1. Markram & Sakmann, *Science*, 1997
2. https://www.pnas.org/doi/abs/10.1073/pnas.94.16.8918
3. https://www.cell.com/neuron/fulltext/S0896-6273(00)81072-7
4. https://www.nature.com/articles/nature00807
5. https://onlinelibrary.wiley.com/doi/full/10.1002/hipo.22472
6. https://journals.sagepub.com/doi/abs/10.1177/107385840100700605

Synaptic plasticity

Groups of neurons which tend to fire together form a cell-assembly whose activity can persist after the triggering event and serves to represent it.

Donald Hebb (1949, Organization of Behavior)

Synaptic plasticity

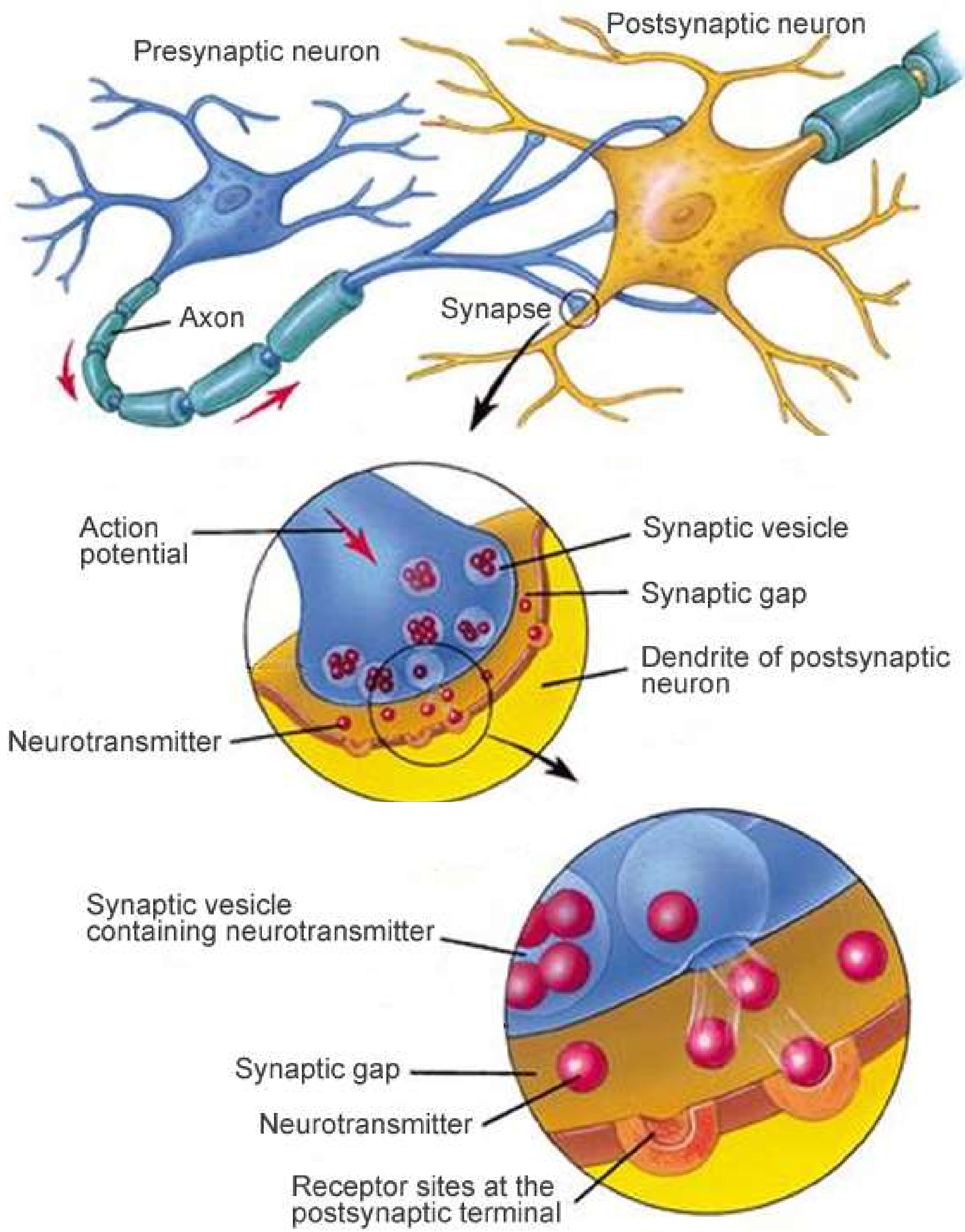
Thinking is the sequential activation of sets of cell-assemblies.

Donald Hebb (1949, Organization of Behavior)

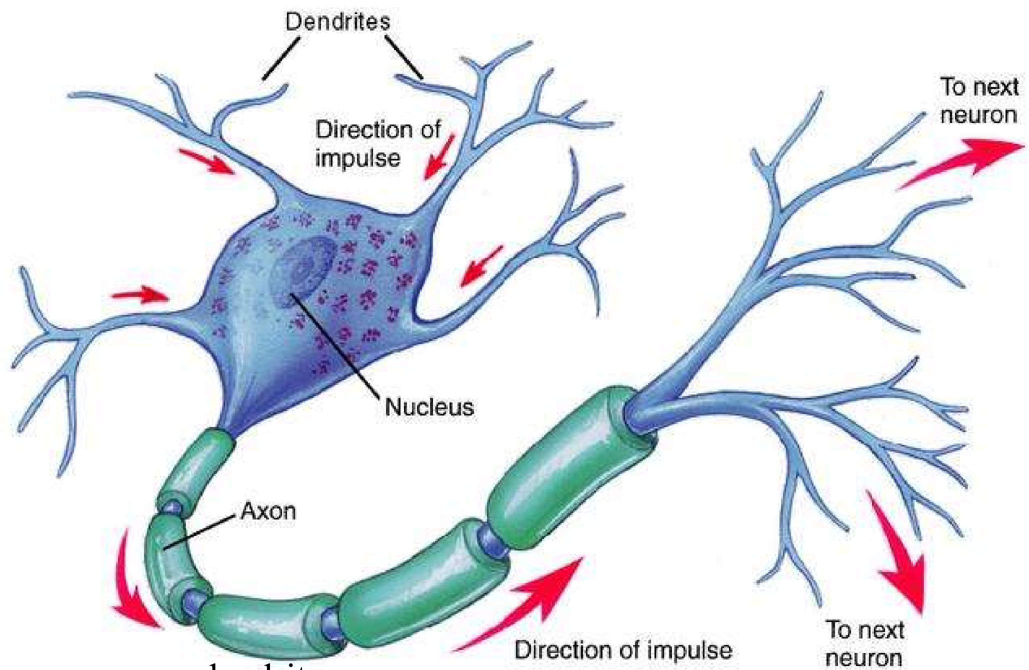
Synaptic plasticity

When an axon of cell A is near enough to excite 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

Donald Hebb (1949, Organization of Behavior)

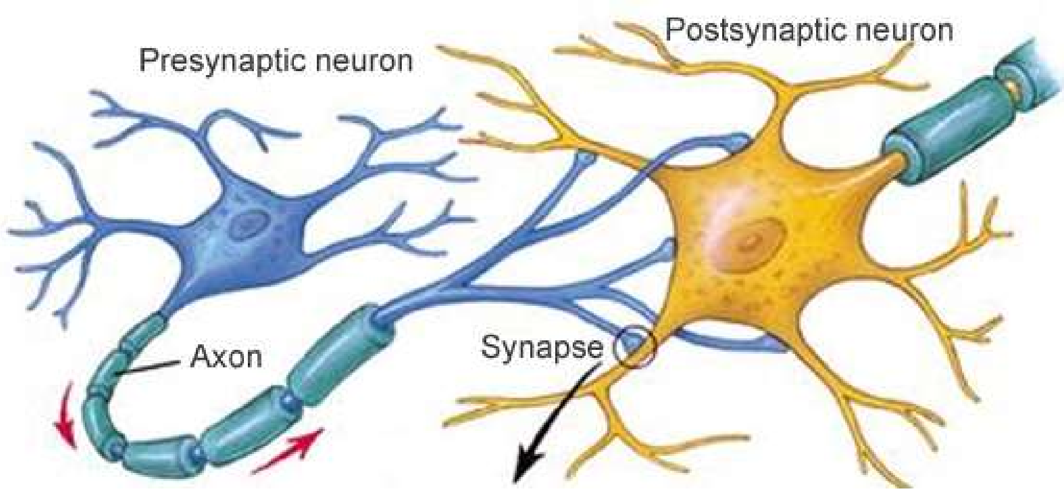

Presynaptic neuron
Postsynaptic neuron
Axon
Synapse
Action potential
Synaptic vesicle
Synaptic gap
Dendrite of postsynaptic neuron
Neurotransmitter
Synaptic vesicle containing neurotransmitter
Synaptic gap
Neurotransmitter
Receptor sites at the postsynaptic terminal

Neurons



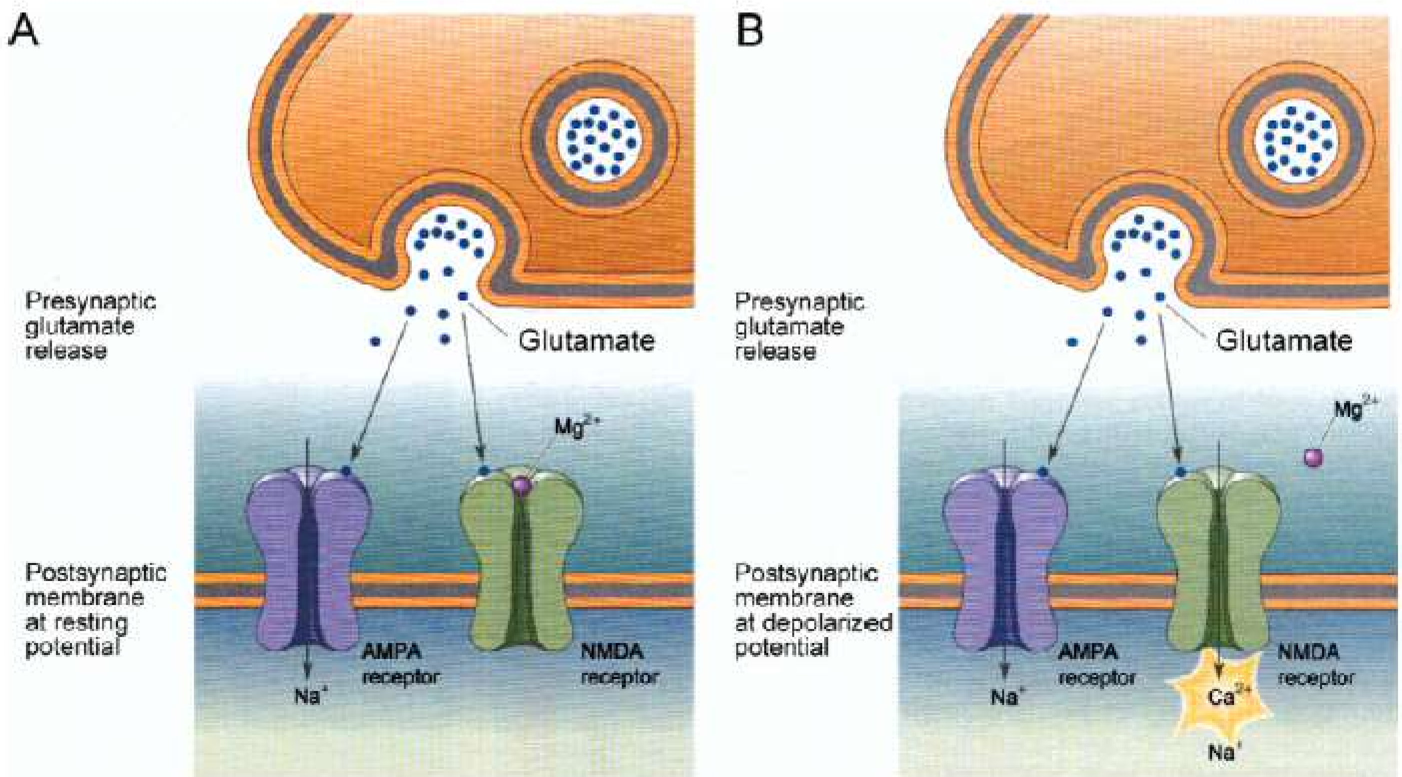
- Inputs arrive at synapses on dendrites.
- These ions travel to the soma.
- If the total voltage thus generated exceeds a threshold at the axon hillock, neuron fires an action potential or a spike.
- Spikes travel rapidly down the axons, especially the mylinated axons.
- Spike reach axon tips and lead to vesicle release and synpatic activity that influences the postsynaptic neuron.

Synapses



- Presynaptic terminal contain vesicles filled with neurotransmitters (eg. Glutamate and GABA).
- These neurotransmitters bind with receptors on the postysynaptic cite and inject ions in the postsynaptic neuron (Na+, K+, Ca++, Cl-)

Neurotransmitter release



•Two types of glutamate receptors on the postsynaptic spine: AMPA & NMDA.

•Calcium influx through NMDA primarily responsible for the induction of plasticity

•In normal conditions, NMDA receptors are blocked by Magnesium.

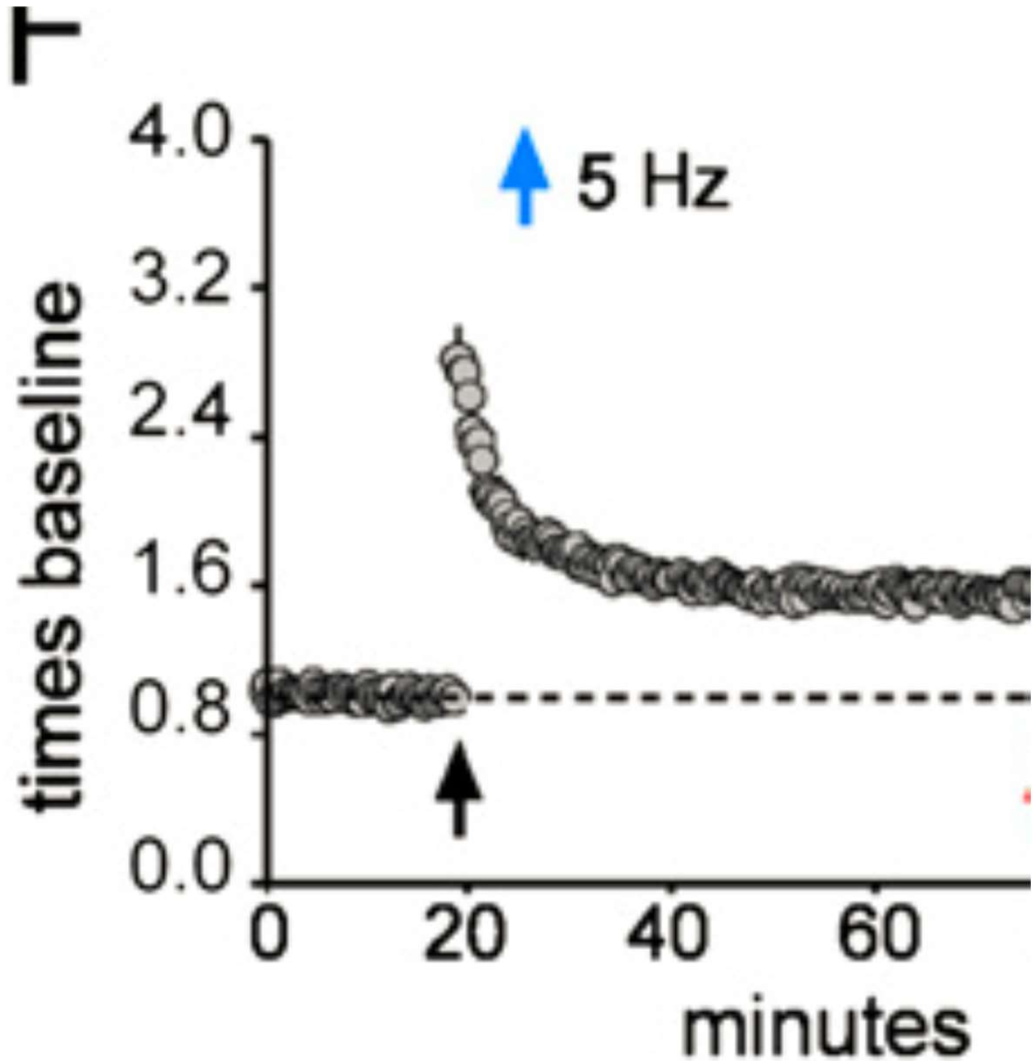
•Large depolarization, such as by back-propagating action potential removes the magnesium block and allows influx of Ca++.

•Low calcium influx: no change. Intermediate calcium influx: LTD. Large calcium influx: LTP.

Synaptic plasticity

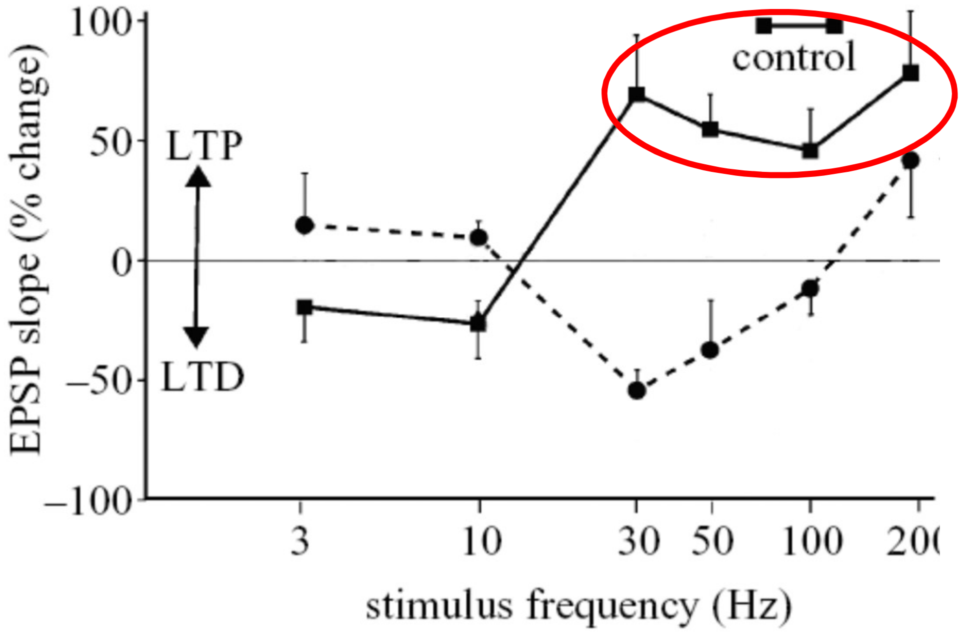
- Rate based protocols
  - ‘Neurons that fire together, wire together’
  - No causal relationship between the input and the output neuron’s activity.
- Timing based protocols
  - Strongly causal learning rules

Long-term potentiation of synapses

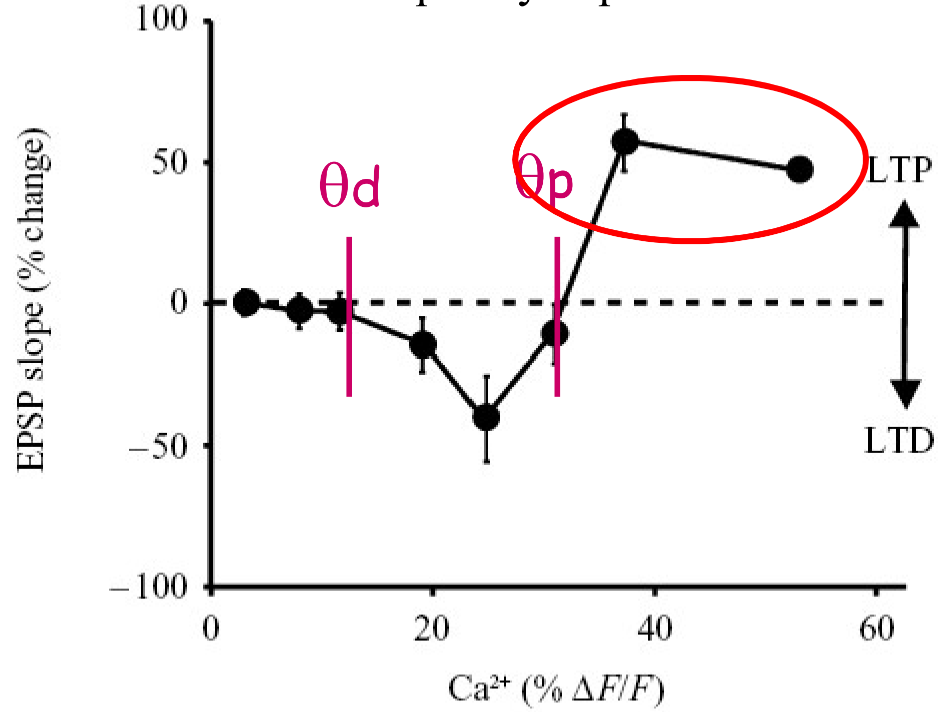


- Stimulate a synapse once every minute to determine its ‘baseline’ strength
- Stimulate the pre- and post-synaptic neurons together at a high rate (> 5 times a second) using about 900 spikes.
- This results in a permanent change in synaptic strength afterwards called long-term potentiation (LTP).

Frequency-dependence of NMDA-mediated synapatic plasticity: Low frequency stimuli induce LTD, high frequency stimuli induce LTP

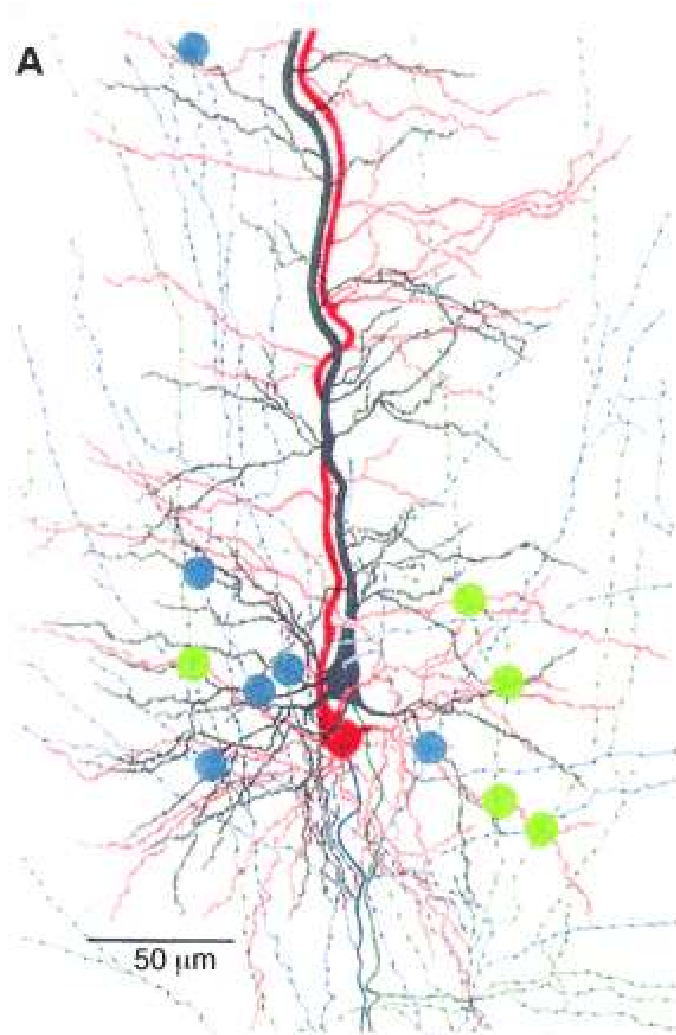


Calcium dynamics determines the frequency dependence



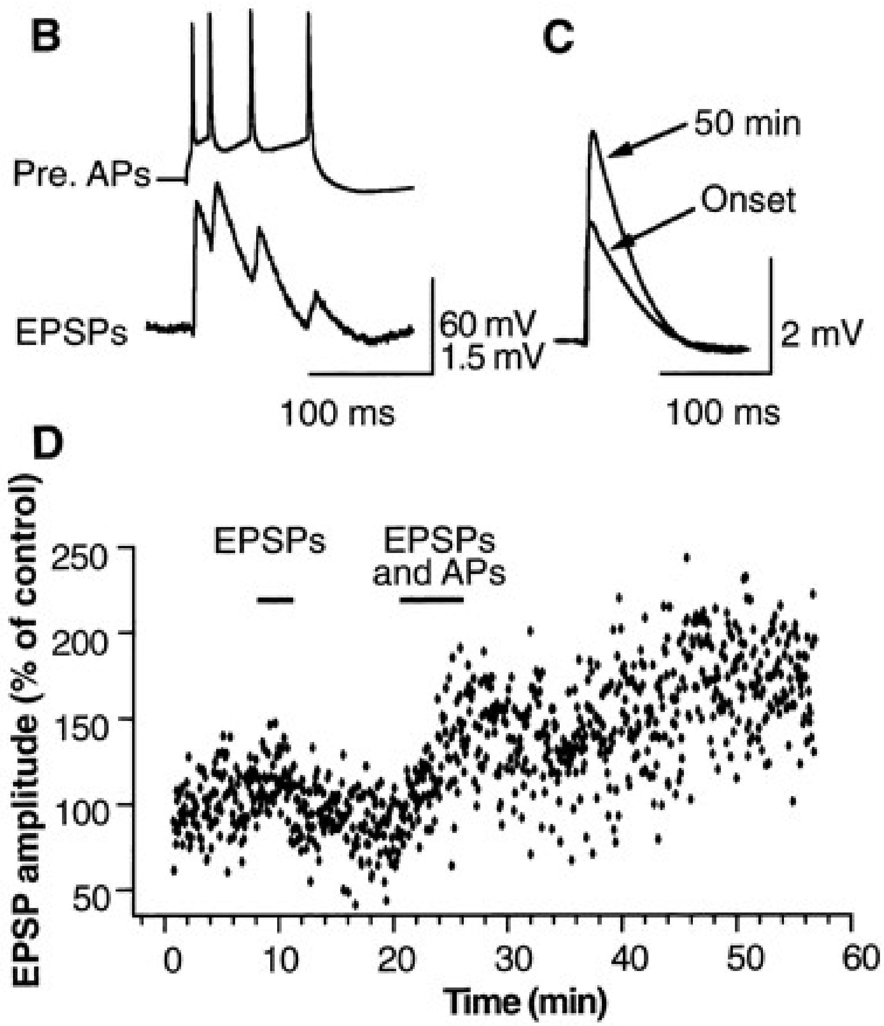
(Johnston et al, Phil Trans R Soc Lond B, 2003)

Stimulation of only one pair of neurons



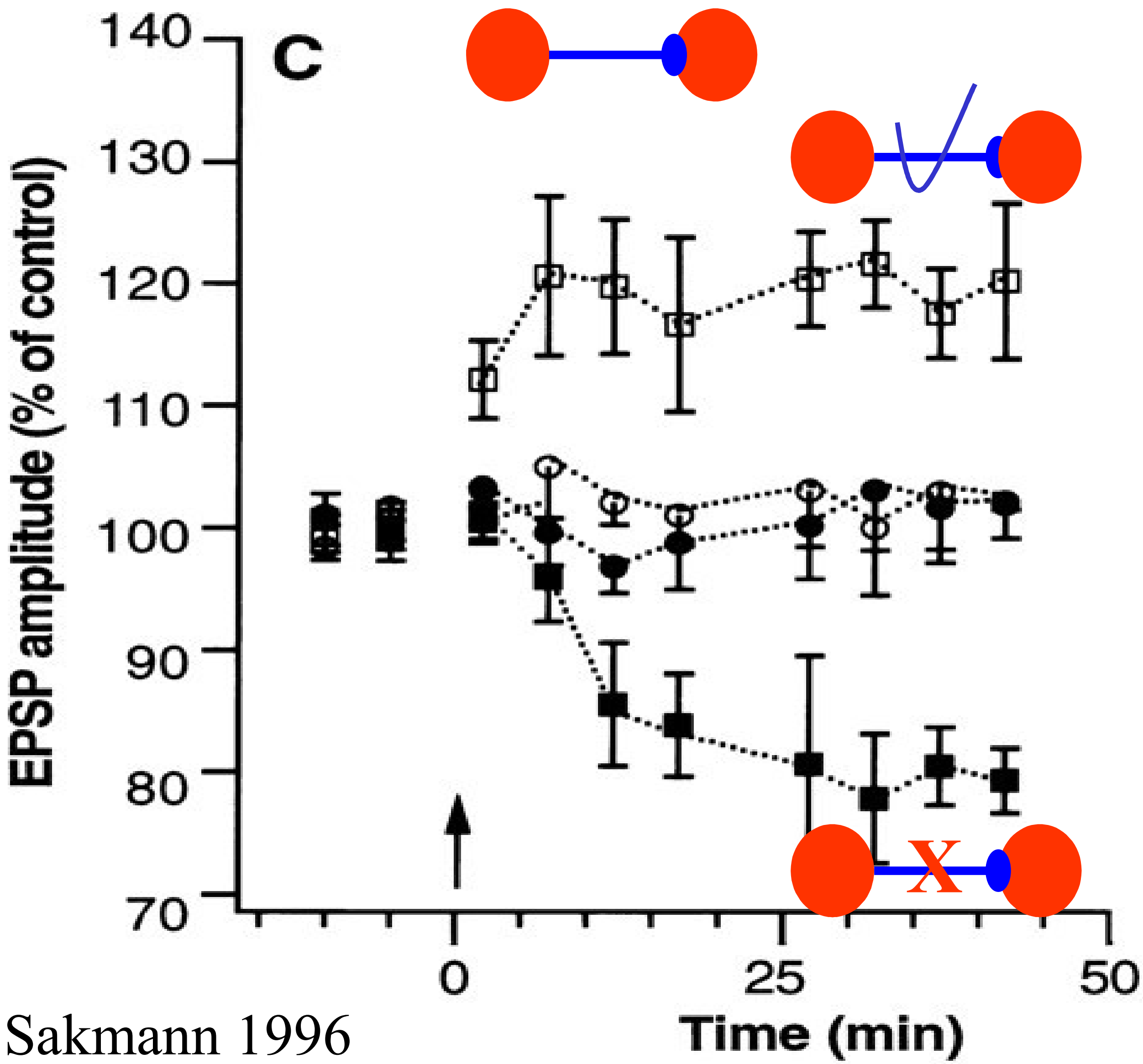
Markram & Sakmann 1996

Presynaptic activity before post-synaptic activity induces LTP



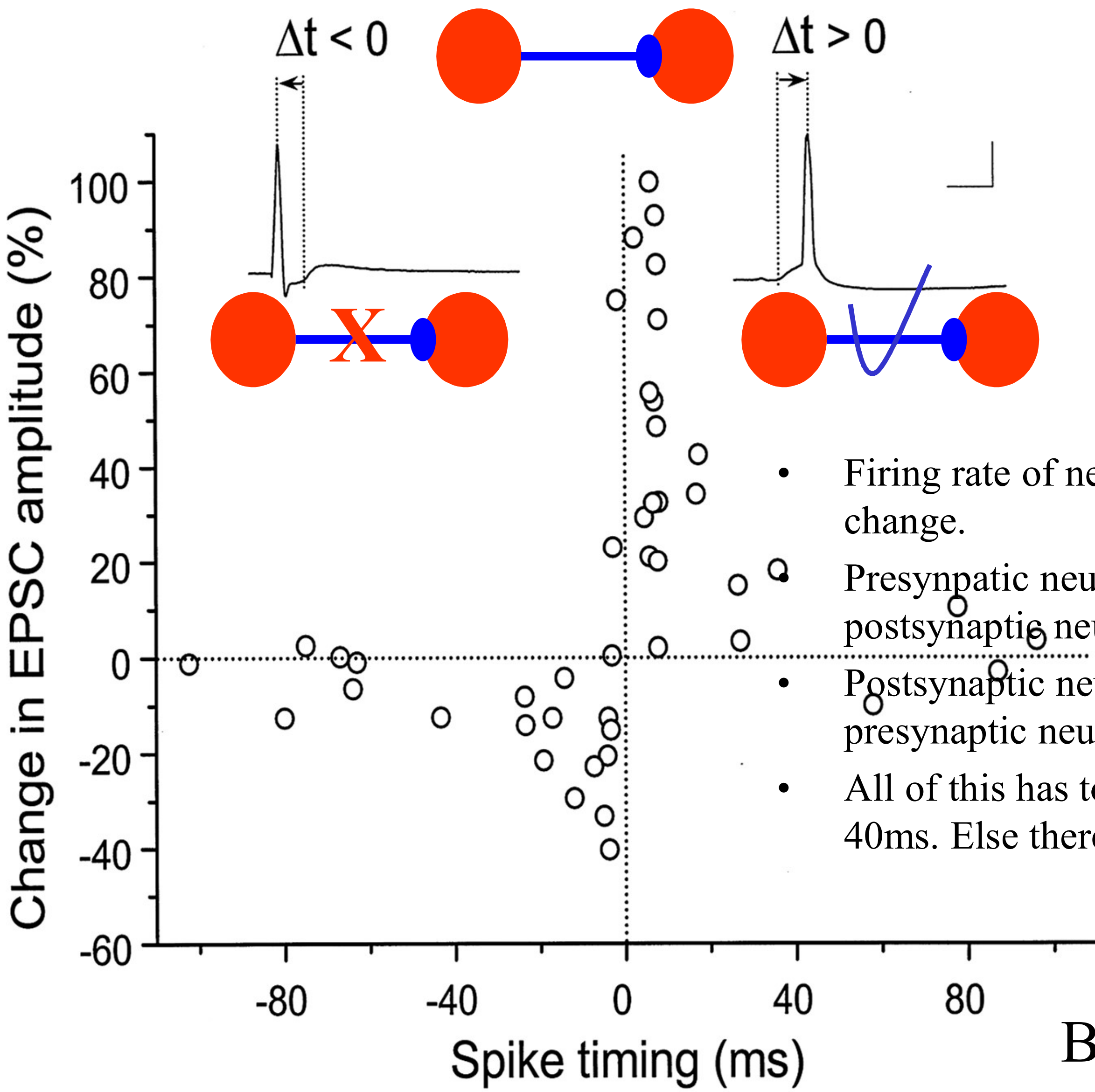
Markram & Sakmann 1996

Timing based protocols for inducing LTP and LTD



Markram & Sakmann 1996

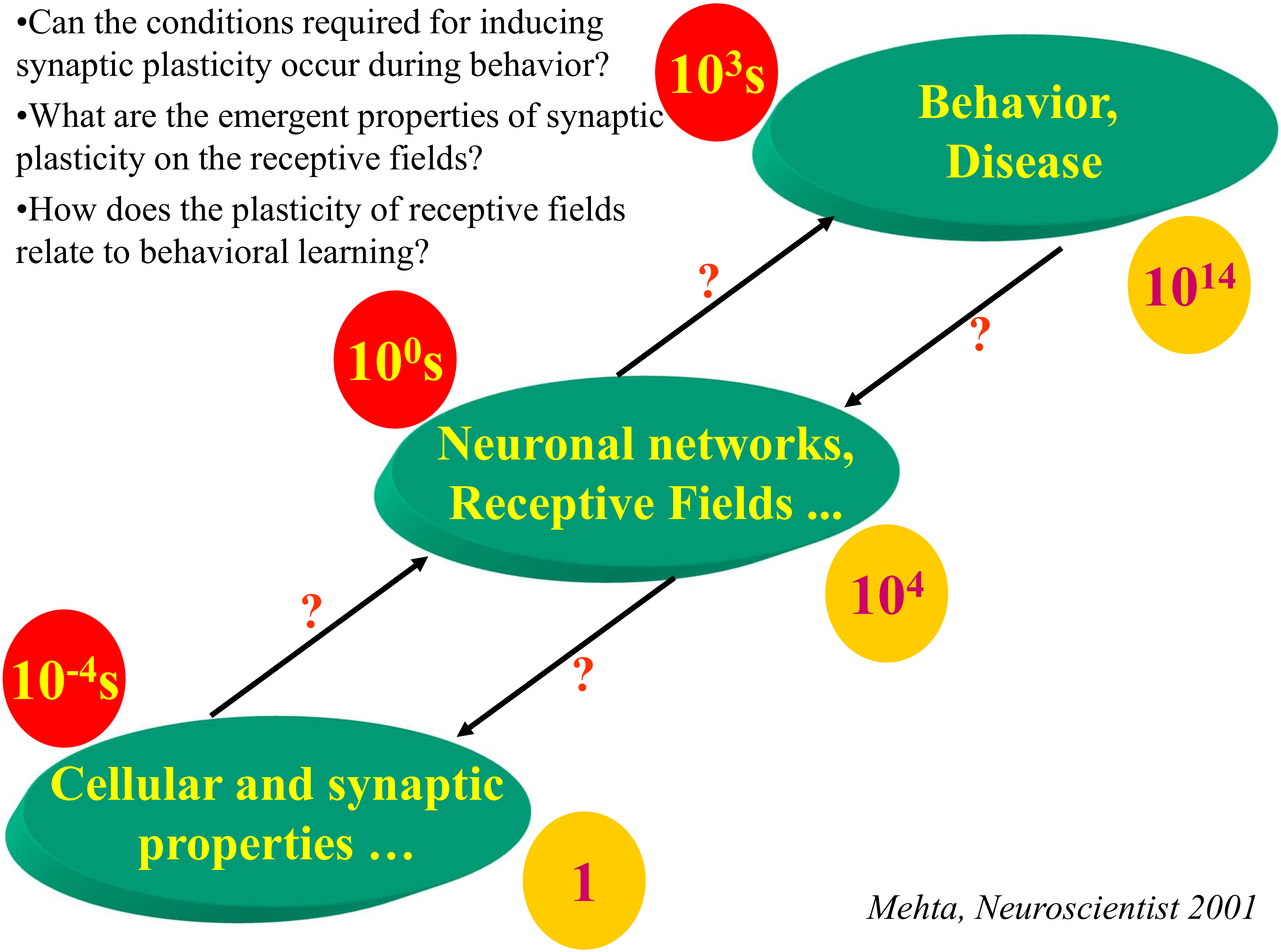
Timing based protocols for inducing LTP and LTD



- Firing rate of neurons dues not change.
- Presynpatic neuron fires before the postsynaptic neuron: there is LTP.
- Postsynaptic neuron fires before the presynaptic neuron: there is LTD.
- All of this has to happen within + or – 40ms. Else there is no plasticity.

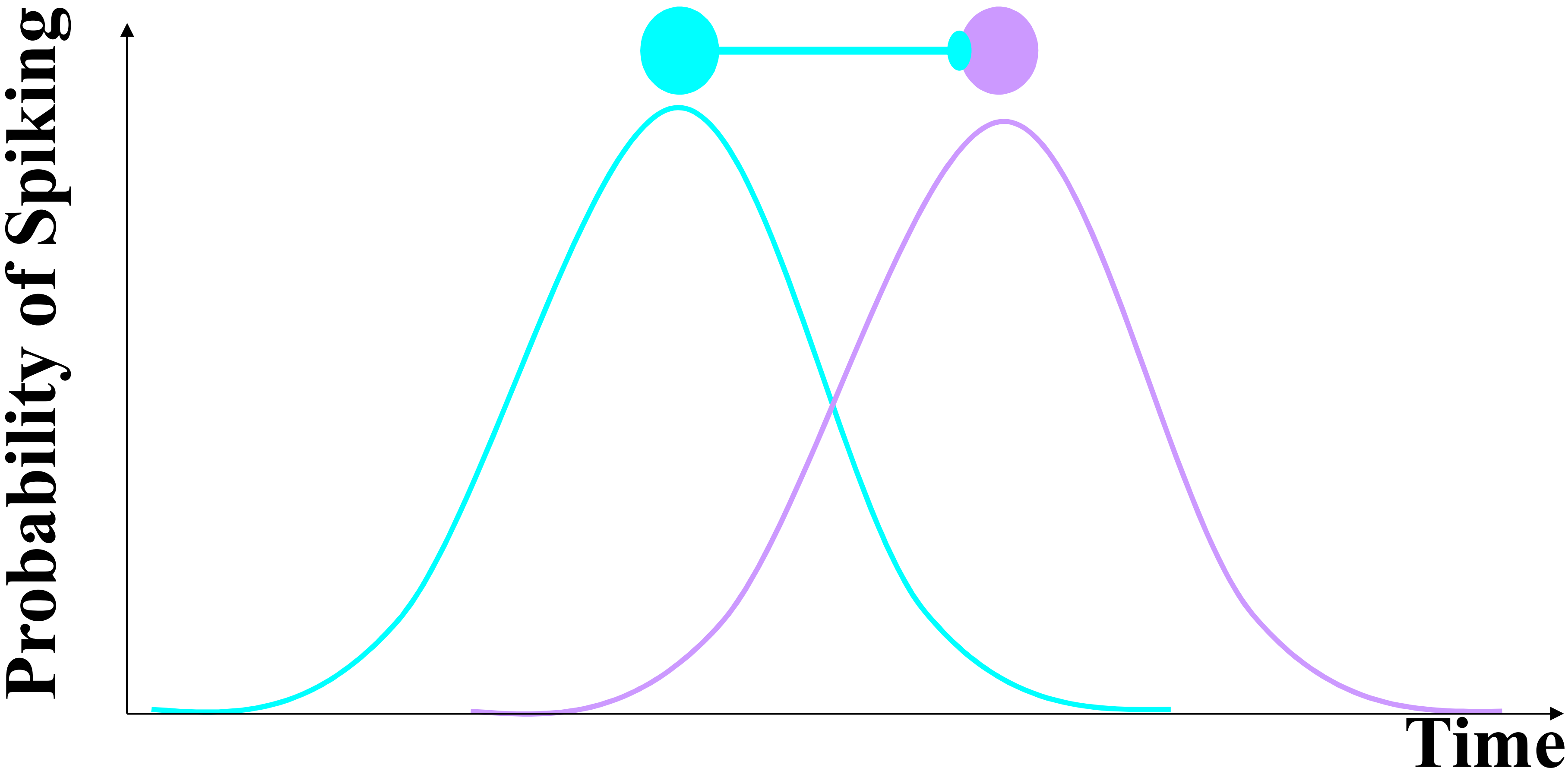
Bi & Poo 1998

- Can the conditions required for inducing synaptic plasticity occur during behavior?
- What are the emergent properties of synaptic plasticity on the receptive fields?
- How does the plasticity of receptive fields relate to behavioral learning?

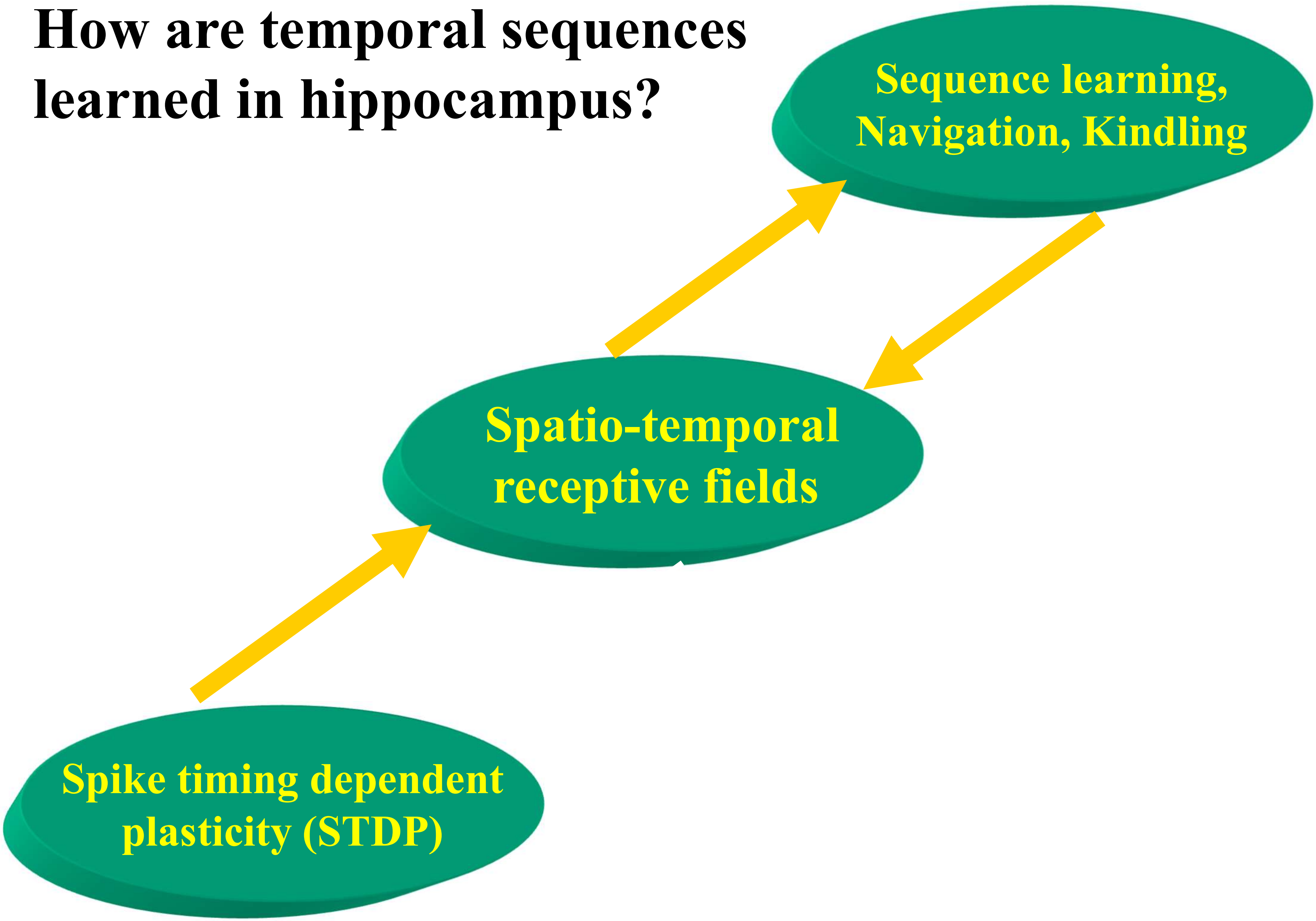


Mehta, Neuroscientist 2001

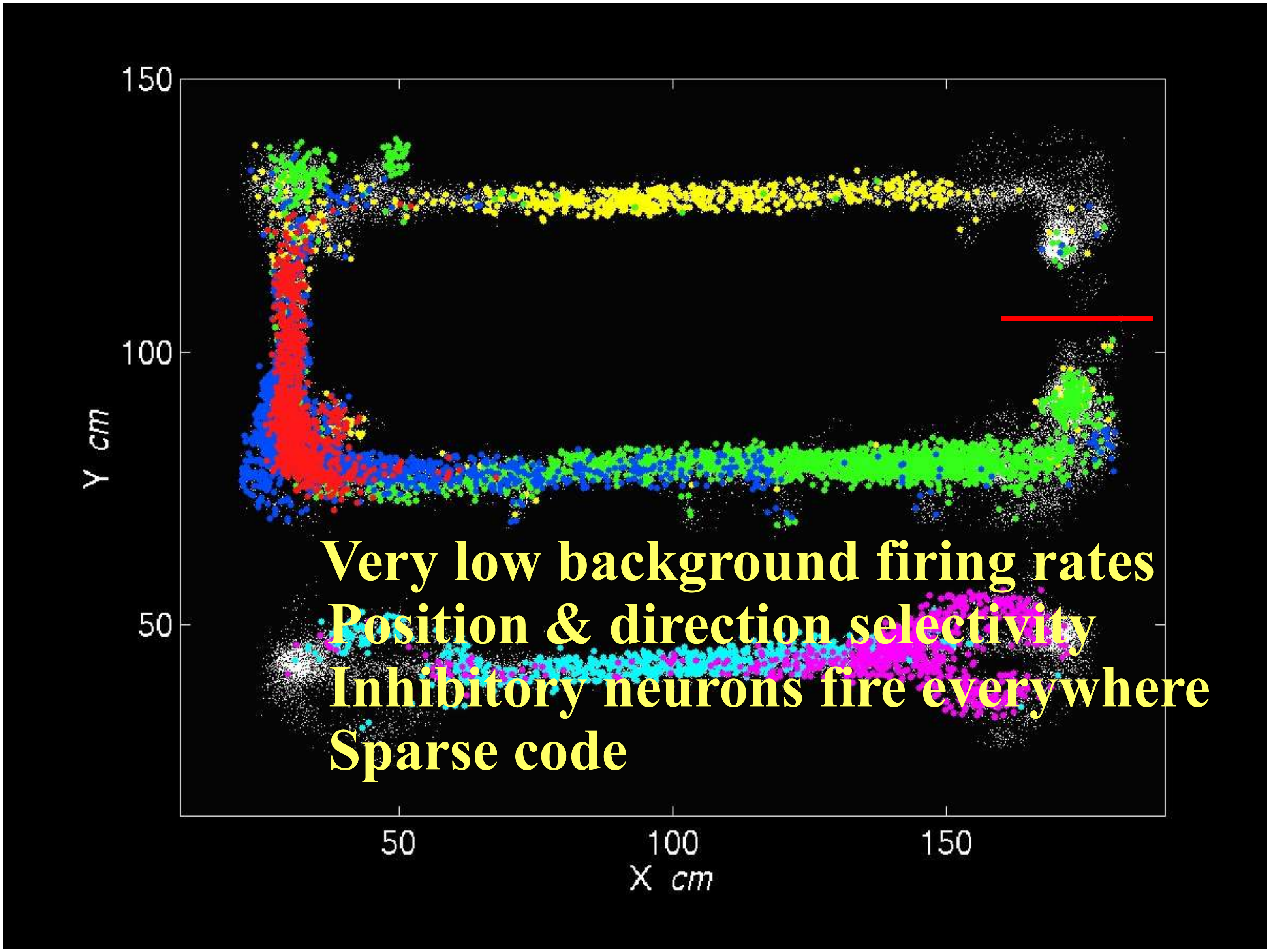
Problem: How do we learn to anticipate?



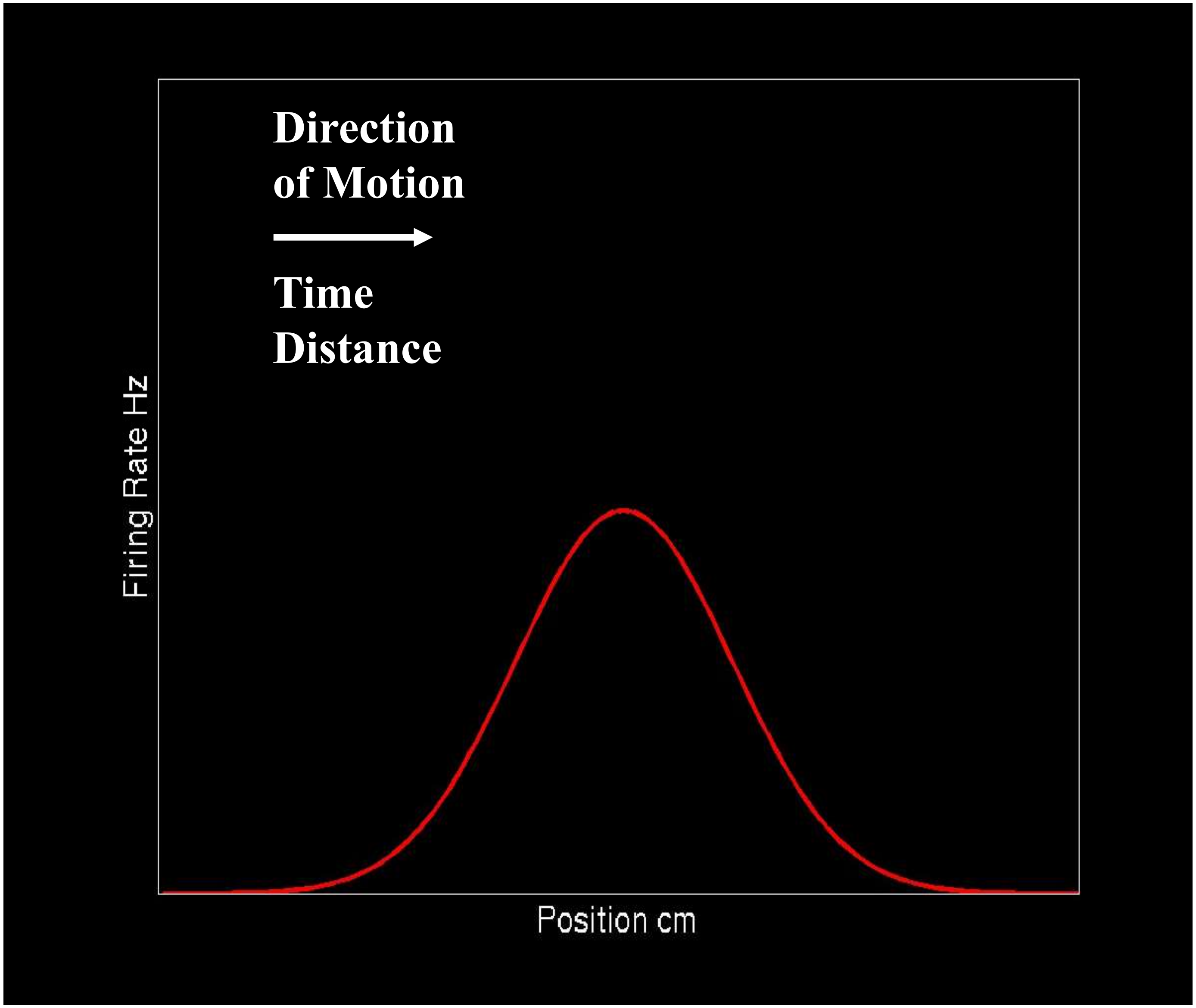
How are temporal sequences learned in hippocampus?



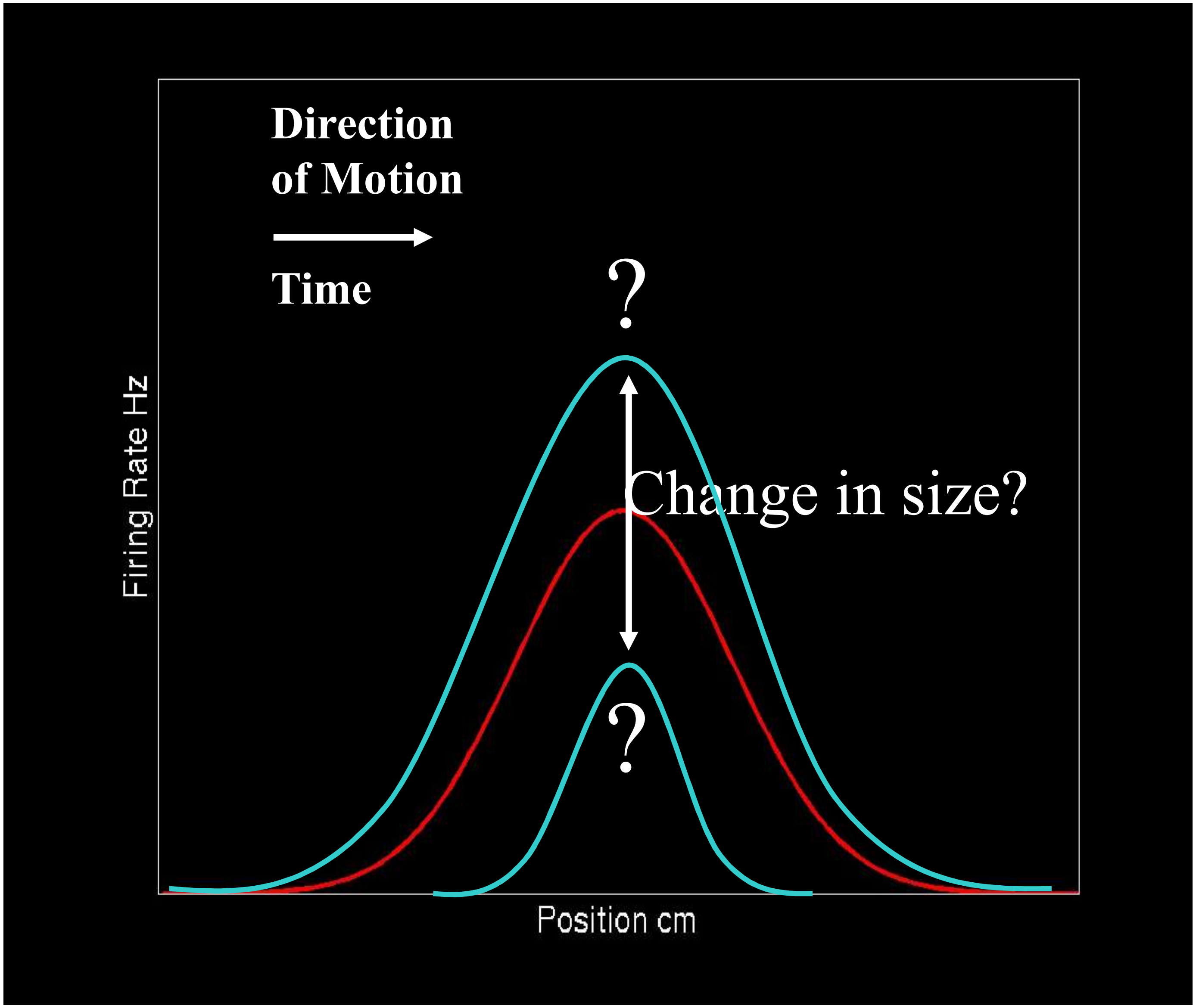
Activity of (excitatory) pyramidal neurons in CA1 depends on rat's position: place cells



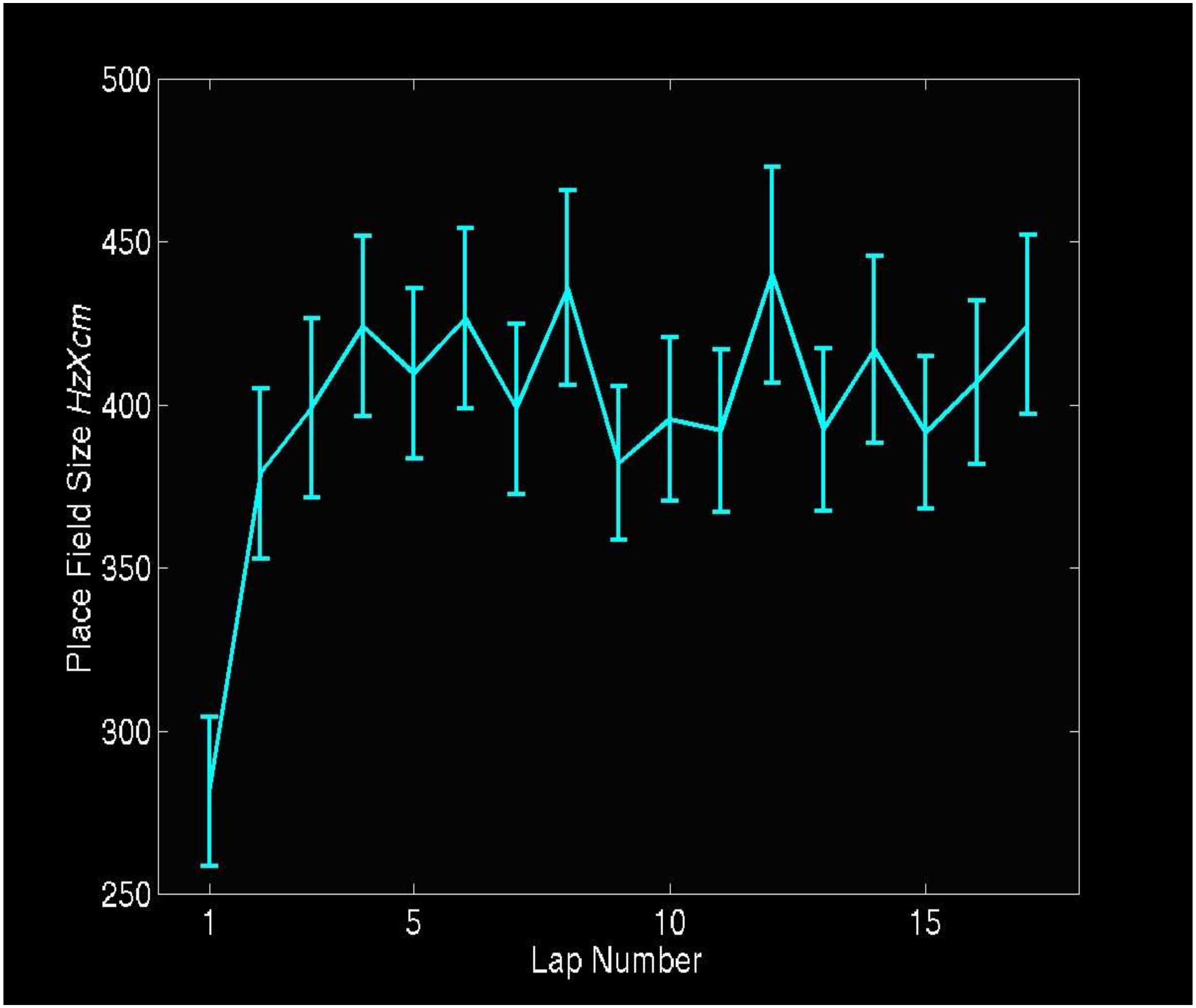
A representation of place fields that takes into account their firing characteristics



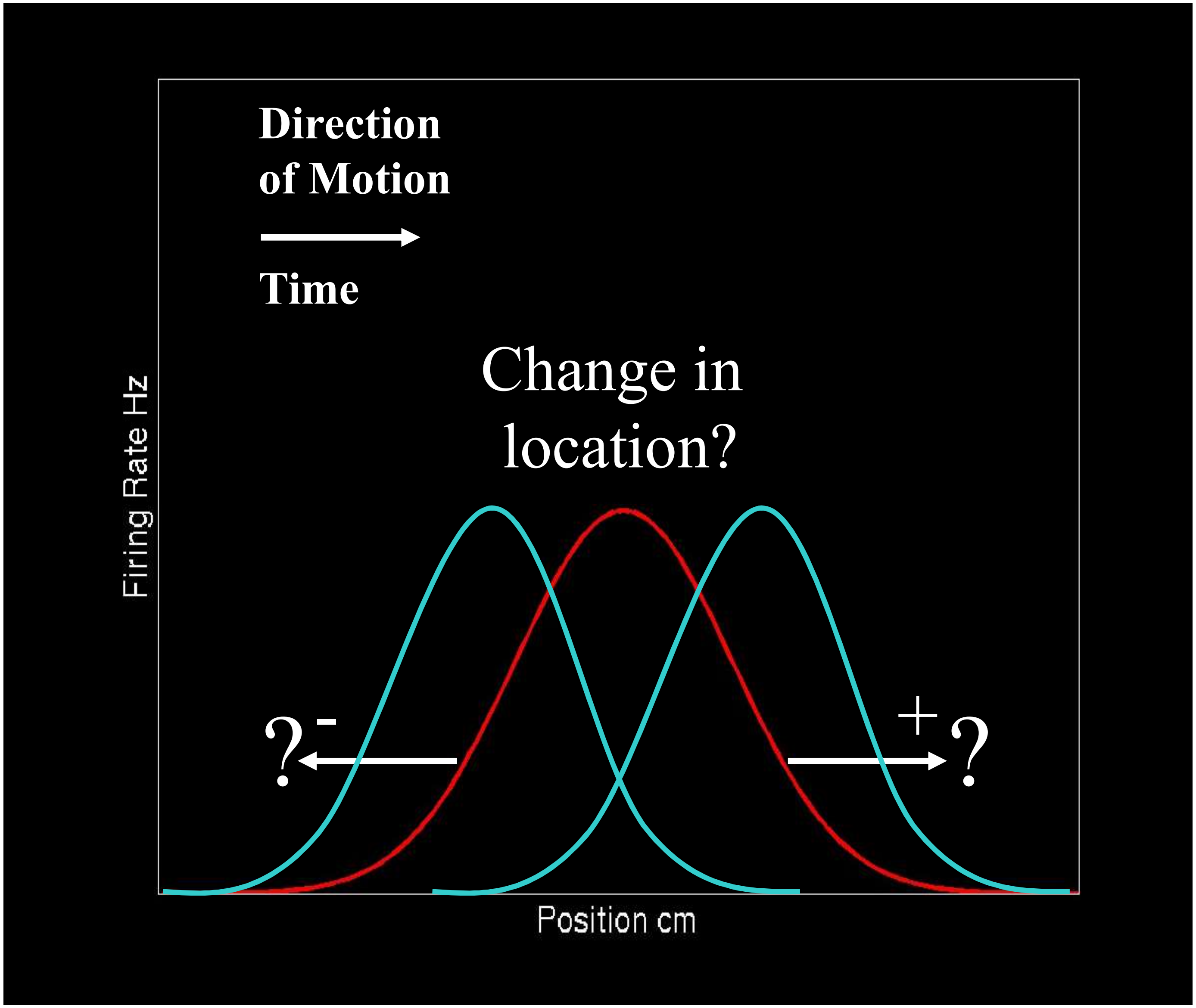
Does the place field size change with experience?



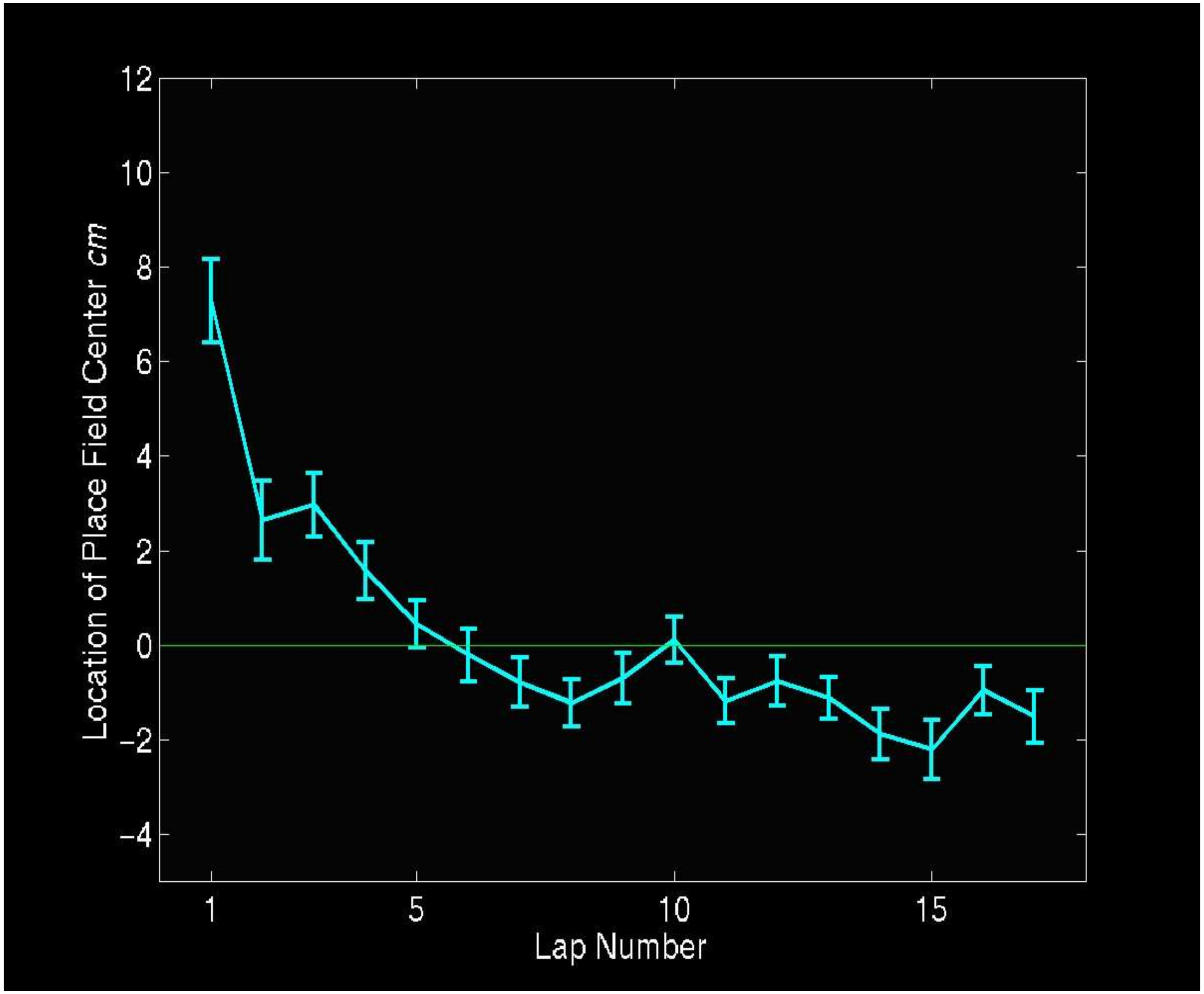
Place field size increases by ~75% within a few trials, lasting a few minutes



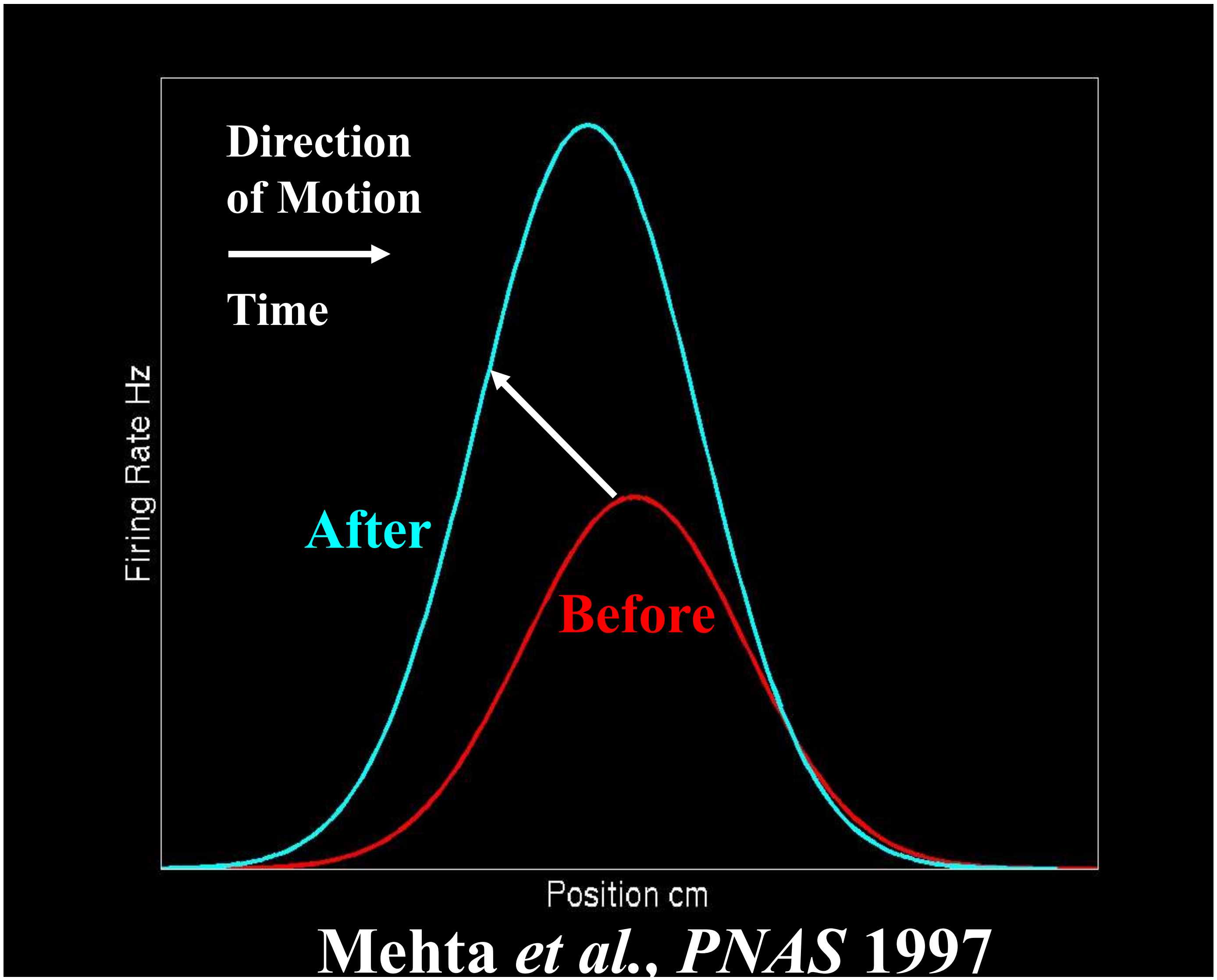
Does the place field location (center) change with experience?



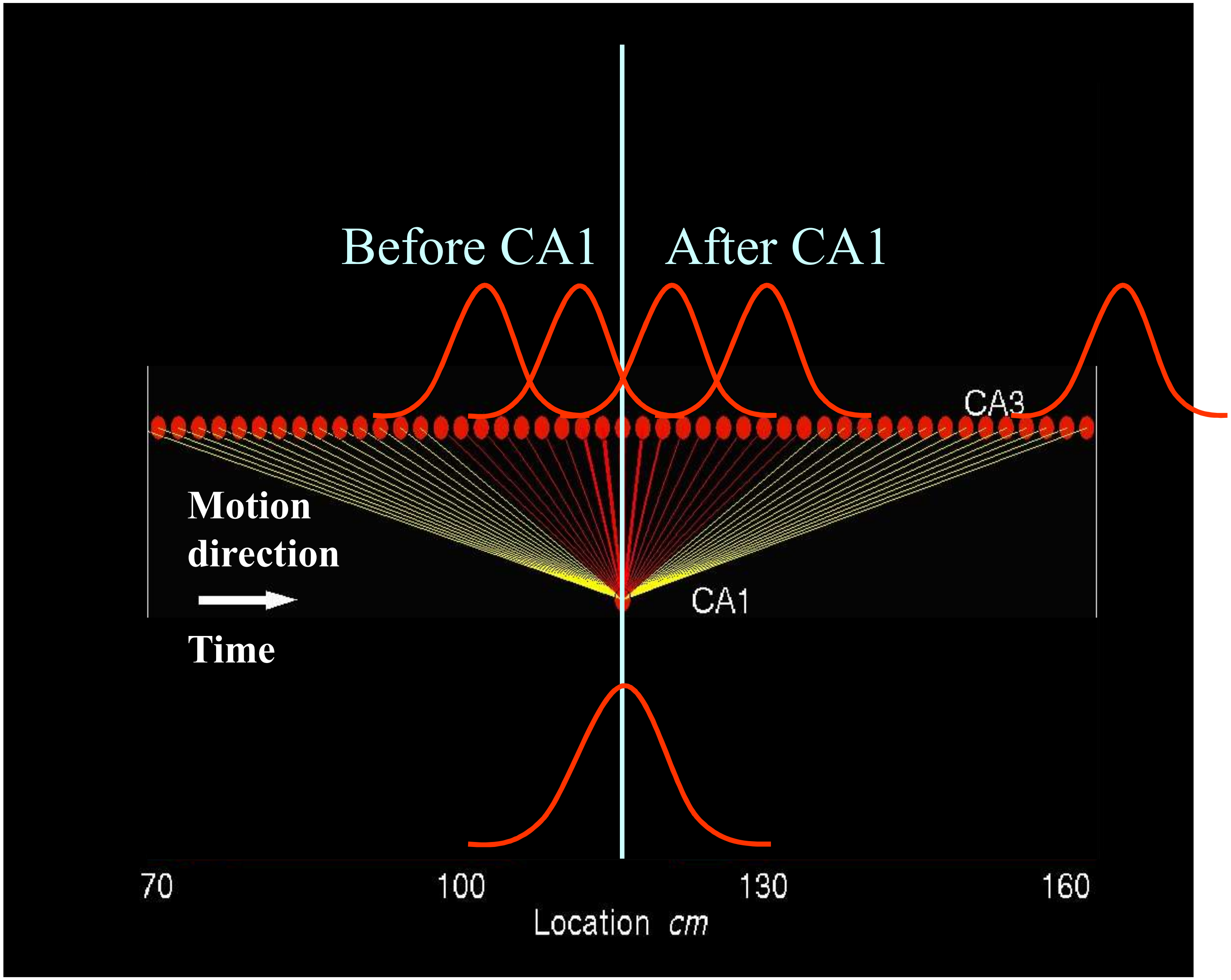
Place fields become more predictive with experience: ~20% ‘backward’ shift in the place field center within a few trials



Summary of experience dependent changes in place fields:

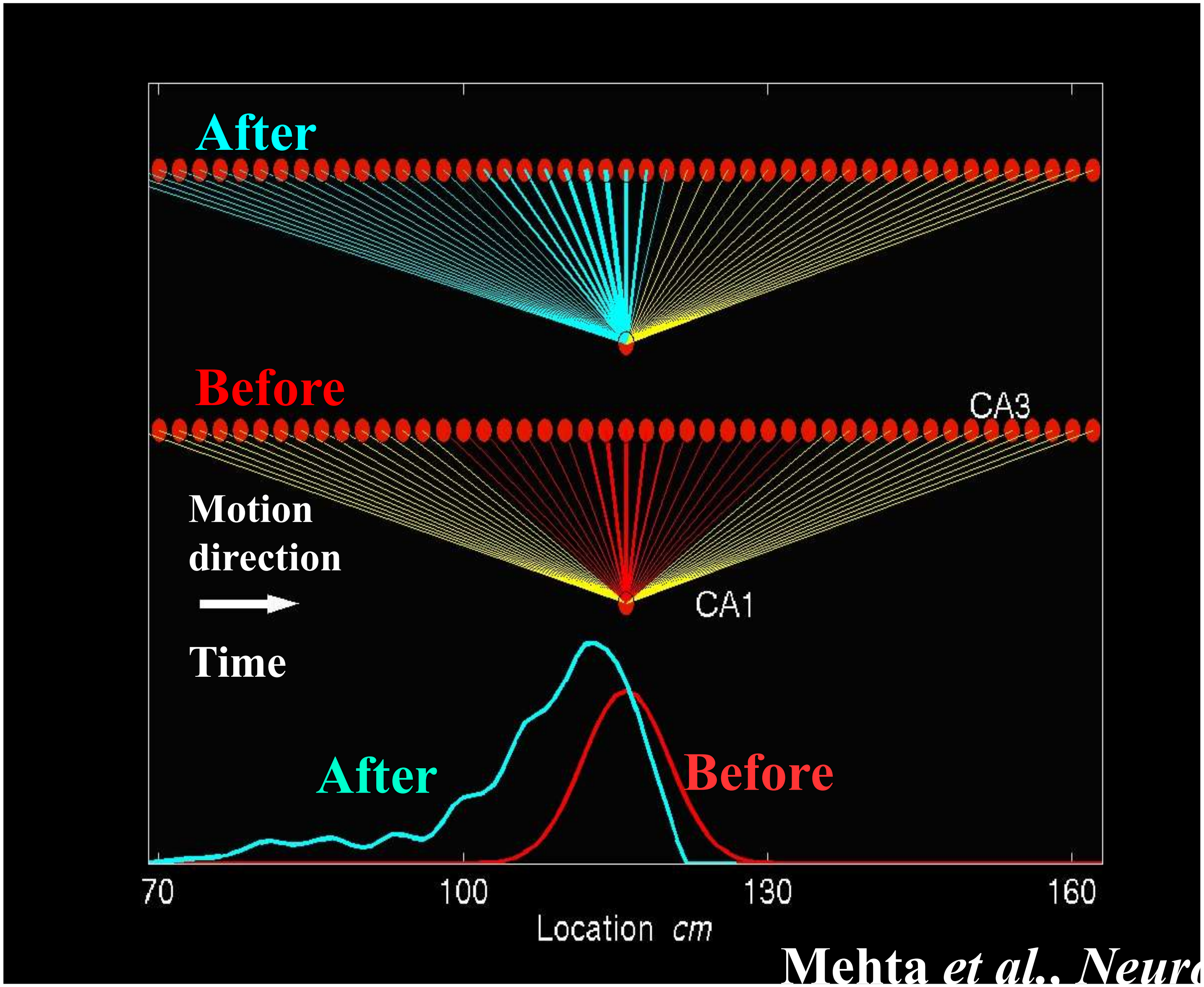


Computational Model of Effect of STDP in CA1

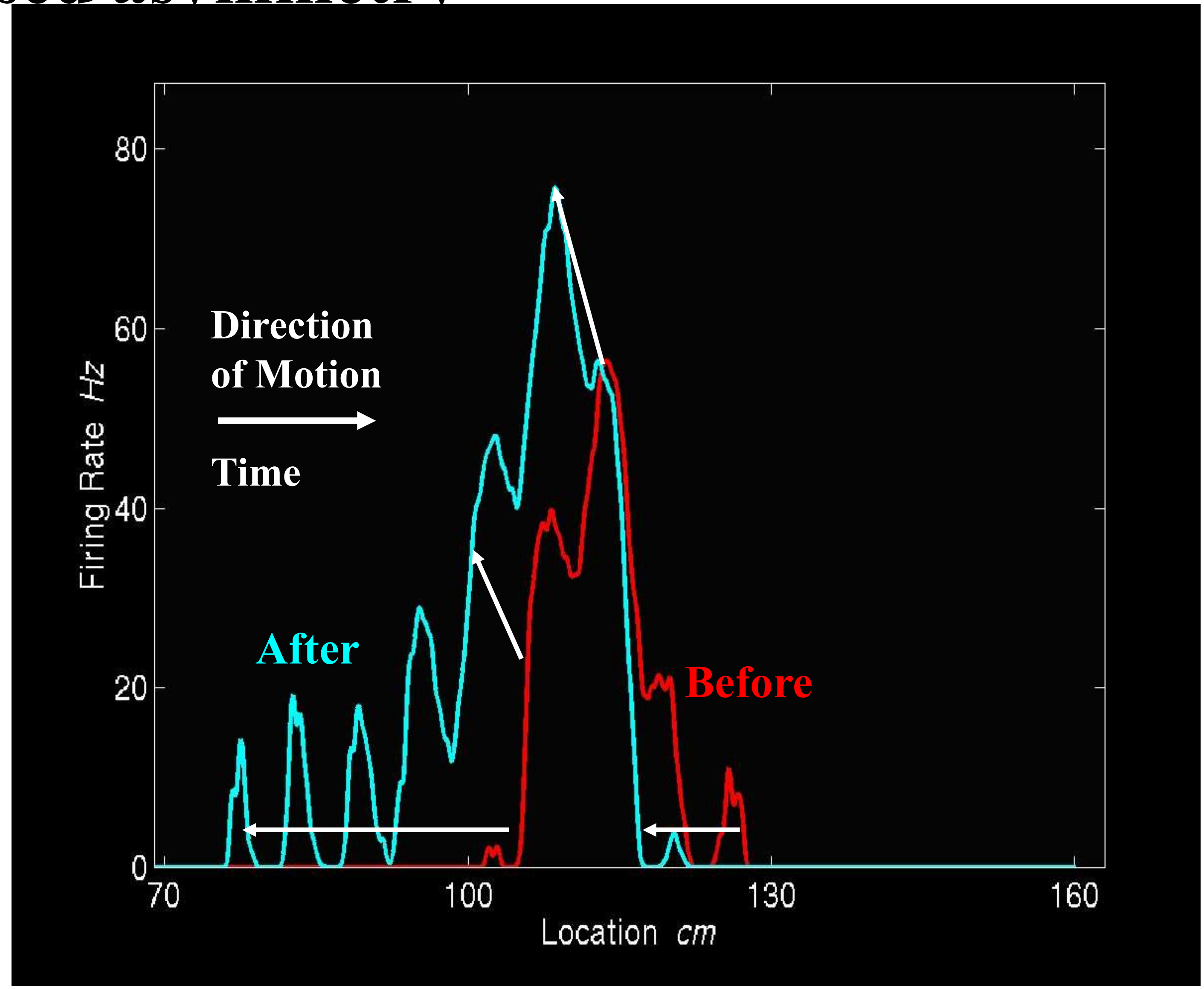


Mehta *et al.*, *Neuron 2000*

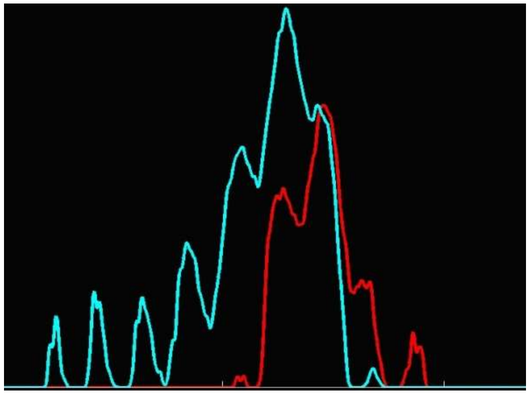
Computational Model of Effect of STDP in CA1



Predictions of model of STDP about the dynamics of place fields: increased firing, predictive shift, increased asymmetry



Predictions of model of STDP in a feed-forward network



•Total activity within a place (size) field should increase with experience.

•Center of the place field should show an anticipatory shift.

•Place fields should be asymmetric.

•Place fields should become more asymmetric with experience.

•First spike in the place field should show a large anticipatory shift, due to LTP.

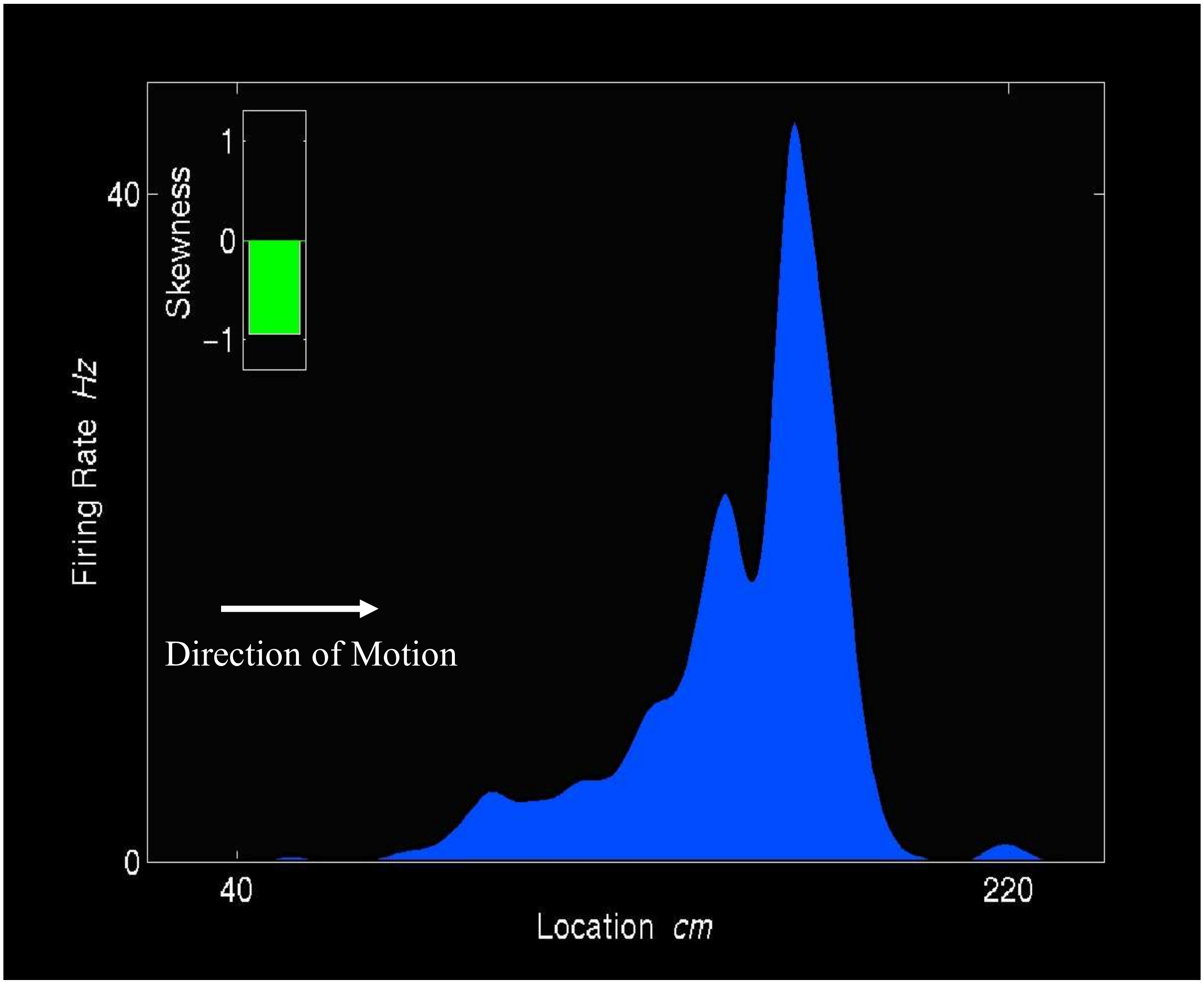
•Last spike in the place field should show a small anticipatory shift, due to LTD.

•Thus place fields should become wider with experience.

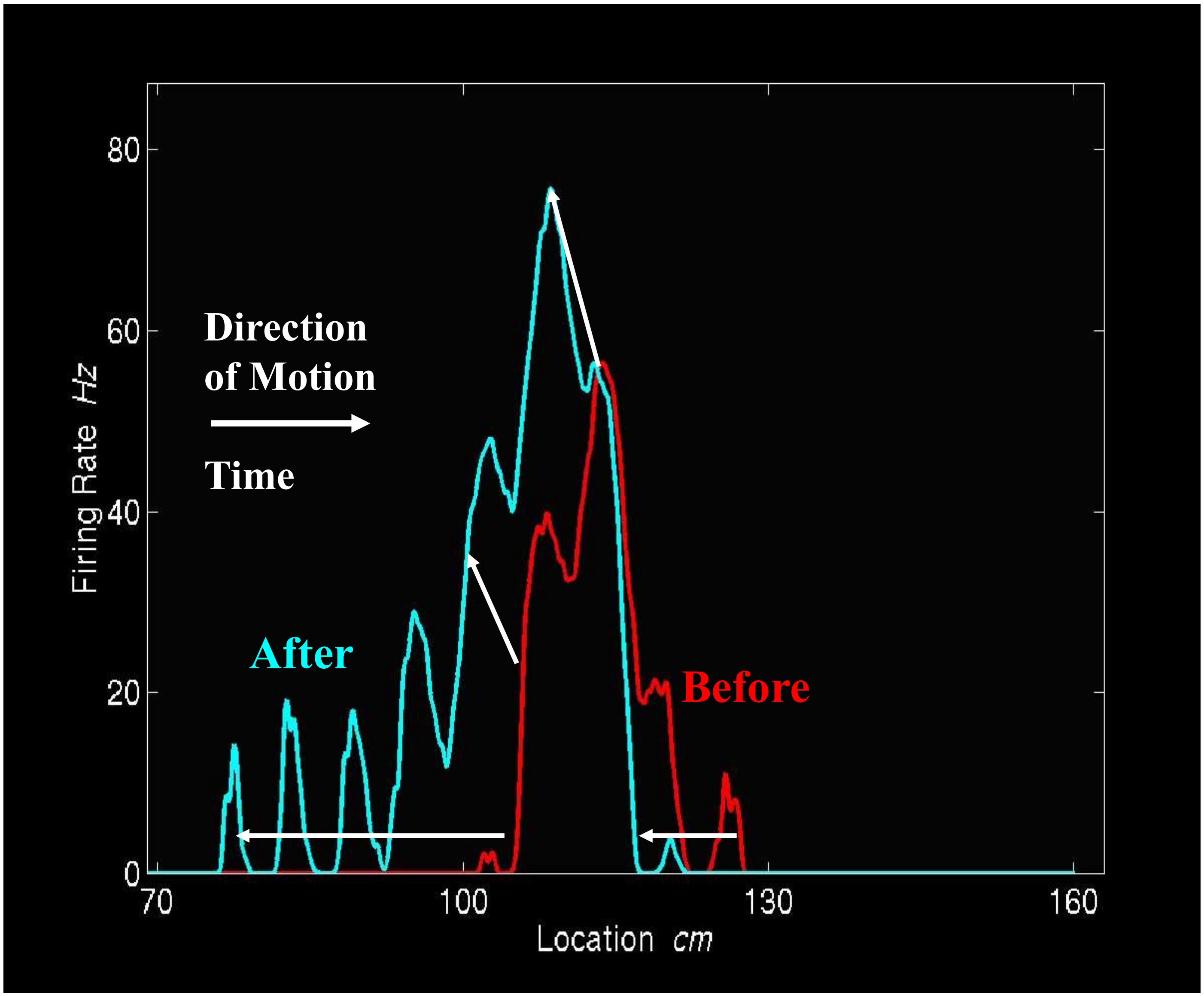
•The asymmetry should be a function of experience, not time.

•Peak firing rate should increase

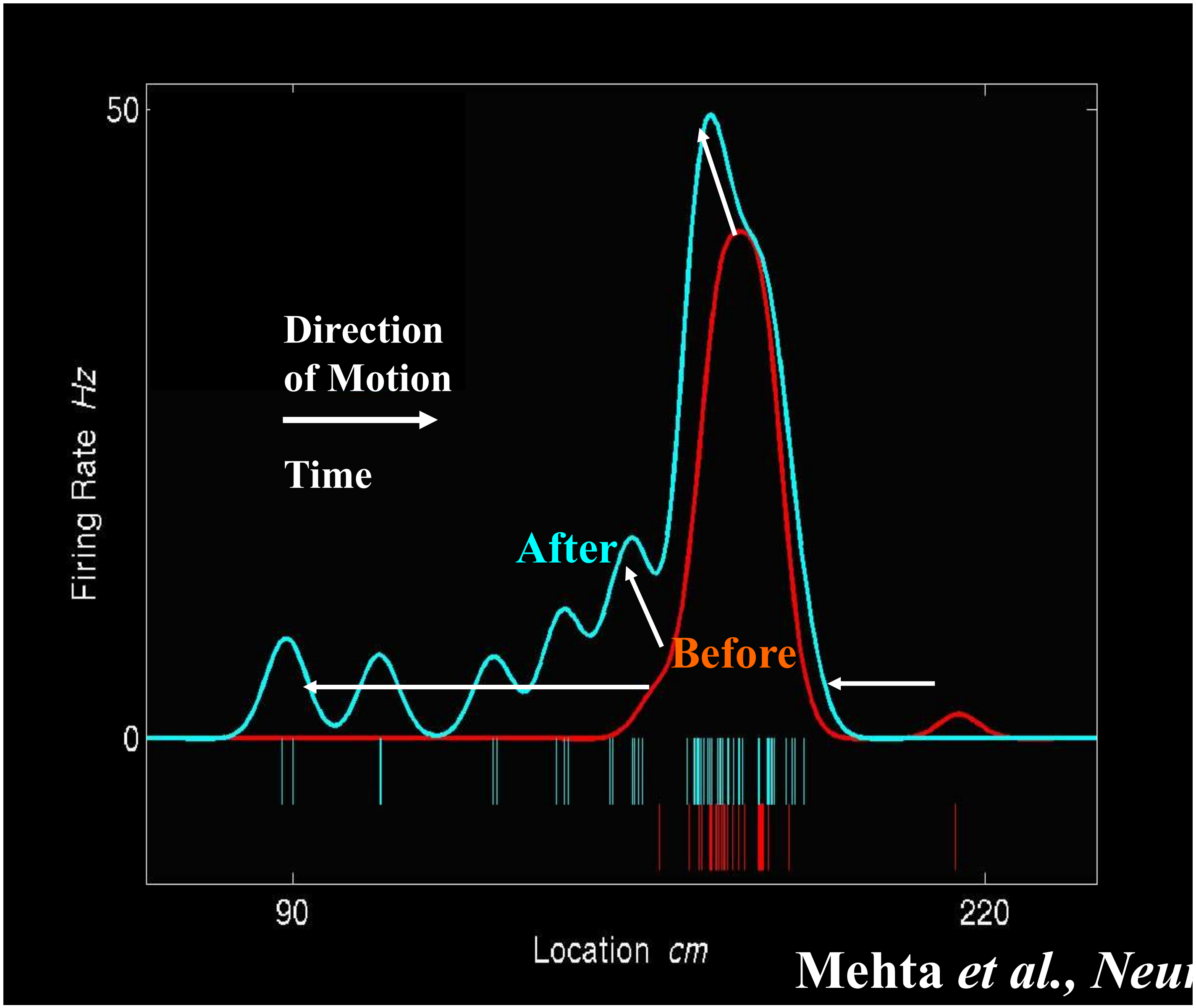
Experimental verification of the predictions of the model: Example of an asymmetric place field:



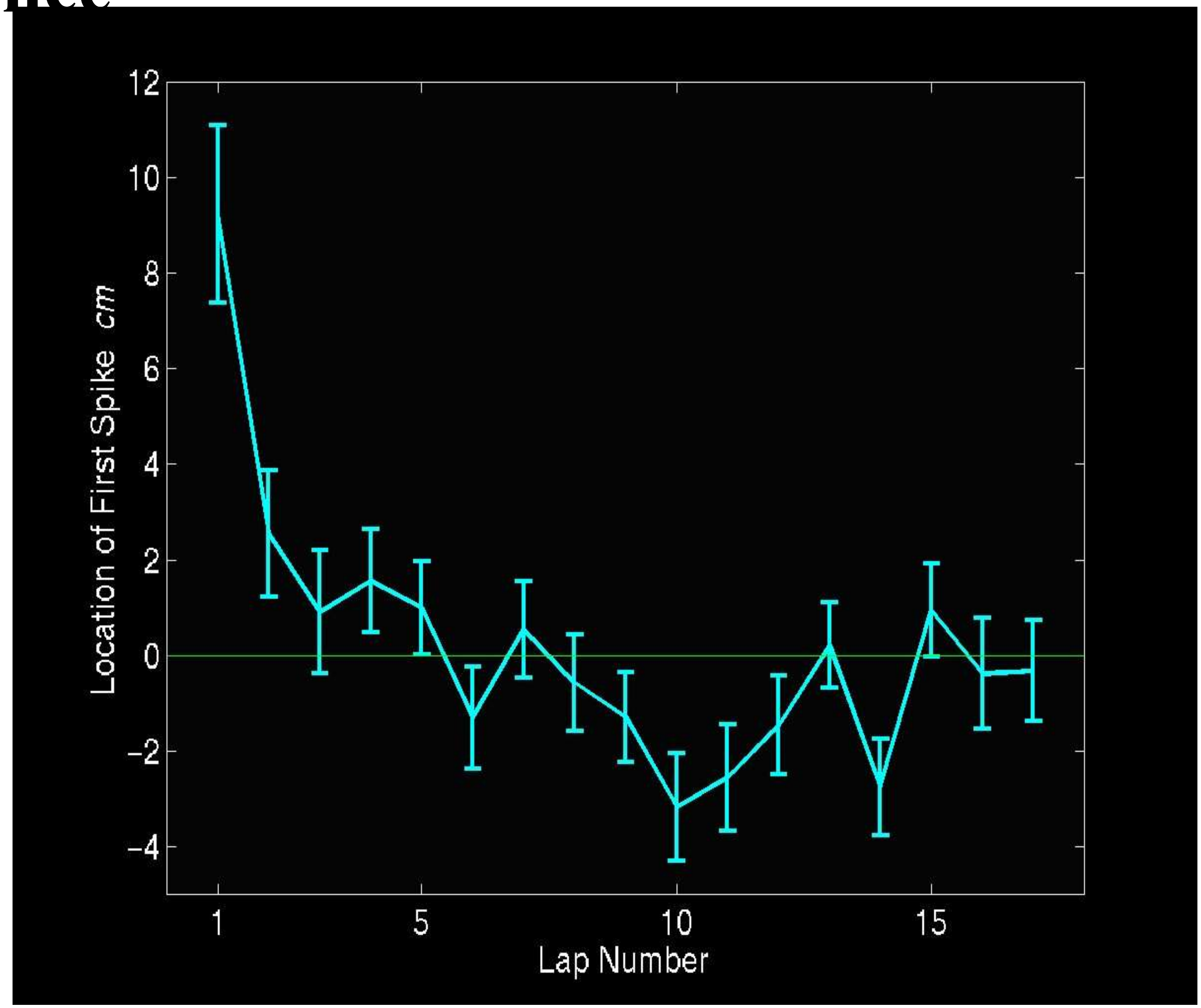
Dynamics of place cells with STDP: Model



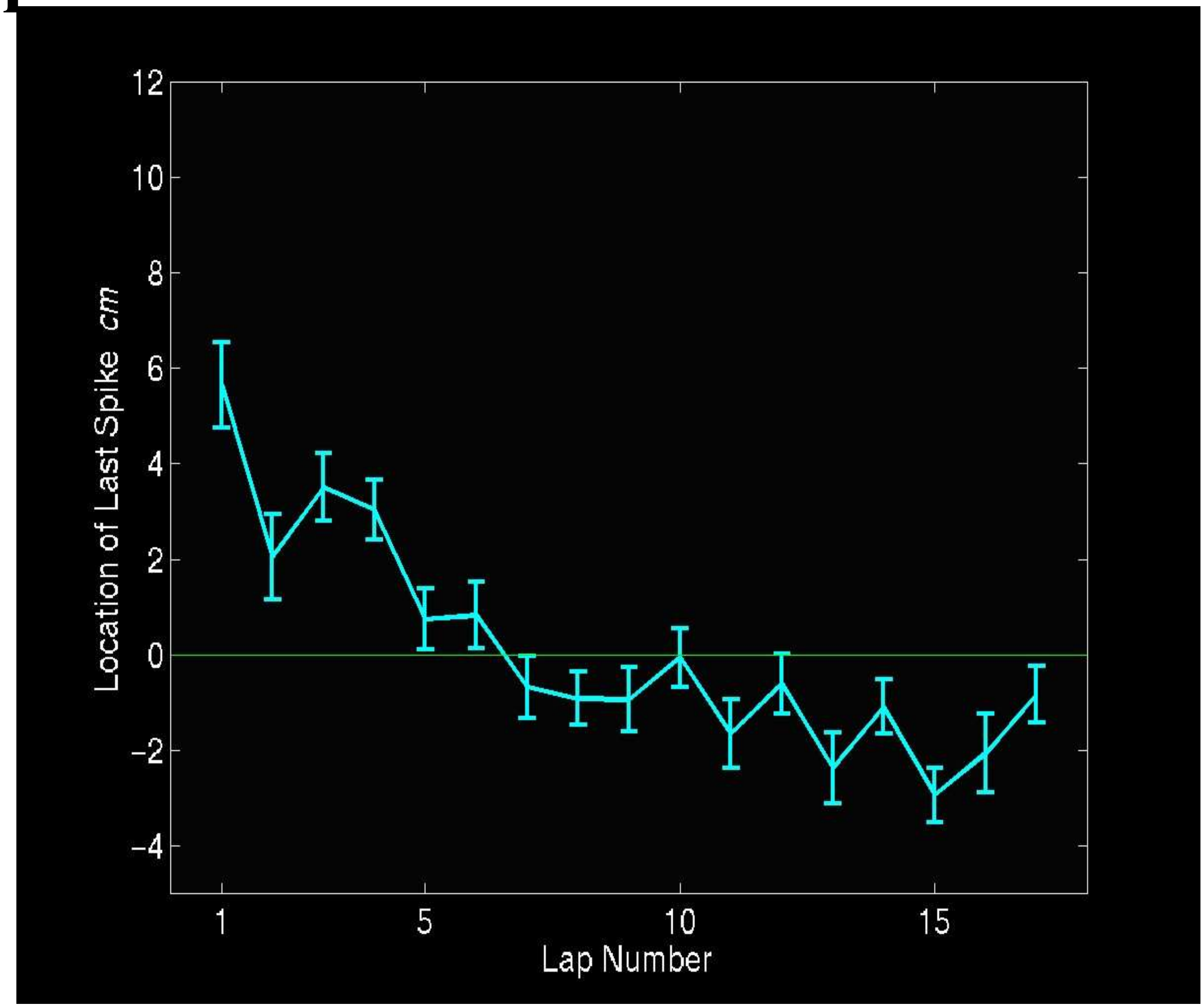
Dynamics of place cells with STDP: Data



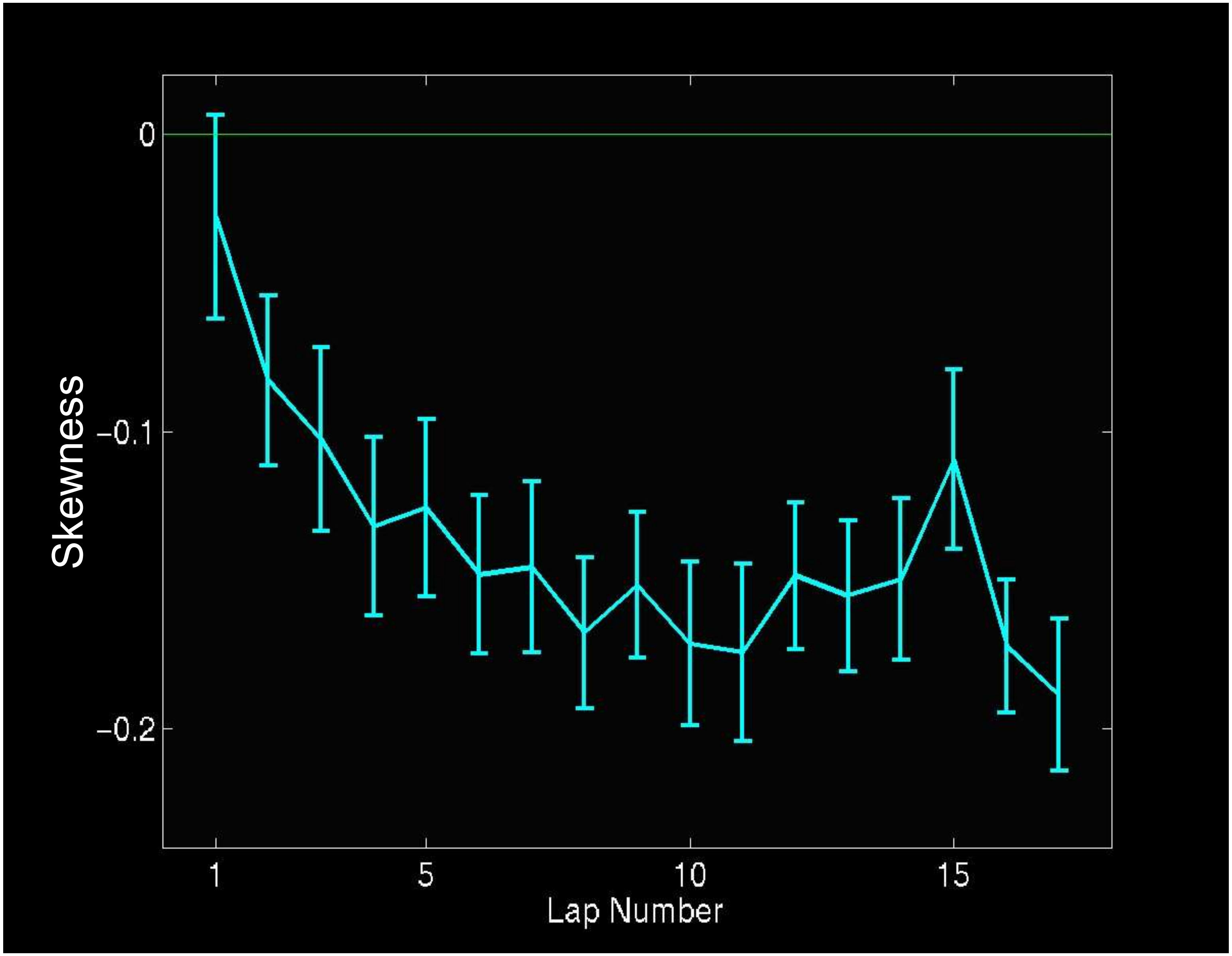
The average first spike of CA1 pyramidal neurons exhibits a 12 cm (25%) 'predictive' shift with experience



The average last spike of CA1 pyramidal neurons exhibits a 'noisy' 6 cm (12%) 'predictive' shift with experience



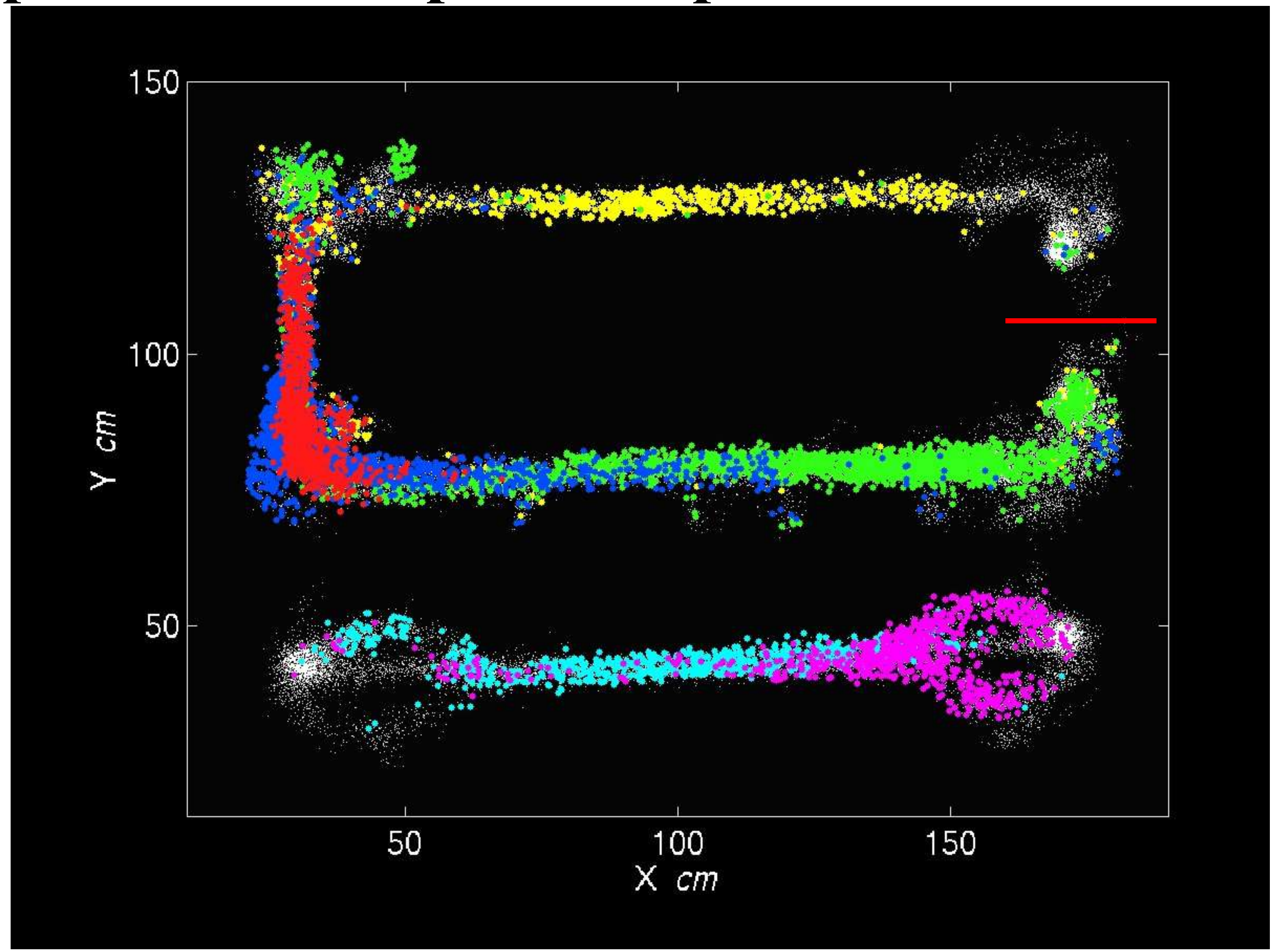
CA1 place fields exhibit a ~ 400% ‘increase’ in asymmetry with experience



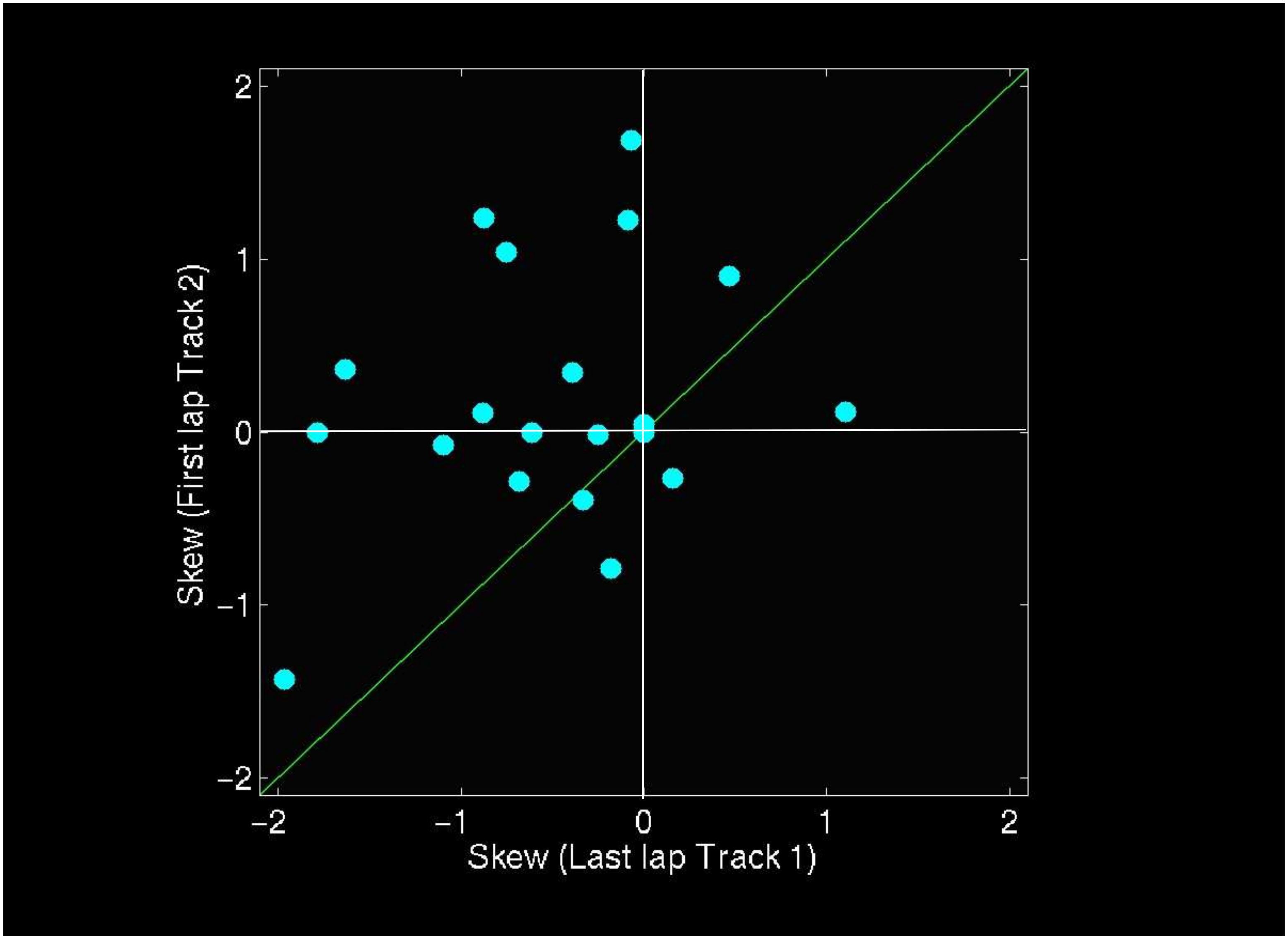
All the (seven) experience dependent changes in place field spiking are consistent with the predictions of the model of STDP in a feed-forward network

Place field size (cm × Hz)	605.8 ± 33.3	426.4 ± 34.6	643.5 ± 41.4	217.1	50.9%
Place field width (cm)	47.4 ± 2.3	40.1 ± 3.0	48.0 ± 2.7	7.9	20.1%
Location of place field center (cm)	0.0	7.3 ± 0.6	−0.9 ± 0.7	−8.2	−17.3%
Location of first spike in place field (cm)	0.0	9.2 ± 1.9	−0.3 ± 1.1	−9.3	−19.6%
Location of last spike in place field (cm)	0.0	5.7 ± 0.9	−0.8 ± 0.6	−6.5	−13.7%
Location of place field peak (cm)	0.0	5.5 ± 1.5	−0.0 ± 1.0	−5.5	−11.6%
Field skewness	−0.27 ± 0.5	−0.05 ± 0.06	−0.21 ± 0.06	−0.16	312.6%
Field FRAI	−0.15 ± 0.02	−0.04 ± 0.04	−0.20 ± 0.03	−0.15	354.5%
Number of neurons with FRAI < 0	134	60	112	52	86%
Number of neurons with skewness < 0	124	67	107	40	60%

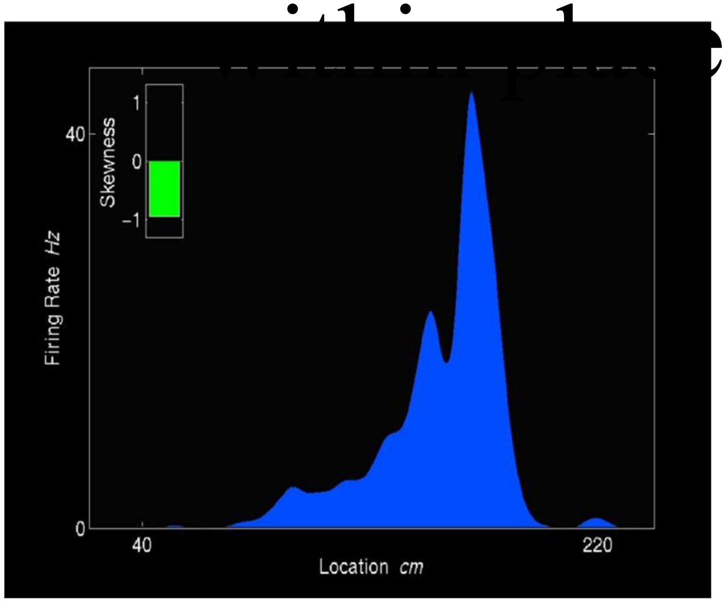
Activity of (excitatory) pyramidal neurons in CA1 depends on rat's position: place cells



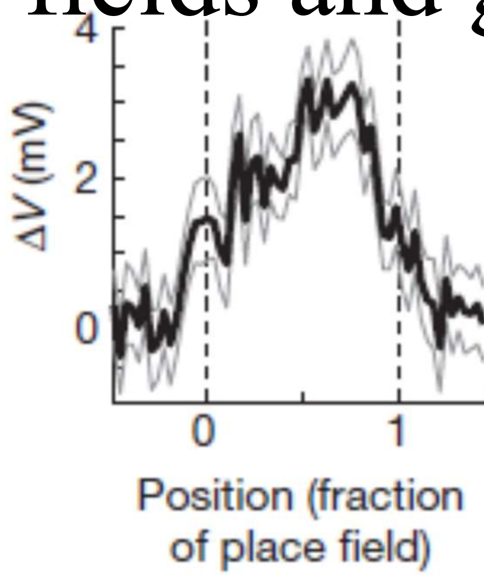
Asymmetry is Environment-dependent, as predicted by the model of learning with STDP



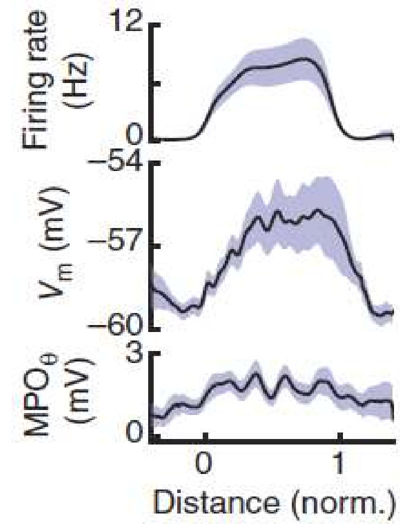
Membrane potential is asymmetric within place fields and grid fields



Place Field



Place Field



Grid Field

- Firing rate within place field is asymmetric
- Subthreshold membrane potential within place field (on linear tracks) is asymmetric (Harvey, Tank, Nature 2010)
- Same is true for the entorhinal grid cells (Schmidt, Hausser, Nature Neurosci 2013).