A(w)P(w,t)] + \frac{1}{2}\frac{\partial^2}{\partial w^2}[D P(w,t)]$$

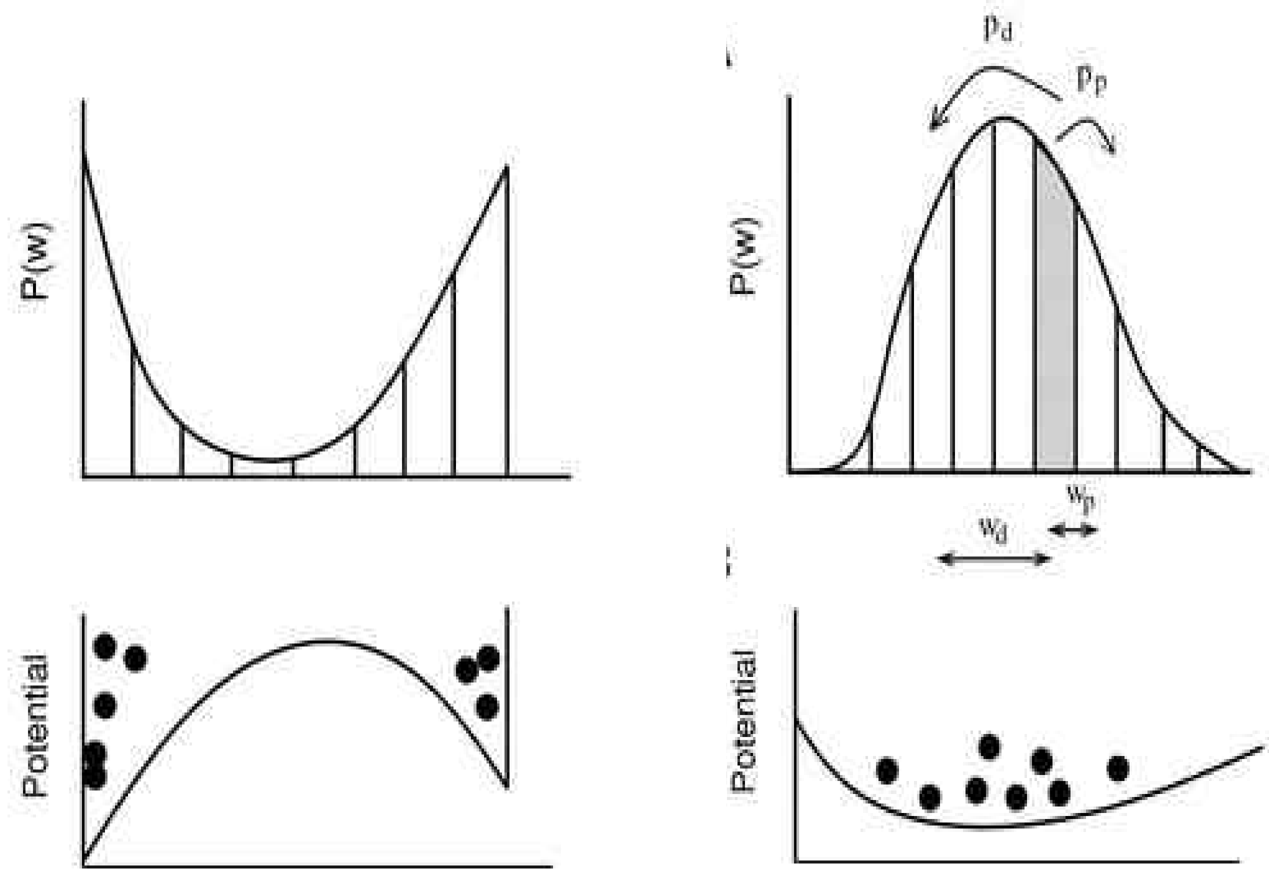
$$A(w) = -p_d c_d w + p_p c_p$$

Weight dependence leads to volatile memories



- Spontaneous activity leads to memory decay
- Decay is exponential
- Decay is much faster for weight dependent STDP

Weight dependence leads to quick forgetting



Weight dependence leads to quick forgetting

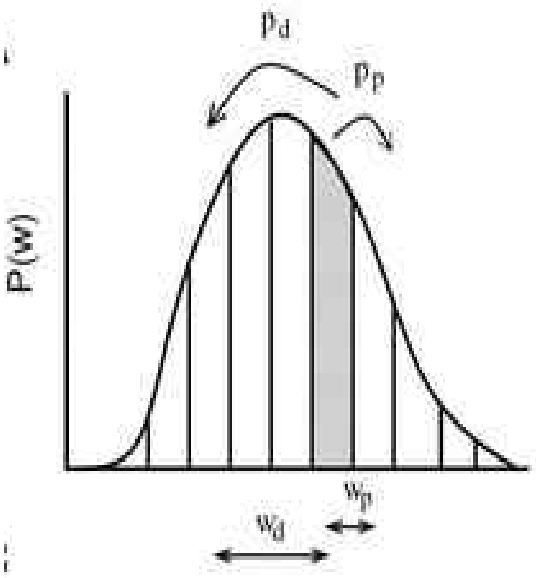
Langevin equation, dominated by drift

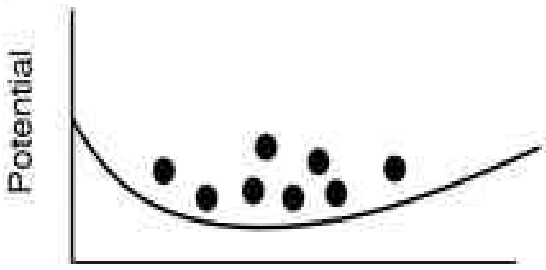
$$w(t+\mathrm{d}t) = w(t) + A(w)\mathrm{d}t + N(0,c)\sqrt{\mathrm{d}t}$$

$$A(w) = \alpha[w_0 - w(t)]$$

$$\langle w(0)w(t+\mathrm{d}t)\rangle - \langle w(0)w(t)\rangle = \alpha[\langle w(0)\rangle w_0 - \langle w(0)w(t)\rangle]\mathrm{d}t$$

$$C(t) = \frac{1}{\sigma^2}[\langle w(0)w(t)\rangle - \langle w(0)\rangle^2]$$
$$= \exp(-\tau\_a\_\nu_{\mathrm{pre}}\nu_{\mathrm{post}}\mathrm{t})$$





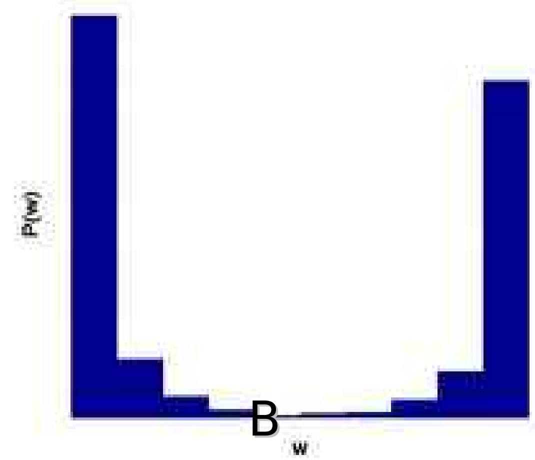
Fluctuation-dissipation theorem

Calculating the nSTDP autocorrelation

From statistical mechanics find the potential that goes with the equilibrium distribution:

$$U(w) = \frac{\sigma}{A_-}\left(\epsilon\, w - \frac{1}{2W_{tot}} w^2\right)(0 < w < w_m)$$

U(w)

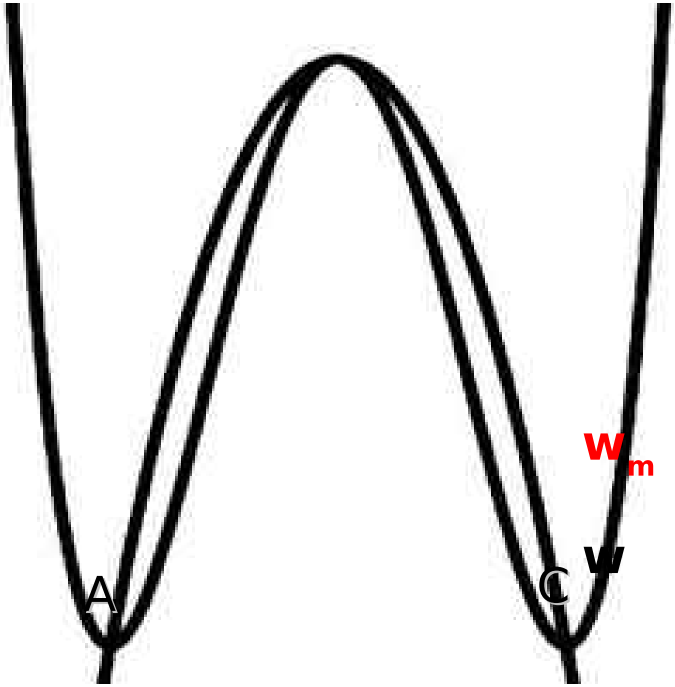


Approximate with a quartic:

$$U_a(w) = \frac{\sigma}{2 w_m^2 A_- W_{tot}} w^2 (4w^2 - 6ww_m + {w_m}^2 - 4\epsilon\, wW_{tot} + 6\epsilon\, w_m W_{tot})$$

Now we can calculate the Kramers escape rate from one well to the other

$$\tau_{\uparrow} = \frac{2\pi}{\sqrt{V_{\text{approx}}''(0)\,|V_{\text{approx}}''(w_p)|}} \exp\left(\frac{V_{\text{approx}}(w_p) - V_{\text{approx}}(0)}{\sigma}\right)$$



From this we find the autocorrelation time

$$\tau_{nSTDP} = \frac{T_{CA} T_{AC}}{T_{CA} + T_{AC}}$$

Weight dependence leads to quick forgetting

Langevin equation, dominated by drift

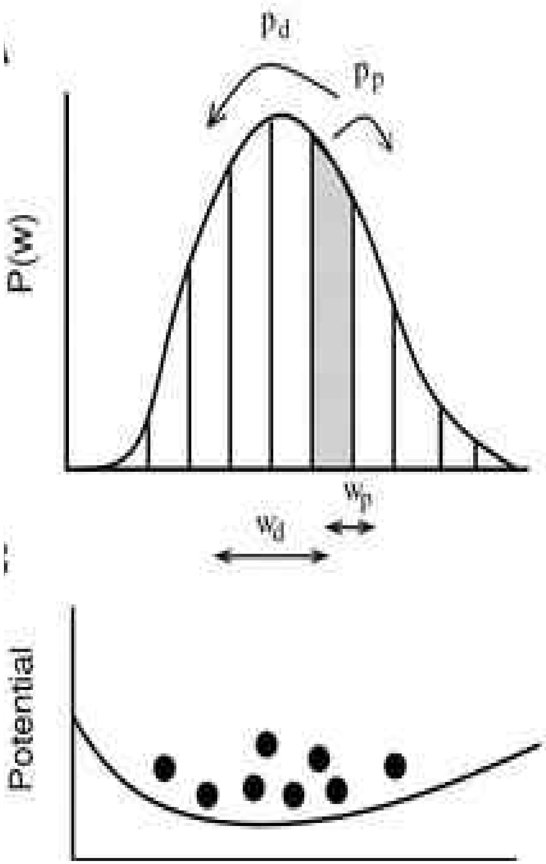
$$w(t + \mathrm{d}t) = w(t) + A(w)\mathrm{d}t + N(0, c)\sqrt{\mathrm{d}t}$$

$$A(w) = \alpha[w_0 - w(t)]$$

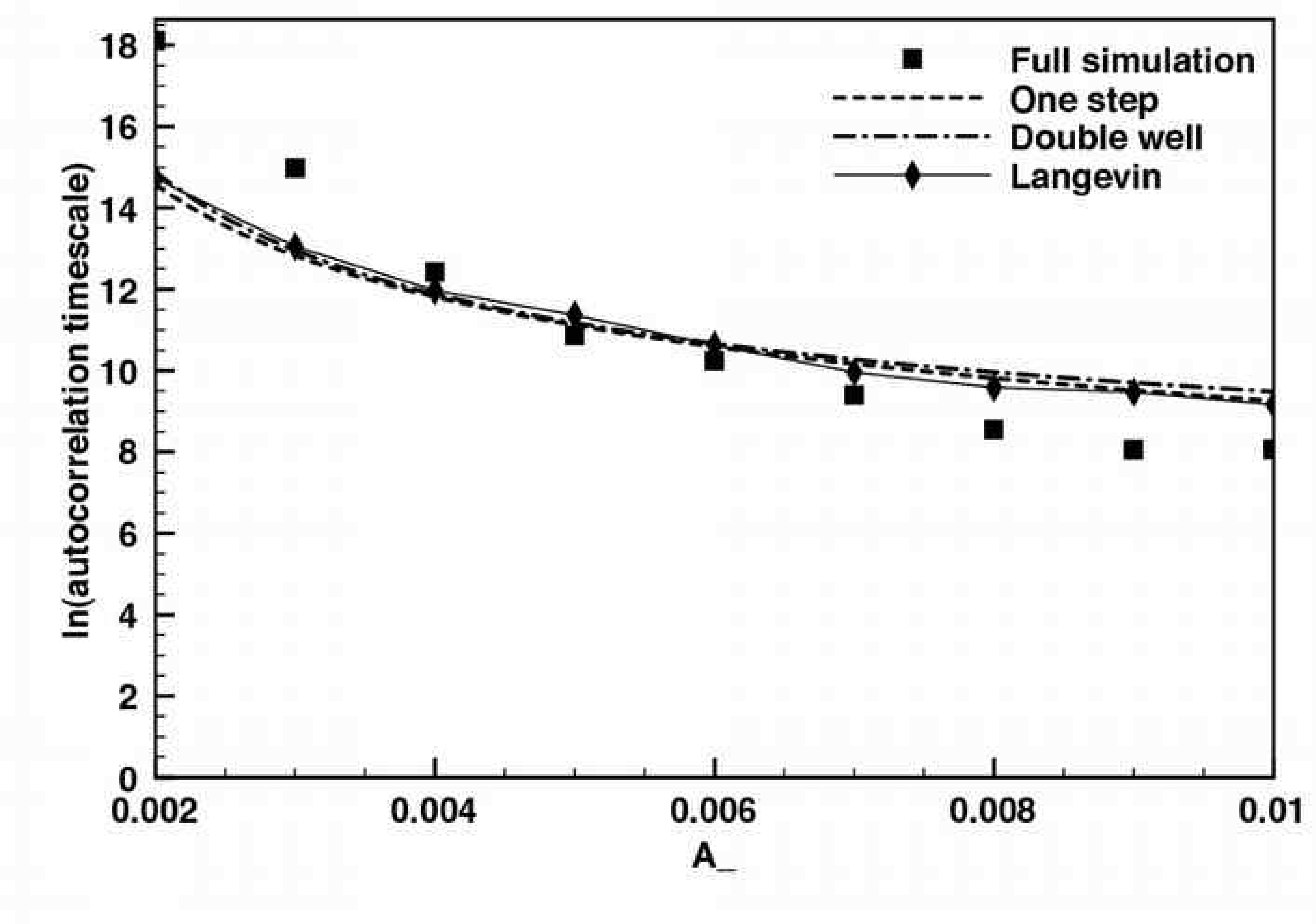
$$\langle w(0)w(t + \mathrm{d}t)\rangle - \langle w(0)w(t)\rangle = \alpha[\langle w(0)\rangle w_0 - \langle w(0)w(t)\rangle]\mathrm{d}t$$

$$C(t) = \frac{1}{\sigma^2}[\langle w(0)w(t)\rangle - \langle w(0)\rangle^2]$$

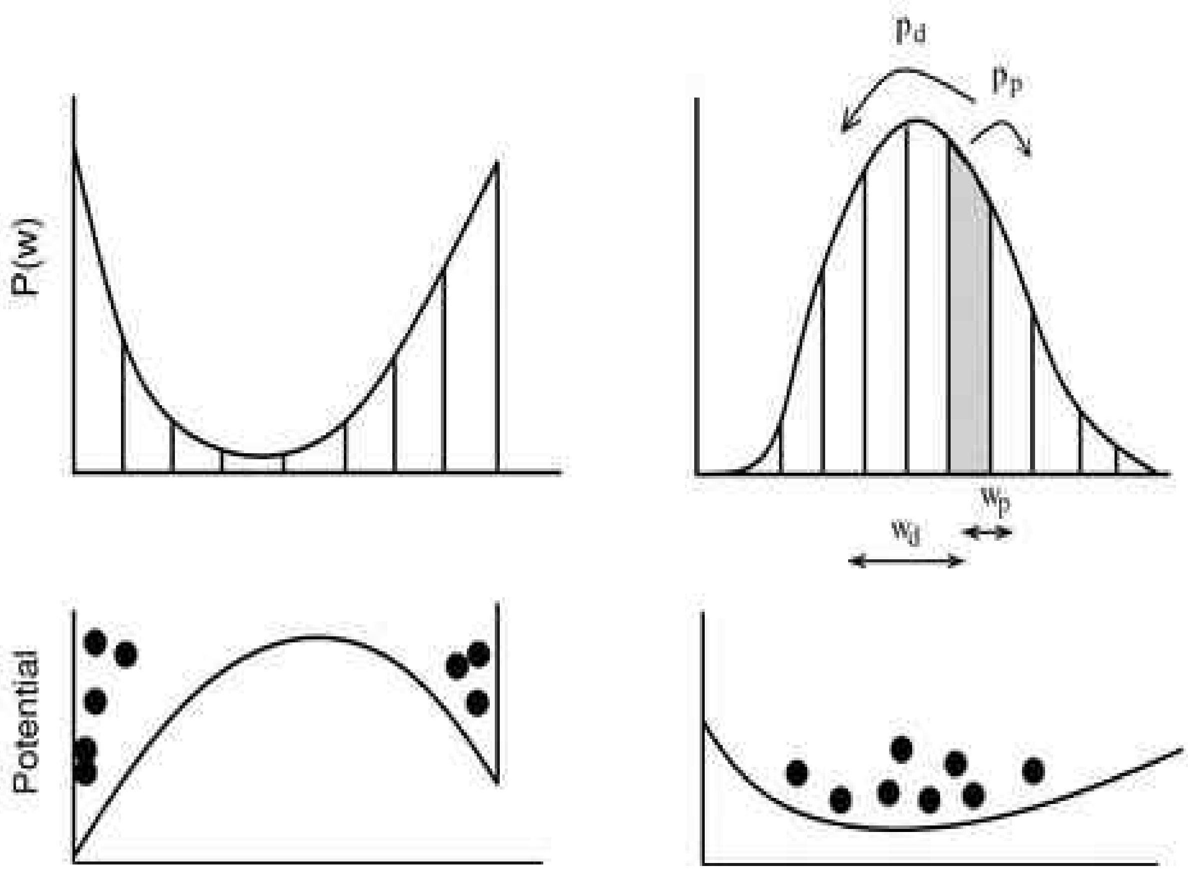
$$= \exp(-\tau\_a\_\nu_{\mathrm{pre}}\nu_{\mathrm{post}}t)$$



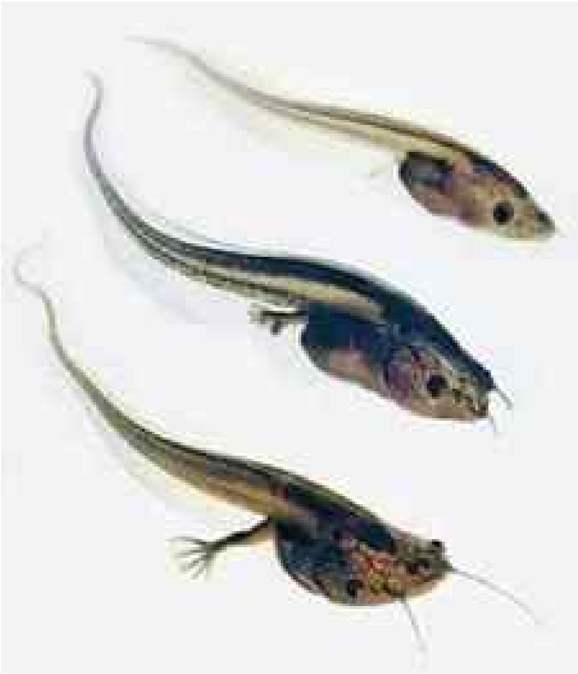
A_ vs autocorrelation timescale for nSTDP

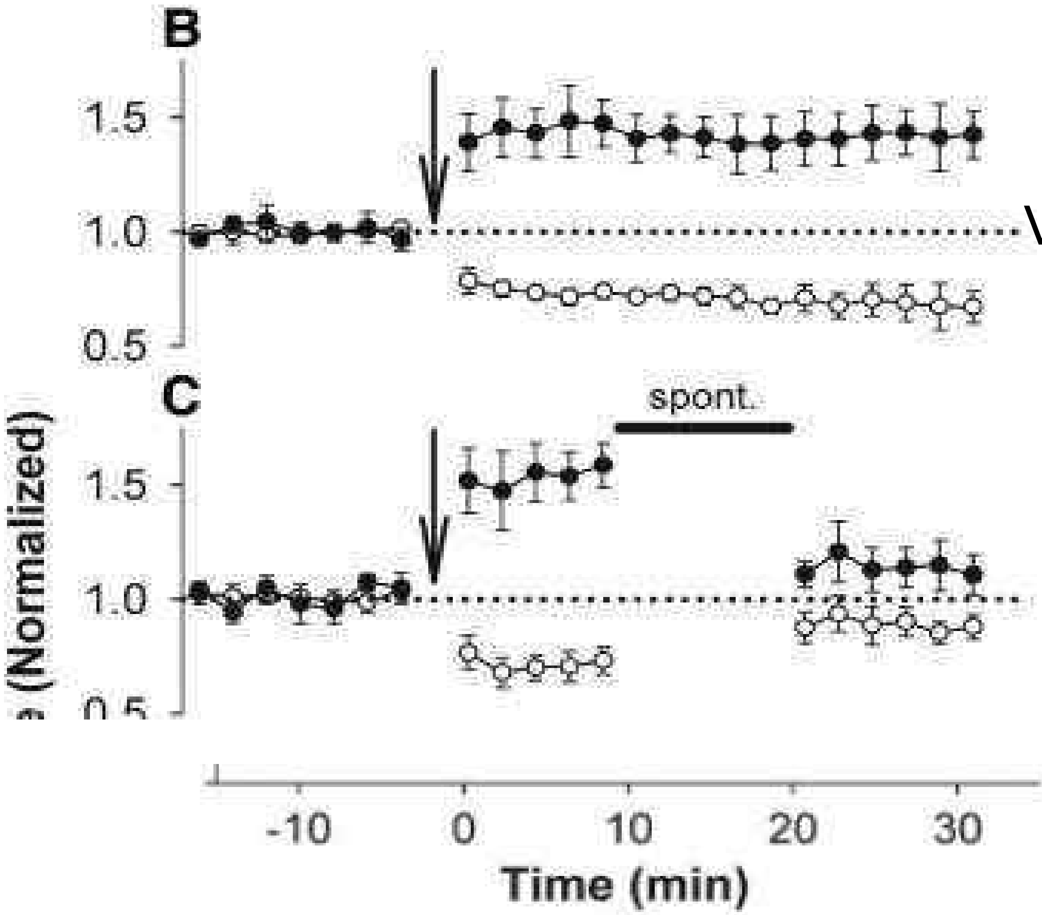


How weight dependence leads to quick forgetting



Experimental data: erasure by spontaneous activity





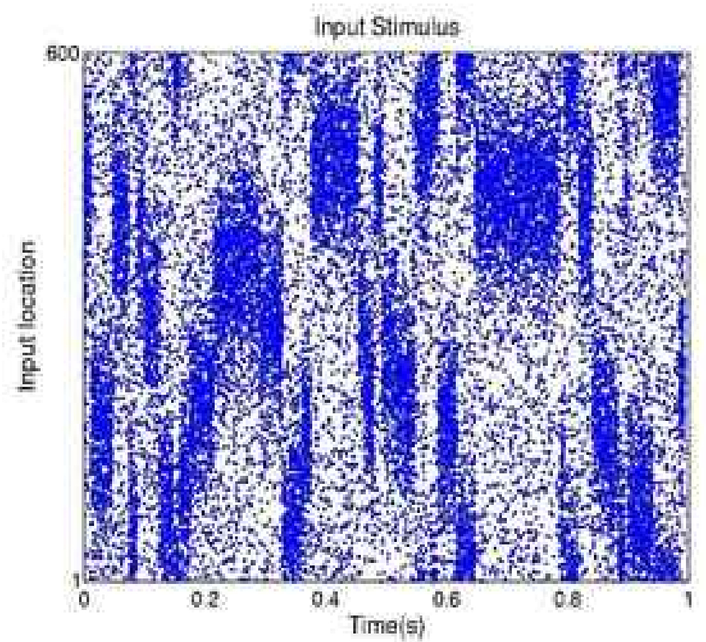
V-clamp

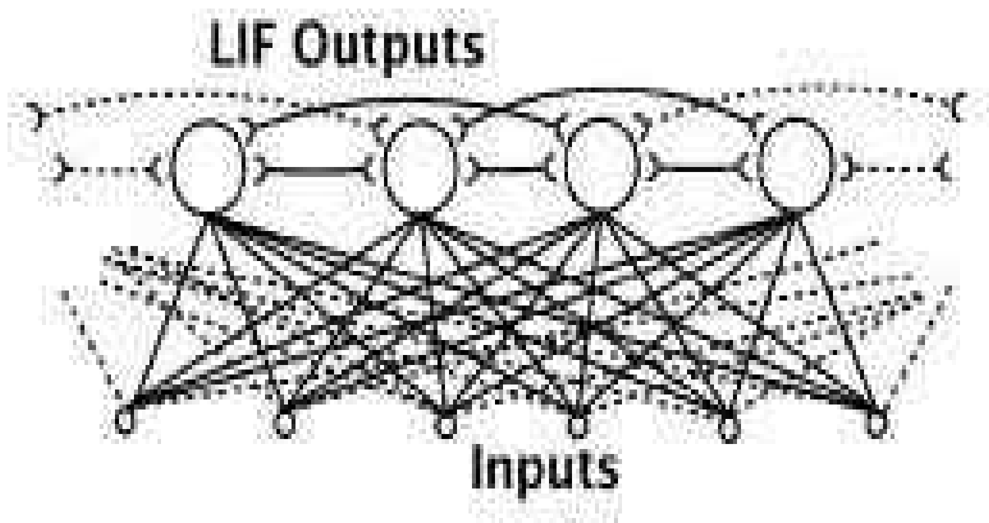
Xenopus tectum [Zhou & Poo, '03]

Are memories in *networks* are unstable?

Stability of receptive fields in networks

"V1"

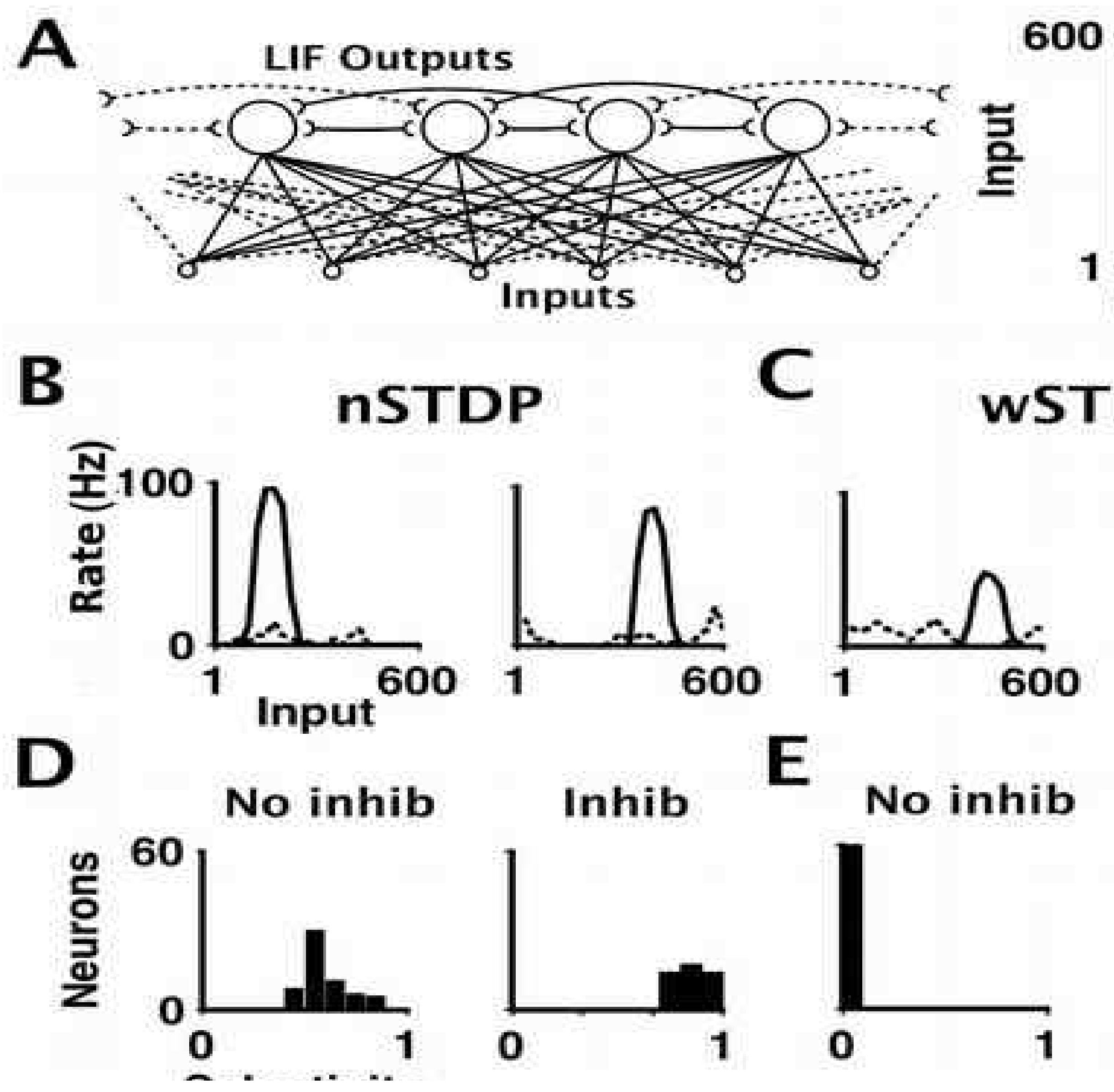




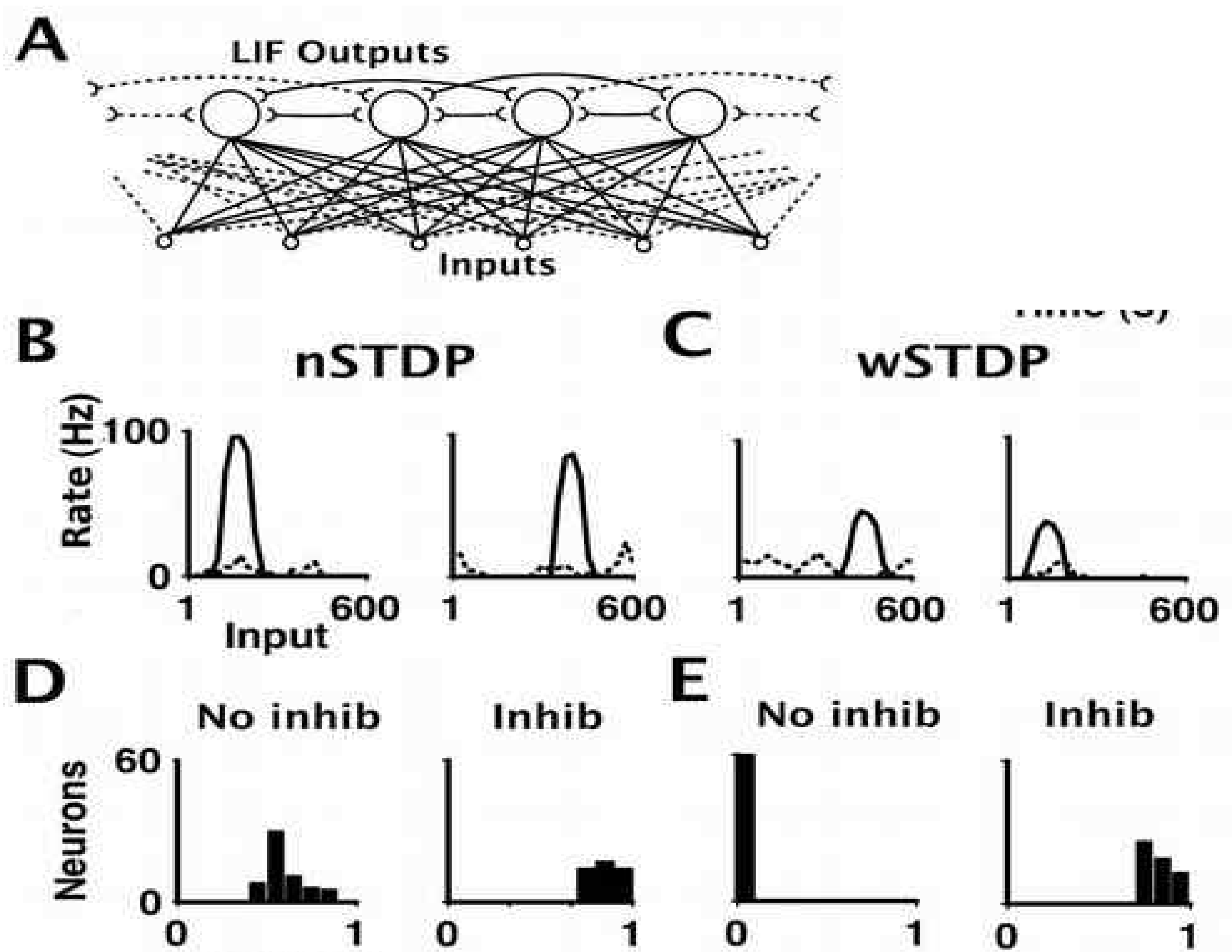
"LGN"

V1-like network

- Integrate and fire
- Variable lateral inhibition
- Sometimes plastic recurrent connections



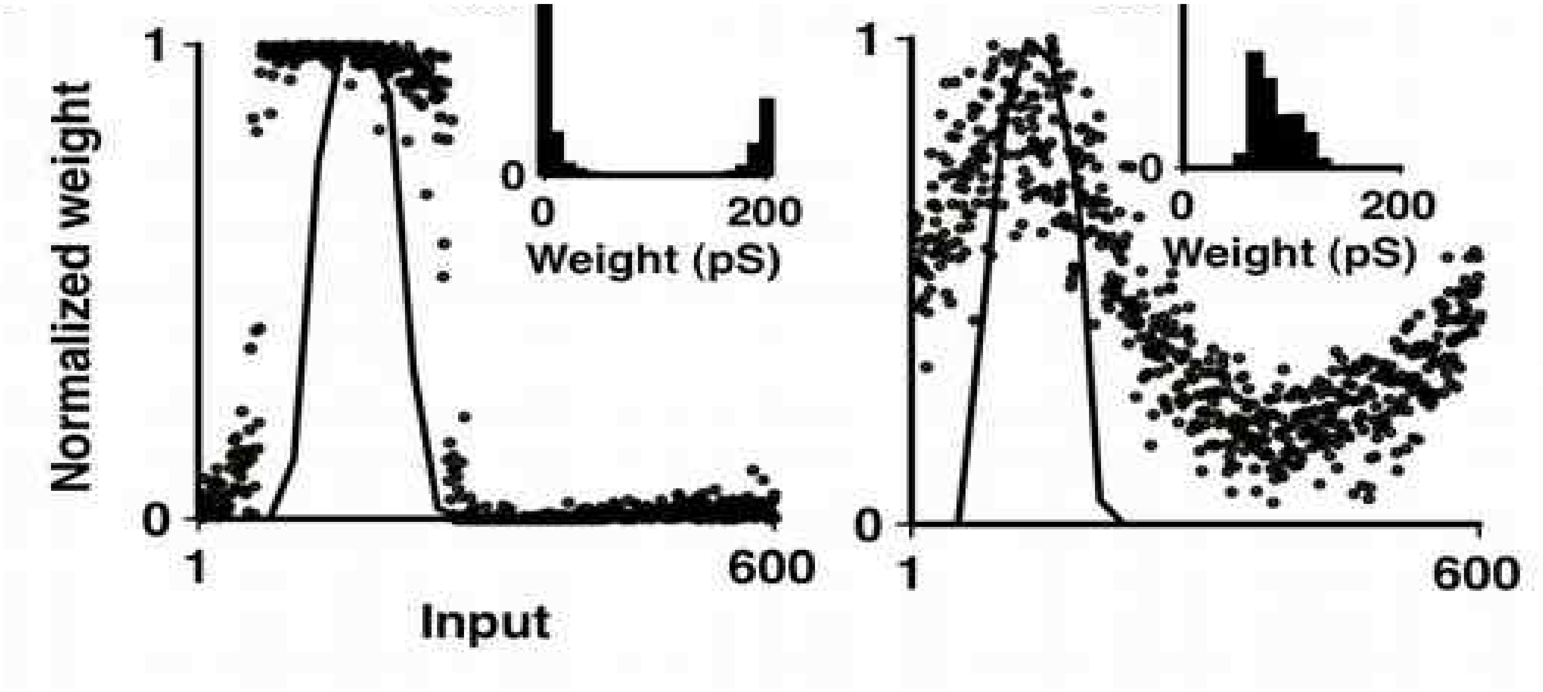
nSTDP: Spontaneous symmetry breaking
[Song &Abbott '01, Delorme '01]



Weight dependent plasticity requires inhibition for selectivity

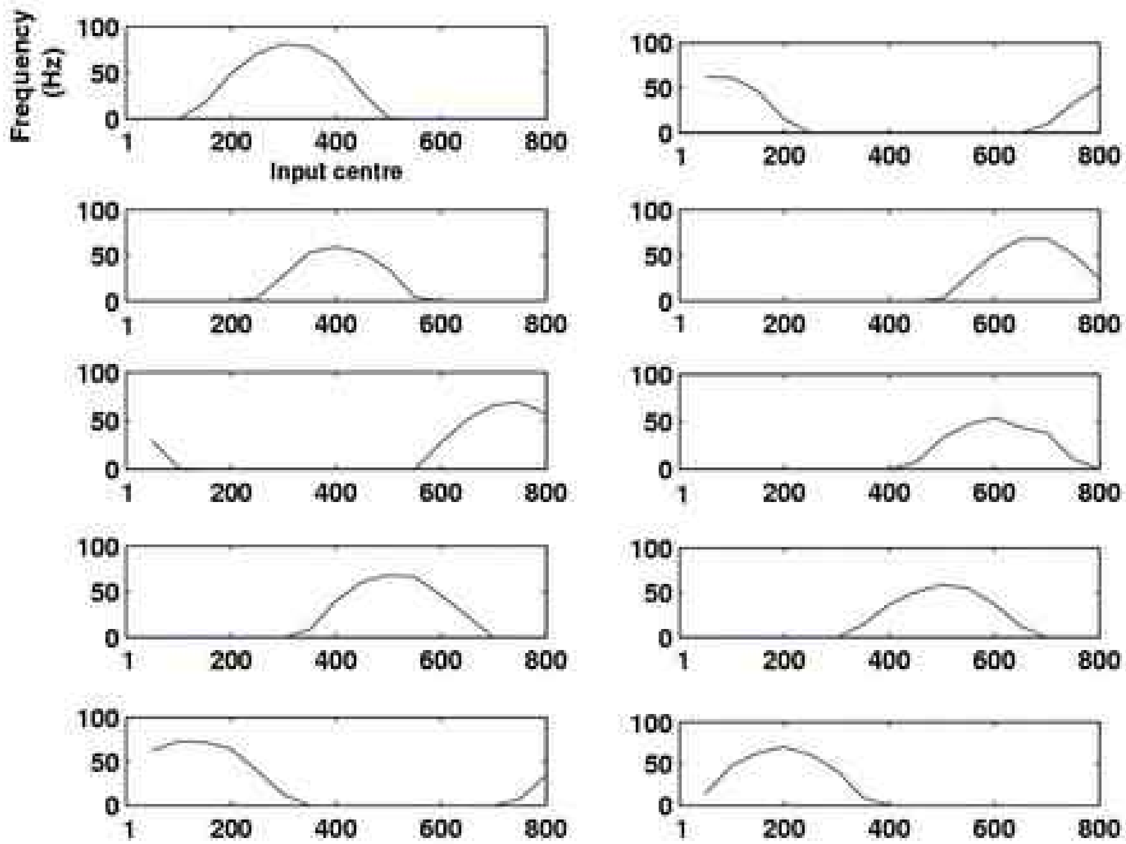
Broad tuning underlies receptive field

nSTDP wSTDP

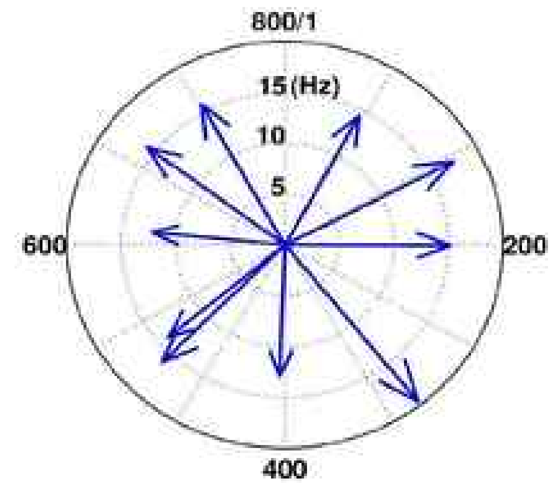


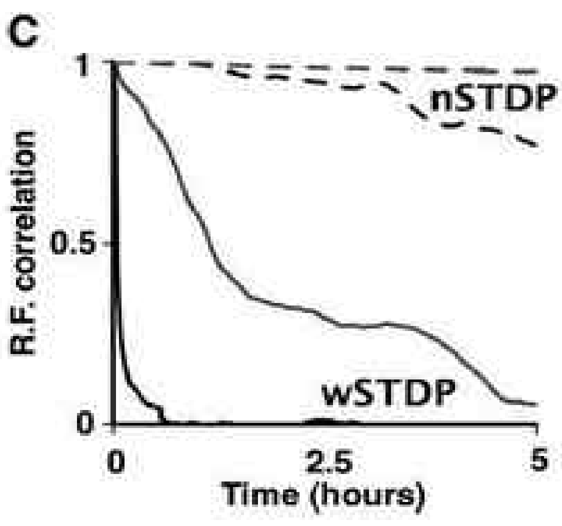
Stability of receptive fields

Receptive fields

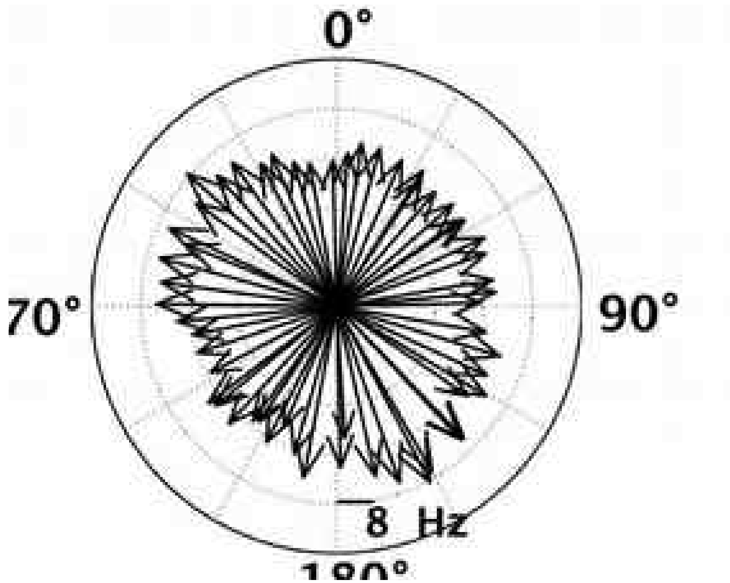


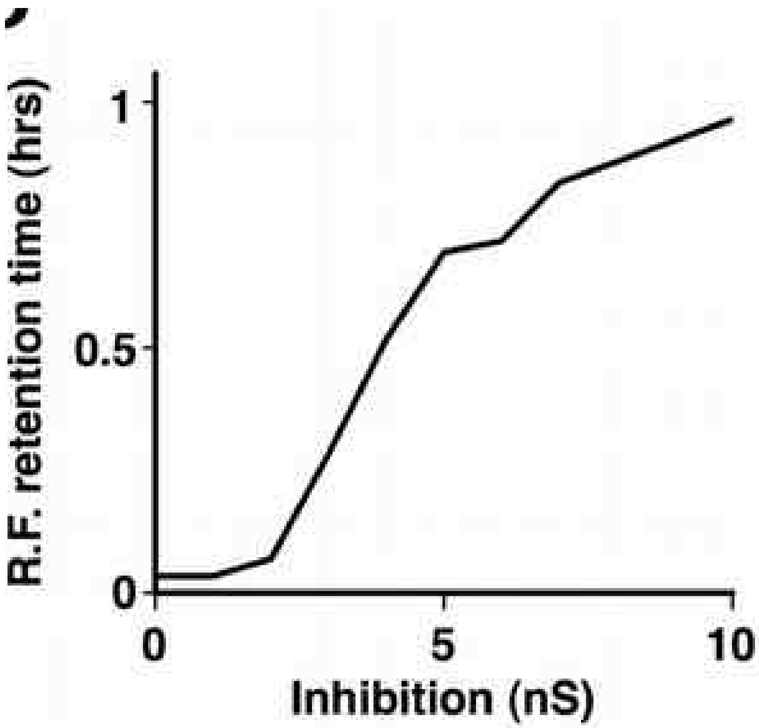
Population vectors





Inhibition rescues network stability



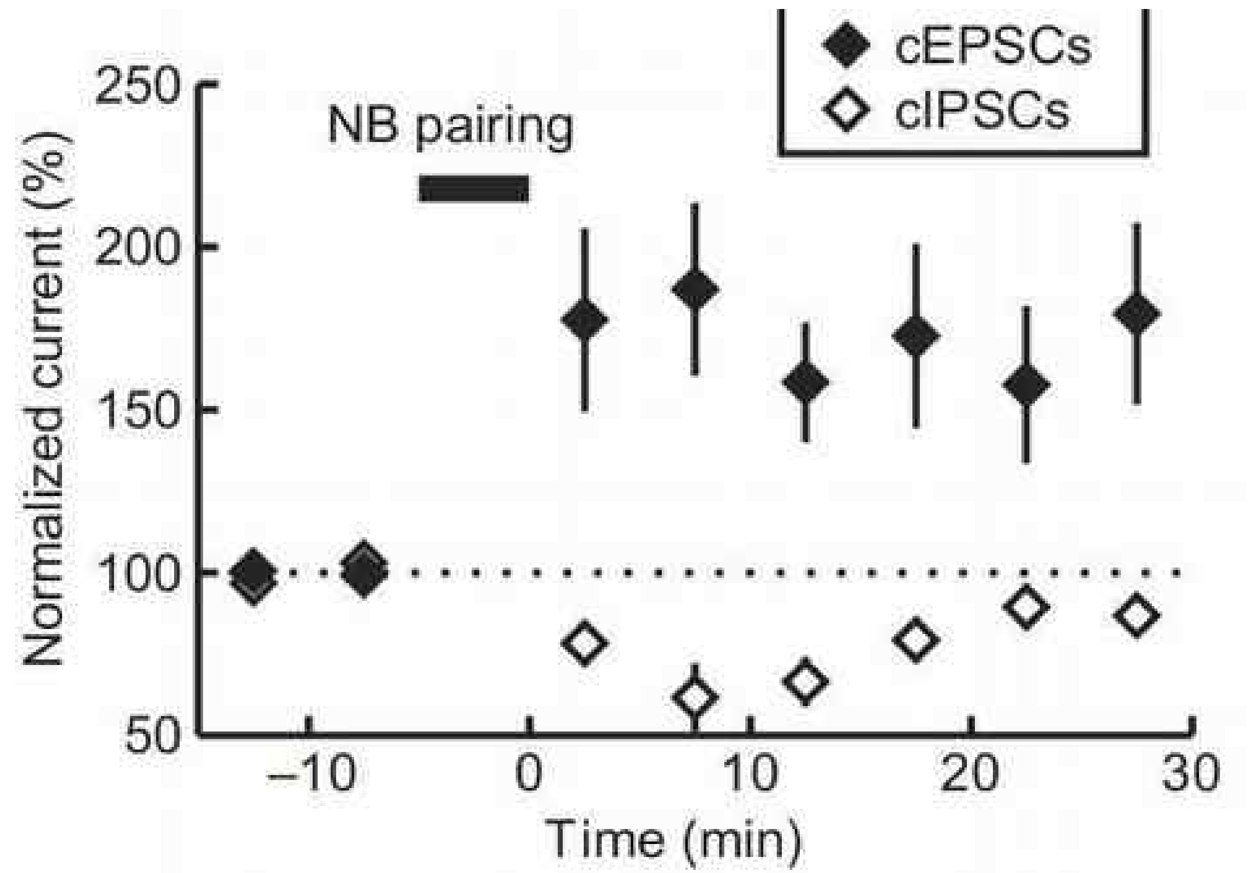


Allows for regulation of retention time

[Billings & MvR 2009]

Experimental evidence for effect of inhibition on stability

- Reduced inhibition in auditory plasticity



[Froemke et al 07]

Experimental evidence for effect of inhibition on stability

LETTER

doi:10.1038/nature12485

A disinhibitory microcircuit initiates critical-period plasticity in the visual cortex

Sandra J. Kuhlman[1]†*, Nicholas D. Olivas[2]*, Elaine Tring[1], Taruna Ikrar[2], Xiangmin Xu[2,3] & Joshua T. Trachtenberg[1]

Stability of plasticity

Stability is regulated on many different levels:

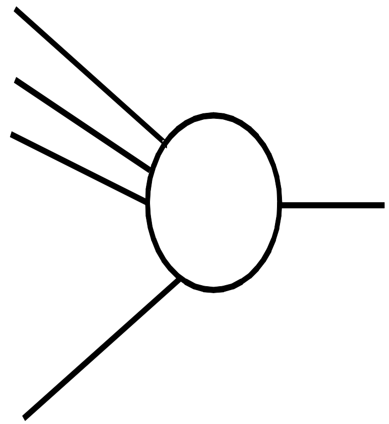
- receptor stability
- weight dependence of the learning rule (here)
- synaptic tagging (Barret and MvR 2008)
- network interactions (here)
- systems level consolidation

Table of contents

- Spines and weight dependent plasticity
- Weight dependent STDP in single neurons and networks
- **Weight dependence increases information capacity**
- Requirements for homeostatic plasticity

Weight dependent learning and information storage

Inputs				Weights
1	0	0…	x^1	w_1
0	1	0…	x^2	w_2
1	1	1…	x^3	w_3
.	.	.	.	.
.	.	.	.	.
.	.	.	.	.
1	0	0…	x^n	w_n



Output

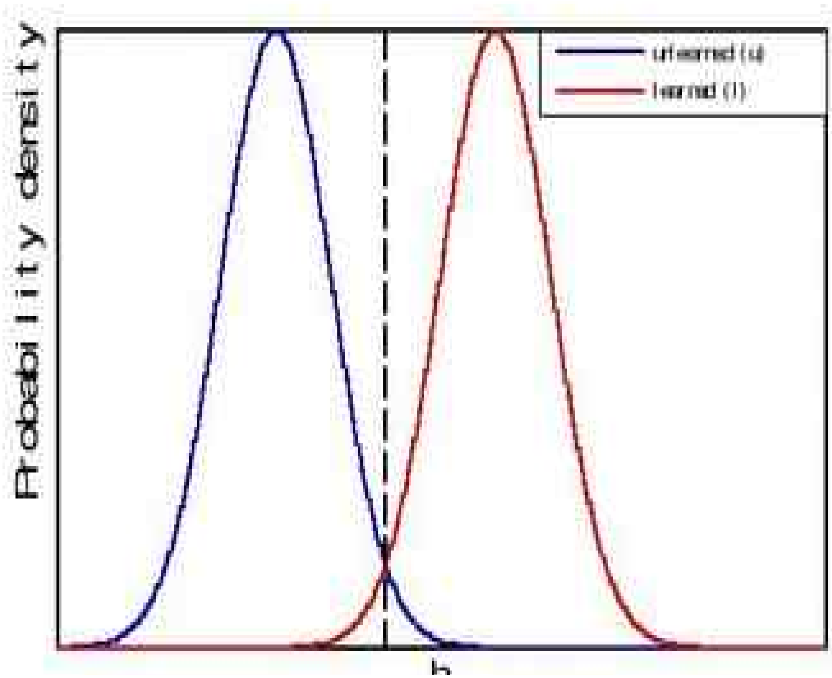
$$y = \sum_{a=1}^{n} w_a x^a$$

- Binary patterns *x*
- Ongoing learning, interrupted by recognition test

Measuring memory storage capacity

Separate learned from novel patterns ('lures')
Response in test phase:

P(y)

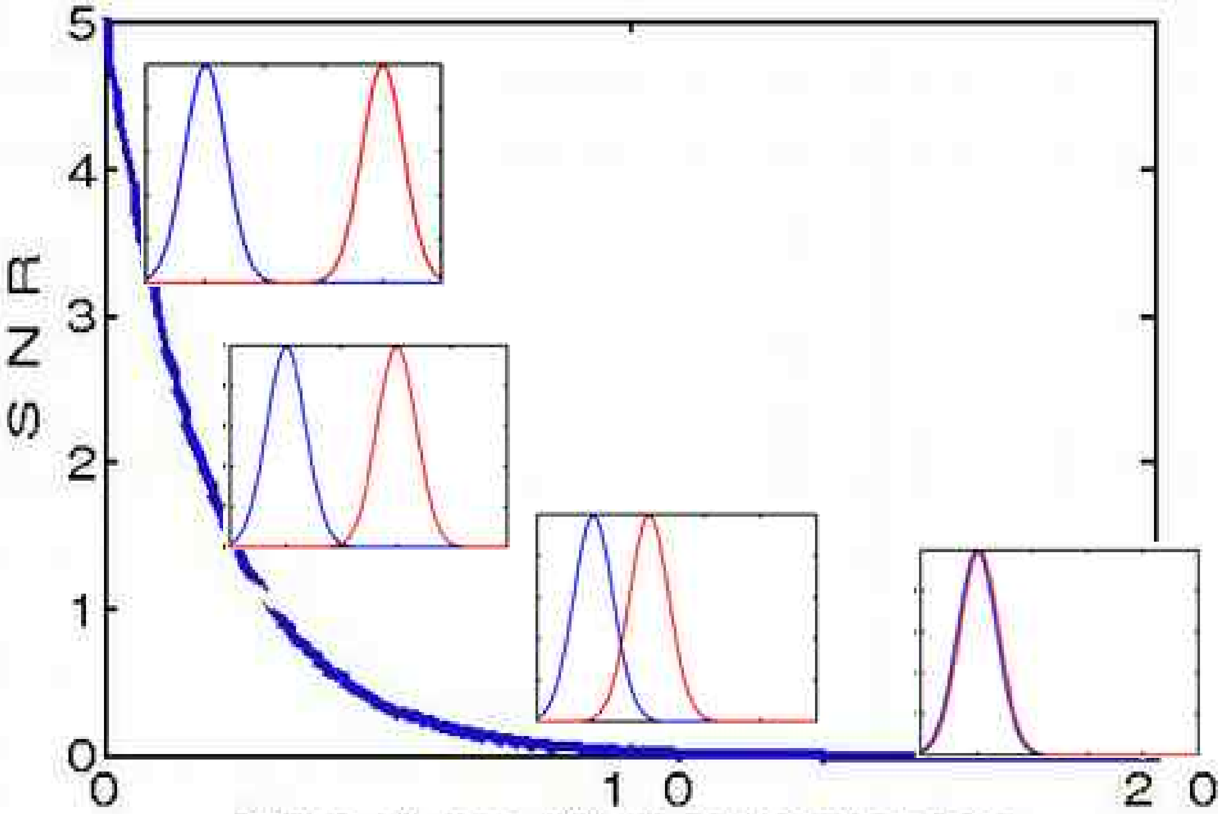


Neuron's output y

Characterize with
Signal-to-Noise Ratio:

$$SNR = \frac{2\left[\langle y_u \rangle - \langle y_l \rangle\right]^2}{Var(y_u) + Var(y_l)}$$

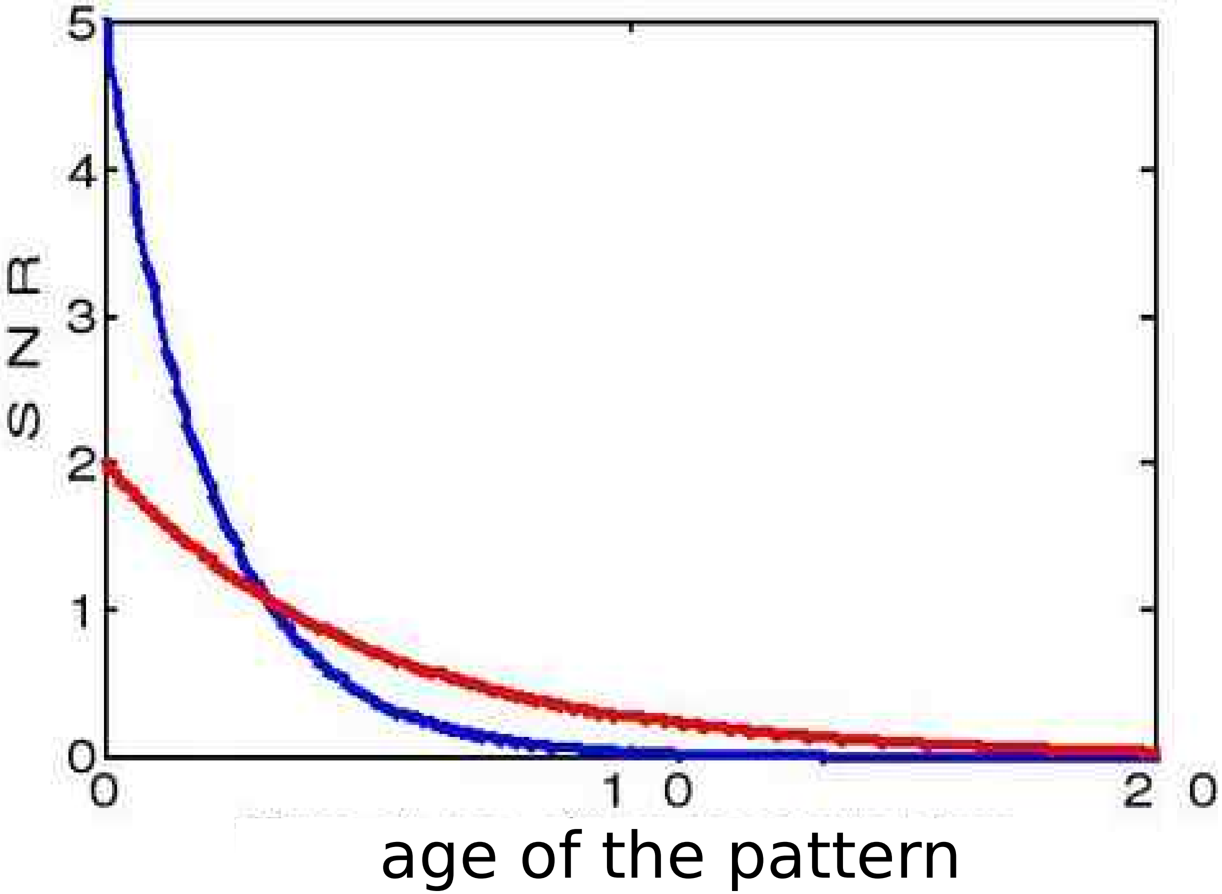
Ongoing learning: new memories overwrite old ones



age of the pattern

Typically, exponential decay

Trade-off: memory strength vs decay



What is better:

- High initial SNR, or slow decay? [Fusi and Abbott '07]

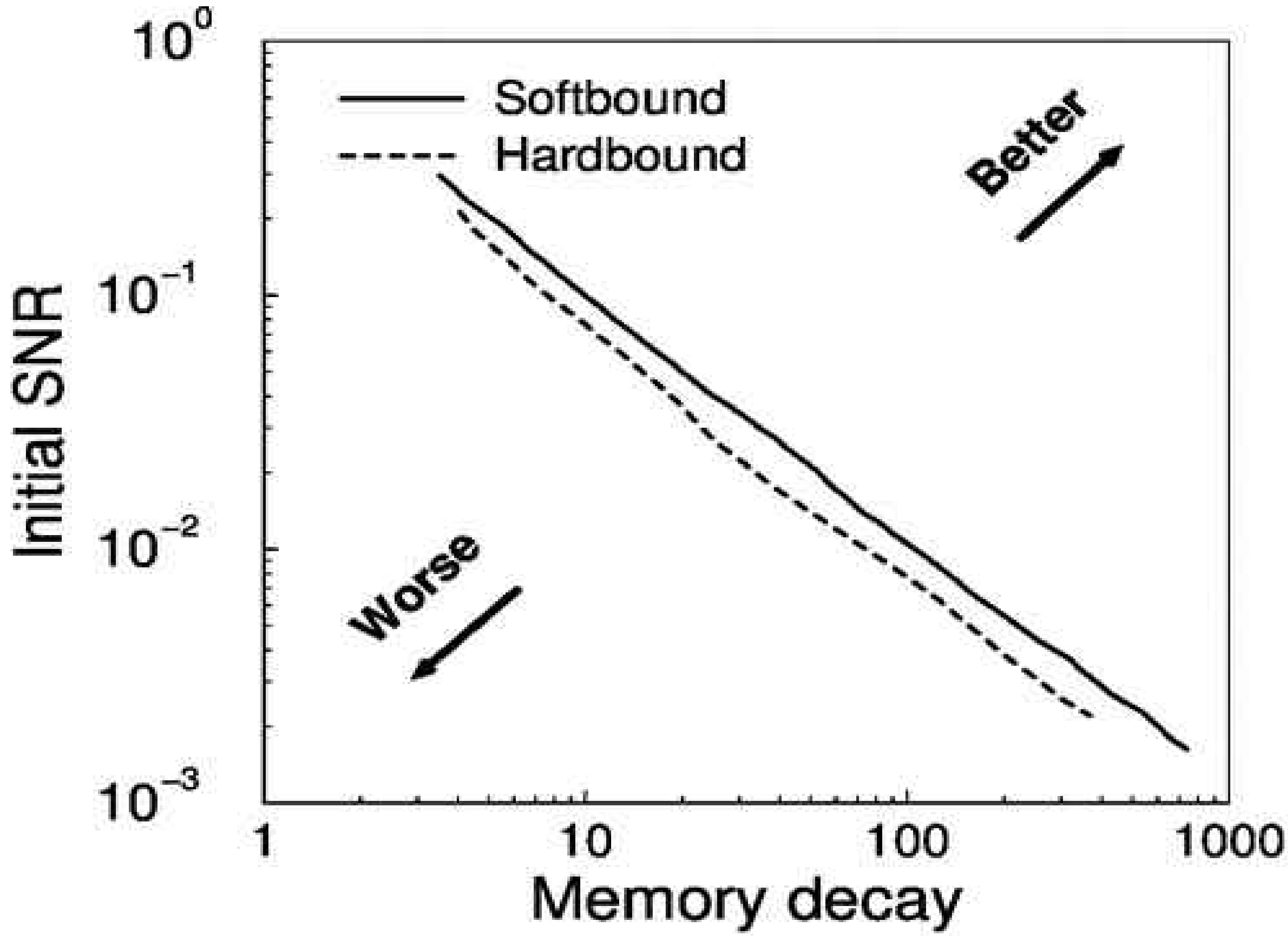
Weight dependence is always better

Hardbound/
Weight indep.

w=w+a
w=w-a

Softbound/
Weight dep

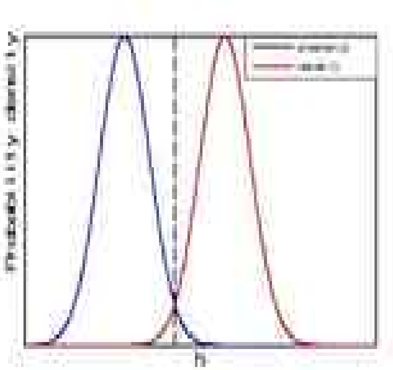
w=w+a
w=b.w

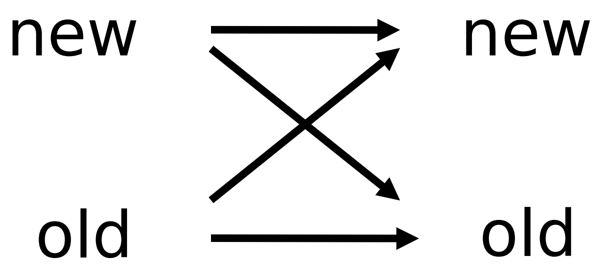


Using Shannon information to resolve trade-off

How much **information** about the pattern is gained by inspecting the output?

<u>test pattern</u> <u>response</u>





$$I = \sum_{s,r} P(r|s)P(s)\log_2 \frac{P(r|s)}{P(r)}$$

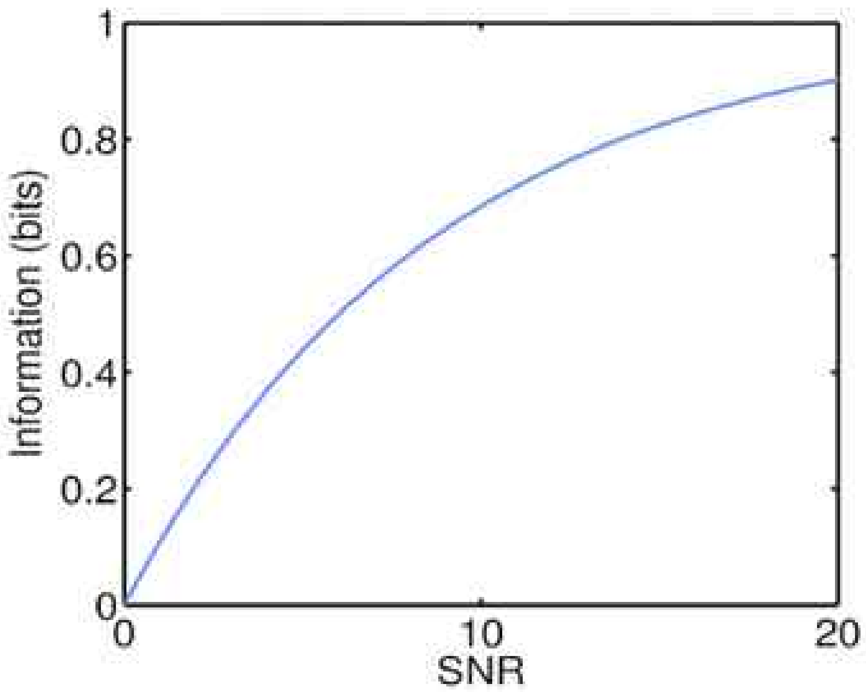
Always correct ~ 1 bit

Chance level ~ 0 bits

[Barrett and MvR' 08]

Using Shannon information to resolve trade-off

Use small learning rates to prevent saturation of Information

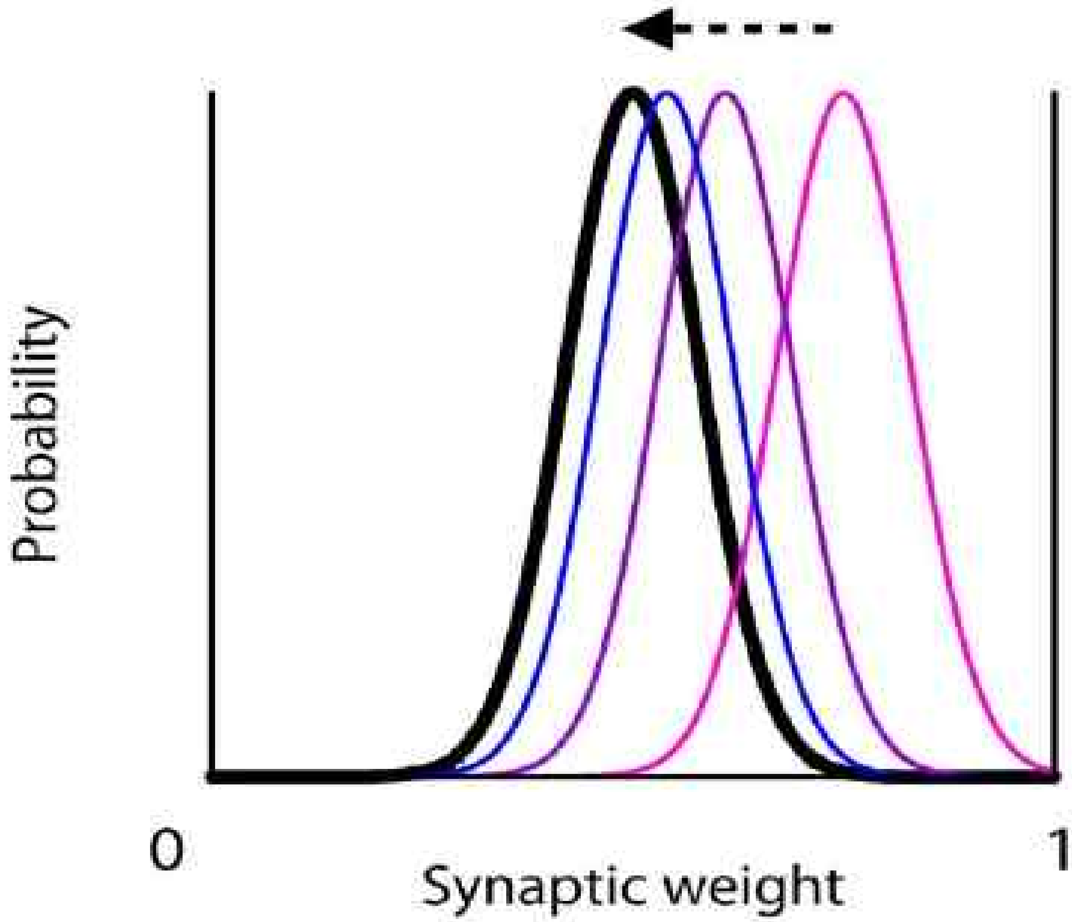


$$I_S^{SB} = \frac{1}{4\pi \ln 2} \sum_{t=0}^{\infty} S(t)$$

$$= \frac{1}{4\pi \ln 2} \int_0^{\infty} S(t)dt$$

Small learning rates, soft-bound

Mean decay of a potentiated synapse



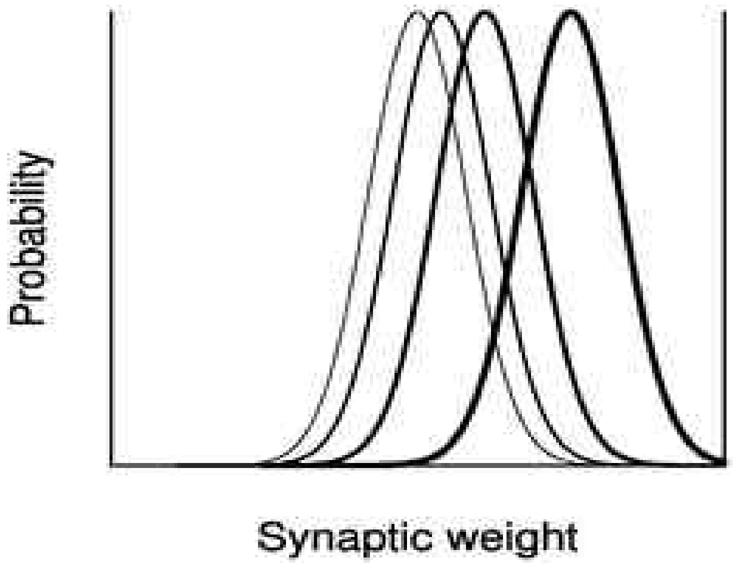
Small learning rates, soft-bound

Fokker-Planck equation:

$$\frac{\partial P(w,t)}{\partial t} = -\frac{\partial[A(w)P(w,t)]}{\partial w} + \frac{1}{2}\frac{\partial^2[B(w)P(w,t)]}{\partial w^2}$$

Right after potentiation

$$P(w,0) = P_\infty(w + v(0)) \approx P_\infty(w) + v(0)P'_\infty(w).$$



Transport equation:

$$\frac{\partial P(w,t)}{\partial t} = -[A'(w)v(t)]\frac{\partial P(w,t)}{\partial w}.$$

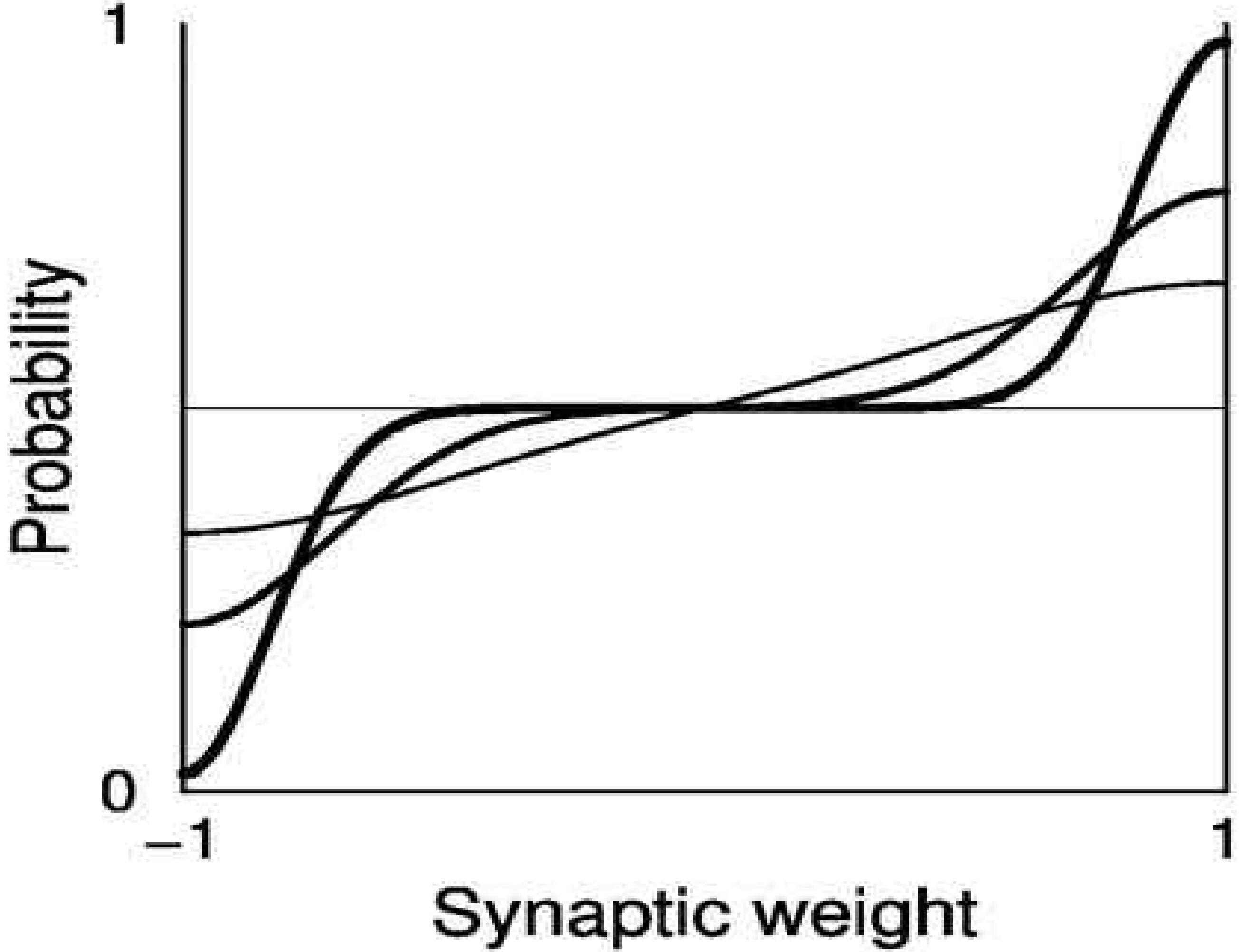
Weight decays as:

$$v(t) = a\exp(-\tfrac{1}{2}bt).$$

Information

$$\begin{aligned} I_S^{SB} &= \frac{1}{4\pi \ln 2}\int_0^\infty S(t)\,dt \\ &= \frac{1}{4\pi \ln 2}.1 \\ &\approx 0.1148 \text{ bits}. \end{aligned}$$

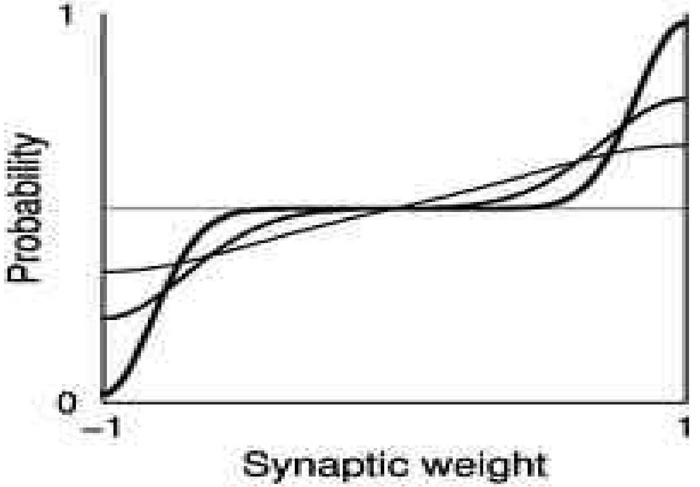
Small learning rates, hard-bound



Small learning rates, hard-bound

$$P(w,t) = P_\infty(w) + a \sum_{k=-\infty}^{\infty} G(w,t;w_0 = 1+4k) - G(w,t;w_0 = -1+4k)$$

$$G(w,t;w_0) = \frac{1}{\sqrt{2\pi Bt}} \exp[-(w-w_0)^2/(2Bt)]$$

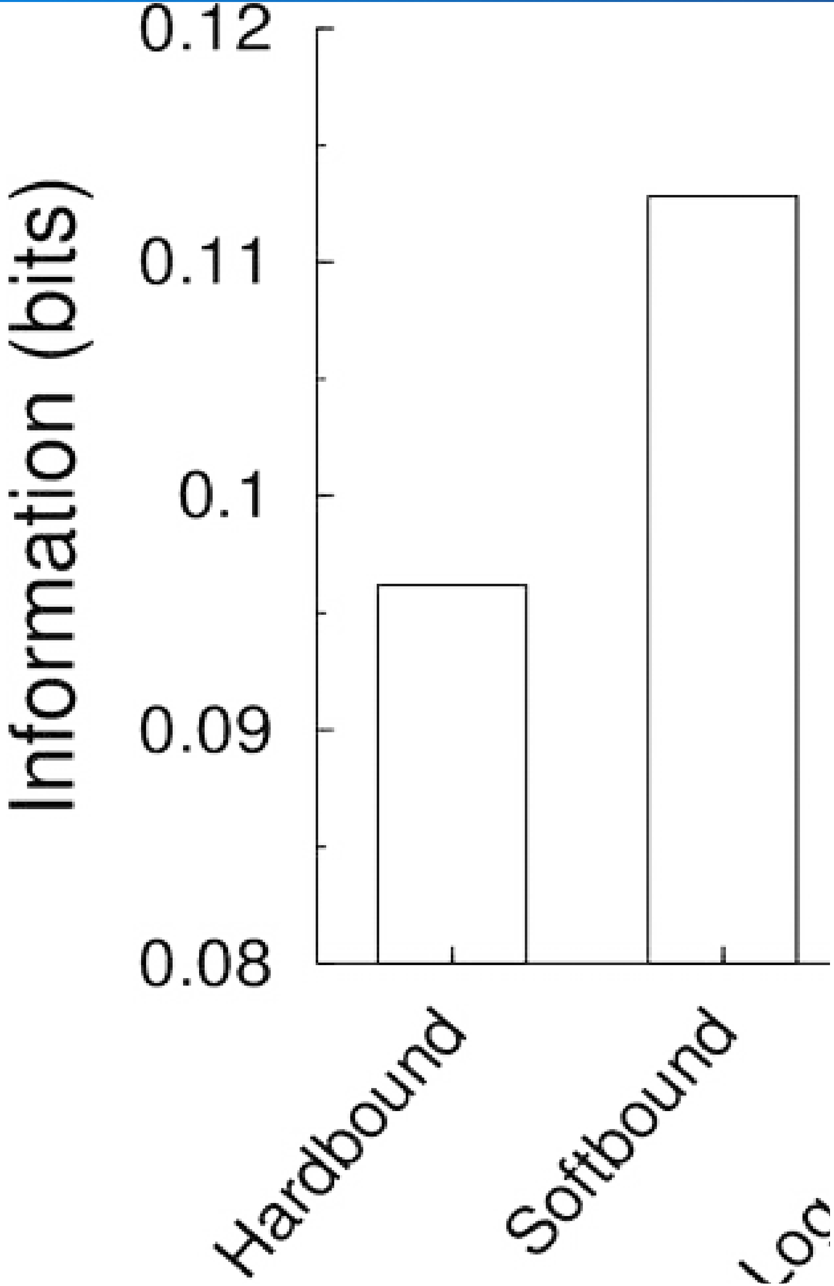


$$\begin{aligned} \frac{\partial \langle w \rangle (t)}{\partial t} &= \int_{-1}^{+1} w \frac{\partial P(w,t)}{\partial t} dw \\ &= \frac{1}{2} B[P(-1,t) - P(1,t)] \\ &= -a^3 \sum_{k=0}^{\infty} e^{-\lambda_k a^2 t} \end{aligned}$$

$$\lambda_k = \tfrac{1}{8}[\pi(2k+1)]^2$$

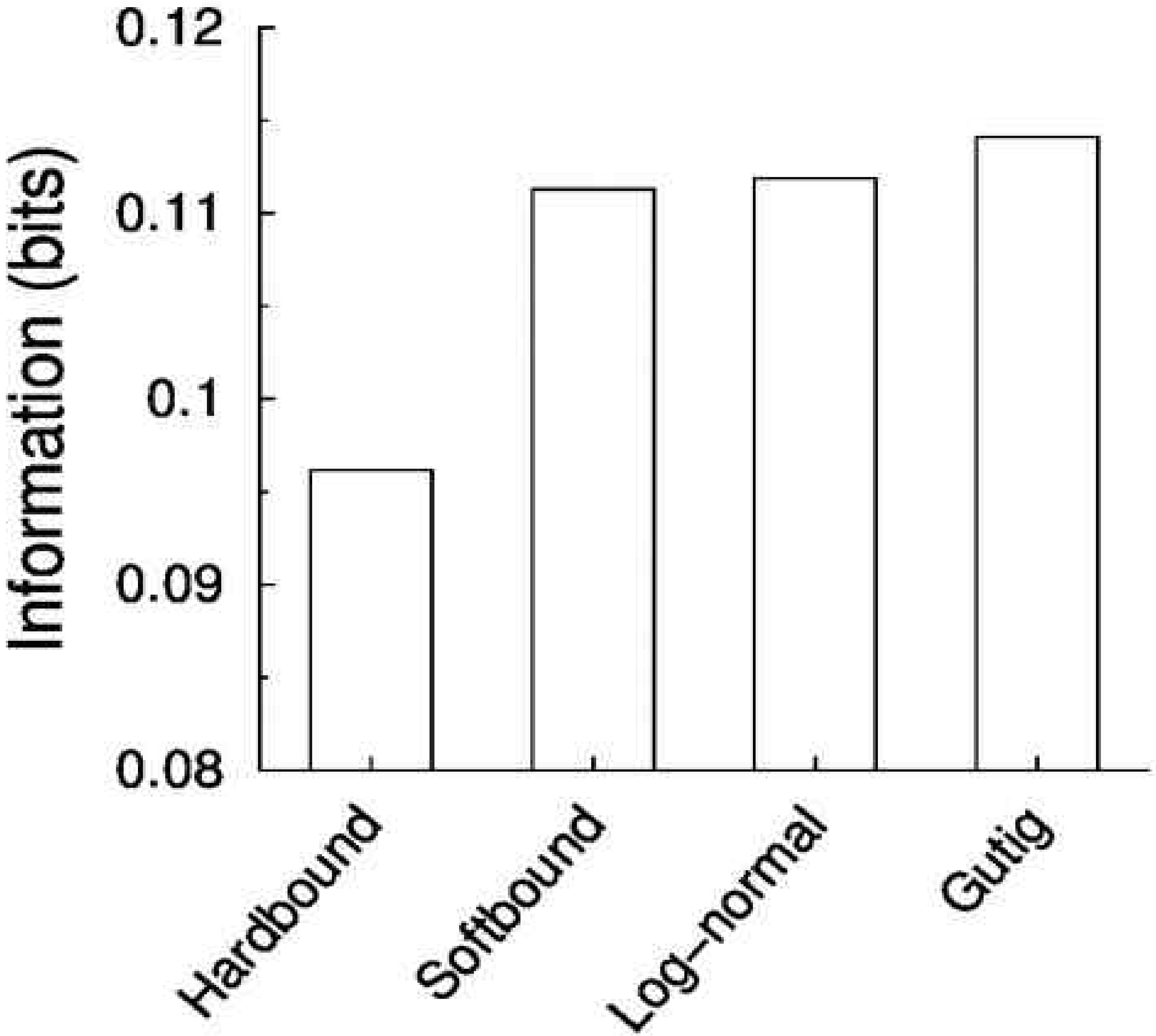
$$\begin{aligned} I_S^{HB} &= \frac{1}{4\pi \ln 2} \int_0^\infty S(t)\, dt \\ &= \frac{1}{4\pi \ln 2} \sum_{k,l=0}^{\infty} \frac{1}{\lambda_k \lambda_l (\lambda_k + \lambda_l)} \\ &\approx 0.096827 \text{ bits} \end{aligned}$$

Weight dependent learning gives superior Information capacity



[MvR et al. '12]

Universality at low learning rates



[MvR et al. '12]

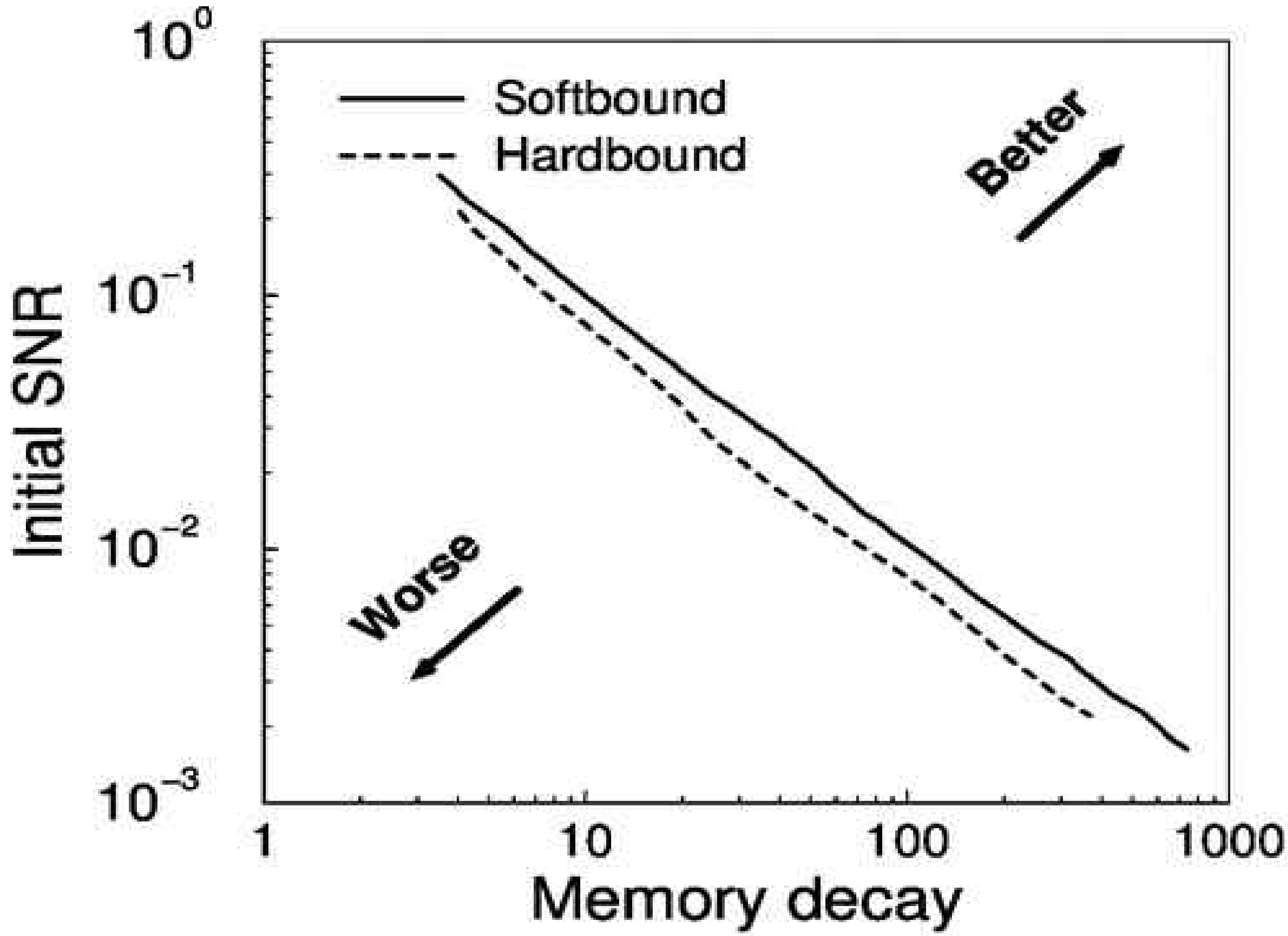
Weight dependence is always better

Hardbound/
Weight indep.

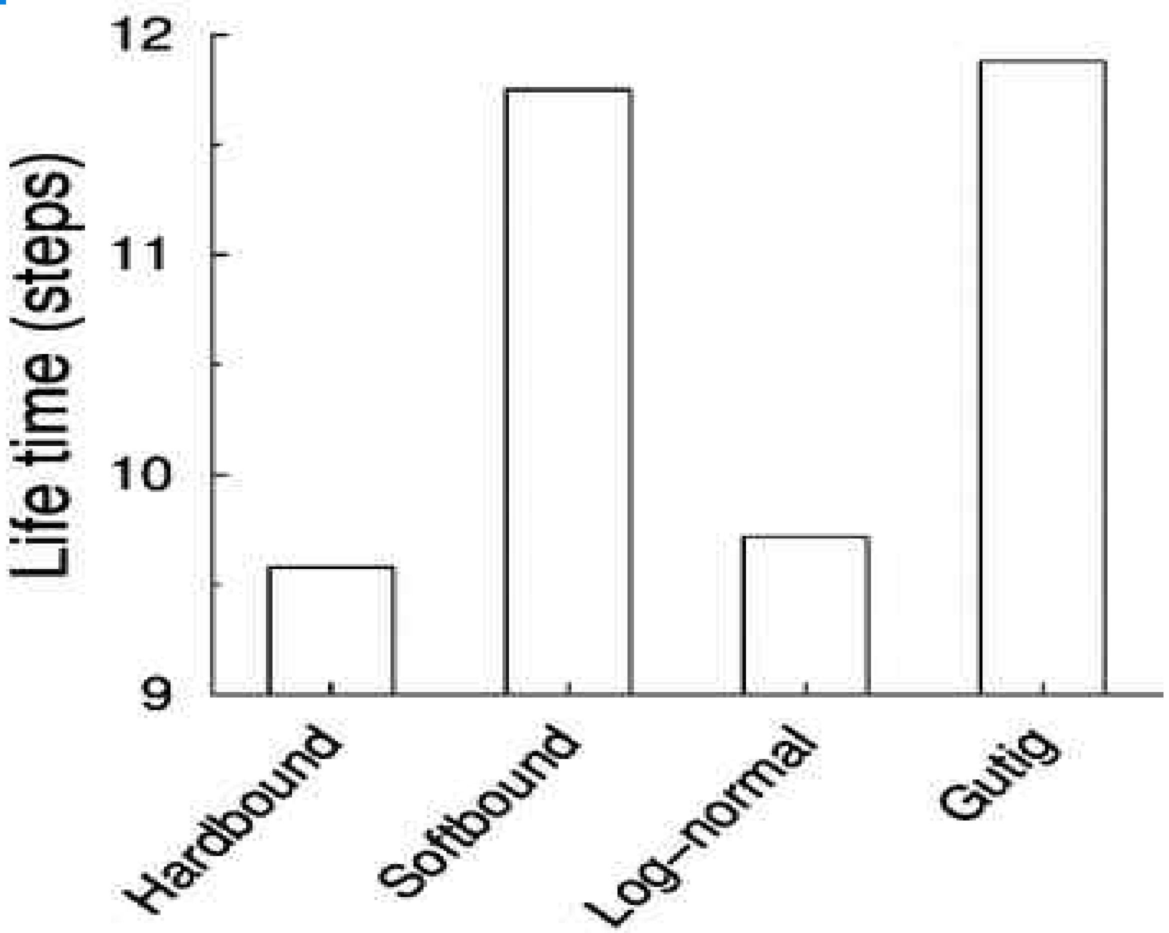
w=w+a
w=w-a

Softbound/
Weight dep

w=w+a
w=b.w



High learning rates



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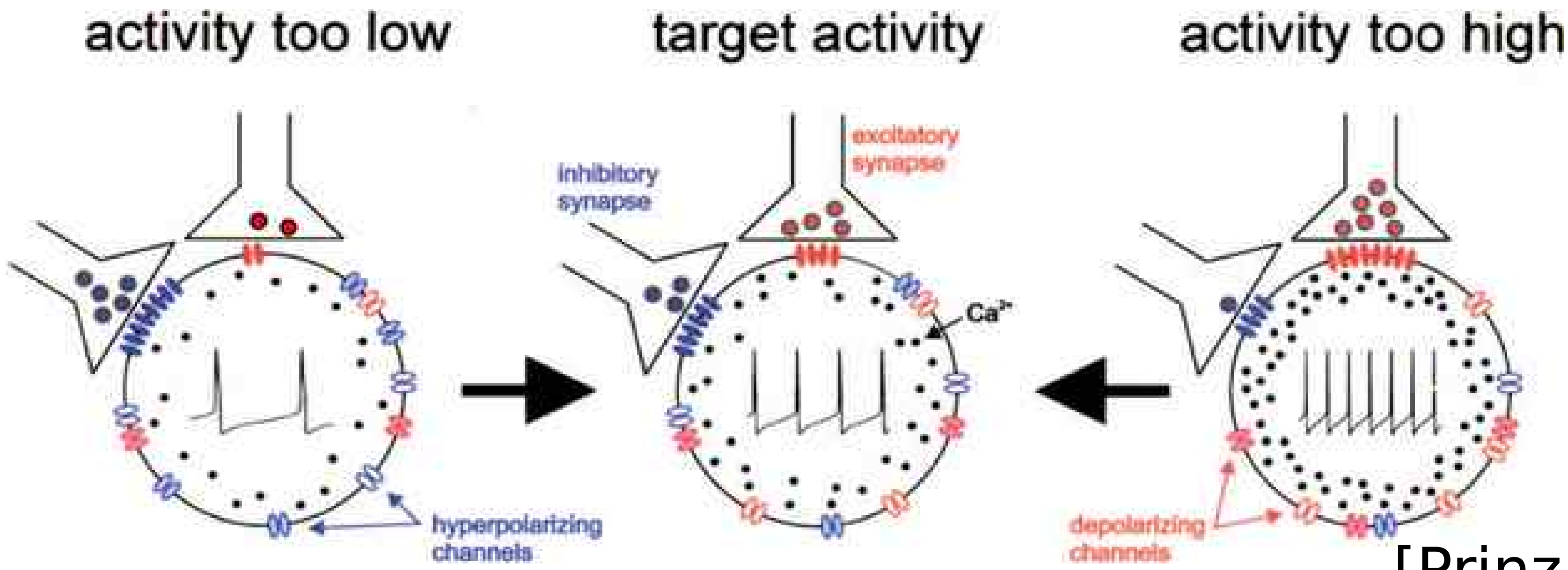
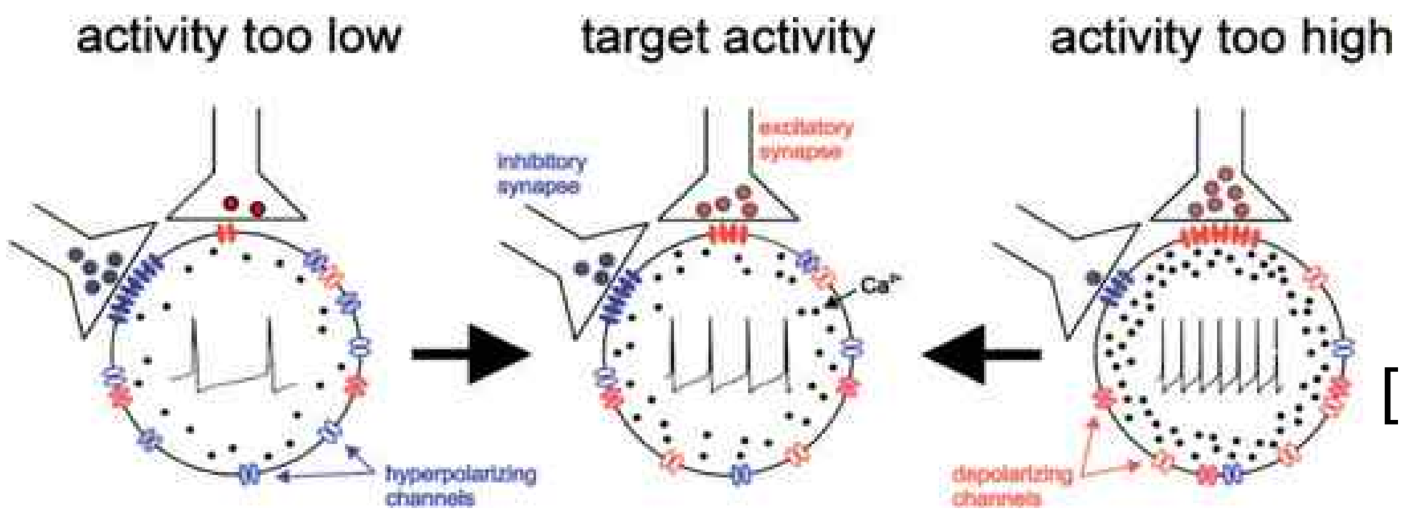
Homeostatic regulation



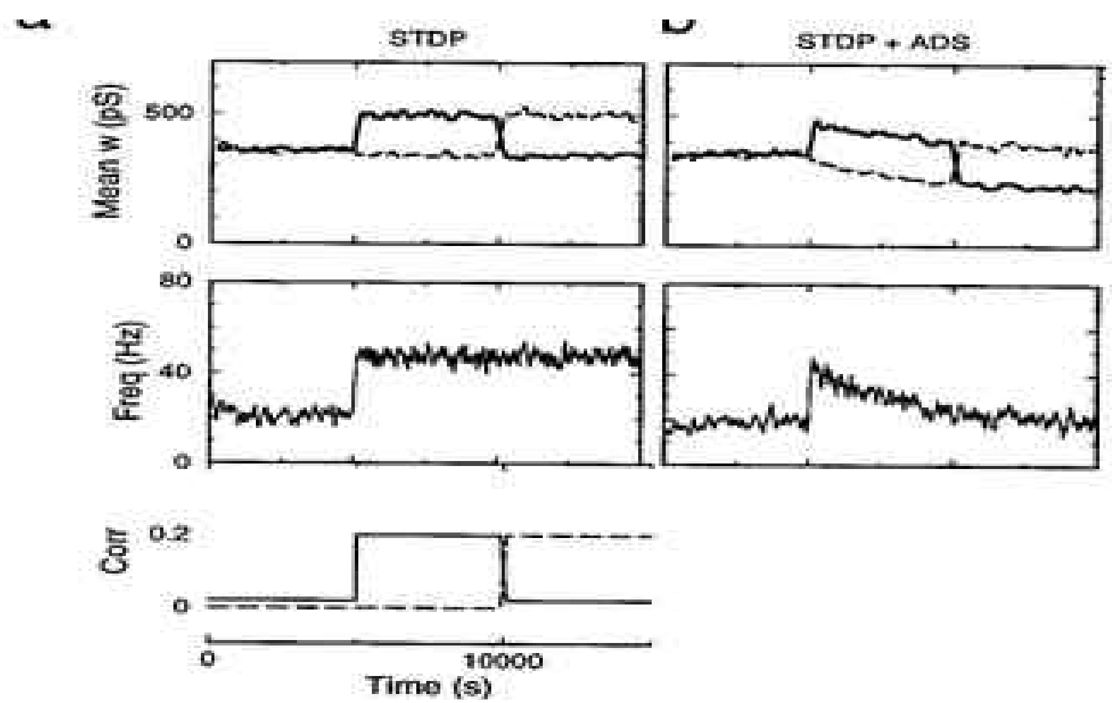
[Prinz '02]

Homeostatic regulation

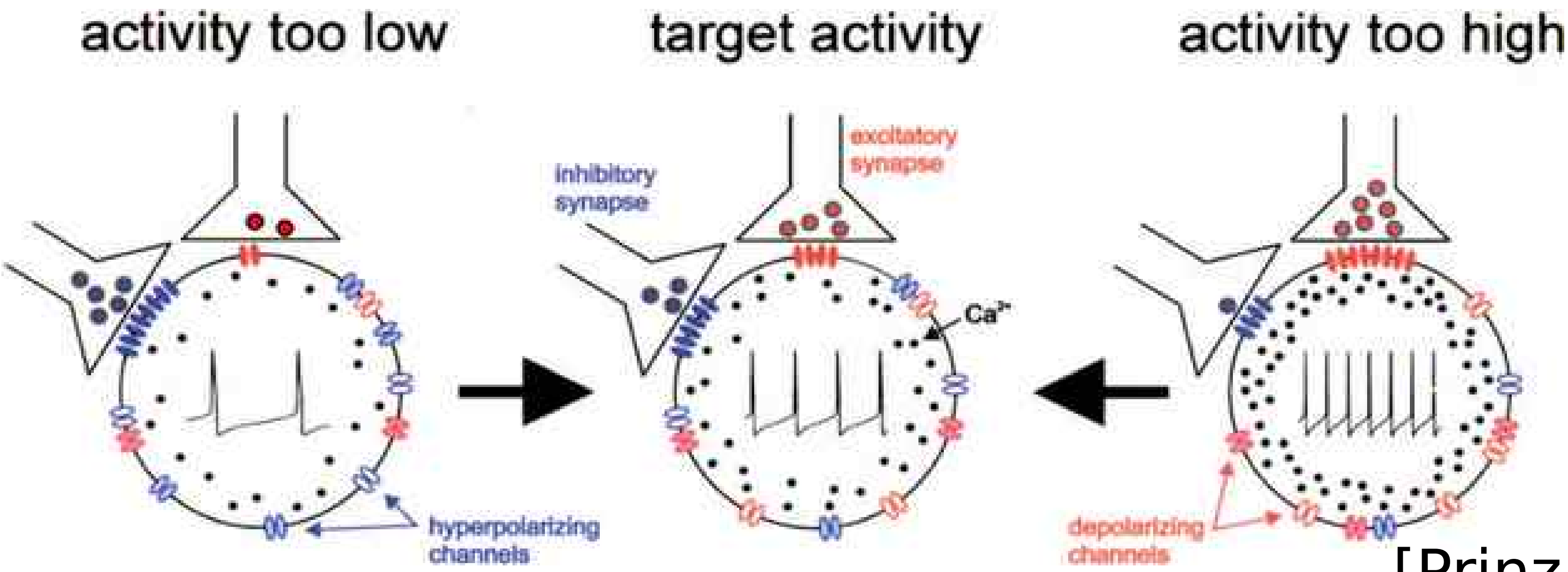


[Prinz '02]

* Synaptic homeostasis (leads to competition)



Homeostatic regulation

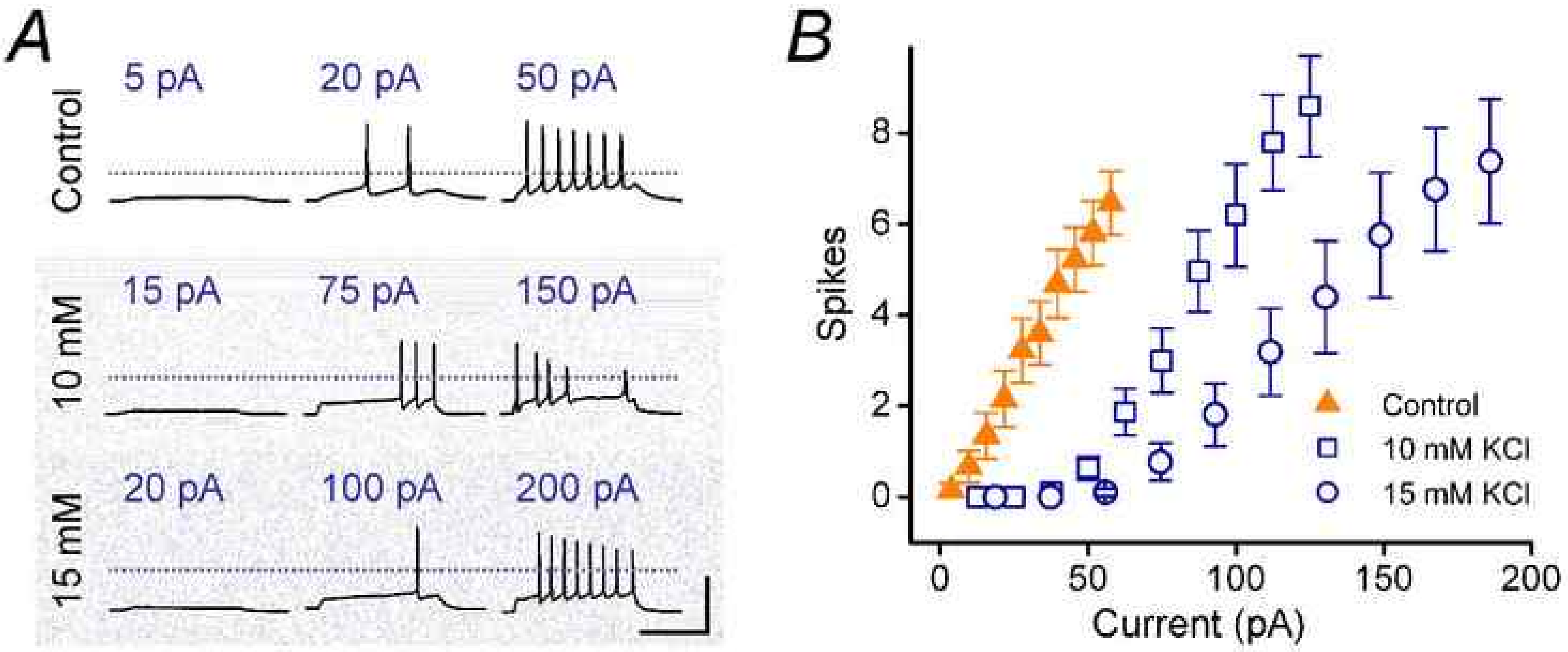


[Prinz '02]

Neural homeostasis in reaction to activity change:

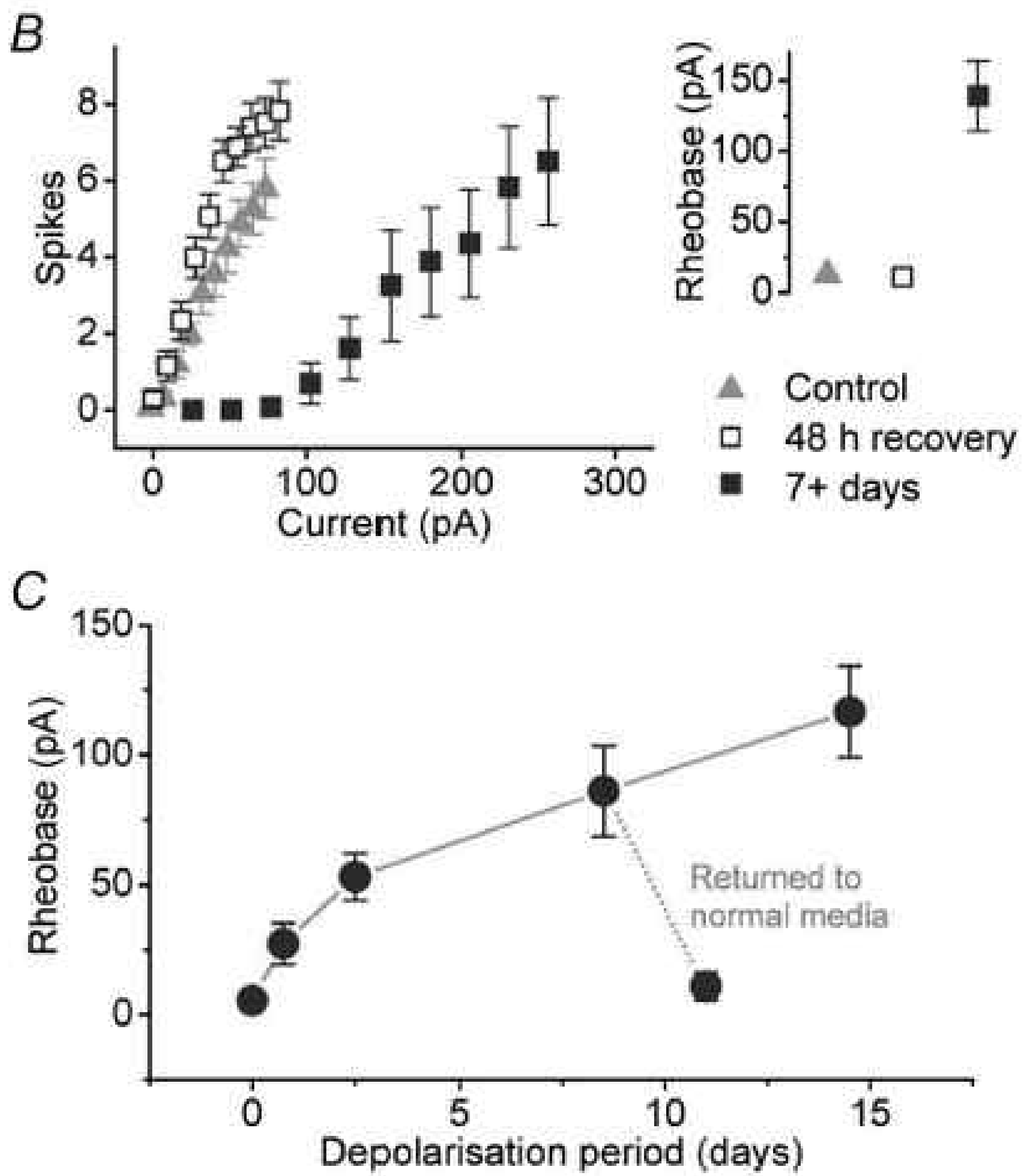
- Synaptic scaling
- **Intrinsic excitability**

Homeostasis of intrinsic excitability



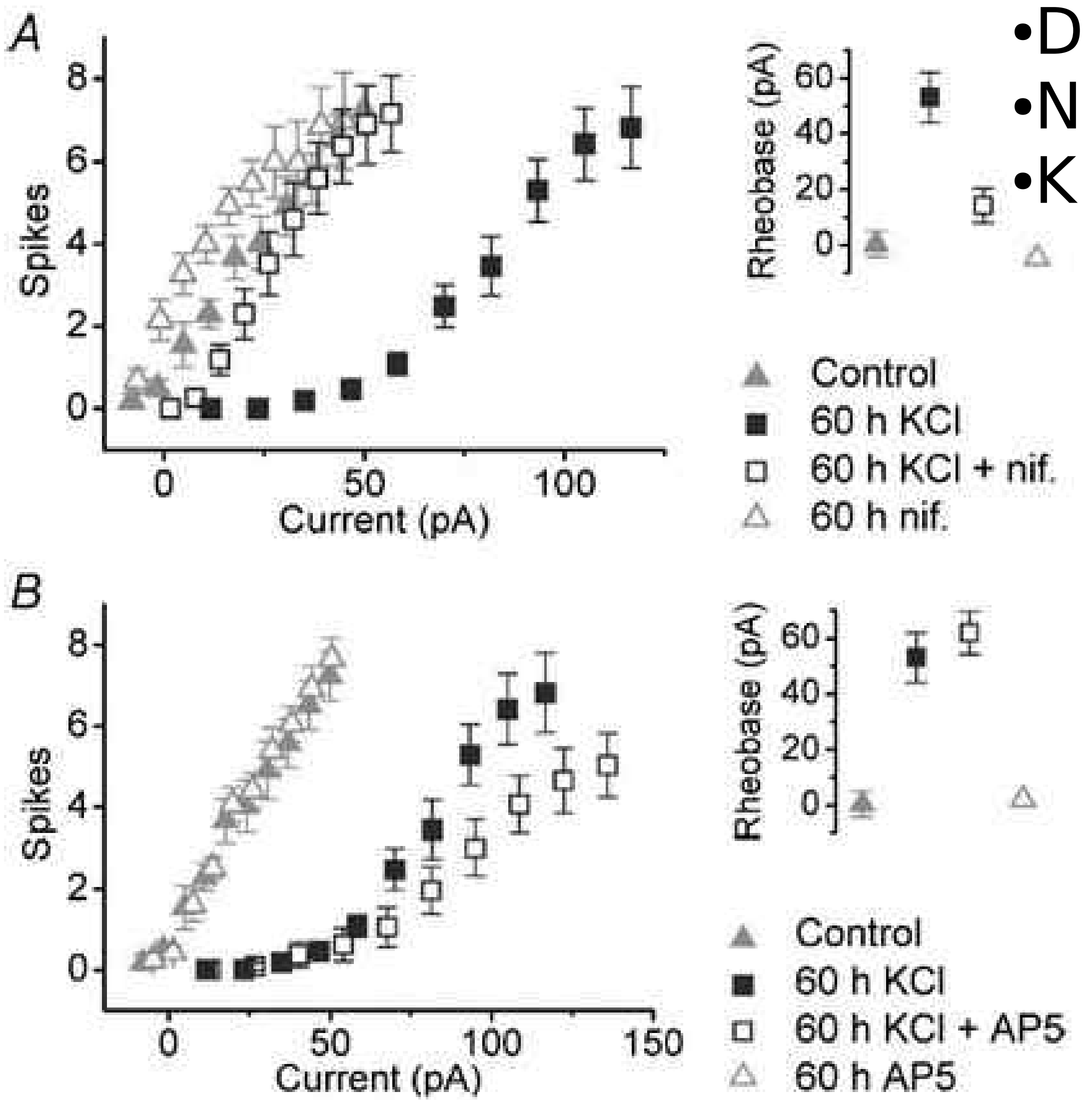
Rat, hippocampal culture.
Manipulation of external K
[O'Leary et al 2009]

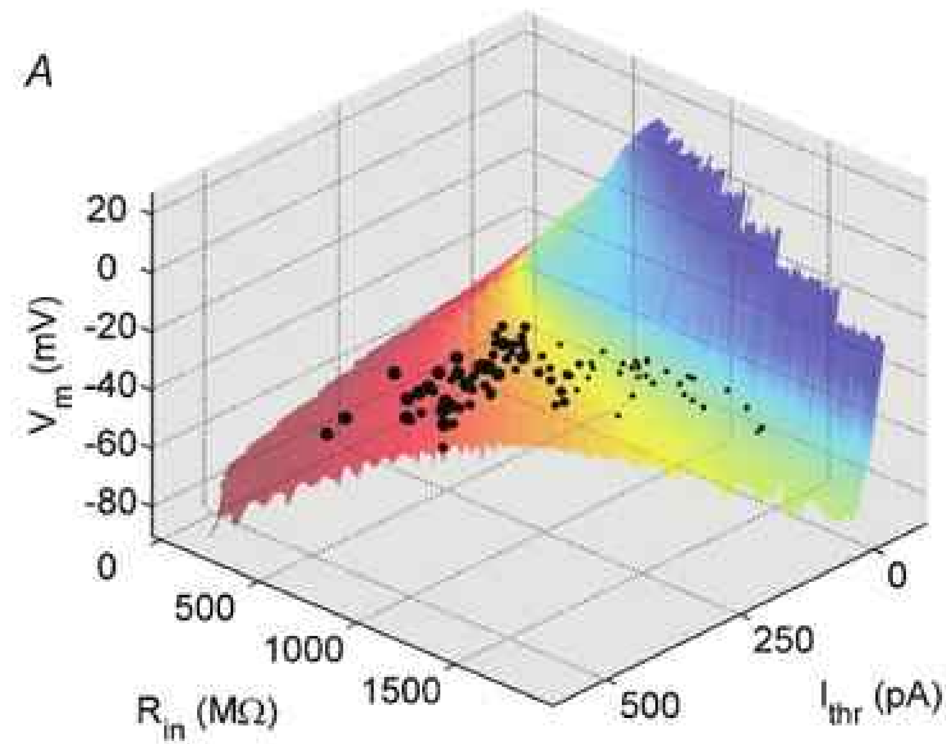
Homeostasis is slow



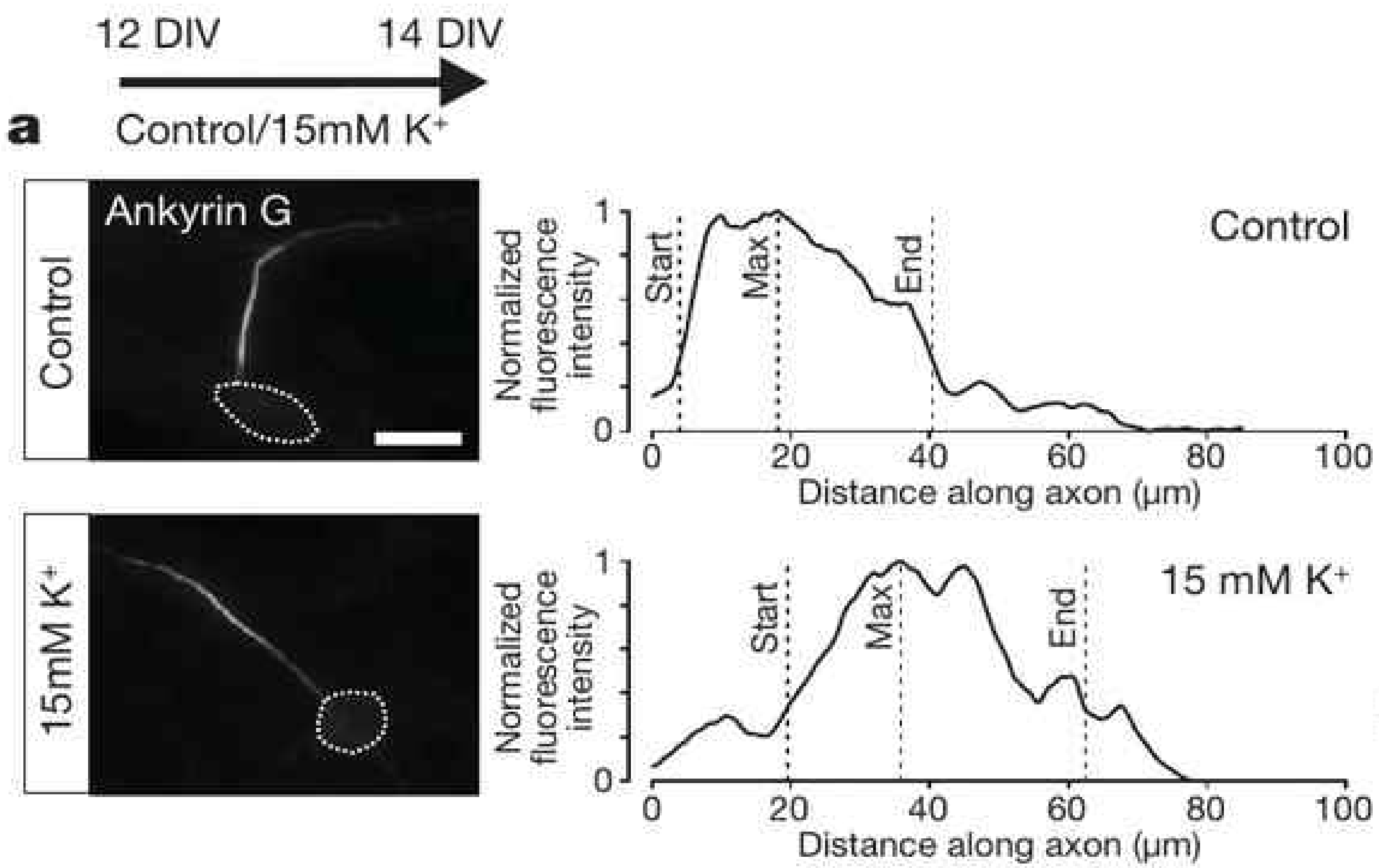
Mechanism: K permeabilty

- Dependent on L-type Ca-channe
- Not dependent on NMDA
- K permeability



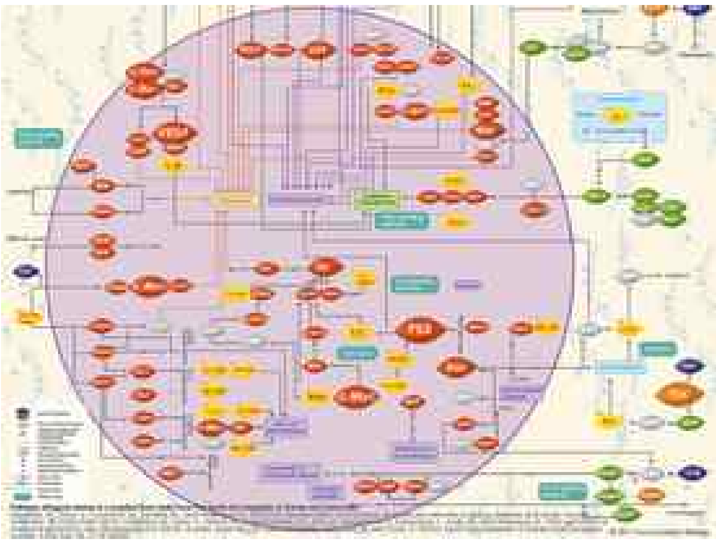


Homeostasis of intrinsic excitability: other pathways



[Grubb & Burrone 2010

Homeostatic regulating of excitability



"Integral controller" Threshold

$$\tau_r \frac{dr(t)}{dt} = -r(t) + g(I - T)$$

$$\tau_{Ca} \frac{dCa(t)}{dt} = -Ca(t) + r(t)$$

$$\tau_T \frac{dT(t)}{dt} = Ca(t) - const$$

Perfect integrator

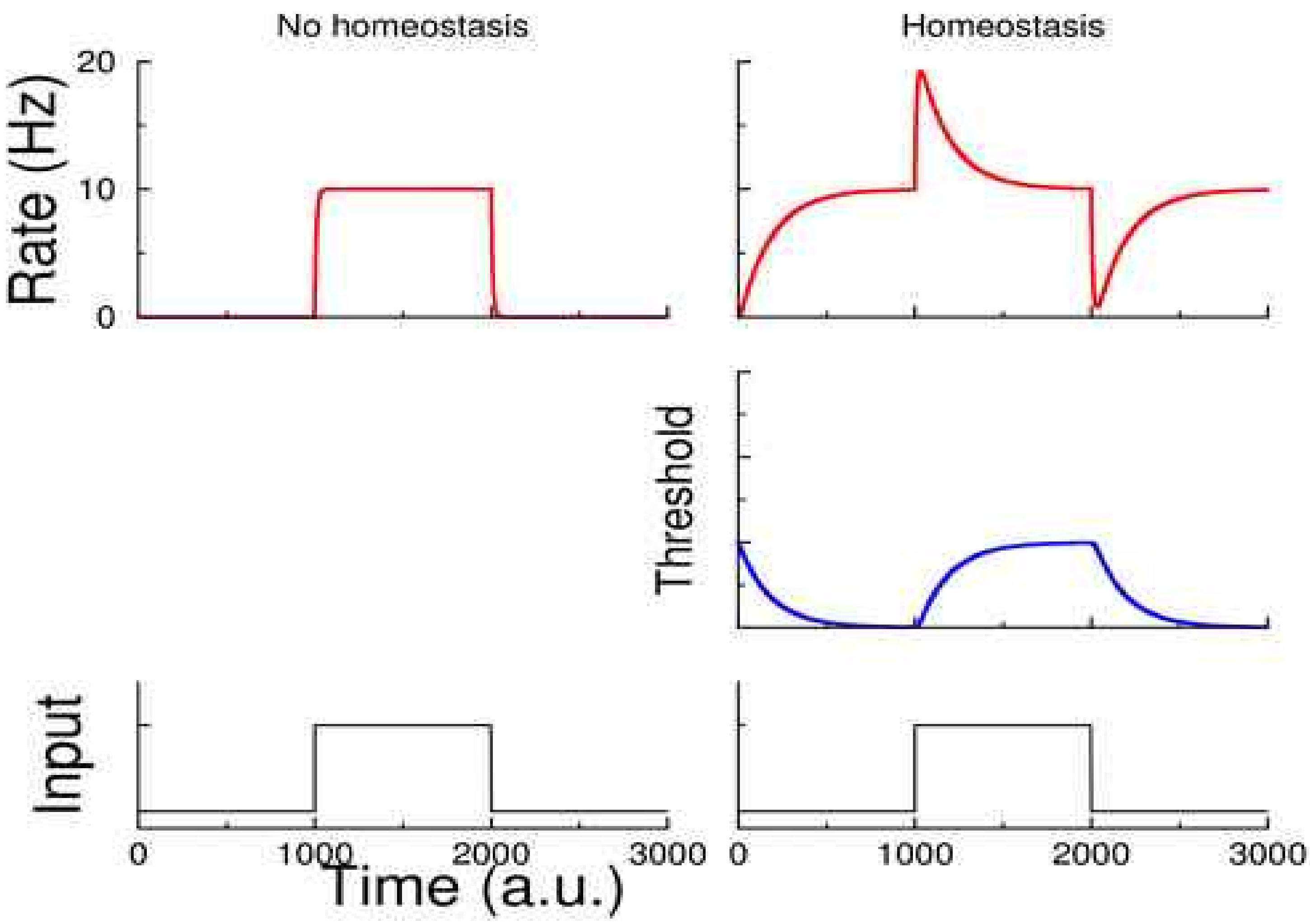
Theoretical challenge

- Fast restoration of operating point
- Stable

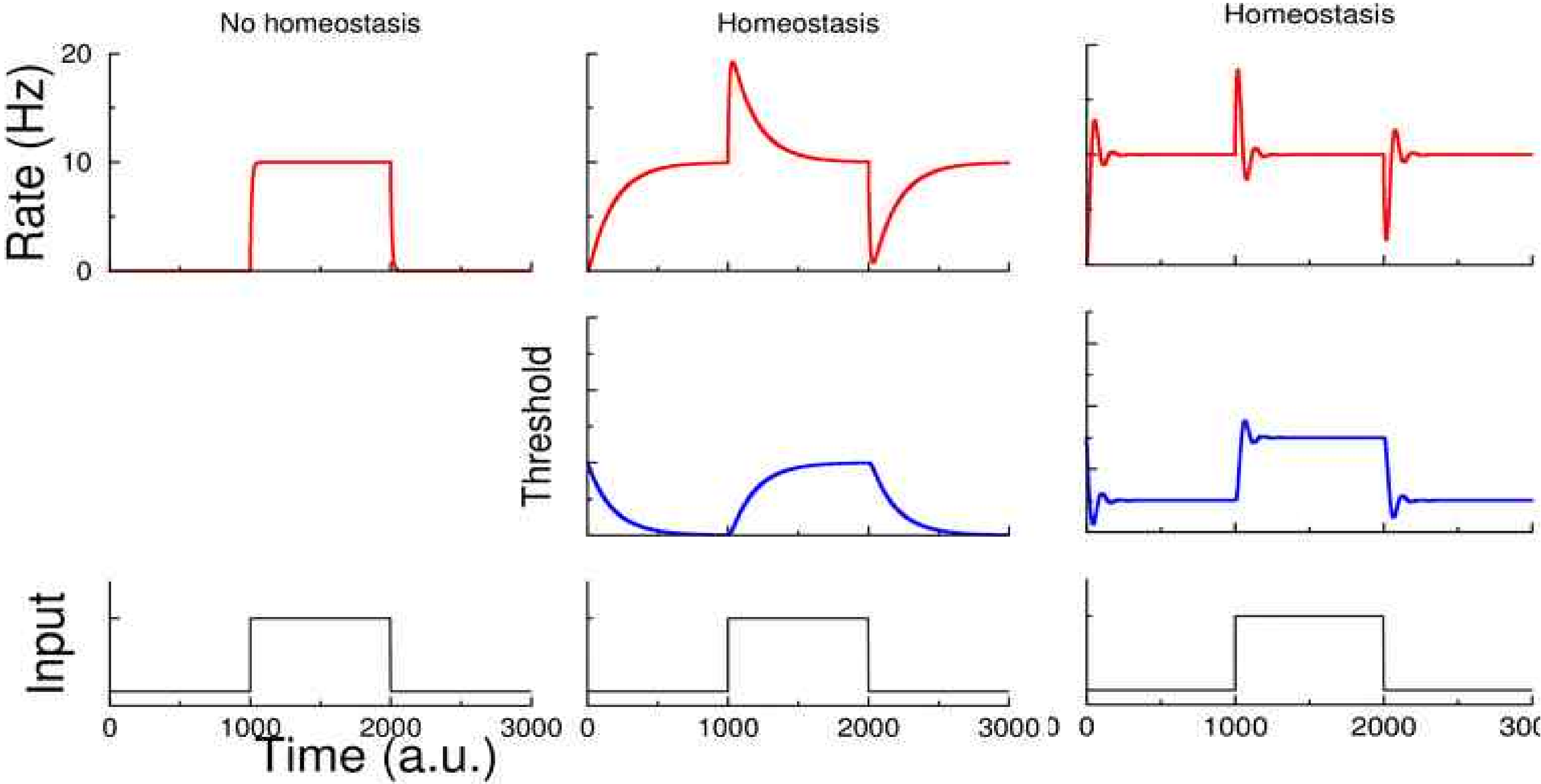
Robust perfect adaptation in bacterial chemotaxis through integral feedback control

Tau-Mu Yi*[†], Yun Huang[†‡], Melvin I. Simon*[§], and John Doyle[‡]

Homeostatic regulation
Single neurons



Homeostatic regulation
Single neurons



Typically a slow feedback will be stable (but slow..)

What time-constants to have stable homeostasis?

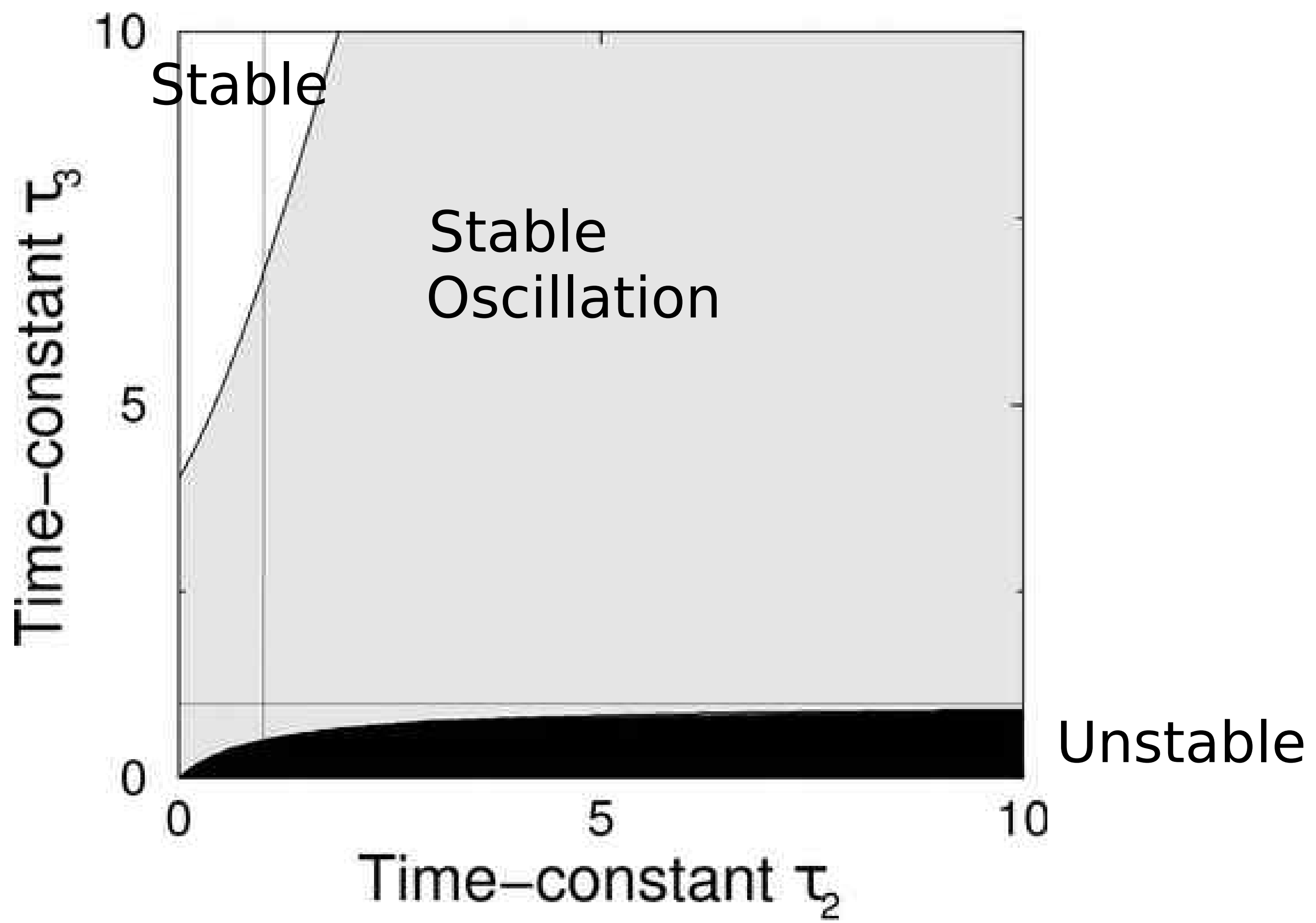
$$\frac{d}{dt}\begin{pmatrix} r_1(t) \\ r_2(t) \\ r_3(t) \end{pmatrix} = M \begin{pmatrix} r_1(t) \\ r_2(t) \\ r_3(t) \end{pmatrix} + \mathbf{b}$$

$$M = \begin{pmatrix} -\frac{1}{\tau_1} & 0 & -\frac{1}{\tau_1} \\ \frac{1}{\tau_2} & -\frac{1}{\tau_2} & 0 \\ 0 & \frac{1}{\tau_3} & 0 \end{pmatrix} \qquad \mathbf{b} = \begin{pmatrix} \frac{1}{\tau_1} u(t) \\ 0 \\ -\frac{1}{\tau_3} r_{goal} \end{pmatrix}$$

Re(Eigenvalues) <0 & Im(Eigenvalues)=0 → Stable

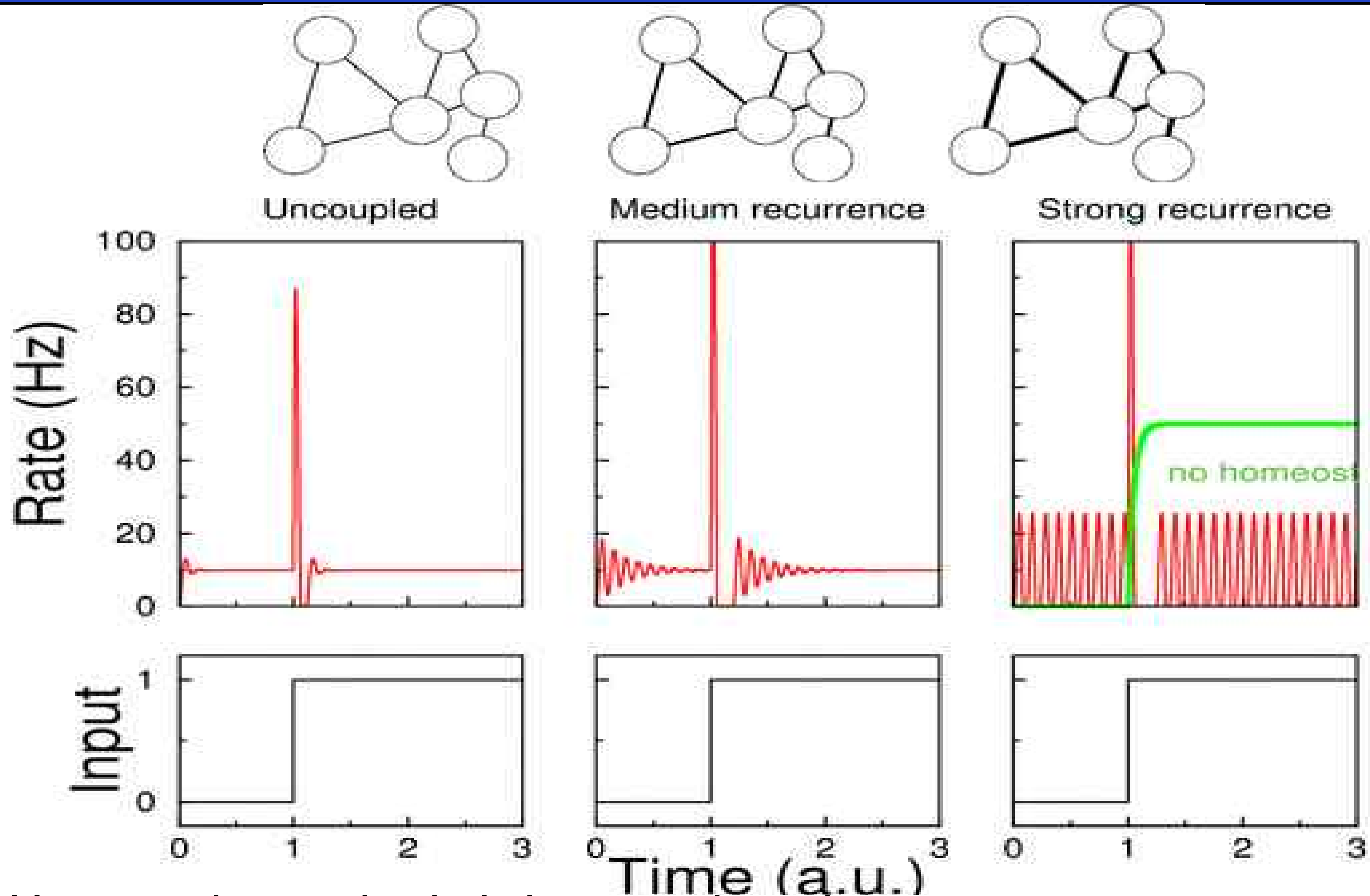
Re(Eigenvalues) <0 → Stable, damped oscillations

Homeostatic regulation
Single neurons



Typically a slow feedback will be stable (but slow..)

Homeostasis in Networks



- Homeostasis destabilizes network
- Critical amount of recurrence

Rate based dynamics

(No homeostasis)
N neurons with fast synapses:

$$\tau_1 \frac{d}{dt}\mathbf{r}_1(t) = (W - I)\mathbf{r}_1(t) + \mathbf{u}(t)$$

Decompose into eigen-modes of W (assume W'=W)

$$\frac{\tau_1}{1-w_i}\frac{d\mathbf{e}_i \exp(\lambda t)}{dt} = -\mathbf{e}_i \exp(\lambda t) + \frac{1}{1-w_i}\mathbf{u}.\mathbf{e_i} \exp(\lambda t)$$

Analysis of homestatic network

3N dimensional system

$$\frac{d}{dt}\begin{pmatrix}\mathbf{r}_1\\ \mathbf{r}_2\\ \mathbf{r}_3\end{pmatrix} = M\begin{pmatrix}\mathbf{r}_1\\ \mathbf{r}_2\\ \mathbf{r}_3\end{pmatrix} + \begin{pmatrix}\frac{1}{\tau_1}\mathbf{u}(t)\\ 0\\ -\frac{1}{\tau_3}r_{goal}\end{pmatrix}$$

$$M = \begin{pmatrix}\frac{1}{\tau_1}(W-I) & 0 & -\frac{1}{\tau_1}I\\ \frac{1}{\tau_2}I & -\frac{1}{\tau_2}I & 0\\ 0 & \frac{1}{\tau_3}I & 0\end{pmatrix}$$

Eigenvectors are of the form:

$$\begin{pmatrix}\mathbf{e}_n\\ \alpha_n\mathbf{e}_n\\ \beta_n\mathbf{e}_n\end{pmatrix}$$

Network stability

Stability of N 3rd order characteristic polynomials

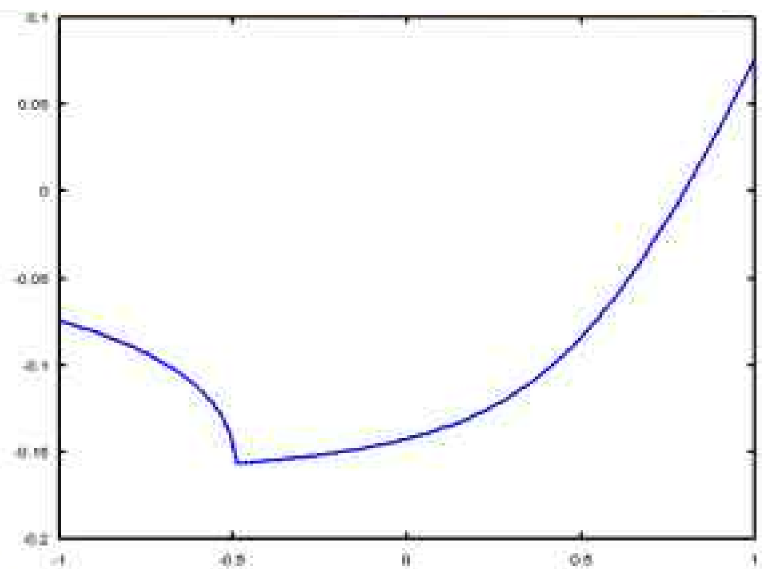
$$(1 - w_i + \tau_1 \lambda)(1 + \tau_2 \lambda)\tau_3 \lambda + 1 = 0$$

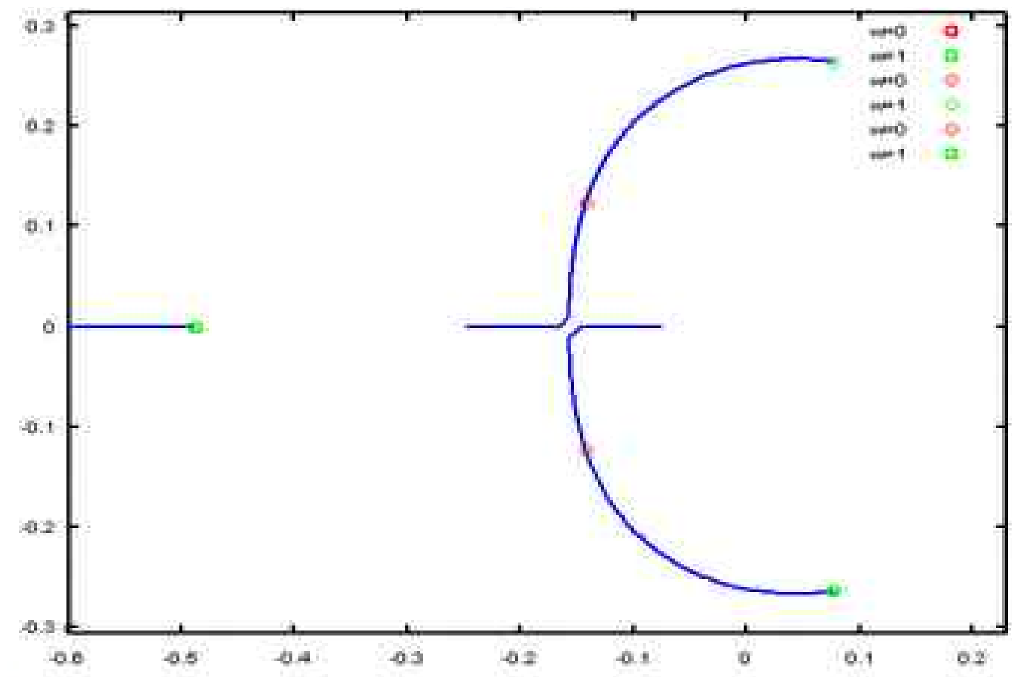
Observation:

mode with largest e.v. w_i de-stabilizes first.

Hence,

network stable *iff* mode with largest eigenvalue is sta





Numerical examples

$$\tau_1 \frac{dr_1(t)}{dt} = -r_1(t) + g\left(I - r_3(t)\right)$$

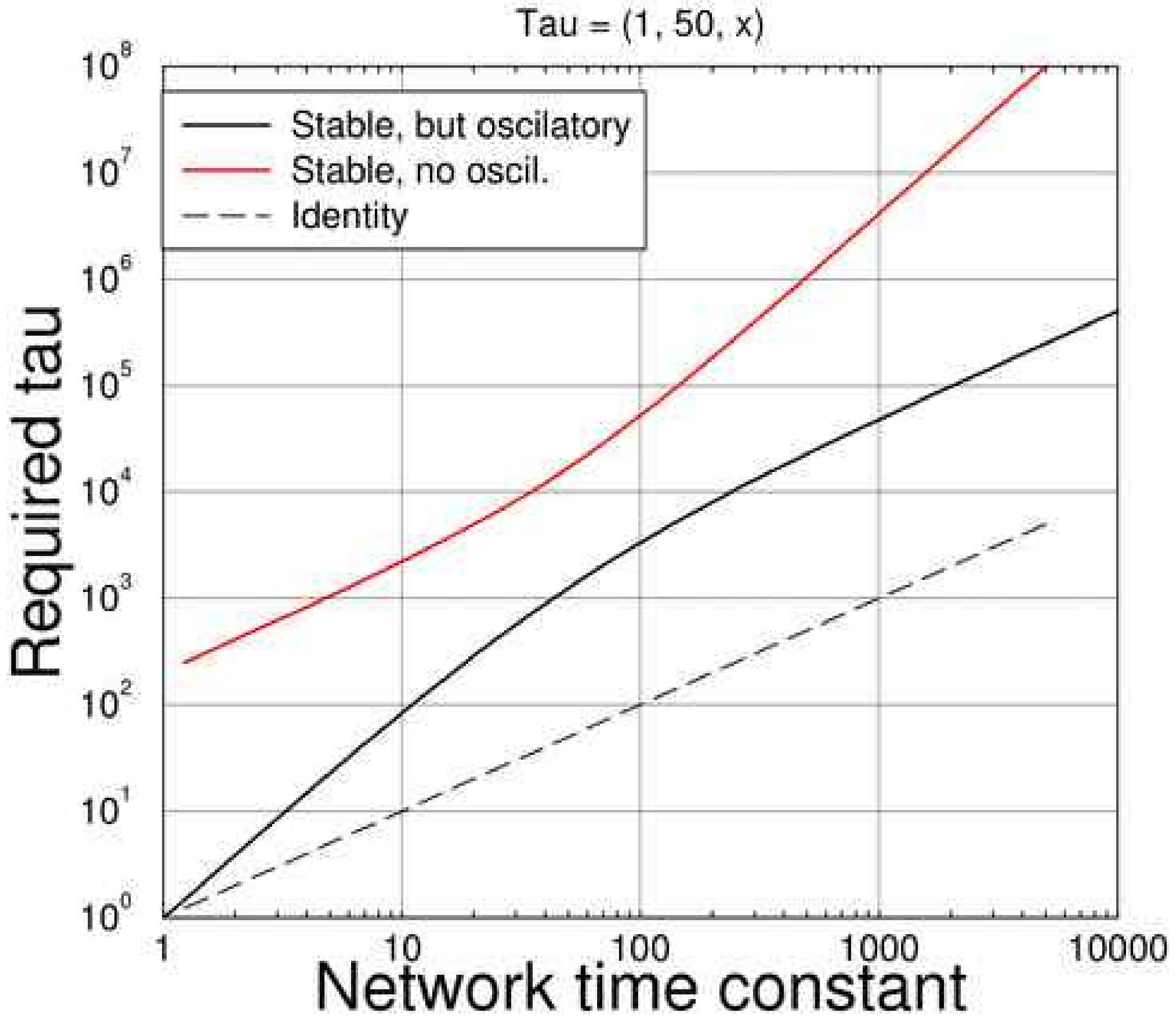
$$\tau_2 \frac{dr_2(t)}{dt} = -r_2(t) + r_1(t)$$

$$\tau_3 \frac{dr_3(t)}{dt} = r_2(t) - const$$

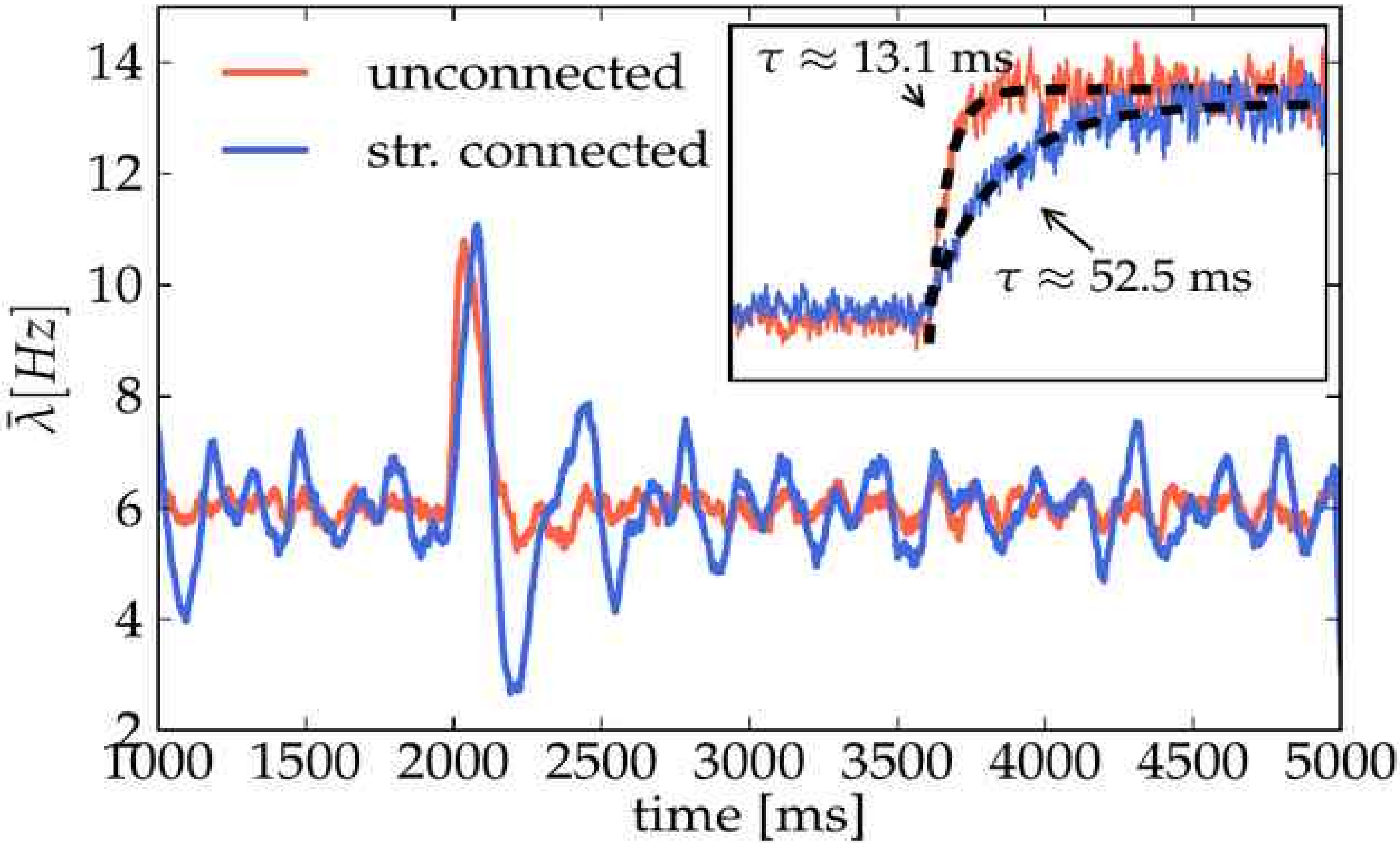
Assume tau1=1ms, tau2=50 ms, examine tau3

Netw. time-const	Recurrence	Stable Oscil.	Stable
1 ms	0	1ms	220ms
100 ms	0.99	3.2s	52s
10 s	0.9999	500s	28hrs

Homeostatic speed vs network recurrence

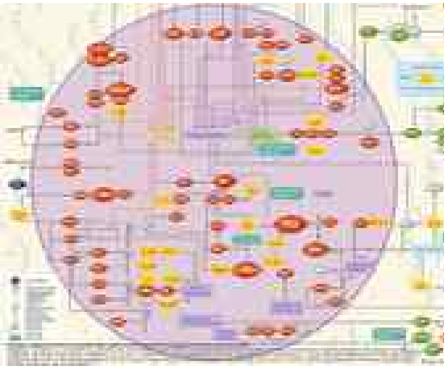


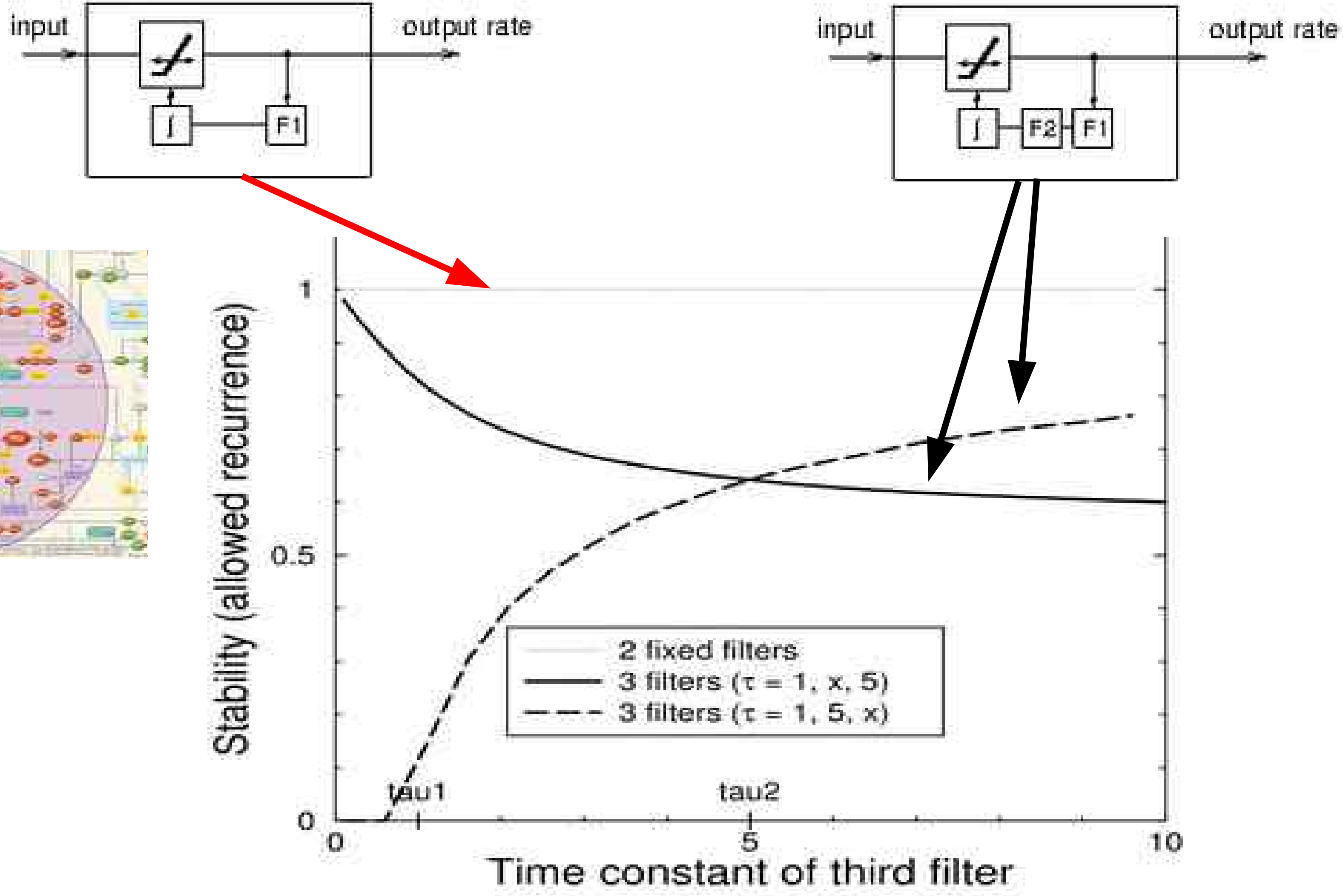
Spiking network simulation



- •Asychronous spiking network
- •Interaction between
- •Currently researching balanced models

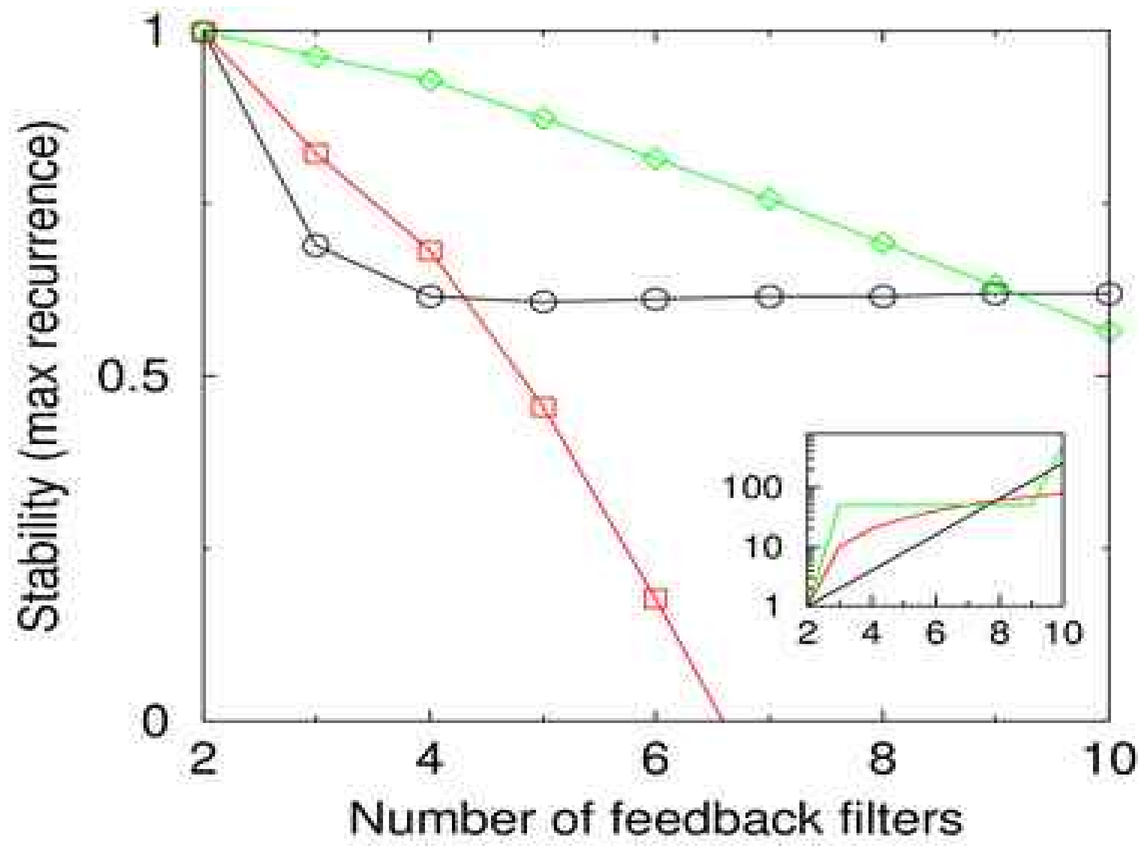
Homeostatic regulation: How many filters?





Counter-intuitively, adding filters tends to de-stabilize.

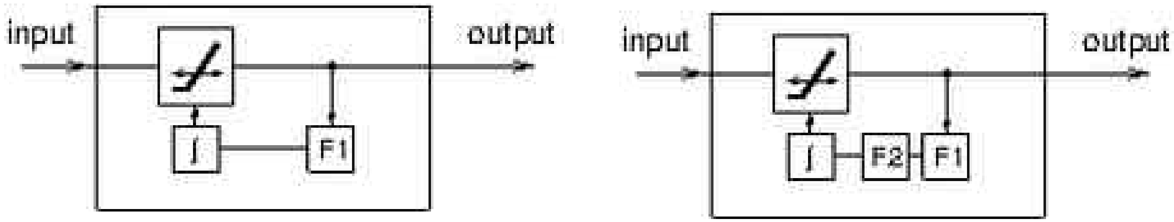
Homeostatic regulation: Adding filters is often bad..



1,50,50,...500

1,10,20,30,....

1,2,4,8, ...



Analysis

N x K dimensional system

$$\tau_1 \frac{dr_1(t)}{dt} = -[1-w]r_1(t) + u(t) - r_K(t)$$

$$\tau_k \frac{dr_k(t)}{dt} = -r_k(t) + r_{k-1}(t) \qquad k = 2 \ldots K-1$$

$$\tau_K \frac{dr_K(t)}{dt} = -r_{goal} + r_{K-1}(t)$$

For each eigenvalue w:

$$1 + \lambda\tau_K(1 - w + \lambda\tau_1) \prod_{k=2}^{K-1} (1 + \lambda\tau_k) = 0$$