Modelling inhibitory control of encoding and retrieval in CA1 pyramidal cells

Bruce Graham

Computing Science & Mathematics

University of Stirling
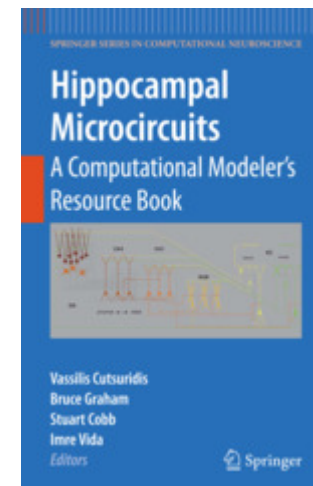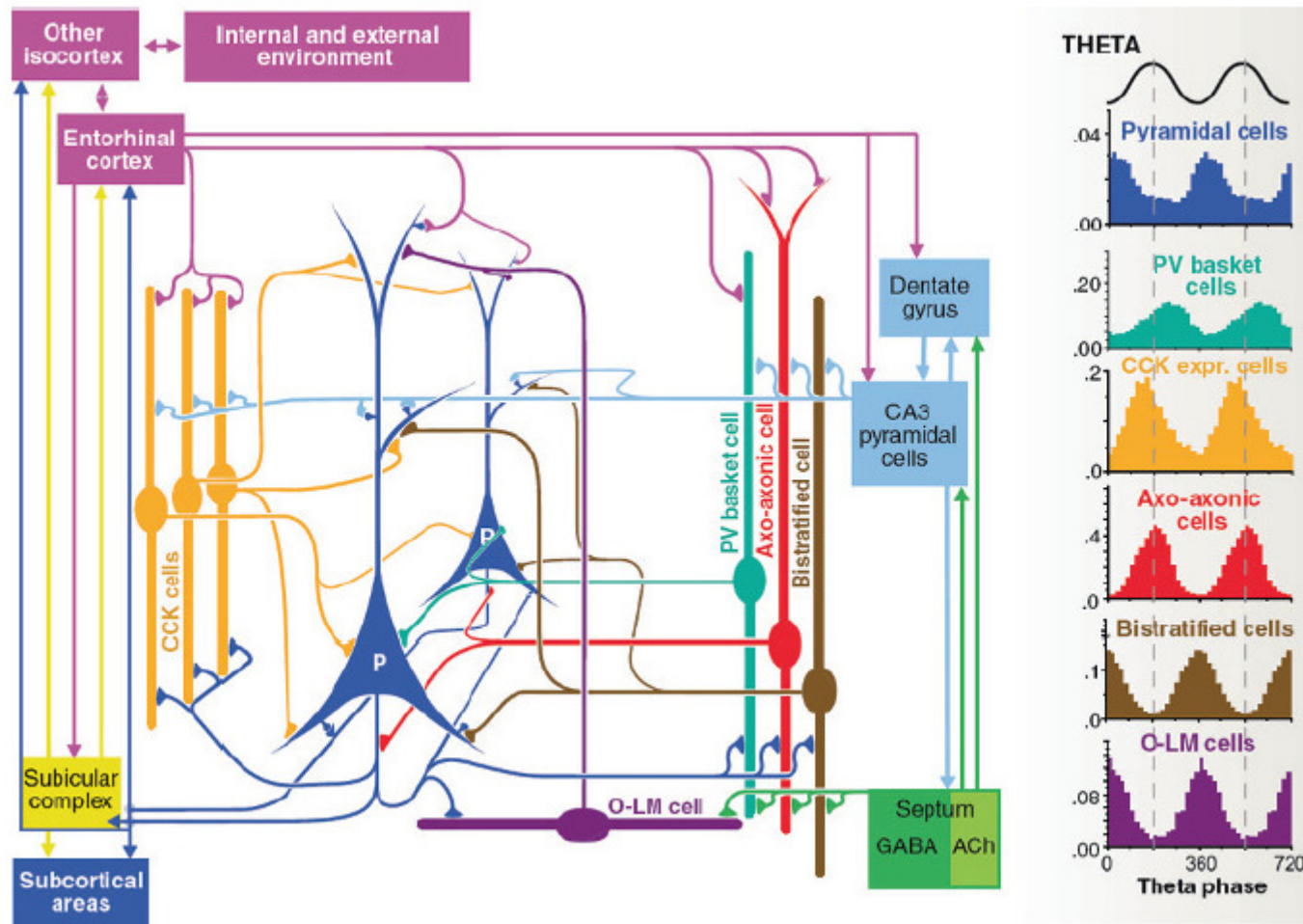
Scotland, UK

UNIVERSITY OF STIRLING

Background...

- Collaborators:
  - Stuart Cobb (Neuroscience, Glasgow)
  - Ausra Saudargiene (Informatics, Kaunas, Lithuania)
  - Vassilis Cutsuridis (RA), Russell Hunter (PhD)
- Funding: EPSRC
- Book:

Hippocampal Microcircuits:
A Computational Modeler's Resource Book
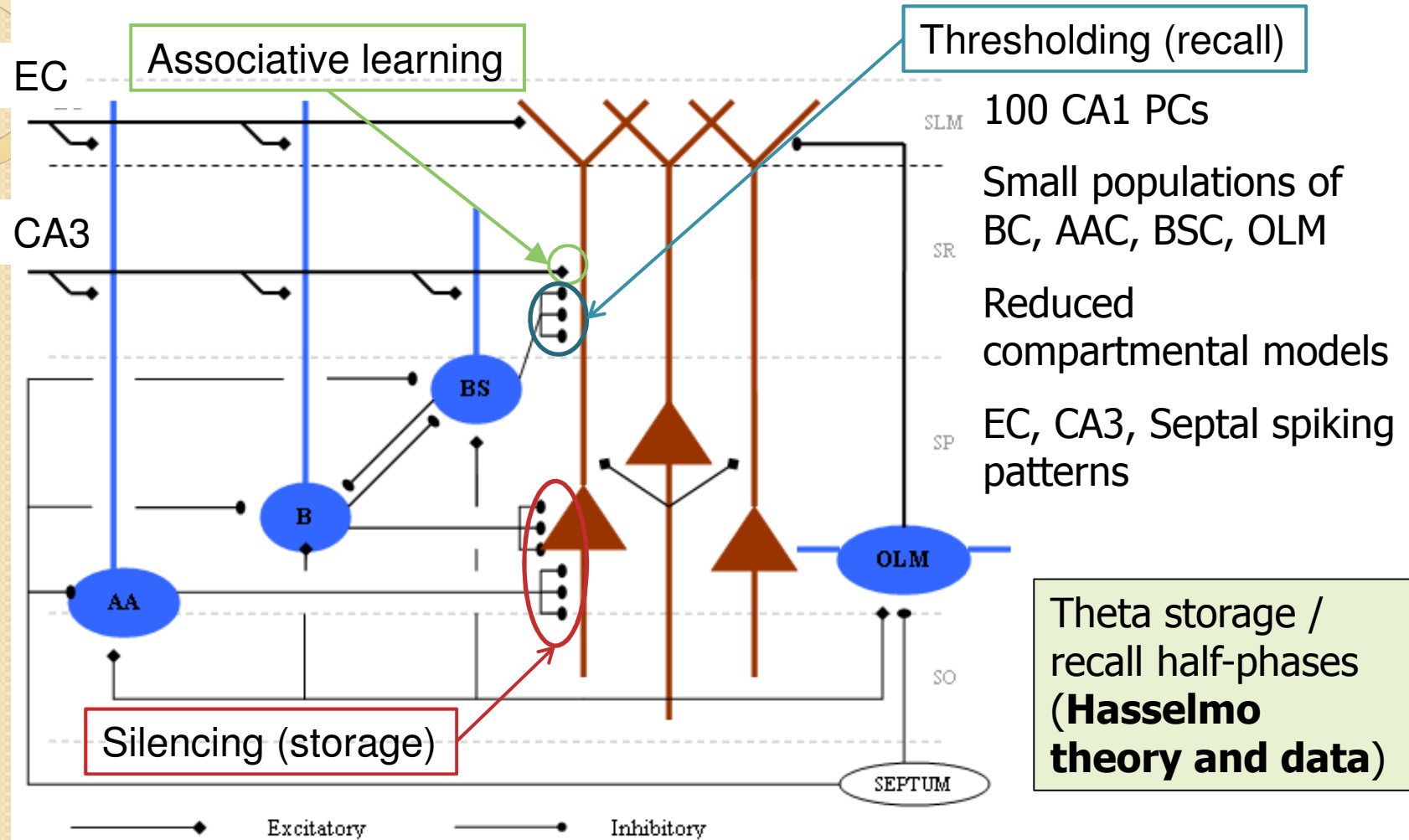Eds: Cutsuridis, Graham, Cobb, Vida
Springer, 2010

Fundamental CA1 Microcircuit?

(Cobb and Vida, Fig 2 Pg 284, Hippocampal Microcircuits, Springer 2010)
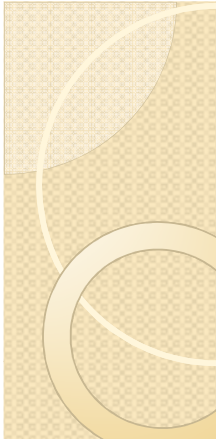
Klausberger data

CA1 Network Model

EC

CA3

Associative learning

Thresholding (recall)

100 CA1 PCs

Small populations of BC, AAC, BSC, OLM

Reduced compartmental models

EC, CA3, Septal spiking patterns

Silencing (storage)

Theta storage / recall half-phases (**Hasselmo theory and data**)

SLM

SR

SP

SO

BS

B

AA

OLM

SEPTUM

Excitatory   Inhibitory

Cutsuridis, Cobb & Graham, Hippocampus 20:423-446, 2010
Saudargiene, Cobb & Graham, Hippocampus 25:208-2018, 2015
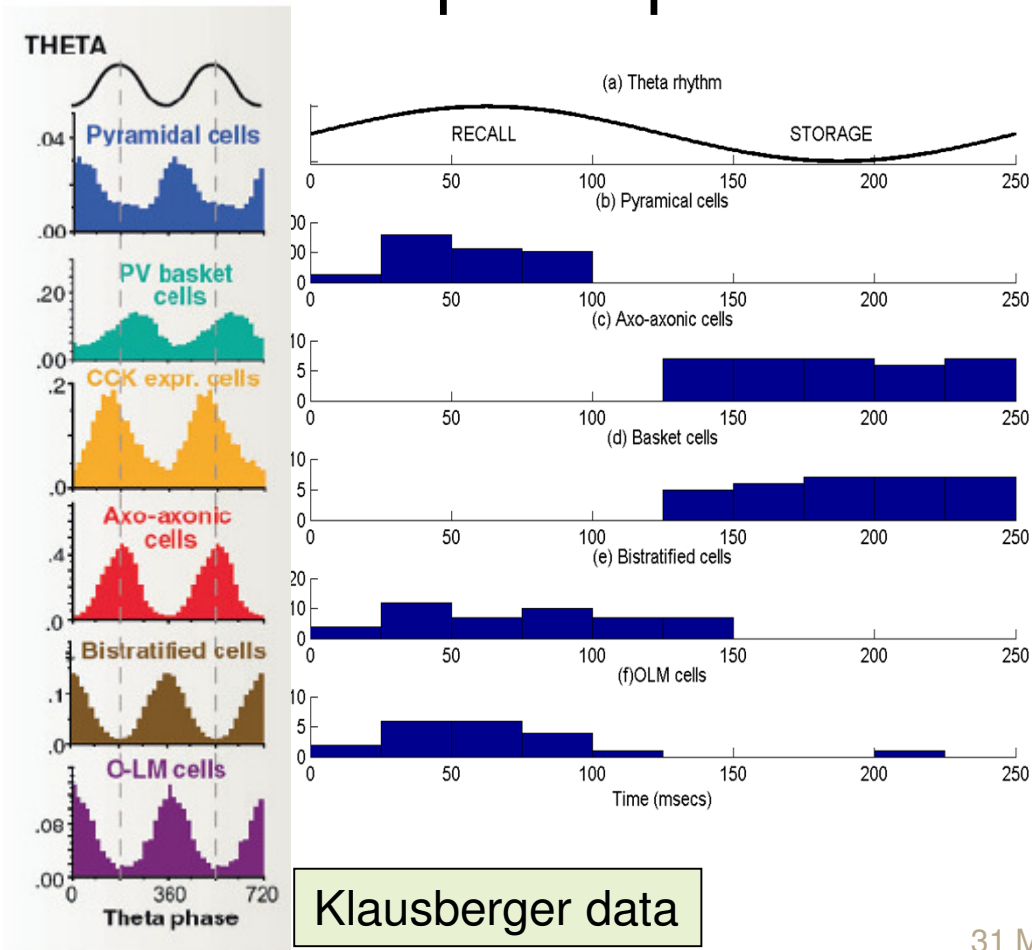
Model Neurons
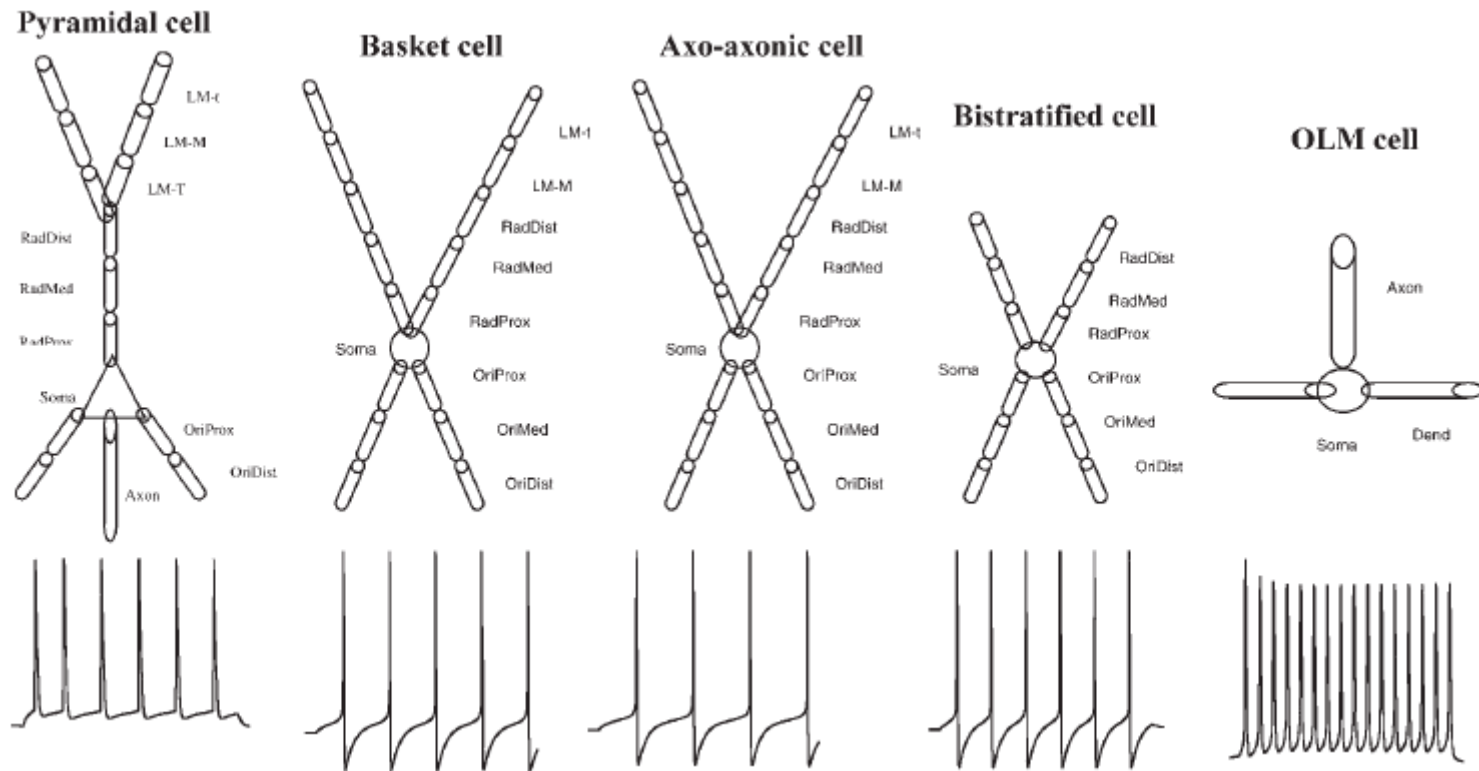
PC based on Poirazi model: ion channels and distributions
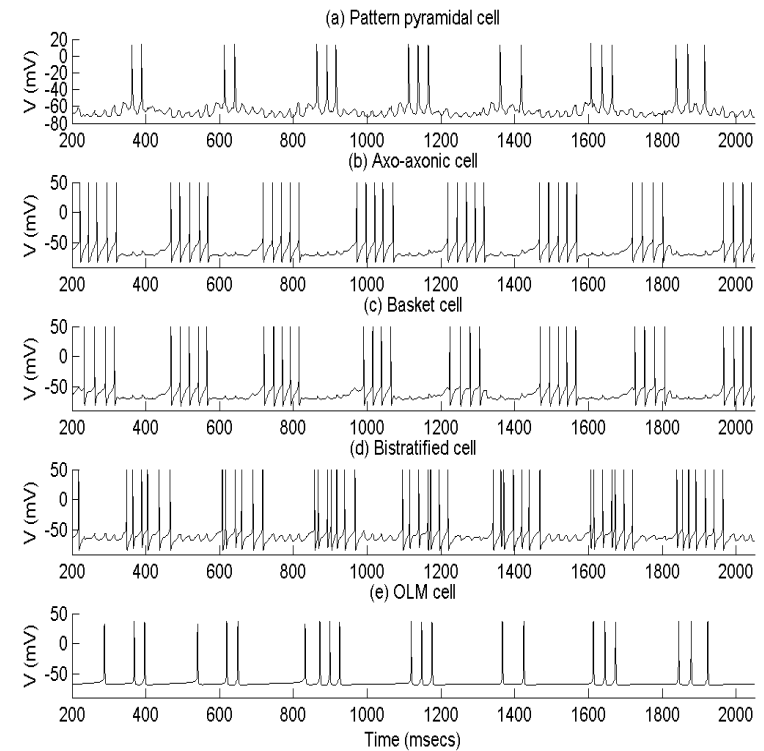IN models based on models from Skinner lab
NEURON code from ModelDB

Patterned Firing of Cell Types

- Theta due to phasic MS input
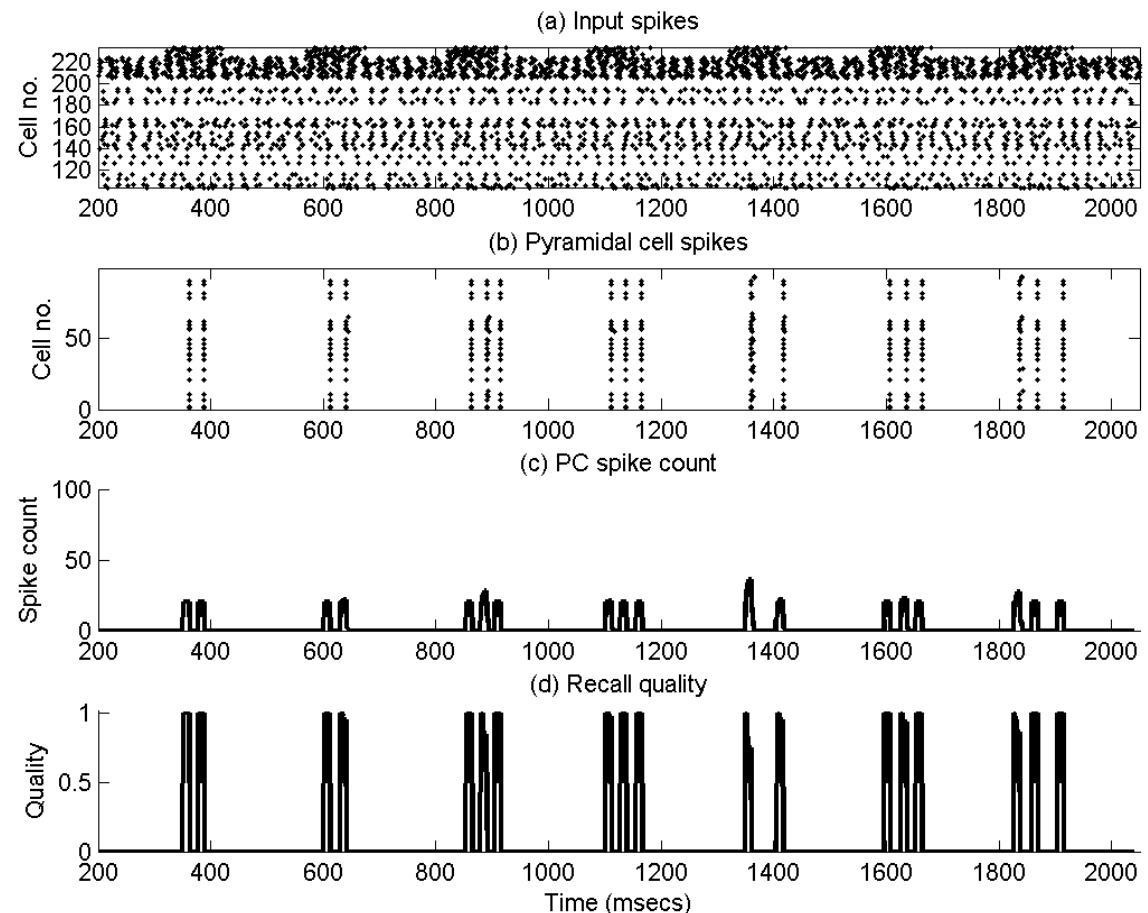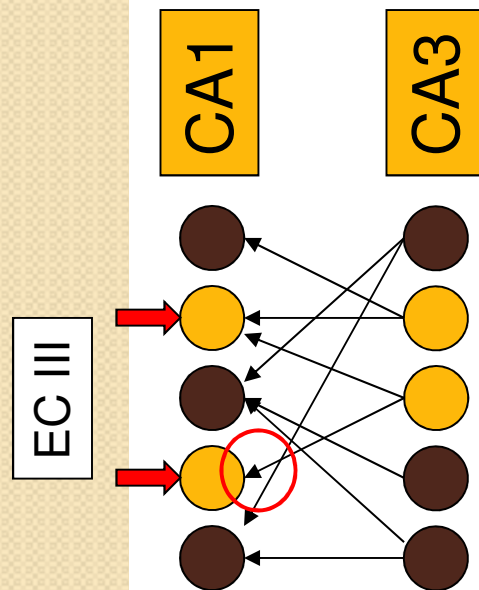- Specific phase relationships as per in vivo data
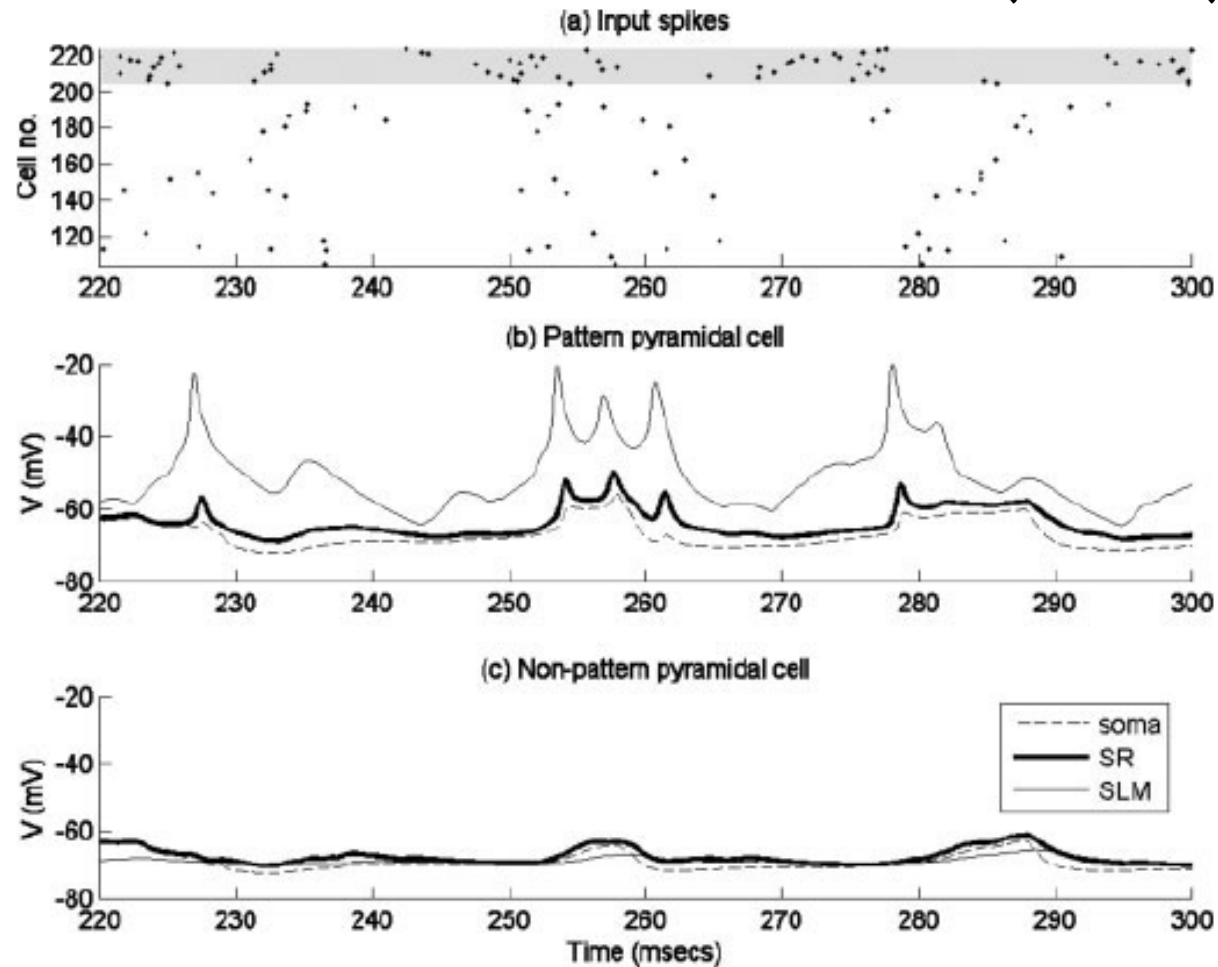

Klausberger data

Phasing Storage and Recall

- Recall at *gamma* frequency in *theta* half-cycles
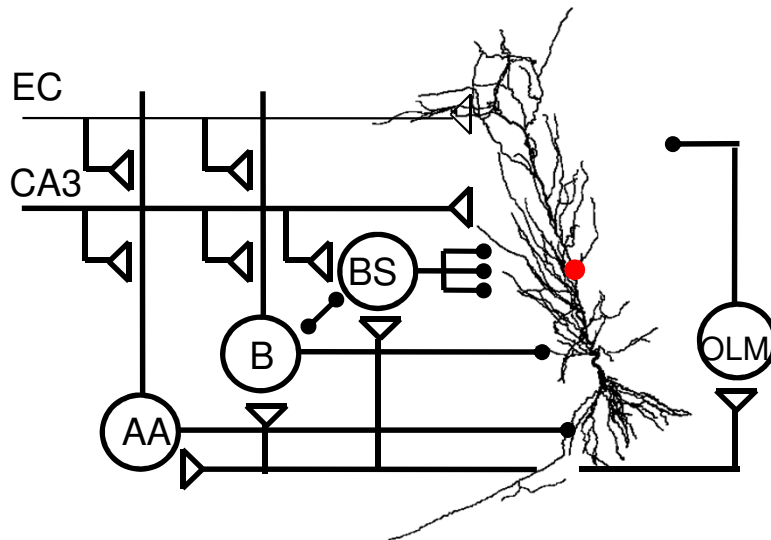- Storage during *silent* theta half-cycles

Storage Signal

- Synaptic (dendritic) voltage: $\Delta w_{ij} = p_i . p_j$

(a) Input spikes

(b) Pattern pyramidal cell

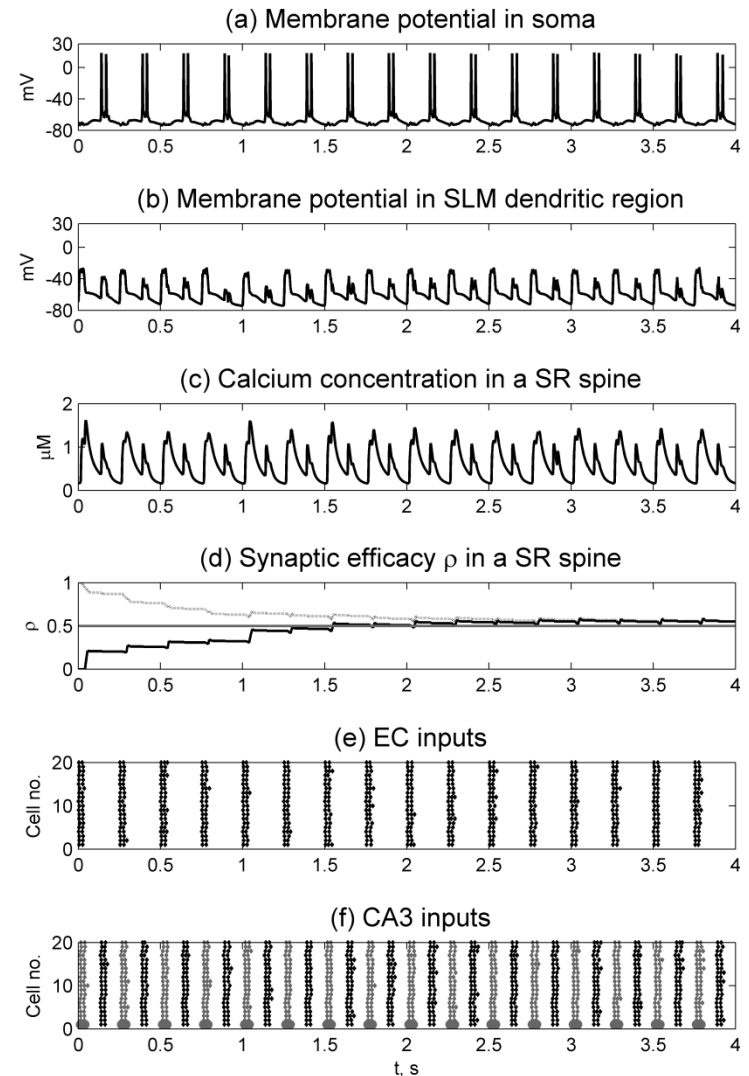(c) Non-pattern pyramidal cell

soma
SR
SLM

Time (msecs)

Calcium-based Learning: Storage

- EC + weak CA3
- Perisomatic inhib
- LTP of CA3 inputs

Saudargiene et al, Hippocampus, 2015
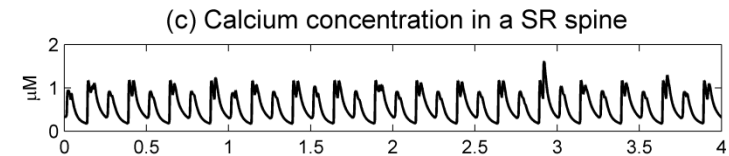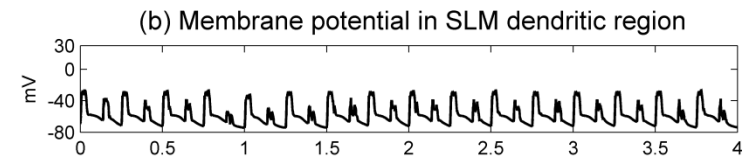Poirazi CA1 PC model, 2003
Graupner & Brunel plasticity rule, 2012

(a) Membrane potential in soma

(b) Membrane potential in SLM dendritic region

(c) Calcium concentration in a SR spine

(d) Synaptic efficacy ρ in a SR spine

(e) EC inputs

(f) CA3 inputs

Calcium-based Learning: Recall

- Strong CA3 input
- Dendritic inhib
- LTD of CA3 inputs

(a) Membrane potential in soma

(b) Membrane potential in SLM dendritic region

(c) Calcium concentration in a SR spine

(d) Synaptic efficacy ρ in a SR spine

(e) EC inputs

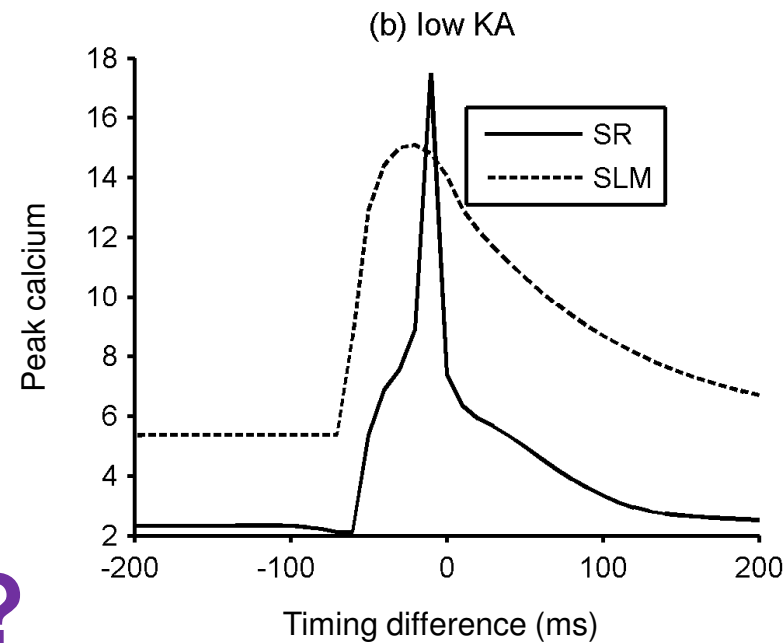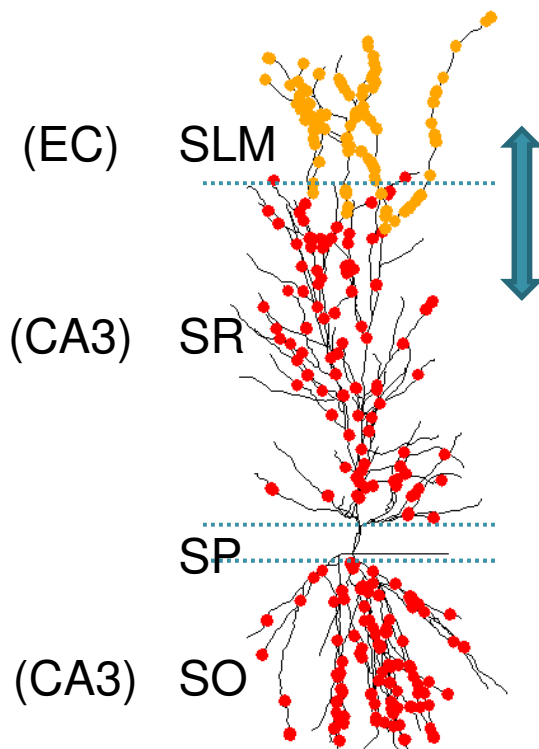(f) CA3 inputs
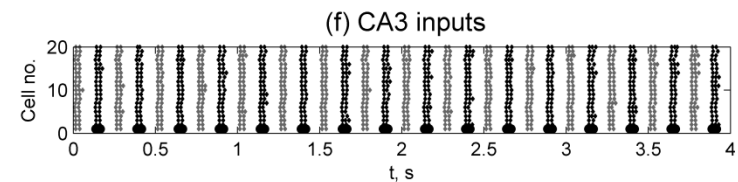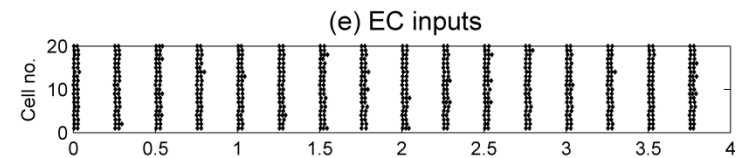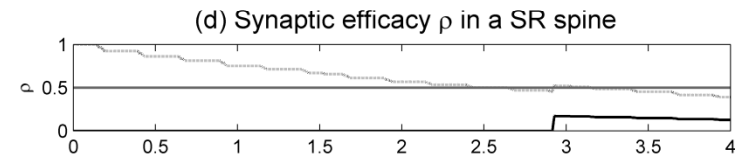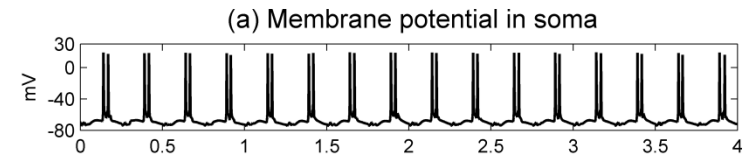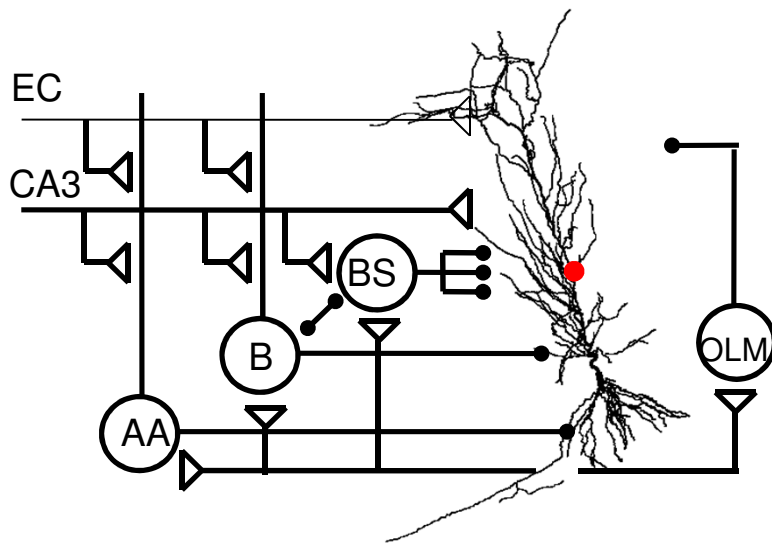
Synaptic Cooperativity

- Peak synaptic calcium as a function of the number of simultaneously active synapses
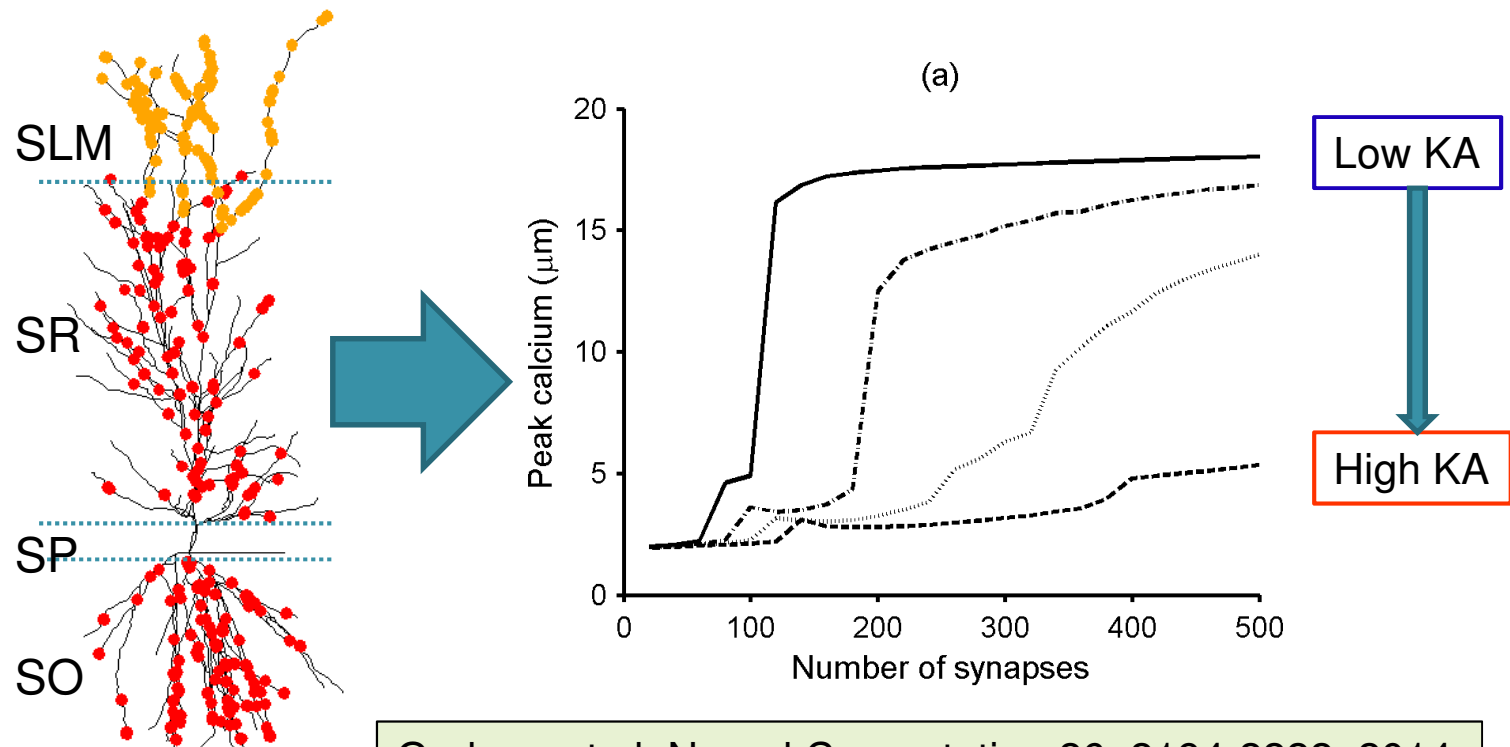
Graham et al, Neural Computation 26: 2194-2222, 2014
Extended Migliore (2005) CA1 PC model

# Cooperativity Between Layers

- Problematic?

(EC) SLM

(CA3) SR

SP

(CA3) SO

?

(b) low KA
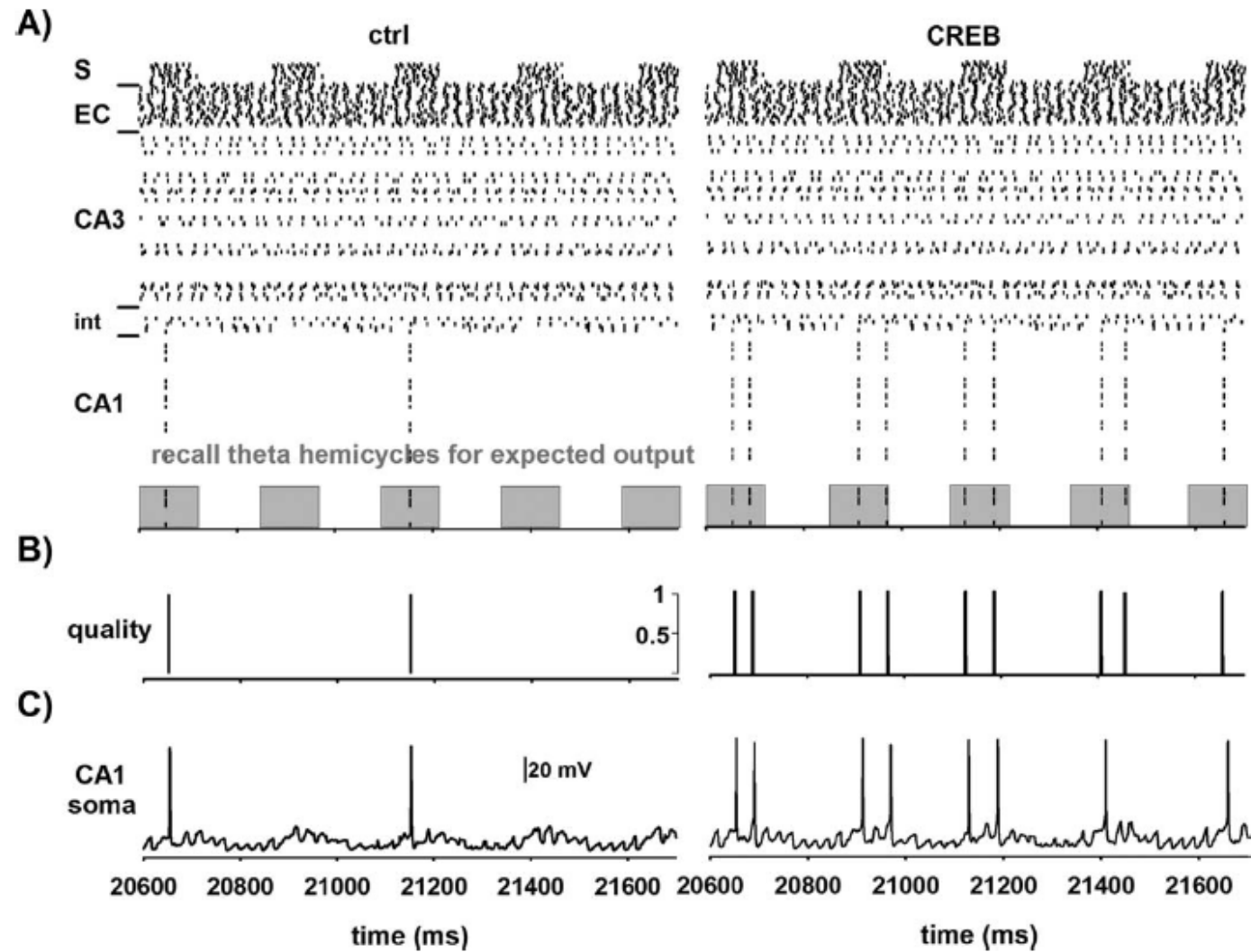
Peak calcium

— SR
---- SLM

Timing difference (ms)

Graham et al, Neural Computation 26: 2194-2222, 2014
Experimental evidence eg Takahashi & Magee (2009)

Model reuse: CREB and AD

- cAMP Response Element Binding protein
  - Enhances plasticity and cell excitability
- CREB signalling down-regulated in AD

Bianchi et al. Hippocampus 24:165-177, 2014
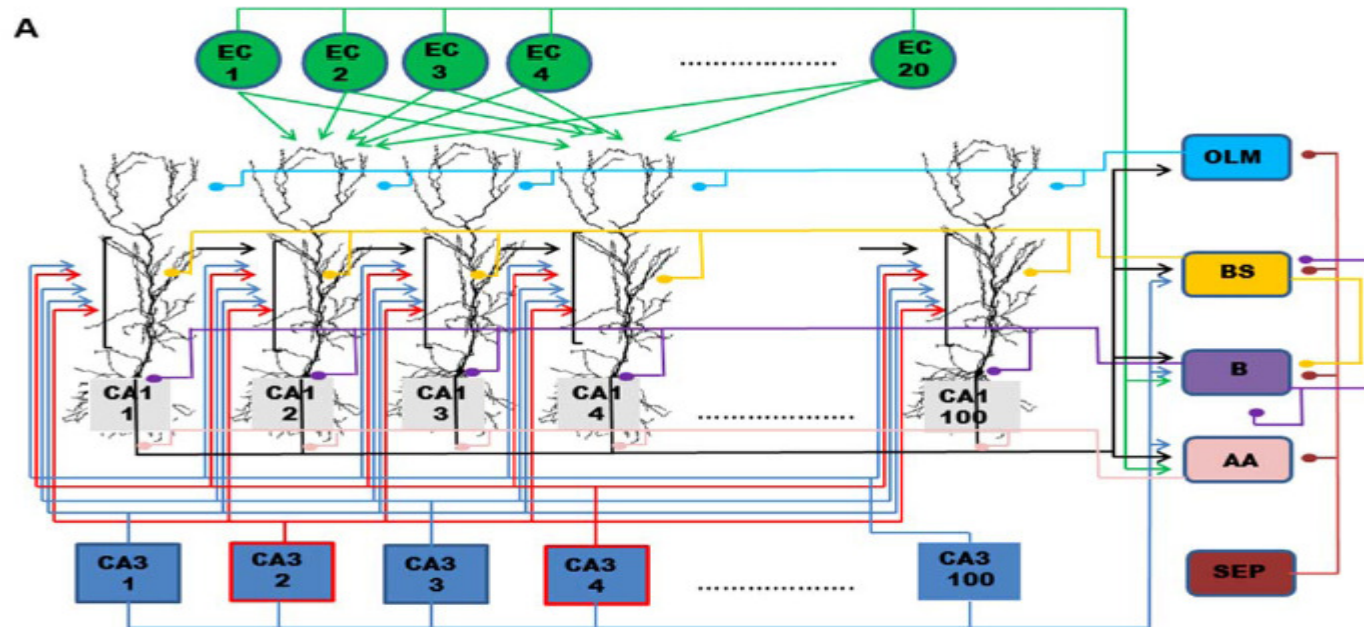
CREB and AD

Bianchi et al. Hippocampus 24:165-177, 2014

Summary

- Model of associative memory in CA1
    - INs control plasticity and recall
- Code repository: ModelDB
    - All NEURON model code on ModelDB
    - Use of ion channel and cell models
    - Model reuse
- Experimental data:
    - Cell-specific physiology and activity patterns
    - Schaffer collateral LTP/LTD