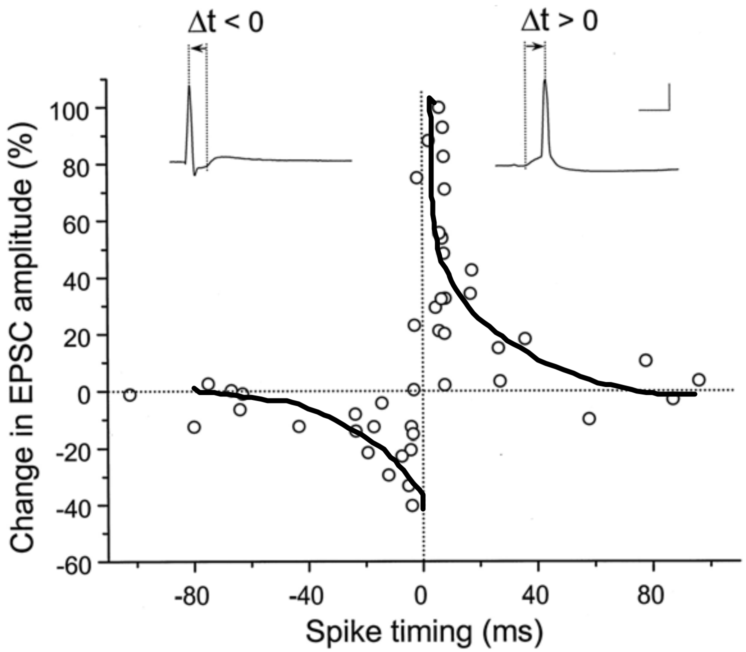
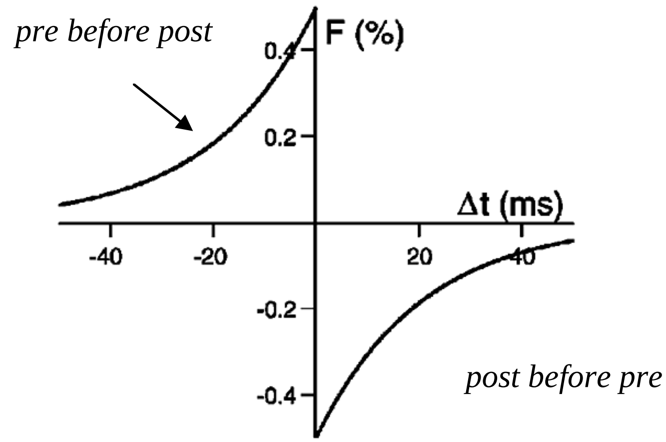




$$\Delta t = \mathrm{time}_{pre} - \mathrm{time}_{post}$$

$$F(\Delta t) = \begin{cases} A_+ \exp(\Delta t/\tau_+) & \text{if } \Delta t < 0 \\ -A_- \exp(-\Delta t/\tau_-) & \text{if } \Delta t \geq 0 \end{cases}$$

Bi, GQ and Poo, MM. Synaptic modifications in cultured hippocampal neurons: dependence on spike timing, synaptic strength, and postsynaptic cell type.
J Neurosci. 1998 Dec 15;18(24):10464-72.

Song, Miller and Abbott, Competitive Hebbian learning through spike-timing-dependent synaptic plasticity.
Nat Neurosci. 2000 Sep;3(9):919-26.

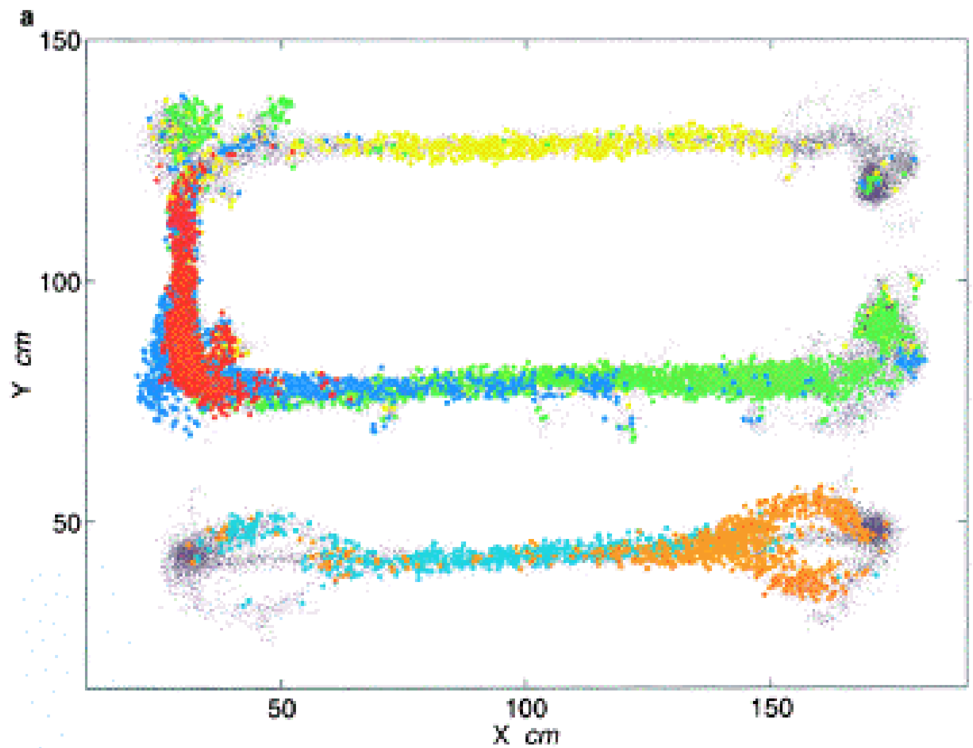
Experience-Dependent Asymmetric Shape of Hippocampal Receptive Fields

Mehta, Quirk and Wilson

* When a rat moves through an environment, neurons in the hippocampus fire in a spatially and directionally selective fashion and provide an accurate estimate of the location of the rat.

* Changes in these fields as a result of experience in novel and familiar environments suggest that mechanisms of plasticity may be involved.

* In this work, it is shown that the hippocampal receptive fields have an asymmetric shape and that this asymmetry is experience dependent.

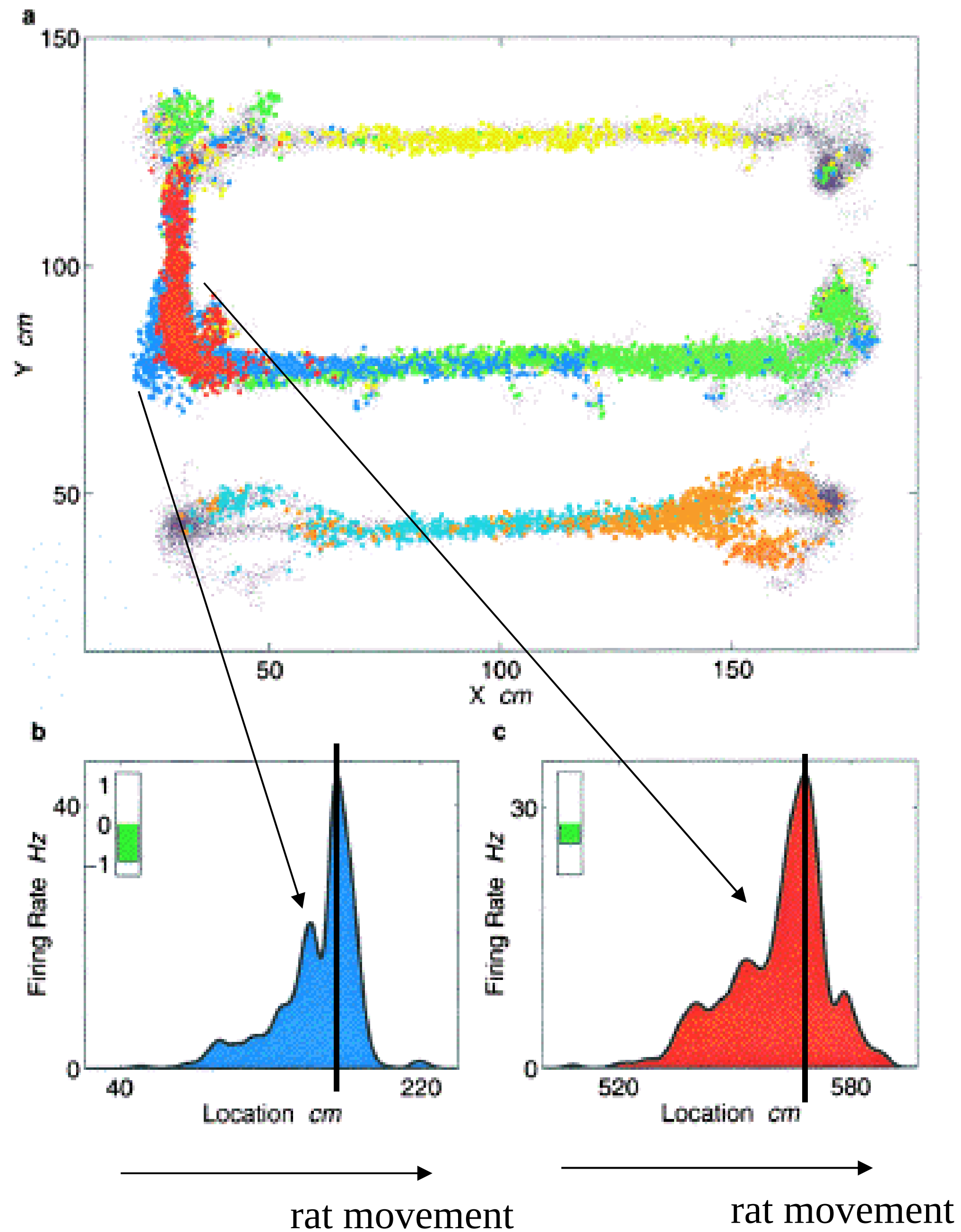


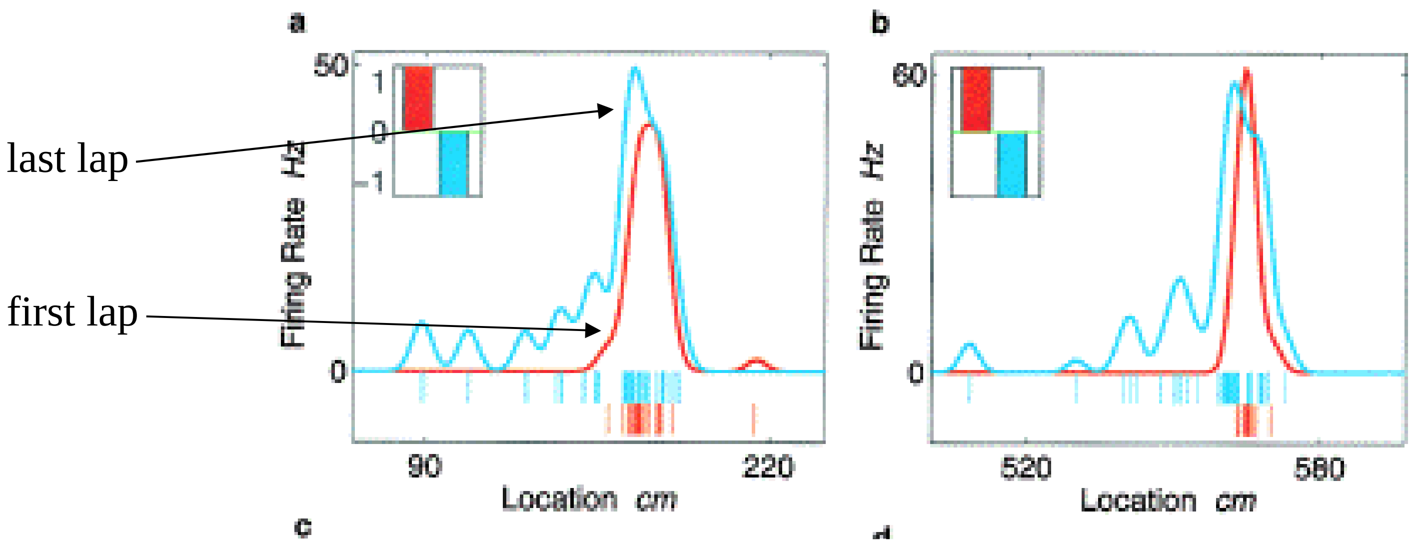
- Hippocampal pyramidal cells fire significantly more than rest when rat moves through a specific place in the environment.

- "Best place" is the exact location for which the cell fires most.

- "Place field" is the environment around the *best place for* which cell fires significantly more than rest.

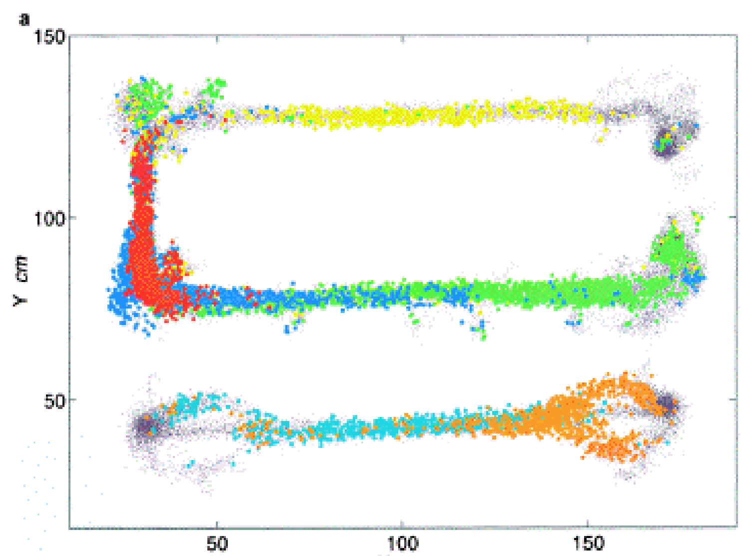
- On a linear track, place fields are asymmetric (or skewed) with respect to the *best place.*





- Asymmetry of place fields depends on rat's experience with a given environment.

- Asymmetry is not just *time dependent*. Place fields of cells that have acquired asymmetry in one environment are symmetric when rat is first placed in a novel environment in which the same cells are active.



* In previous work experience-dependent changes in place field location and firing rate were reported.

* A 51% increase in the place field size (from 426 to 643 cm × Hz) and a predictive or backward (i.e., in a direction opposite to the direction of movement of the rat through the place field) shift in the location of the center of mass of the place fields by 8.2 cm were observed.

* Further, the location of the peak of the place field shifted backward by 5.5 cm, and the first spike in the place field occurred 9.2 cm earlier, whereas the last spike in the place field occurred 6.5 cm earlier.

* This resulted in an experience-dependent widening of place fields by 7.9 cm.

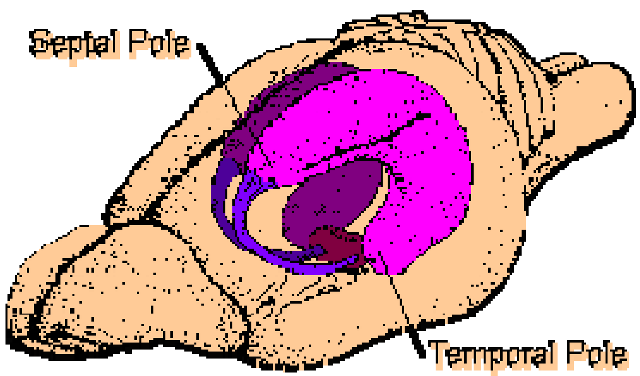
* Experience-dependent changes of place fields could result from the LTP and LTD of NMDA-dependent synapses.

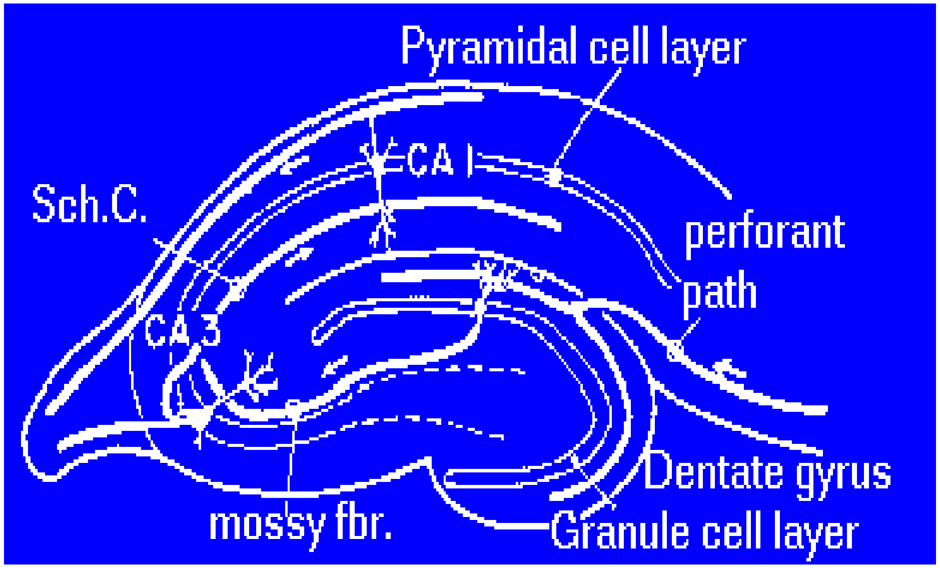
* NMDA-dependent synapses are strengthened if postsynaptic activity lags behind presynaptic spiking and depotentiated if the converse is true

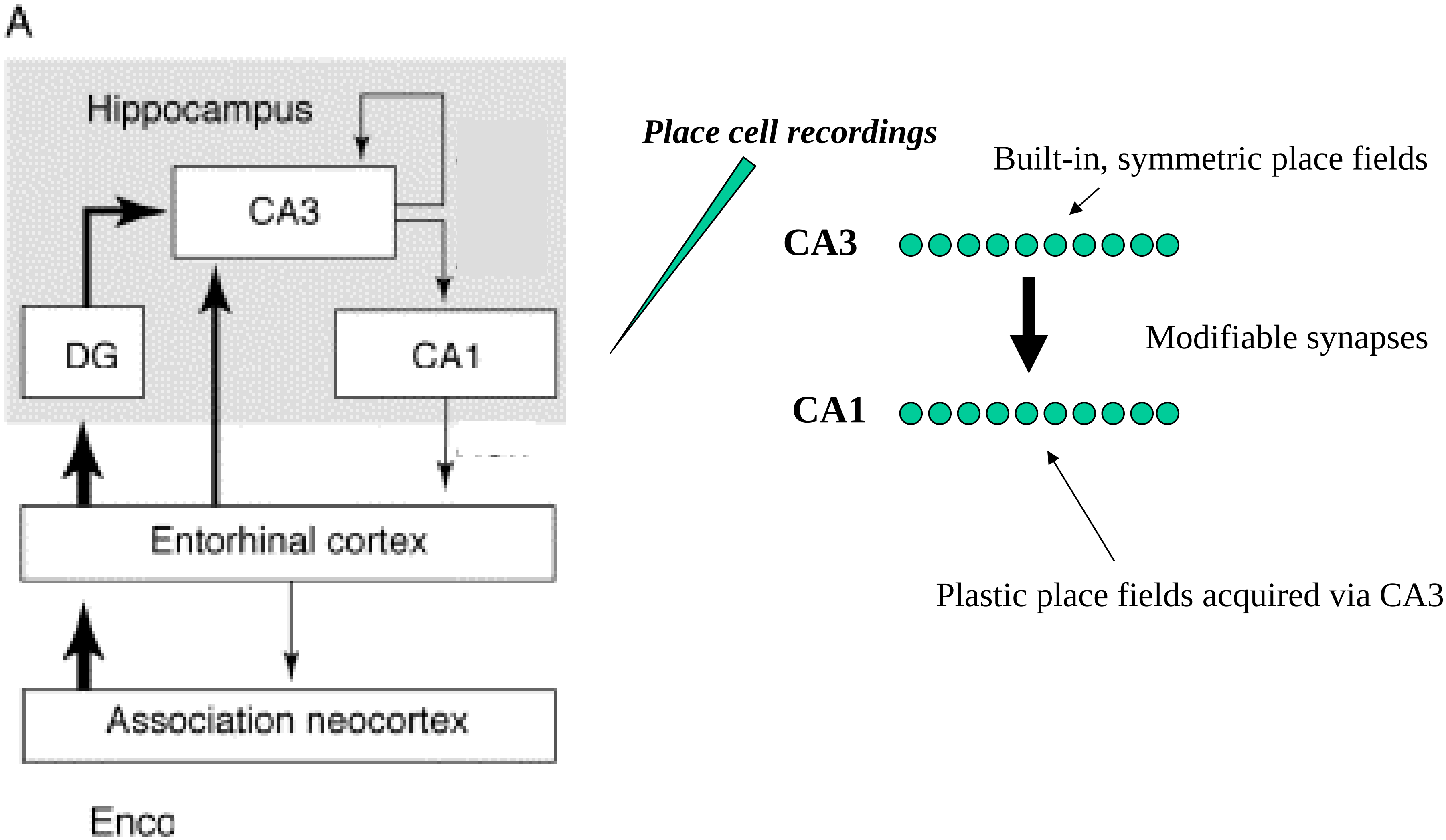
*Further, the amount of LTP/LTD is inversely related to the absolute value of the time lag between the pre- and postsynaptic neuronal spike times.

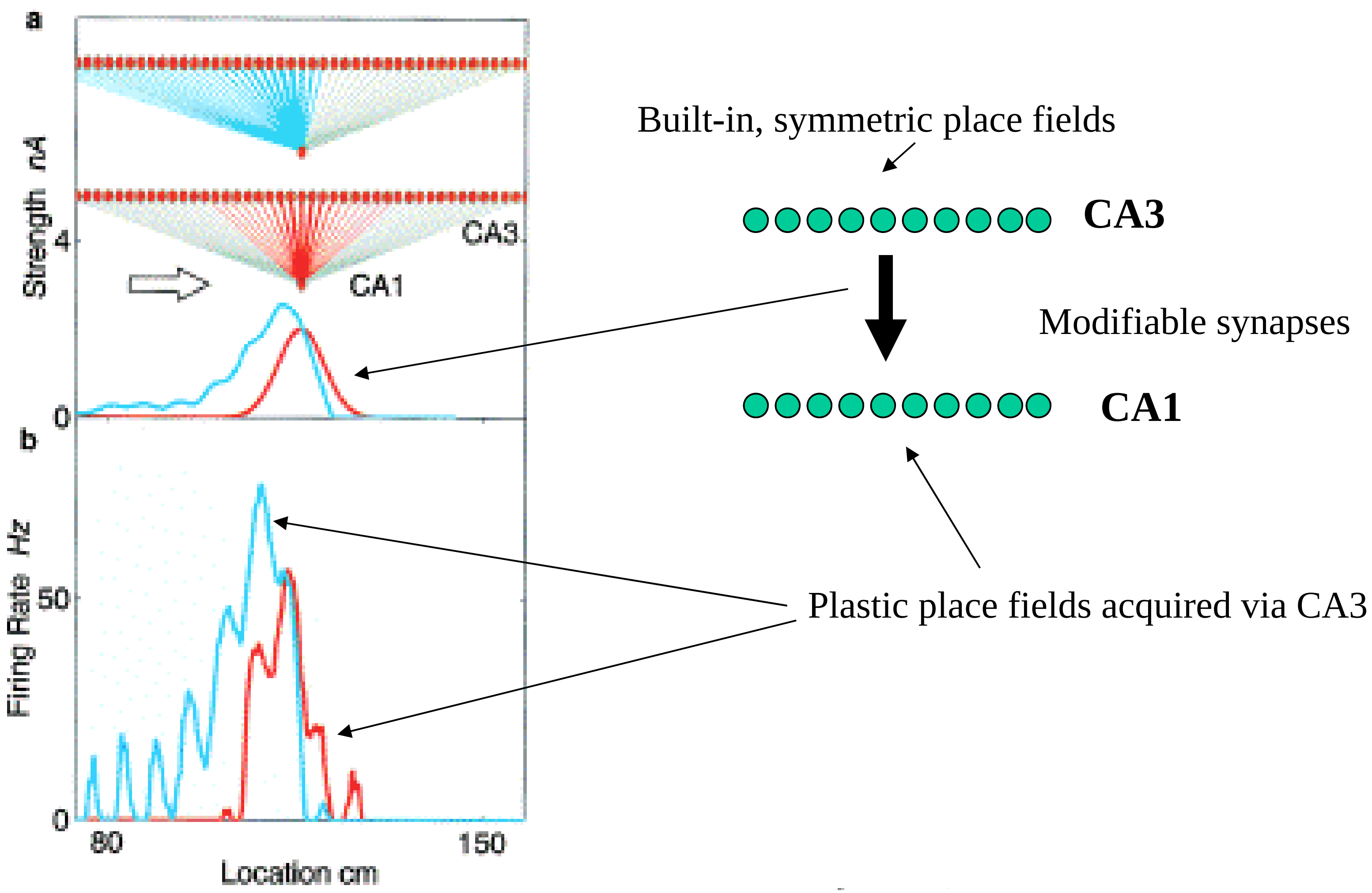
* It is known that pyramidal neurons in CA1 receive excitatory inputs from pyramidal neurons in CA3, which also exhibit place-specific firing. LTP of these CA3 CA1 connections has been shown to be NMDA dependent.

A very simple computational model

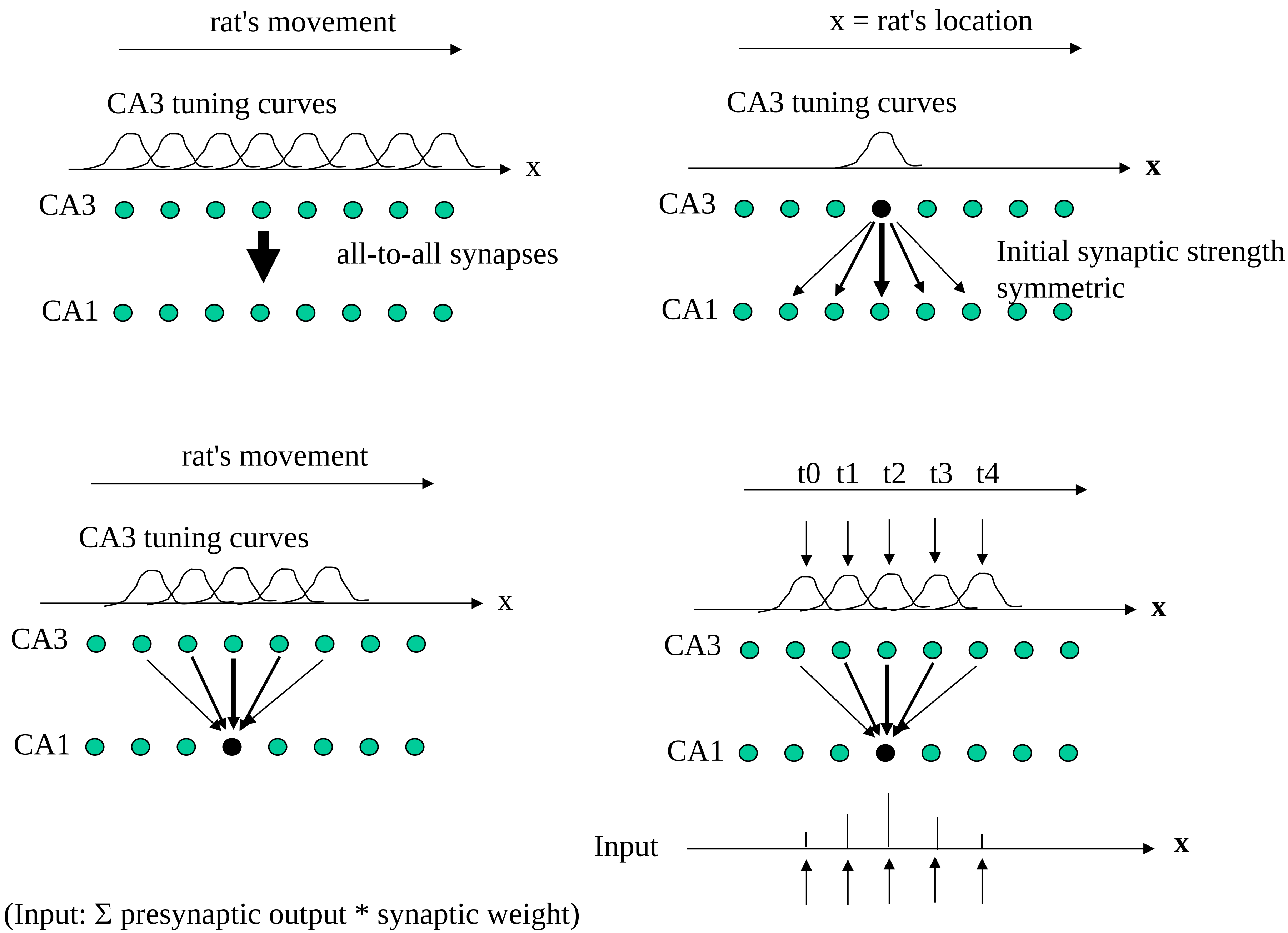


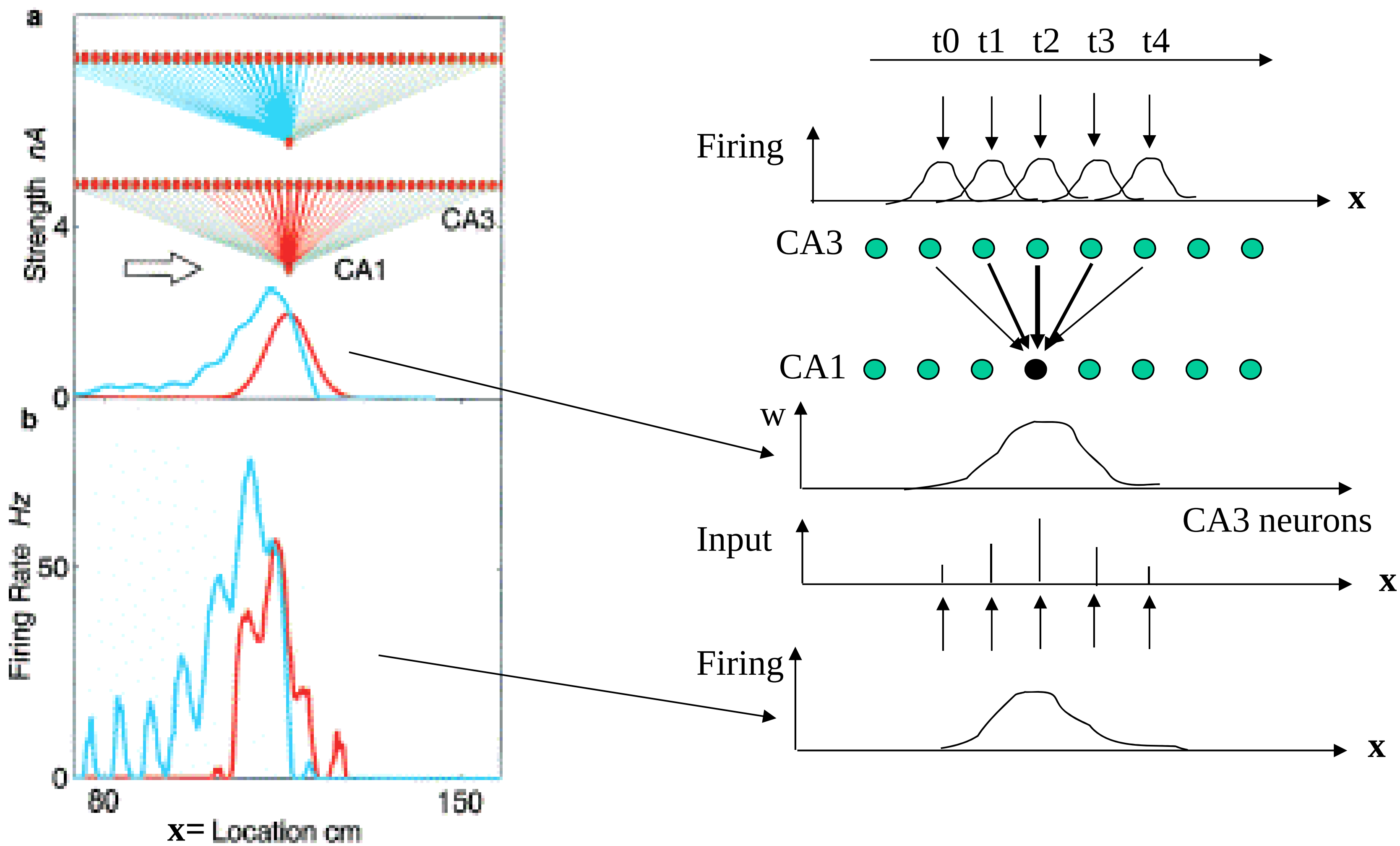


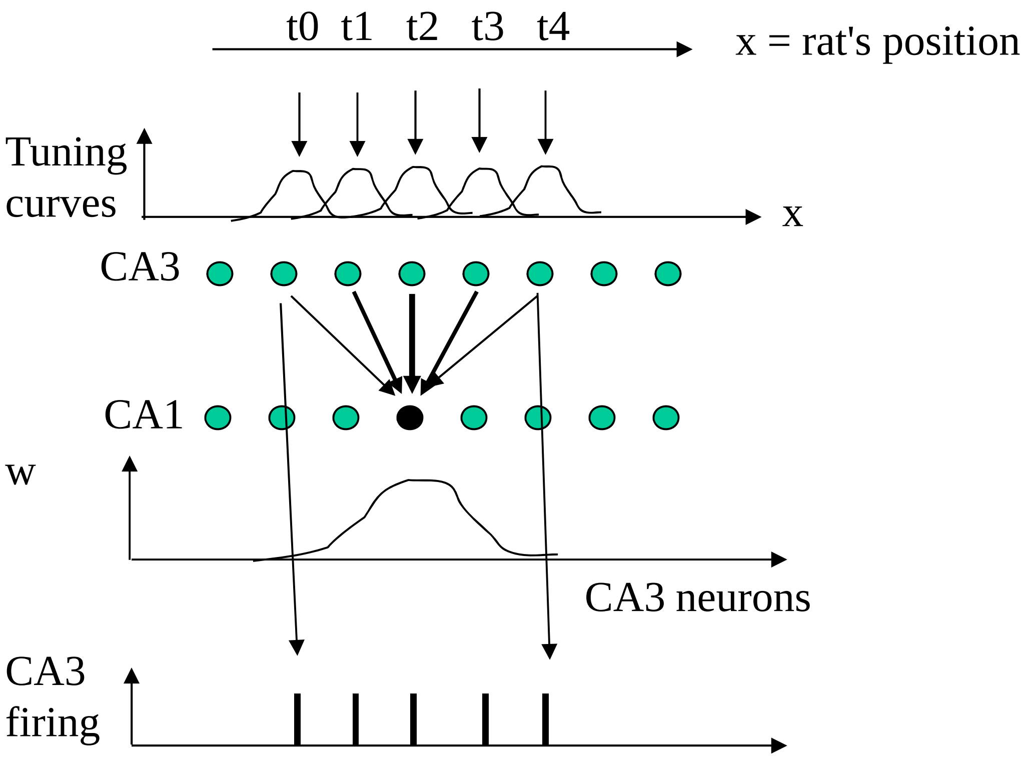

A
Hippocampus
CA3
DG
CA1
Entorhinal cortex
Association neocortex
Enco
Place cell recordings
Built-in, symmetric place fields
CA3
Modifiable synapses
CA1
Plastic place fields acquired via CA3

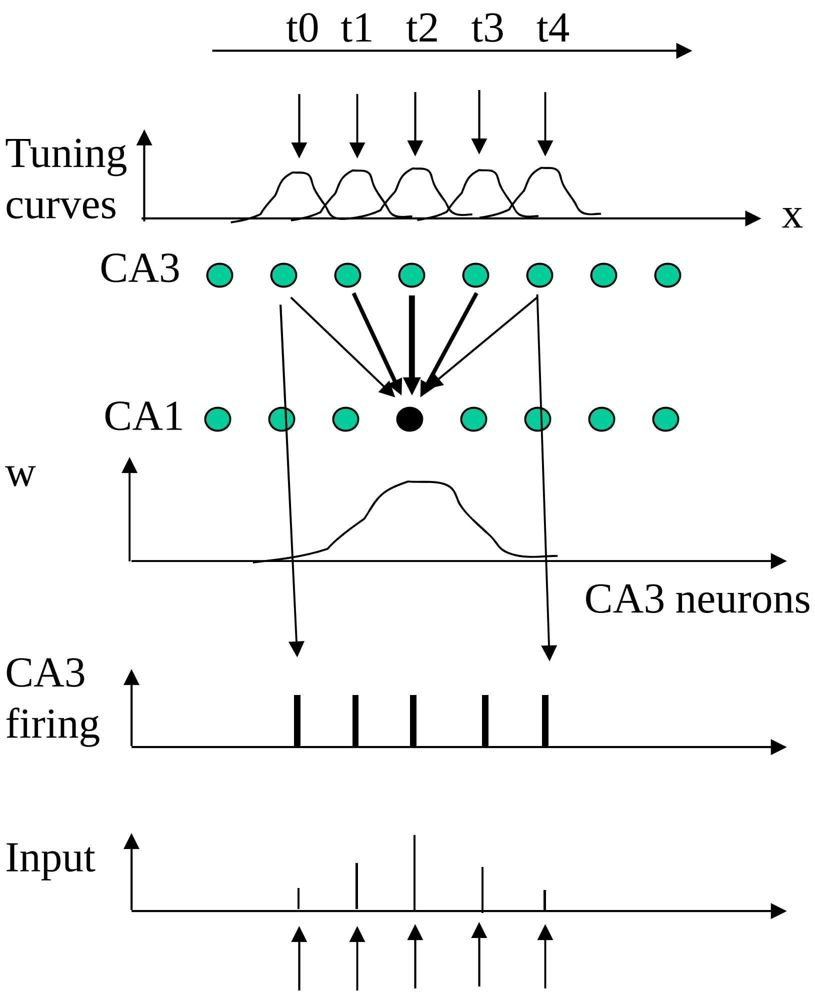


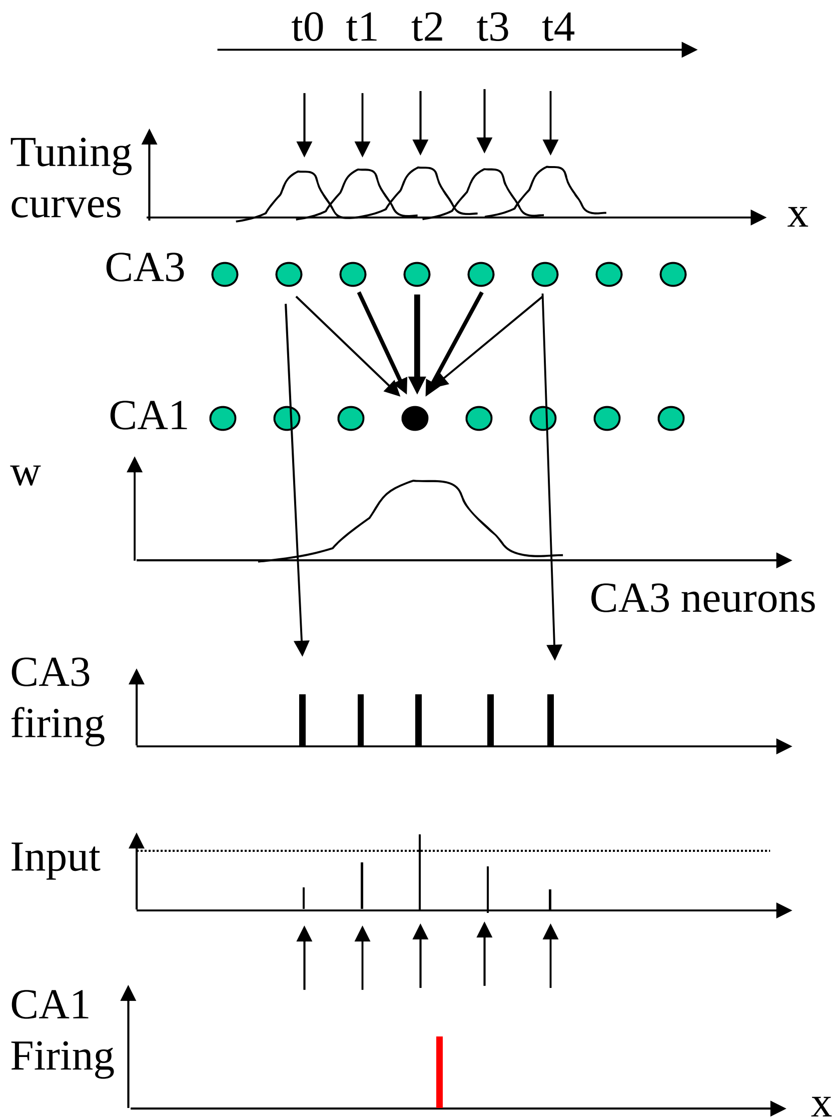
a
b
Strength nA
4
0
CA3
CA1
Firing Rate Hz
50
0
80
150
Location cm
Built-in, symmetric place fields
CA3
Modifiable synapses
CA1
Plastic place fields acquired via CA3


rat's movement
CA3 tuning curves
x
CA3
all-to-all synapses
CA1
x = rat's location
CA3 tuning curves
x
CA3
Initial synaptic strength
symmetric
CA1
rat's movement
CA3 tuning curves
x
CA3
CA1
t0 t1 t2 t3 t4
x
CA3
CA1
Input
x
(Input: Σ presynaptic output * synaptic weight)

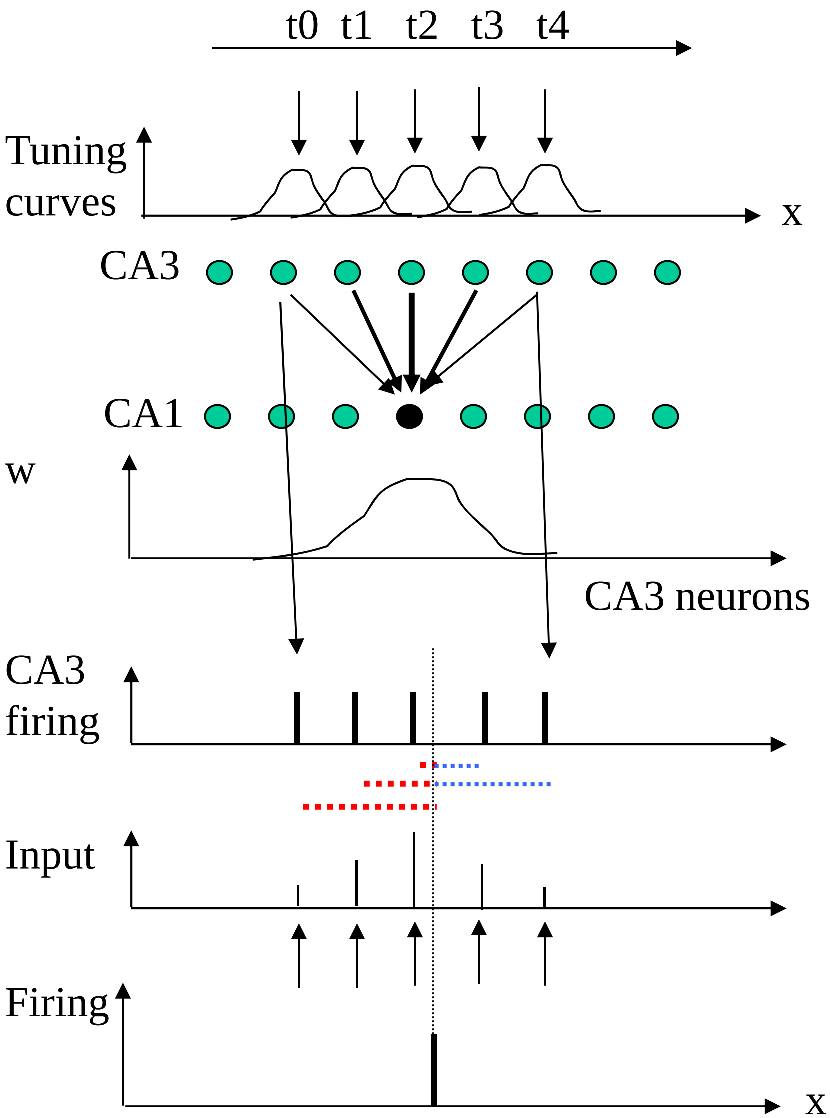

a
b
Strength nA
4
0
CA3
CA1
Firing Rate Hz
50
0
80
150
x= Location cm
t0 t1 t2 t3 t4
Firing
x
CA3
CA1
w
CA3 neurons
Input
x
Firing
x

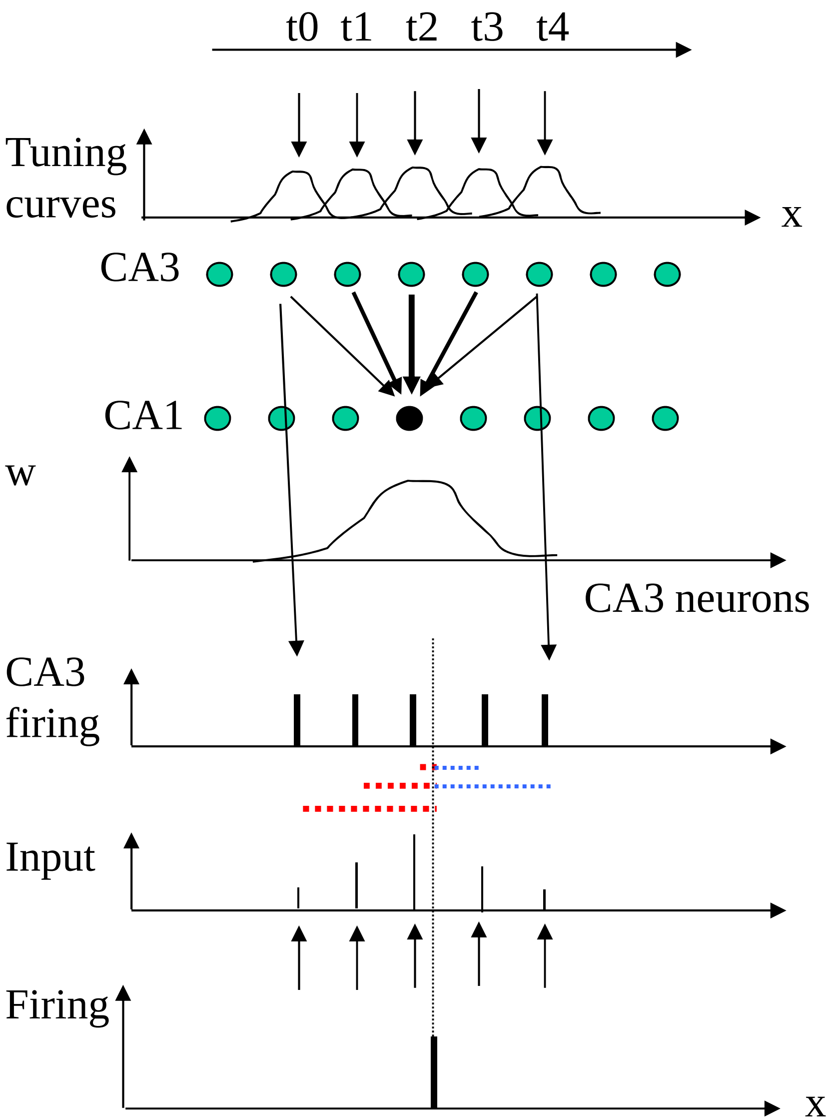

t0 t1 t2 t3 t4
x = rat's position
Tuning curves
x
CA3
CA1
w
CA3 neurons
CA3 firing

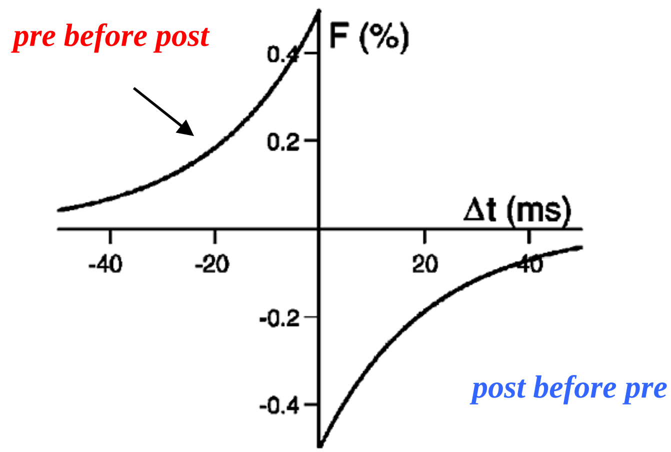

t0 t1 t2 t3 t4
Tuning curves
x
CA3
CA1
w
CA3 neurons
CA3 firing
Input



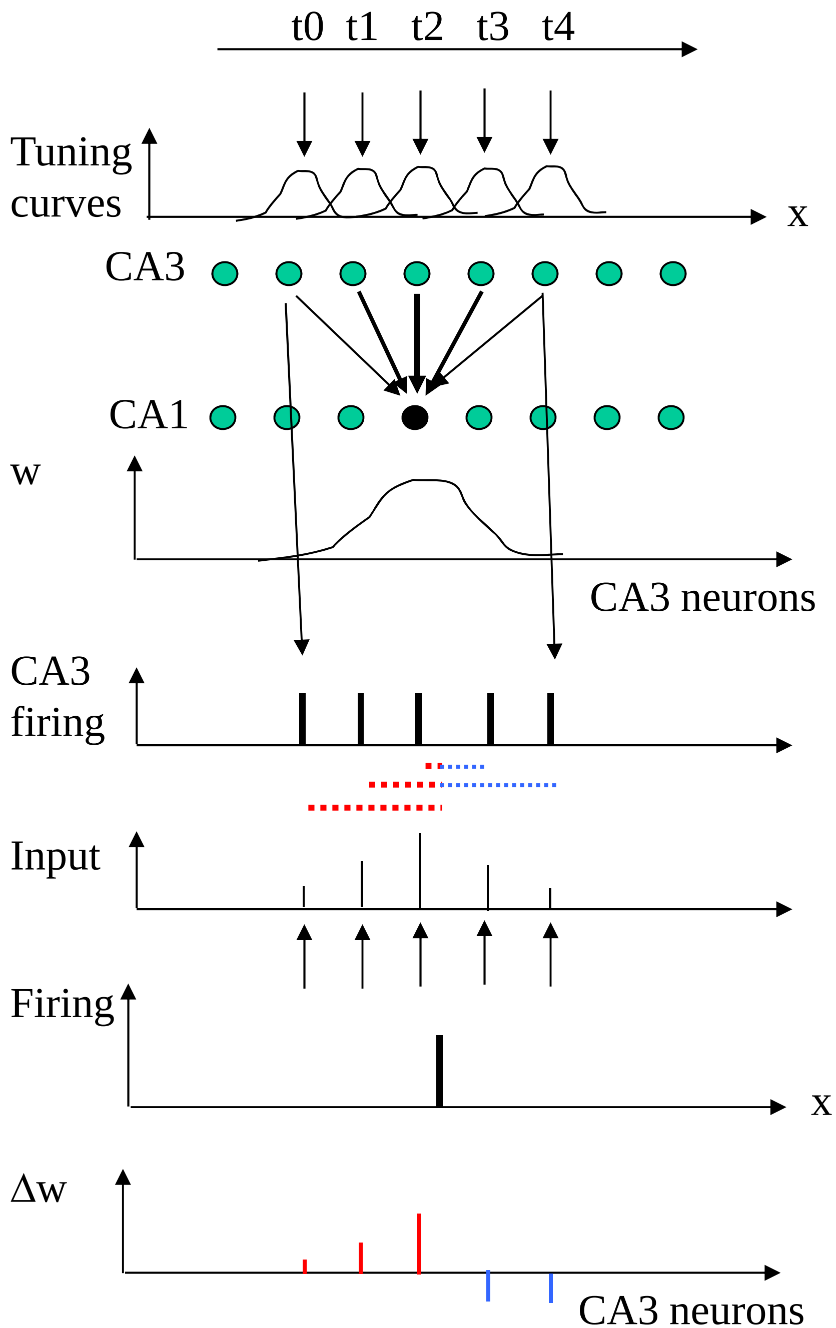
t0 t1 t2 t3 t4
Tuning curves
x
CA3
CA1
w
CA3 neurons
CA3 firing
Input
CA1 Firing
x

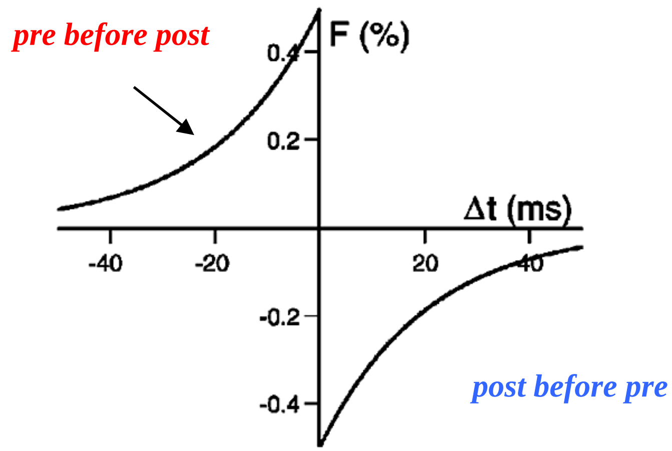

t0 t1 t2 t3 t4
Tuning
curves
x
CA3
CA1
w
CA3 neurons
CA3
firing
Input
Firing
x



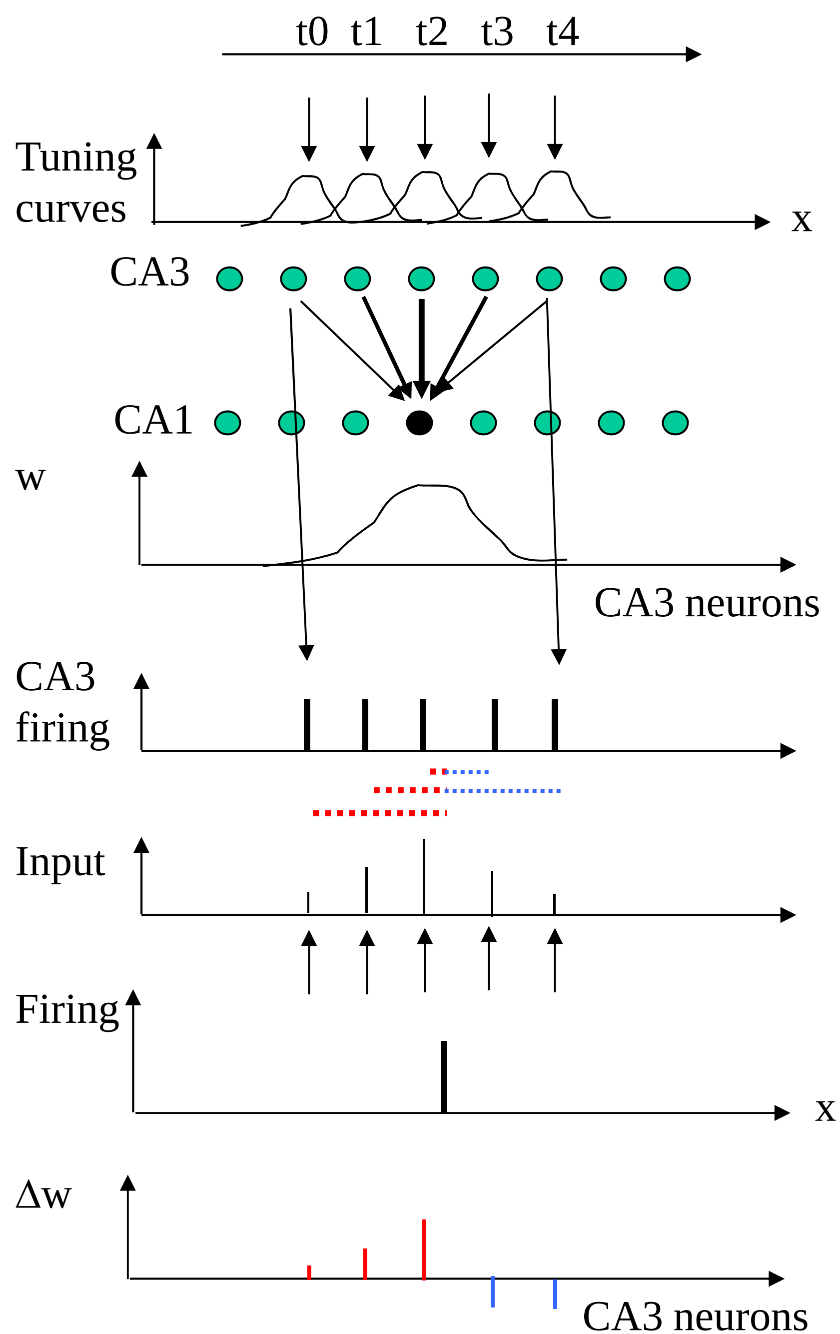


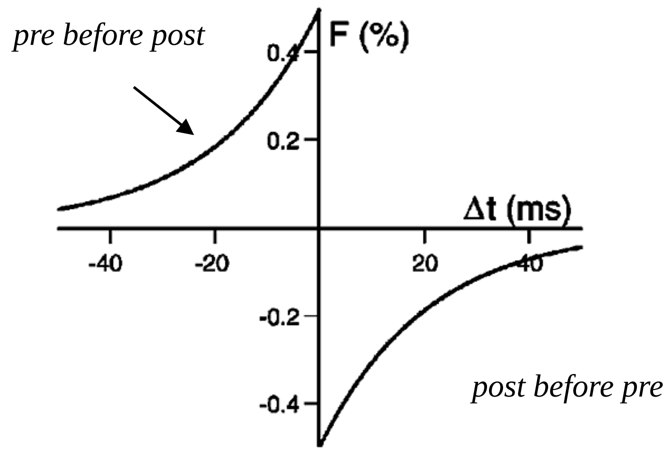
$\Delta t = \text{time}_{pre} - \text{time}_{post}$



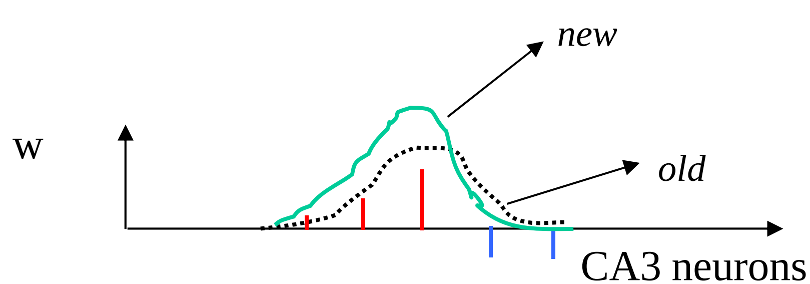


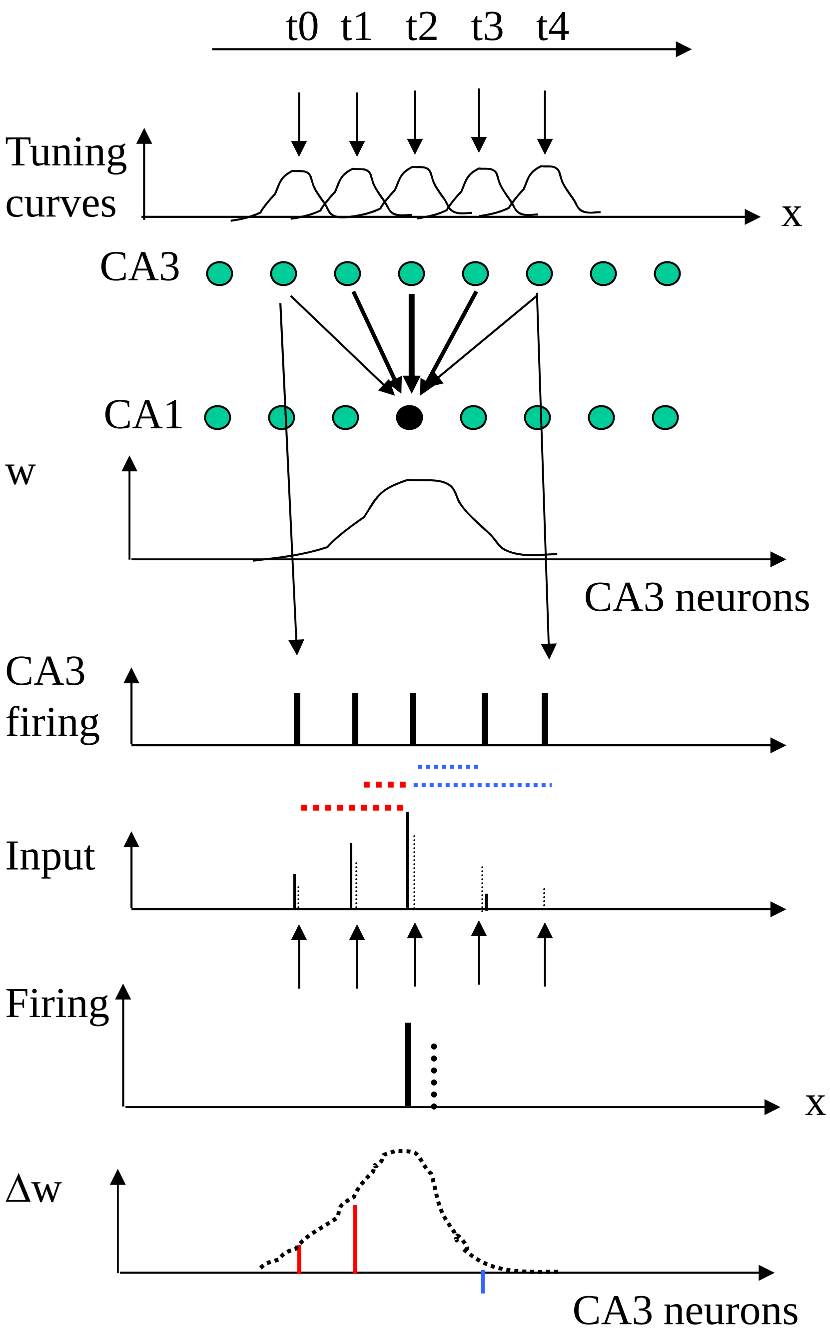
$\Delta t = \text{time}_{pre} - \text{time}_{post}$



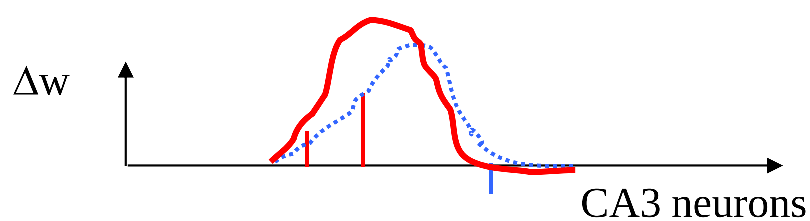


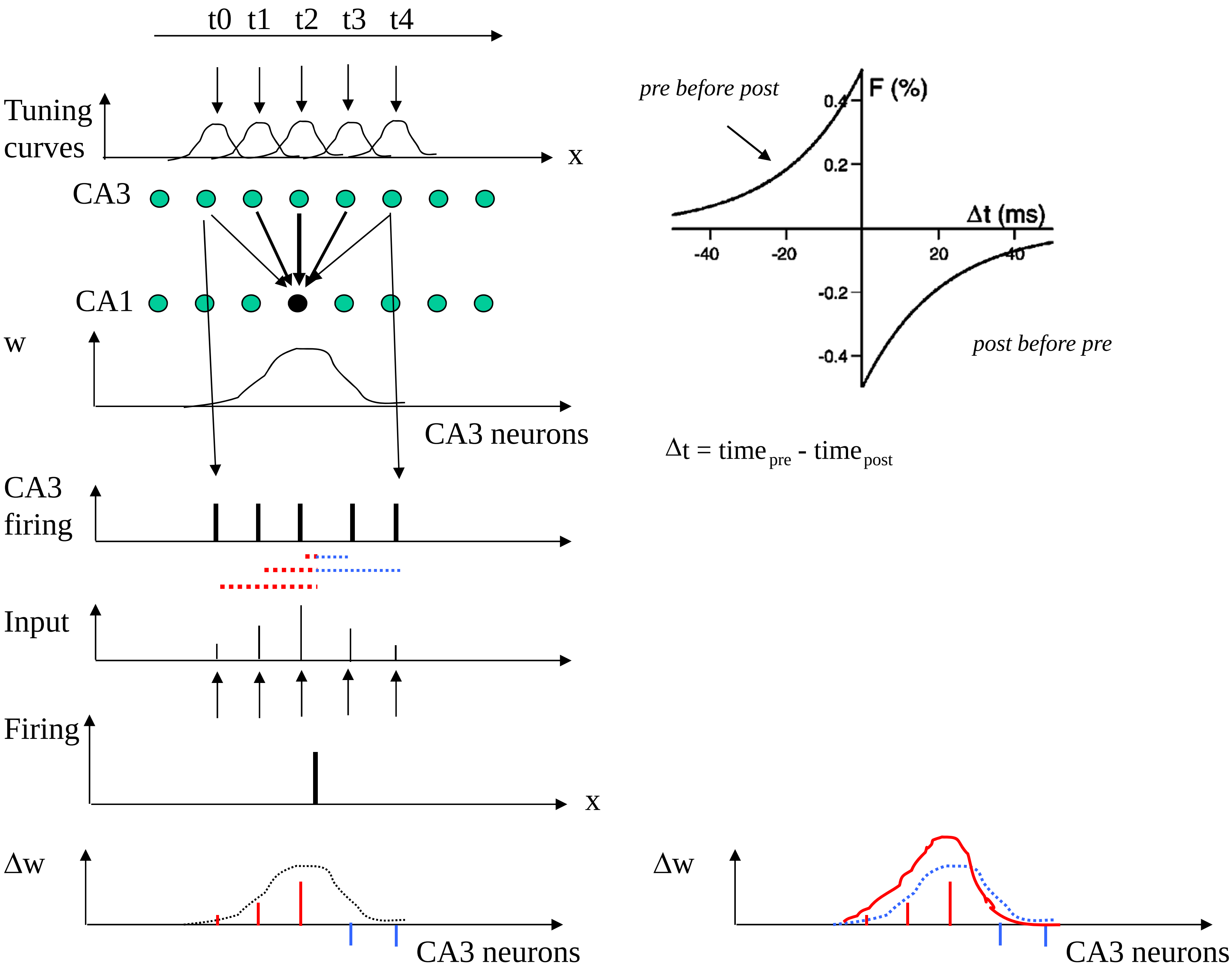
$\Delta t = \text{time}_{pre} - \text{time}_{post}$



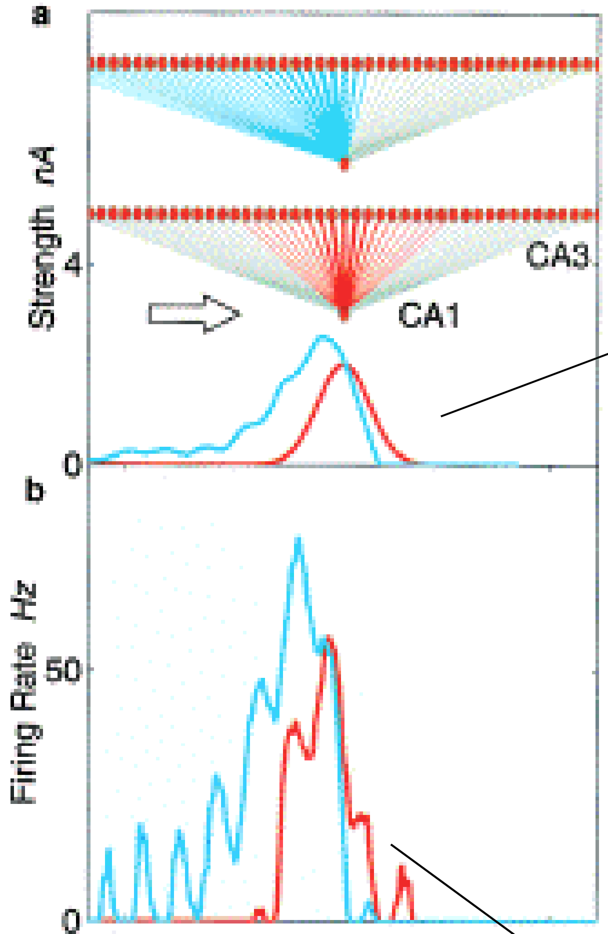


Because of the spike-timing dependent plasticity rule, the place fields tend to move to earlier positions and become asymmetric as the rat moves through the track more and more often

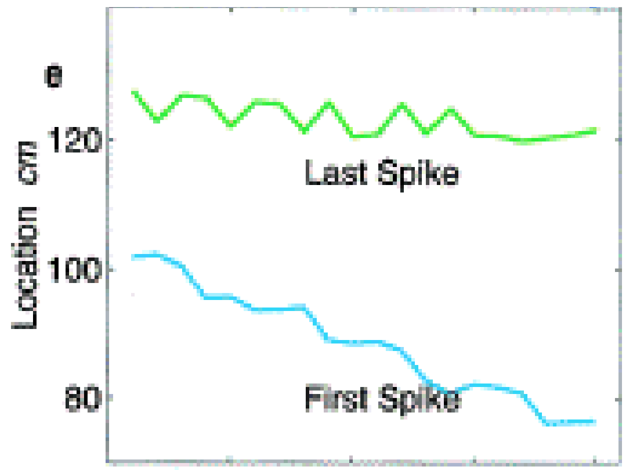




t0 t1 t2 t3 t4
Tuning curves
x
CA3
CA1
w
CA3 neurons
CA3 firing
Input
Firing
x
Δw
CA3 neurons
pre before post
F (%)
0.4
0.2
Δt (ms)
-40
-20
20
40
-0.2
-0.4
post before pre
Δt = time_pre - time_post
Δw
CA3 neurons



Distribution of synaptic weights becomes asymmetric



Place fields move to earlier positions and become asymmetric

Intracortical mechanism of stimulus-timing-dependent plasticity in visual cortical orientation tuning

Yao, Shen and Dan

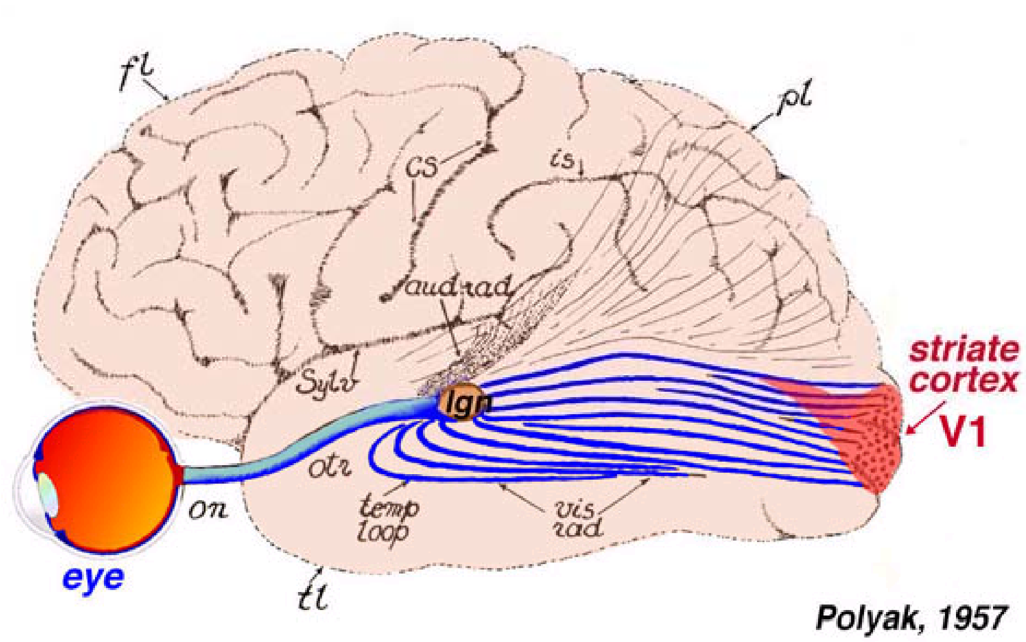


Figure 8. Visual input to the brain goes from eye to LGN and then to primary visual cortex, or area V1, which is located in the posterior of the occipital lobe.
Adapted from Polyak (1957).

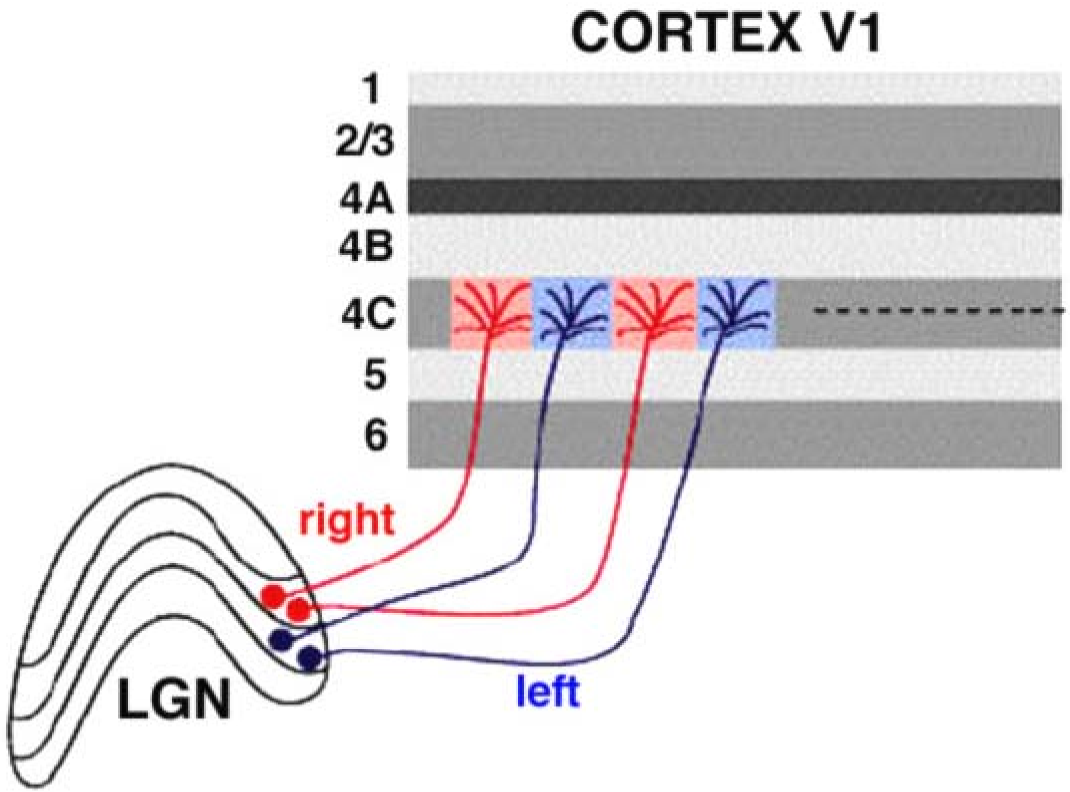


Figure 14. The signals from each eye are segregated within the LGN and go into different ocular dominance columns within area V1, layer 4C.

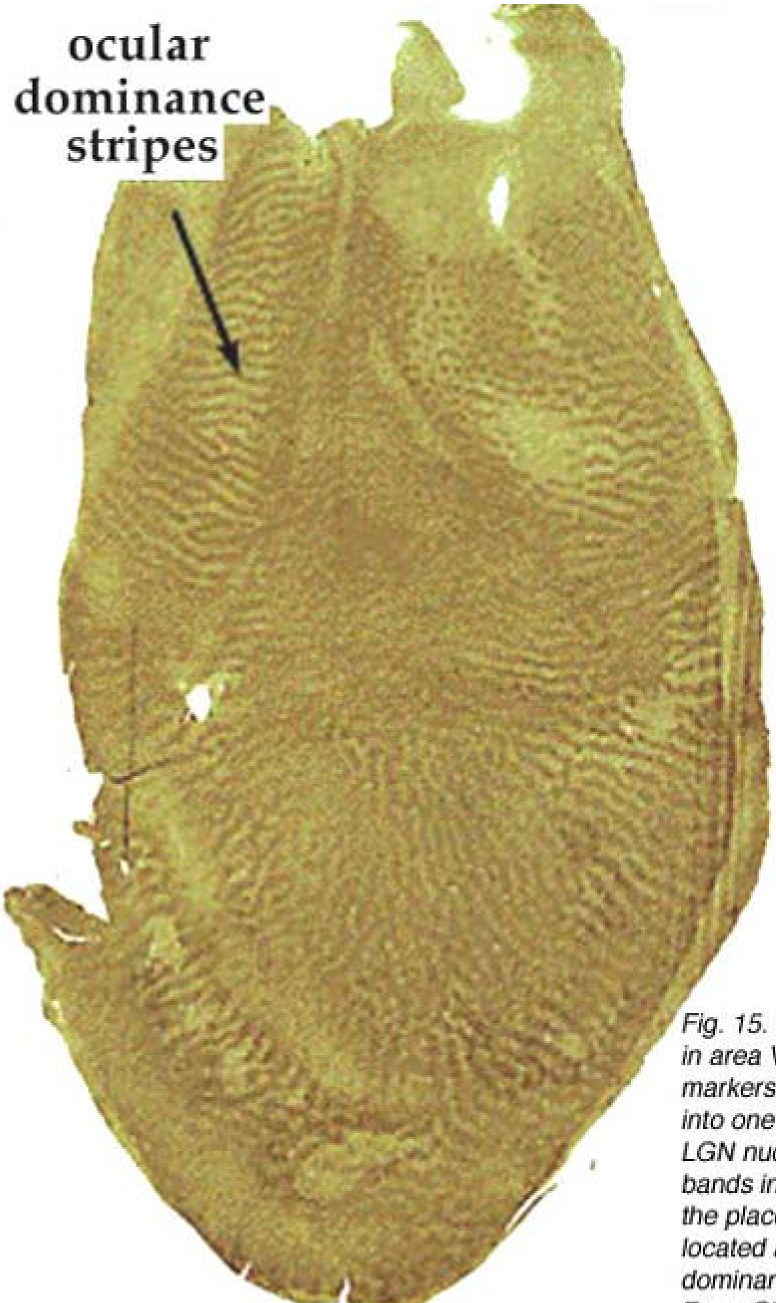


Fig. 15. The ocular dominance columns in area V1 can be visualized by using markers. When the marker is injected into one eye it is transported via the LGN nucleus to the cortex. The light bands in this tangential section show the places where the marker was located and thus reveal the ocular dominance columns.
From Olavarria & van Essen, 1997.

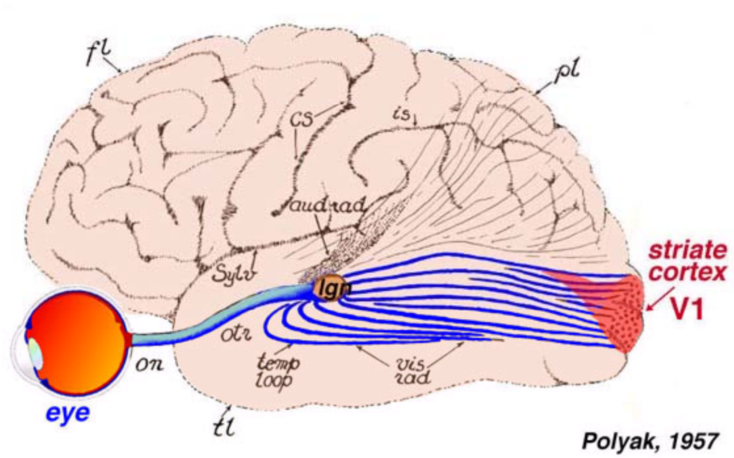


Figure 8. Visual input to the brain goes from eye to LGN and then to primary visual cortex, or area V1, which is located in the posterior of the occipital lobe.
Adapted from Polyak (1957).

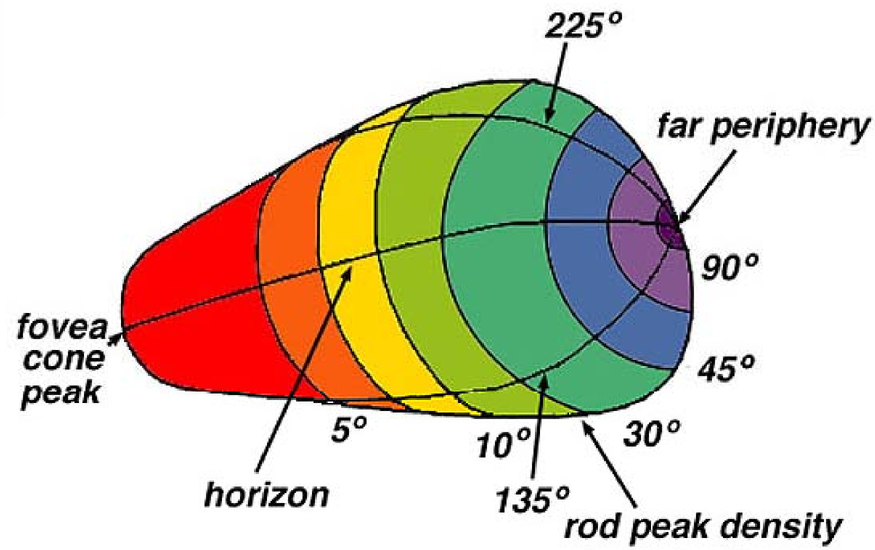


Figure 20. The unfolded striate cortex has a shape like a pear. It would be a quarter sphere if the visual fields were equally represented everywhere, but instead it is greatly distorted by the disproportionate representation of parts near the center of gaze (fovea), a feature termed "cortical magnification". In contrast, the far periphery is greatly underrepresented.

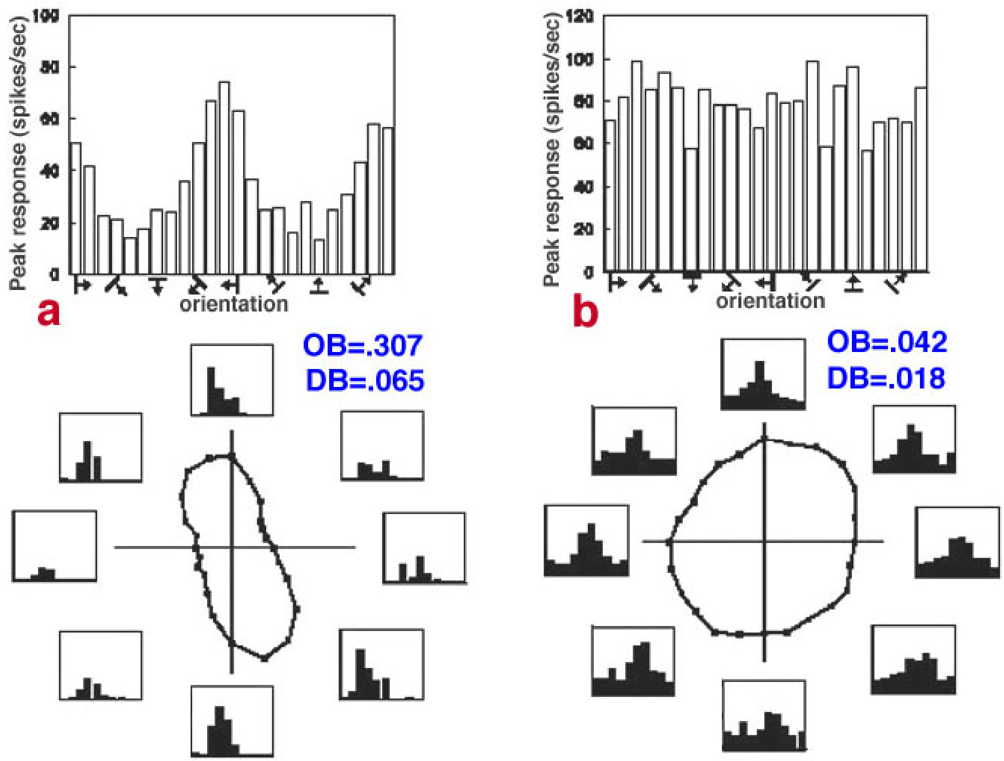
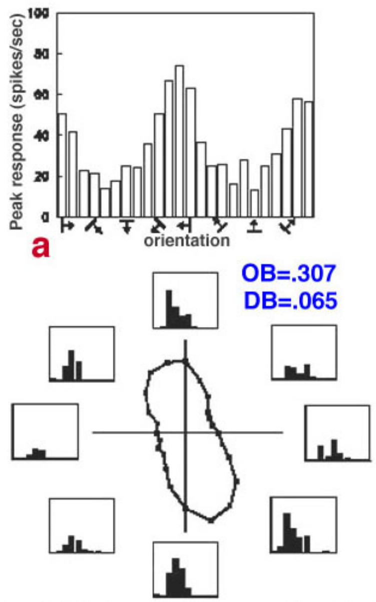


Figure 21. A tuning curve and corresponding polar plot obtained from two macaque V1 cells in response to drifting luminance bars of systematically varied orientation and direction. The responses of one orientation selective cell and one nonselective cell are provided for comparison. Histograms surrounding the polar plots demonstrate the cellular response as a function of time. Orientation bias (OB) and direction bias (DB) are measures of how selective a cell is, where >0.1 is significant, and 0.3 is approximately an 8:1 maximum firing rate to minimum firing rate ratio. From Schmolesky et al. (2000).



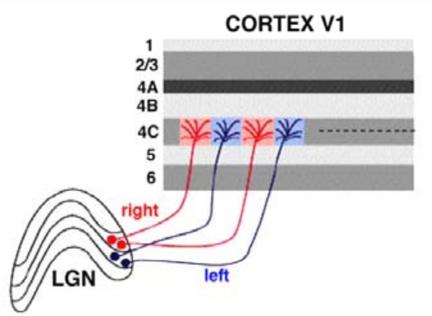
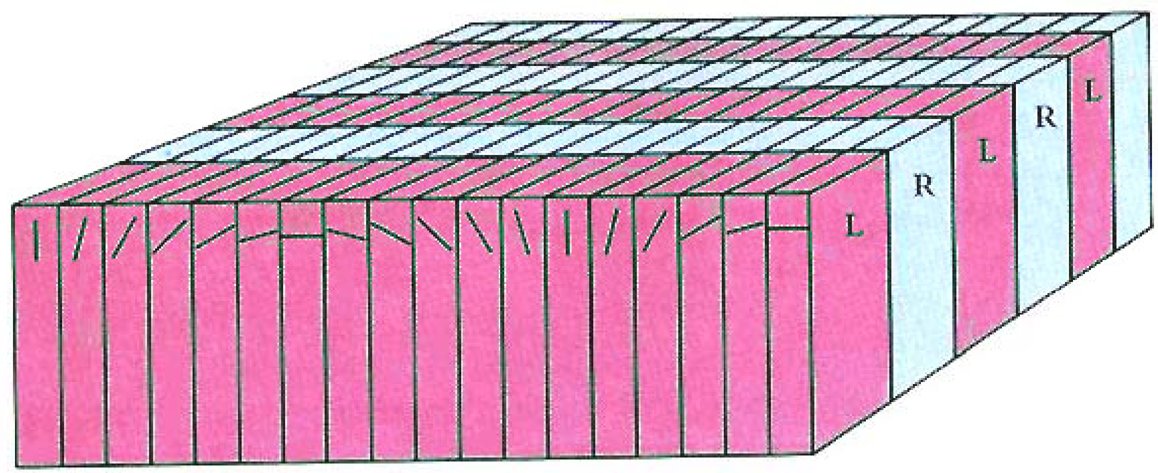


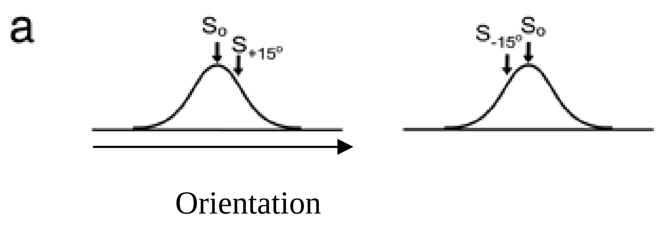
Figure 14. The signals from each eye are segregated within the LGN and go into different ocular dominance columns within area V1, layer 4C.

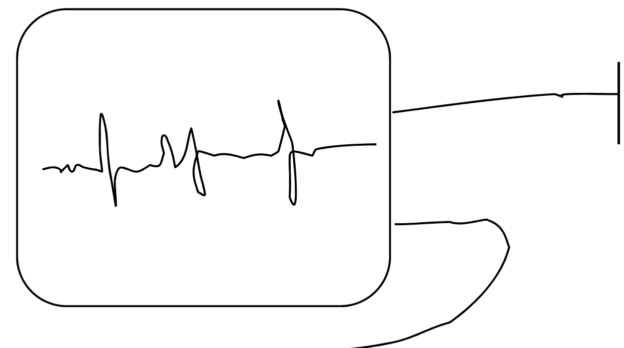


Orientation and ocular dominance columns

Figure 23. The ice-cube model of the cortex. It illustrates how the cortex is divided, at the same time, into two kinds of slabs, one set of ocular dominance (left and right) and one set for orientation. The model should not be taken literally: Neither set is as regular as this, and the orientation slabs especially are far from parallel or straight.

1) Measure orientation selectivity of cell in response to stimulation of each eye. This results in an orientation tuning curve for each cell with an optimal orientation S_0.





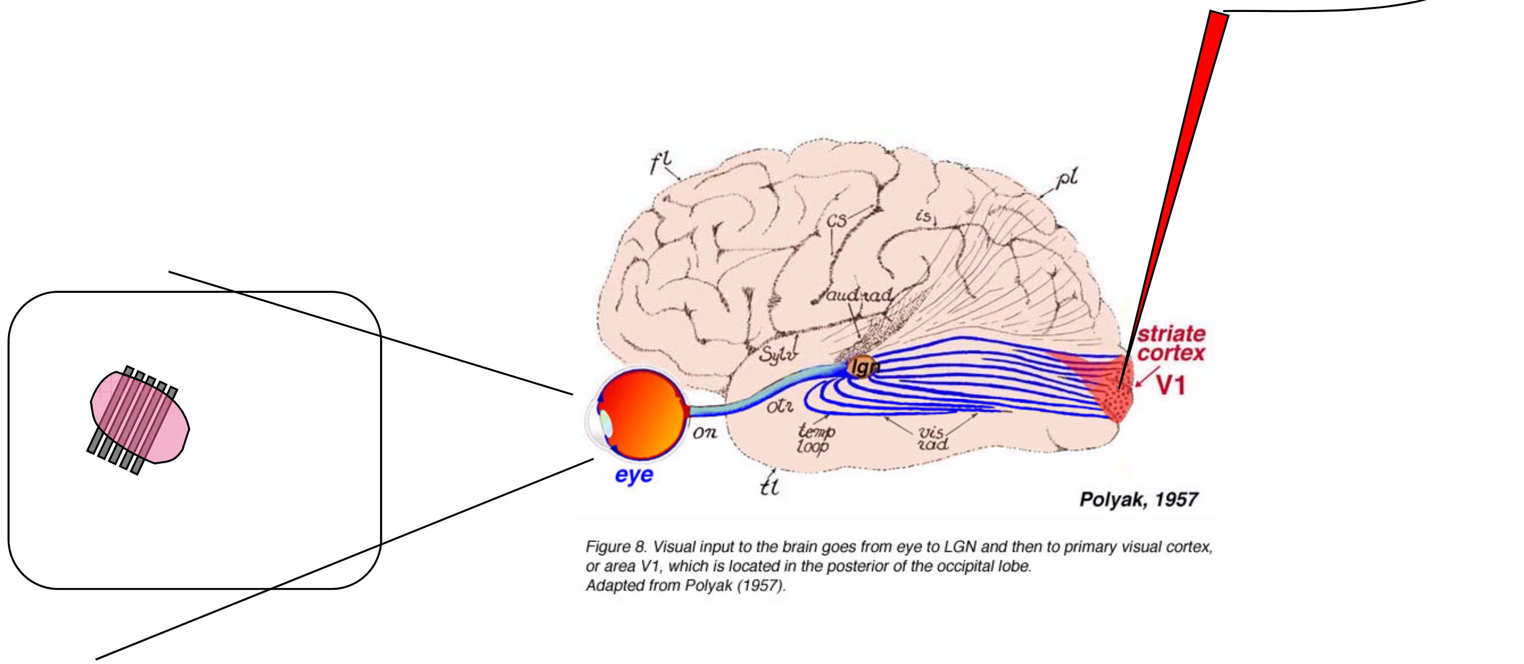
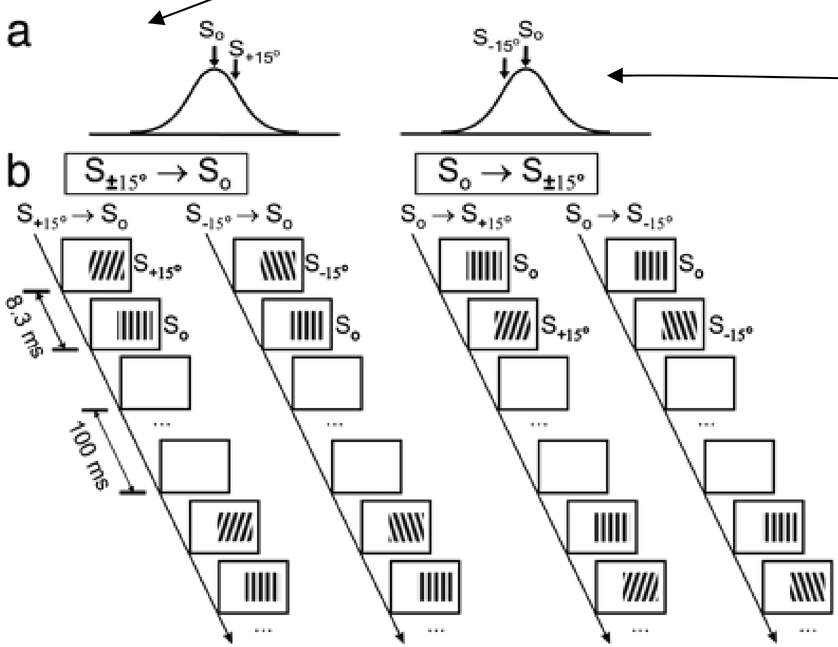
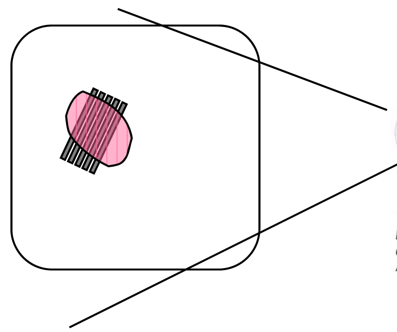


Figure 8. Visual input to the brain goes from eye to LGN and then to primary visual cortex, or area V1, which is located in the posterior of the occipital lobe. Adapted from Polyak (1957).

1) Measure orientation selectivity of cell in response to stimulation of each eye. This results in An orientation tuning curve for each cell with an optimal orientation S_0.

2) Then “condition” the cell by repeatedly presenting two stimuli at 8.2 ms intervals. Two conditioning paradigms were used:
A) $S_0 – S_{+/-15}$ separated by 8.2 ms
B) $S_{+/-15} – S_0$ separated by 8.2 ms.





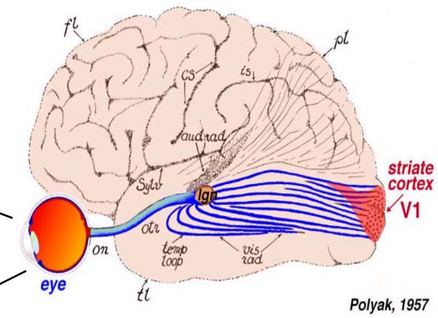
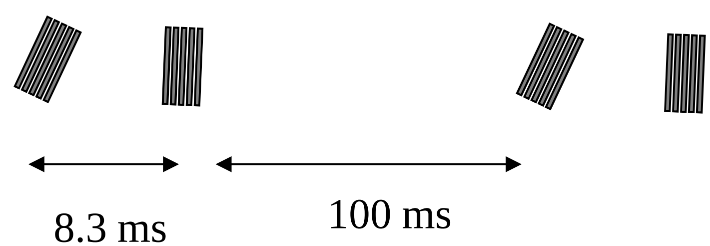


Figure 8. Visual input to the brain goes from eye to LGN and then to primary visual cortex, or area V1, which is located in the posterior of the occipital lobe.
Adapted from Polyak (1957).



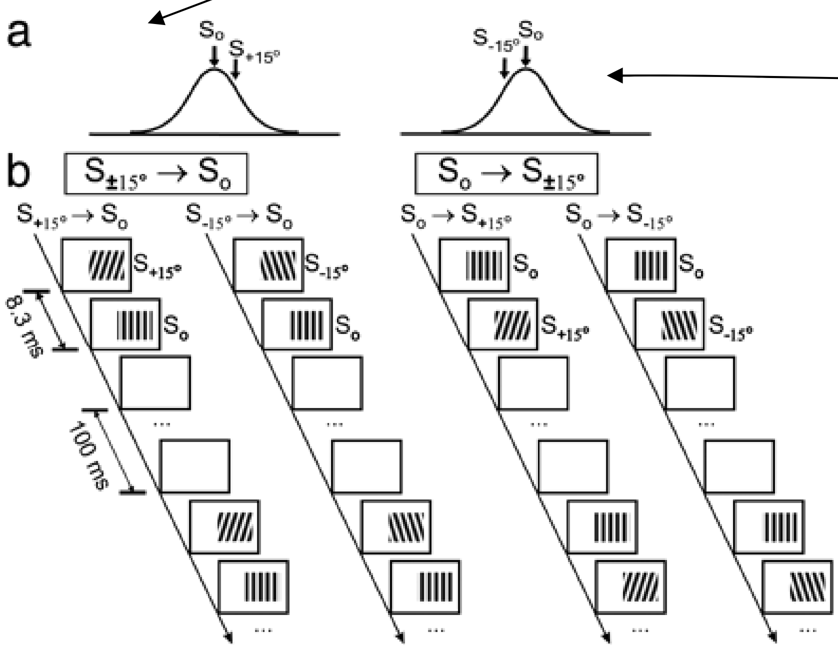
A) Shifted followed by best orientation
B) Best followed by shifted orientation

1) Measure orientation selectivity of cell in response to stimulation of each eye. This results in An orientation tuning curve for each cell with an optimal orientation S_0.

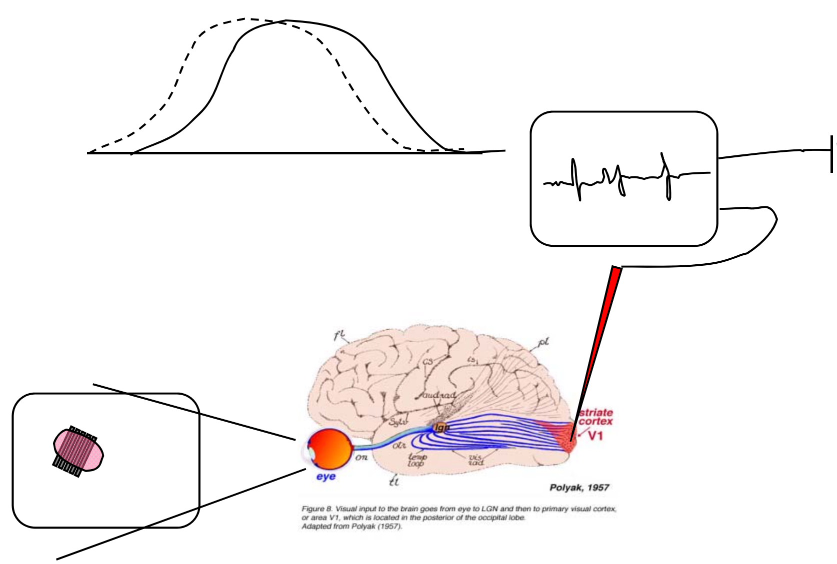
2) Then "condition" the cell by repeatedly presenting two stimuli at 8.2 ms intervals. Two conditioning paradigms were used:

A) $S_0 - S_{+/- 15}$ separated by 8.2 ms

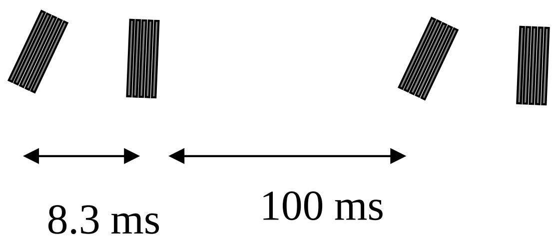
B) $S_{+/-15} - S_0$ separated by 8.2 ms.

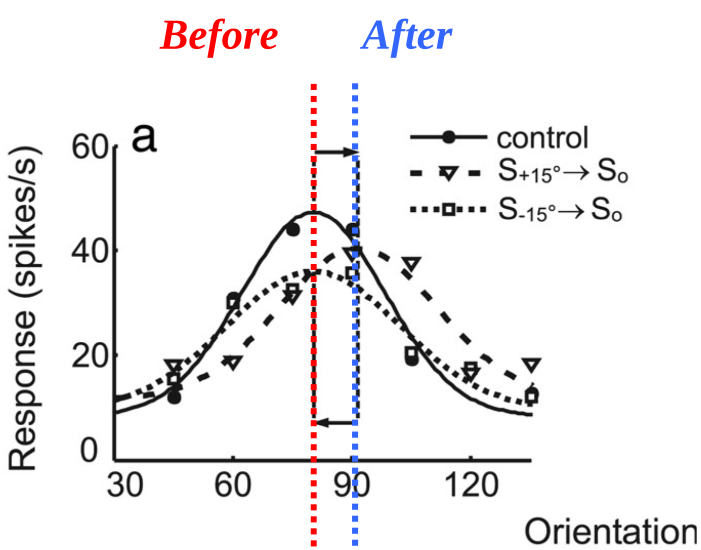


3) After the conditioning phase, the orientation selectivity was measured again by presenting stimuli to the non-conditioned eye!



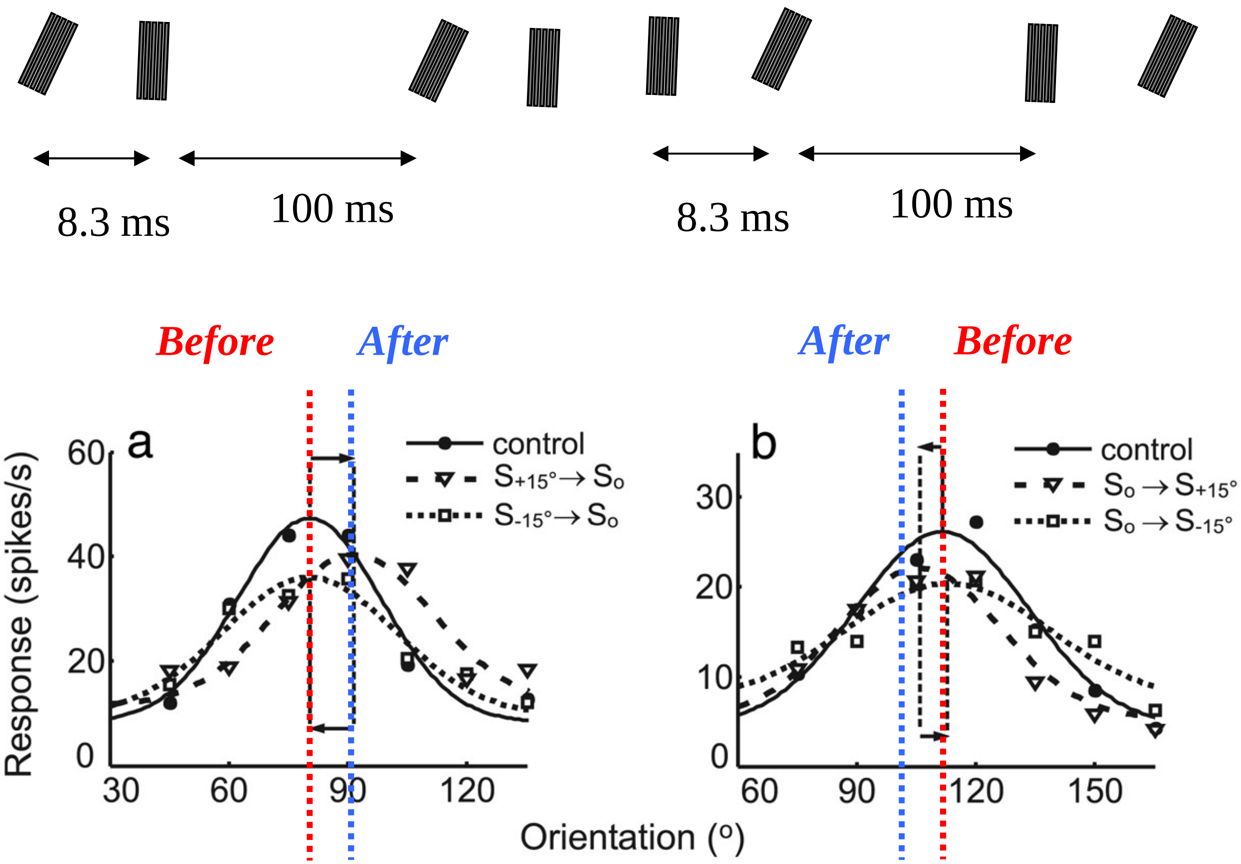
a) Shifted followed by best orientation





a) Shifted followed by best orientation

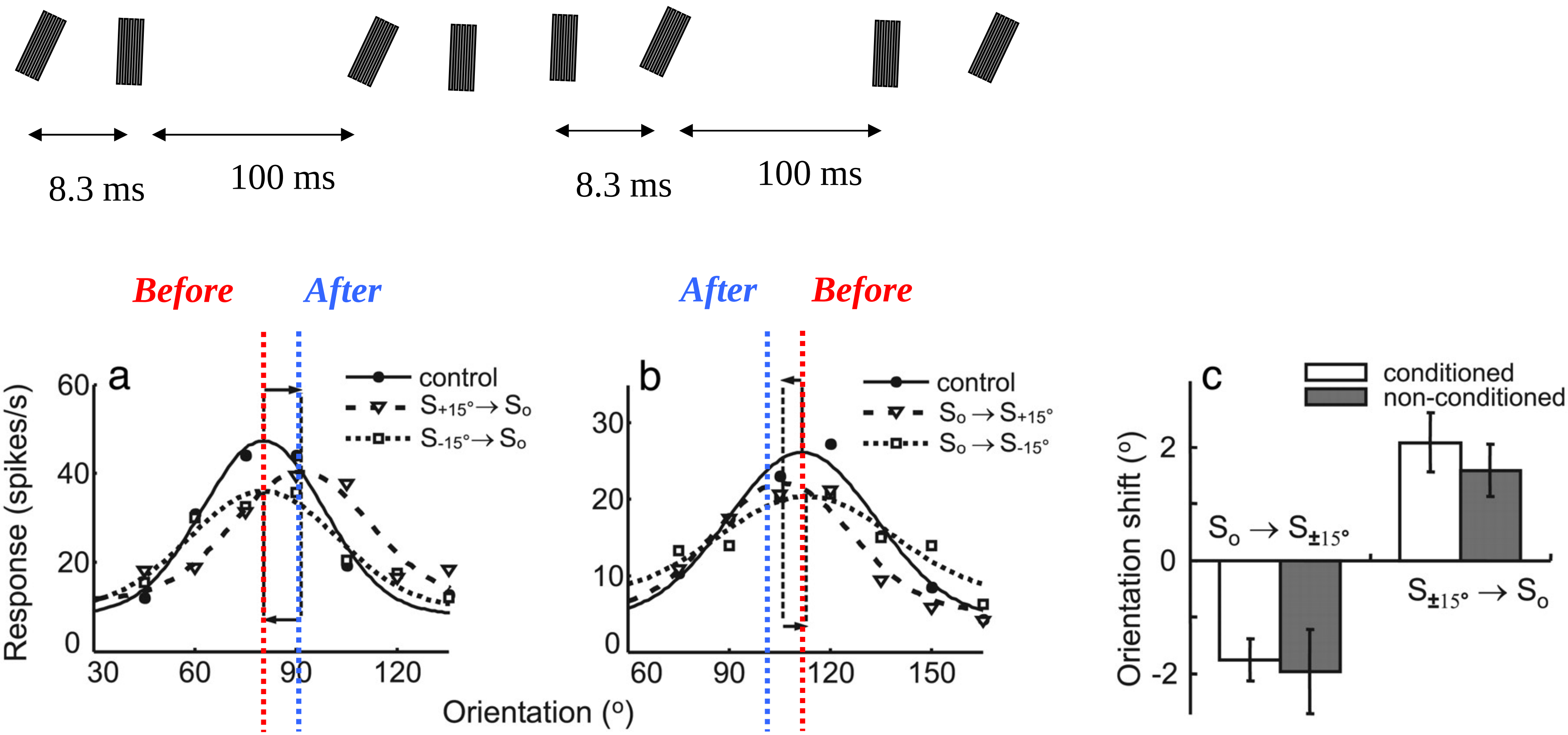
b) Best followed by shifted orientation



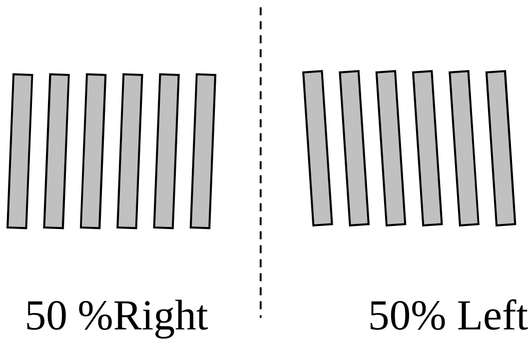
a) Shifted followed by best orientation

b) Best followed by shifted orientation

c) Conditioning leads to similar shifts in orientation tuning in response to stimuli in both eyes



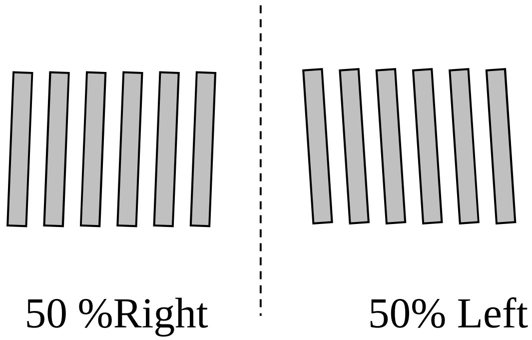
Human psychophysics



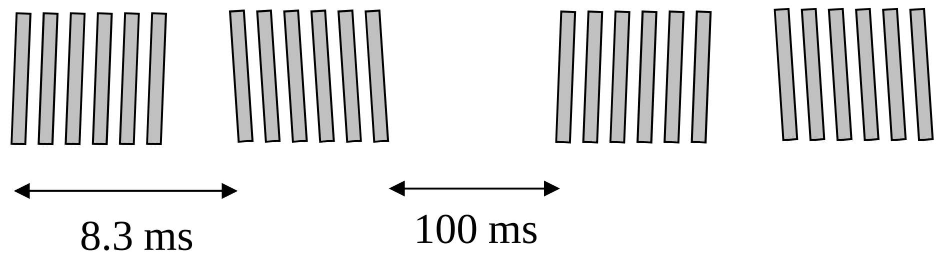
300 ms presentations,
1 sec ITI
orientations 1, 2 or 3^o from vertical

Test: Percentage of gratings judged to be on left or right side.
Control subjects usually judge an average of 50% to be on either side

Human psychophysics



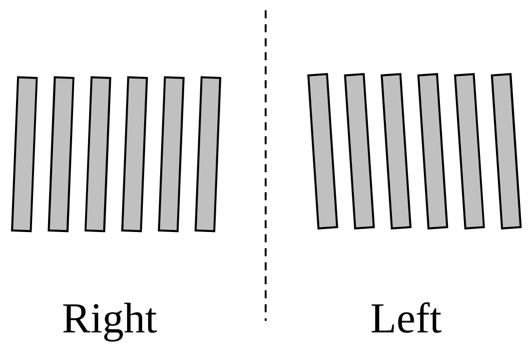
Conditioning:



300 ms presentations,
1 sec ITI
orientations 1, 2 or 3^o from vertical

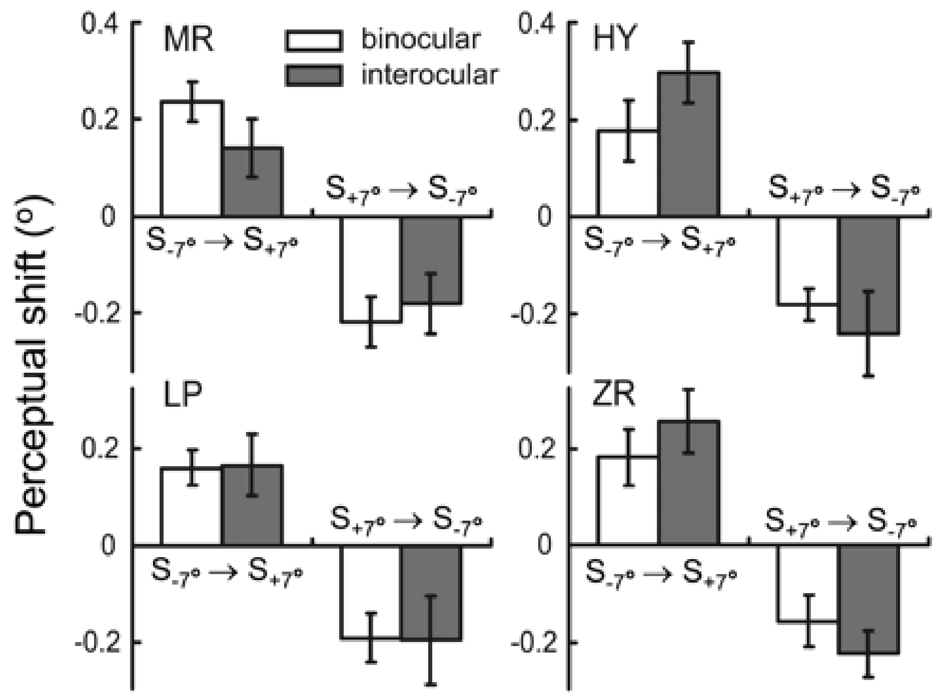
Test: Percentage of gratings judged to be on left or right side.
Control subjects usually judge an average of 50% to be on either side

Human psychophysics



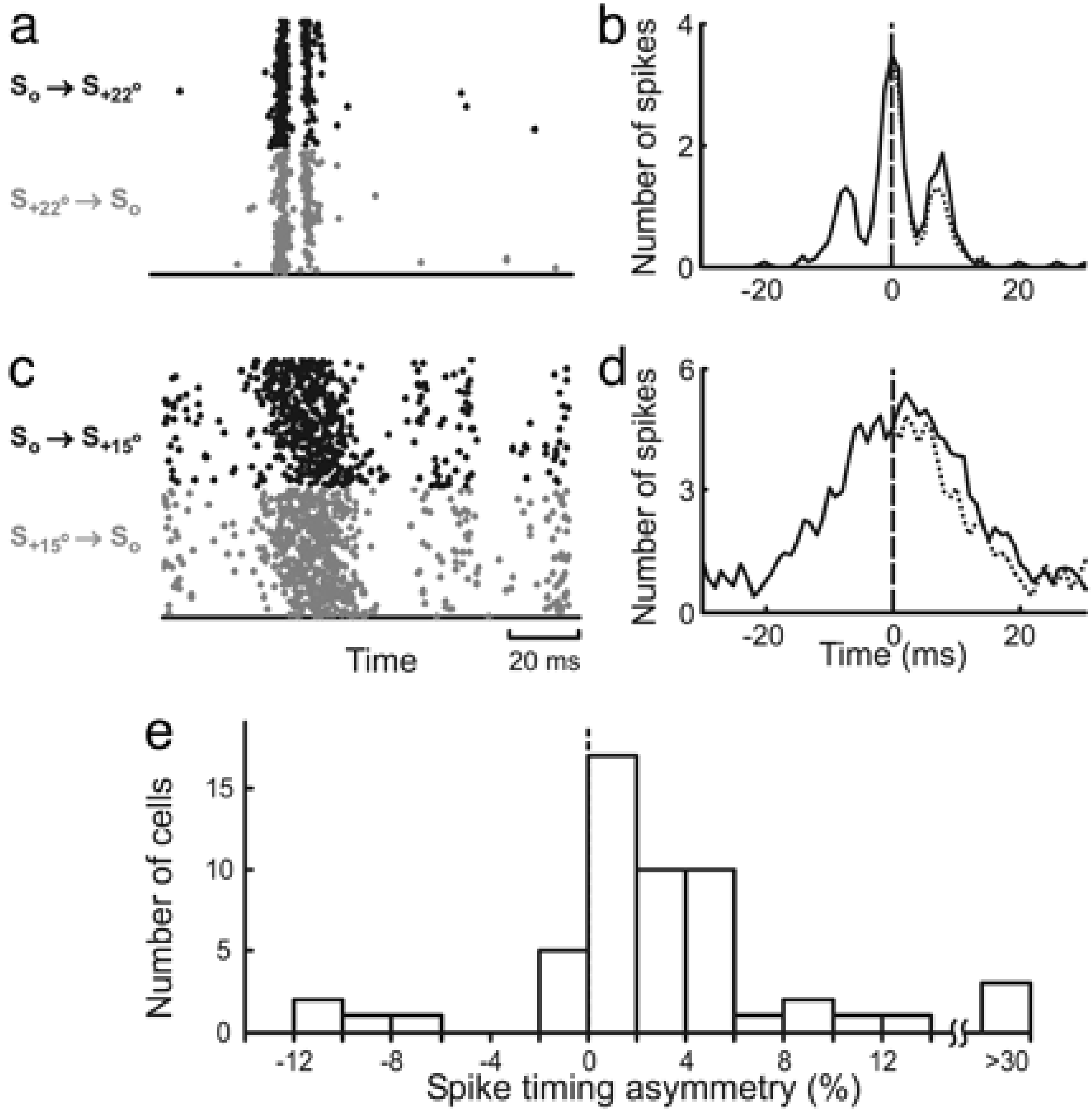
300 ms presentations,
1 sec ITI
orientations 1, 2 or 3^o from vertical

Result: Perceptual shifts in agreement with electrophysiological data

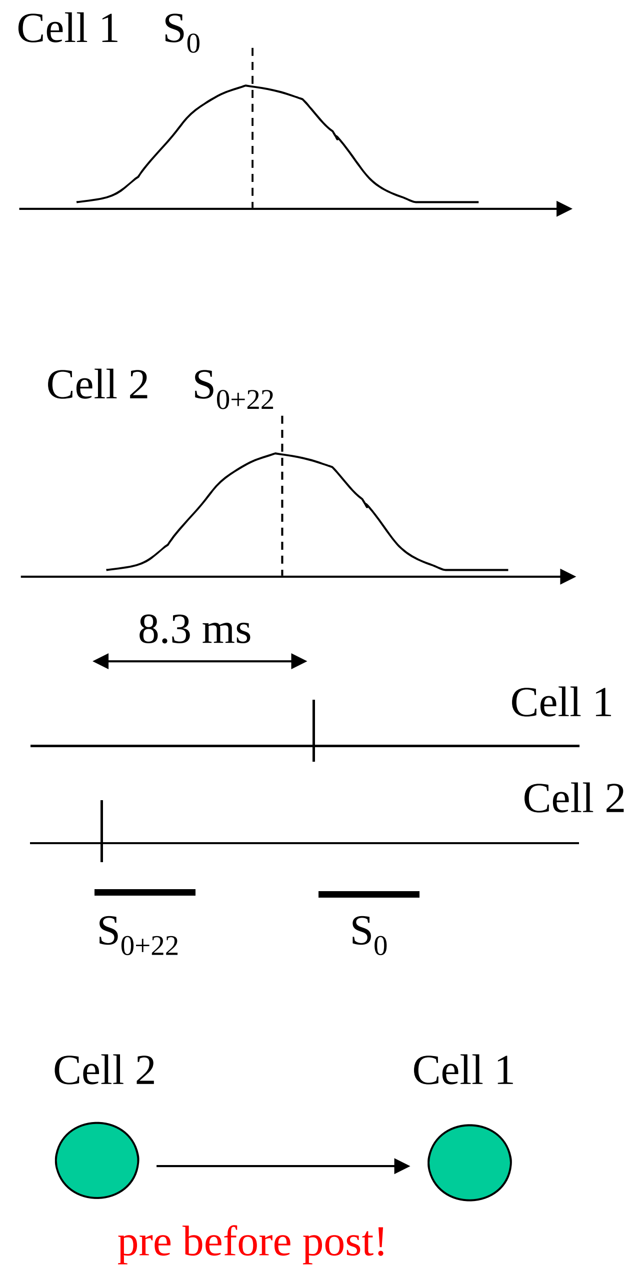


Mechanism?

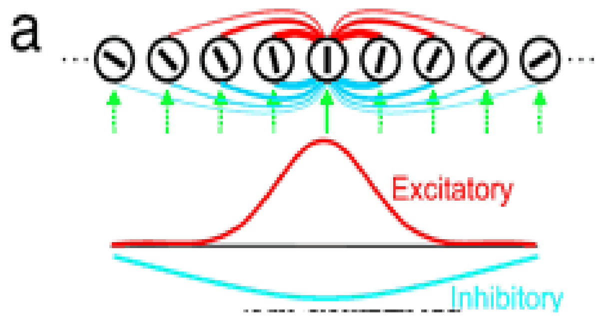
Mechanism?



a
$S_o \rightarrow S_{+22°}$
$S_{+22°} \rightarrow S_o$
b
Number of spikes
c
$S_o \rightarrow S_{+15°}$
$S_{+15°} \rightarrow S_o$
Time
20 ms
d
Number of spikes
Time (ms)
e
Number of cells
Spike timing asymmetry (%)



Cell 1
S_0
Cell 2
S_{0+22}
8.3 ms
Cell 1
Cell 2
S_{0+22}
S_0
Cell 2
Cell 1
pre before post!



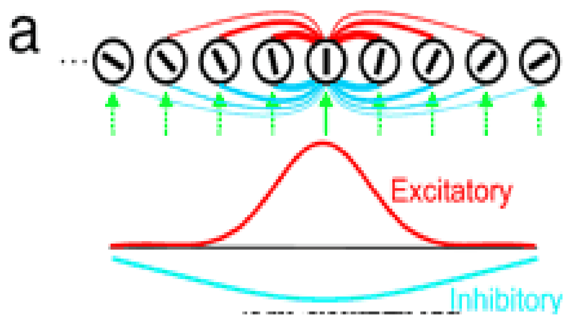
$$\tau_0 \frac{\partial V_k(t)}{\partial t} + V_k(t) = V_k^{ff}(t) + \sum_{j=1}^{j=36} V_{k,j}^{\text{rec}}(t),$$

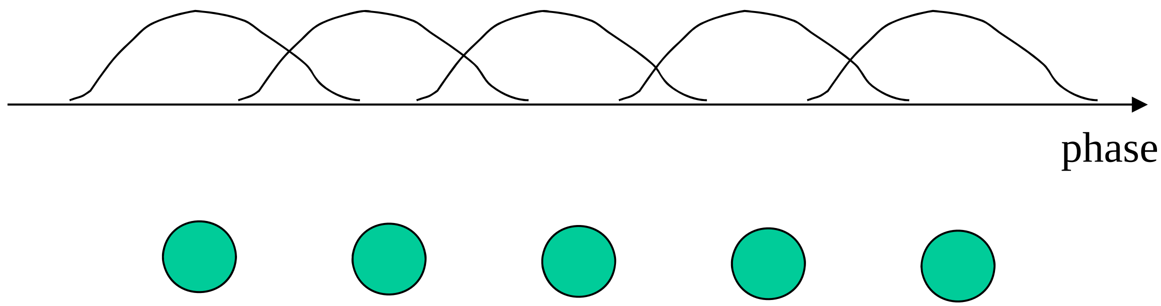
$V_k(t)$: membrane voltage of pyramidal cell k.
To: membrane time constant
$V_k^{ff}(t)$: feedforward (afferent) input (green arrows)
$V_{k,j}^{rec}(t)$: recurrent input from other cells.

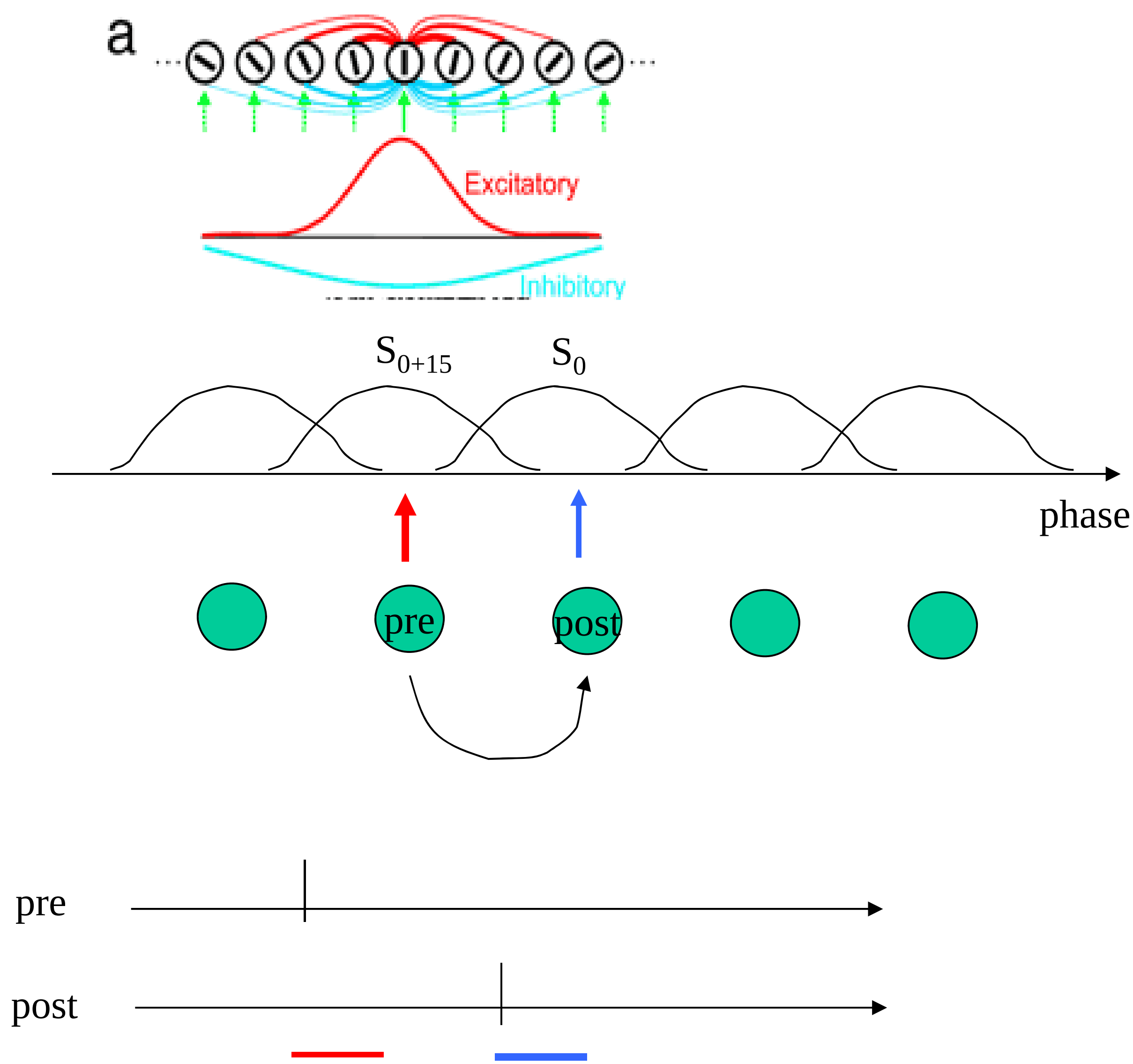
This equation describes how the membrane voltage evolves in time due to external inputs (leaky integrator).

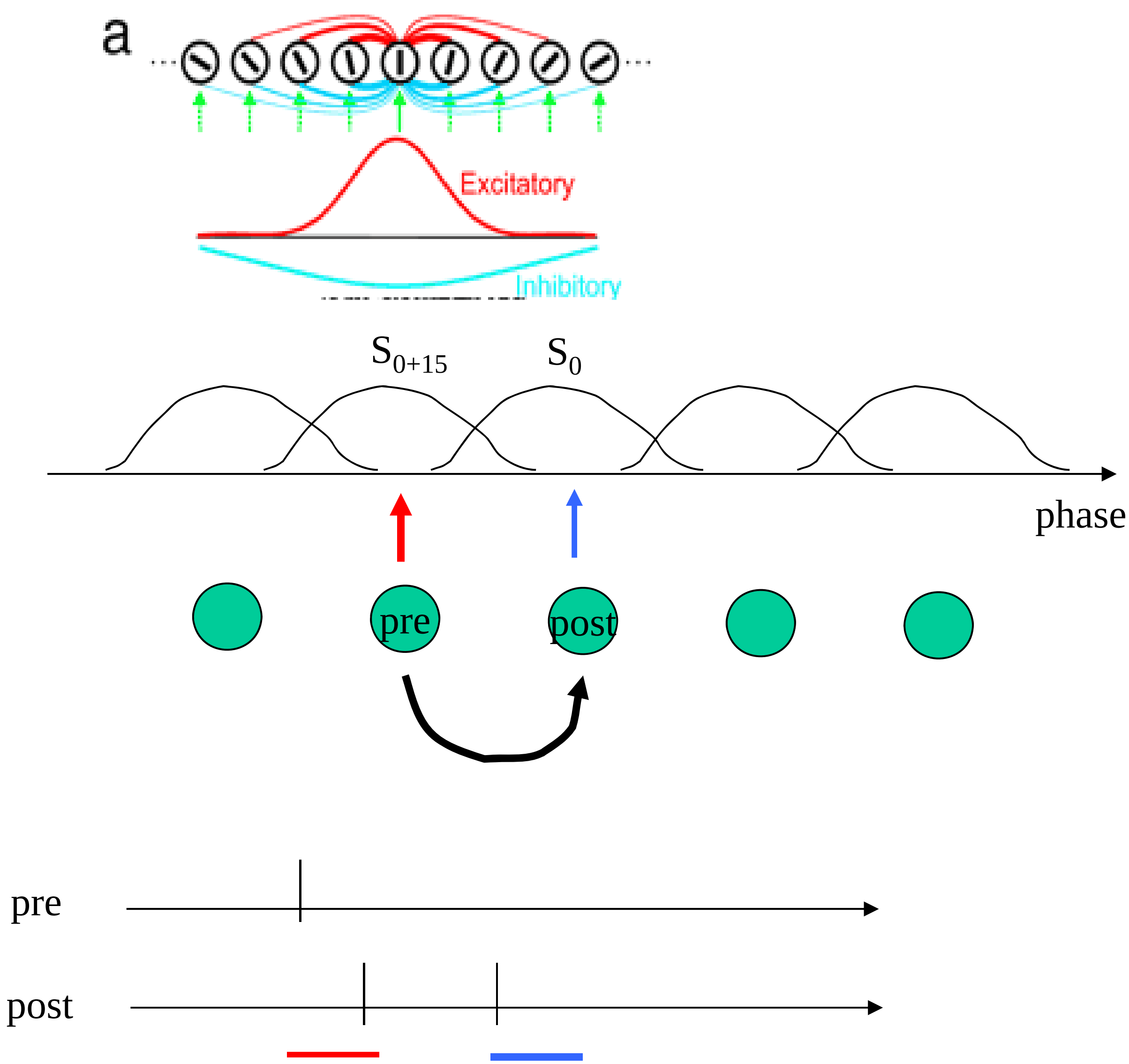
Remember: $\tau\ dv/dt = -v + \text{inputs}$

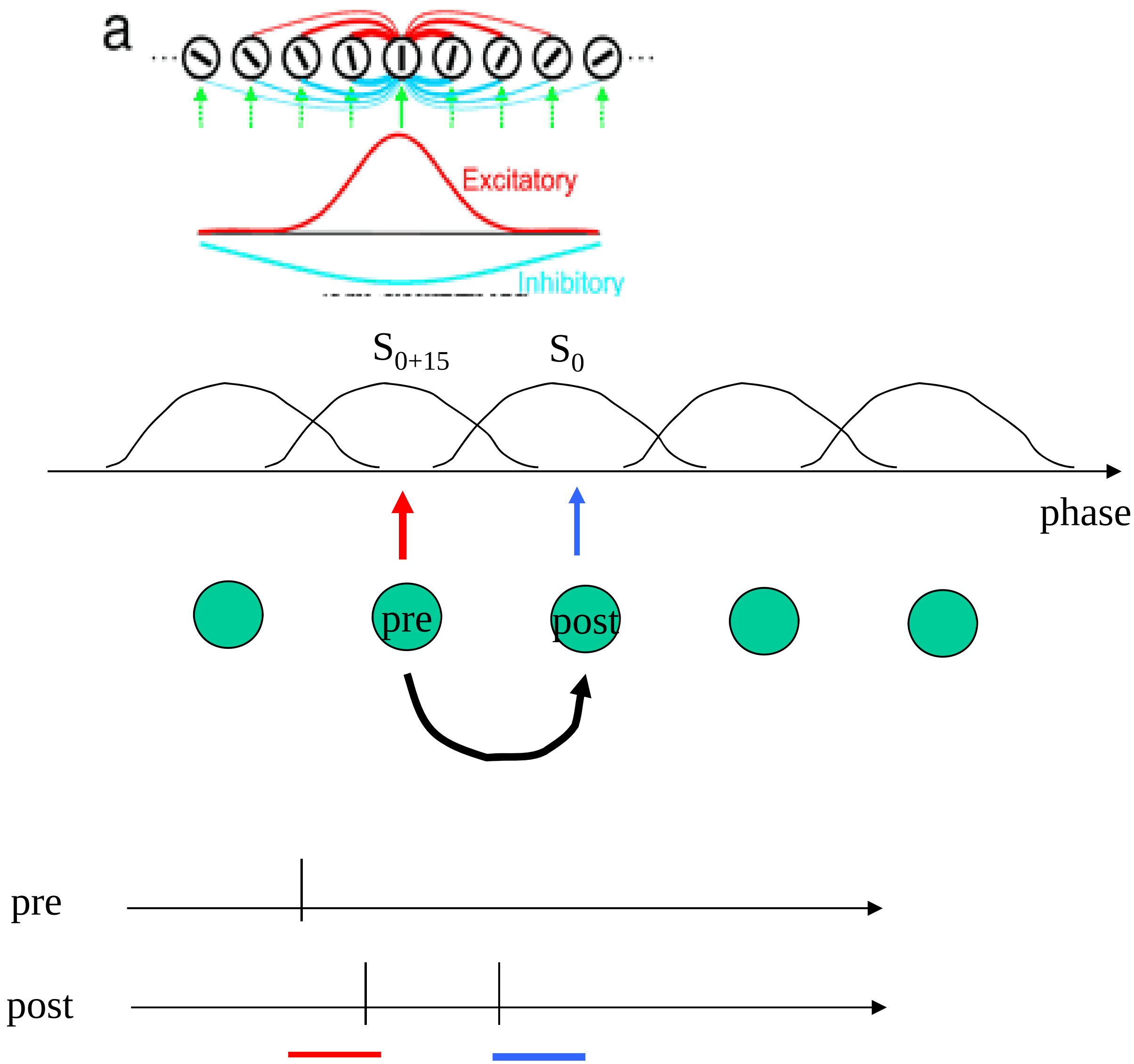
In response to a give stimulus orientation, each cell receives a combination of feedforward input, output of other Cells (narrowly tuned) and input of more broadly tuned cells.


a
Excitatory
Inhibitory

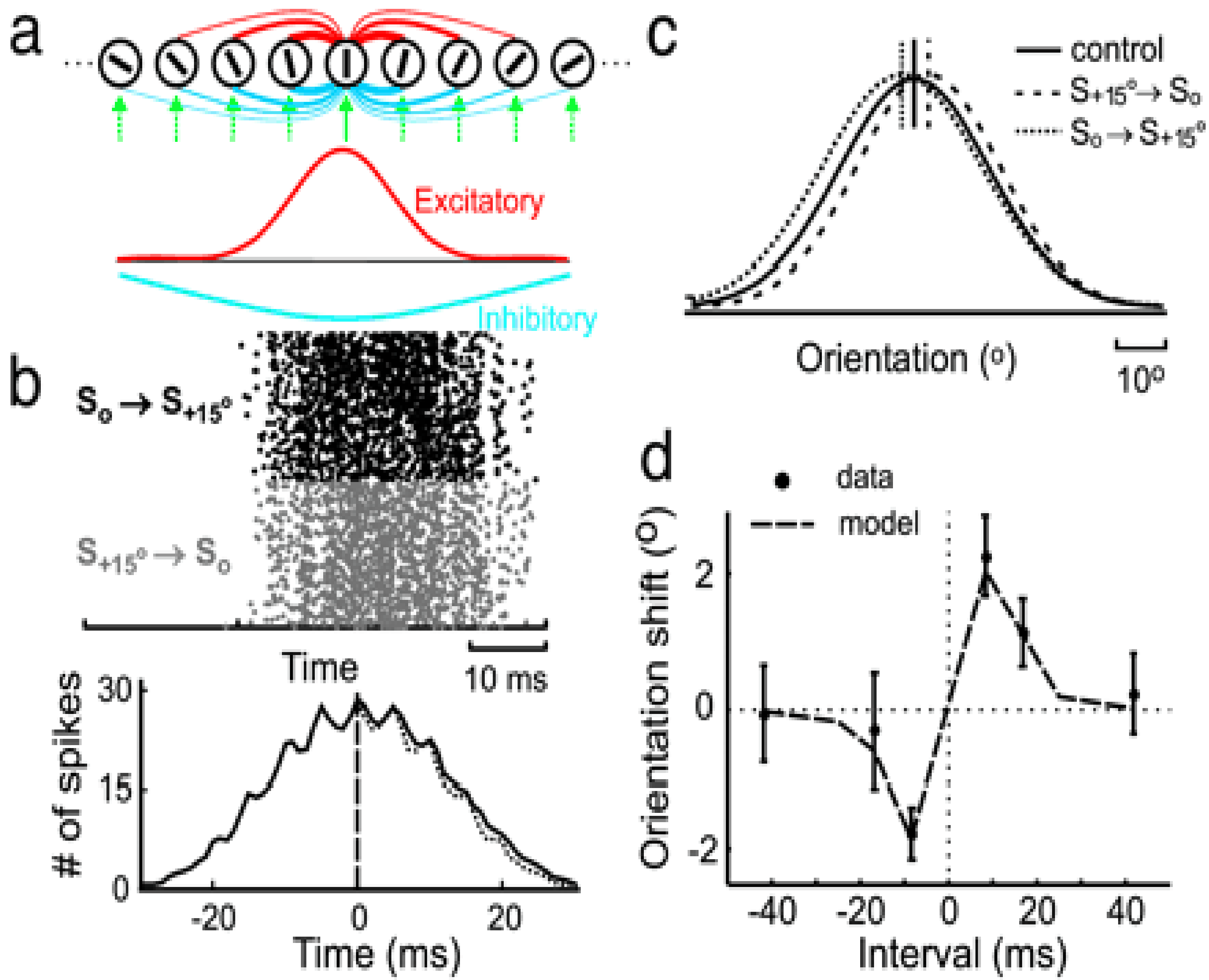

phase


a
Excitatory
Inhibitory
S_{0+15}
S_0
phase
pre
post
pre
post

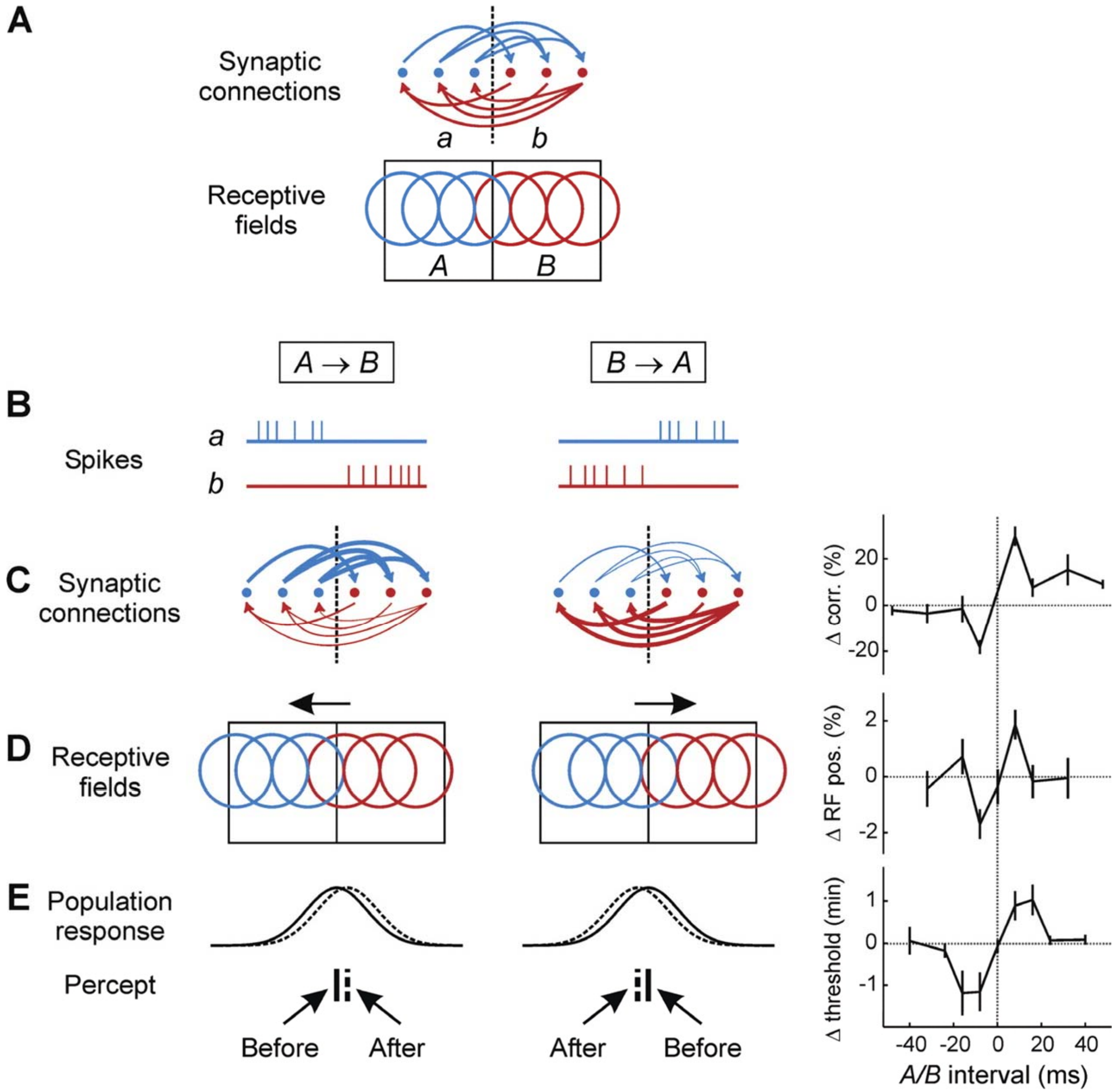

a
Excitatory
Inhibitory
S_{0+15}
S_0
phase
pre
post
pre
post

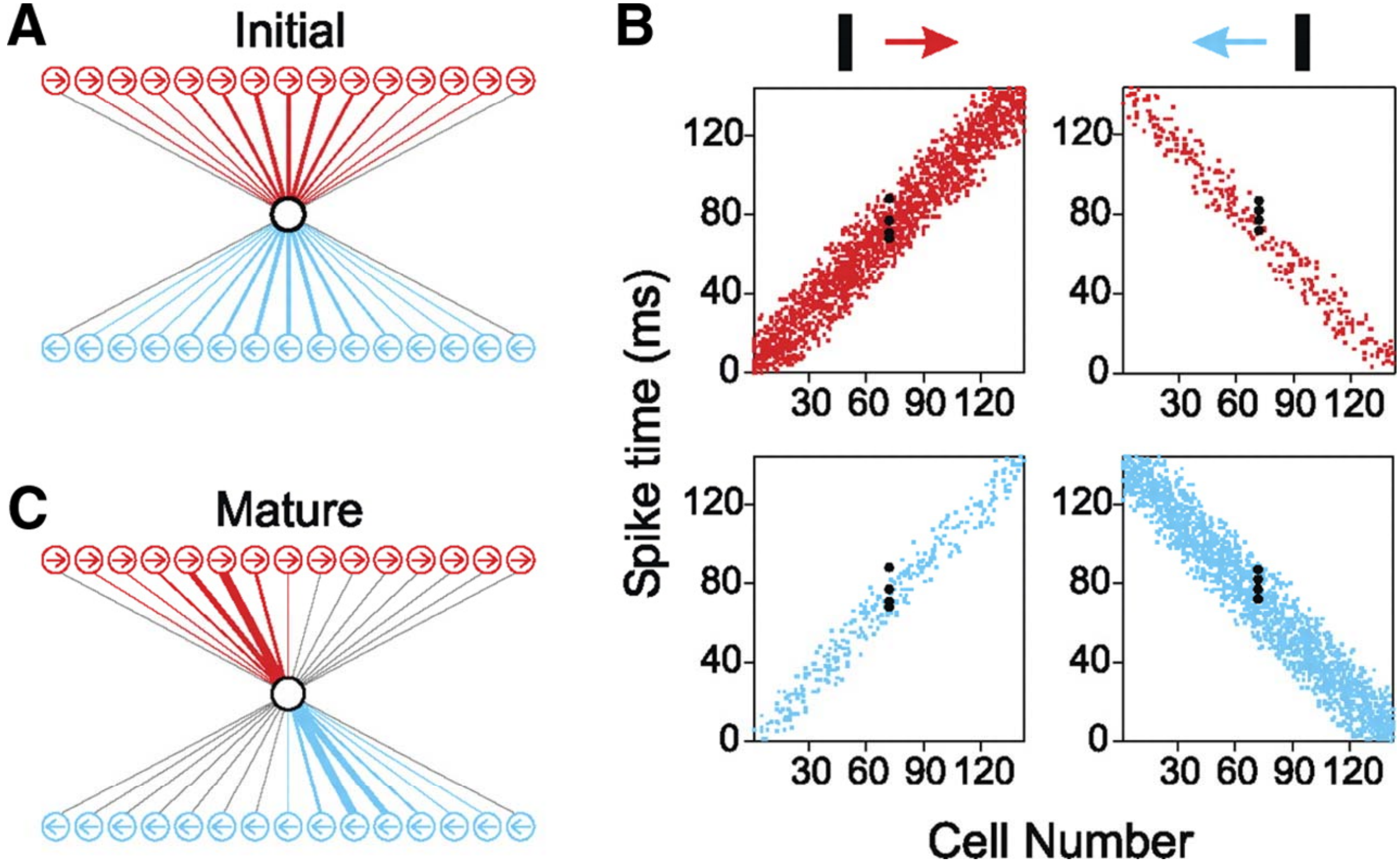


a
Excitatory
Inhibitory
S0+15
S0
phase
pre
post
pre
post



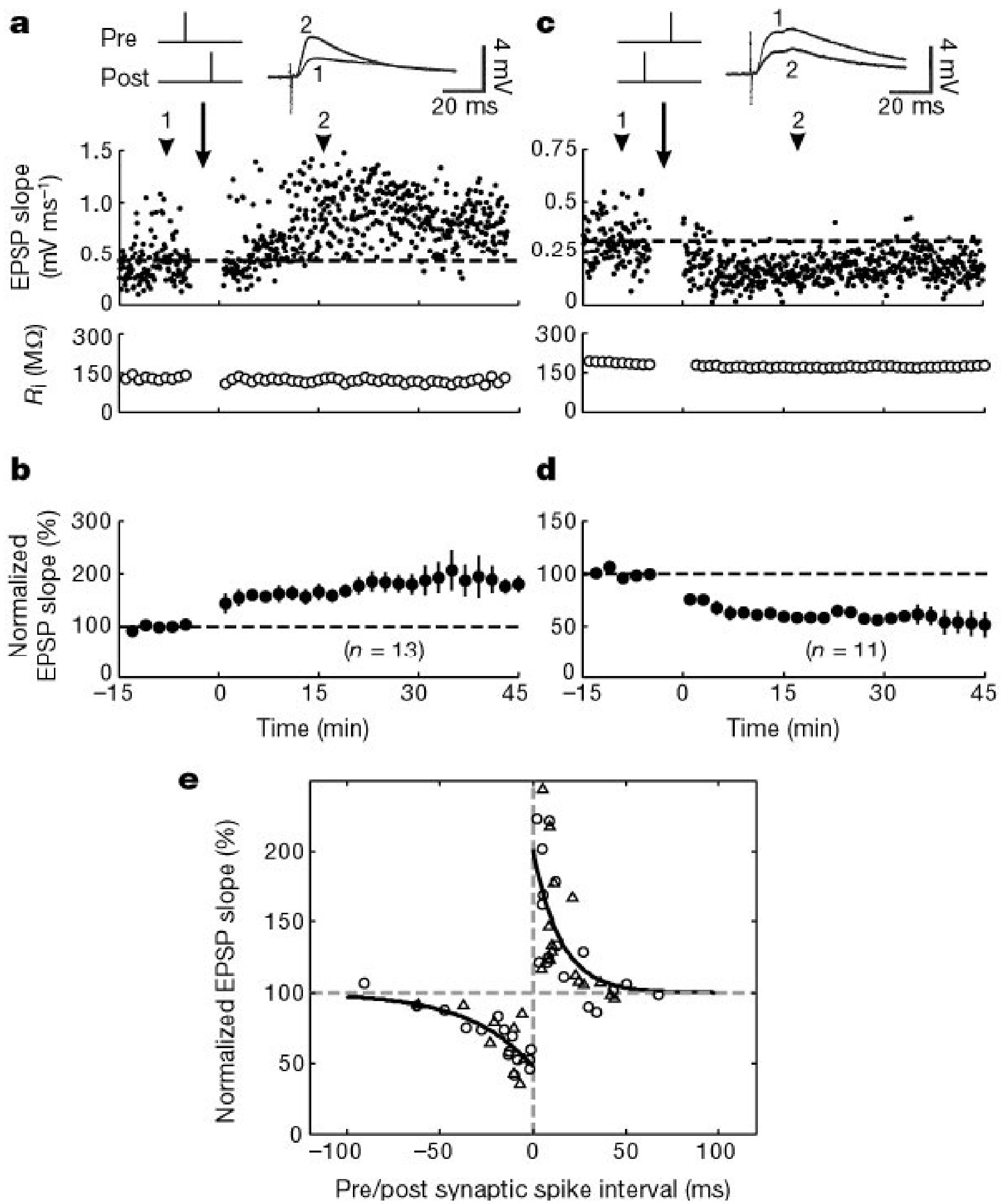
a
Excitatory
Inhibitory
b
So → S+15°
S+15° → So
Time
10 ms
# of spikes
30
15
0
-20
0
20
Time (ms)
c
control
S+15° → So
So → S+15°
Orientation (°)
10°
d
data
model
Orientation shift (°)
2
0
-2
-40
-20
0
20
40
Interval (ms)

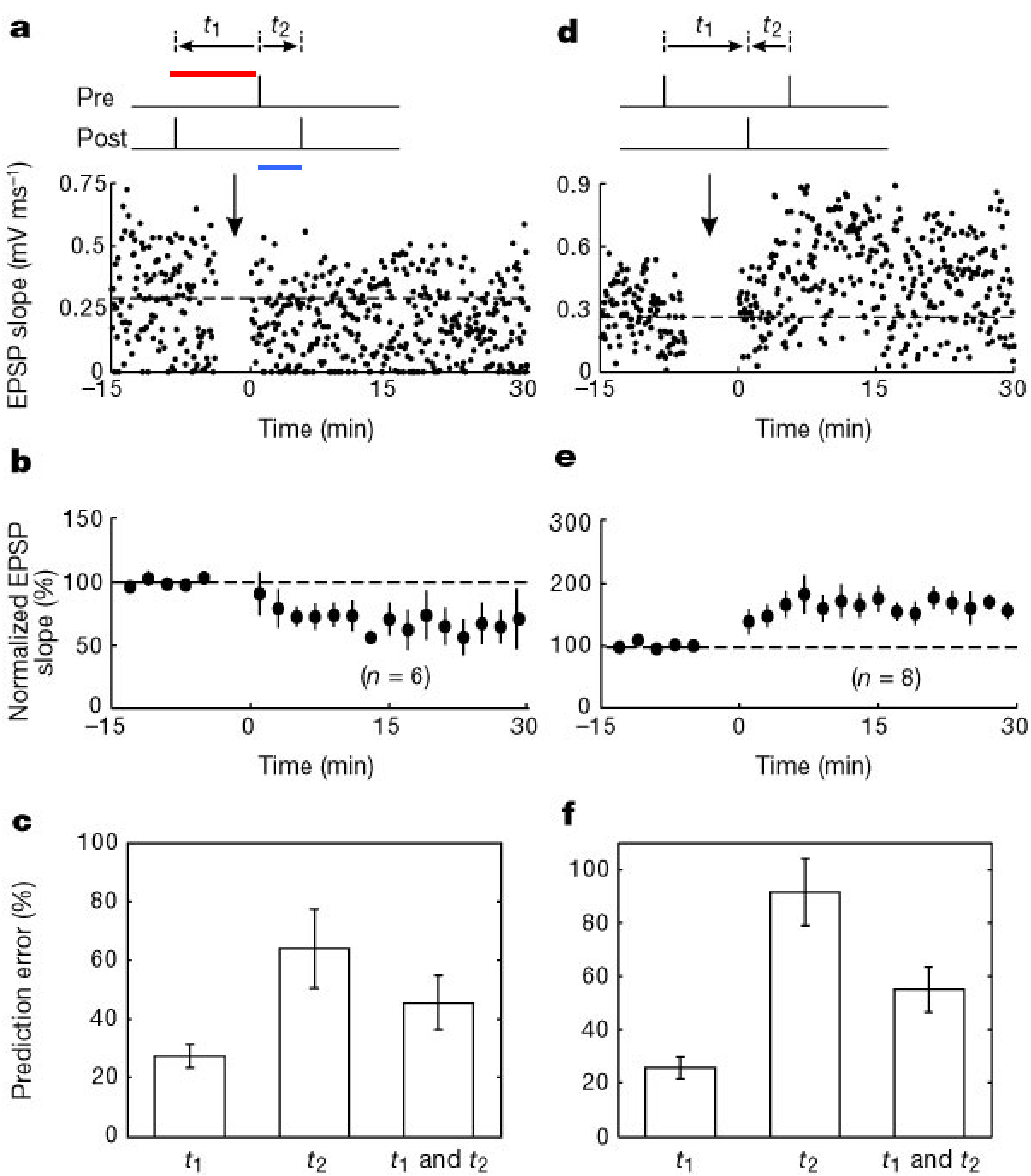

A
Synaptic connections
a
b
Receptive fields
A
B
A → B
B → A
B
Spikes
a
b
C
Synaptic connections
D
Receptive fields
E
Population response
Percept
Before
After
After
Before
Δ corr. (%)
20
0
-20
Δ RF pos. (%)
2
0
-2
Δ threshold (min)
1
0
-1
-40
-20
0
20
40
A/B interval (ms)



A
Initial
B
120
80
40
0
30
60
90
120
Spike time (ms)
Cell Number
C
Mature

Froemke, Dan, Nature 2002

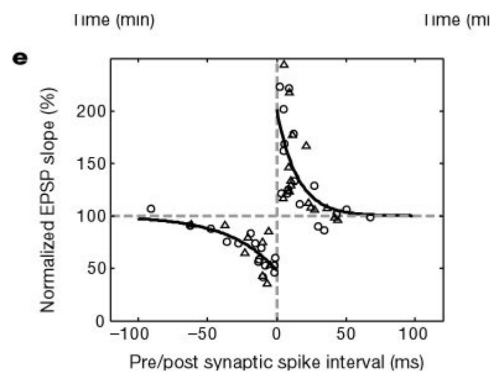




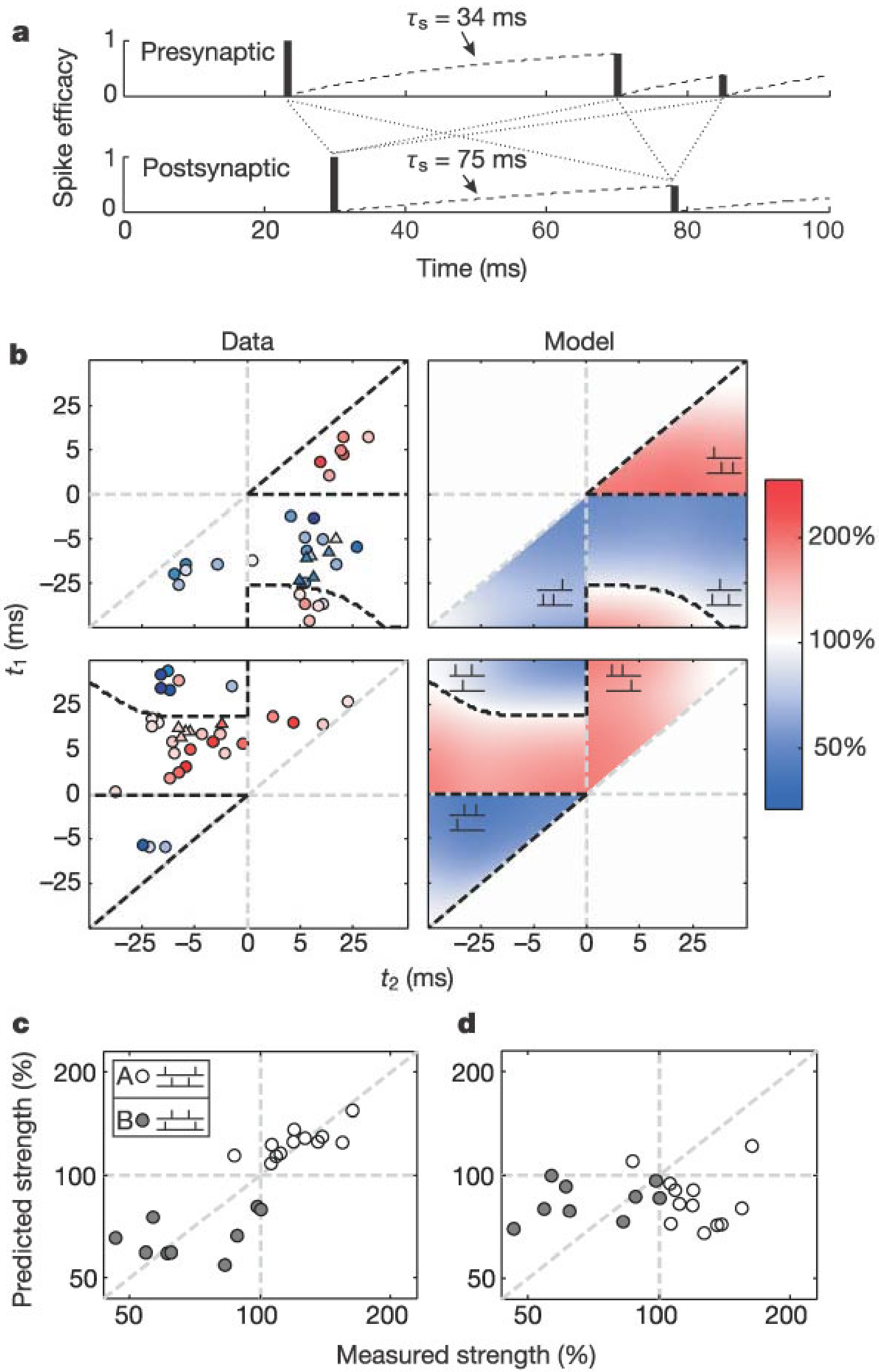
-26%

+67%

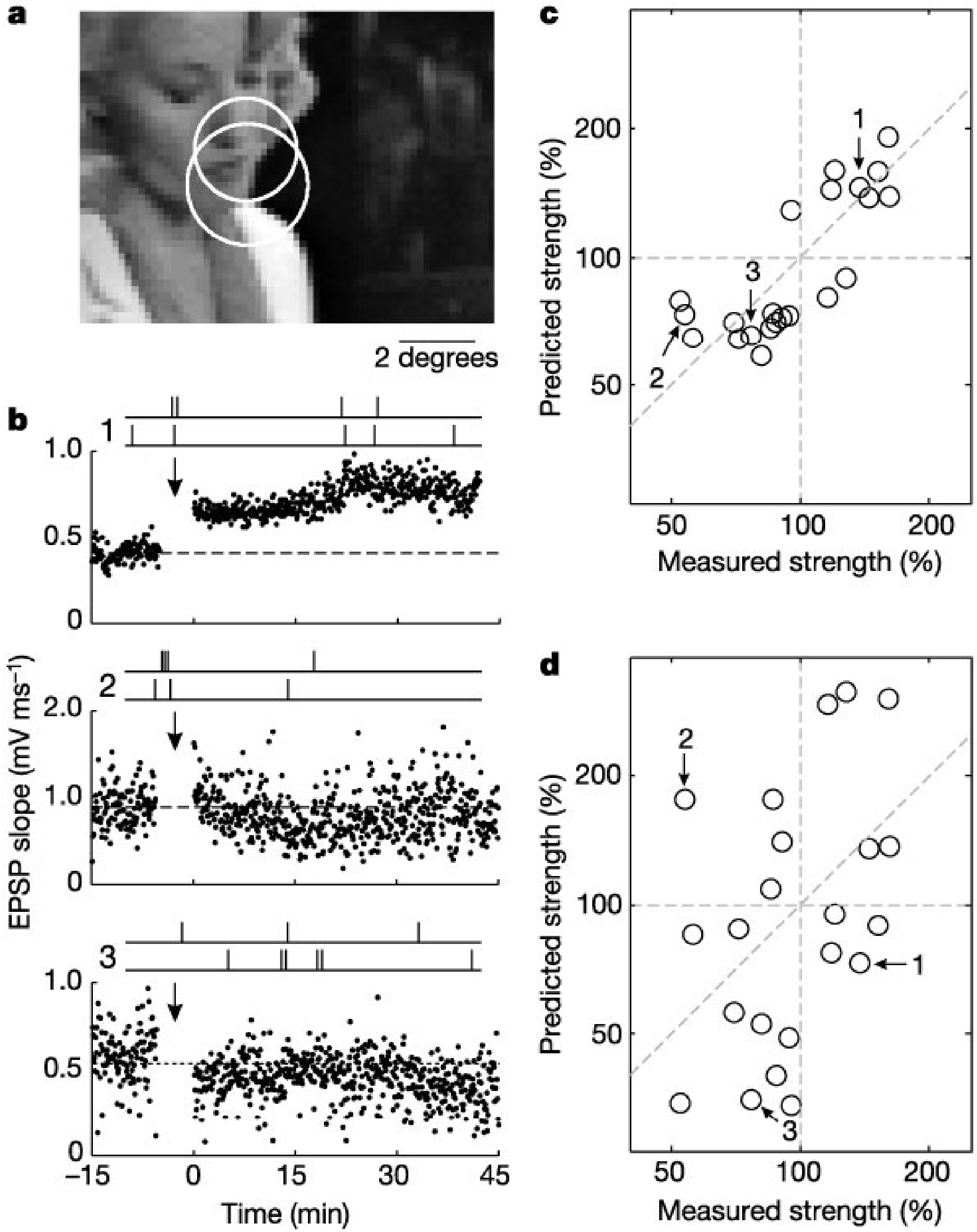
Independent contribution -> +2



Contribution of second spike is suppressed!



Efficacy of nexy spike is suppressed and recovers exponentially.



a
2 degrees
b
1
2
3
EPSP slope (mV ms^{-1})
Time (min)
c
d
Predicted strength (%)
Measured strength (%)