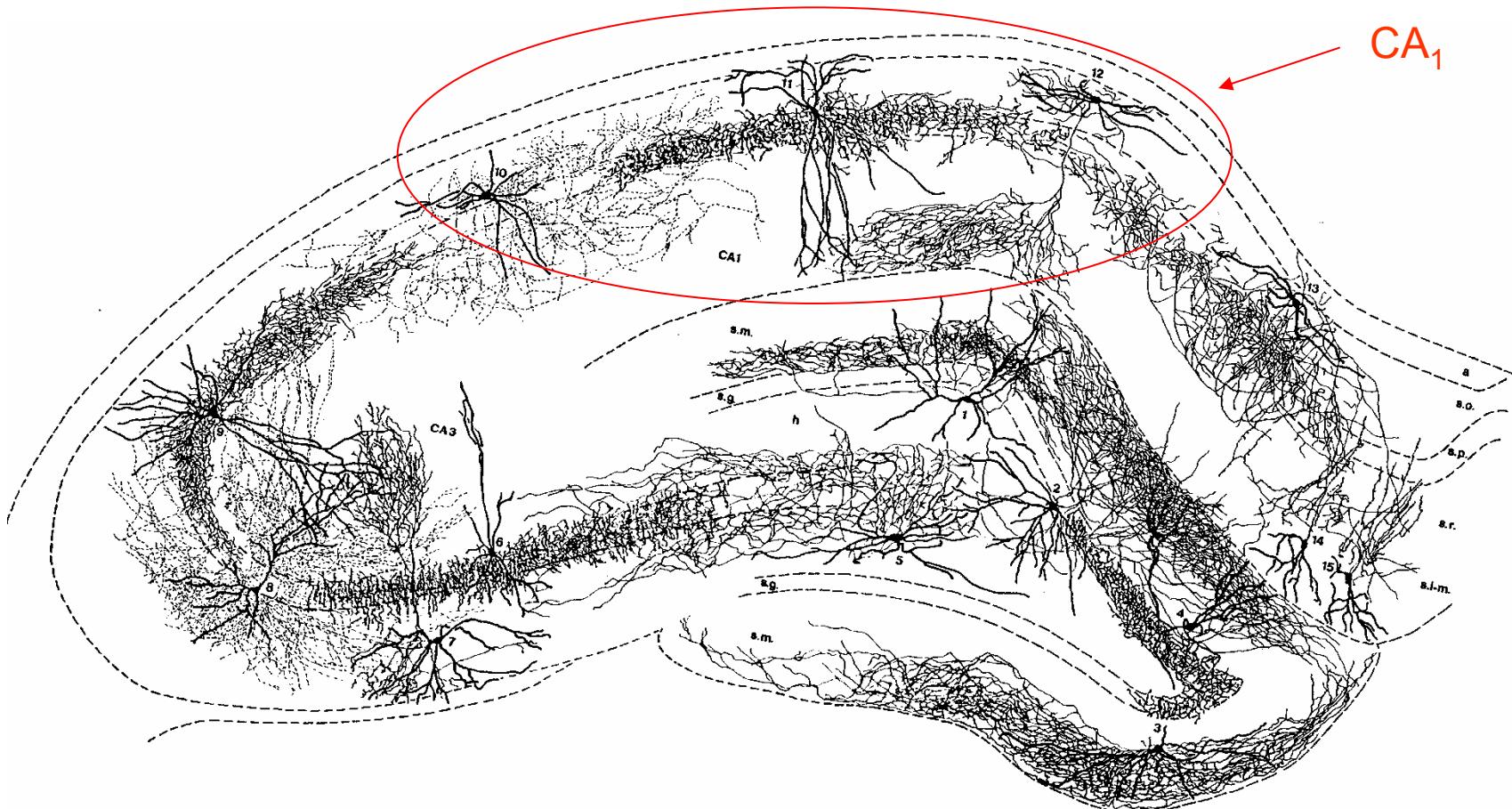


Encoding and Retrieval of Memories in the Animal Hippocampus

Vassilis Cutsuridis

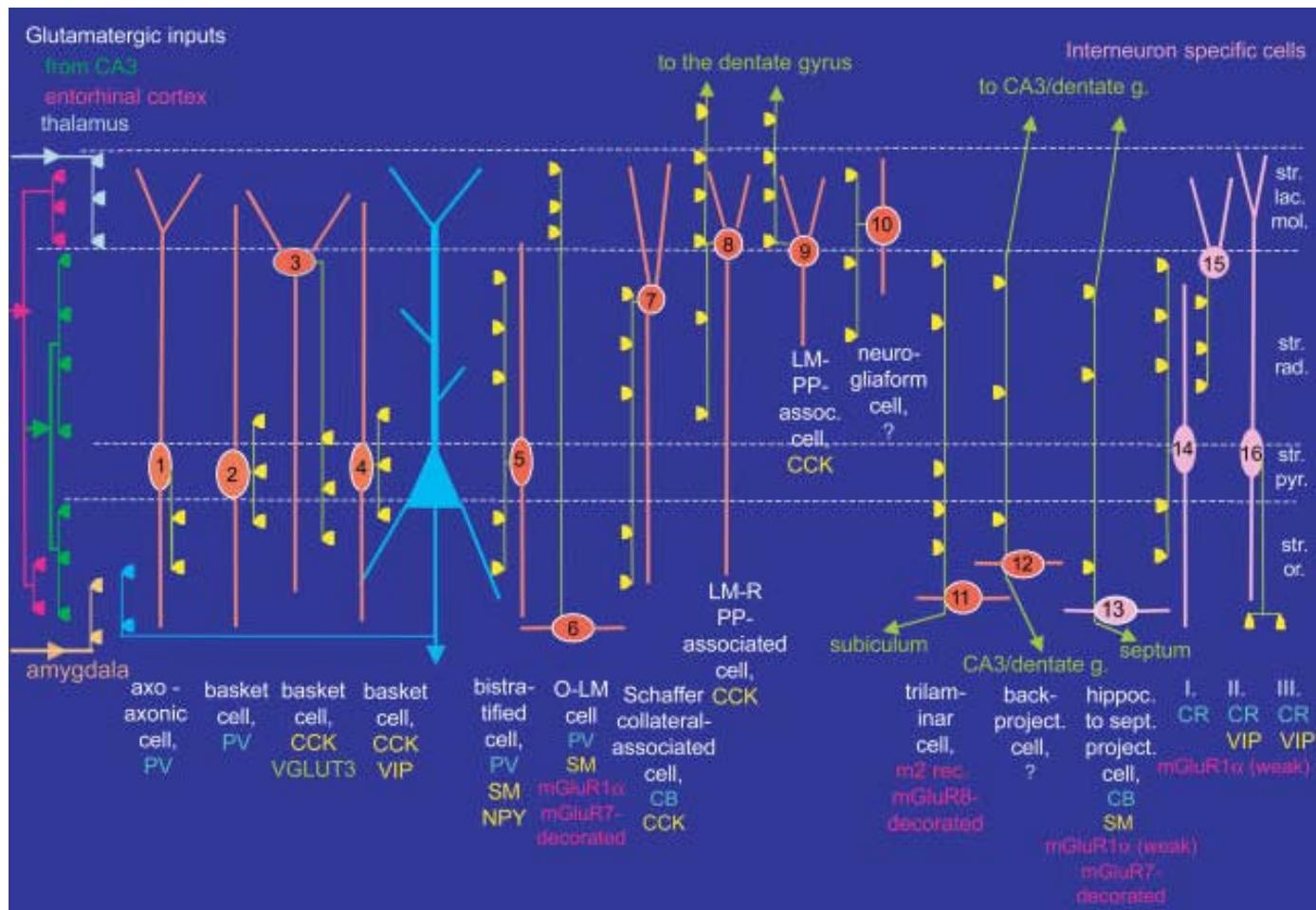
Kings College London, U.K.

The Hippocampus



Freund and Buzsaki. 1996

Hippocampal CA1 Microcircuit

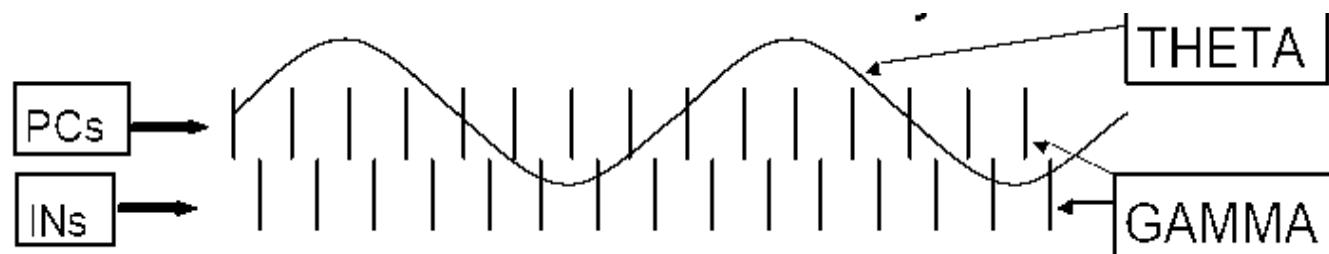


Functions of the Microcircuit

- Rhythm generation
 - temporal reference signals
 - synchronisation of PC activity
- Controlling plasticity
 - storage (learning) and recall modes
 - spatial and temporal control of internal PC signals
 - BPAPs and calcium spikes
- Threshold setting for PC output
 - recall mode
 - general control of network excitability

Dynamics of Operation

- Gamma rhythm (30-80Hz)
 - Circuit dynamics of feedback inhibition leads to rhythmic firing of PCs and INs
- Theta rhythm (4-8Hz)
 - External inhibitory and modulatory input causes coincident slower rhythm

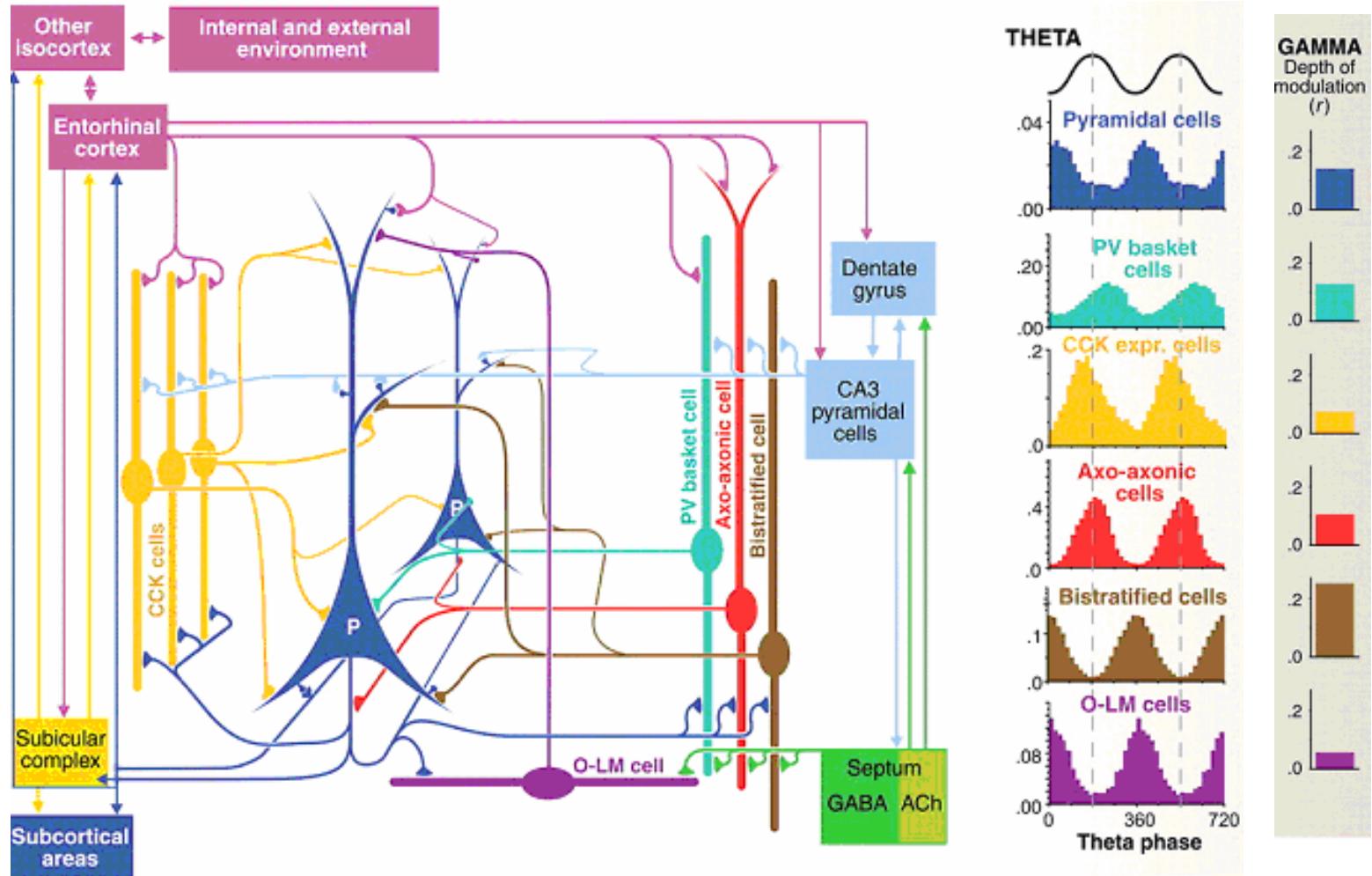


adapted from Graham, 2003

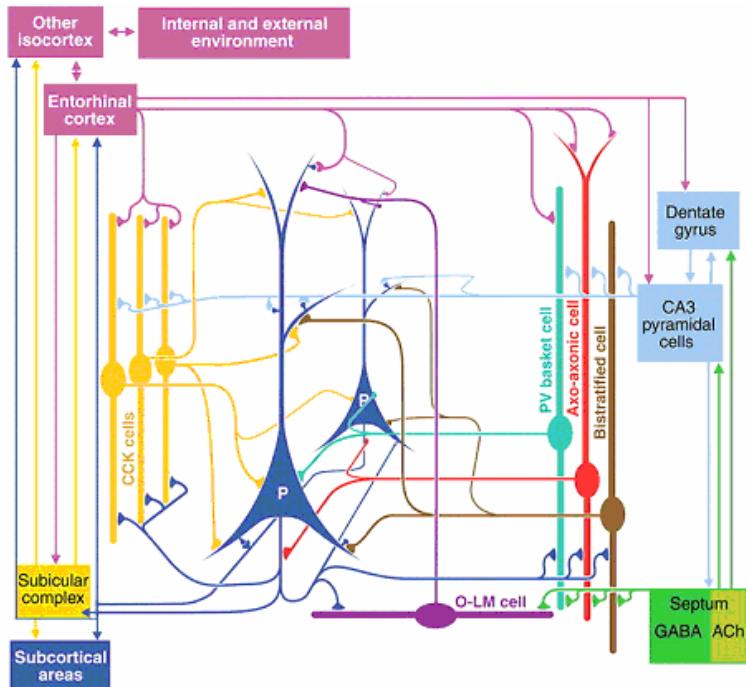
Roles of Rhythms

- Gamma rhythm (30-80Hz)
 - Internal clock
 - Memory pattern is active PCs on a gamma cycle
 - Recall takes place at gamma frequency
- Theta rhythm (4-8Hz)
 - Phase storage and recall
 - Recall compressed to a theta cycle

In Vivo Firing Patterns

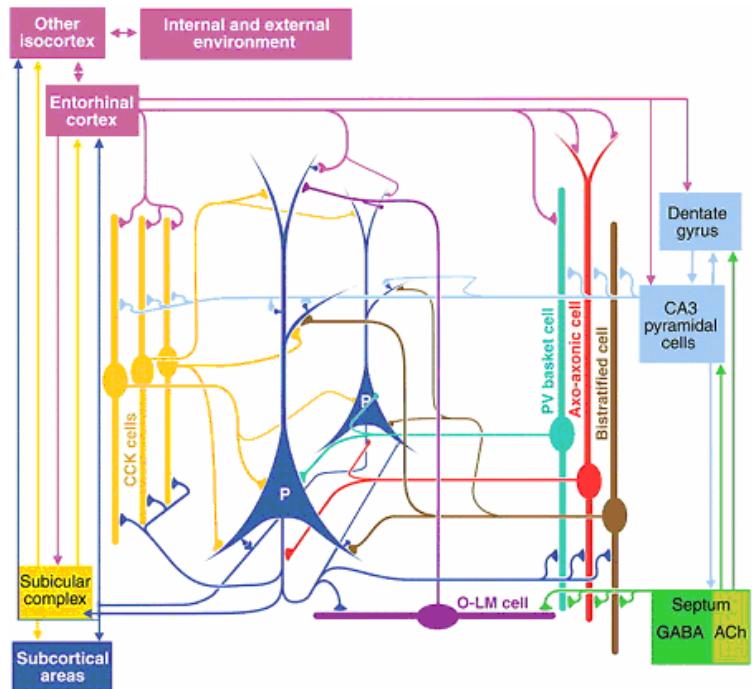


Medial septum

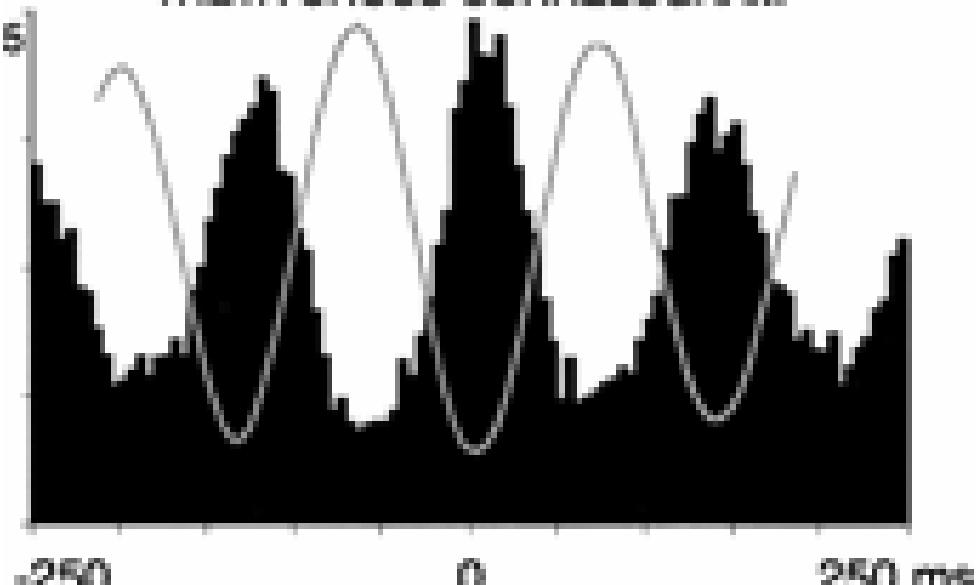


Klausberger, & Somogyi , Science, 2008

Medial septum



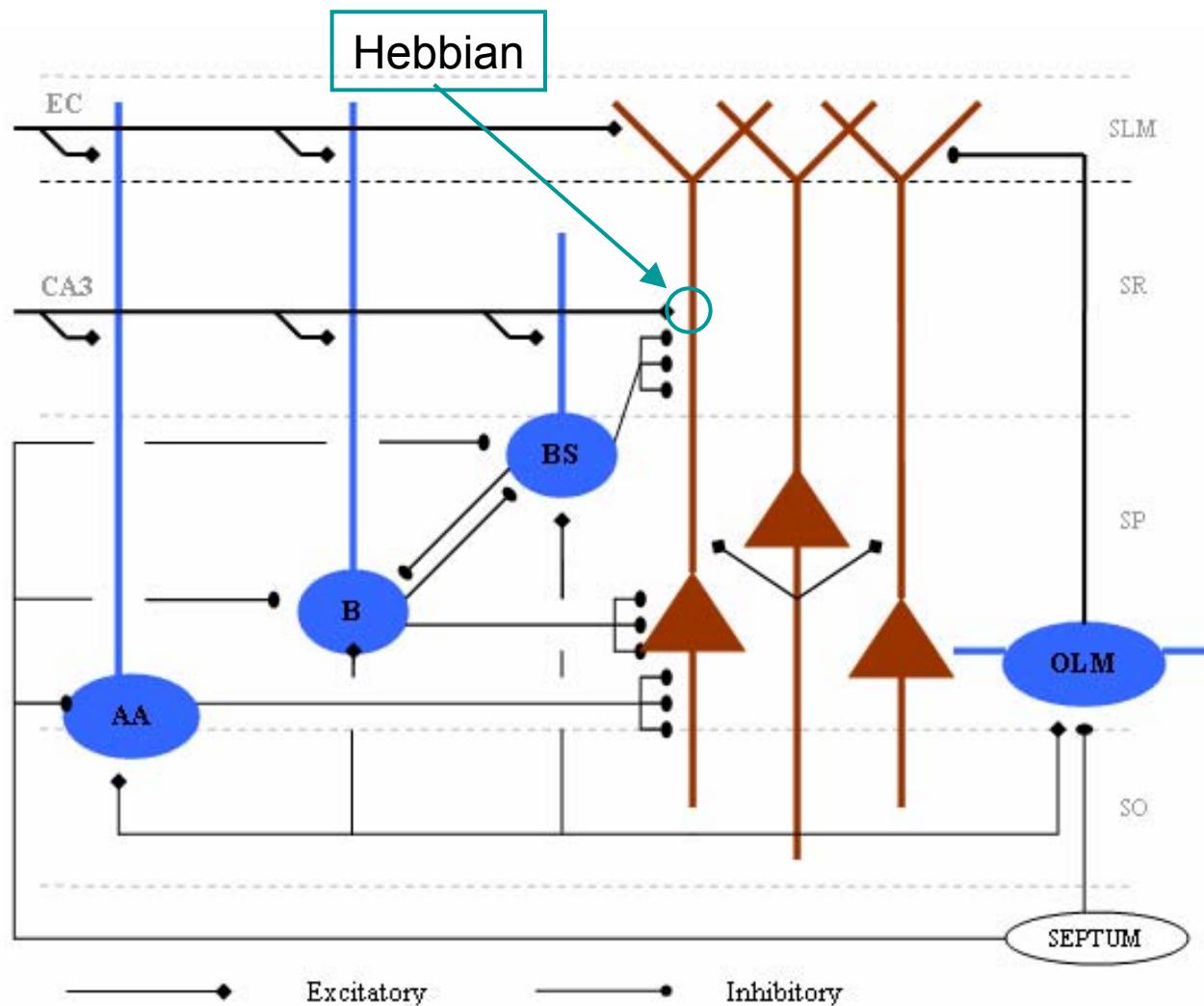
THETA CROSS-CORRELOGRAM



Klausberger, & Somogyi , Science, 2008

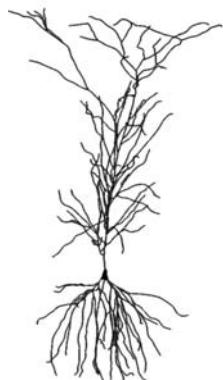
Dragoi et al. J. Neurosci 1999

The Model



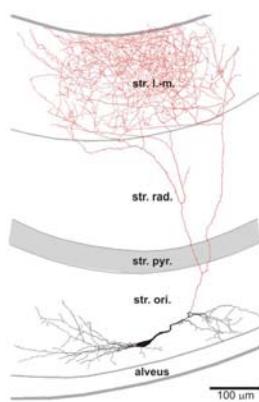
Model Neurons

CA1 pyramidal cell

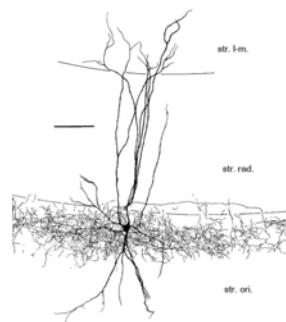


Front

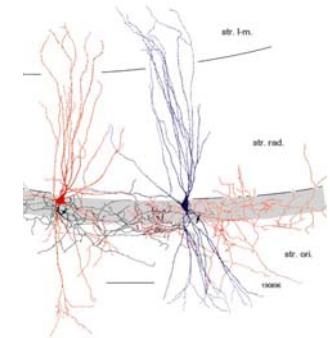
OLM cell



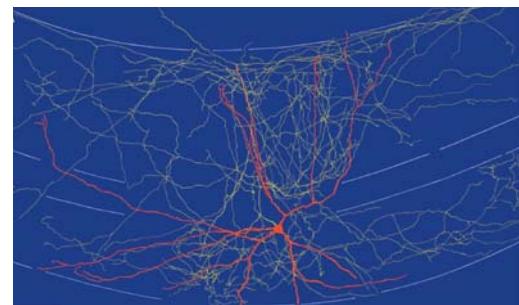
Axoaxonic cell



Basket cells

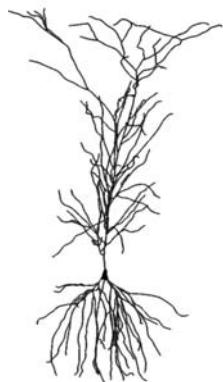


Bistratified cell

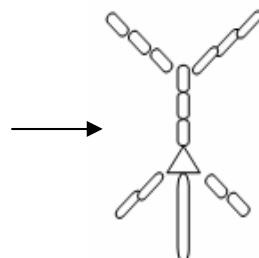


Model Neurons

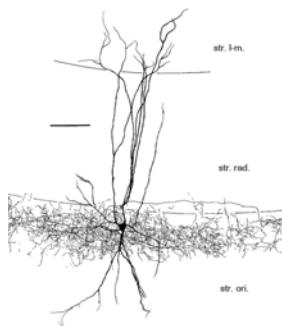
CA1 pyramidal cell



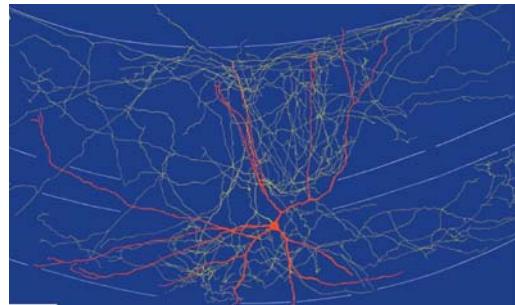
Front



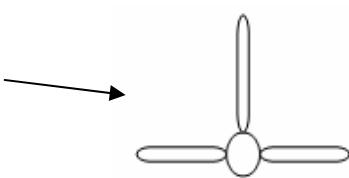
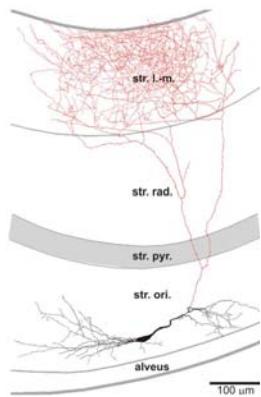
Axoaxonic cell



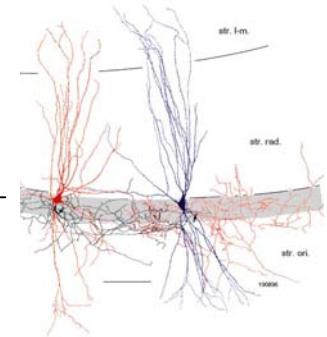
Bistratified cell



OLM cell



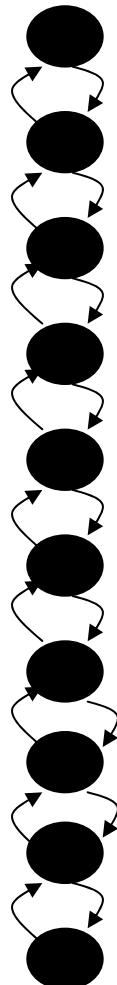
Basket cells



Ionic Properties

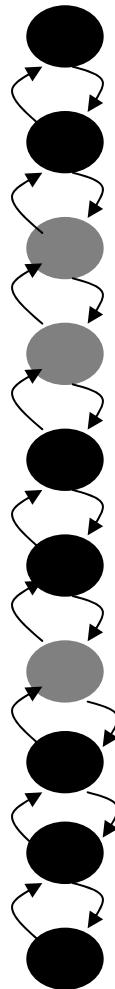
- **Pyramidal cells (Poirazi et al, (2003) *Neuron*)**
 - Calcium pump and buffering mechanism
 - Calcium activated mAHP potassium current
 - LVA L-type Ca^{2+} current
 - HVA L-type Ca^{2+} current
 - MVA R-type Ca^{2+} current
 - HVA T-type Ca^{2+} current
 - h current
 - HH current that includes both a sodium and a delayed rectifier current
 - Slow Ca^{2+} - dependent potassium current
 - Slow non-inactivating potassium channel with HH style kinetics
 - K^+ A current
 - Leak current
- **Basket, Axoaxonic and Bistratified cells (Santhakumar et al, (2005) *J Neurophysiol*)**
 - Leak current
 - Sodium current
 - Fast delayed rectifier K^+ current
 - A-type K^+ current
 - L- and N-type Ca^{2+} currents
 - Ca^{2+} -dependent K^+ current
 - Ca^{2+} - and voltage-dependent K^+ current
- **OLM cells (Saraga et al. (2003) *J Physiol*)**
 - Sodium (Na^+) current
 - Delayed rectifier K^+ current
 - A-type K^+ current
 - h-current

Model Inputs



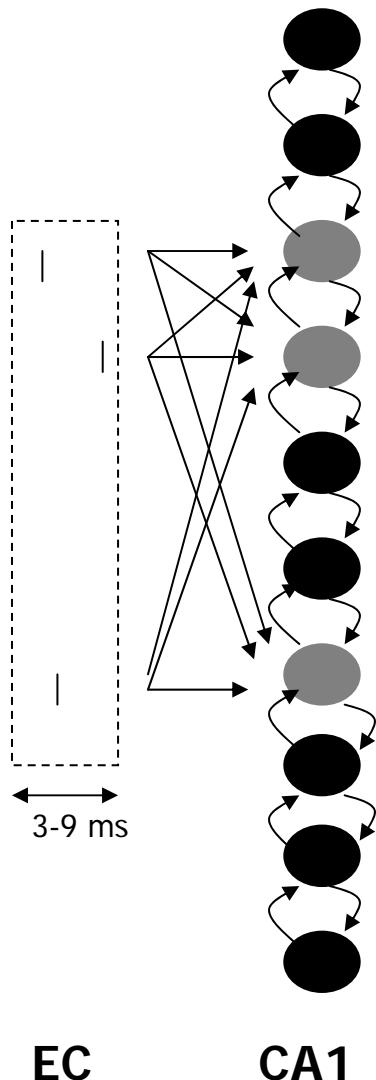
CA1

Model Inputs

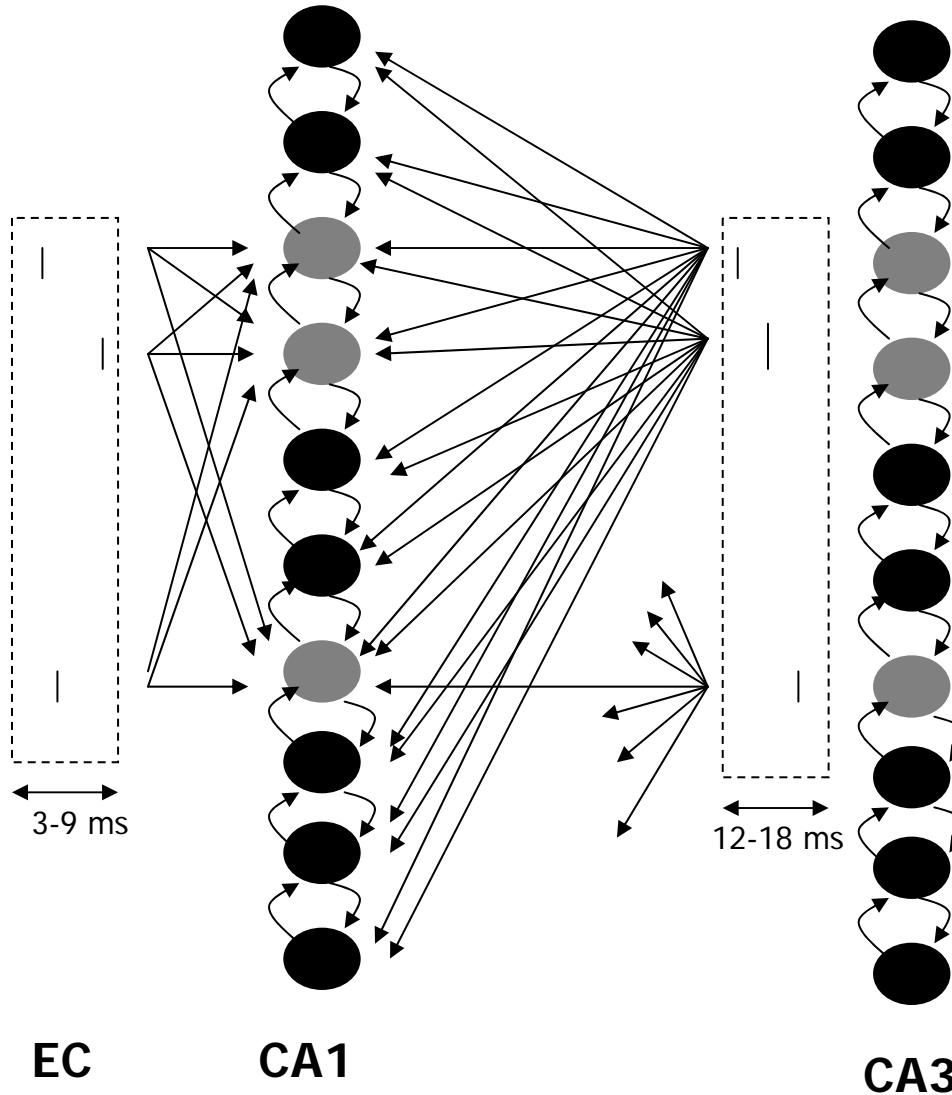


CA1

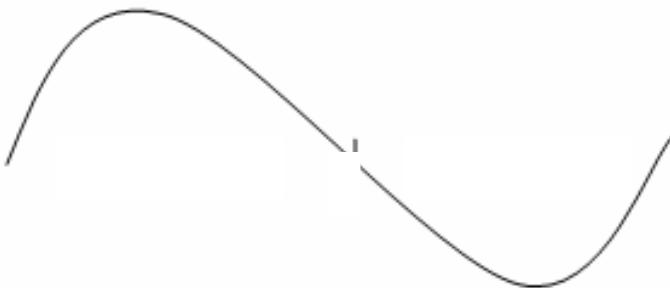
Model Inputs



Model Inputs

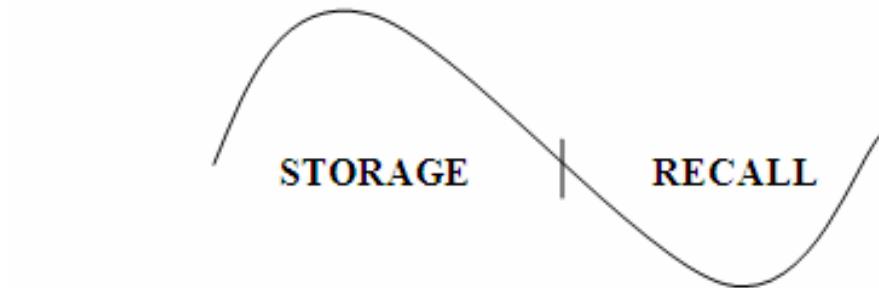


Input presentation

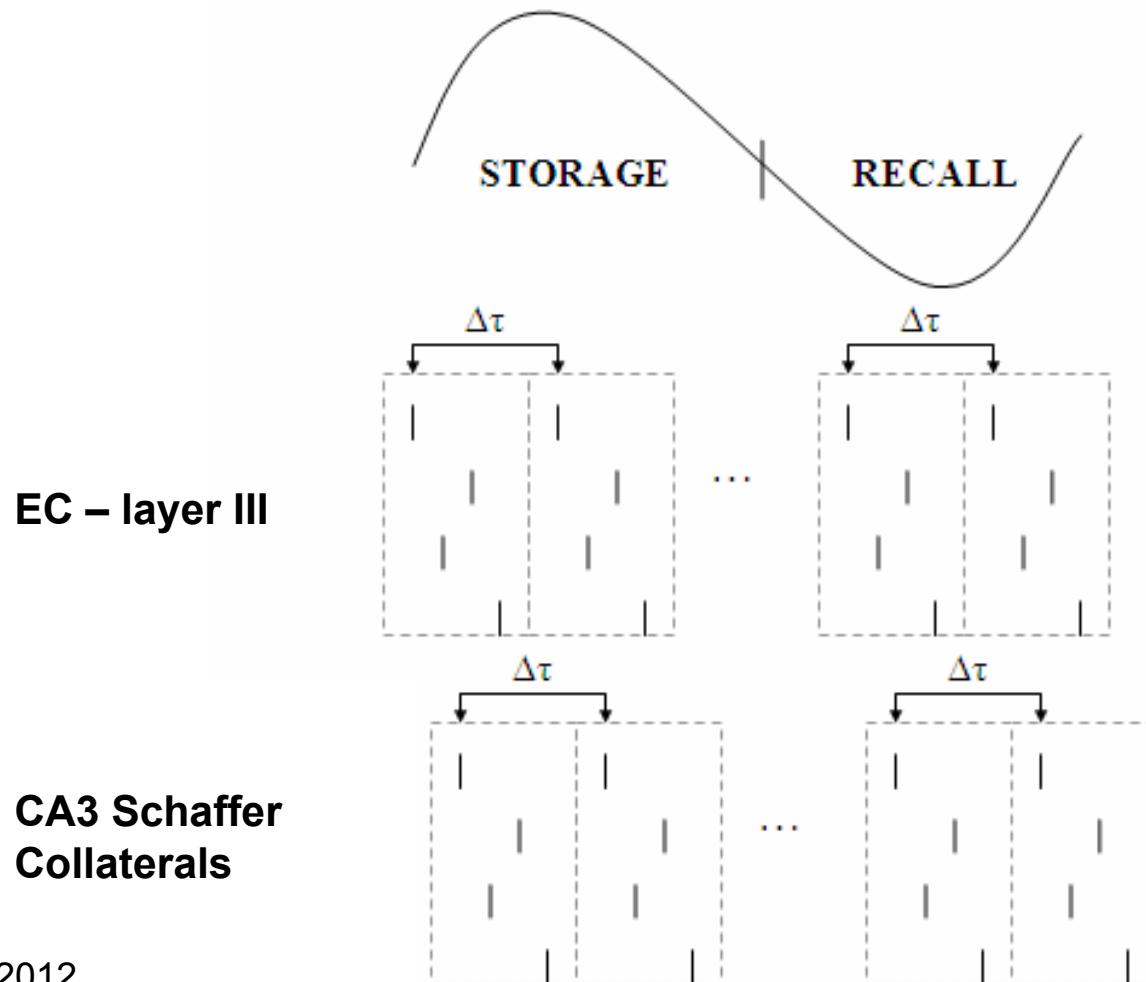


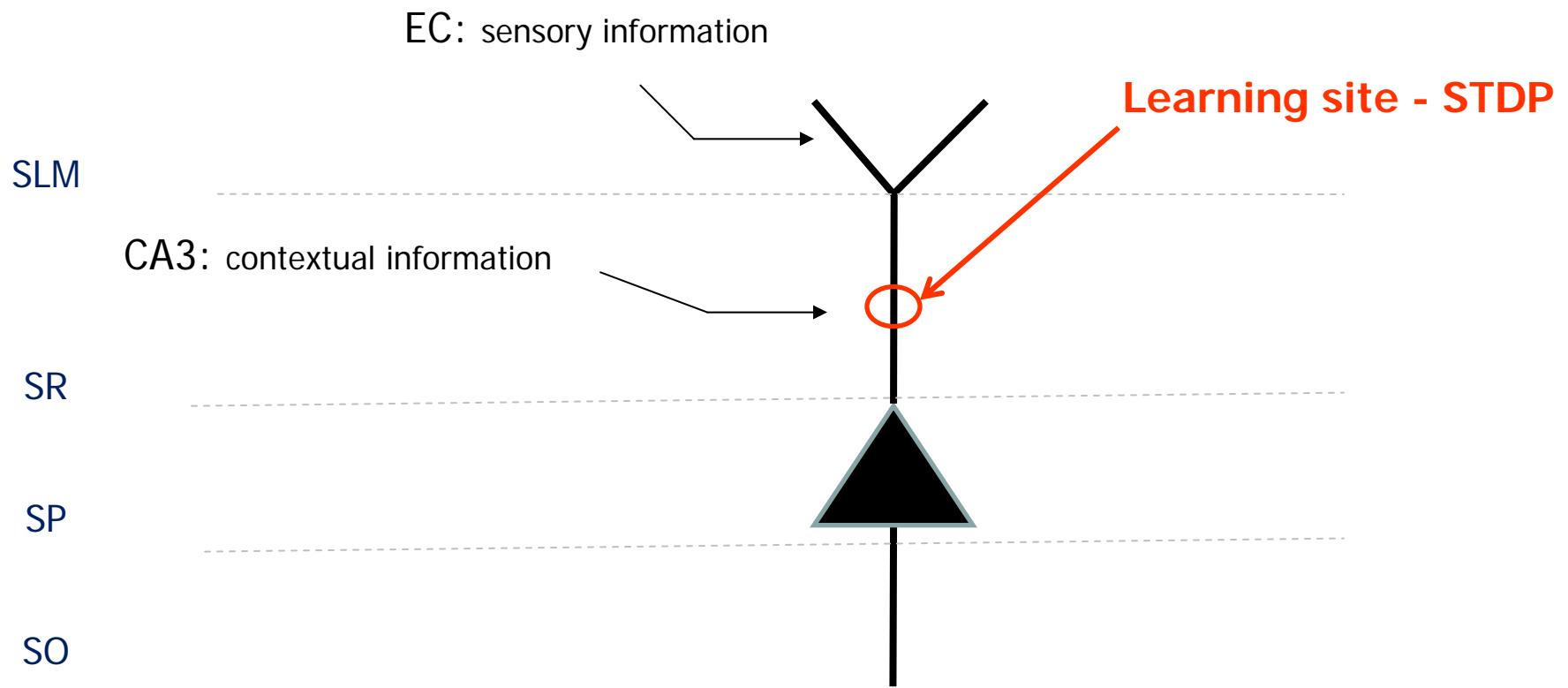
Paulsen & Moser, 1998;
Hasselmo et al., 2002

Input presentation



Input presentation



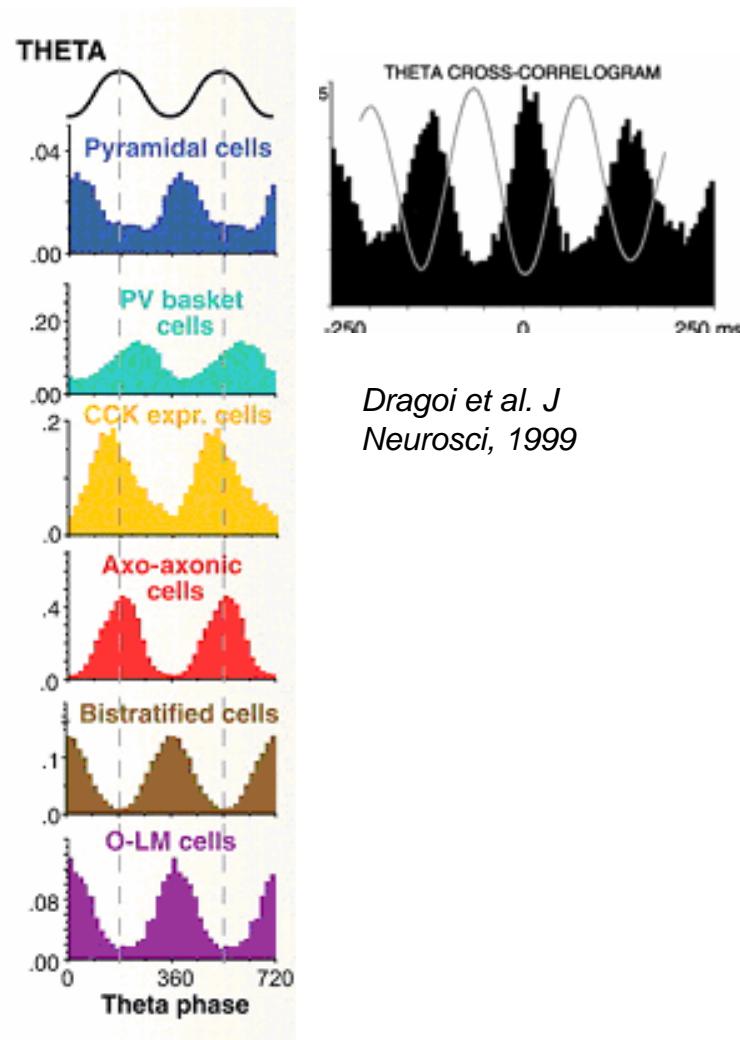
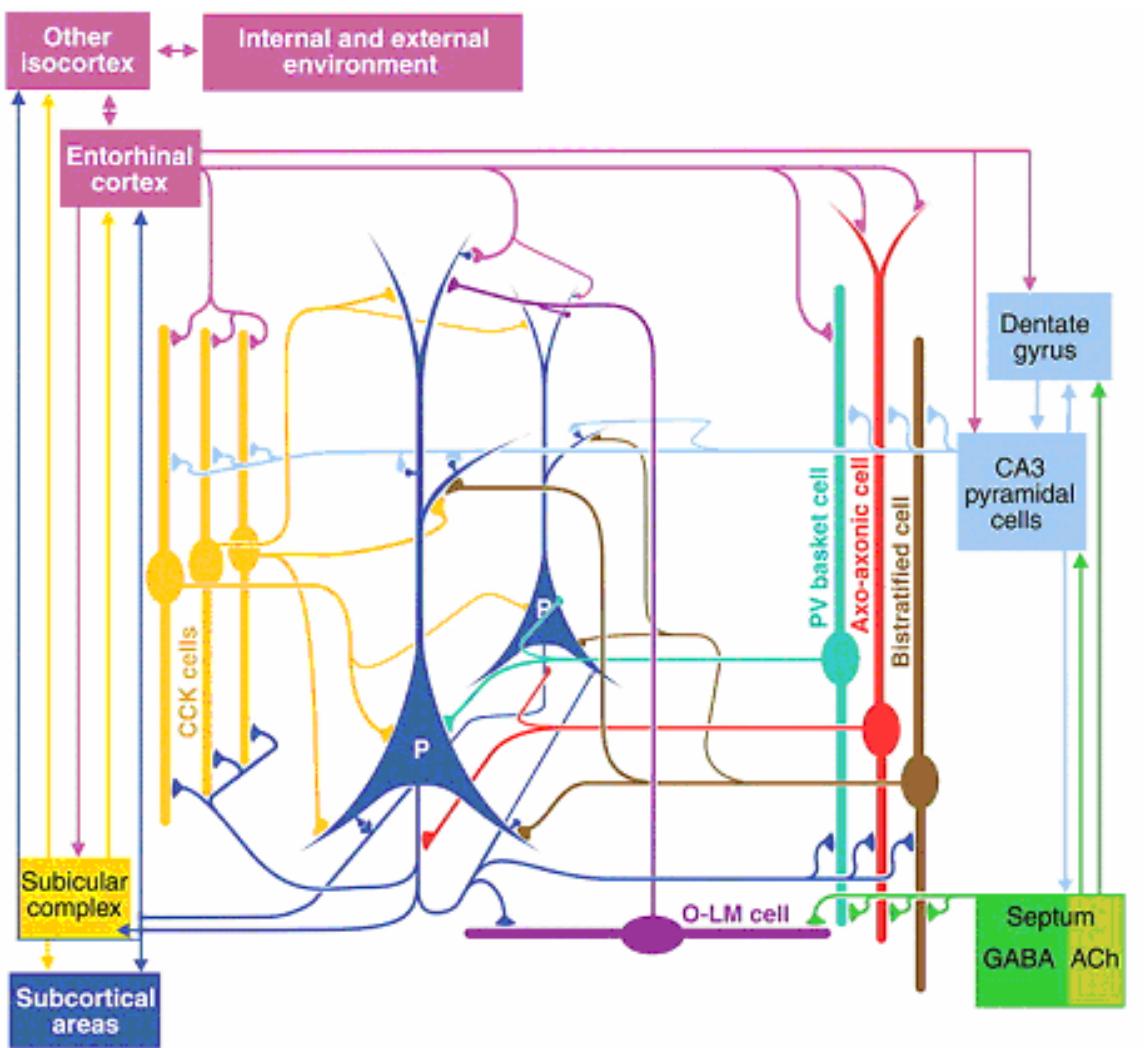


Model STDP Rule

$$g = g + w \cdot (1 + A)$$

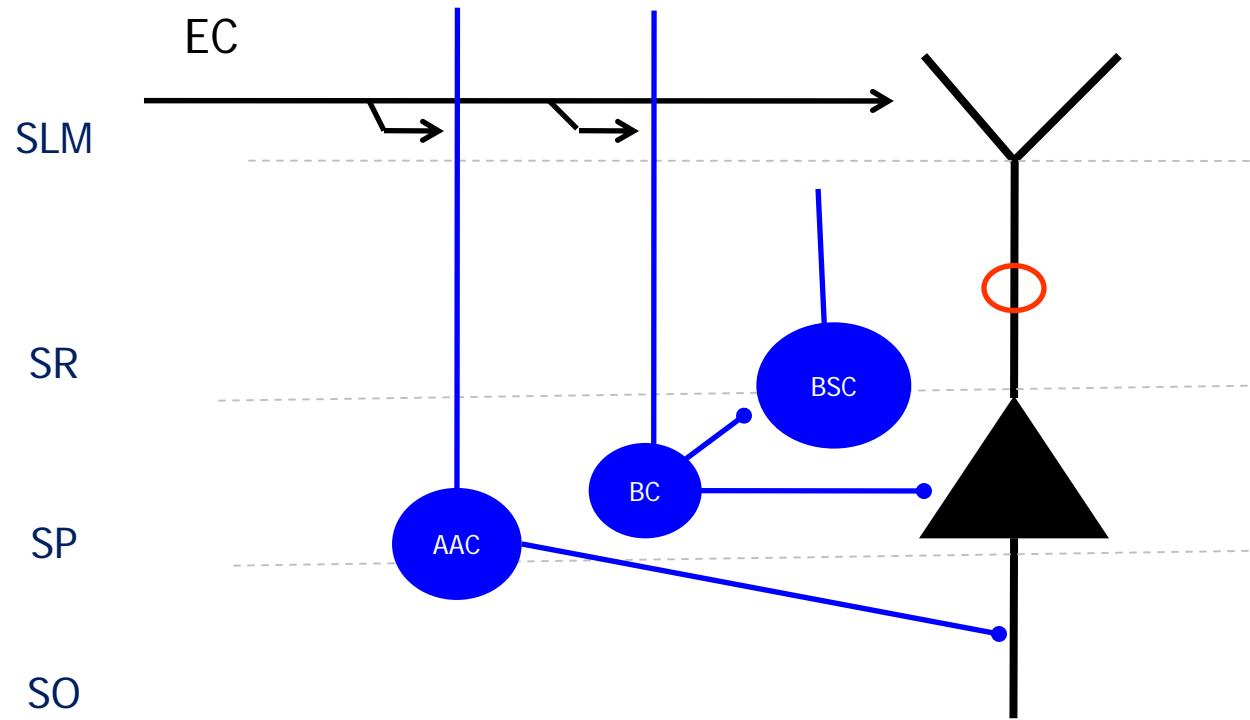
$$A = p \cdot e^{\frac{\Delta t}{\tau_p}} \quad \text{if} \quad \Delta t = t_{post} - t_{pre} \geq 0$$

$$A = A \cdot (1 - \alpha \cdot e^{\frac{\Delta t}{\tau_d}}) \quad \text{if} \quad \Delta t = t_{post} - t_{pre} < 0$$



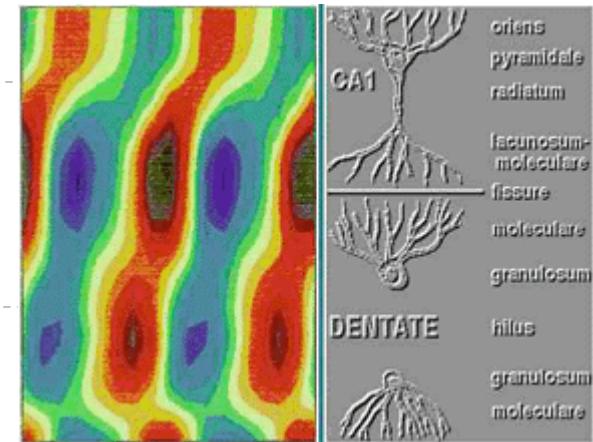
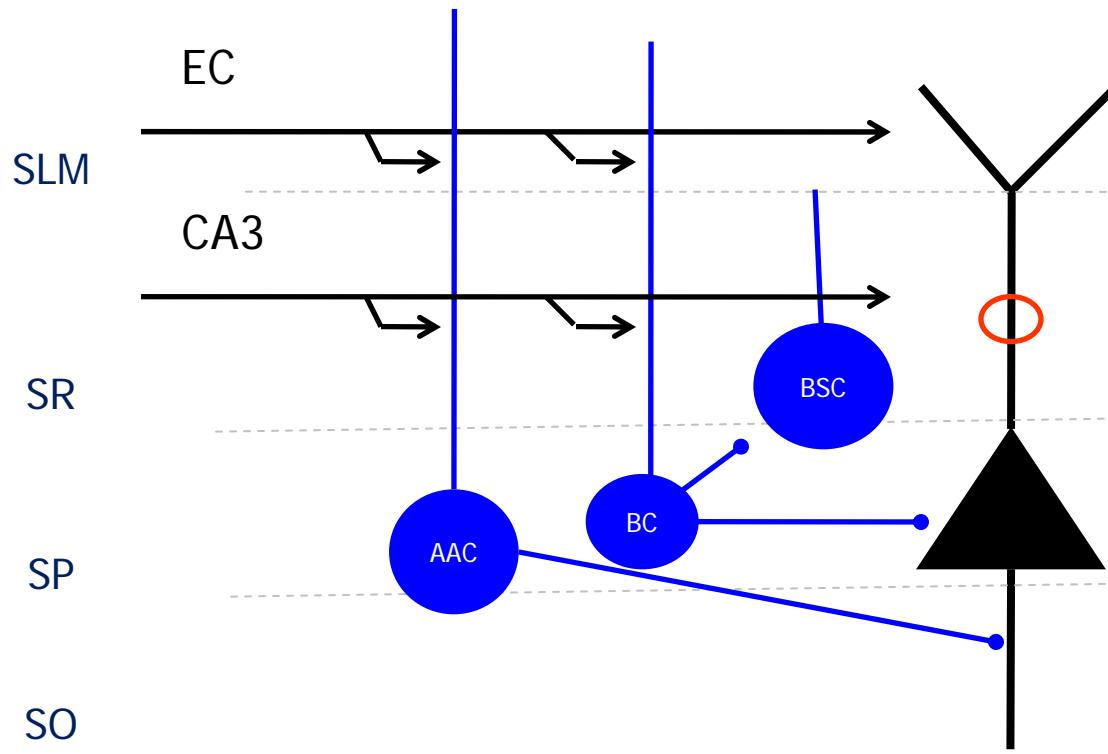
Klausberger, & Somogyi , Science, 2008

Storage cycle (first half-cycle of theta)



BC Basket cell AAC Axo-axonic cell BSC Bistratified cell Pyramidal cell

Storage cycle (first half-cycle of theta)



Brankack J, Stewart M, Fox S. Current source density analysis of the hippocampal theta rhythm: associated sustained potentials and candidate synaptic generators. *Brain Res* 310–327, 1993.



Basket cell



AAC

Axo-axonic cell



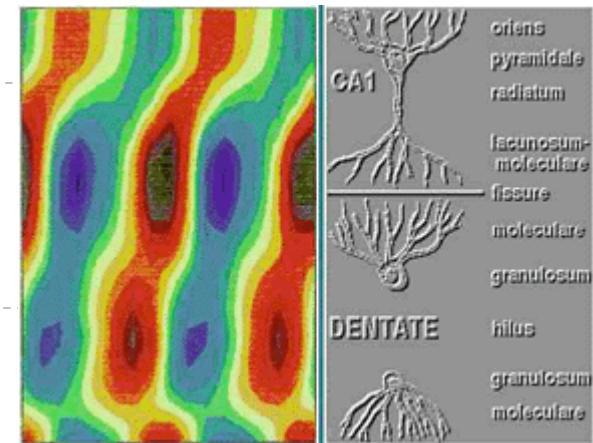
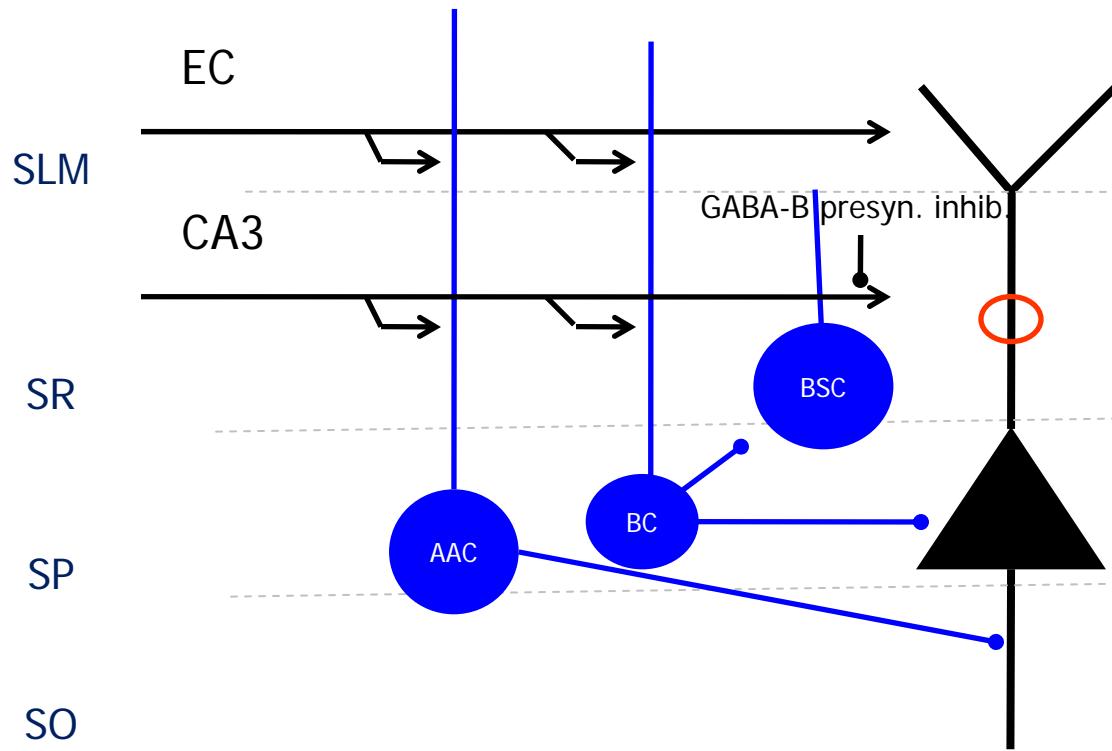
BSC

Bistratified cell



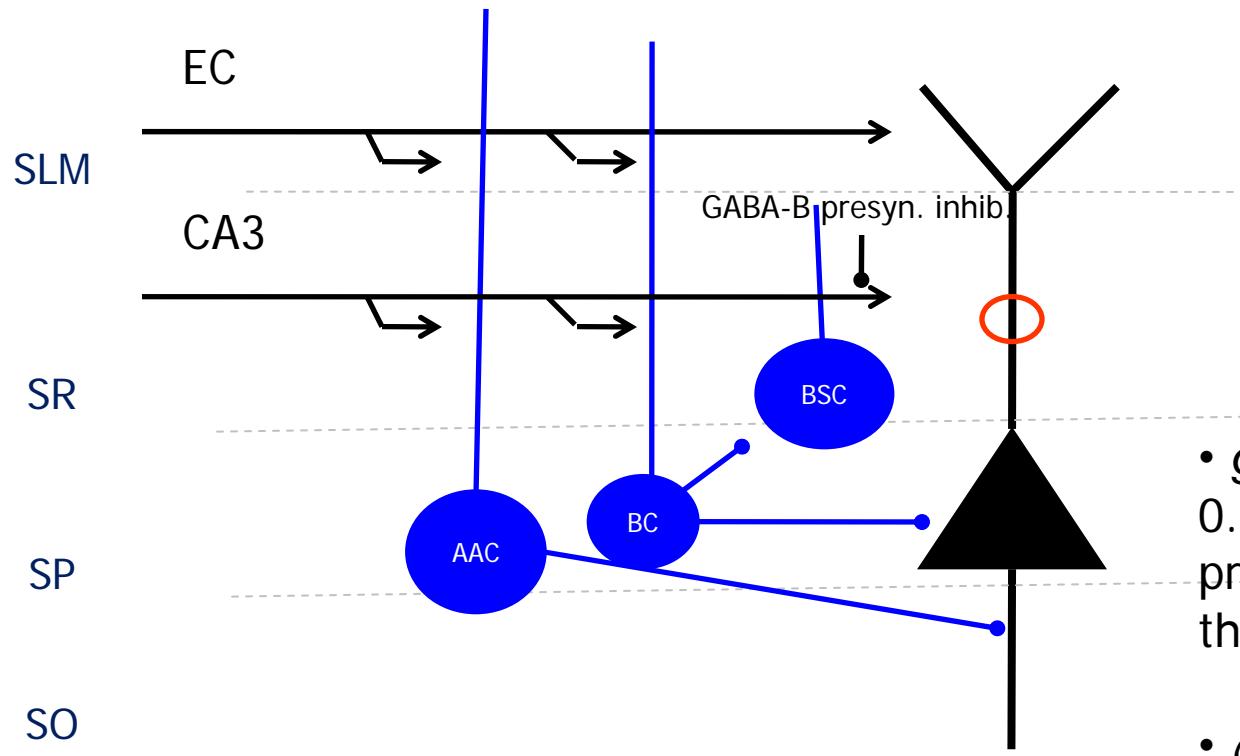
Pyramidal cell

Storage cycle (first half-cycle of theta)



Brankack J, Stewart M, Fox S. Current source density analysis of the hippocampal theta rhythm: associated sustained potentials and candidate synaptic generators. *Brain Res* 310–327, 1993.





$$g' = g_s \cdot g$$

- g_s is a scaling factor (set to 0.4) representing the presynaptic GABA-B inhibition that is present during storage
- $g_s = 1$ during recall



BC
Basket cell



AAC
Axo-axonic cell

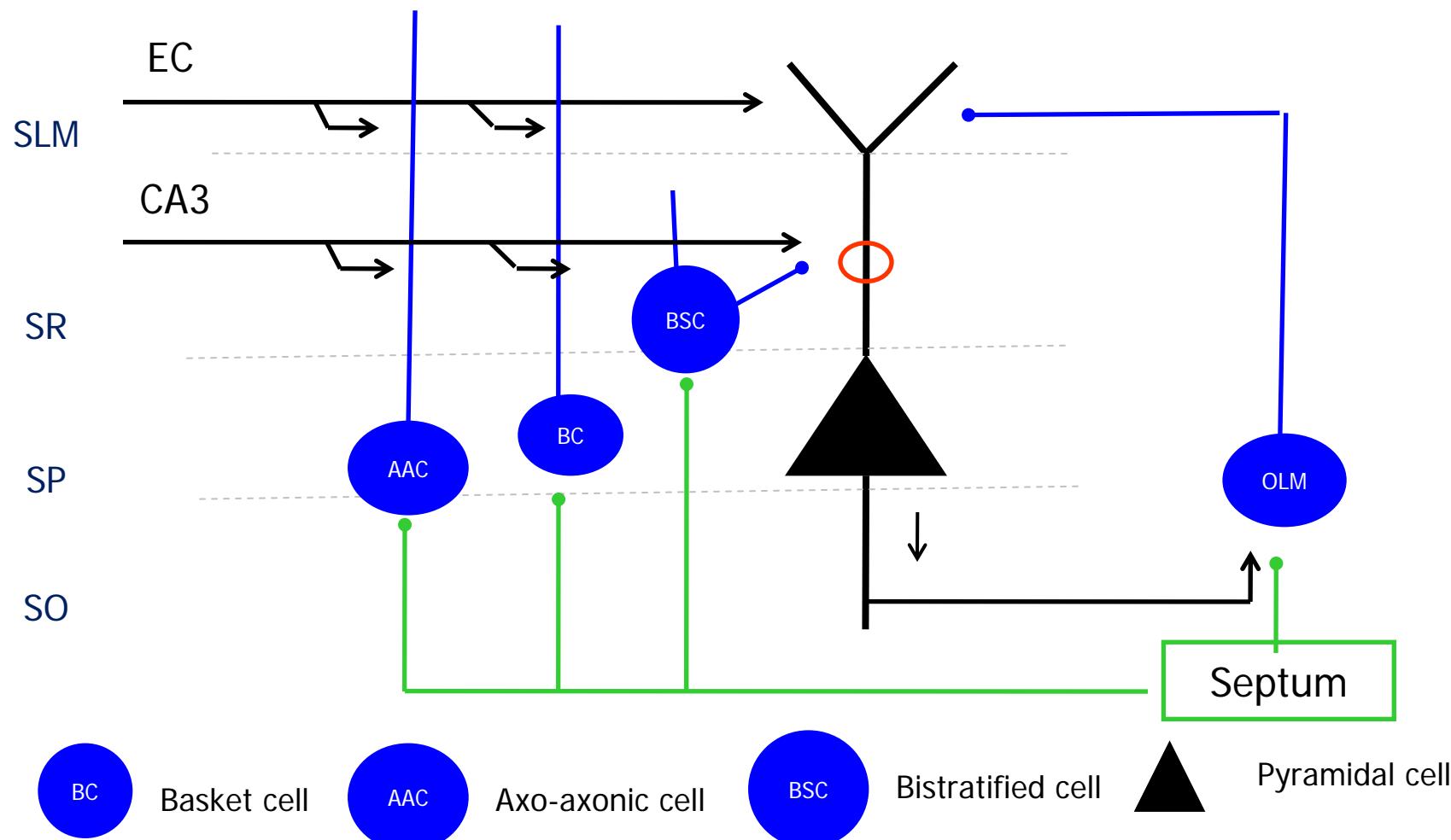


BSC
Bistratified cell

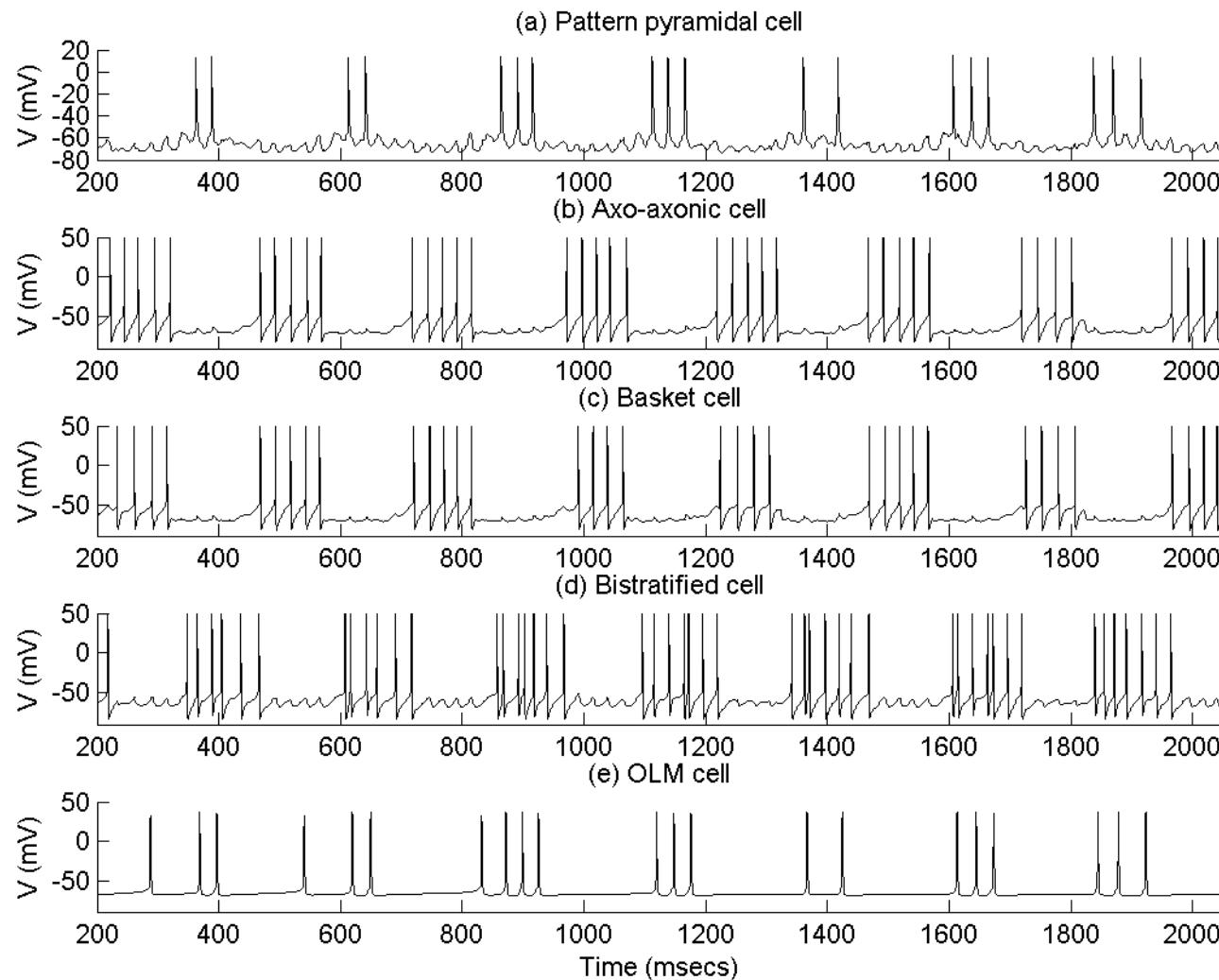


Pyramidal cell

Recall cycle (second half-cycle of theta)



Neuronal firing activities



Recall Performance Measure

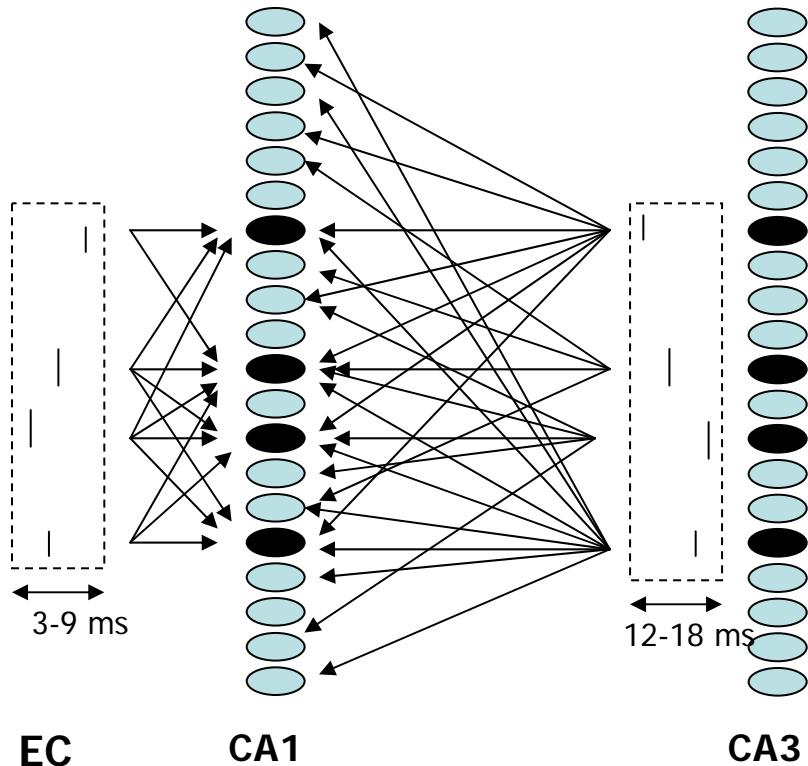
$$C = \frac{B \times B^*}{\left(\sum_{i=1}^{N_B} B_i \times \sum_{j=1}^{N_B} B_j^* \right)^{1/2}}$$

B: recalled output pattern

B*: desired output pattern

N_B: number of output units

Recall Performance Measure



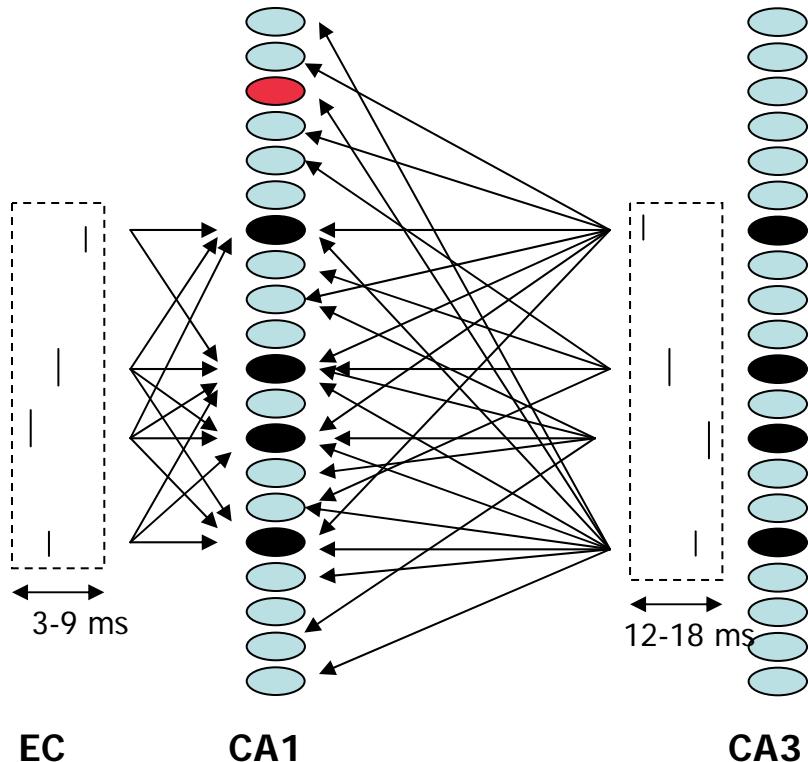
$$C = \frac{B \times B^*}{\left(\sum_{i=1}^{N_B} B_i \times \sum_{j=1}^{N_B} B_j^* \right)^{1/2}}$$

B: recalled output pattern

B*: desired output pattern

N_B: number of output units

Recall Performance Measure



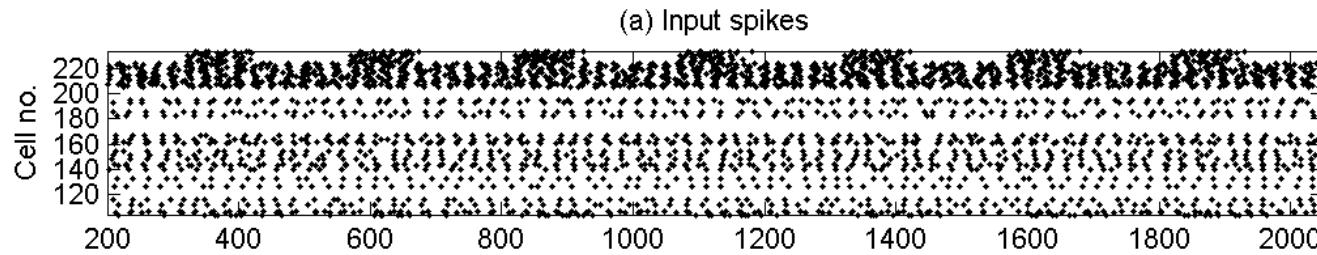
$$C = \frac{B \times B^*}{\left(\sum_{i=1}^{N_B} B_i \times \sum_{j=1}^{N_B} B_j^* \right)^{1/2}}$$

B: recalled output pattern

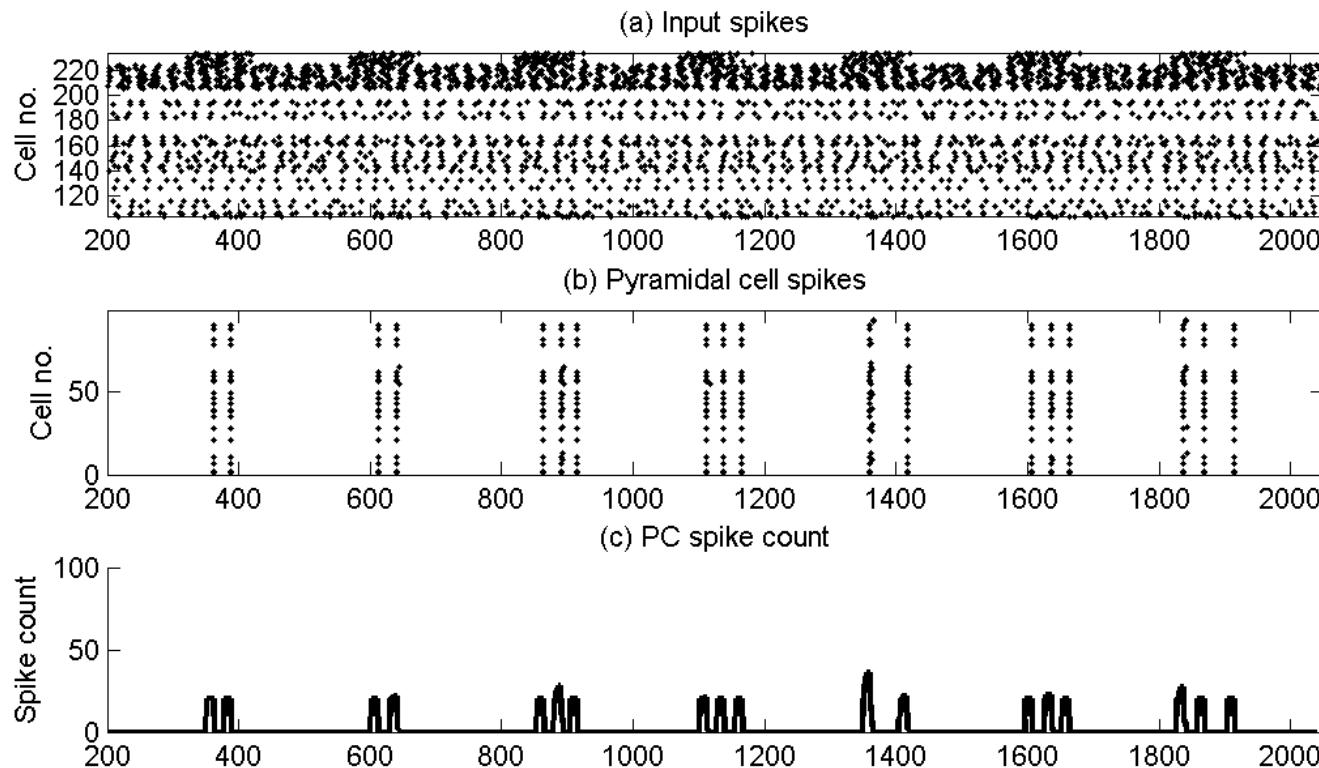
B*: desired output pattern

N_B: number of output units

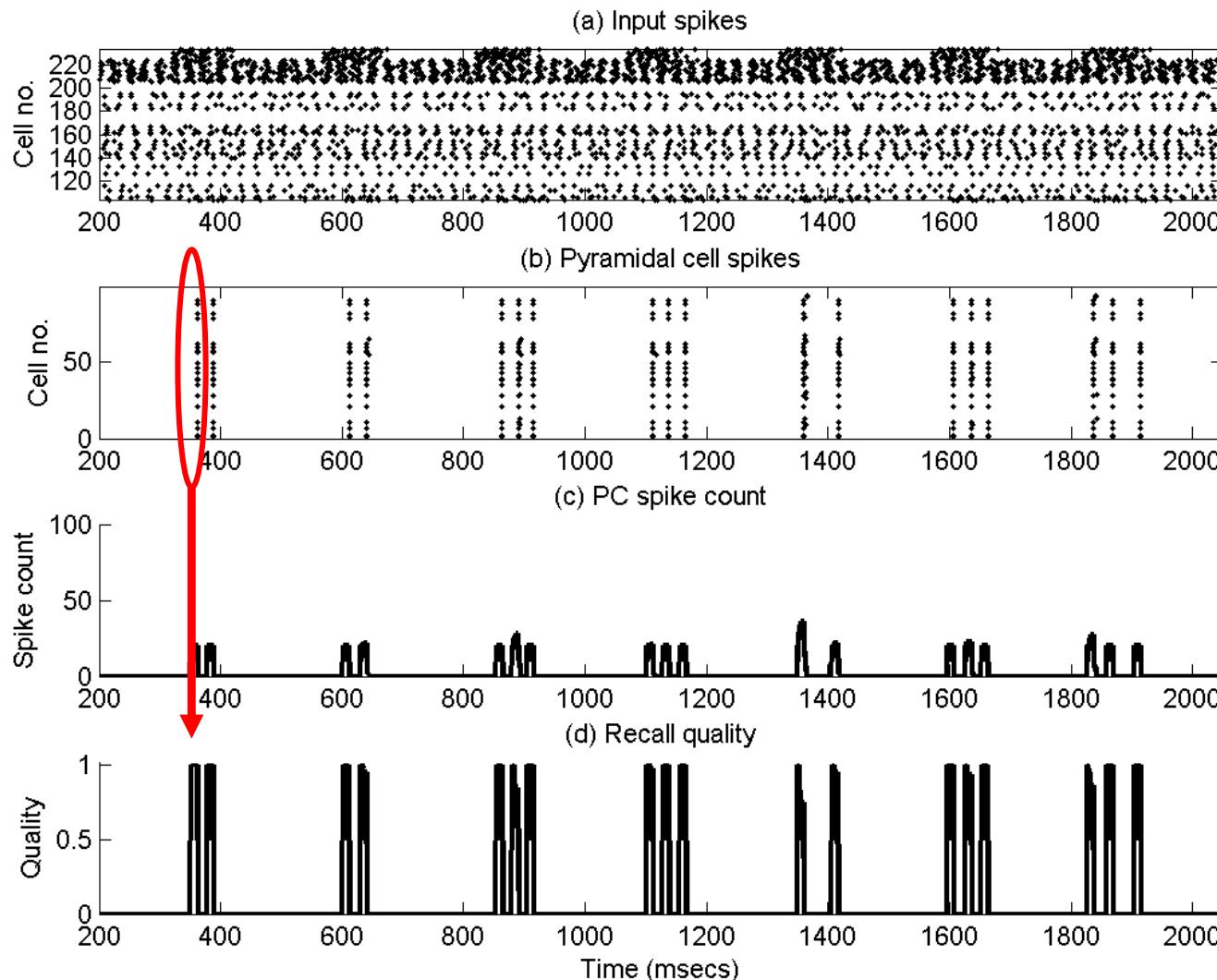
Recall performance



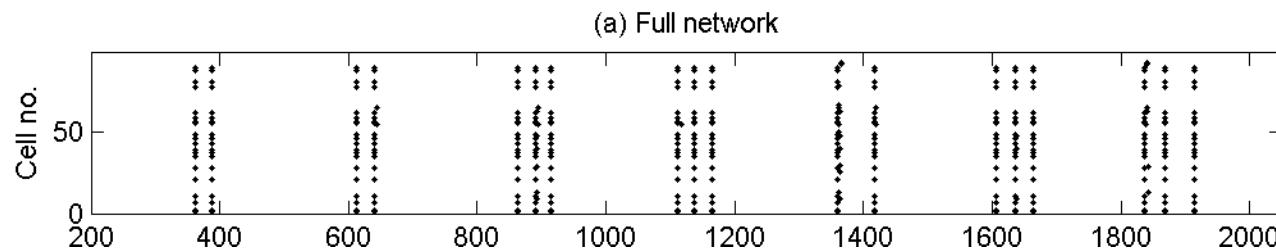
Recall performance (2)



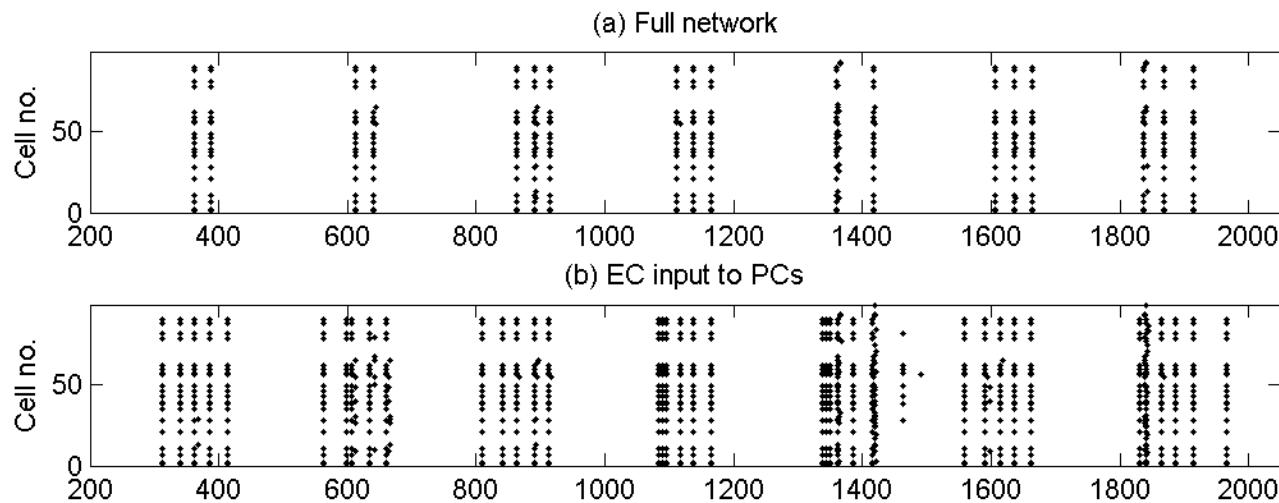
Recall performance (3)



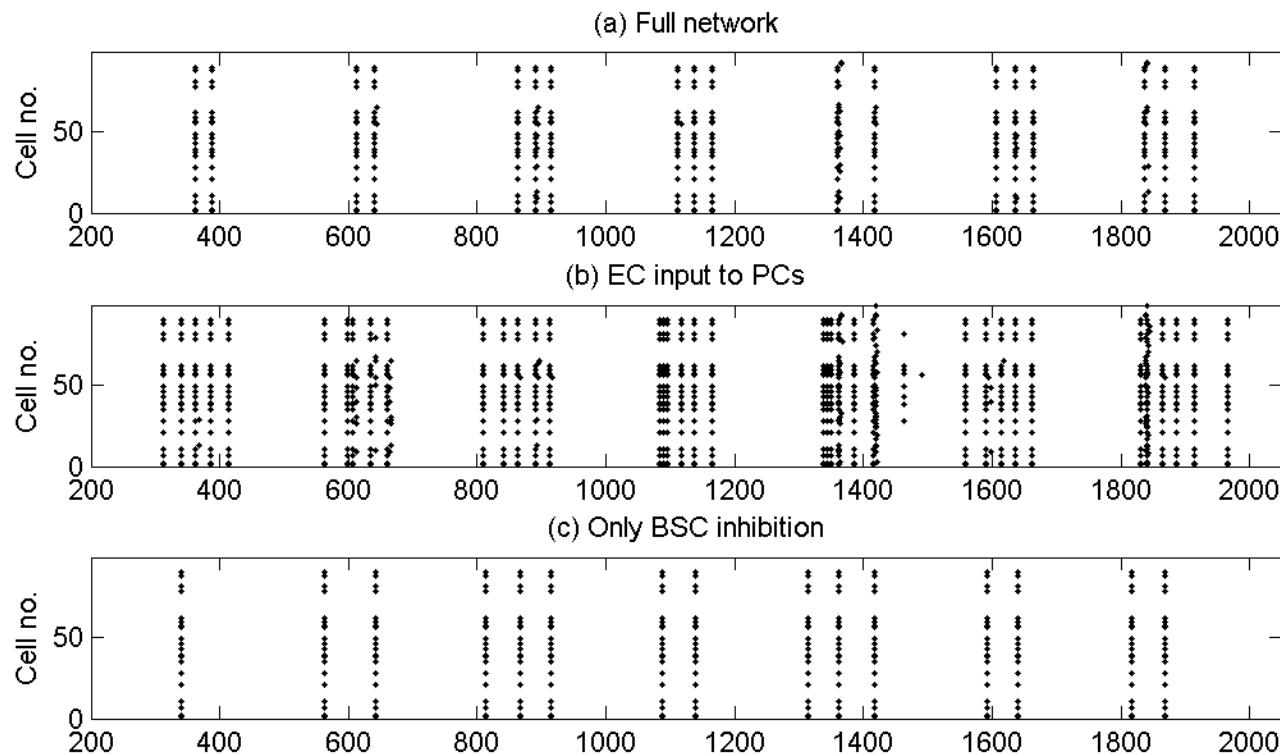
Recall performance (4)



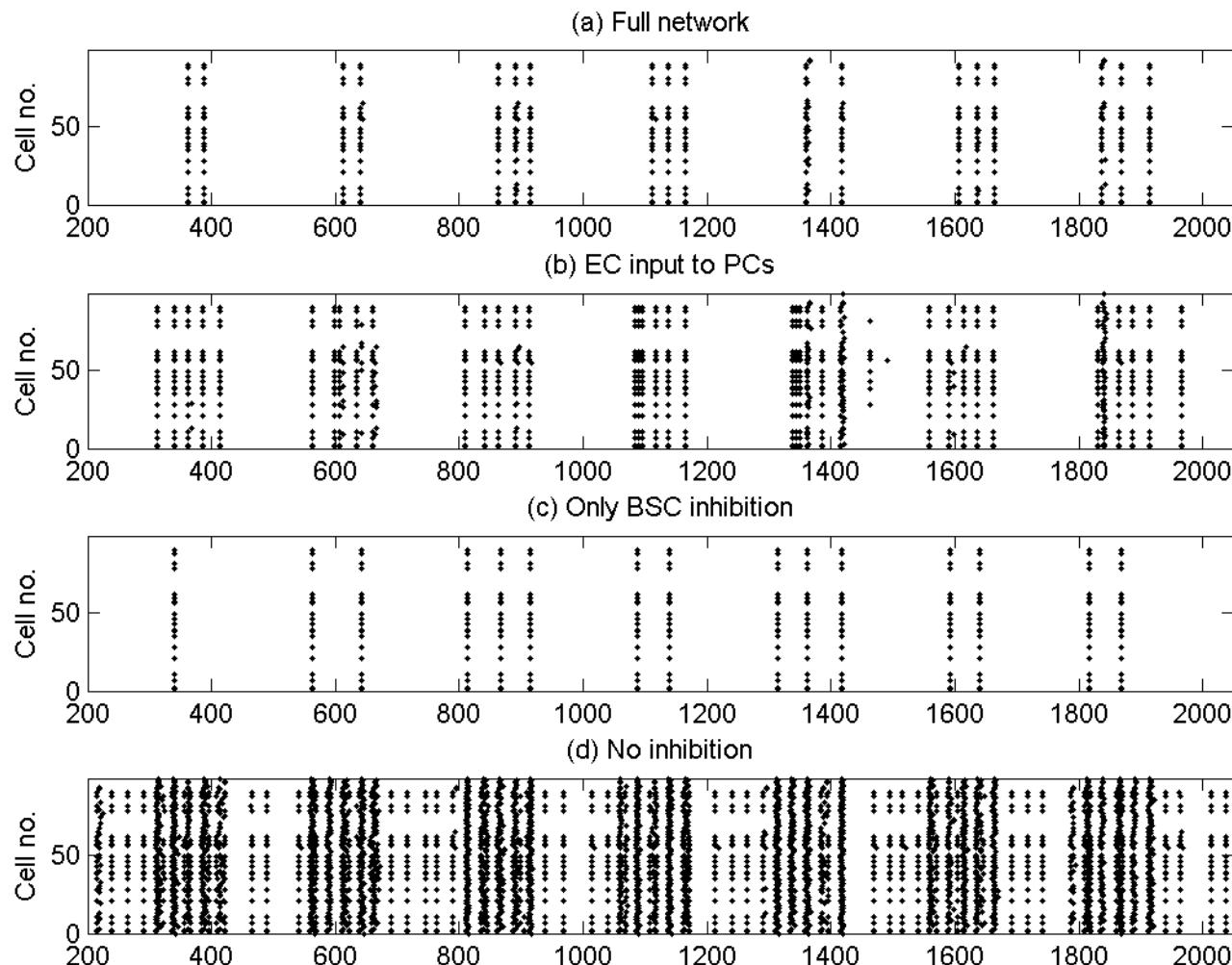
Recall performance (5)



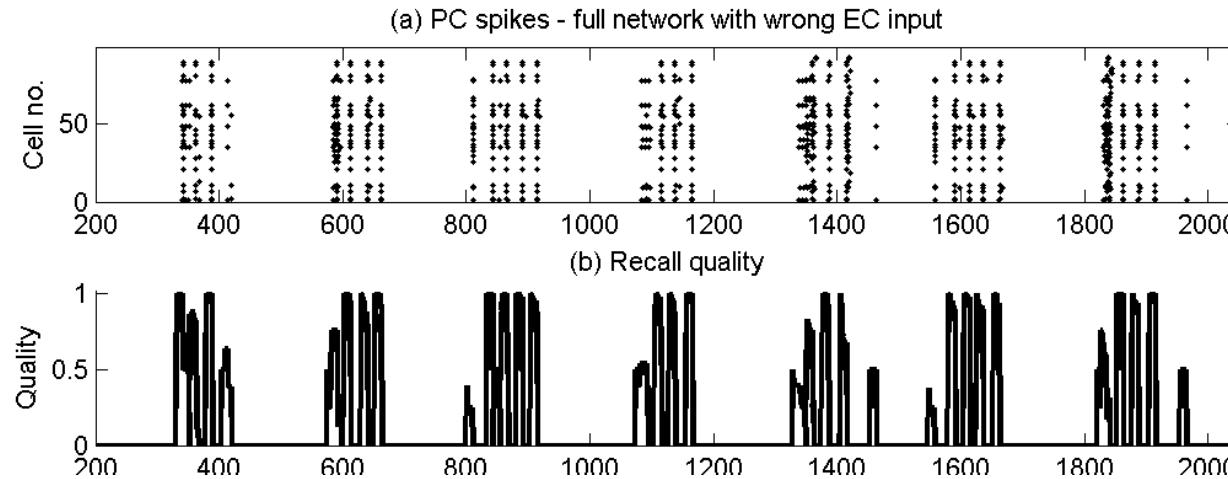
Recall performance (6)



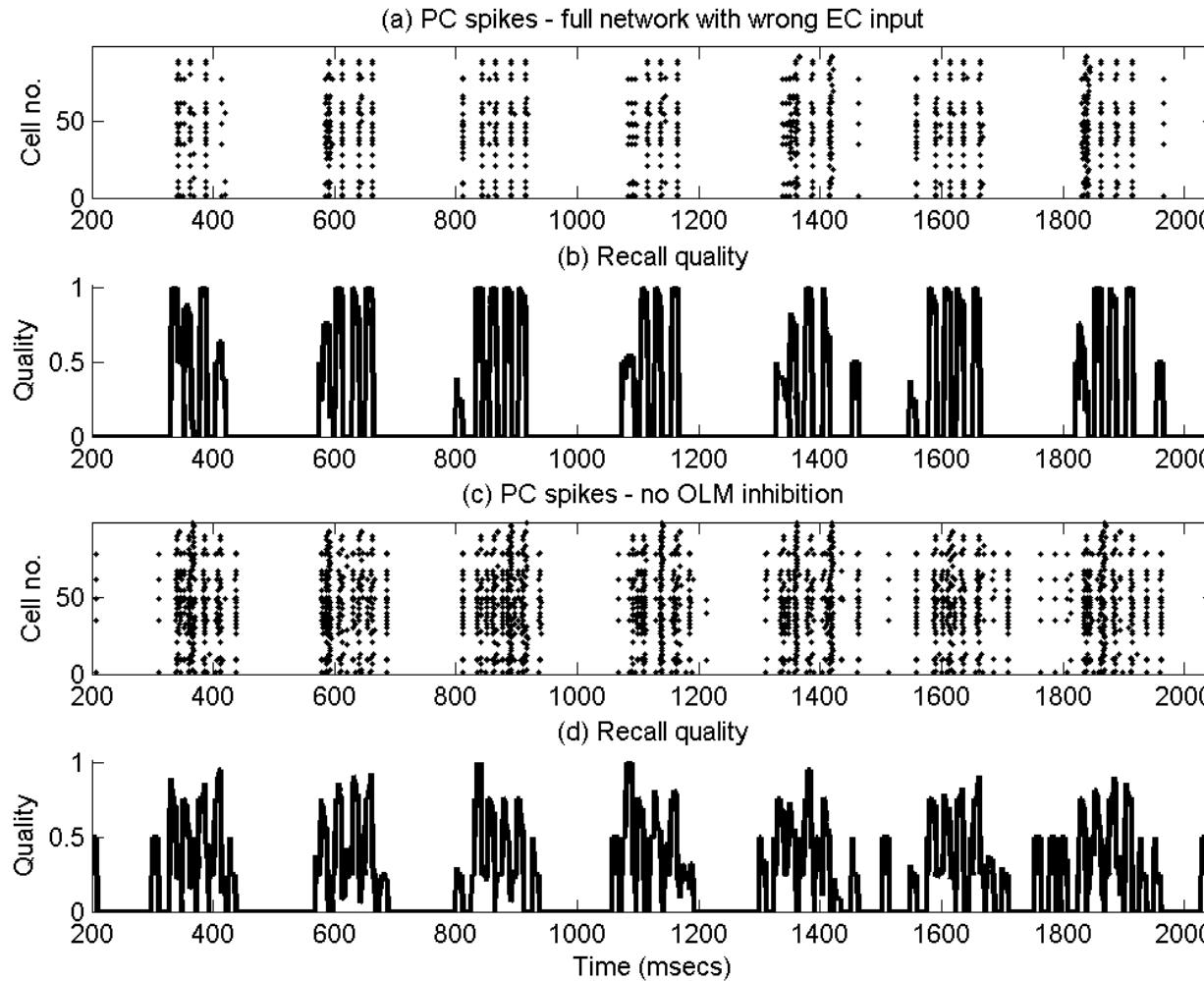
Recall performance (7)



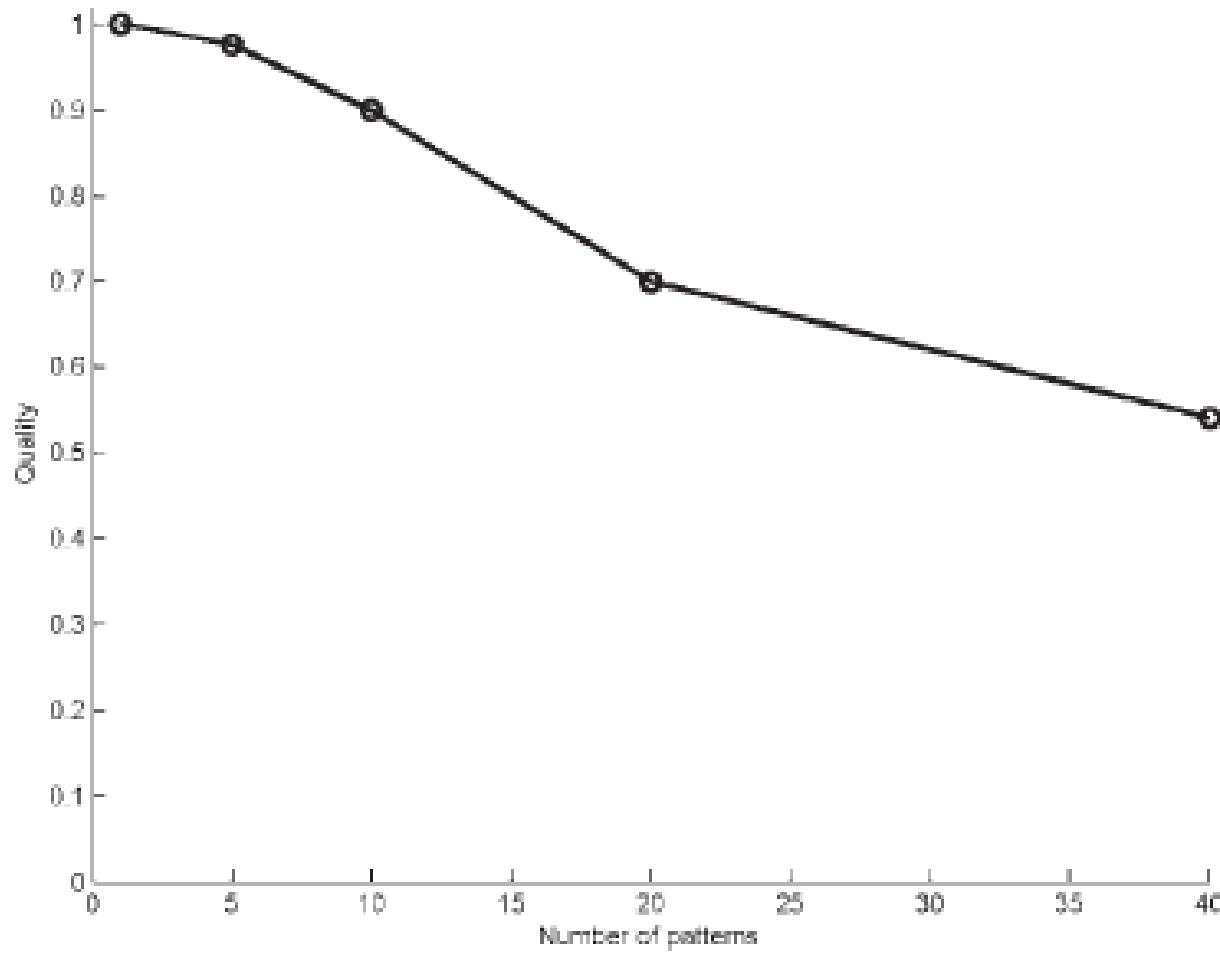
Recall performance (8)



Recall performance (9)

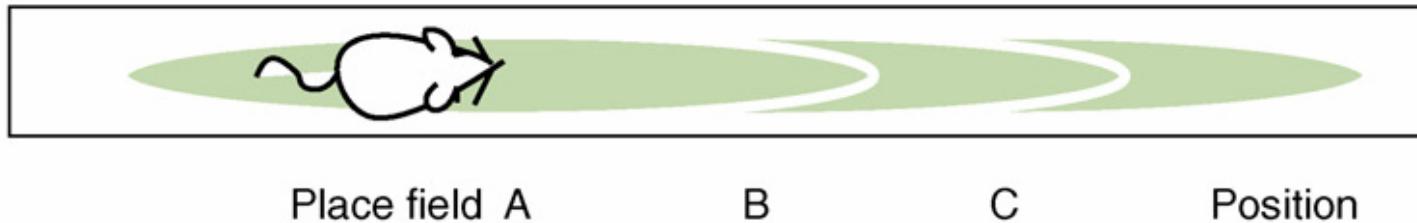


Memory Capacity

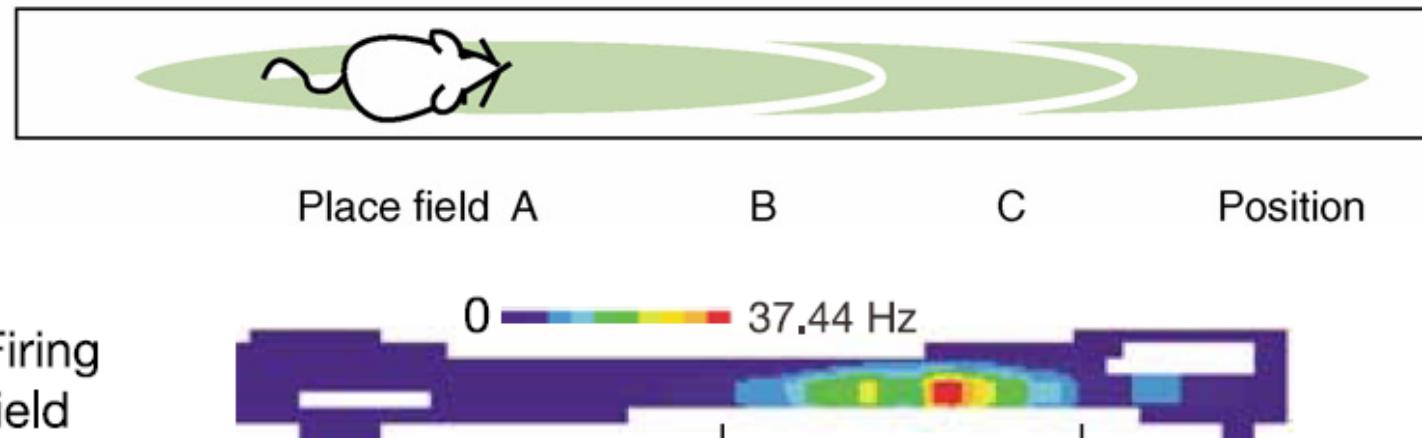


In Vivo Firing Patterns

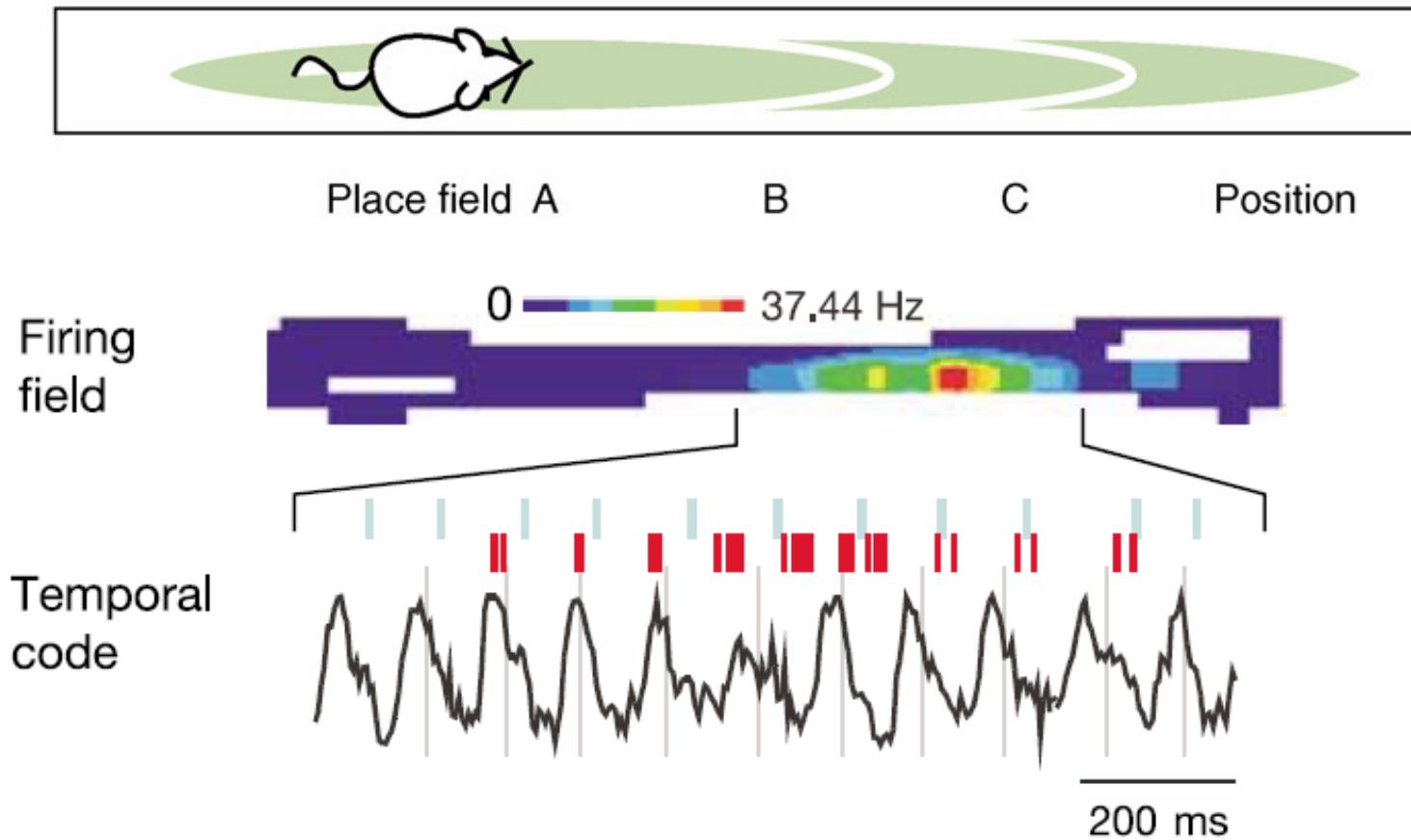
(freely moving animals)



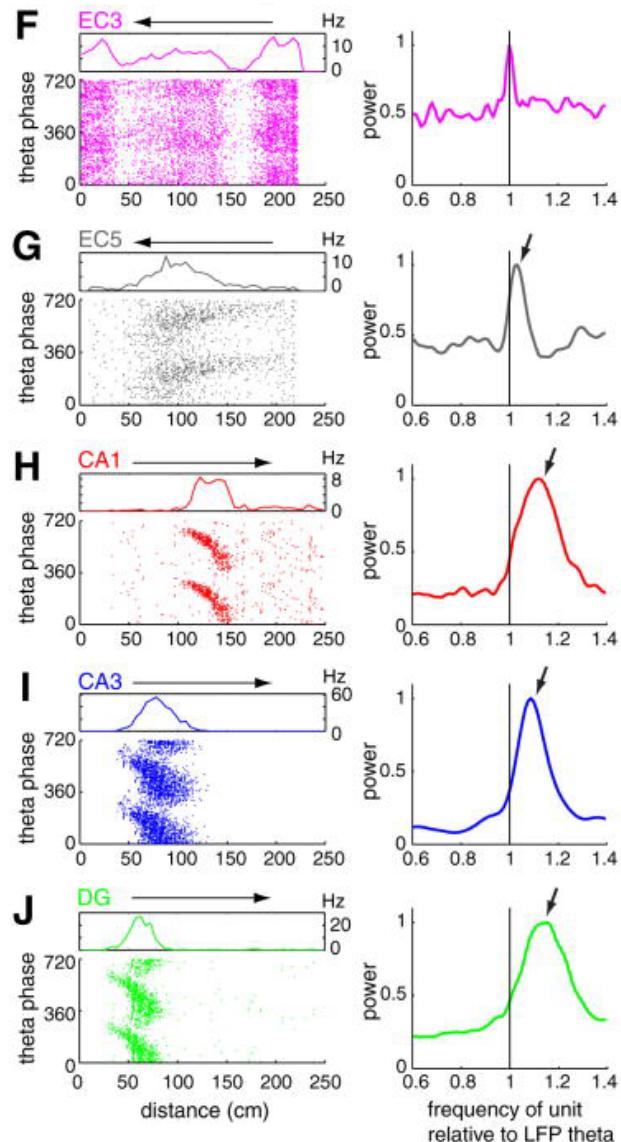
In Vivo Firing Patterns (freely moving animals)



In Vivo Firing Patterns (freely moving animals)



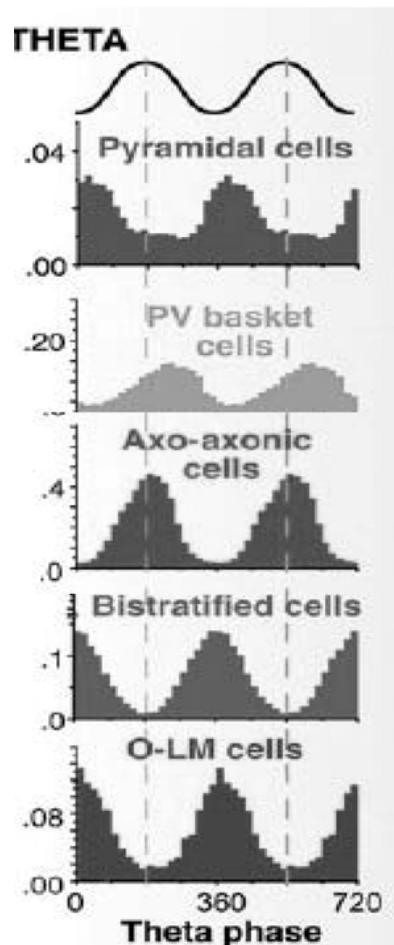
Theta Phase Precessing EC and HPC Cells



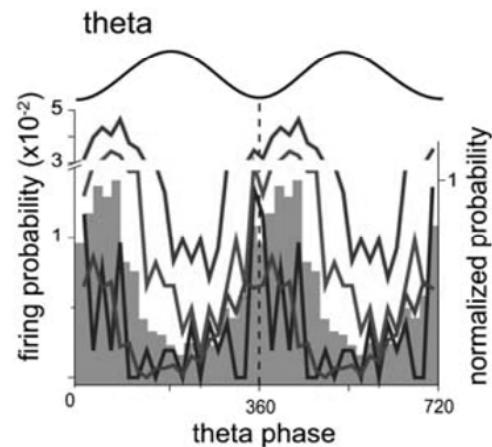
Mizuseki et al. (2009) Neuron

In-vivo Cell Firings

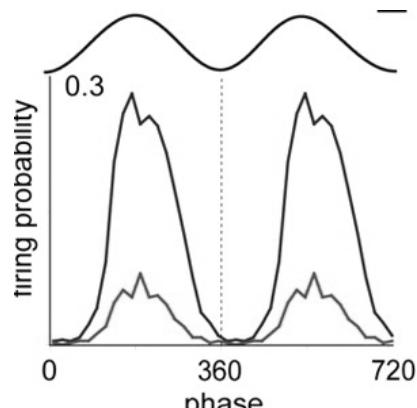
CA1



CA1 – IVY cells



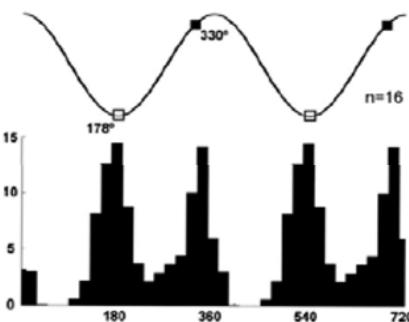
CA1 – NGL cells



Klausberger & Somogyi, 2008

04/06/2012

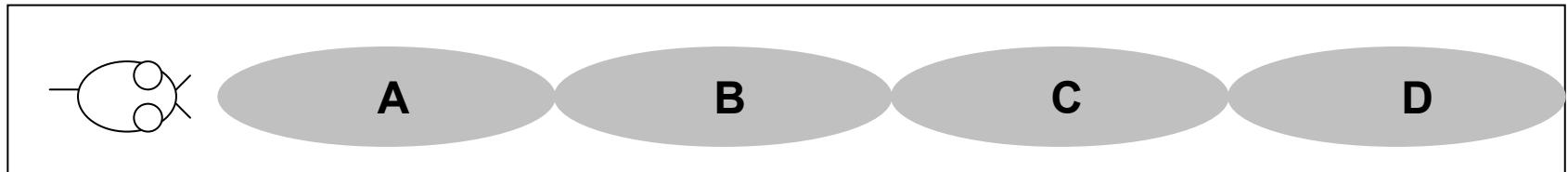
Medial Septum



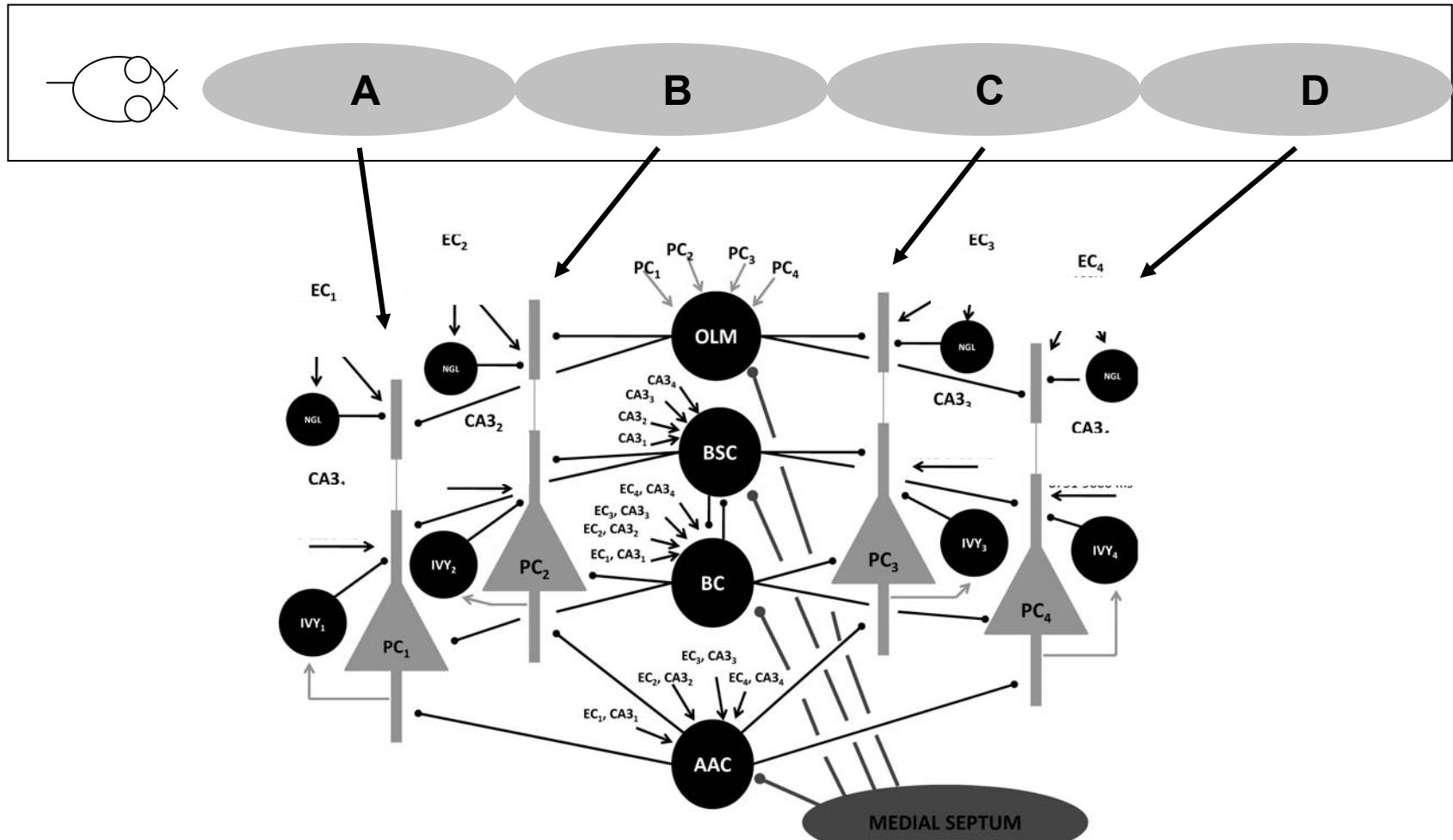
Borhegyi et al., 2004

- Given how different CA1 cells wax and wane w.r.t. theta, can I explain how CA1 supports place cells' rate and phase coding?

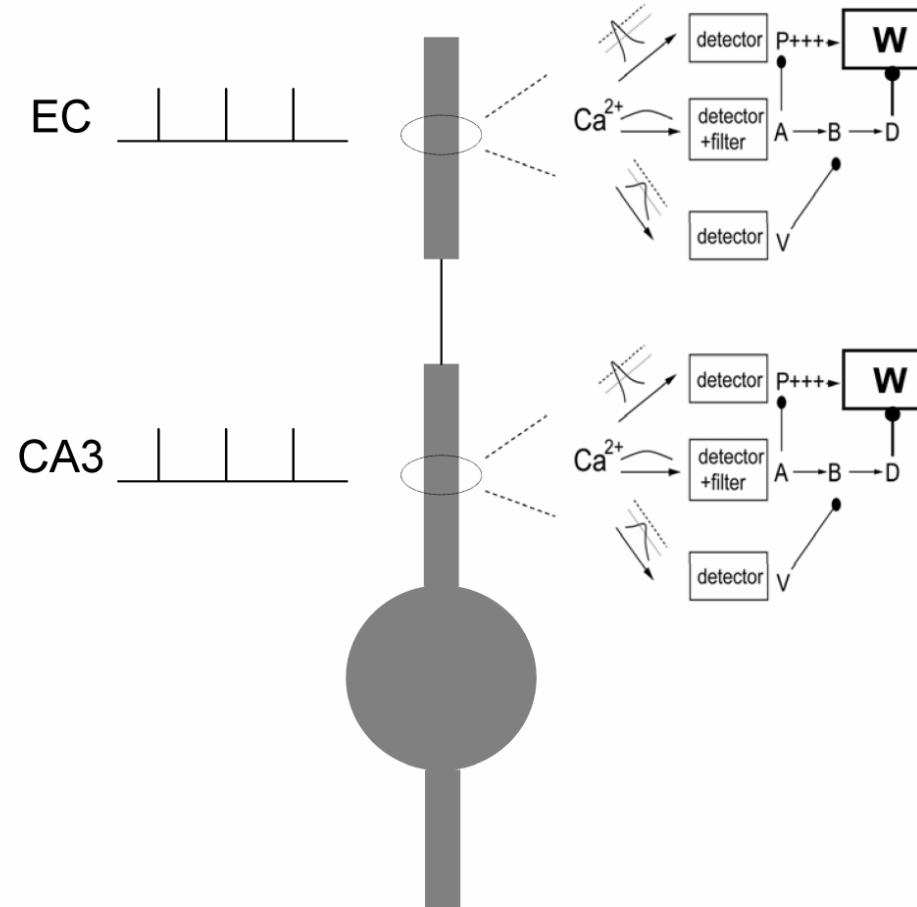
The New Model



The New Model

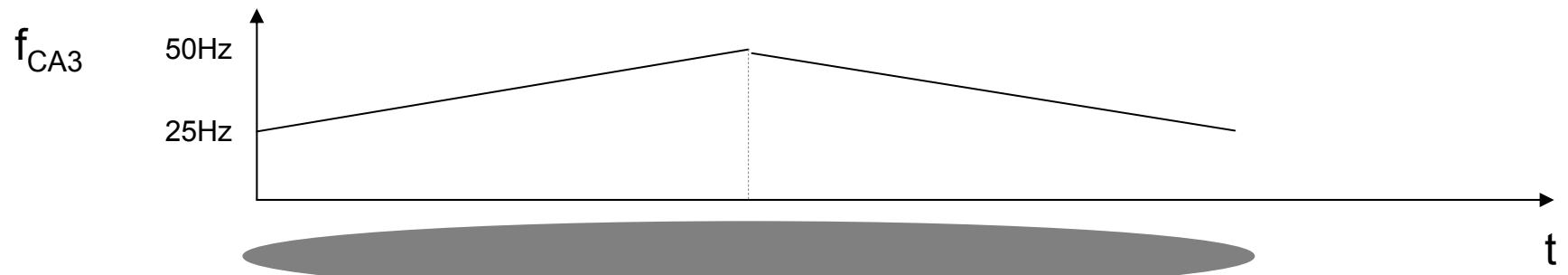


Model Pyramidal Cell

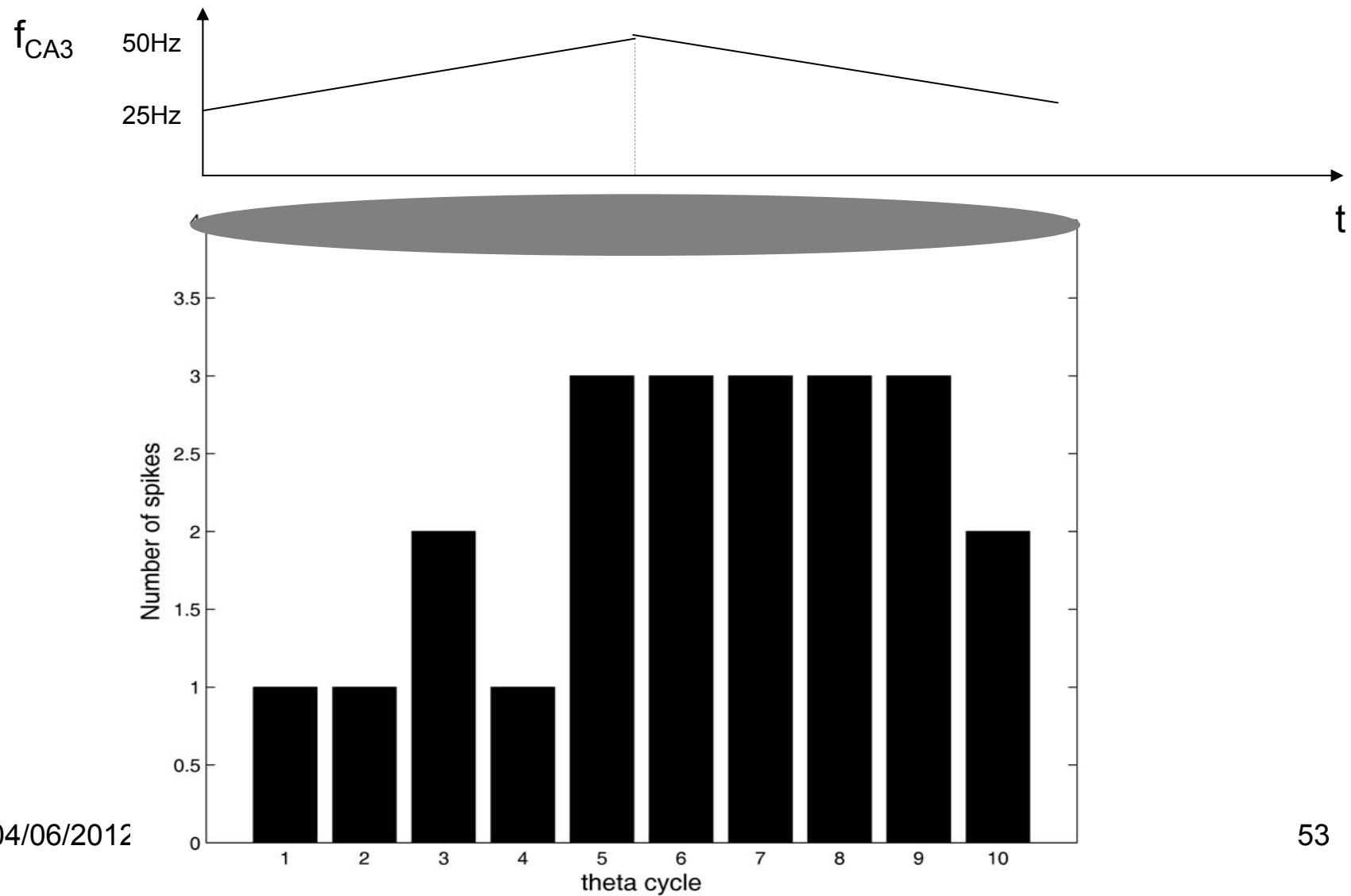


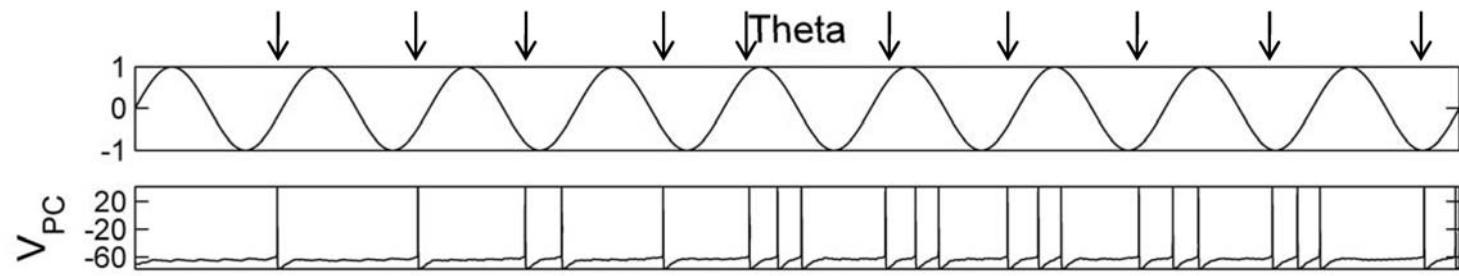
Rubin et al. (2005)

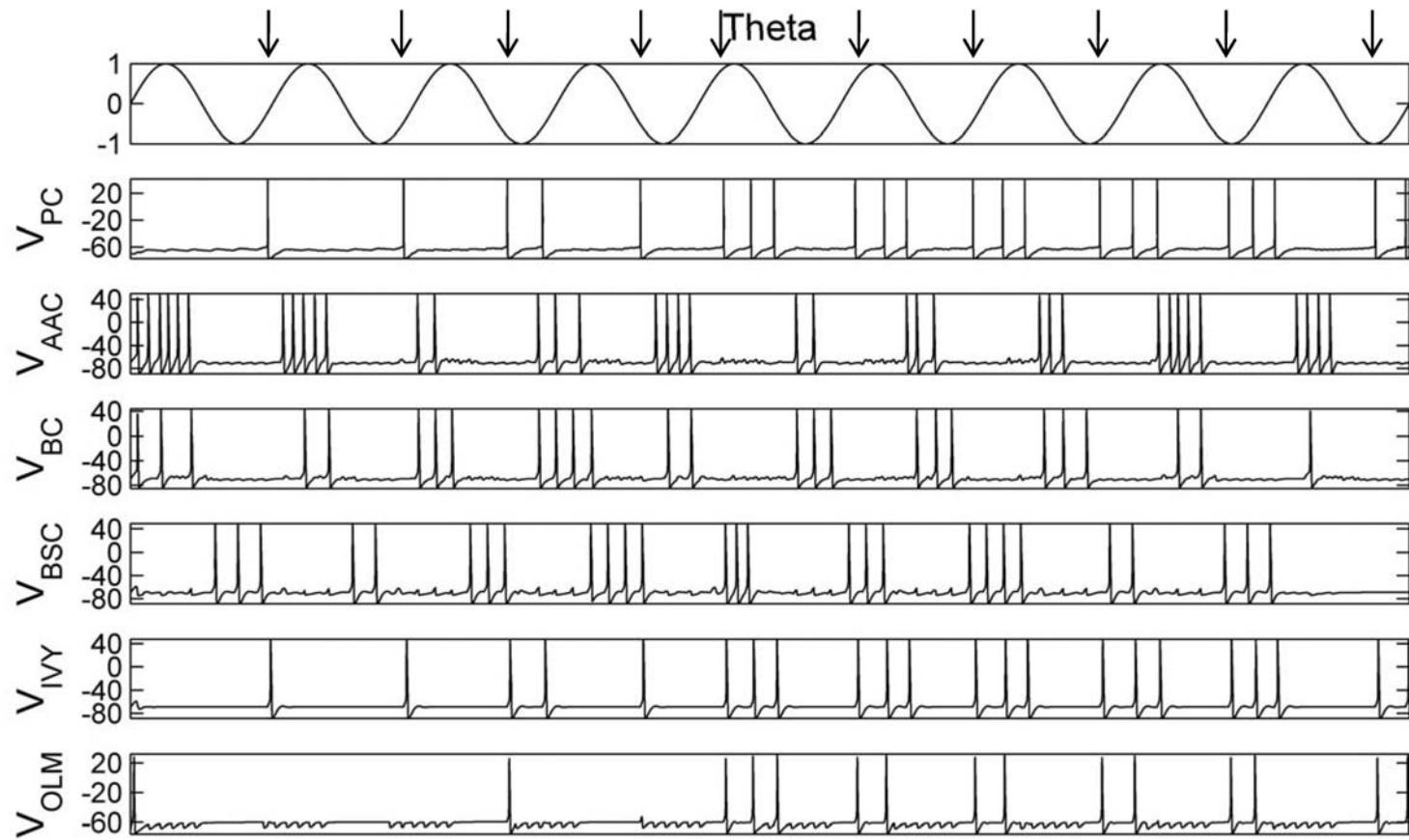
Firing Rate Code

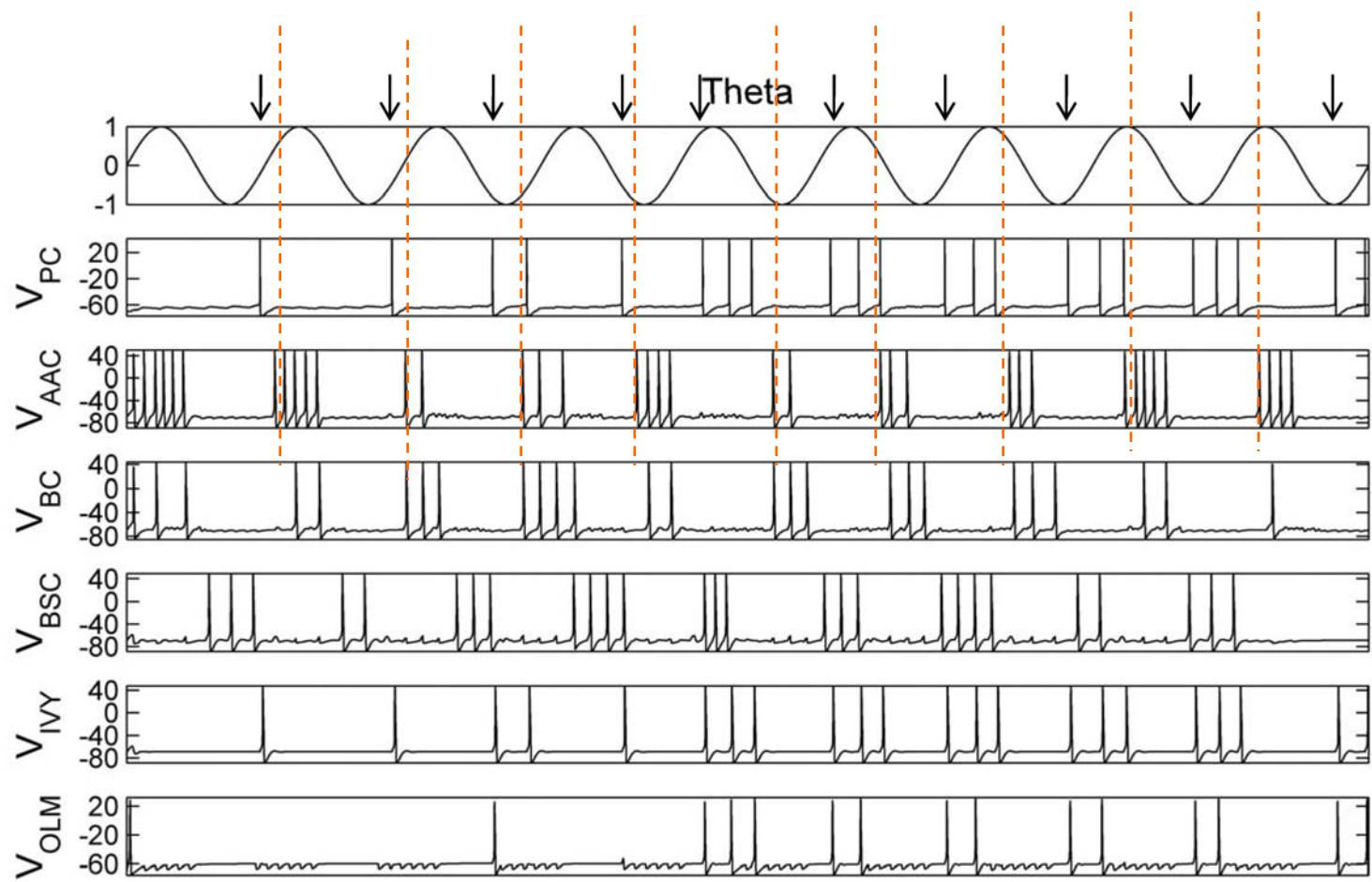


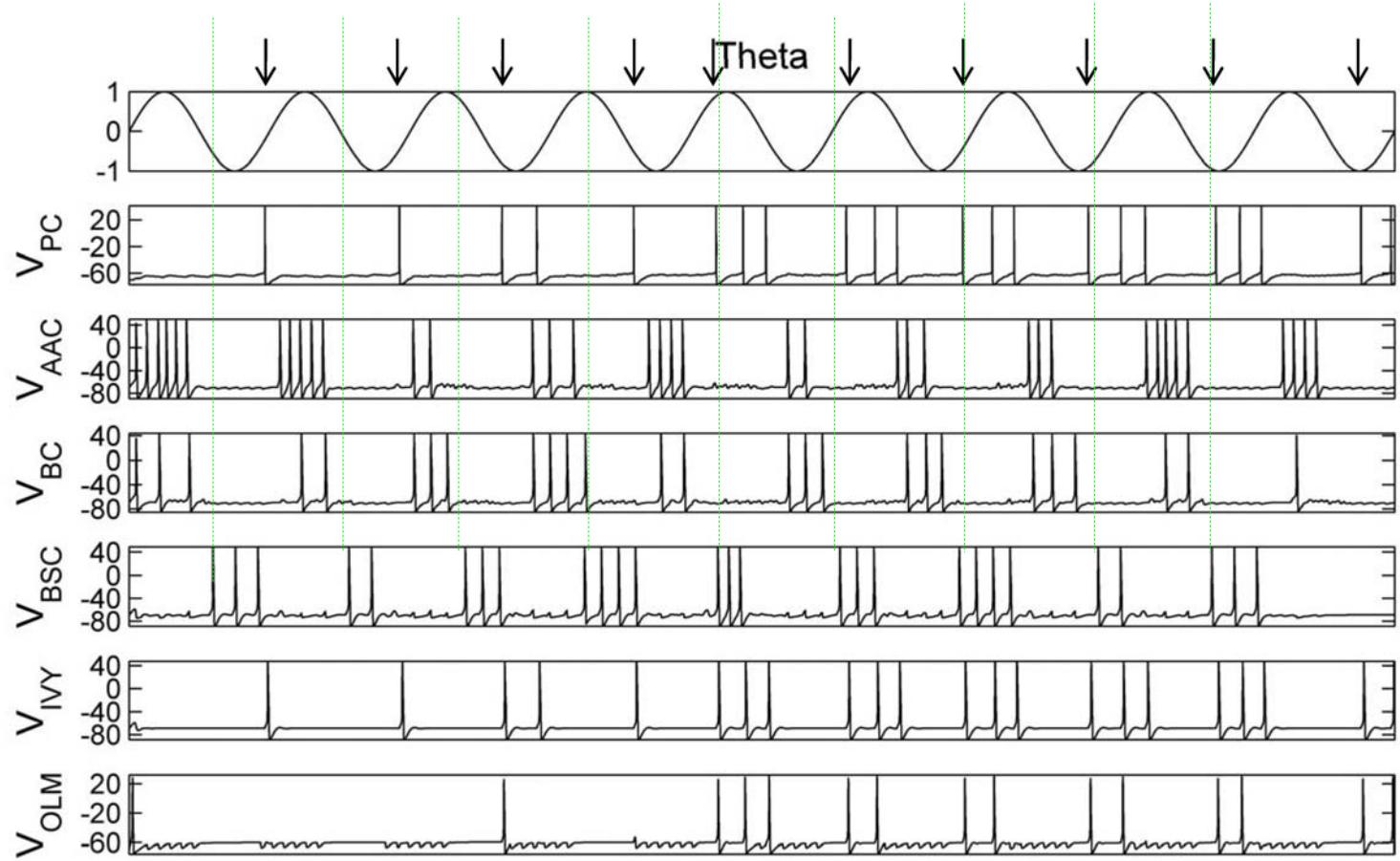
Firing Rate Code

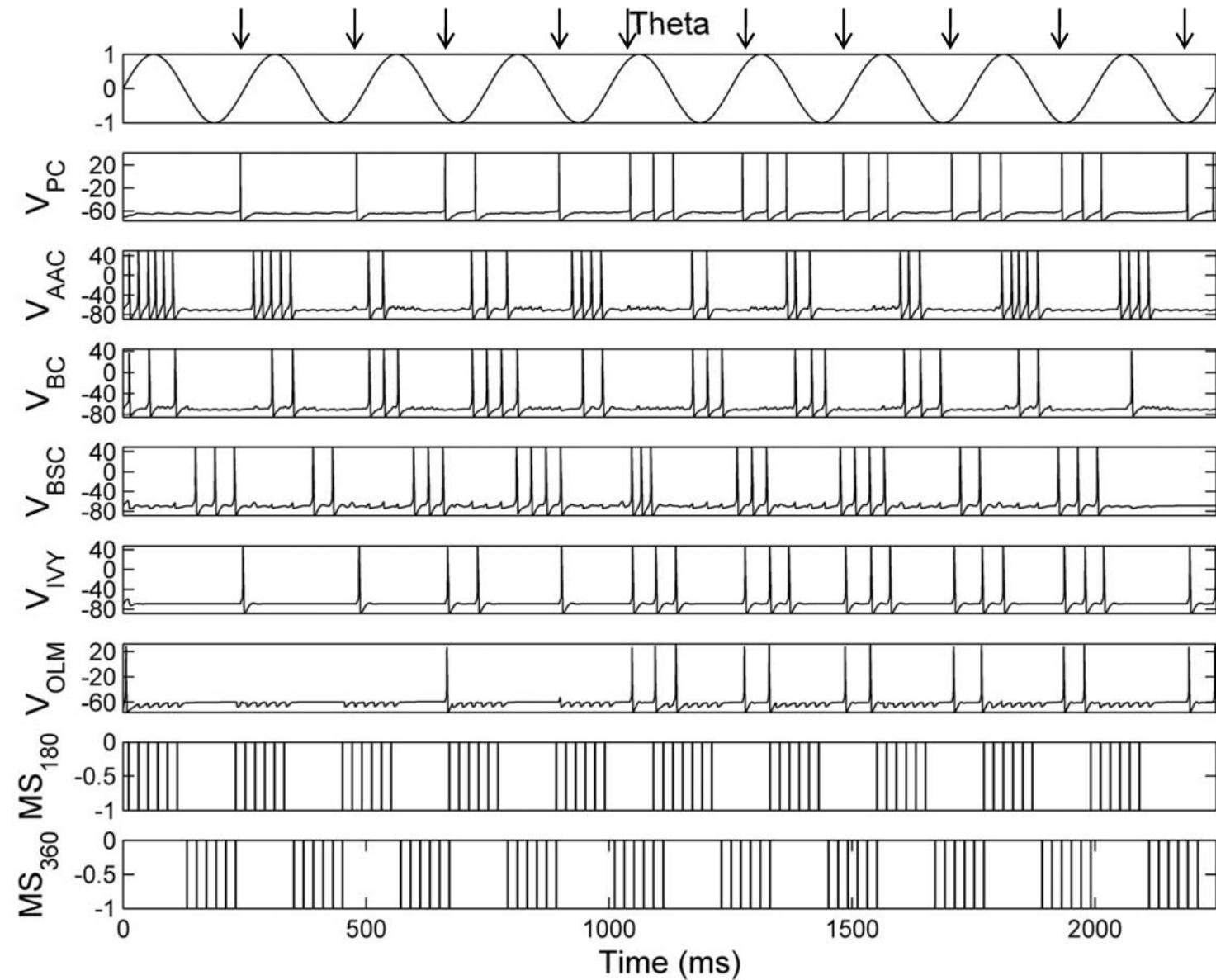


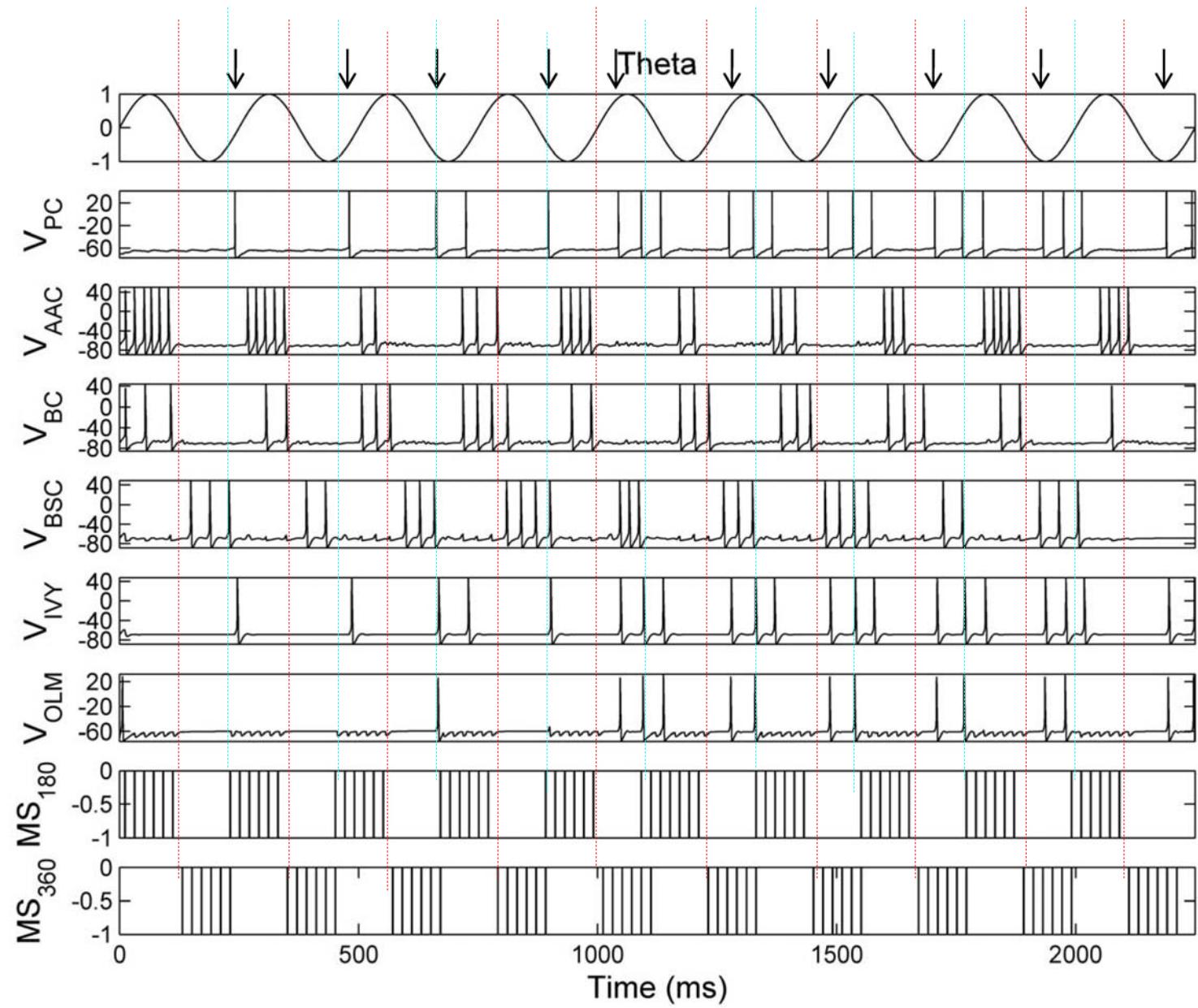




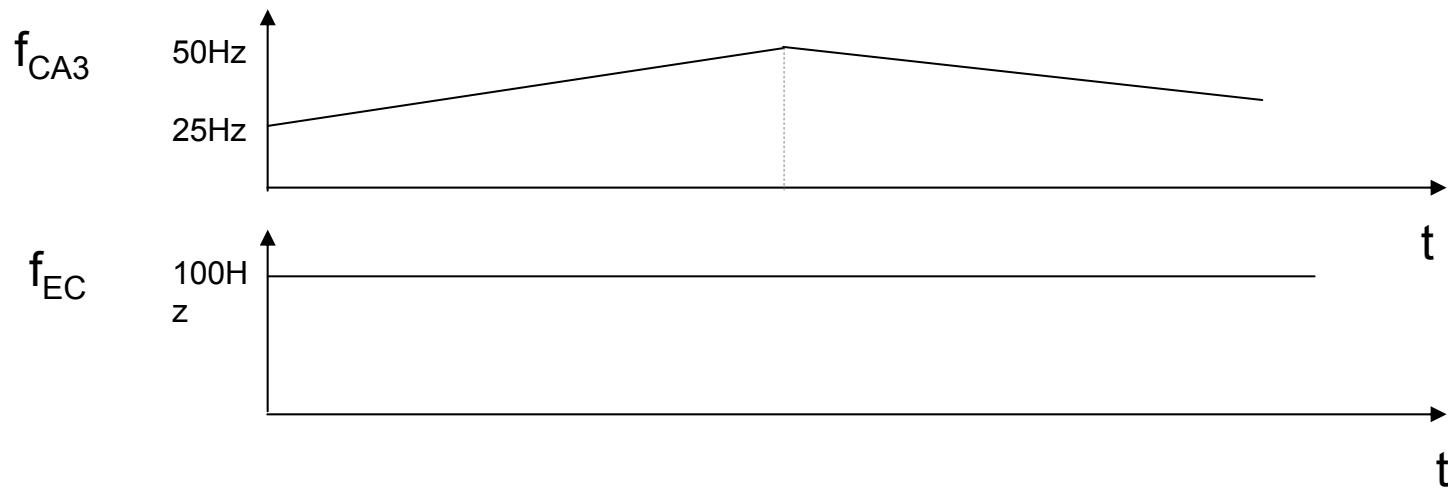




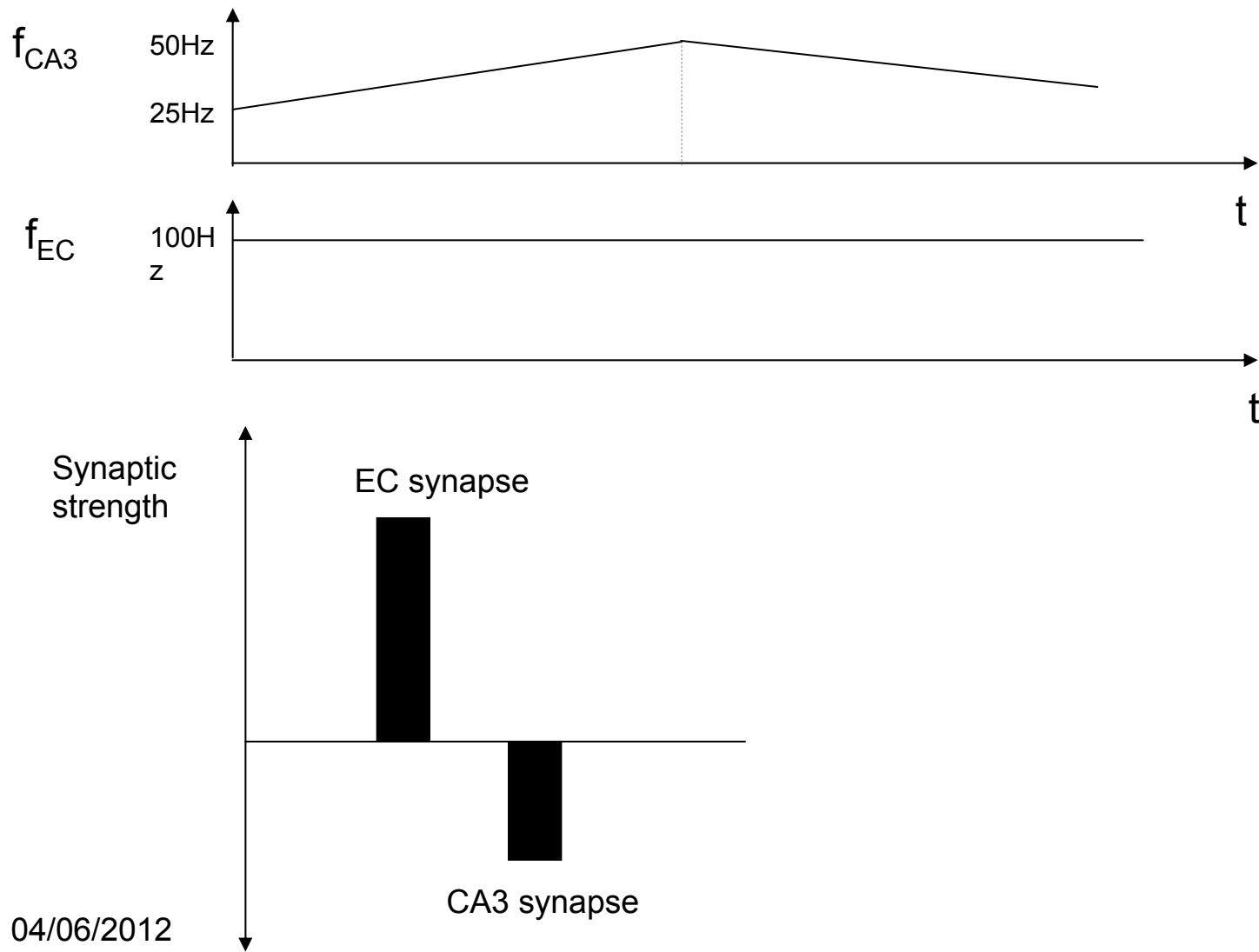




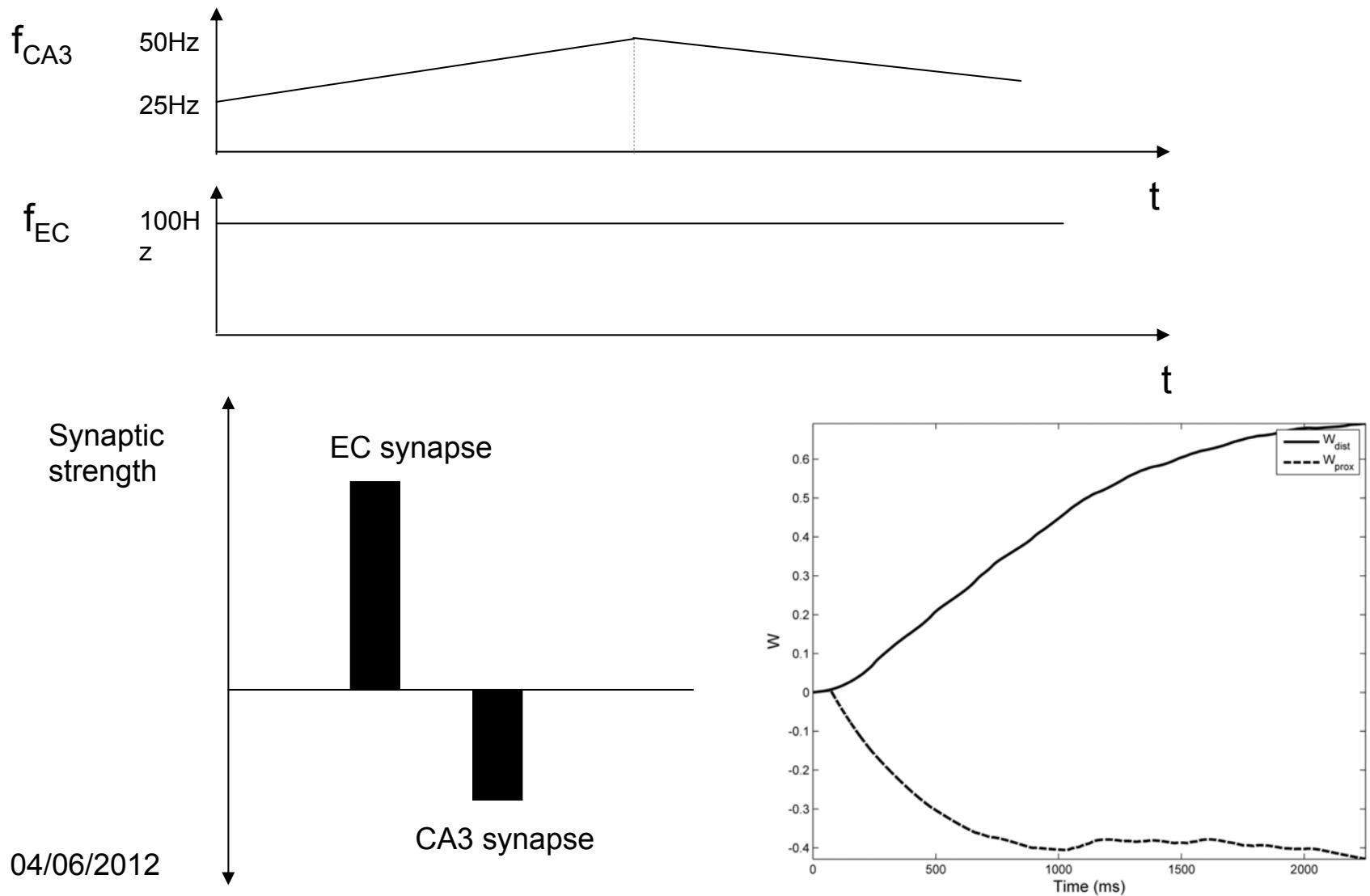
Depressed CA3 Synapse



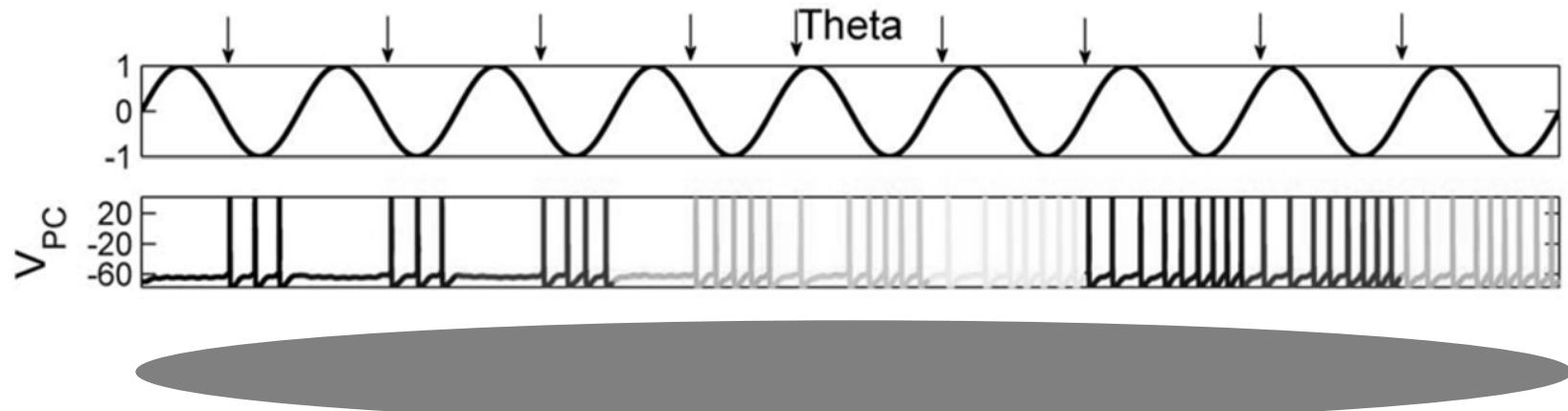
Depressed CA3 Synapse



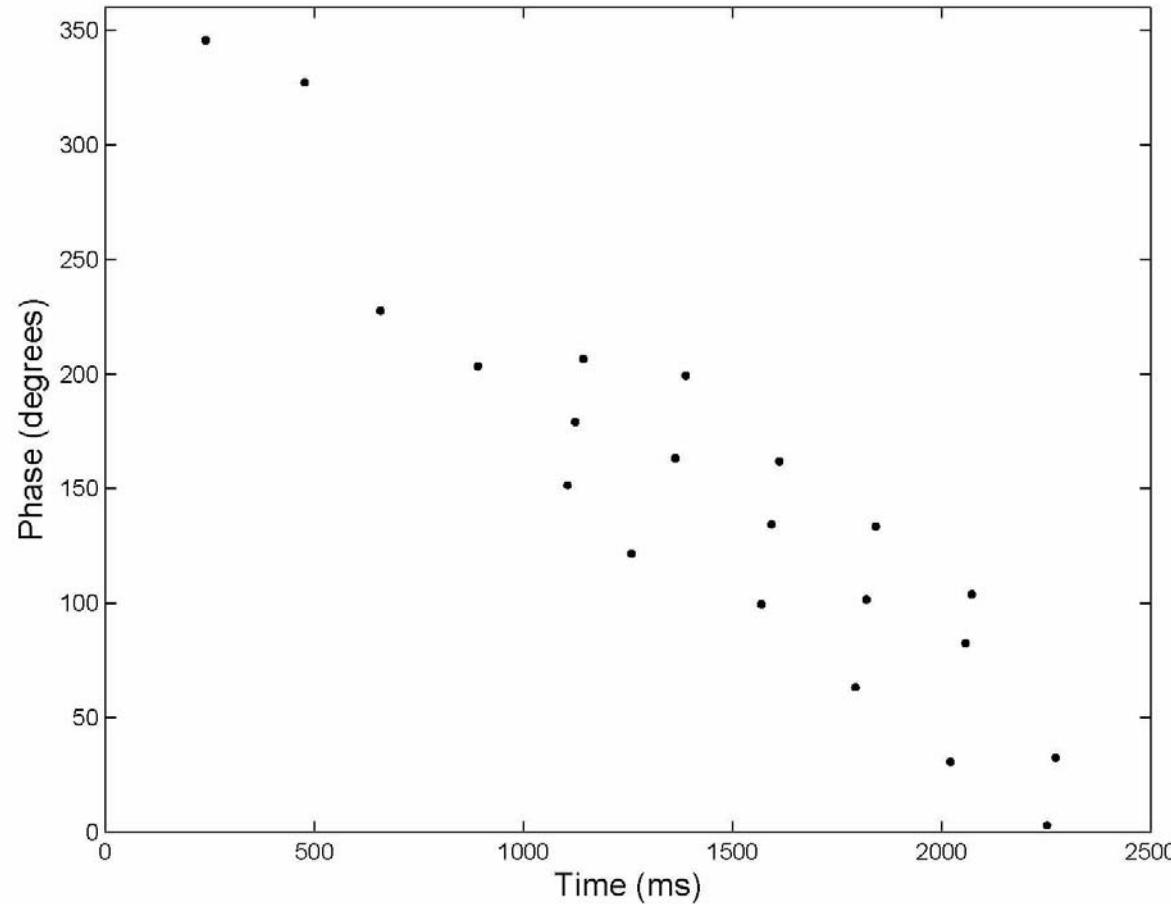
Depressed CA3 Synapse



Why a potentiated CA3 synapse may destroy both rate and phase code



Rate and Phase Code of Model Place Cell



Extensions to Alzheimer's Disease

- Alzheimer's disease (AD) is the most common neurodegenerative disorder characterized by cognitive and intellectual deficits and behavioural disturbance
- The hallmark disturbance in AD is a memory impairment
- This impairment may result from a number of factors:
 - **Cholinergic deprivation.** Cholinergic neurons from the medial septum project to both excitatory and inhibitory interneurons in the hippocampus (Cobb & Lawrence, 2010)
 - **Accumulation of beta-amyloid (A β) peptide.** A β affects several ionic currents in pyramidal cells (A-type K $^{+}$ current, L-type Ca $^{2+}$ current, delayed rectifier K $^{+}$ current, Ca $^{2+}$ - activated K $^{+}$ current, etc.), thus altering their excitability. An increase in PC excitability may account for the observed increase in hippocampal-septal theta band power (Coben et al., 1983; Jeong, 2004).