Hippocampus, memory and dynamics.

From neurophysiological observations to computational models.

Colin Molter and Naoyuki Sato

Lab. For Dynamics of Emergent Intelligence RIKEN - Brain Science Institute— Japan

*"In order to understand the brain, we have used the computer as a model for it. Perhaps it is time to reverse this reasoning.
To understand where we should go with the computer, we should look to the brain for some clues,"*

Orlando - IJCNN 2007

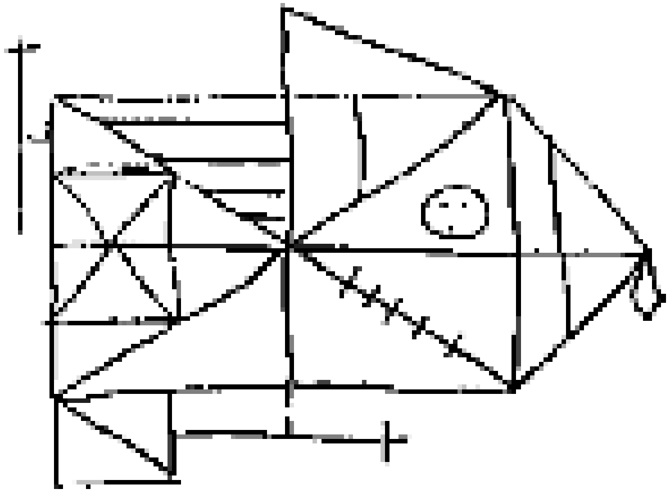
Overview

1. Introduction and Neuroanatomy
2. Rhythms of the Brain
3. Modeling and artificial neural networks
4. Computational Models
    1. Rat computational models
        1. Head directional cells
        2. Path integration
        3. Place cells
        4. Memory formation and consolidation
    2. Human computational models
        1. View cells
        2. Object-place memory
5. Conclusion

The hippocampus? What for !

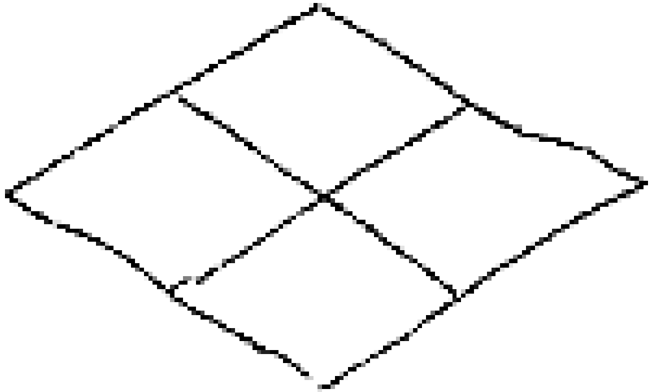
Cognitive Roles of the Hippocampus

Scientist and Experiments

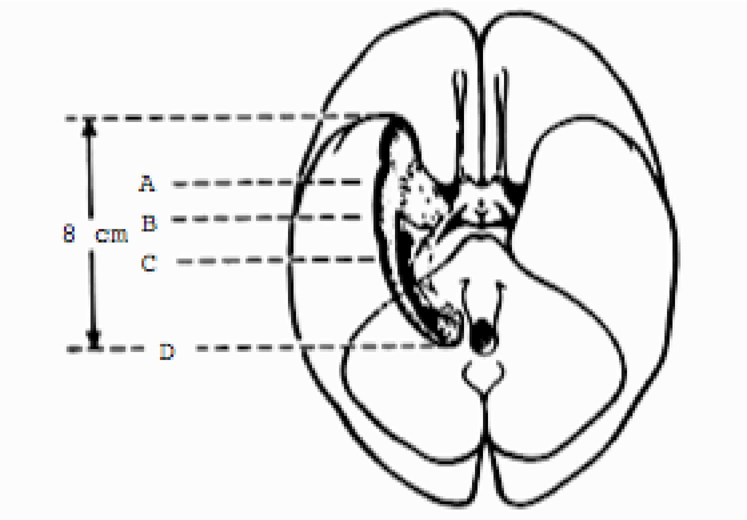


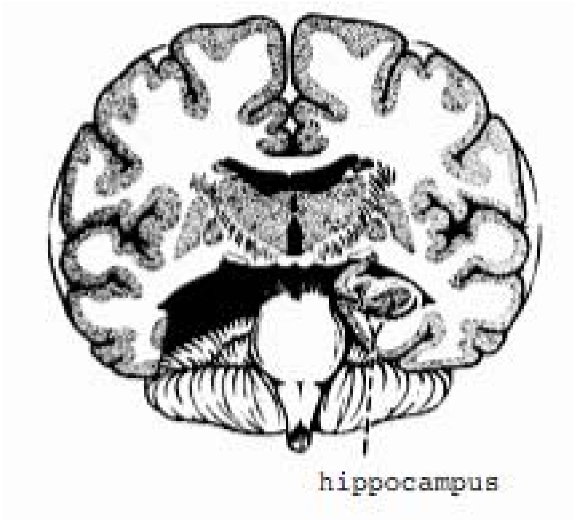
Can you remember this picture?
Can you draw it back?

(Rempel-Clower et al., 1996)



The patient H.M.



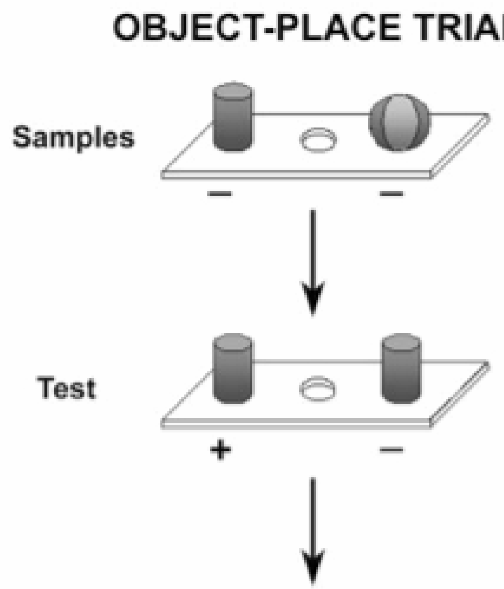


(Scoville & Milner, 1957)

- Bilateral hippocampal removal
- Lost the ability to form new declarative memories
- Normal in procedural learning

Essential for the conscious recall
of specific experiences from one's past (episodic memory)
of general facts about the world (semantic memory)

Hippocampal damage in monkeys

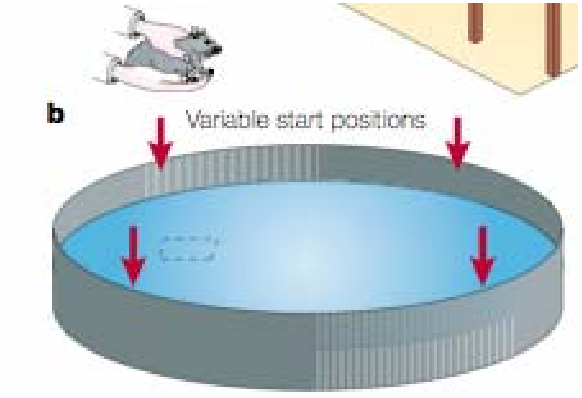


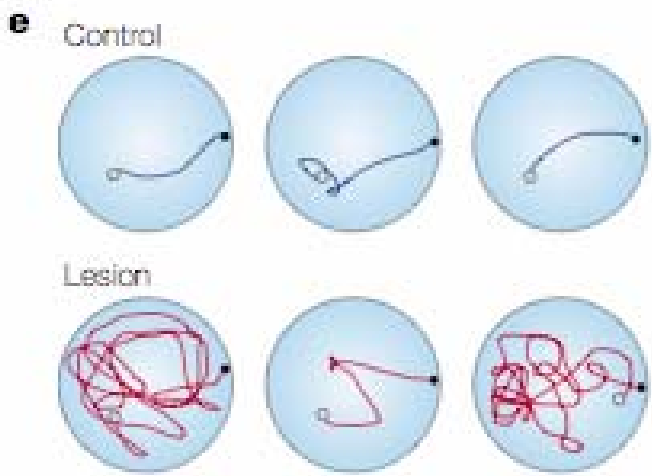
(Malkova & Mishkin, 2003)

- The hippocampus maintains the memory (>15min)
- Task Procedure:
  - Delayed nonmatching to sample, retention of object discrimination, pattern discriminatin
  - Example : an object-place associative memory task,

Selective loss of declarative memory (episodic memory)

Hippocampal damage in rodents



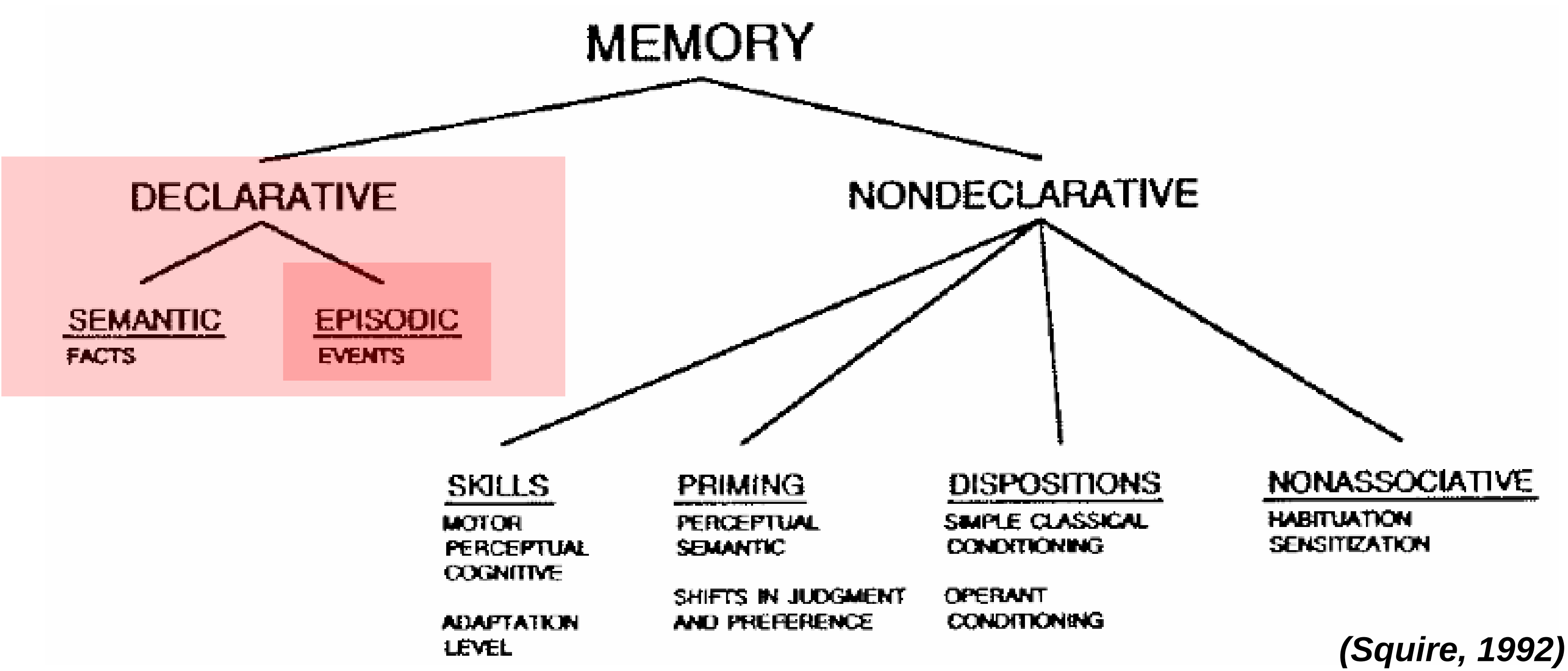


(Eichenbaum, 2001)

- Spatial learning or navigation
- Environmental memory called "cognitive map"
- "Water maze", odor discrimination, timing of events, cue-relation learning, non-spatial alternation, radial maze

Selective loss of spatial navigation system

Hippocampal memory



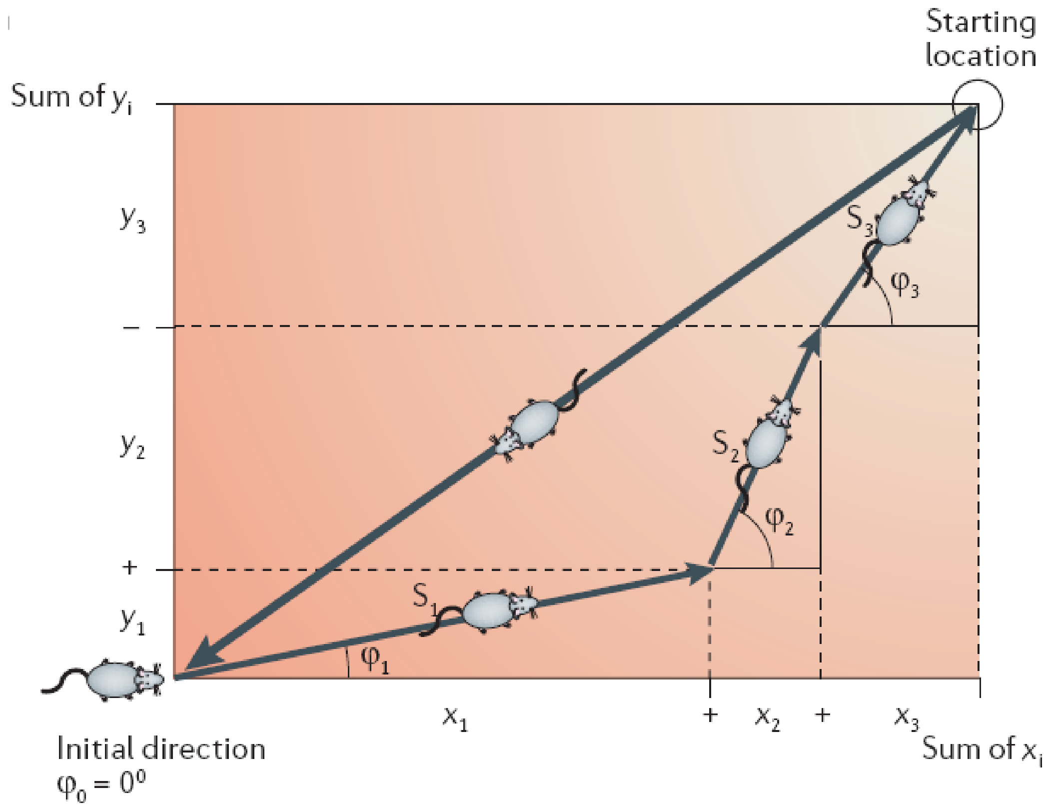
(Squire, 1992)

- All these medical observations stress the importance played by the hippocampus in Cognitive and behavioral role (function in memory)

The hippocampus for path integration … a metric?

- Mittelstaedt and Mittelstaedt 1980

(gerbil looking for her childs in the dark)



Questions

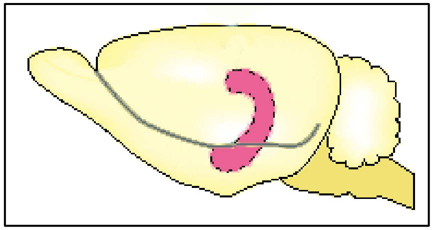
- The Hippocampus for episodic memory
- The hippocampus for path integration → definition of a metric

→ ***HOW ?***

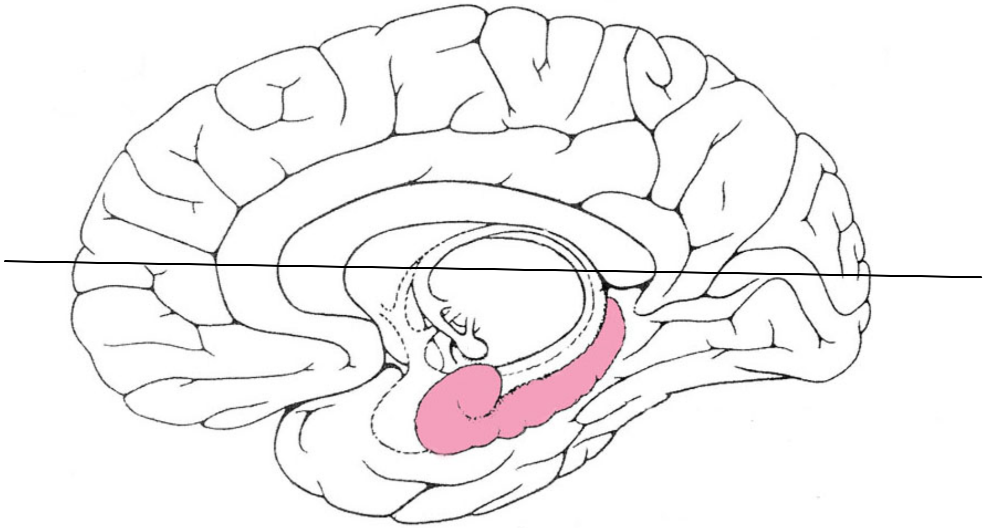
How the Hippocampus
-1- Anatomy

Anatomical structure: the hippocampal formation

rats

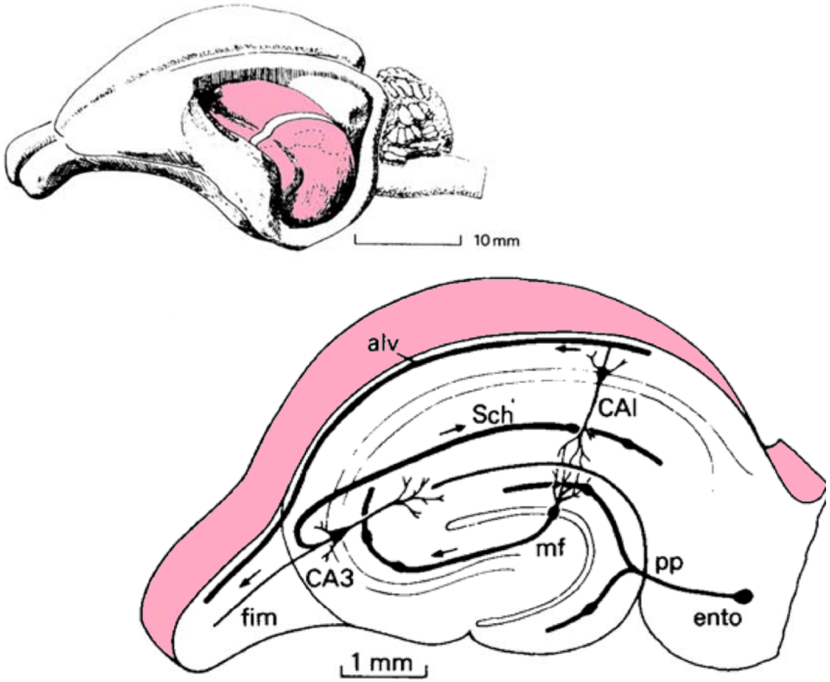


human

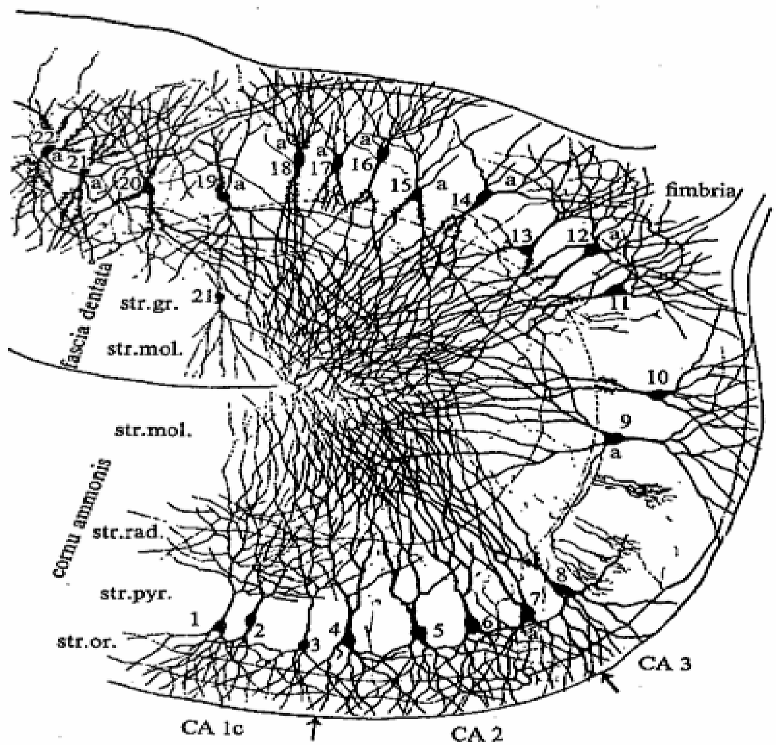


- Limbic system
  - Basal Ganglia (heart beat
  - Amygdala
  - Hippocampus (Dentate Gyrus – CA3 – CA1 – Subiculum)
- All mammalian brains have similitude in their hippocampus

Anatomical structure: the laminar structure



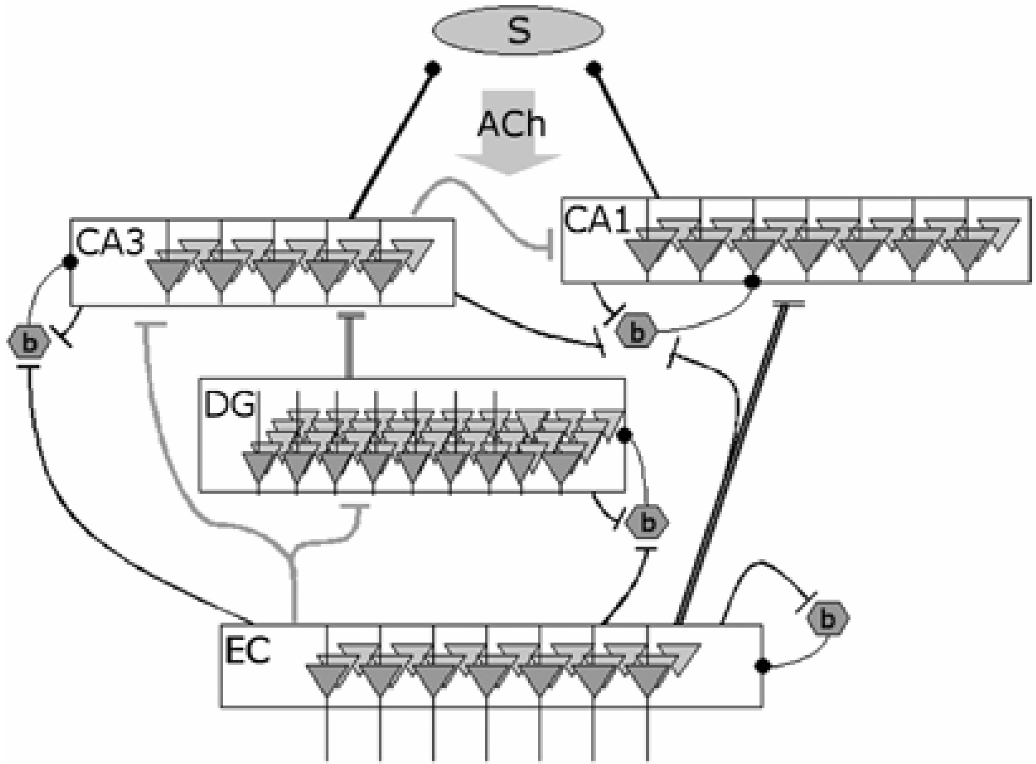
(O'Keefe & Nadel, 1978)



- Three-layered structure → old architecture
- Massive dendrites …. Including a massive number of recurrent connections

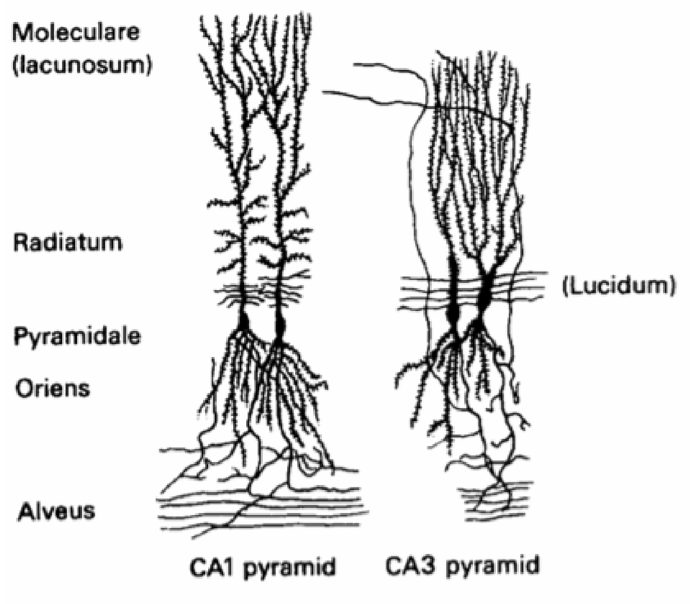
- O'Keefe & Nadel,1978,http://www.cognitivemap.net/

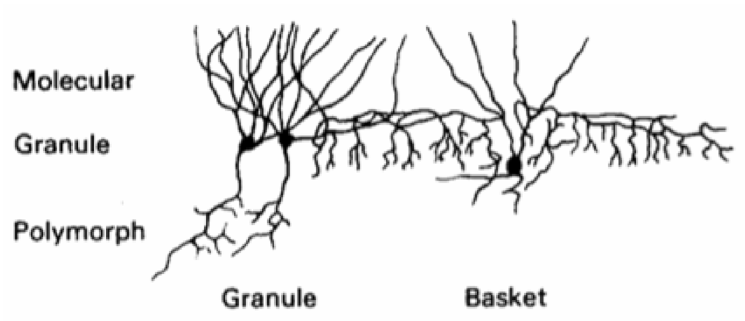
Connectivity in the hippocampus



- Closed circuit
- EC, DG, CA3, CA1, SUB, EC

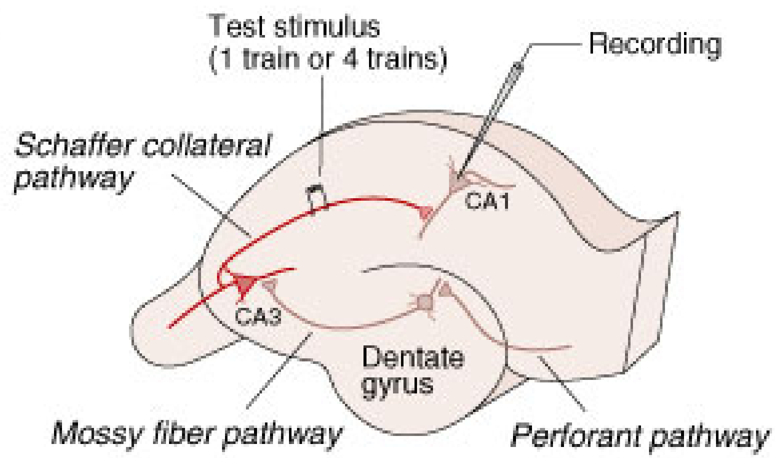
Different kinds of neurons



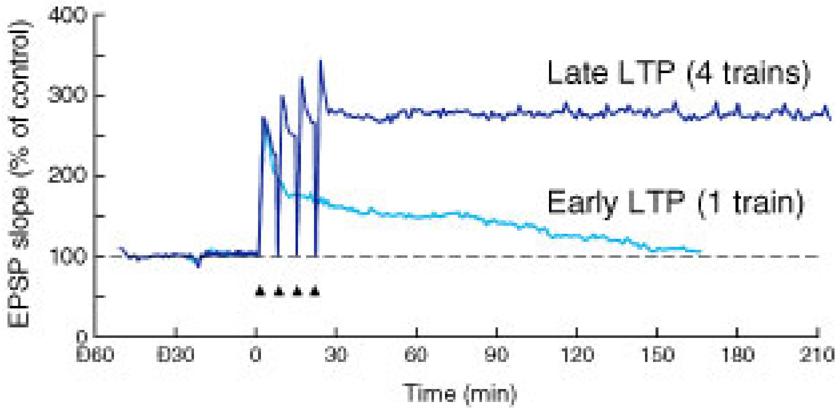


- Pyramidal – interneuron system
  - → Networks with 2 populations
    - Excitatory neurons (principal neurons: pyramidal and granule cells)
    - Inhibitory neurons (interneurons: basket cells and … more than dozens of different cells)
  - → Interneuron for global inhibition

Learning: Long-tem potentiation



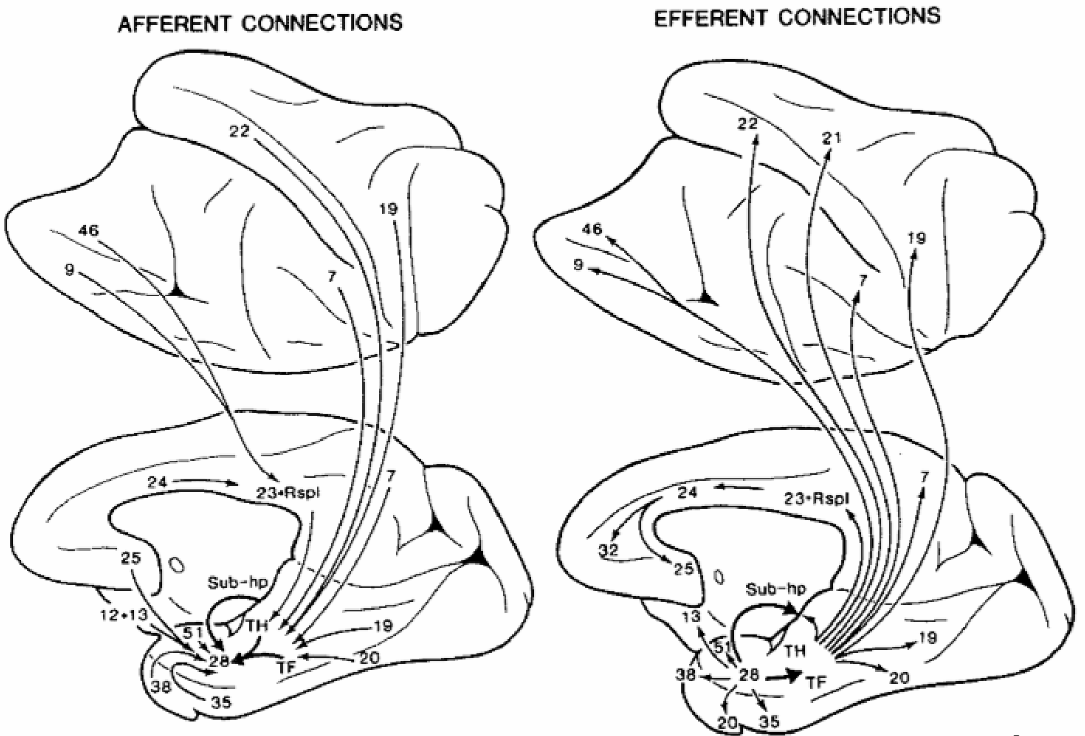
The early and late phases of LTP in the Schaffer collateral pathway



Kandel et al. (2000) *Principles of Neural Science*:New York

- A single train of stimuli for one second at 100 Hz elicits an early LTP, and four trains at 10-minute intervals elicit the late phase of LTP. The early LTP lasts about two hours and the late LTP lasts more than 24 hours.

Cortico-hippocampal connectivity



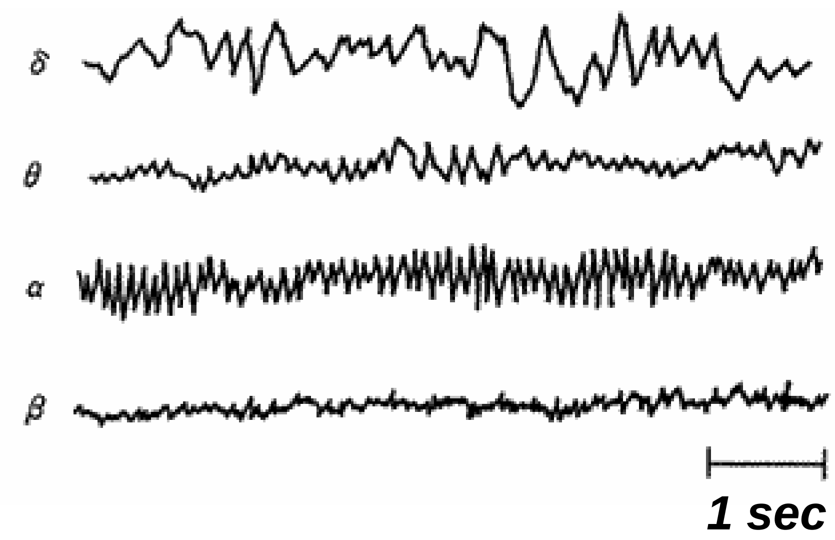
(van Hoesen, 1982)

- Entorhinal cortex : gate of the hippocampus to the neocortex
- These neuroanatomical evidences support that the hippocampus maintain the memory function.

– 2 –
Rhythms of the Brain

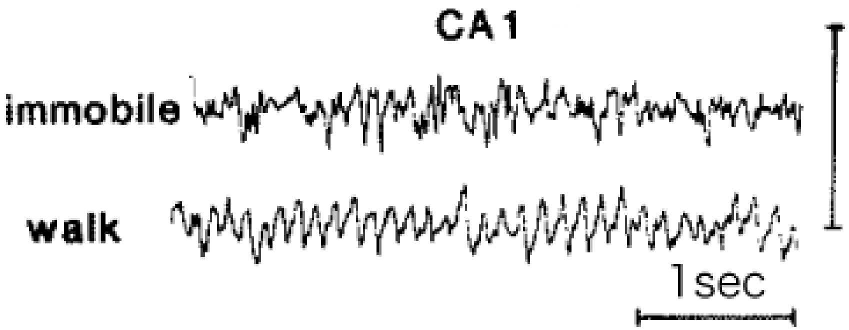
Rhythms of the Brain

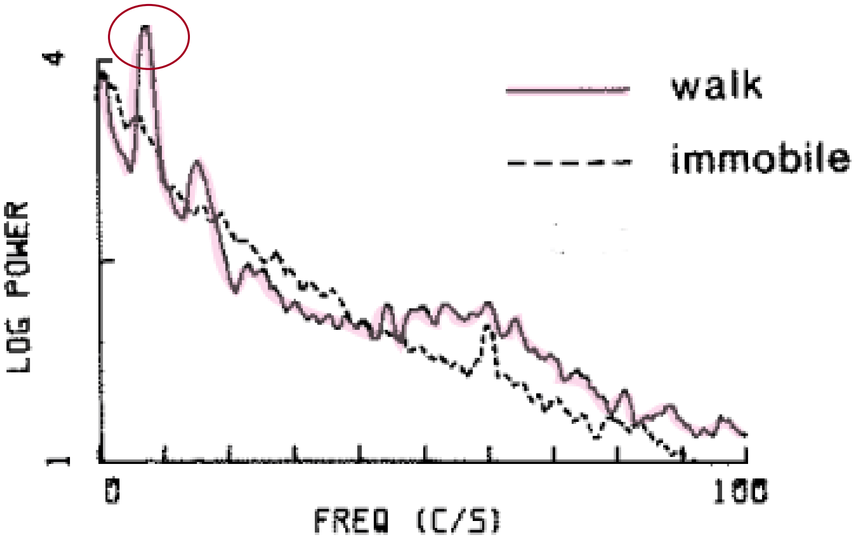
- Various behavior reflects a specific brain rhythm
  - 1-4 Hz Delta: sleep
  - 4-8 Hz Theta: memory
  - 8-12 Hz Alpha: resting
  - 12-20 Hz Beta: attention
  - 20-100 Hz Gamma: feature linking
  - 100-400Hz Sharp Waves:
    memory consolidation?



The hippocampal theta rhythm in cognition

LFP depending on the behavior





(adapted from Bland, 1986, Progress in Neurobiol)

- Important role in cognition
- Kahana: human navigation

Rat: locomotion

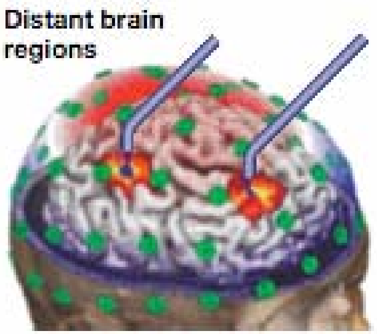
Rabbit: alert

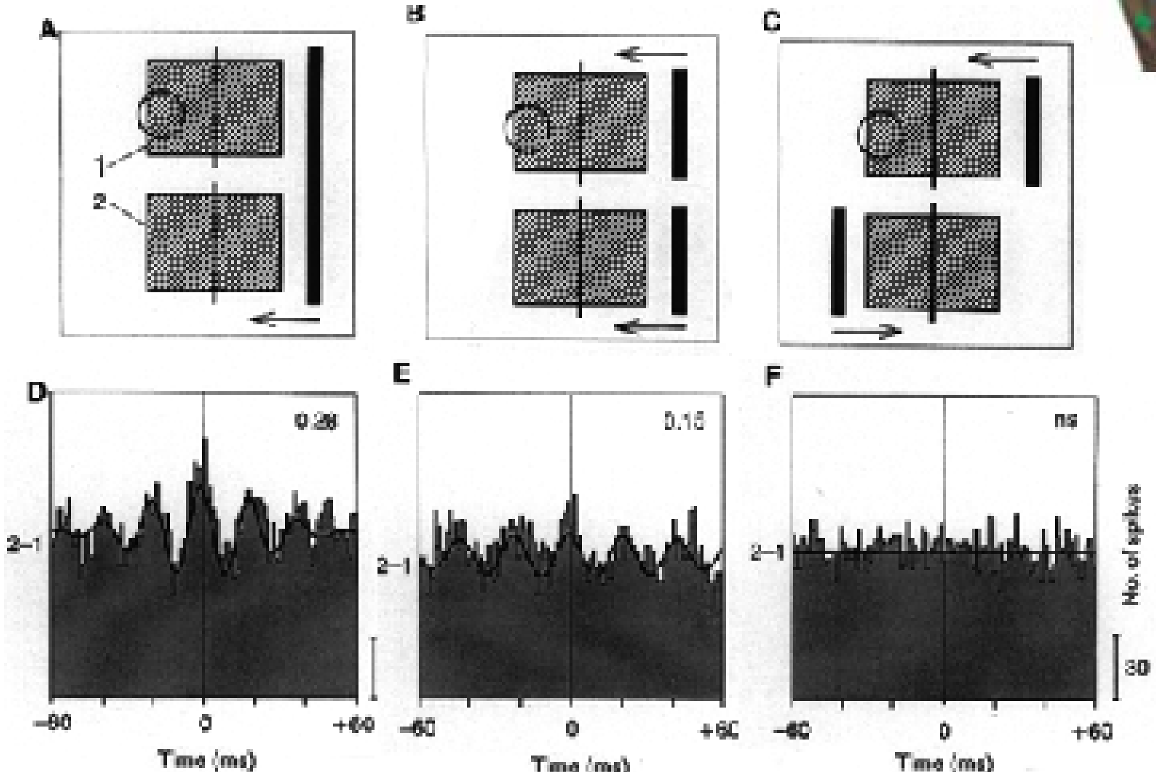
Human : memory formation

Rhythm and synchronization

- The binding problem (Singer)

- Example for Visual Cortex cells





Gamma synchronization between cell1 and cell2

(Engel et al., 1992, Trends in Neurosci.)

-3-
Modeling and artificial neural networks

Historic: the first steps

- 1943 MCCulloch & Pitts : proposition of the formal neuron
  - abstraction of the physiological neuron → first wave
  - Goal: the brain is a Turing machine

  "Plus nous apprenons de choses au sujet des organismes, plus nous sommes amenés à conclure qu'ils ne sont pas simplement analogues aux machines, mais qu'ils sont machine."

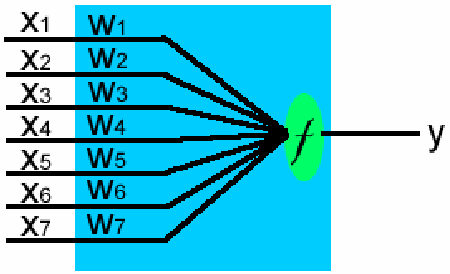
- 1949 Hebb: link between behavioral conditioning and synaptic reinforcement

  → Non supervised learning

- 1958 Rosenblatt: Perceptron model
  - Two layer feedforward network inspired from the visual cortex
  - First artificial system capable of learning

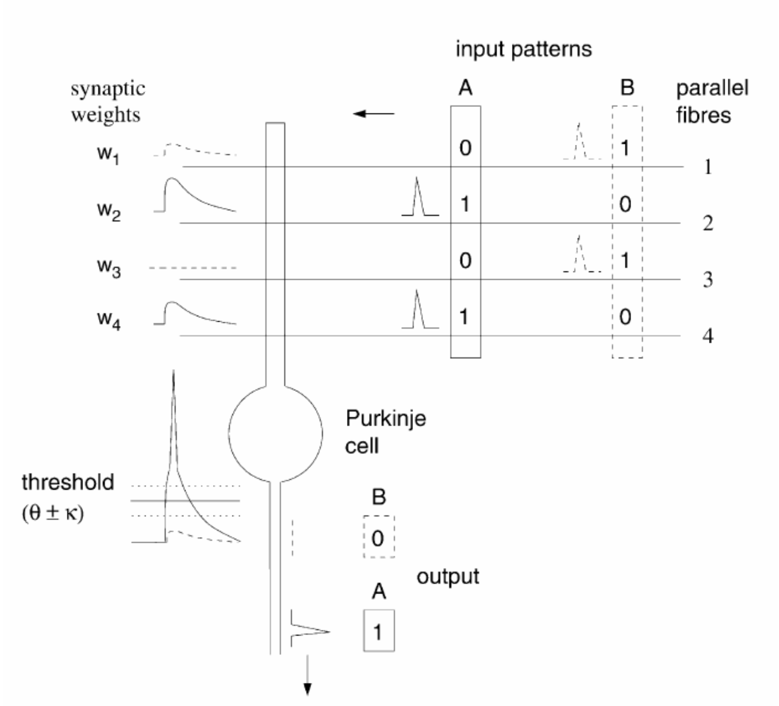
$$w(j)' = w(j) + \alpha(\delta - y)x(j)$$

δ is the expected output

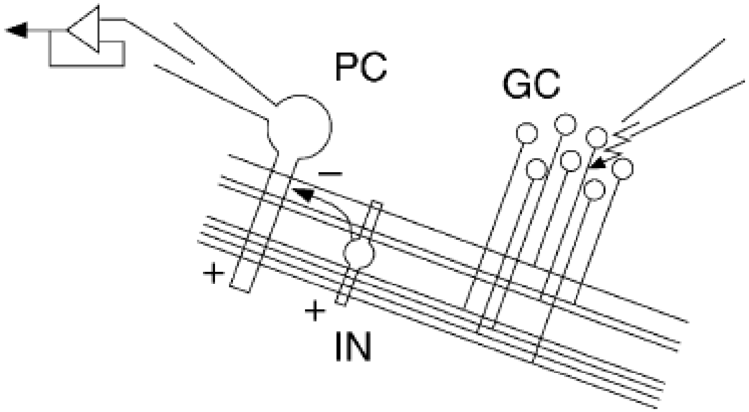


Historic: the perceptron in neuroscience

- Marr (1969): analogy between the cerebellum and the perceptron
  - statistical physics has a framework for analyzing the perceptron
  - Marr estimated that more than 200 associations could be stored



150 000 granule cells



Gardner 1985: detailed mathematical analyze of the maximum capacity (at the thermodynamic limit)

Historic: the perceptron in neuroscience

- Masao Ito (1982) confirmed the plasticity of the granule cell-Purkinje cell synapses

- Nicolas Brunel (2004) analyzed the weight distribution of the learned granule cell-Purkinje cell synapses
  - Assumes that both inputs and output are binary and that synaptic inputs sum linearly
  - Verify these assumptions experimentally: due to feedforward inhibition, only coincident granule cell inputs can excite a Purkinje cell effectively. The coincident inputs sum reasonably linearly.
  - The mathematical analyze shows that near the maximum capacity, the majority of synapses should be silent, the rest of the weights follow a monotonic weight distribution.

Historic: decline and new boom

- 1969 Minsky & Papert: severe critic of the Perceptron
  - No way to learn the logical function XOR

  ➔ 13 years of crisis

- (1972 Kohonen → associative memories)

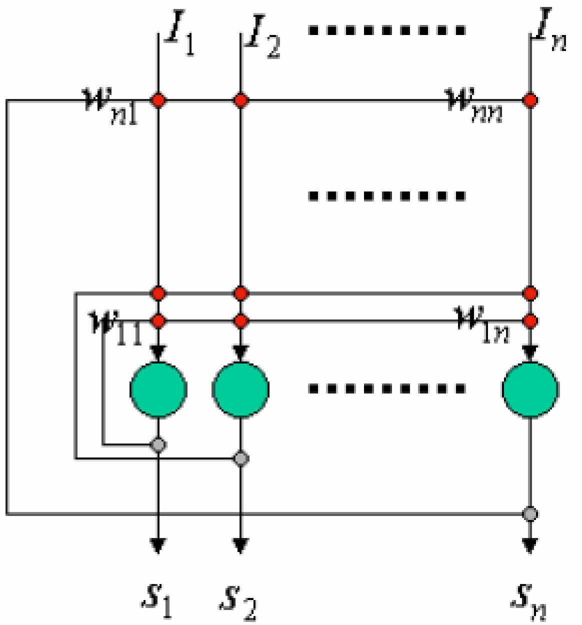
- 1982 Hopfield: dynamics of recurrent network
  - Hebbian learning → gap with cognitivist psychology
  - Mathematical model obtain from spin glass theory → gap with statistical physics

- 1985 Rumelhart → backproagation algorithm for multi-layer feedforward networks
  - Data analysis, classification

Historic: Hopfield networks
recurrent networks and memories

$$h_i(t) = \sum_{j=1}^{N} w_{ij} s_j(t) + \theta_i$$

$$s_i(t+1) = \mathrm{sgn}\left[h_i(t)\right]$$

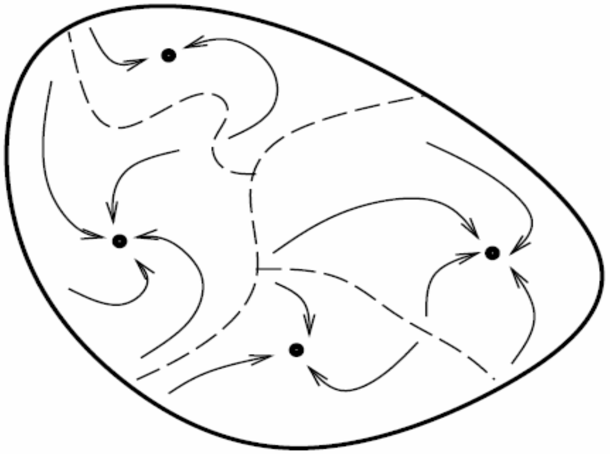


1. Statistical analysis using spin models
   → According to weight constrains (weights have to be symmetric), the dynamics iterates to stable patterns: fixed point attractors, i.e. '**memories**'

2. Hebbian learning of the desired attractors

$$\{\xi^\mu = (\xi_1^\mu, \xi_2^\mu \ldots \xi_N^\mu); 1 \le \mu \le M\}$$

$$w_{ij} = \frac{1}{N} \sum_{p=1}^{M} \xi_i^p \xi_j^p$$



Historic: Hopfield networks recurrent networks and memories

- Importance of the hippocampus in memory formation (Marr 1971)
- Rolls (1987): proposition that the CA3 network operates as an auto-associative memory system

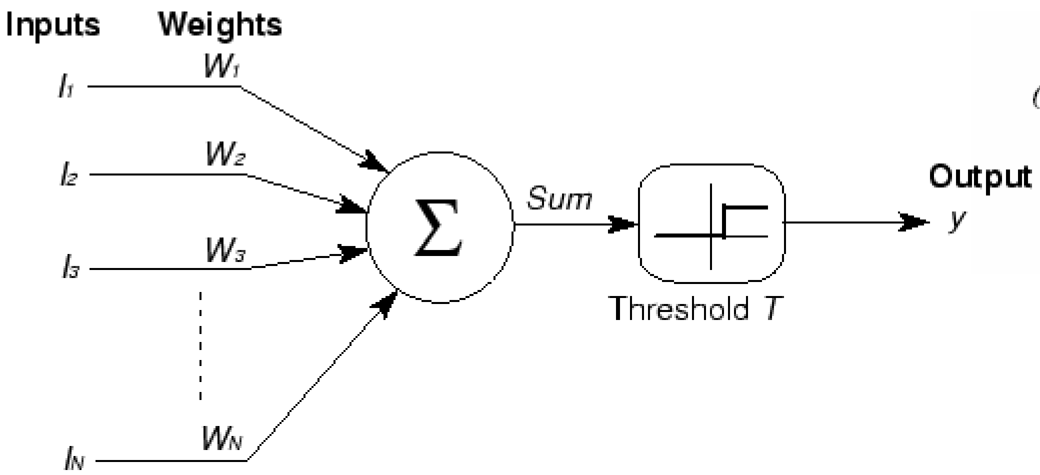
How to create a neural network

1. Definition of the formal neuron and its activation function
2. Design of the architecture (topology)
3. Definition of learning rules to modify synaptic weights

No rules

Formal neuron model

- Since Mc Cullogh and Pitts' neuron (digital input – digital output), known as the first generation neuron → many different types of units

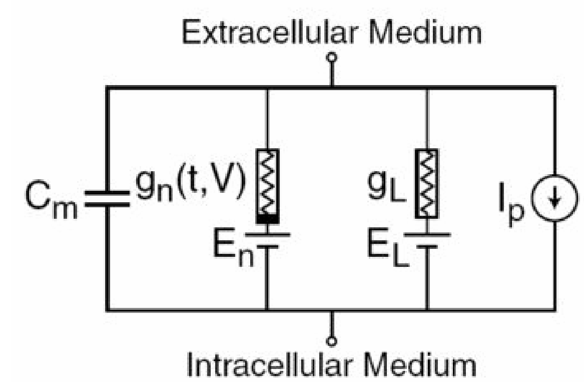


$$\sigma_i(t+1) = f(o_i(t))$$

$$o_i(t) = \sum_{i=0}^{N} w_{ij}\sigma_j(t) + \theta_i(t)$$

MCCulloch & Pitts 1943

- Hodgkin-Huxley Model (1952)
  - Developed the voltage clamp model
  - First mathematical model of the action potential
  - Problem 7 parameters to tune!!
  - Simplified form: the FitzHugh-Nagumo Model (1955)

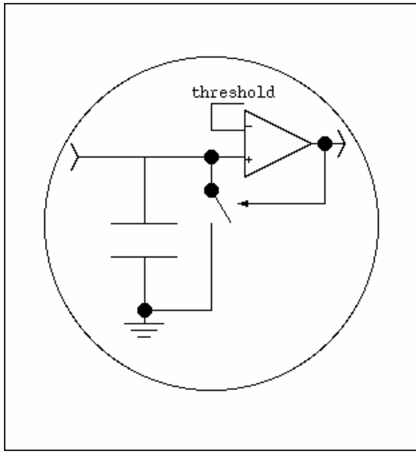


Temporal coding versus rate coding

- Exemple of spiking neurons: integrate and fire model

$$C\frac{dV(t)}{dt} = I(t)$$

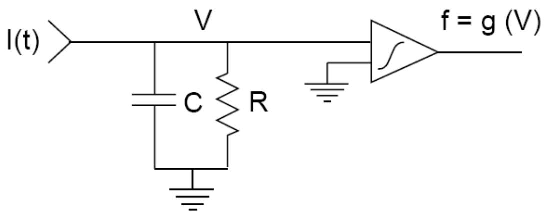
  - Subthreshold time course of the membrane potential determined by passive integration of synaptic inputs
  - Once the potential reaches Vth a pulse is triggered and the charge that has accumulated on the capacitance is shunted to zero



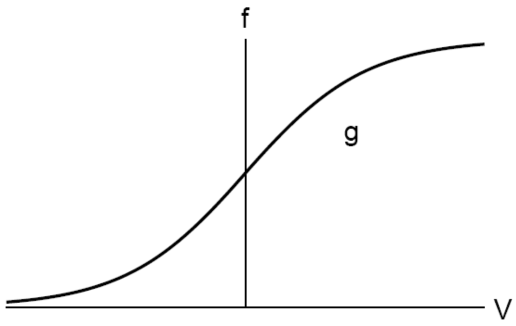
- Firing rate model

$$C\frac{dV(t)}{dt} = -\frac{V(t)}{R} + I(t)\,.$$

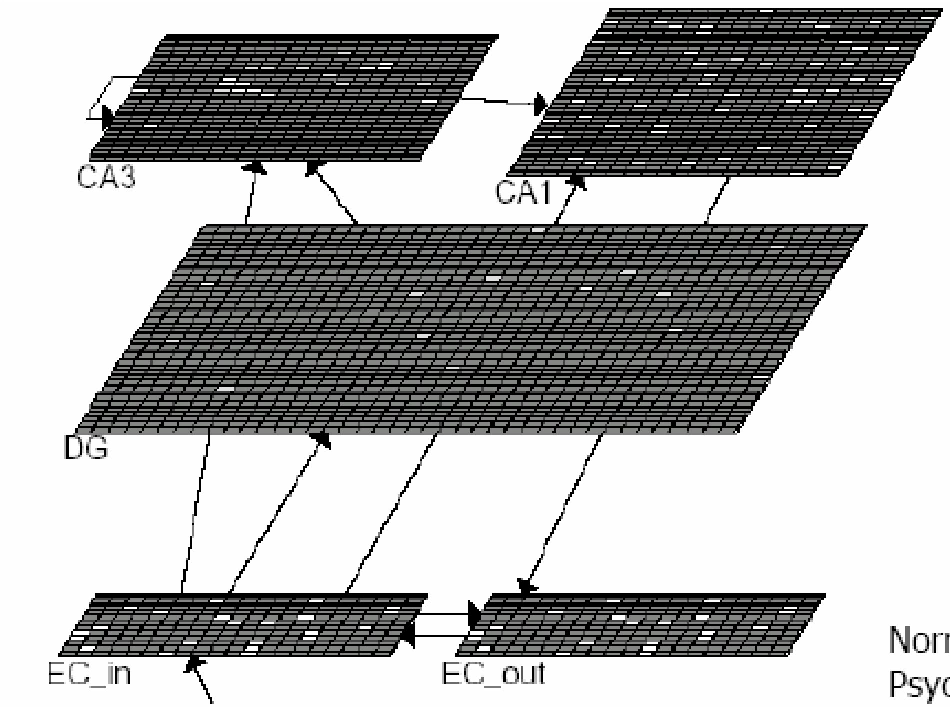
$$f = g(V)$$



  - Used by Hopfield
  - Used in many hippocampal memory model



Neuronal architecture



Norman & O'Reilly (2003)
Psych. Rev., 110, 611-646.

- Recurrent network vs. feedforward networks
- Fully connected vs. sparse connections, small world networks
- Type of connections: excitation vs. inhibition

Legacy of David Marr

- how functional groups of neurons within the hippocampus and neocortex interact, store, process, and transmit information

- But before all:

  "… Marr's work provided a solid proof that a good theory in behavior and brain sciences need not have to trade off mathematical rigor for faithfulness to specific findings. More importantly, it emphasized the role of explanation over and above mere curve fitting, making it legitimate to ask *why* a particular brain process is taking place, and not merely what differential equation can describe it." (***Edelman***)

-4-
Computational Models

Rat

no subject … information

precise data acquisition (electrophysiology possible)

Human

subject feedback

less precise data acquistion (non invasive techniques)

-4.1-
Rat Hippocampal models

Path integration models

Memory models

1: Place cells - Hippocampal cell firing has place selectivity

Firing rate encode “where I am”

OKeefe 1971

Place cells

- Hippocampal pyramidal cells have place field property (Okeefe&Dostrovsky 1971);
- In one environment, 10 to 20 % of ca3 pyramidal cells fire, each cell firing at different locations;
- The environment is fully covered by place fields

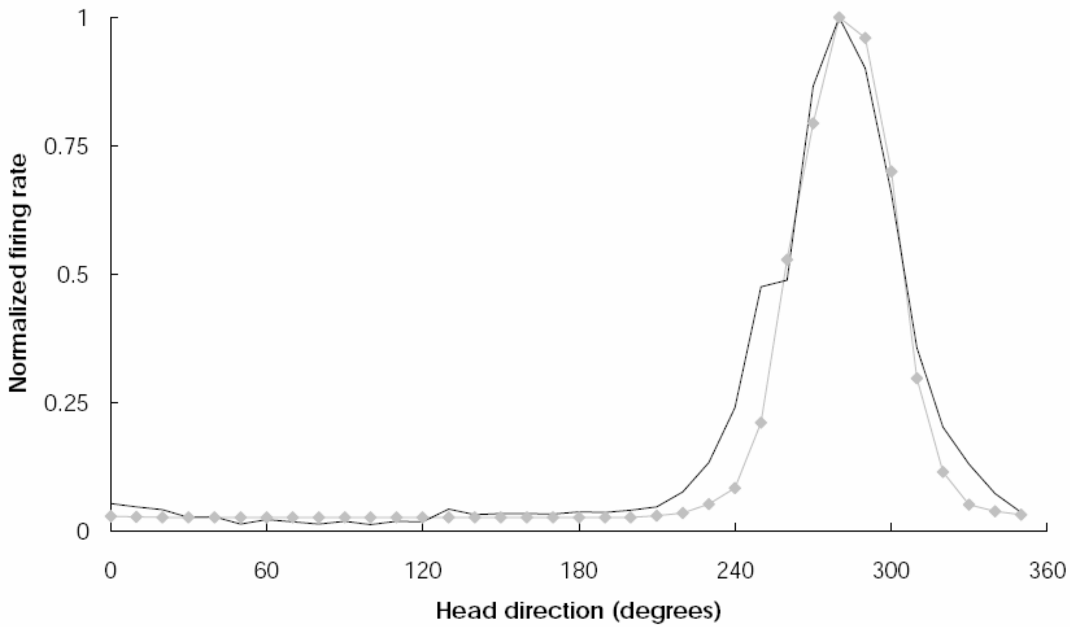
- Cognitive map theory:
  - The environment is represented by a cognitive map
  - The hippocampus plays an important role in spatial navigation and in path integration

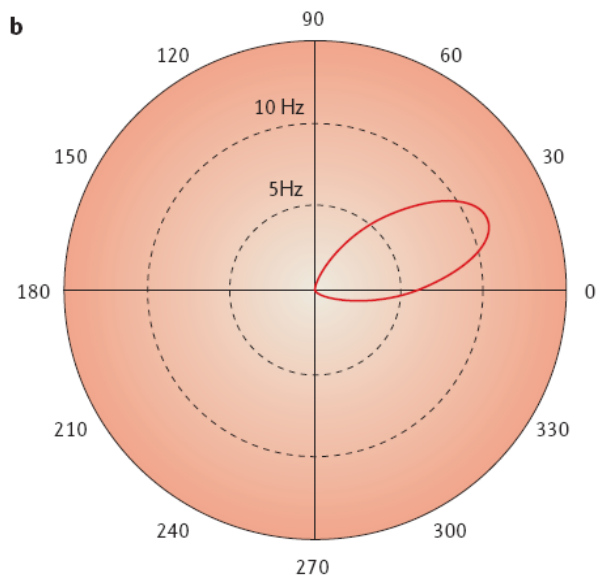
(*OKeefe-Nadel 1978*)

2: Head direction cells (Subiculum)

Ranck 1985

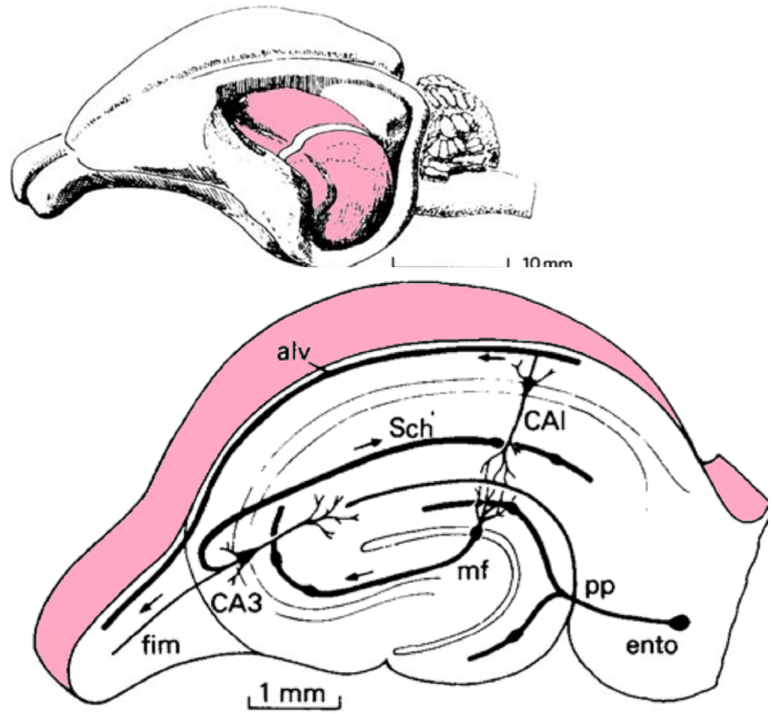
- Discovered in the postsubiculum (Ranck *et al* – 1985), also present in the anterior thalamic nuclei
- Characterized by a triangular tuning curves (Taube *et al – 1990)*

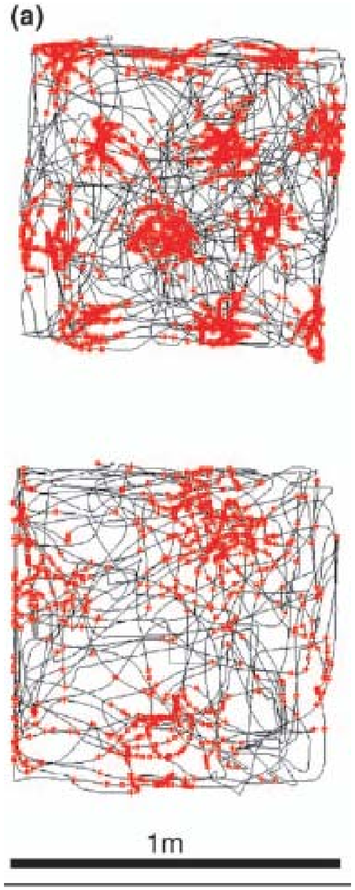




3: Grid cells (medial entorhinal cortex -mEC)

Moser 2003





Fhyn et al. 2003
Hafting et al. 2005

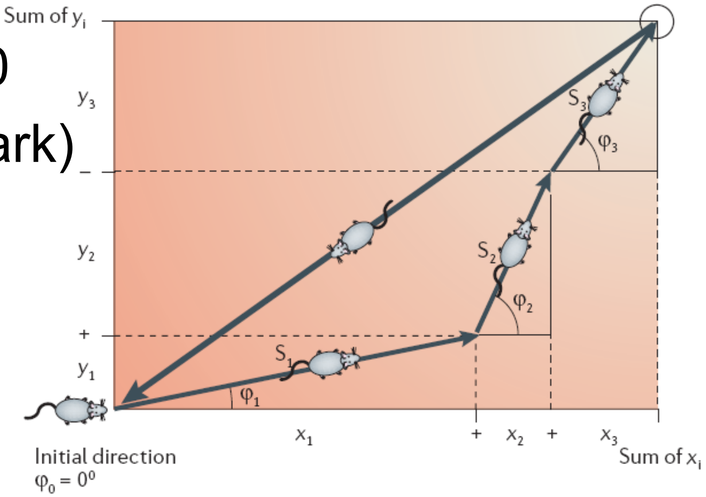
One synapse upstream the hippocampus, cells fire when the rat is at different locations in the environment, these locations having a grid like structure

-4.1.1-
Path integration models

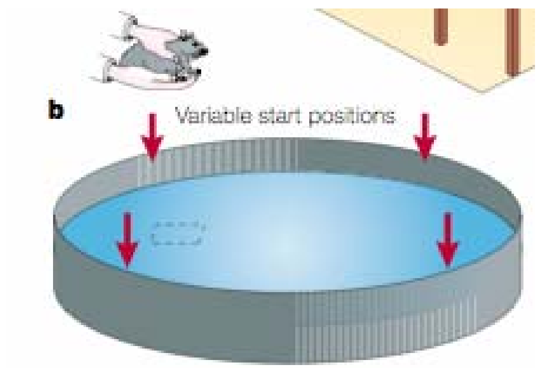
The hippocampus for spatial navigation and path integration

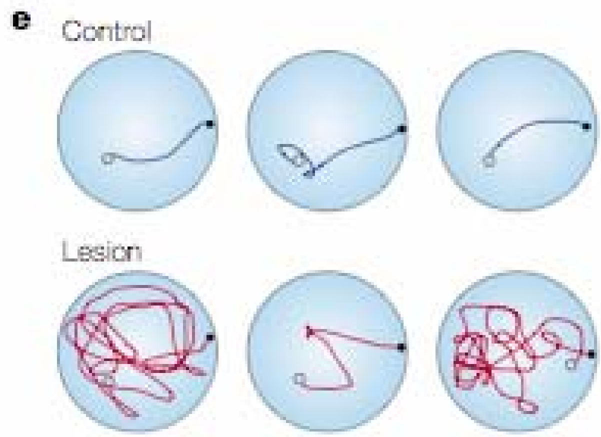
- Mittelstaedt and Mittelstaedt 1980

(gerbil looking for her childs in the dark)



- Morris et al. 1982



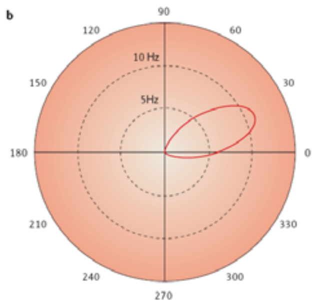


A model for retrieving its direction

Head direction cells → How to maintain directional tuning?

- 1985: discovery of cells having directional selectivity (Ranck et al.)

- Given an ensemble of head directional cells



→ How it is possible to avoid multiple cells having directional tuning to fire simultaneously?

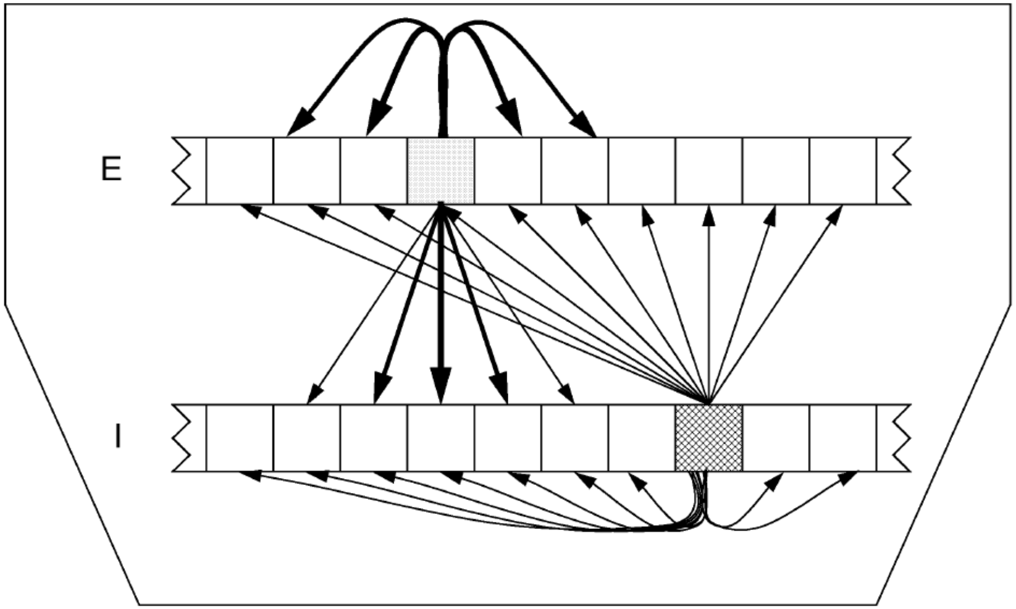
→ Most obvious solution : through attractor dynamics

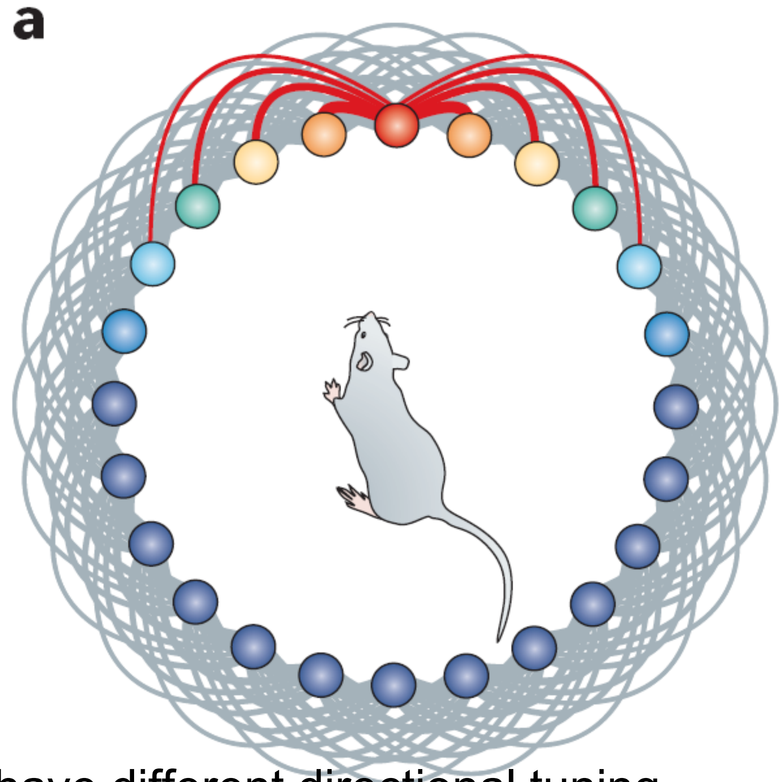
Head direction cells … an attractor network?

Skaggs et al. 1995
Zhang 1996
Redish & Touretzky 1996

- Local excitation
- Global inhibition

It defines an attractor module

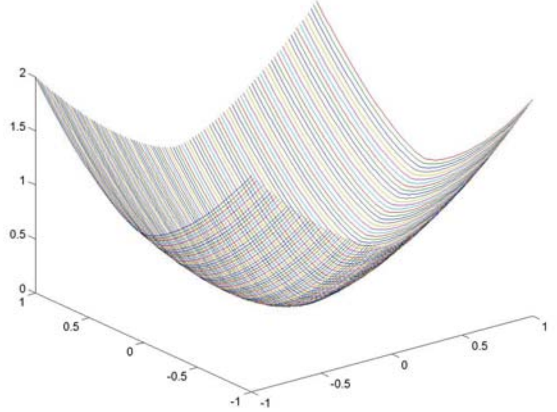




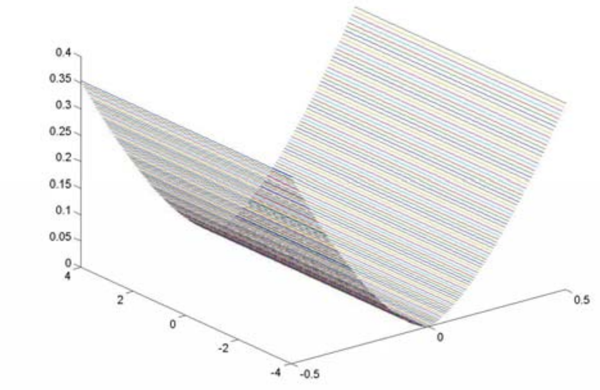
One clue: nearby head directional cells have different directional tuning which are preserved in different environments
This could be tested

This defines a “**continuous attractor**”

- Attractor dynamics
  - → one or more stable states determined by the weights of the recurrent connections between the units (neurons) in the network.
  - → Depending on the initial conditions, the network will end up in one of the stable states.
- Continuous attractor
  - → a stable activity state can be maintained over time and possible states can vary continuously.



Point attractor: the steady state is only the bottom of the bowl.



Line attractor: the system is stable on the whole valley.

Property of continuous attractors

- The steady states of the system (the memorized stimulus values) forms a continuous space, on which the system is *neutrally* stable

  → All directional tunings are equally stable

- The system can change smoothly its state, following a fixed path

  → The system can track smooth change of stimulus.

- Drawback: the neutrally stability implies the system is sensitive to fluctuations along the attractor space.

  → This, can be overcome through on-line coding.

All directional tunings are equally probable.
Only one direction can appear at one time

How to modify directional tuning

- When the rat rotates?

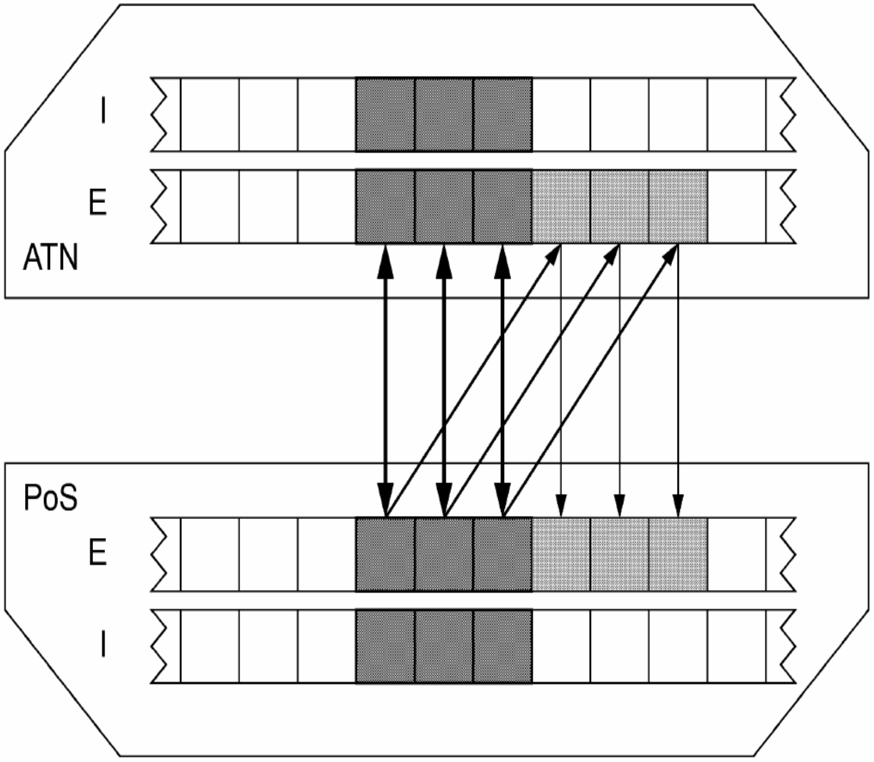
  → motion information must update the firing rates of head direction cells.

  → How?

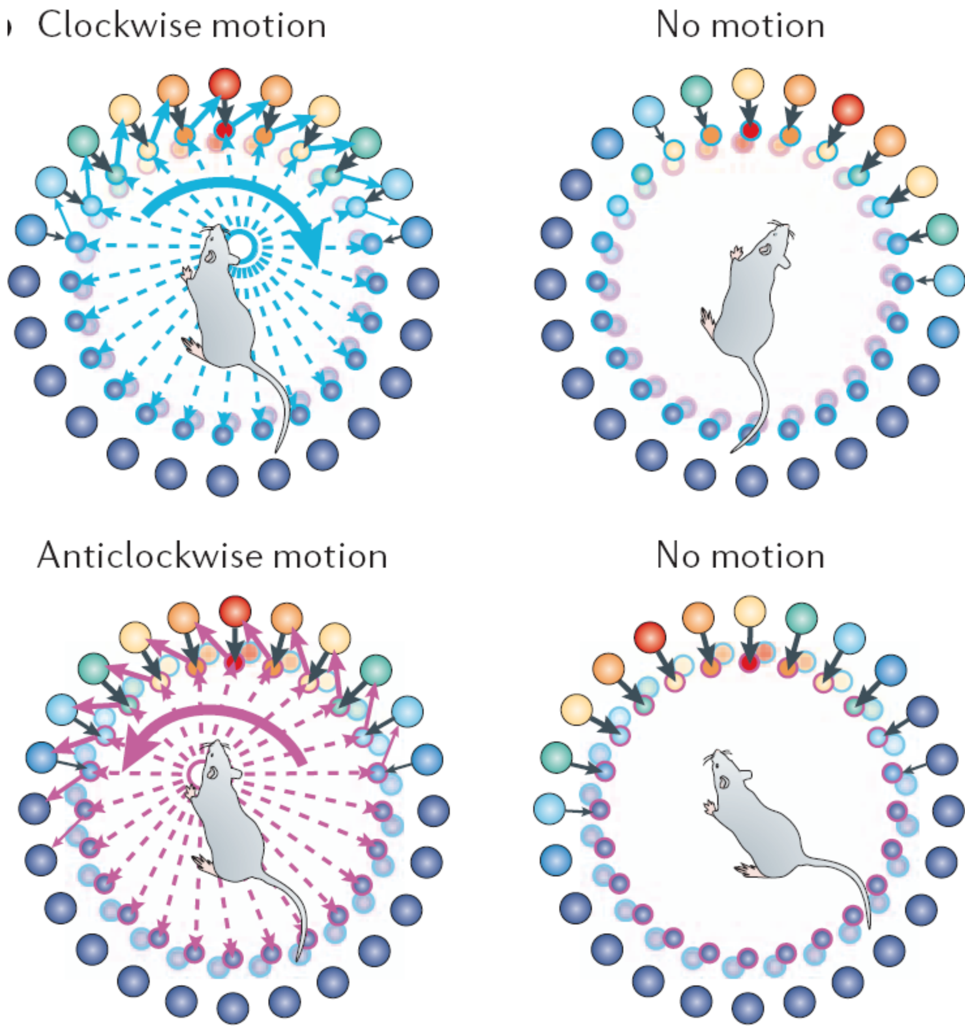
  - Visual motion cues → update based on observed angular velocity
  - Familiar landmarks → enable to correct velocity integration errors.
  - vestibular cells → enable to work in darness

- Slow rotation in the dark
  - Subthreshold input to the vestibular cells → the rat fails to update its head direction cells

How to modify directional tuning



Redish & Touretzky 1996



Skaggs et al. 1995
McNaughton et al. 2006

What kind of units

- Action potentials are Boolean events with infinitesimal duration.
- Postsynaptic potential (PSP) in neuron *i* has an instantaneous rise and exponential fall-off with time constant -->

$$\alpha_j(t-s) = \mathrm{e}^{-(t-s)/\tau_j}.$$

$$V_i(t) = \gamma_i + \sum_j w_{ij} S_j(t)$$

$$F_i(t) = \frac{1 + \tanh(V_i(t))}{2}$$

$$\tau_i \frac{\mathrm{d}S_i(t)}{\mathrm{d}t} = -S_i(t) + F_i(t).$$

Redish & Touretzky 1996

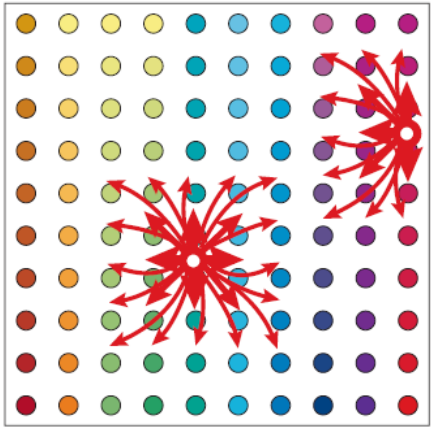
- Also implemented with classical spiking neurons (e.g. Brunel et al. 2003) and with rate models (e.g. Rolls et al. 1998)

Path integration

Two-dimensional attractor network

- A bump of activity of ‘CA3 cells’ emerge from interactions between
  - Local excitation (specified by the current environment)
    - → ***Extensive use of the CA3 recurrent connections***
  - Global inhibition

➔ It explains place cells !!

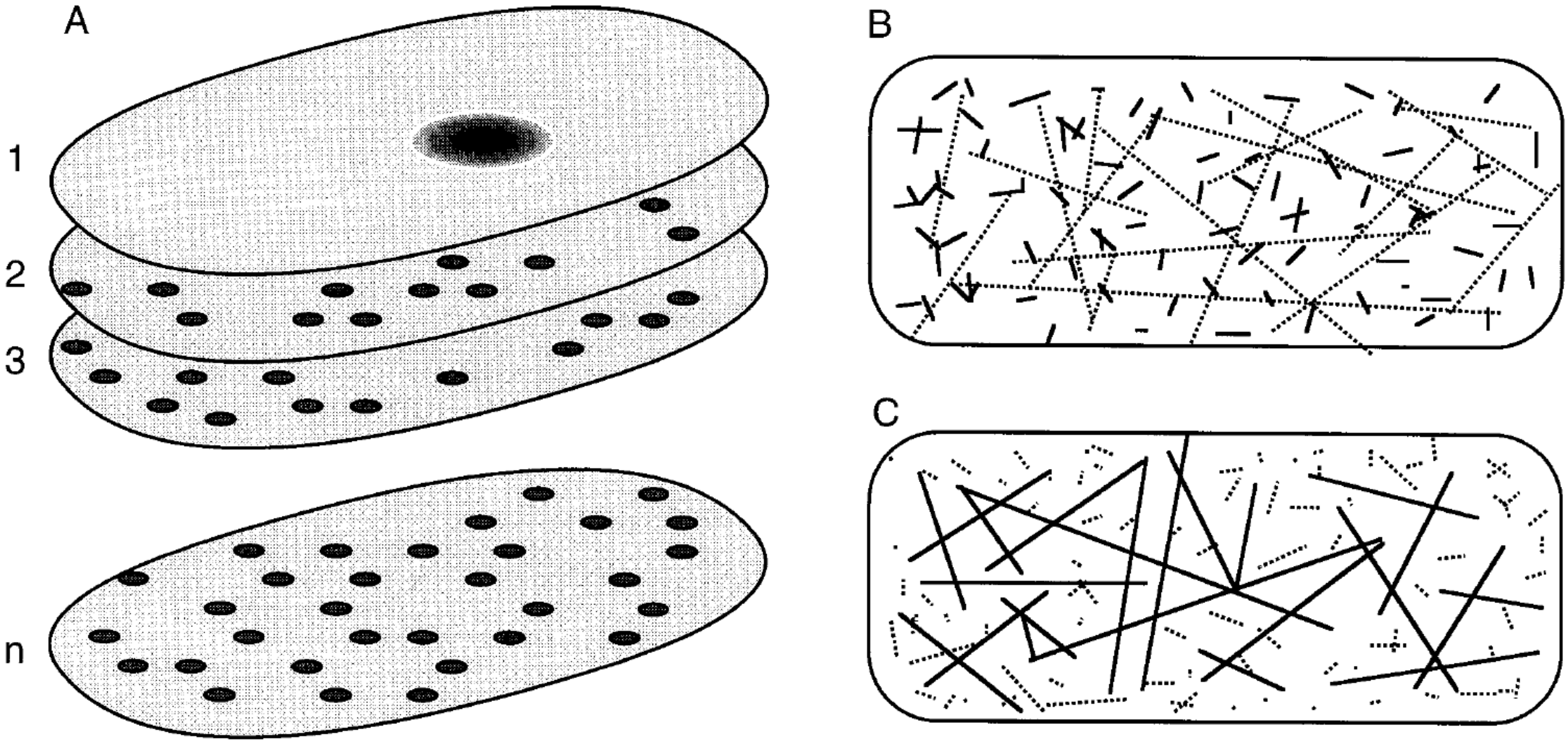


McNaughton et al. 1995
Samsonovich et al. 1996

Problems:
1/ Boundary problem (not known)
2/ Learning multiple environments → multiple charts

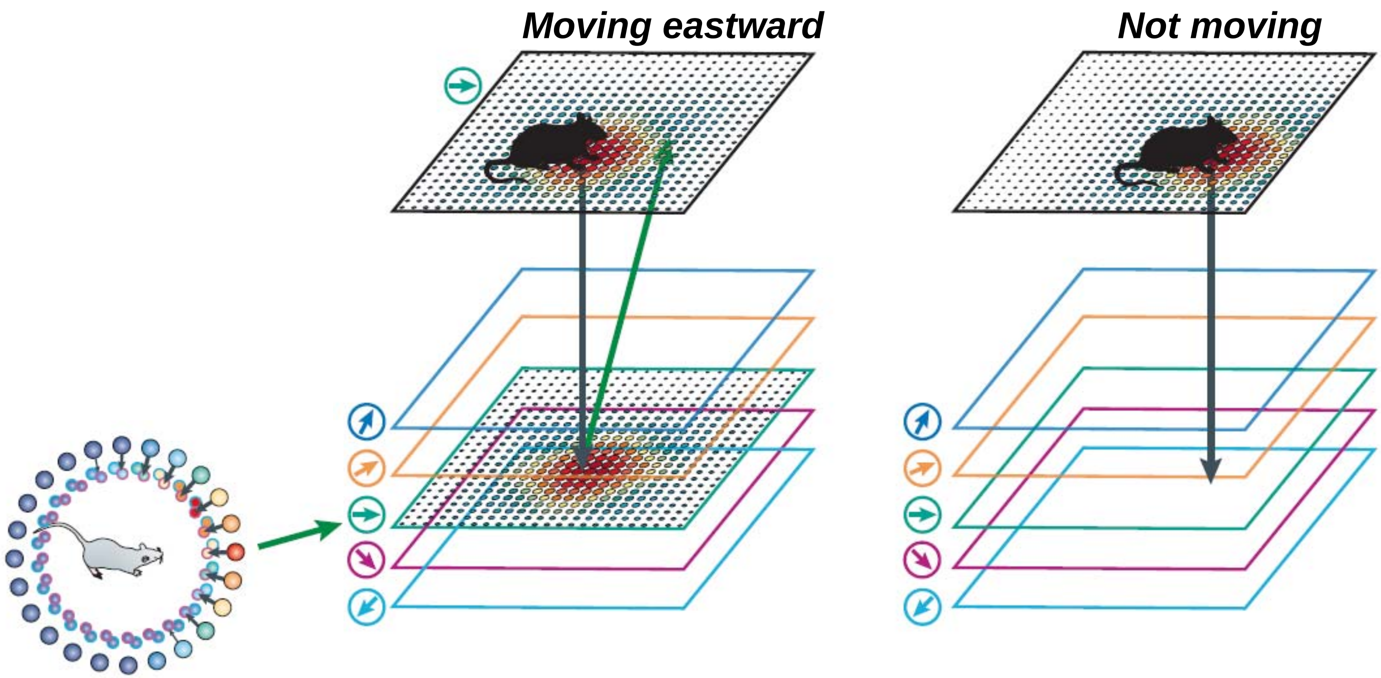
Two-dimensional attractor network with multi-chart

Samsonovich et al. 1997



Hopfield like capacity measure → 100 chart for the rat

Path integration network

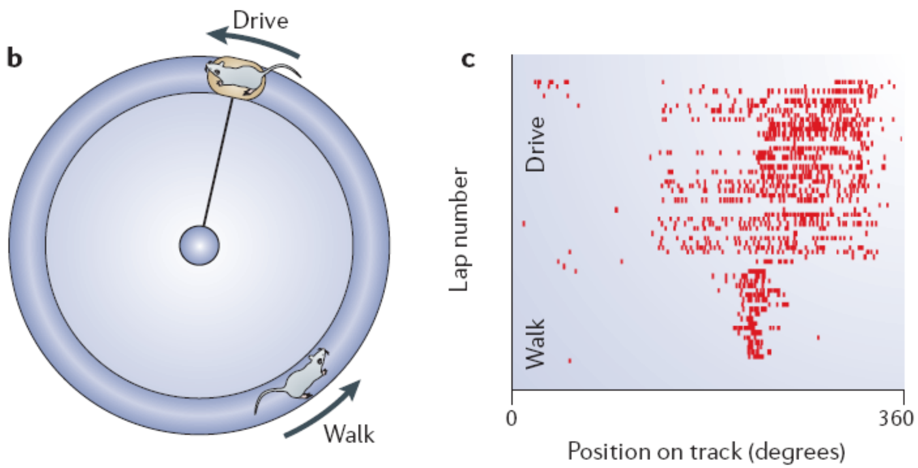


Activation if: speed and direction

- Continuous attractor network → any perturbation moves the attractor position
  1. The bump sends activity to N different hidden layers of cells
  2. Each layer receives input from head direction having different directional tuning
  3. Activity of these cells is suprathreshold only if the rat moves AND receives inputs from HD
  4. These layers project asymmetrically to the corresponding side of the cells in the attractor layer

Importance of speed

- This model predicts that place field size is controlled
  - Not by external inputs
  - But by the way the speed of the rat moves the speed of the bump across the attractor layer.
  - (this defines the scale at which space is represented in the brain)
- Importance of self-motion (VanderWolf 1966-1973, OKeefe 1983)



Terrazias et McNaughton 2005

The scale metric determined by speed

- The scale of hippocampal place fields
  - "determined by a movement-speed signal that is generated outside the hippocampus through a summation of components related to ambulation, vestibular activation and optic flow."

Maurer & McNaughton 2005

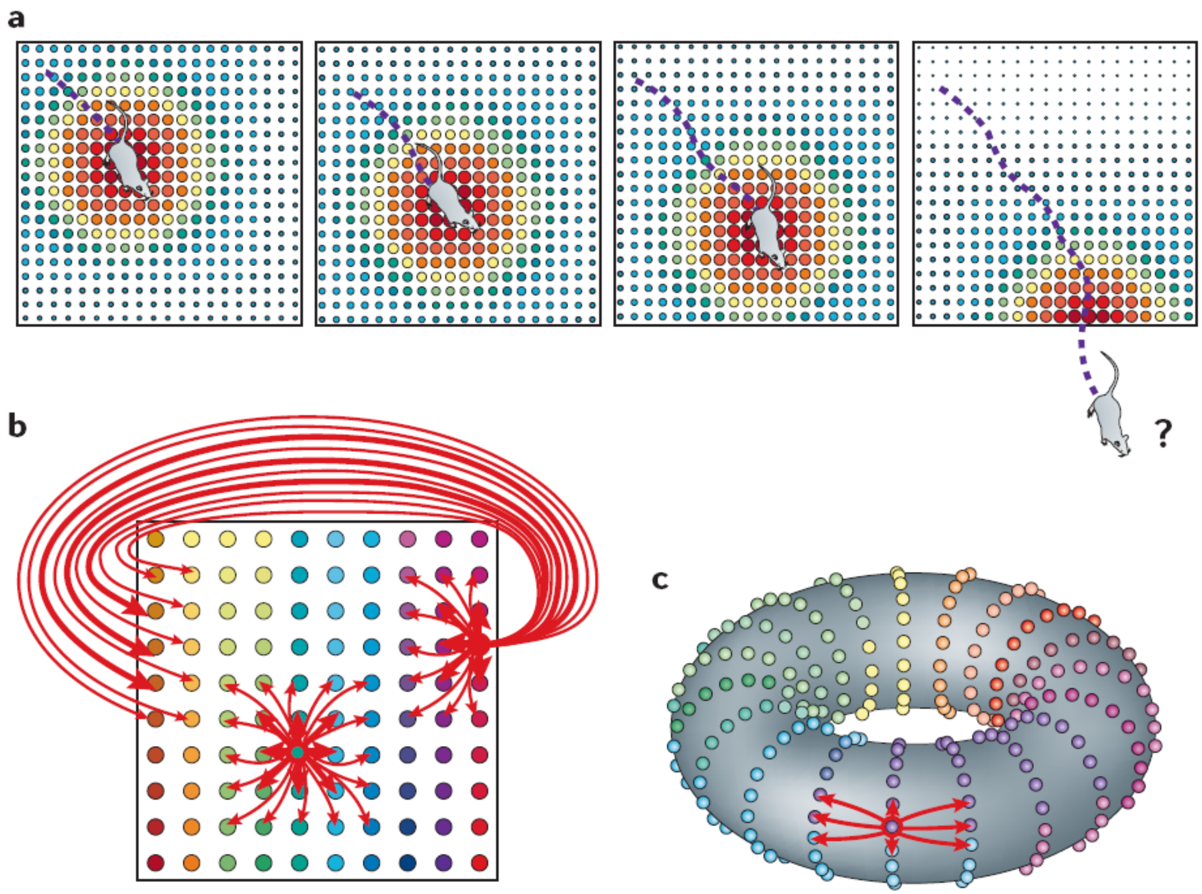
- The observed change in spatial scale along the septotemporal axis of the hippocampus
  - explained by a systematic variation in the gain of the motion signal.

→ confirmed by the observation that the function relating theta amplitude and relative firing rates of CA1 cells to running speed become systematically less steep as the recording location moves temporally along the septotemporal axis.

Hippocampal place cell assemblies are speed-controlled oscillators (Buzsaki 2007)

Boundary problems

- Among the many problems … only one was discussed, the boundary problem … solution : a torus!
  - But problem: predict periodic fields.

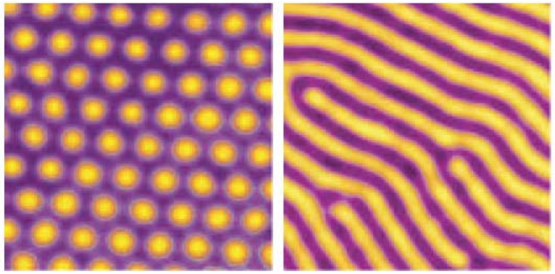


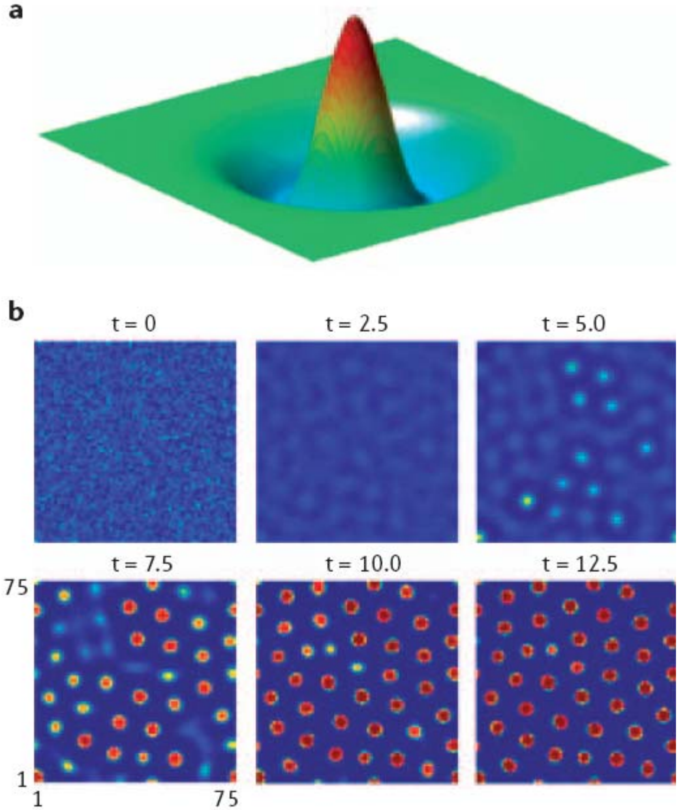
Grid cells solve the problem

- According to this model, the path integration
  - Is no more in a loop involving the CA3 network
  - Is in a loop involving the EC network

How to explain grid fields

- Alan Turing proposed the emergence of ‘Turing stuctures’:
  - Structures emerge spontaneously as diffusion-driven instabilities in a 2-component chemical reaction with activator and inhibitor.
  - The diffusion rate of the inhibitor MUST be larger than that of the activator;
  - Fundamental mechanism in morphogenesis



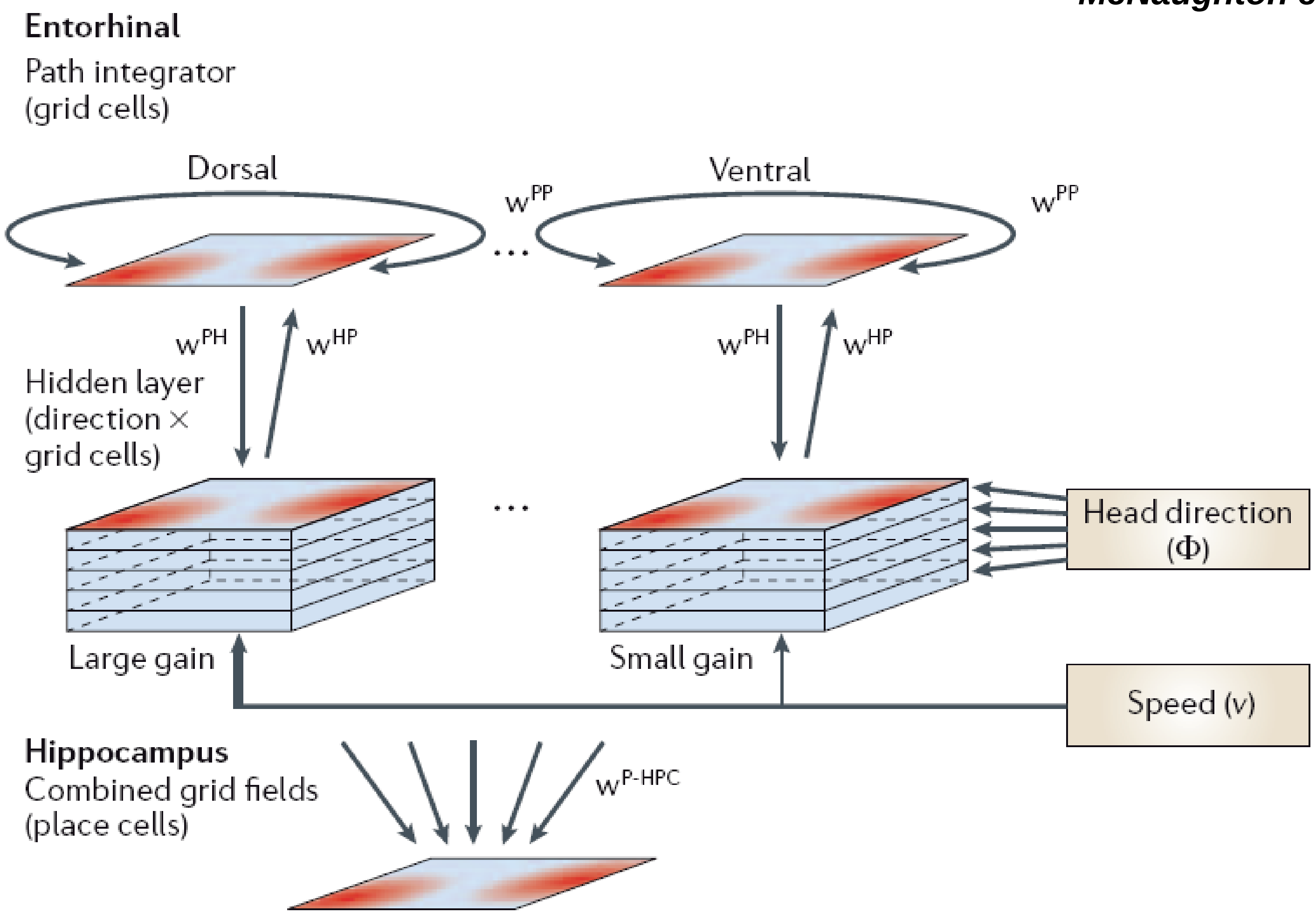


- In Neural network
  - Short excitation and longer inhibition
  - → Mexican hat → grid fields

Fuhs & Touretzky 2006
McNaughton et al. 2006

The full version of the path integrator

McNaughton et al. 2006

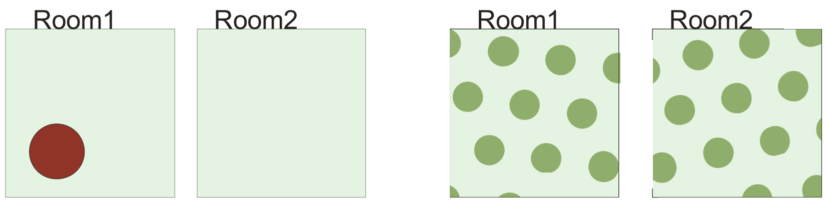


From entorhinal grid fields to hippocampal place fields

Solstad and Molser 2006
Rolls 2006
Molter and Yamaguchi 2007

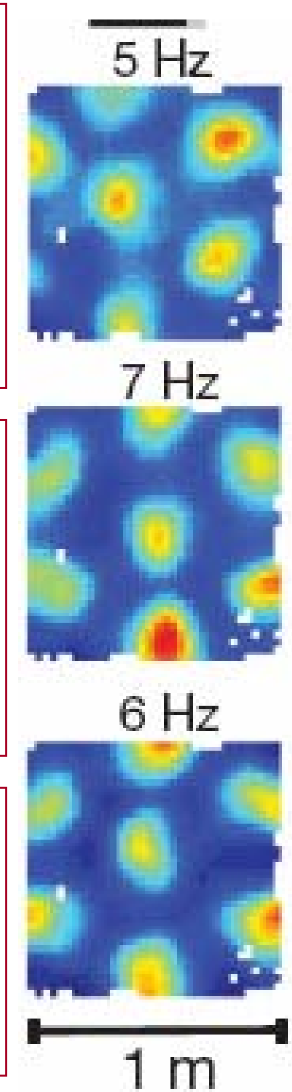
Grid cells in the medial entorhinal cortex (mEC)

- Place cells fire in some environments
- Grid cells fire in every environments



- Place cells are not related to each other (in some environments, their firing field can be overlapping while in other environments they are clearly separated, or inexistent)
- The relative offset of the spatial phase of grid fields for any two cells appears to be universal

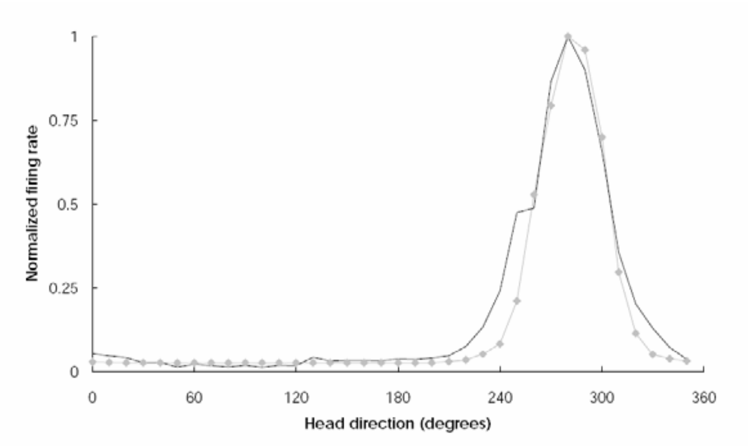
- Nearby grid cells have similar orientation and scale
- More distant cells have different orientation
- Along the dorso-ventral axis grid cells have different scales:
    - From 30 cm to 70 cm



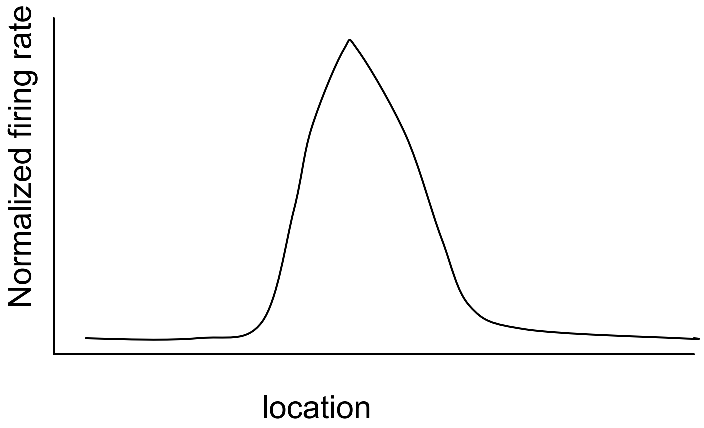
Using rate coding neurons

When the rat crosses a specific place field, or moves its head, corresponding place cells or head direction cells increase their firing rates

➔ suggest the possibility to use a rate coding mechanism to code these cells



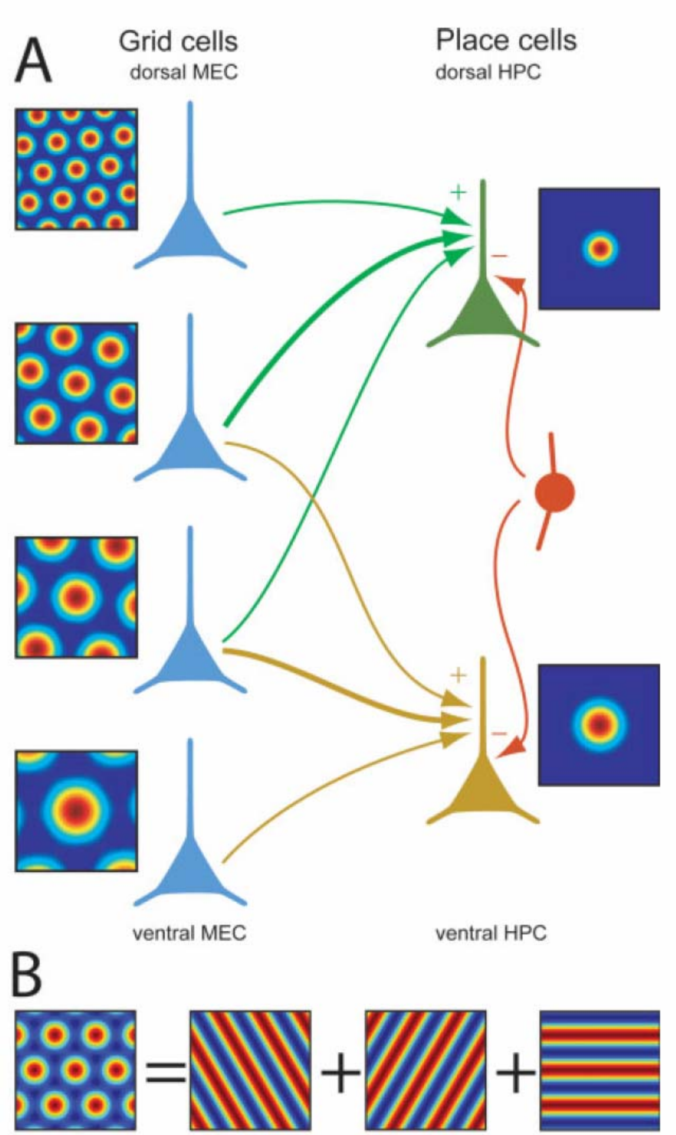
Head direction cell

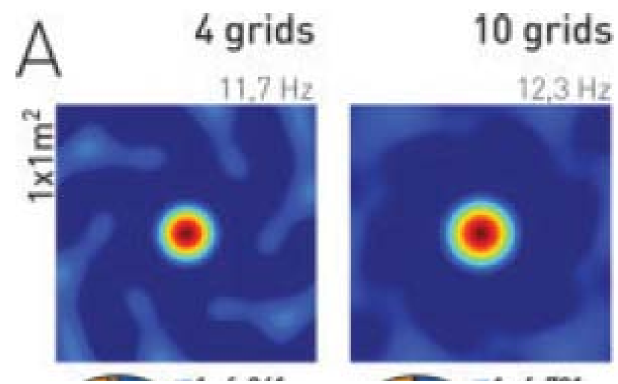


Place cell

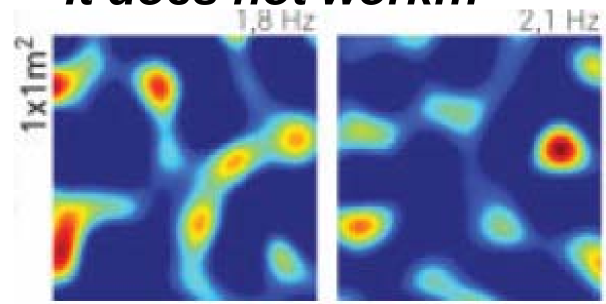
Superposition of Grid Fields

Solstad et al. 2006





But with random phase
It does not work!!!



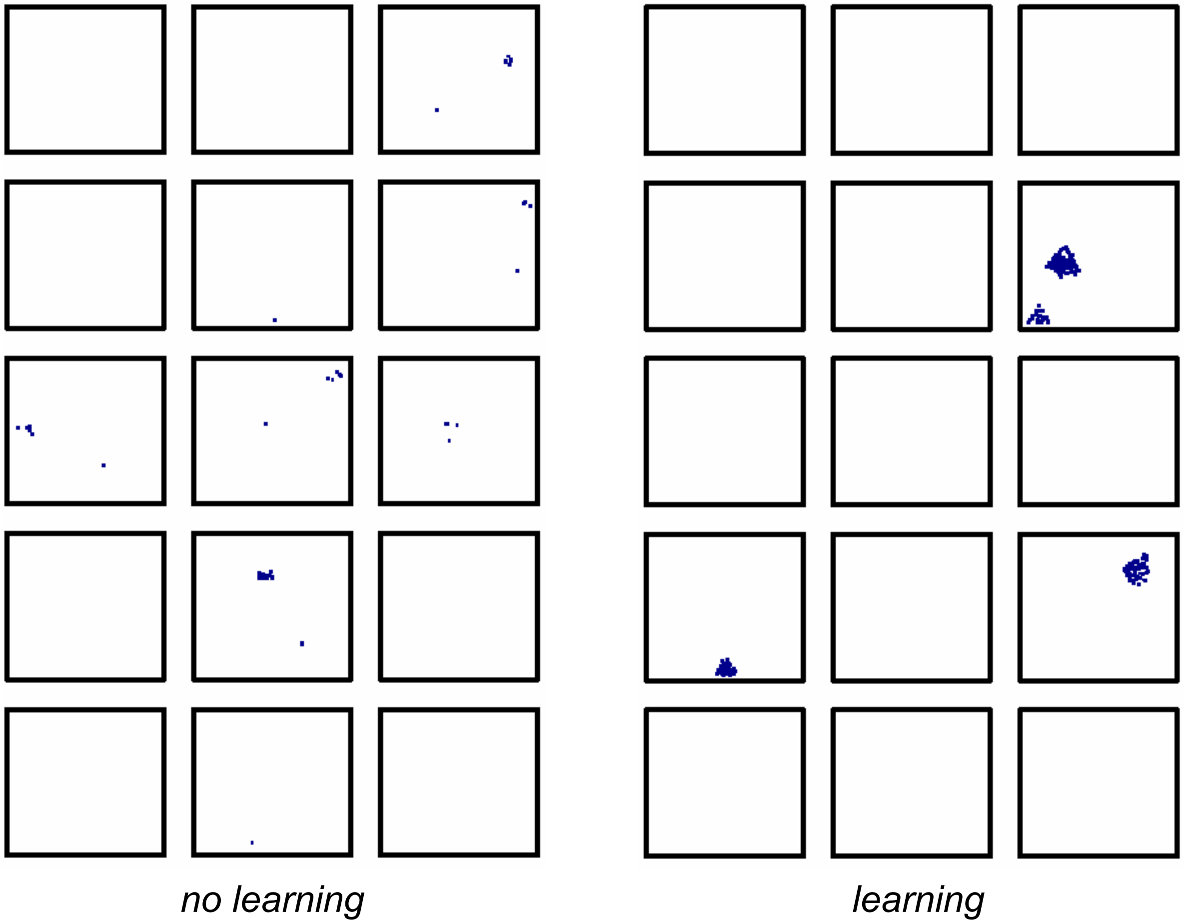
Competition and Learning

Rolls 2006

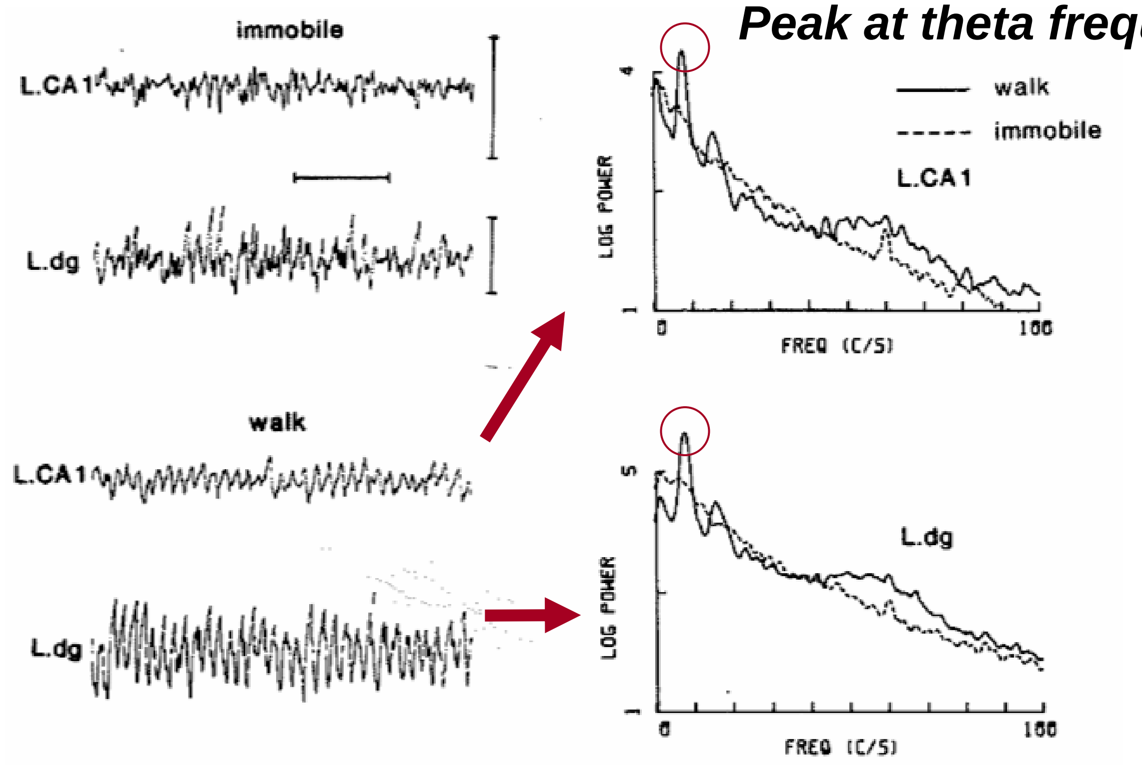
→ Learning should enhance this firing

→ Classical hebbian learning

$$\delta w_{ij} = k r_i^{\mathrm{DG}} r_j^{\mathrm{EC}}$$



What is missing? Theta rhythm?



– Important role in cognition
– Kahana: human navigation

Rat: locomotion

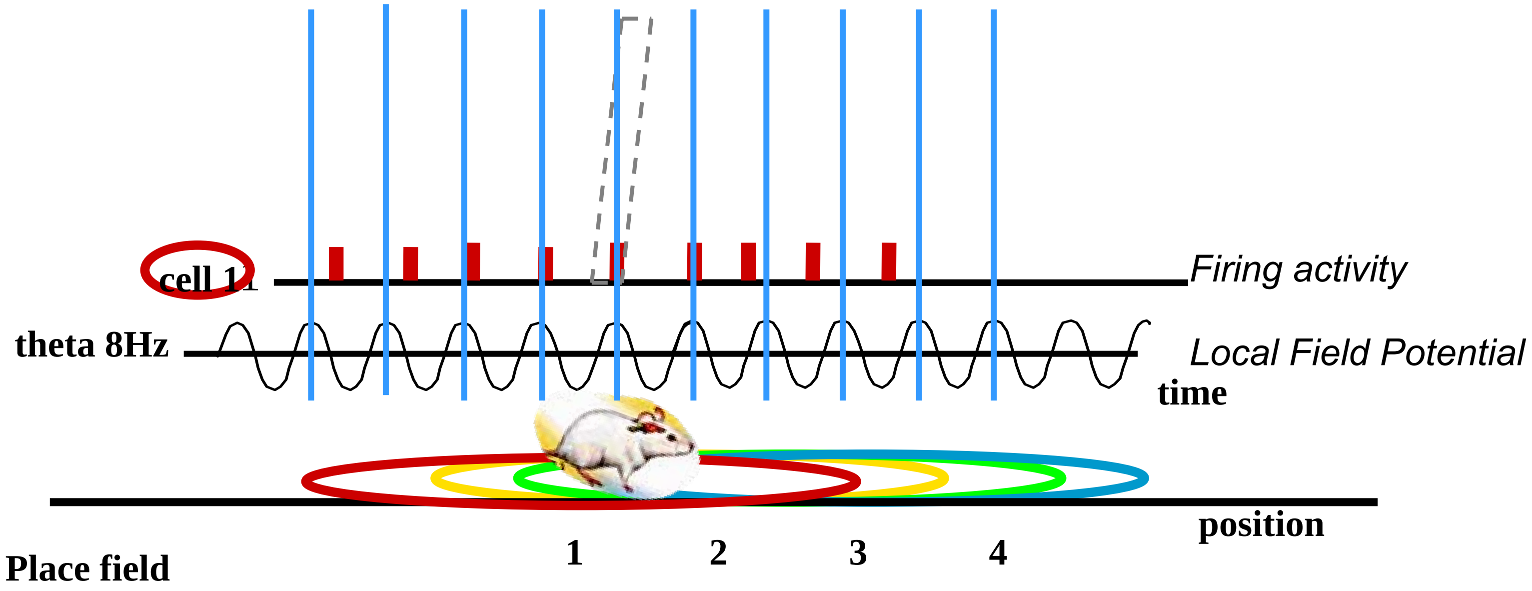
Rabbit: alert

Human : memory formation

Hippocampal dynamics: Temporal coding?

Theta phase precession: theta phase coding of “where I goes”

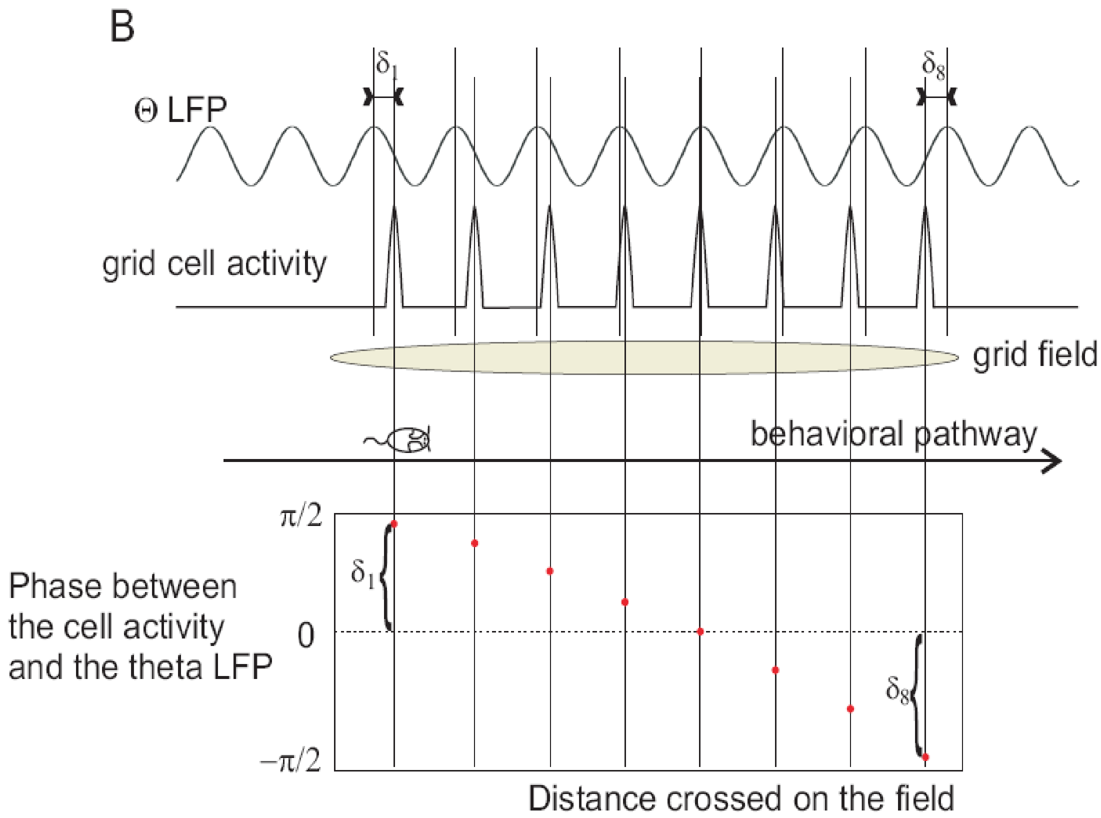
O’Keefe and Recce 1993; Skaggs et al., 1996

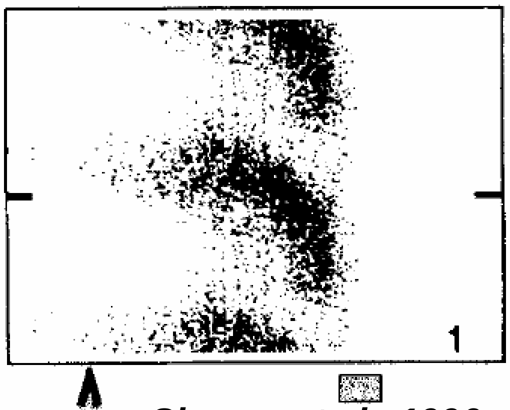


Firing phase of a place cell advances as the rat traverses the place field.

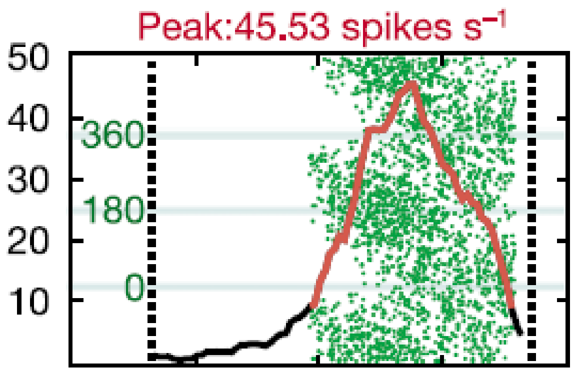
Relative firing phase of place cells represents a temporal sequence of running behavior (10cm/sec) in a compressed form within each theta cycle (1/8 sec).

Theta phase precession





Skaggs et al., 1996



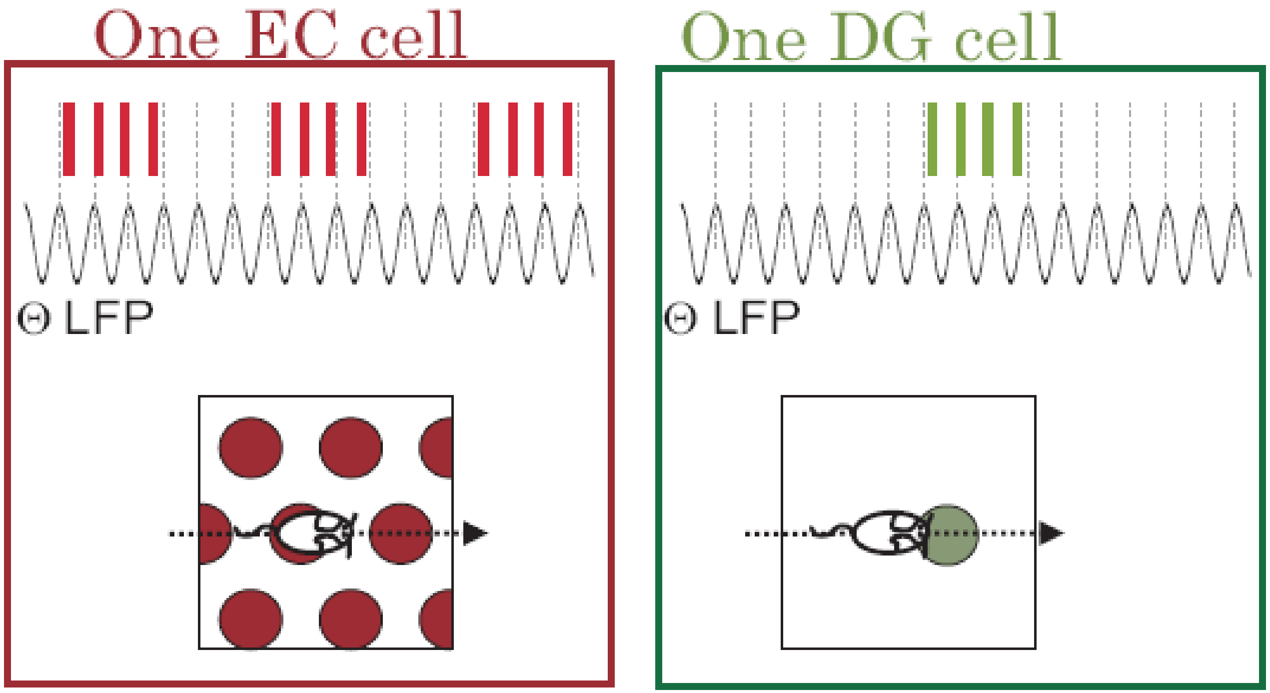
O'Keefe et al., 2006

Phase precession appears in the CA3-CA1-DG
…… and in the mEC layer II

A functional role for the phase precession dynamics

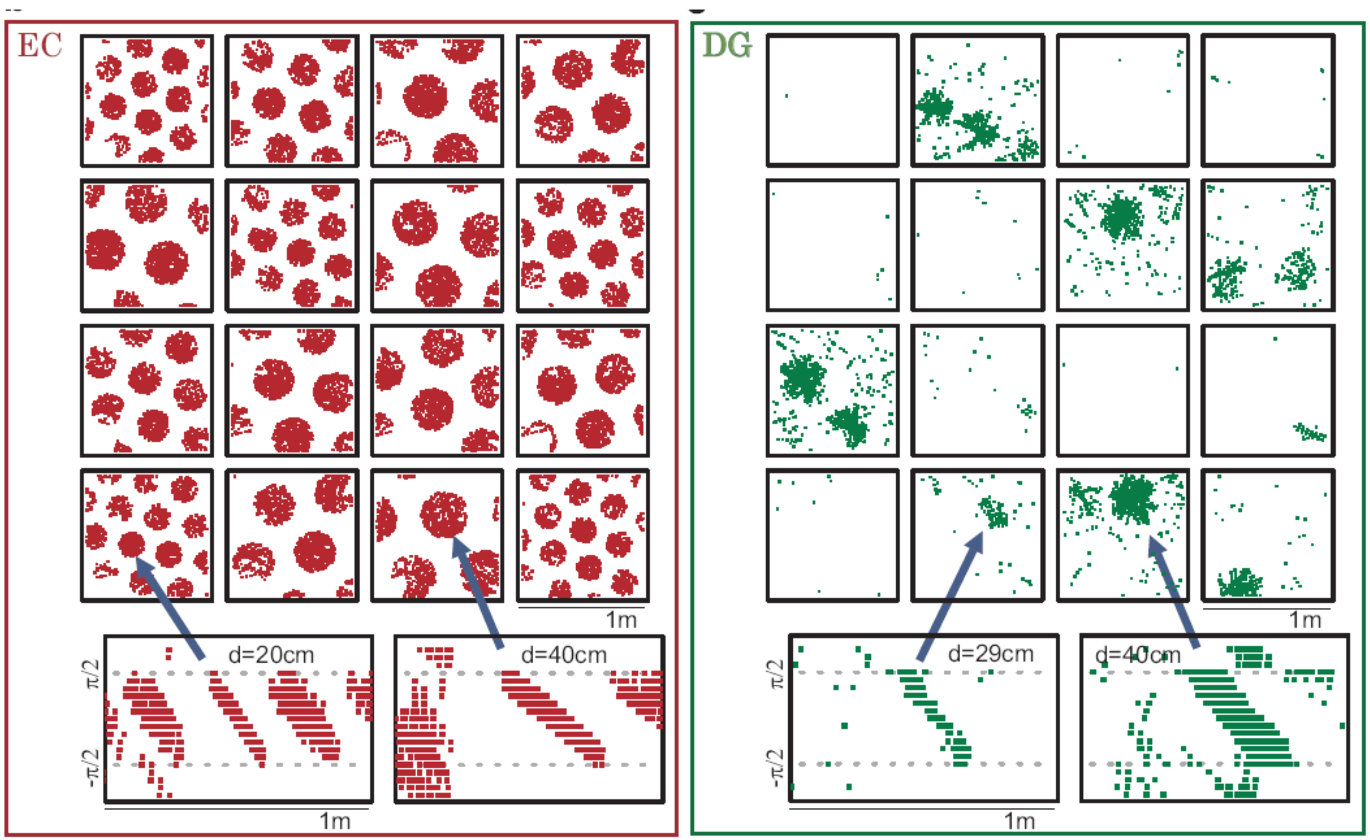
Molter & Yamaguchi 2007

- What we know:
  - Existence of grid cells
  - Entorhinal phase precession
- What we want:
  - Place fields representation
  - Hippocampal phase precession



Hippocampal dynamics

Molter & Yamaguchi 2007

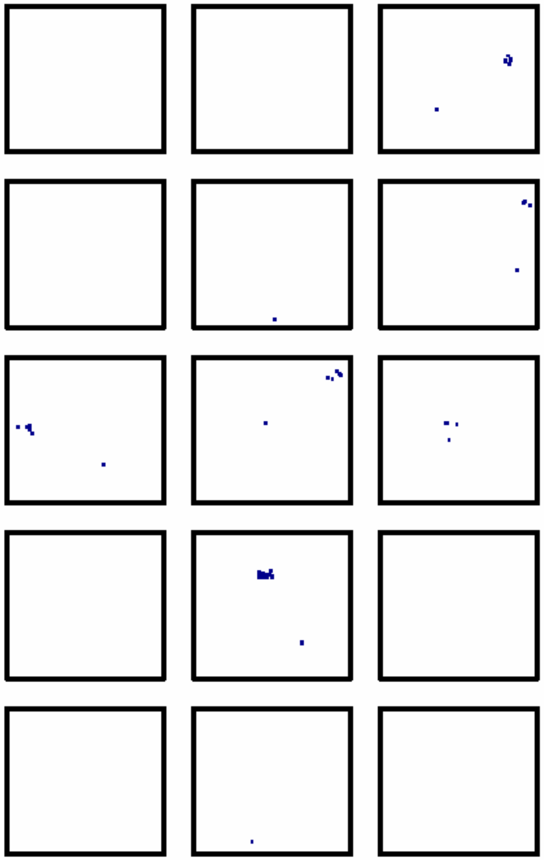


Molter et al. 2007

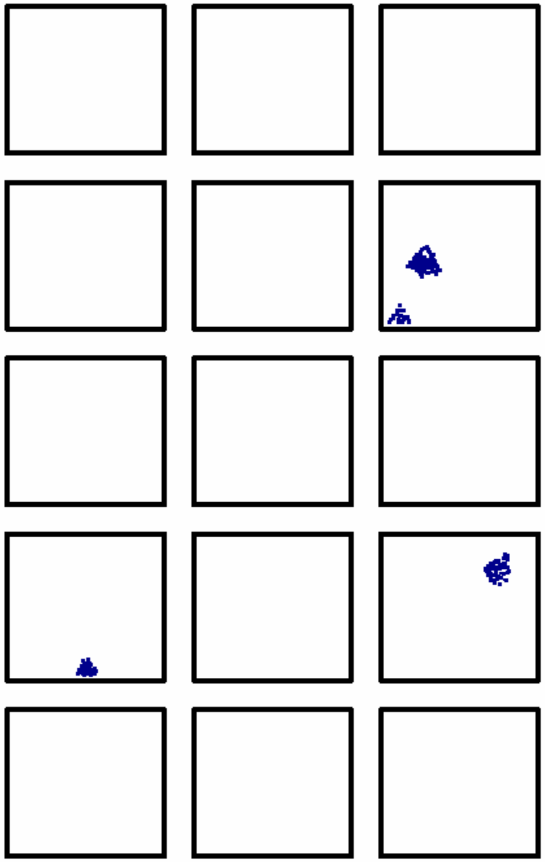
Leutgeb et al. 2007

To validate the impact of phase precession

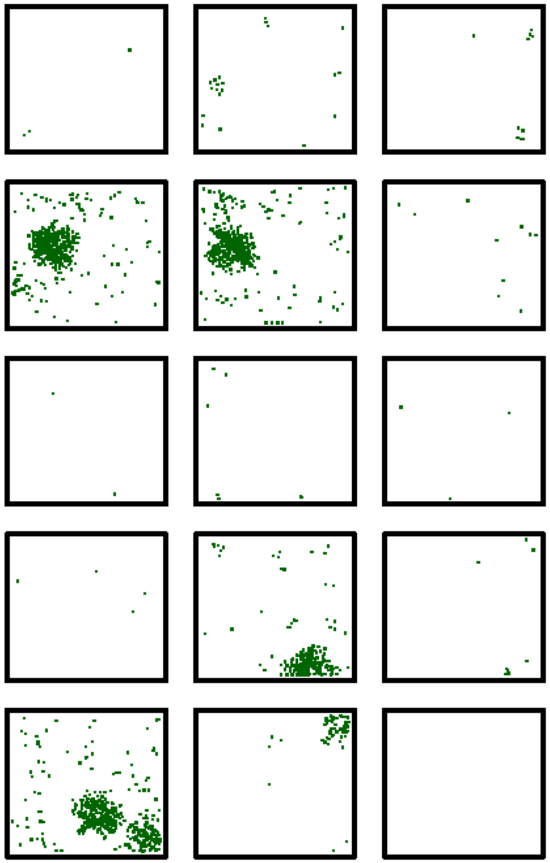
Molter & Yamaguchi 2007



No phase precession – no learning



No phase precession – learning

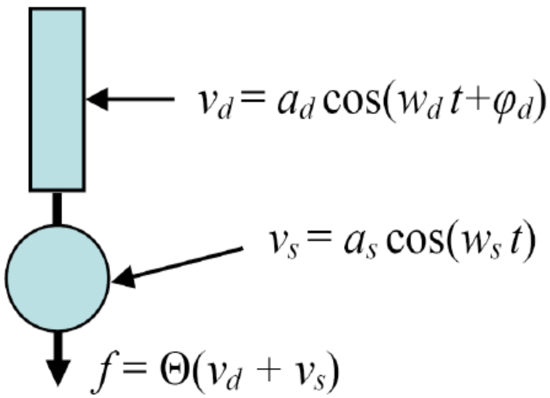


Phase precession – learning

Apparition of grid fields

An oscillatory interference model

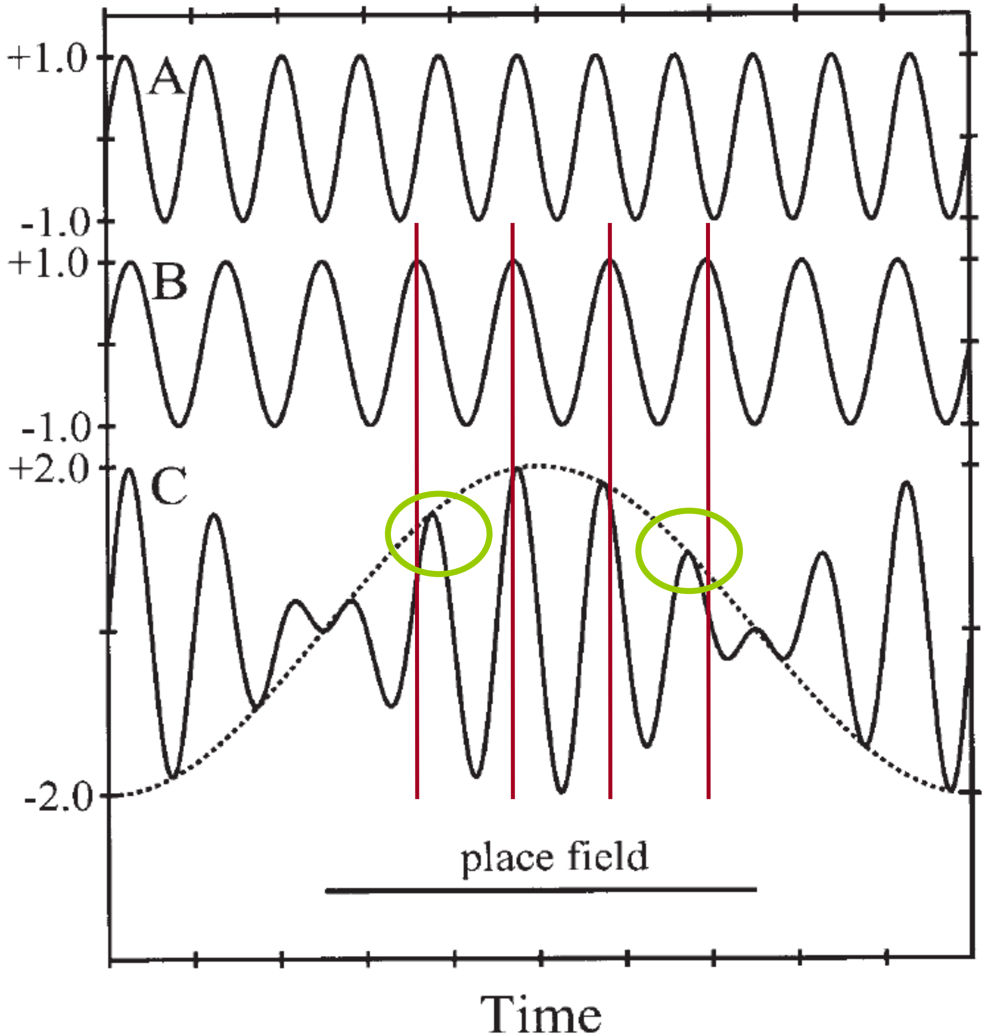
OKeefe et al. 1996-2005-2007



- an interference pattern between two oscillatory inputs
  - The 'somatic' input
    - angular frequency *ws* corresponding to the theta rhythm in the extracellular EEG recorded near the soma
    - reflects the inputs from the medial septal pacemaker
  - The 'dendritic' input
    - angular frequency *wd* which increases with running speed *s: wd* = *ws* + *βs*,
    - Reflects intrinsic oscillation of the dendritic membrane potential, whose frequency increases above theta frequency in response to a speed dependent input (e.g., 'speed cells', O'Keefe, Burgess, Donnett, Jeffery, & Maguire,1998).
    - Availability in mEC of speed-modulated head-direction information (Sharp, 1996) from the presubiculum

An oscillatory interference model

OKeefe et al. 1996-2005-2007



Intrinsic frequency of the cell

Local Field Potential

Proposed in 1996 to explain place cells with phase precession

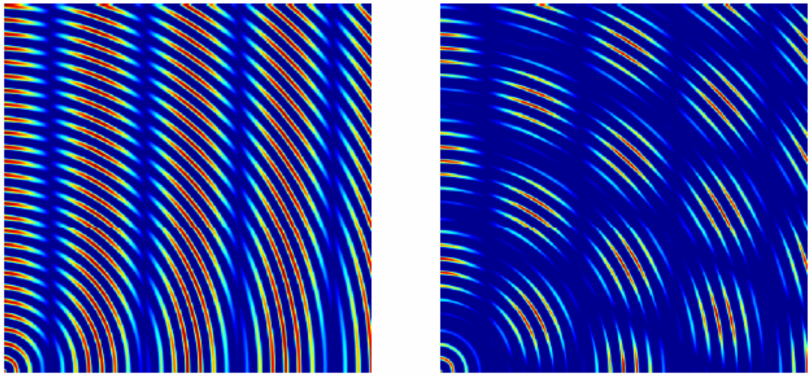
→problem: periodic structure

→Perfect for a grid cell model

An oscillatory interference model

OKeefe et al. 2007

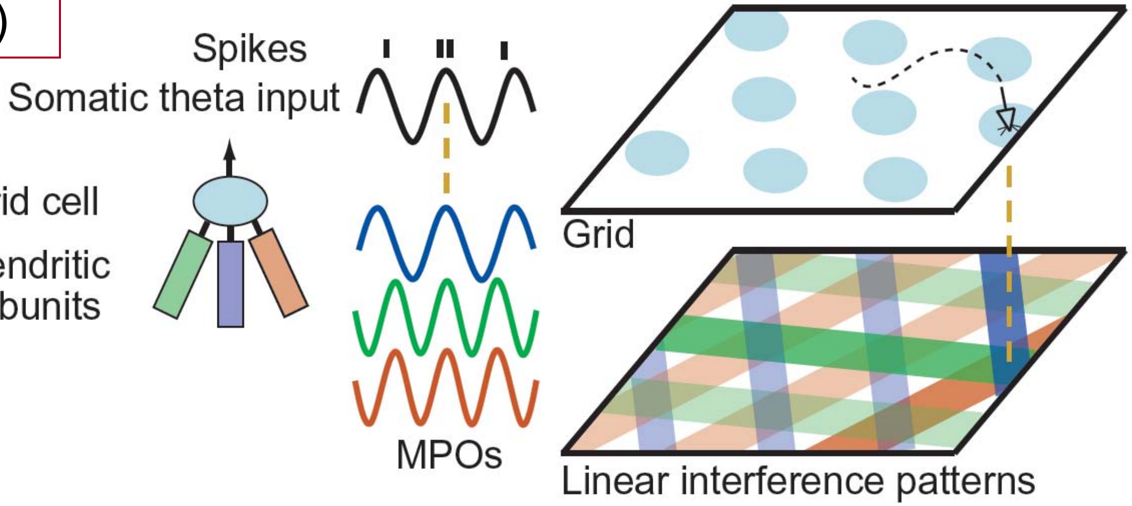
- the dendritic oscillator has a "preferred direction"
  - phase precesses according to distance traveled along a specific running direction: $wd = ws + \beta s\cos(\o - \o d)$



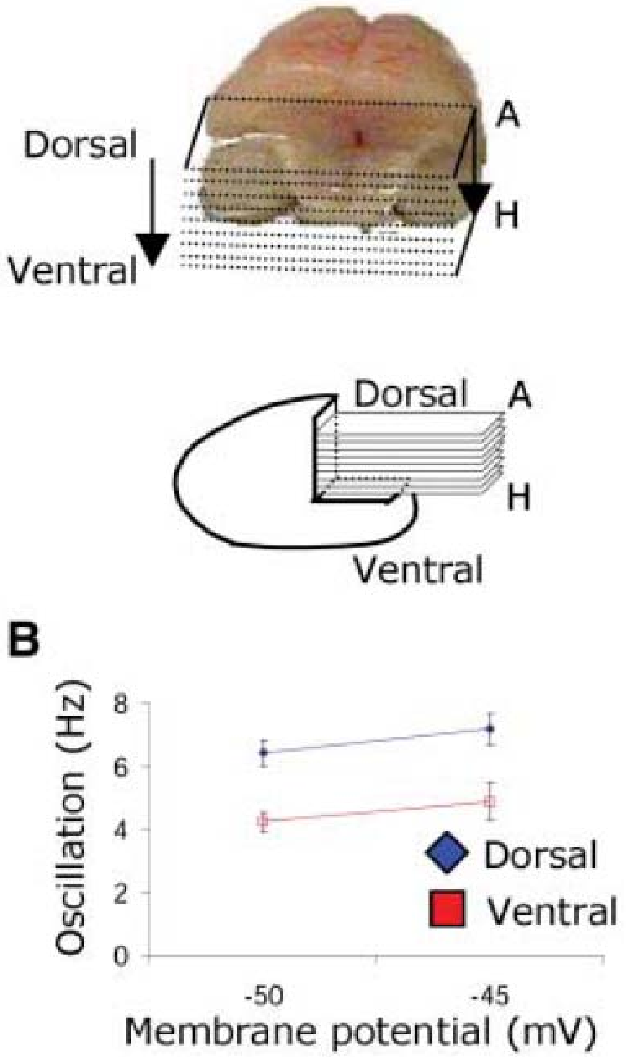
- Different dendrites have different preferred directions

Layer II stellate cells have 4 to 8 (mode 5) noticeably thick proximal dendrites (Klink & Alonso, 1997a)

appropriate subsets of head-direction cells needs to be connected to grid cells



An oscillatory interference model



- Entorhinal cortical stellate cells
  - Existence of subthreshold membrane potential oscillations (due to a a single-cell mechanism involving voltage-sensitive currents)

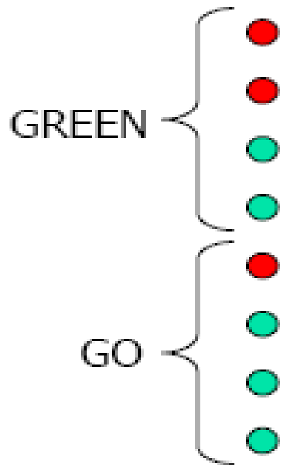
- Higher frequency of subthreshold oscillations in dorsal versus ventral entorhinal cortex.

Giocomo et al. 2007

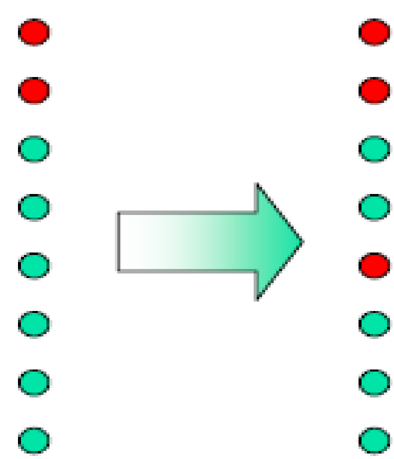
-4.1.2-
Hippocampus and memory

Introduction: Auto associative memory

- Storage
  - Memories represented by assemblies of neurons active together



- Retrieval
  - GOAL: Complete the pattern, given partial cue



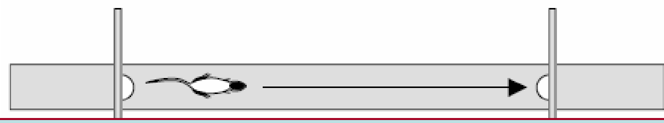
- The **CA3** network is considered to operate, in part at least, as an **autoassociative memory**, in which neuronal representations of different events, or episodes, experienced by the organism may be stored (on the modifiable synapses of the collateral connections), and from which they may be retrieved following a partial cue

Introduction: Two stage hippocampal dynamics

During running behavior and REM sleep

Functional role in memory

→ hippocampal neurons (**place cells**) fire selectively at particular locations in space (place fields).



- Place cells and the cognitive map theory

OKeefe and Nadel

From Huxter et al. 2003

During slow wave sleep (SWS), awake immobility and consummatory behaviors

→ cells activated are representative of previous behavioral activity

Wilson et al. 1994 – Kudrimoti et al. 1999 – Hirase et al. 2001

The encoding and consolidation of memories results from the reactivation and the transfer of information acquired during awake activity in the hippocampal formation to other cortical areas during awake immobility and slow wave sleep

Marr 1971 – Buzsaki 1986

We learn when we sleep !!

From Battaglia et al. 2004

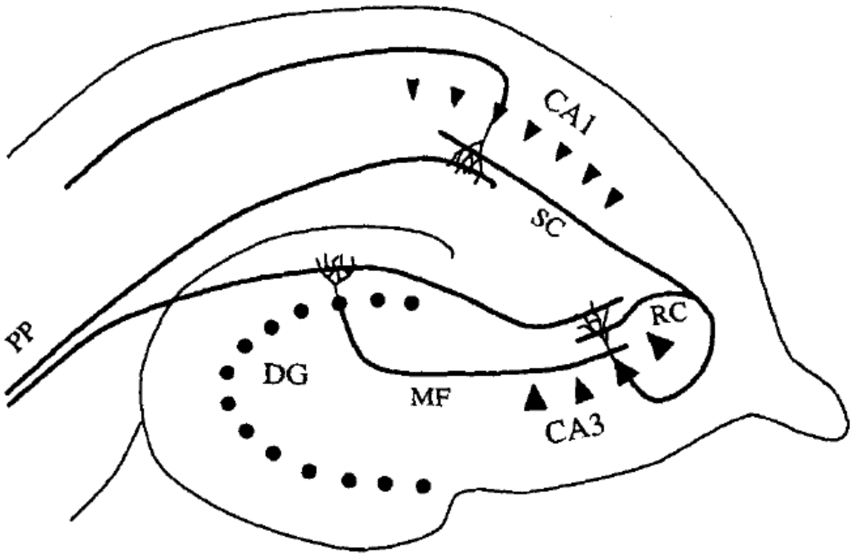
1 s

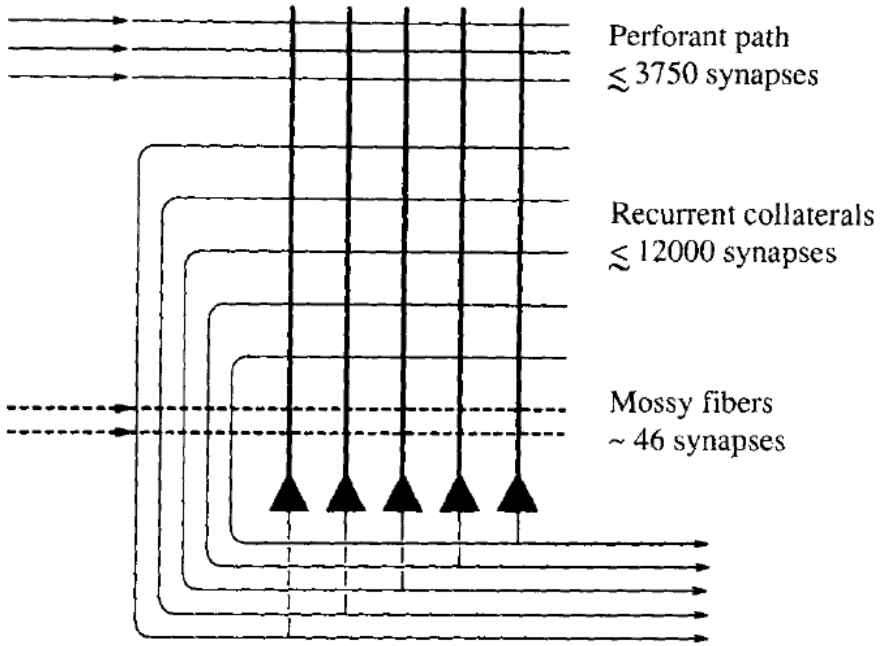
The Need for Two Distinct Input Systems to the Hippocampal CA3 Network

Rolls and Treves 1993

The CA3 Inputs

Granule cells: 1.000.000
CA3 pyramidal cells: 300.000





- CA3 is unique (in the hippocampus) since it is the only system where recurrent connections are dominant
- Beyond the interesting detailed connectivity patterns of the CA3, recurrent collaterals are divergent enough to guarantee that excitation can spread from any ca3 cell to any other cell within a few synaptic steps, i.e. a few tens of millisecond

The problem

- How is it possible to store information
- Suppose no mossy fibers:
  - the synaptic current reaching the soma of a ca3 cell is given by

$\boxed{\Delta h_i^{PP}}$ Contribution from the PP through the apical dendrites. Because many synapses, the integrated current can be seen as a random gaussian with a variance proportional to the number of synapses

$\boxed{\Delta h_i^{RC}}$ Contribution from the recurrent collaterals. Gaussian with variance proportional to the number of synapses.

- The two distributions are independent since RC synapses reflect previous events, unrelated to the new one.

$$\boxed{h_i = \bar{h} + \Delta h_i^{PP} + \Delta h_i^{RC}}$$

After a short mathematical development ….

→ RC are giving too much noise to the effective signal. Only an insufficient amount of information provided by the PP can be stored.

Importance of the Mossy fibers

- The mossy fibers force efficient information storage
  - Presumed strength of MF (large size and proximity to the soma)
  - Small number of synapses and sparse firing in the DG
    → highly structured signal to CA3 cells (far from gaussian)
  - The type of plasticity in the MF
    - NOT hebbian or associative:
    - a consistently firing mossy fiber would, in contrast to an occasionally firing one, produce nonlinearly amplified currents in the postsynaptic **CA3** cell.
  - While storing the information through the Mossy Fibers, PP synapses can be learned in an associative way (NMDA receptors).

Retrieving the information

- Once a pattern has been stored, the CA3 network, stimulated with a partial cue, should retrieve the ‘original’ pattern.
- (Marr proposed a correlation of 0.3 between the two patterns)

- Mathematics becomes nearly impossible …
- It can be proved that information provided by the perforant path can be sufficient.

Storage and retrieval

- During retrieval, or at its initiation:
  - the mossy fiber input should be nearly silent to not perturb the PP signal

- During storage
  - the perforant path input has to be active, to enable associative modifications to take place at its synapses.
  - → synaptic modification on the distal dendrites should reflect depolarizations produced close to the soma by the mossy synapses.
  - → the time scale for information the depolarizations produced by mossy fiber should be consistent with the time scale for associative plasticity.

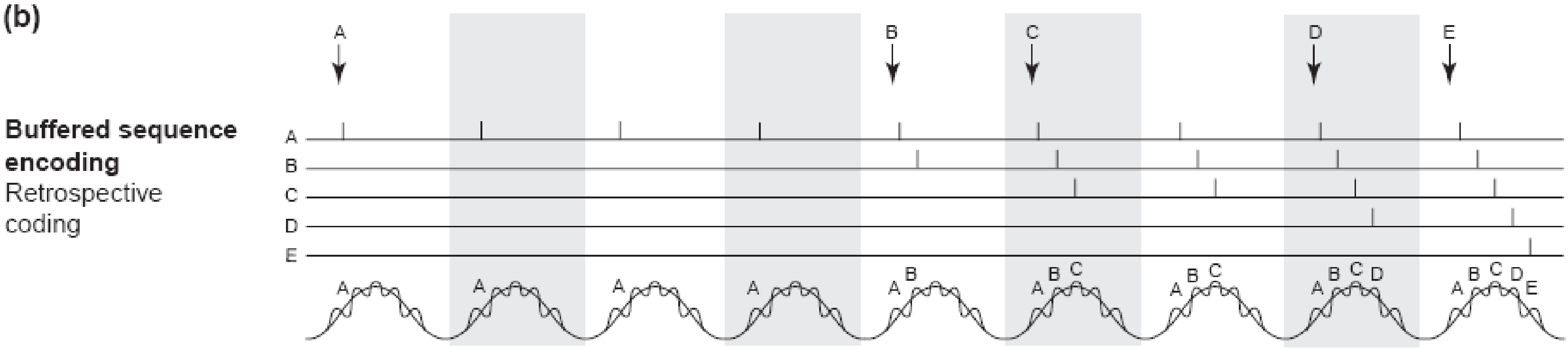
Hippocampal sequence-encoding and cortical working memory

Jensen Lisman 1996-2005

Short term memory buffer

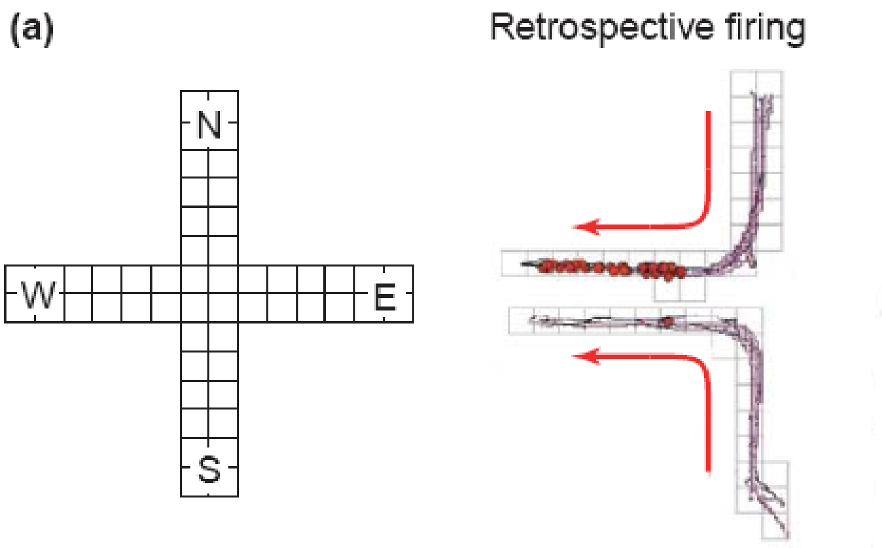
- Miller (1951): the magic number 7
- Sternberg (1966):
  - N objects are presented
  - A test item is presented → question: in the list or not
  - Response time increases of 30 ms per item

➔ Short term memory in the neocortex



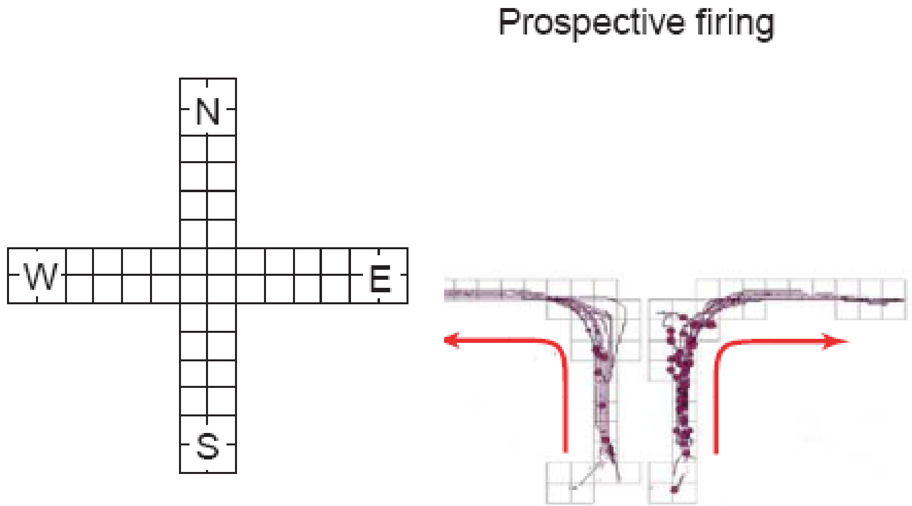
Encoding in the hippocampus

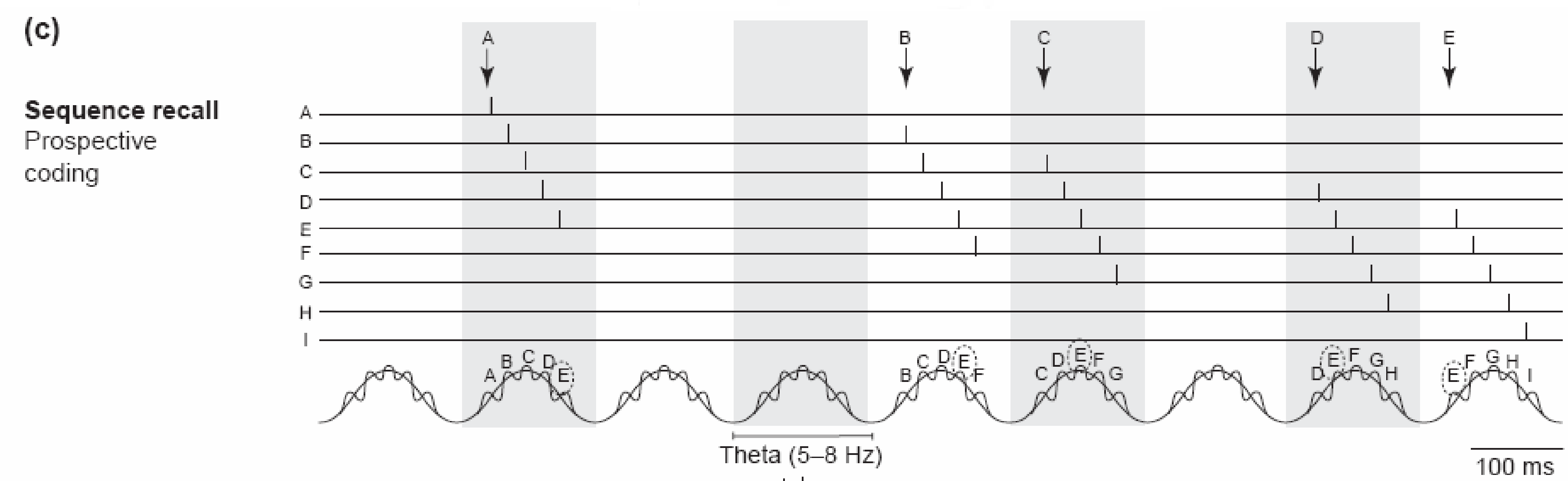
- Buffer learned through the entorhinal pathway to the CA3 recurrent collaterals with asymmetric connections due to an asymmetric STDP learning rule
- Existence of a buffer in EC proved by existence of retrospective firing cells
- Idem in the hippocampus



Phase precession in the hippocampus

- Phase precession corresponds to prospective coding





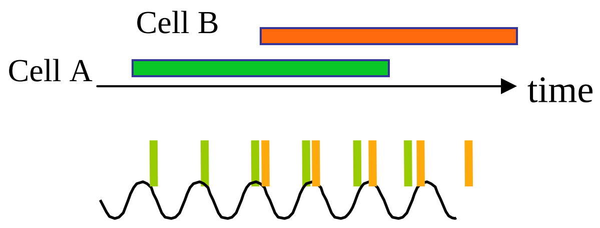
Online encoding during theta reactivation during Sharp Waves

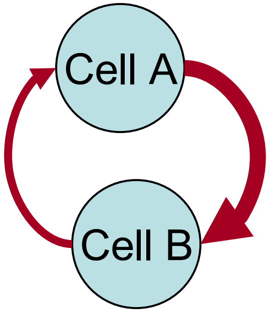
Plasticity during the running behavior?

Skaggs et al., 1996

CA3 associative memories
Time asymmetric Hebb Rule

Levy & Steward, 1983 etc.

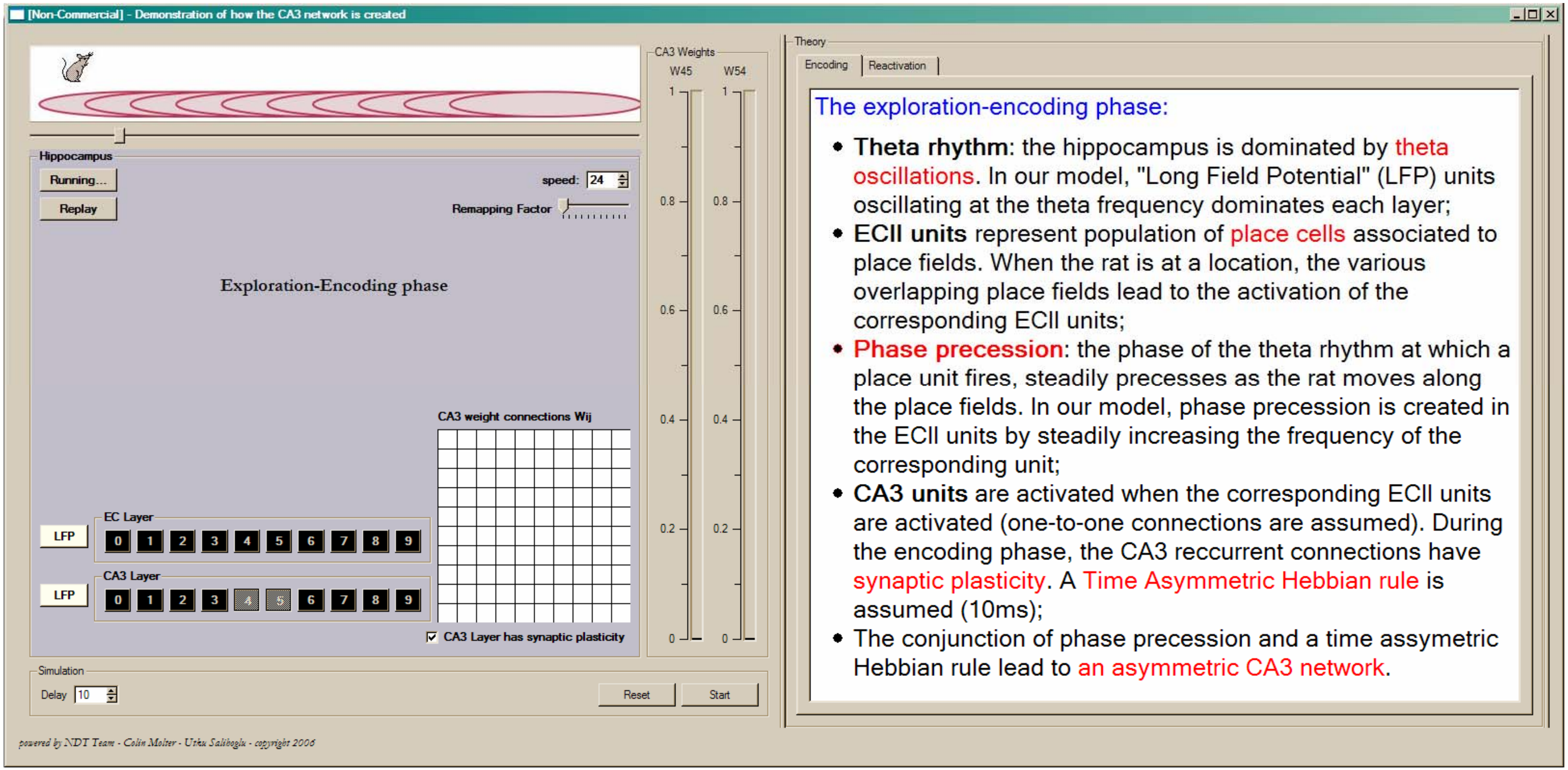




A two-stage model of memory trace formation

Synaptic plasticity during theta in the CA3

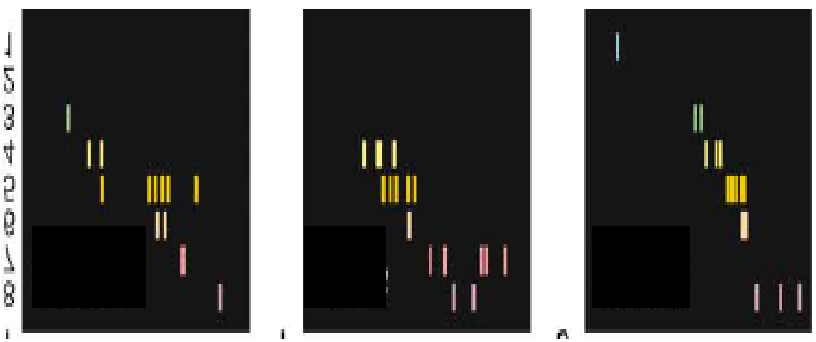
Yamaguchi (2003)



Temporal coding?
Sharp Waves replay

- Reactivation of the sequential pathway during SPWs

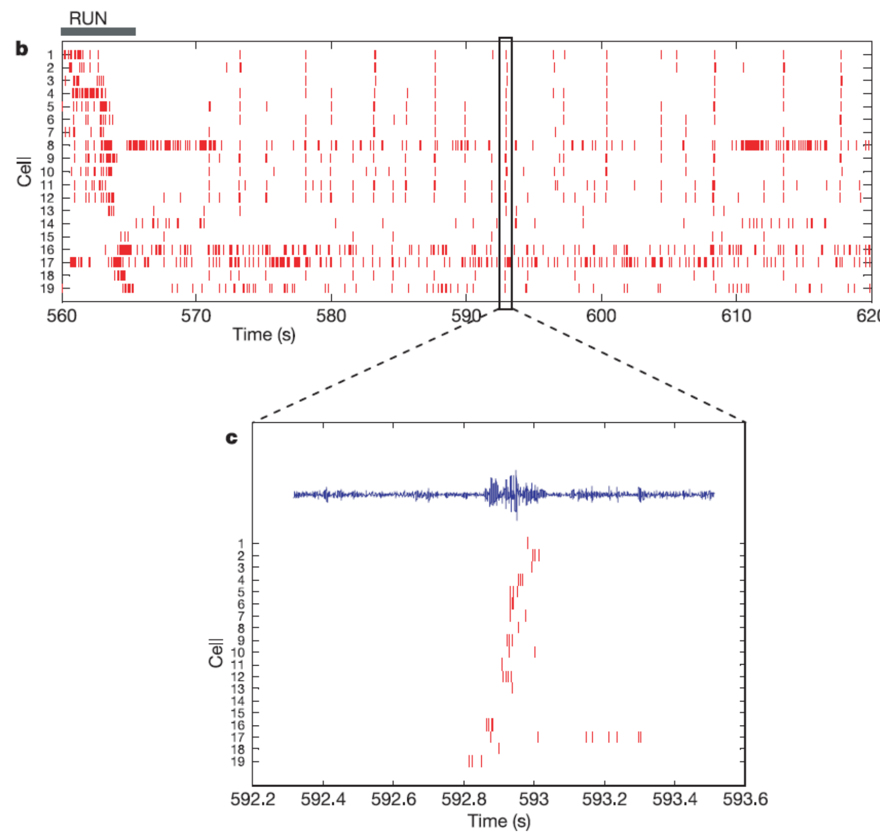
Forward replay
During slow wave sleep



50 ms

Lee and Wilson 2002

Reverse replay
During consummatory behavior

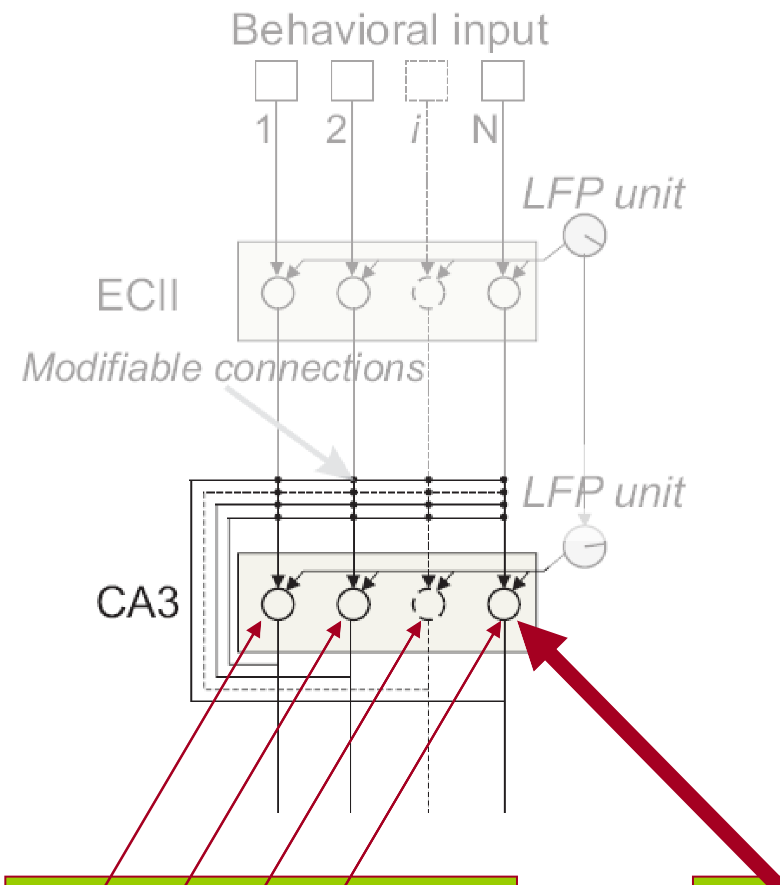


288 ms

Foster and Wilson 2006

A two-stage model of memory trace formation
Reactivation during SPWs

Molter, Sato and Yamaguchi (2006)



Two different kinds of inputs are assumed to initiate global discharges.

- *Irregular non-specific input* during SWS and consummatory behavior

- *Specific place unit activation* during the consummatory behavior: after the running behavior, in addition to the irregular non-specific input, an additional input feed the CA3 units corresponding to the place fields at the eating location.

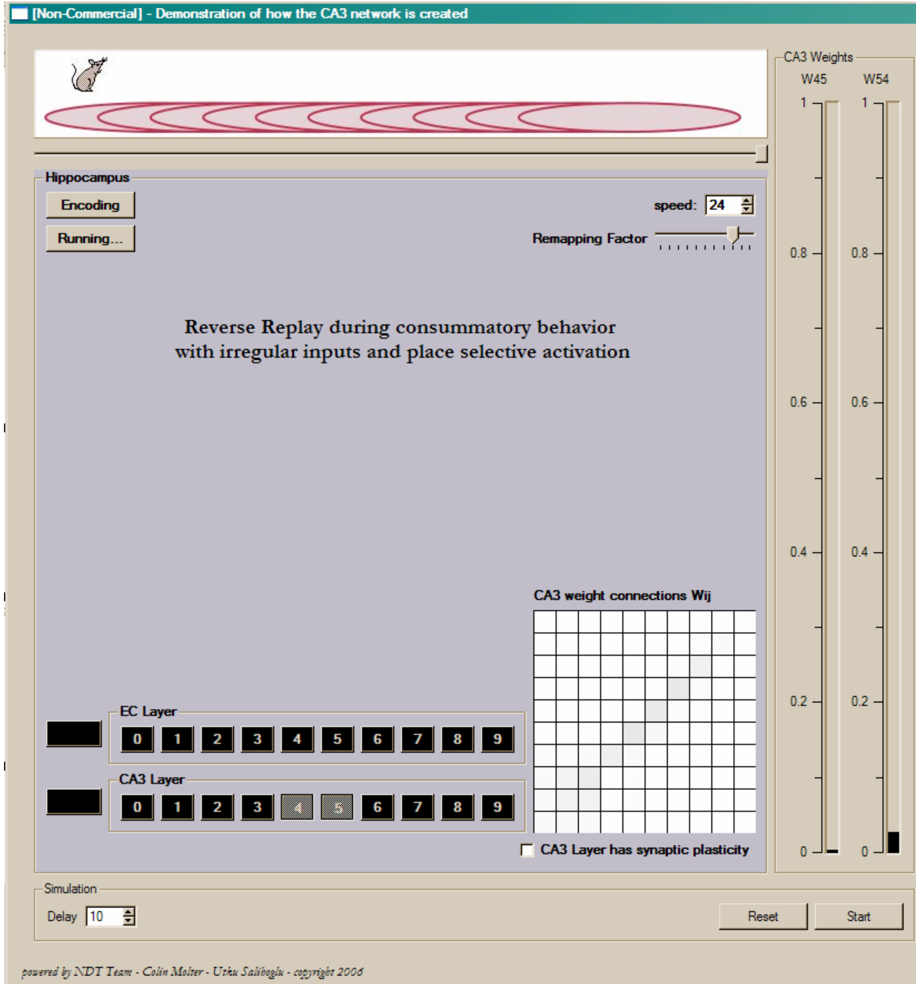
Irregular non specific inputs
Slow Wave Sleep

Specific place unit activation
Consummatory behavior

Csicsvari et al. (2006)

A two-stage model of memory trace formation
Reactivation during SPWs

Molter, Sato and Yamaguchi (2006)



Theory

Encoding | Reactivation

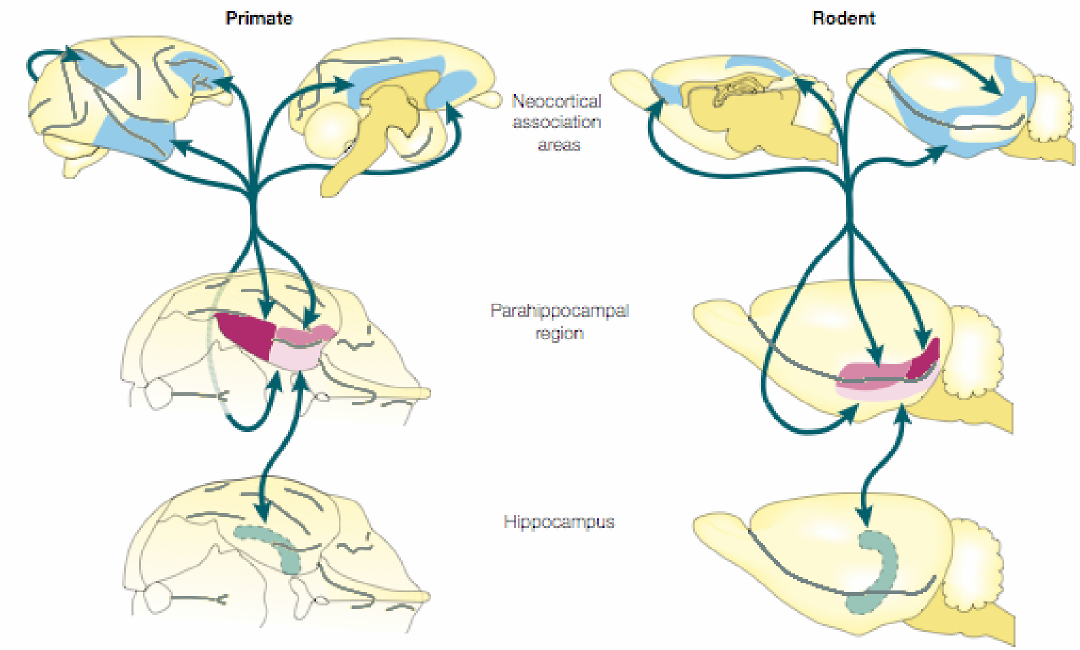
The reactivation phase during sharp waves:

- During slow wave sleep and awake immobility , large irregular transient bursts of CA3 and CA1 pyramidal cells associated with sharp waves (SPW) occurs in the hippocampus;
- **To simulate SPWs events**, rapid irregular inputs *Gi(t)* are assumed, such that the probability for a unit to get reactivated is small but not null.
- **Forward replay during SWS**. Once a unit is reactivated, its activation is propagated along the asymmetric connections. This lead to the forward replay of the behavioral sequence.
- **Reverse replay during consummatory behavior**. The mean of the distribution *Gi(t)* is increased for the CA3 units at the end of the track. Accordingly, these cells are more sensitive. This intents to reproduce observations of place selective firing at the rat's location during awake SPWs. The propagation through the small but non negligible backward connections leads to the reverse replay of the behavioral sequence.
- **Learning leads to place cells remapping**: more place cells appear at the reward location and diminish elsewhere. This remapping is simulated by diminishing the mean of the distribution *Gi(t)* for the CA3 units outside the reward location (the end of the track). The diminution of the subthreshold input leads to slower the propagation of the reverse replay. This is supported by Figures appearing in Foster and Wilson's paper.

-4.2-
Human Hippocampal models

Memory models

Transition slide



Eichenbaum, 2001

- Is the primate hippocampus is different from the rat hippocampus?
  - Yes: anatomical structures of rat and primate hippocampus are similar
  - No: number of cells
- But: different cortical inputs

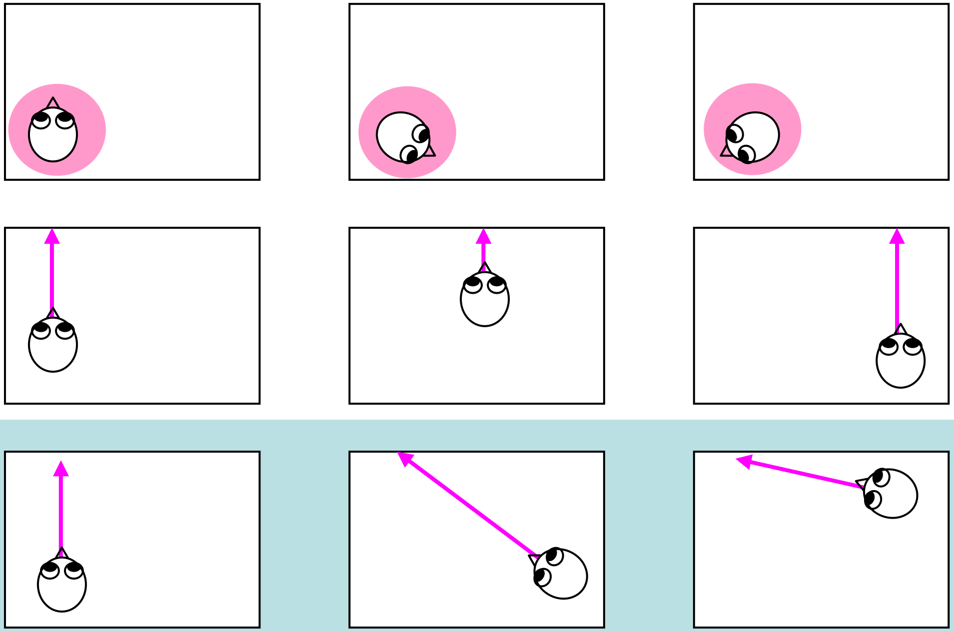
Monkey hippocampus - View cells

Place cell

Head-direction cell

View cell

(Rolls, 1999)



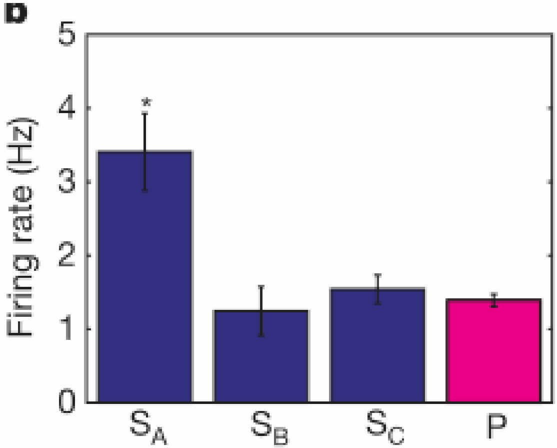
- Spatial view cells (in conjunction with whole body motion cells in the primate hippocampus, and head direction cells in the primate presubiculum) would also be useful as part of a spatial navigation system. (Rolls, 1999).

Human hippocampus: view cells and place cells

Example of visual scene

Virtual environment

View selectivity of a hippocampal cell



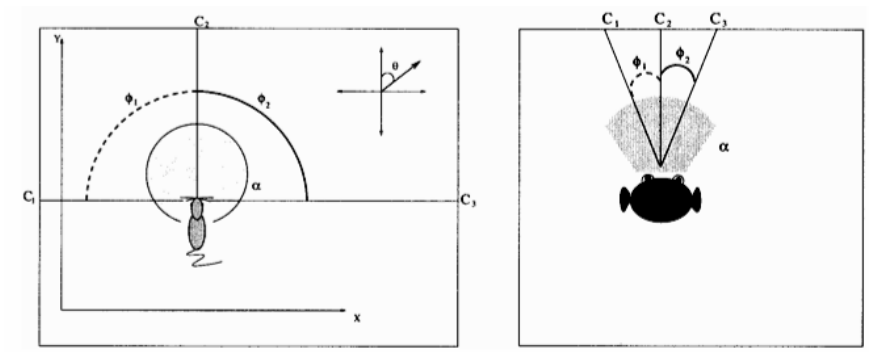
(Ekstrom et al., 2003)

- Virtual navigation task. Hippocampal cells responds at specific spatial locations and cells that respond to views of landmarks.
- Is there any common neural mechanism for place cells and view cells?

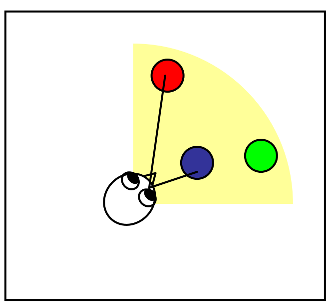
A computational model: Inclusion of visual receptive field size difference between

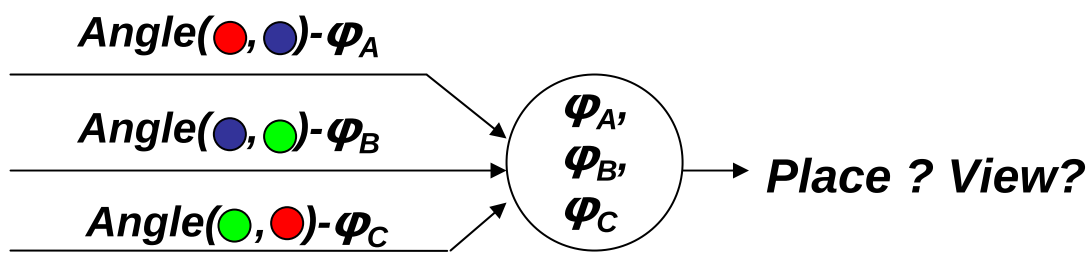
(Araujo et al., 2001)

Rat visual field



Monkey visual field

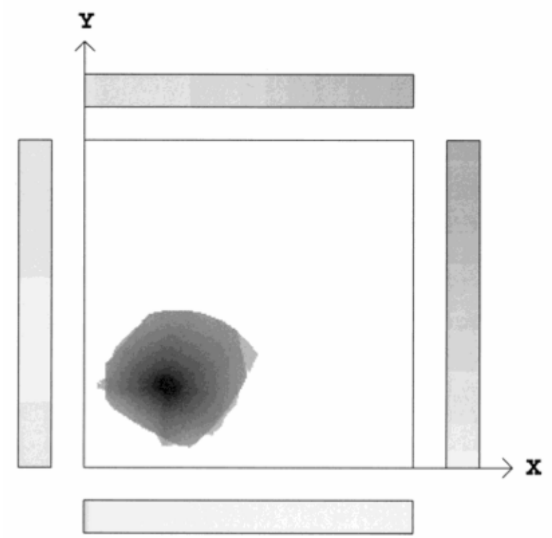




- Influences of visual receptive field sizes were evaluated whether these could account for both place cells in rodents and spatial view cells in primates.

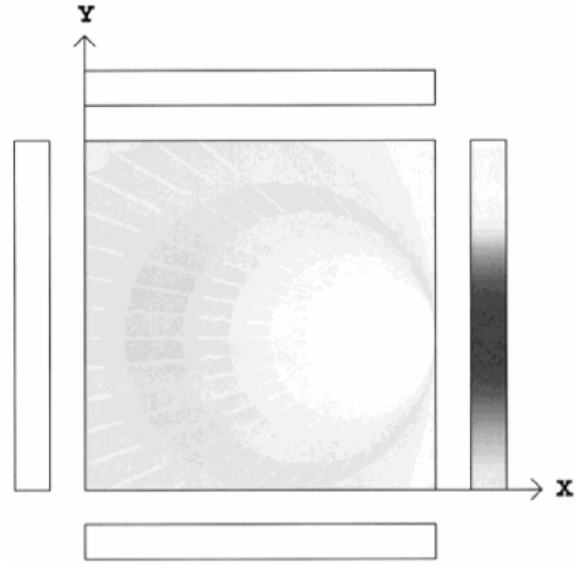
Visual receptive field size difference accounts for view cells and place cells

(Araujo et al., 2001)



Place cell

(visual field size= 270 deg)



View cell

(visual field size= 30 deg)

Araujo et al., 2001

- A common hippocampal mechanism operating with different visual receptive field sizes could account for some of the visual properties of both place cells in rodents and spatial view cells in primates.

Discussion and questions

- human episodic memory appears different than rodents memory
  - E.g. object-place episodic memory

→ How to attribute this difference

  - Primates hippocampal dynamics is expected to be similar to rodents dynamics.
  - Inputs are known to be different

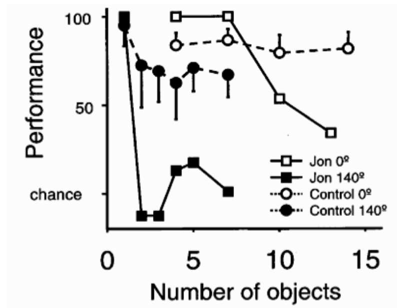
A experimental model of episodic memory: object – place memory

Cave & Squire, 1991

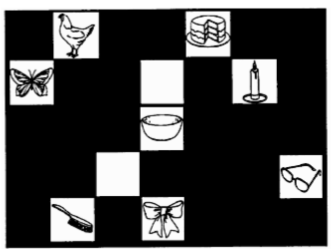
- A model of episodic memory (what-where) (Rolls, 1999)
- Subjects are asked to remember the object-place associations.
- Subject with hippocampal damage has a great difficulty to perform the task (Smith & Milner 1981, Cave& Squire 1991, King et al., 2002, Stepankova, 2004).

Variation of object-place memory tasks

Human:

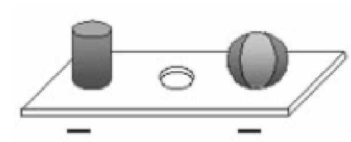


King et al, 2003



Johnsrude et al., 1999

Monkey:



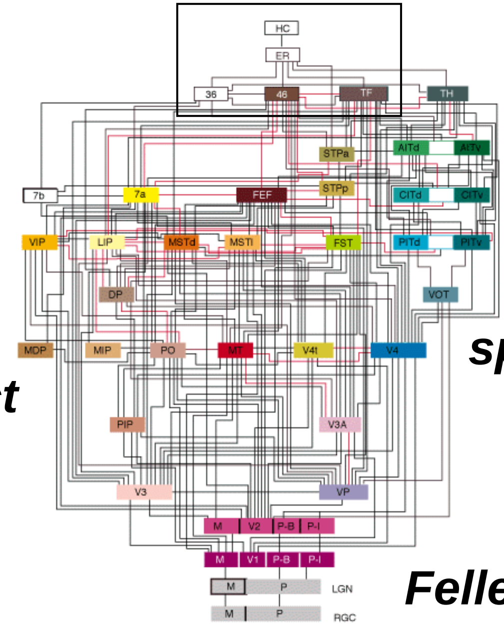
Malkova & Mishkin, 2003

Gaffan, 1996

- Common experimental paradigm to investigate object-place memories
  - To human (King et al., 2003)
  - To monkeys (Gaffan 1996; Malkova & Mishkin, 2003)
  - To rats (Ennaceur et al., 1997; Eacott & Norman, 2004).

- Hippocampus is necessary for high capacity object-place memories (King et al., 2003).

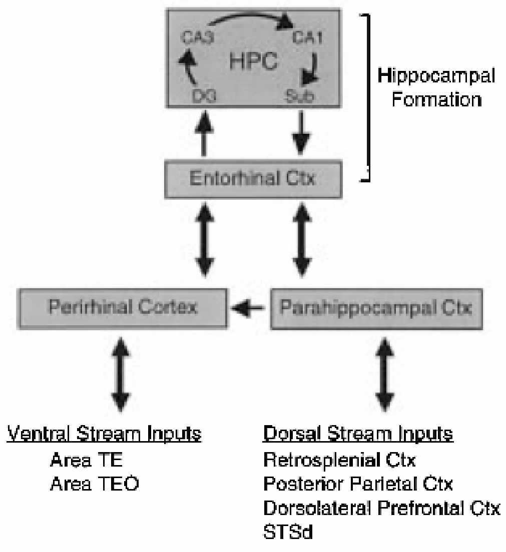
Cortical inputs: “object” and “space”



object

space

Felleman & van Essen., 1991



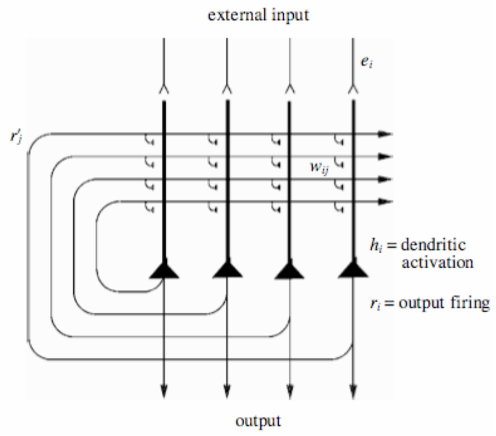
Mishikin et al., 1997

- Two visual input pathways converge into the hippocampus.
  - Retina: Parvo/ magno celler system
  - Visual cortex: ventral/ dorsal system (“object”/”space” information)
  - Parahippocampal region: perirhinal/ parahippocampal cortices
- Object-place memory is a good example to evaluate the hippocampal memory.

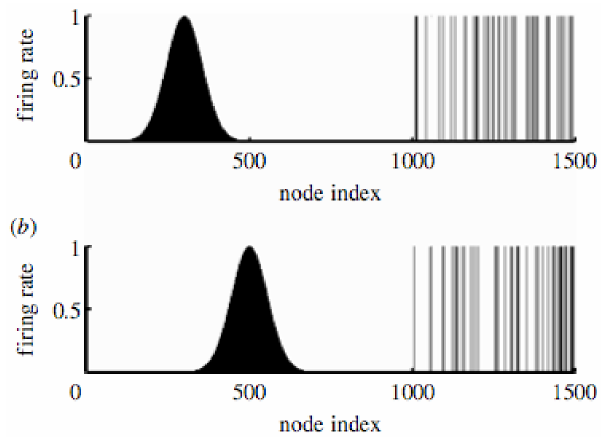
A computational model: continuous and discrete inputs

Rolls et al., 2002

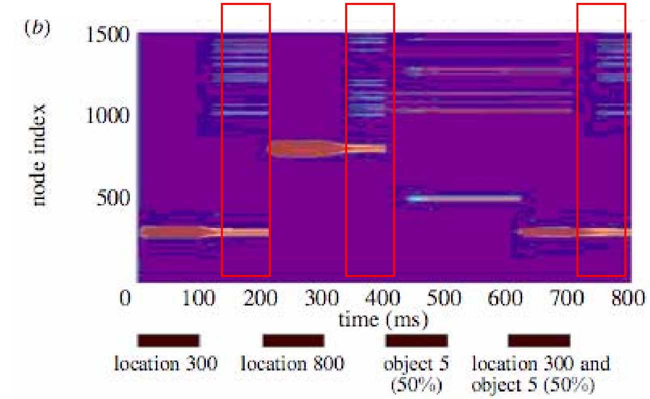
Network model



Continuous & discrete inputs



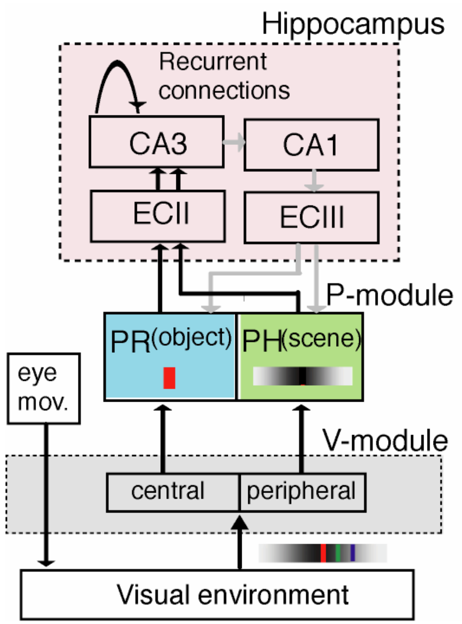
Result of recall



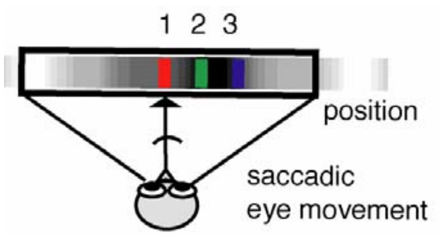
- A single recurrent attractor network can store both the discrete memories that characterize episodic memory and the continuous representations that characterize physical space.
- Combining both types of representation in a single network is necessary for object-place memory storage.

A computational model: object-place visual input sequence with theta phase coding

Sato & Yamaguchi, 2005



Visual environment



retinal images and inputs

- Hippocampal input is given by saccadic visual sequence.
- -Object-place associations are stored in CA3 associative network.
- -Parameters of visual system is determined by human evidences.

Memory encoding with theta phase coding

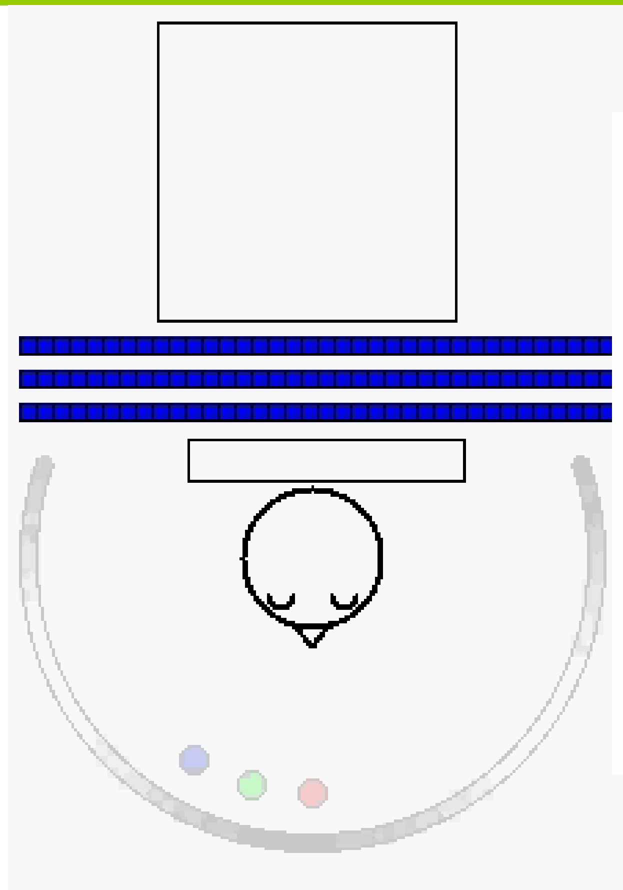
Sato & Yamaguchi, 2005

CA3 Connection weights

CA3

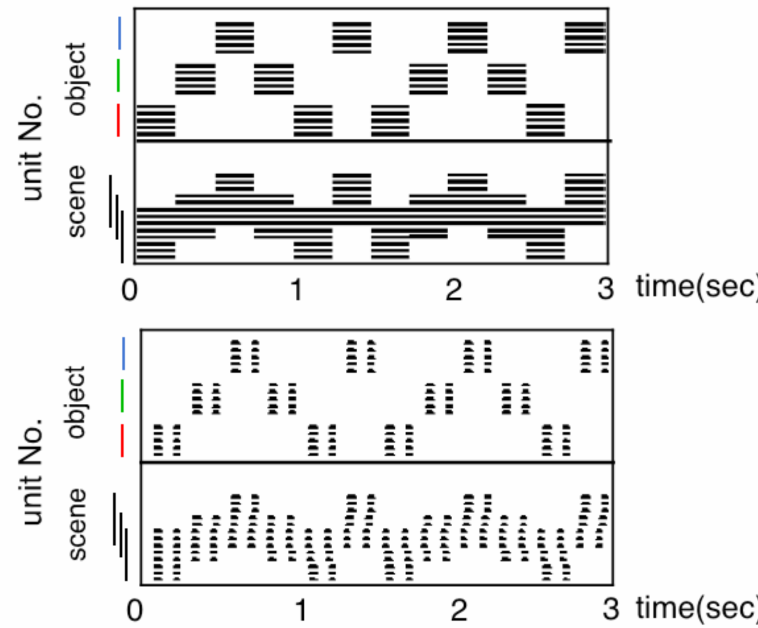
EC

Visual input



Visual input

Activities in CA3



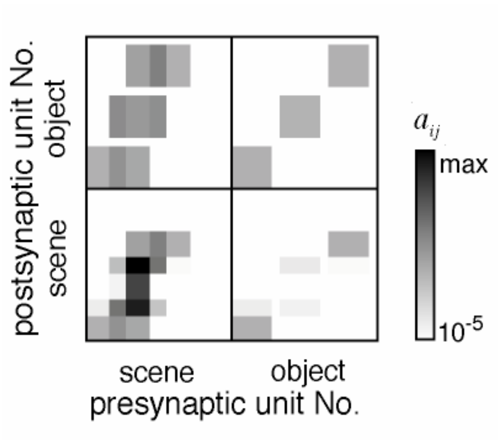
- Object and scene visual inputs are translated to theta phase coding, and stored into CA3 connection weights.

A hierarchical cognitive map for object-place associations

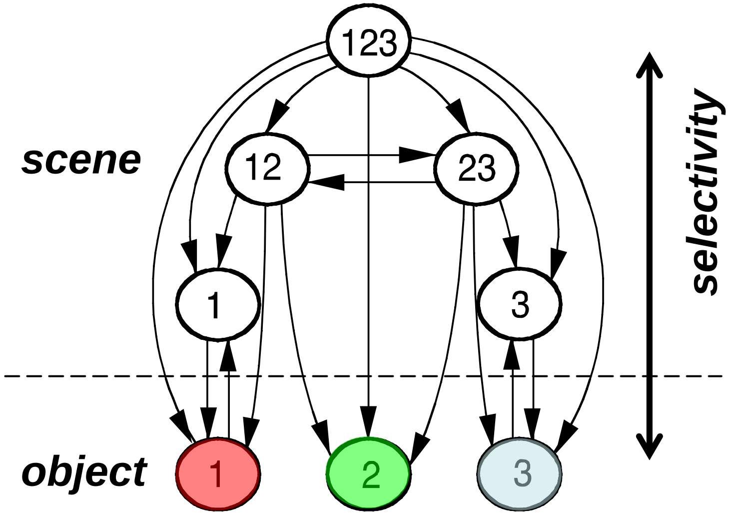
Sato & Yamaguchi, 2005

Visual environment

Connection weights formed in CA3



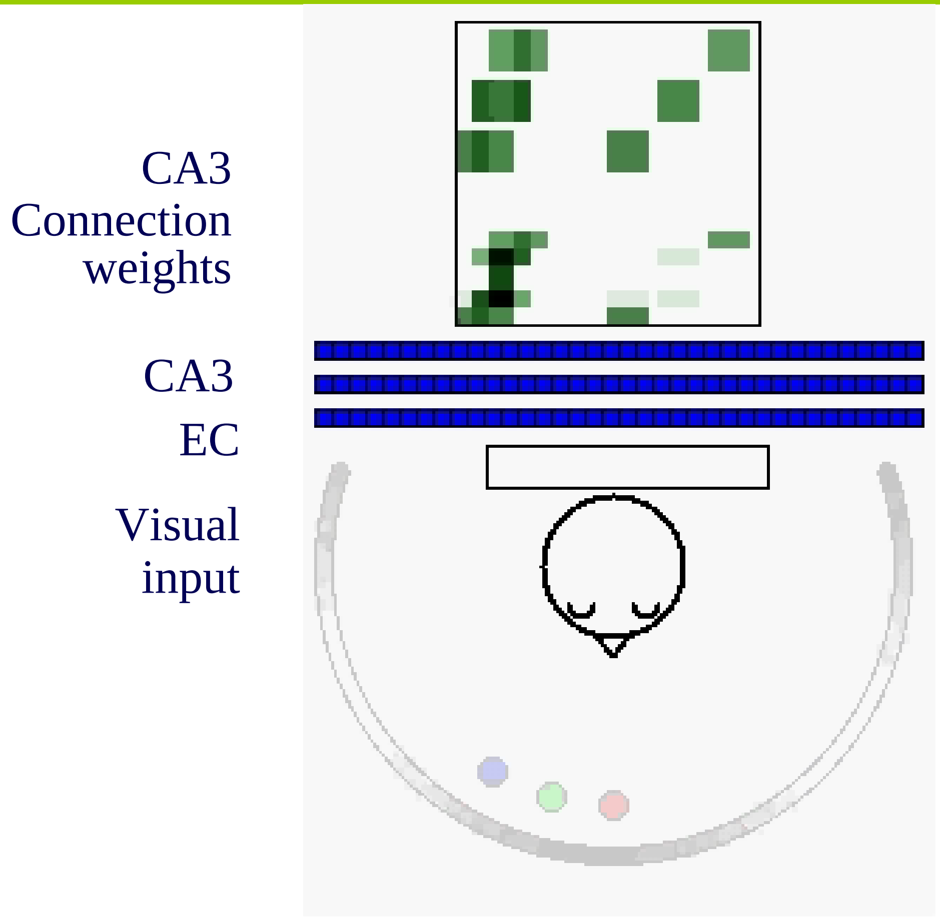
Connections between populations of object units and scene units



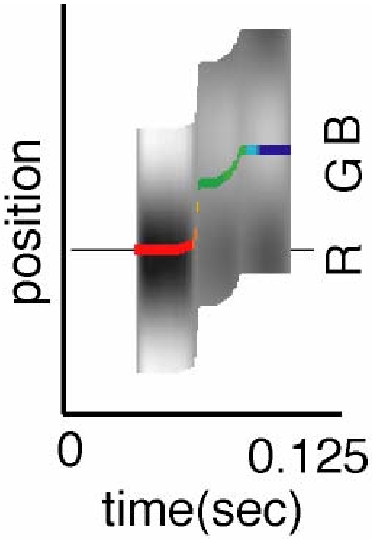
- Asymmetric connections are formed by random saccade sequence.
- Asymmetric connections appears between units of different spatial selectivity.
- Object-place memory is formed as a hierarchical structure of the network

Memory recall in the cognitive map

Sato & Yamaguchi, 2005



Recalled object-place associations in a sequence



- A set of object-place associations appears simultaneously.
- Individual sets appears sequentially one by one.

Discussions and questions

- The theta phase coding observed in the rat hippocampus can facilitate the online memory storage of complex environments in humans as a hierarchical cognitive map.
- In the recall process, not only the hippocampal dynamics but also the cortico-hippocampal interaction is necessary. What is the cortico-hippocampal interaction during recall?

End of tutorial

Conclusion

"In order to understand the brain, we have used the computer as a model for it. Perhaps it is time to reverse this reasoning. To understand where we should go with the computer, we should look to the brain for some clues,"

- The hippocampus
  - assumes several important functional roles
  - has a unique laminar structure made of several layers
  - Is known for its plasticity
  - has unique dynamical features

- The cognitive roles should be explainable by developing ANN reproducing these features