Theta, Gamma, and Working Memory

Computational Models of Neural Systems
Lecture 3.8

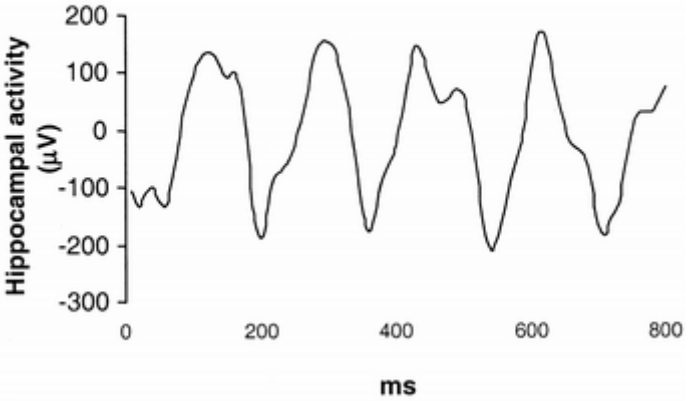
David S. Touretzky
October, 2023

Outline

- Theta rhythm and gamma rhythms
- Phase precession in hippocampus
- Theta and gamma in entorhinal cortex
- Lisman working memory proposal
- Hasselmo theory of EC as buffer

Hippocampal Theta Rhythm

- 3-12 Hz oscillation in local field potential
  - when the animal is moving or engaged in voluntary behavior: frequency increases with running speed
  - during REM sleep

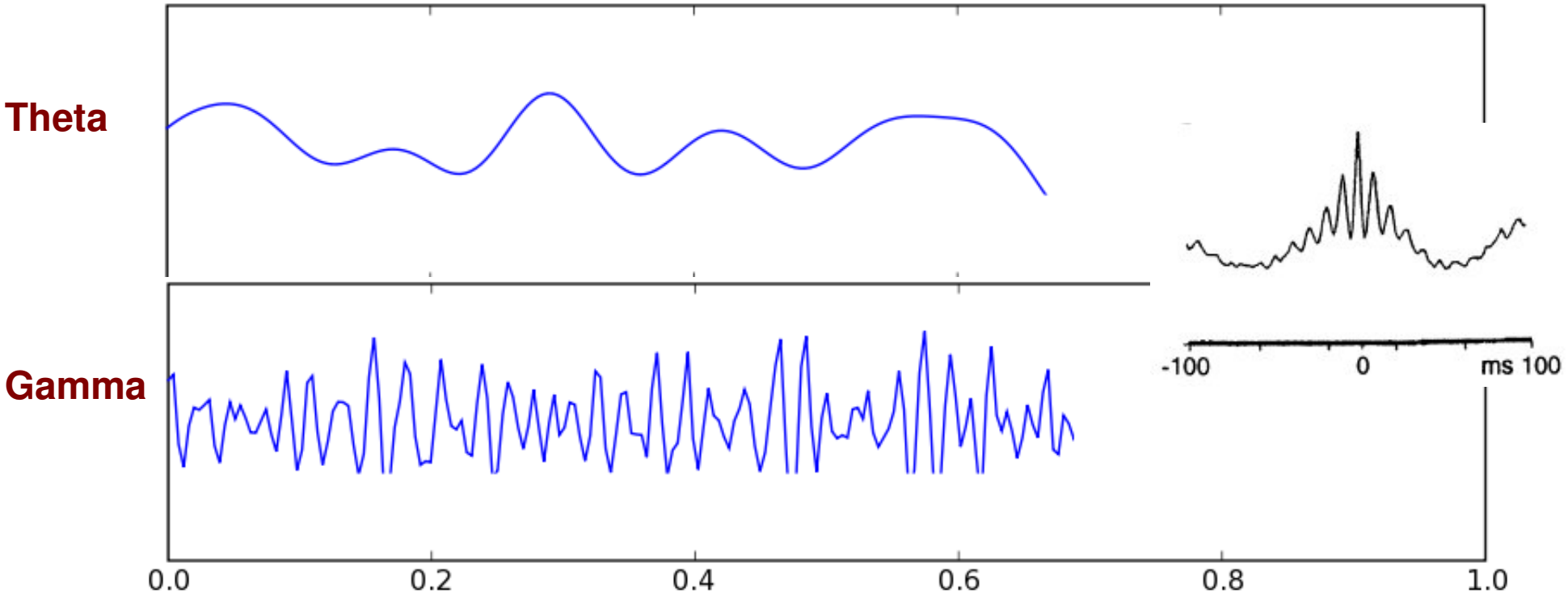


- Entorhinal cortex also exhibits theta rhythm and is the principal source of hippocampal theta.

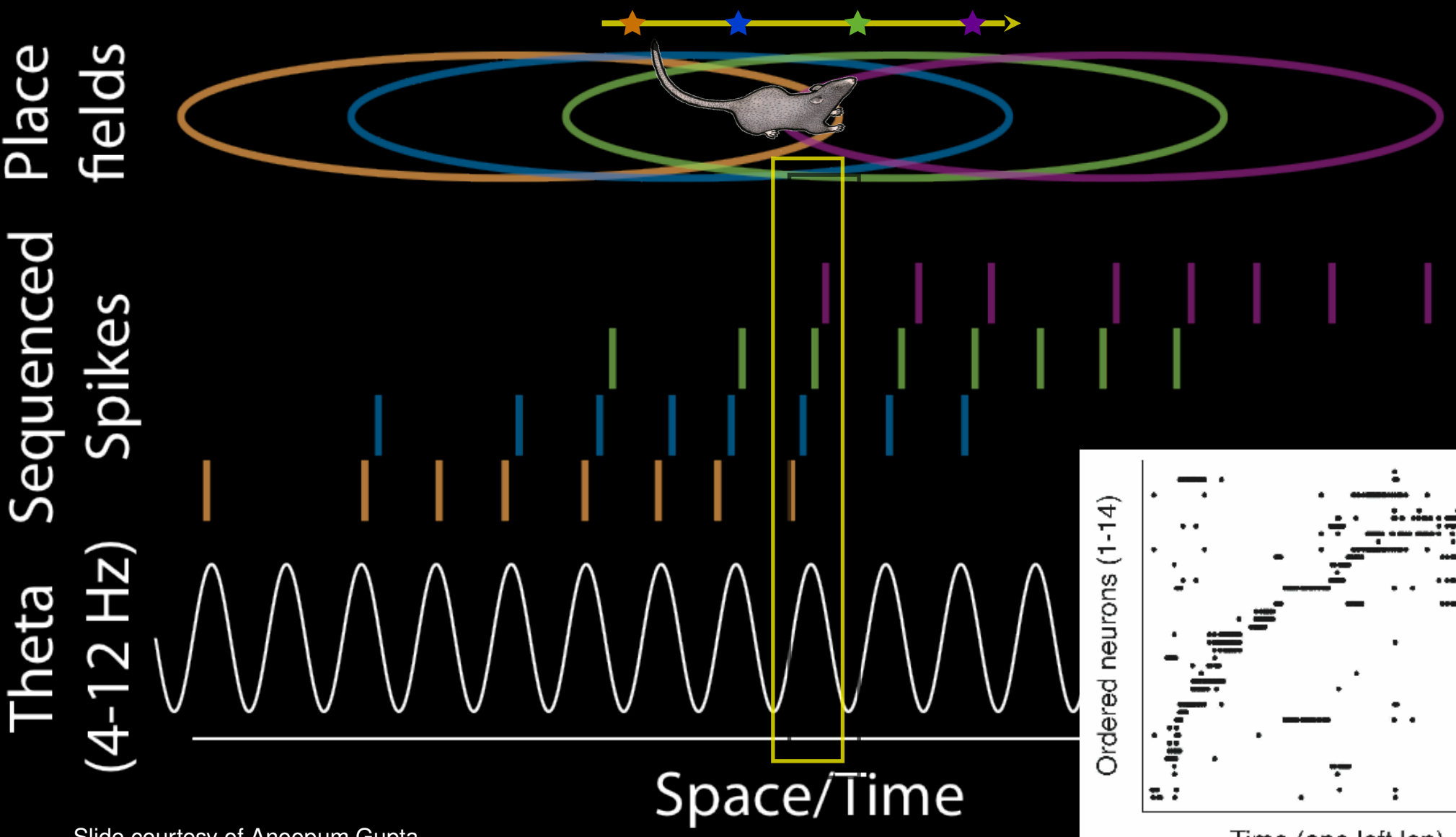
- The theta pacemaker is the medial septal nucleus, which has a GABAergic projection to the hippocampal formation via the fornix. (Also a significant cholinergic projection.)

Gamma Rhythm

- Roughly 40 Hz oscillation (could be from 25 to 100 Hz)
  - "Slow gamma" is 25-50 Hz; "fast gamma" is 50-90 Hz.`
- Gamma is superimposed on top of theta in hippocampus.
- There is speculation that gamma rhythm synchrony may play a role in binding cortical areas together. Consciousness?

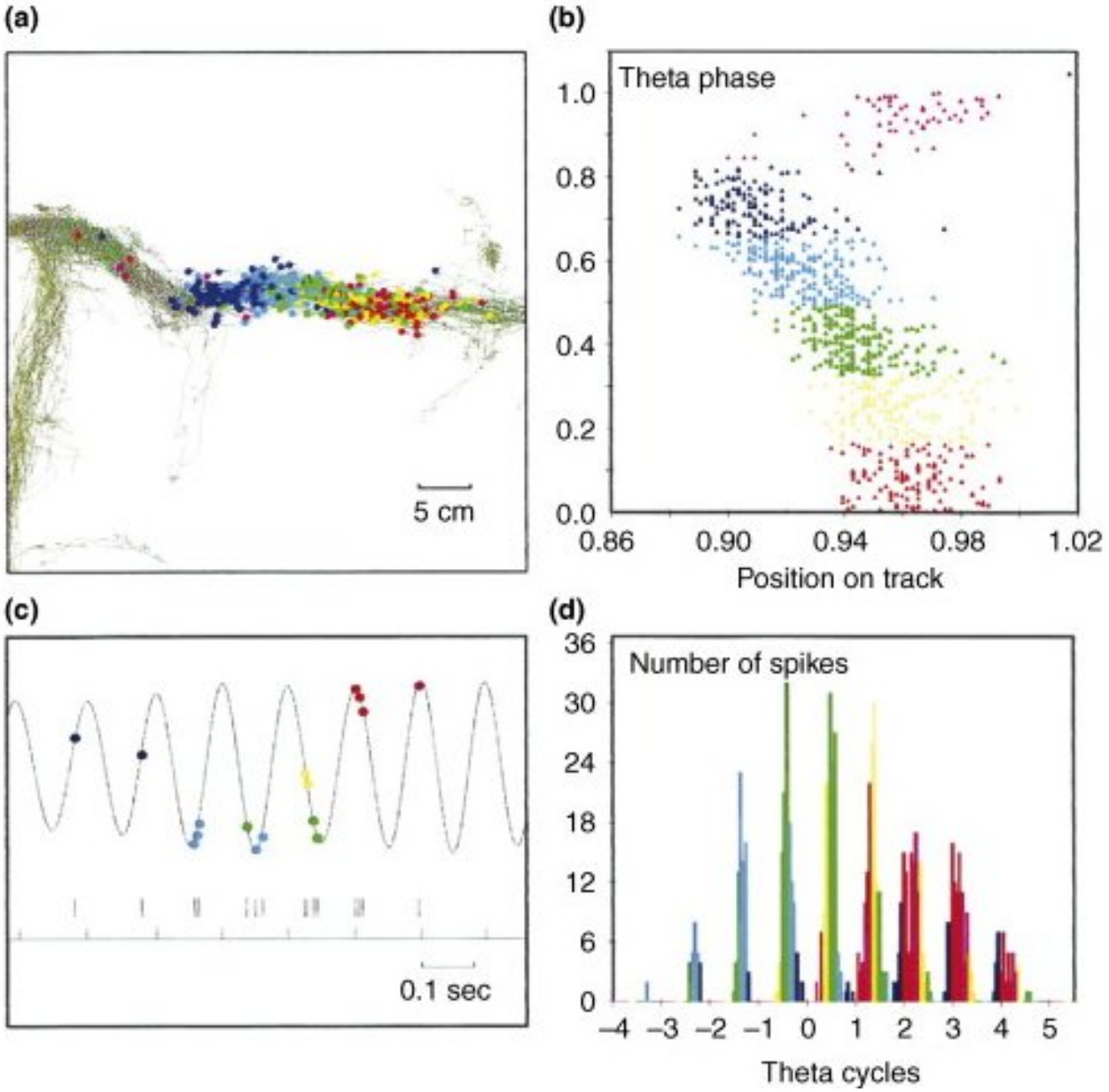


Theta Phase Precession



Slide courtesy of Anoopum Gupta

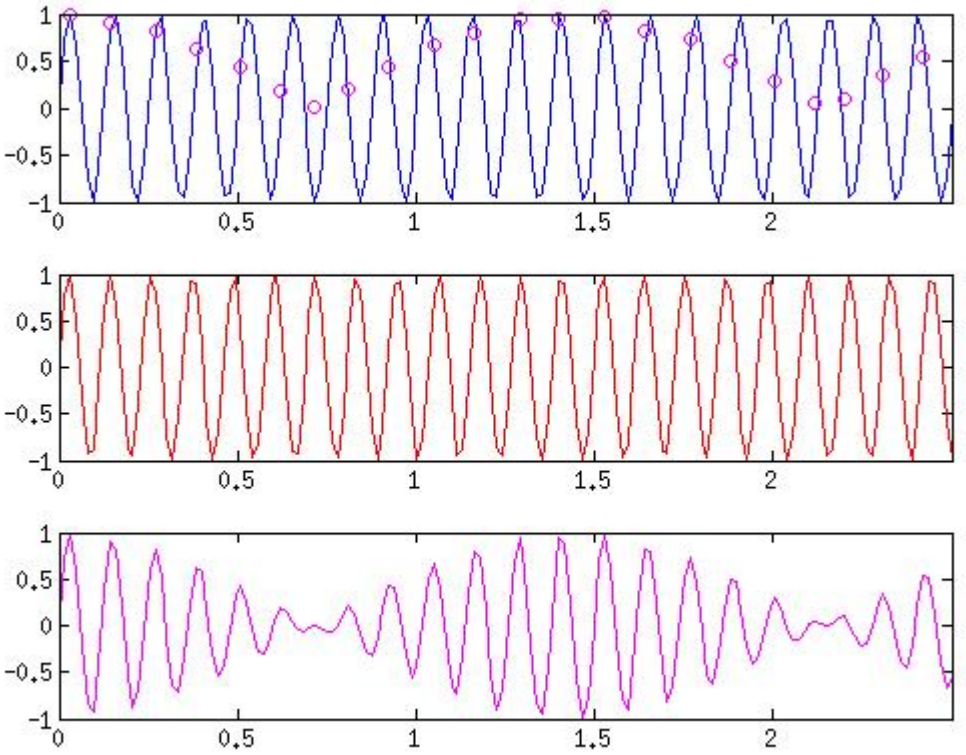
Phase Precession In One Hippocampal Place Cell



Maurer & McNaughton, TINS 2007

Theories of Phase Precession

- Network theory: caused by interactions among cells; cells learn to predict firing ahead of the rat.
- Oscillator interference mechanism: slightly faster cellular oscillator beats against the theta rhythm.



Problems for Both Theories

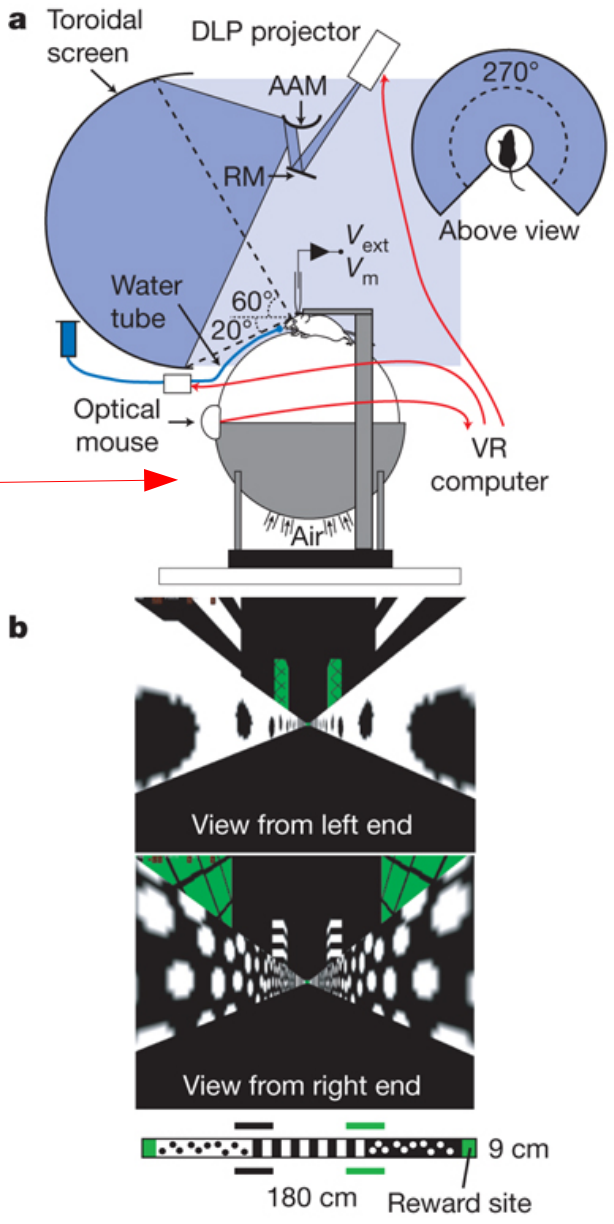
- Network theory depends on learning, but phase precession has been observed on the first pass through a firing field.

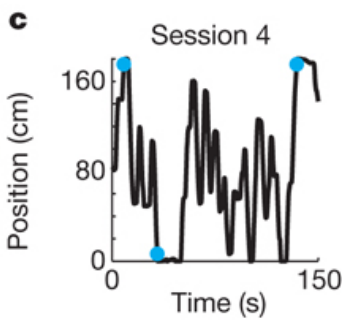
- The oscillator interference model depends on a specific phase relationship between the intrinsic oscillator and the rat's location. But some cells with multiple overlapping firing fields will fire spikes at both phases of the theta cycle, which a simple oscillator couldn't do.

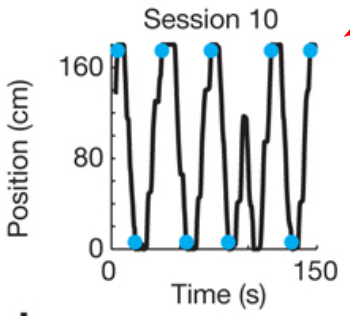
Mice In a Virtual Reality Environment

Harvey et al.
Nature 2009

Spherical treadmill

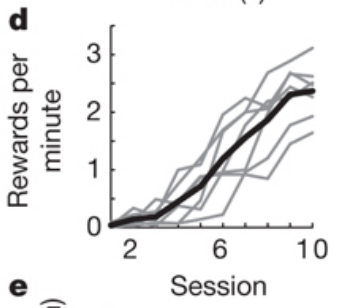


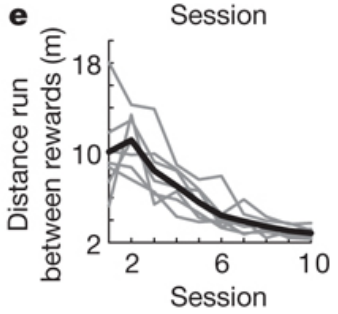




Sample trajectories

= water reward



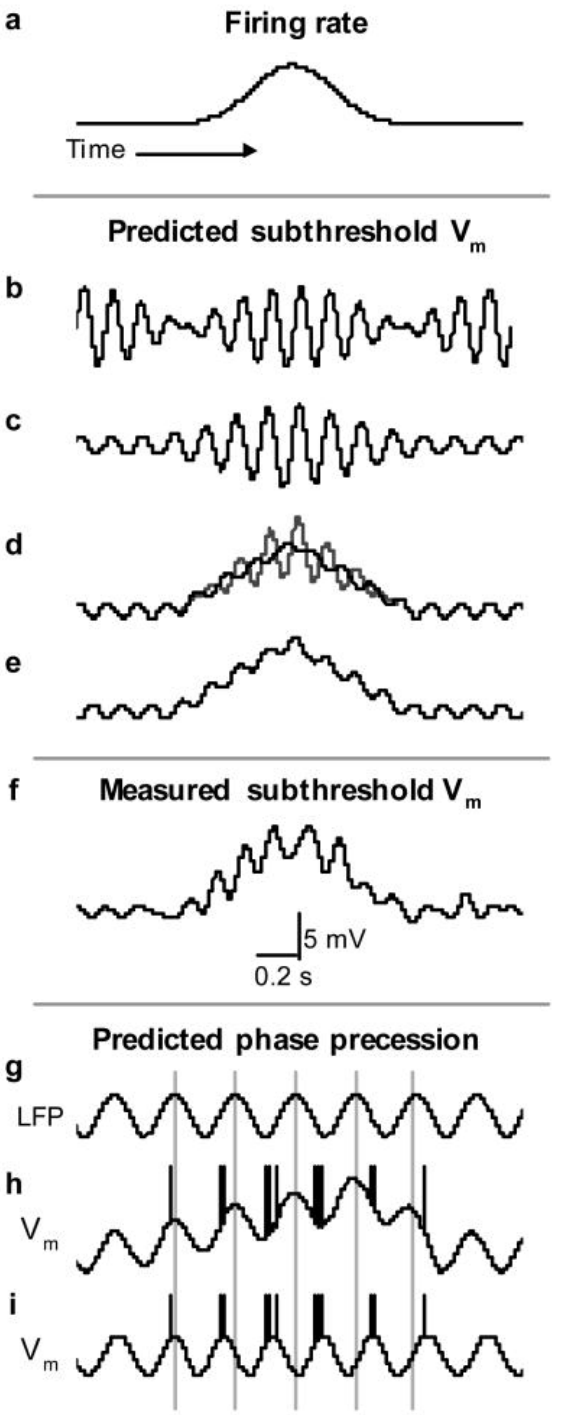


Sub-Threshold Membrane Oscillations and Place cell Phase Precession

Predictions from dual oscillator models

Measured intracellular membrane potential; spikes removed

Harvey et al. Nature 2009



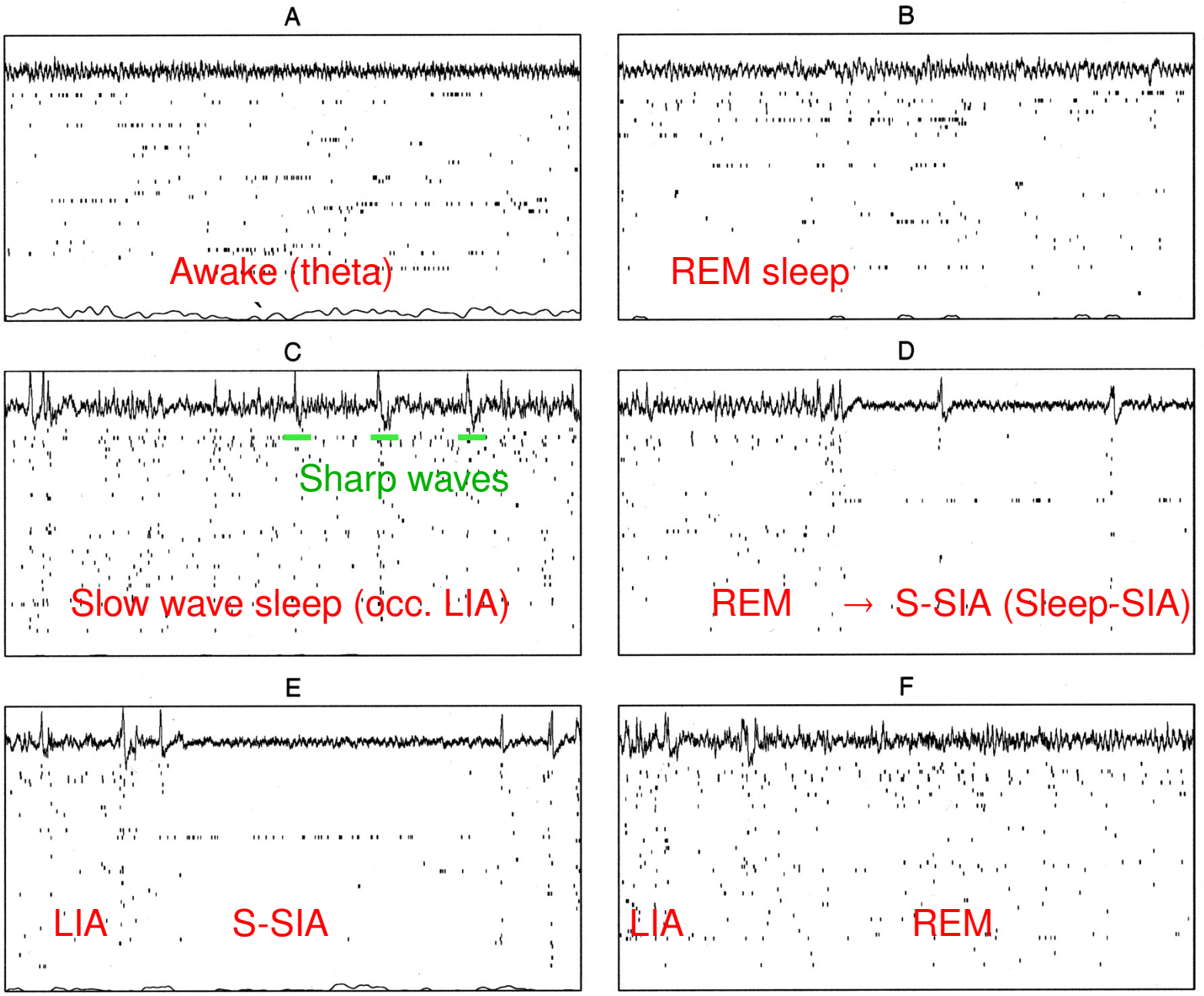
Intracellular Oscillations

- Harvey et al. recorded *intracellularly* from place cells in mice running on a treadmill.
- Observations as the animal proceeds through the field:
  - Ramp-like depolarization of baseline membrane potential
  - Increasing amplitude of membrane potential theta
  - Phase precession of intracellular theta relative to LFP
  - Spike times advance relative to LFP but not relative to intracellular theta
- Most compatible with a somato-dendritic interference model of phase precession.

Why Is Phase Precession Useful?

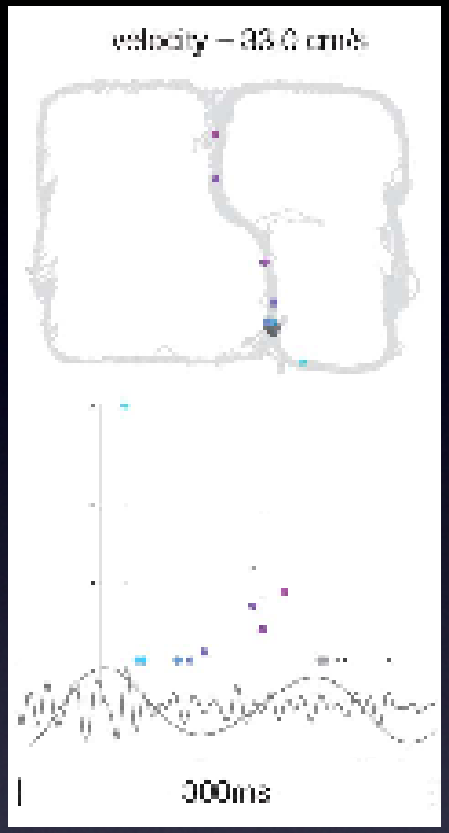
- At any given location, place cells behind the rat fire earlier in the theta cycle than place cells ahead of the rat.
- This sets up the necessary conditions for Hebbian learning: if cell A fires before cell B, strengthen the A $\rightarrow$ B connection.
- On each theta cycle the hippocampus is playing a short *sequence* of activity representing a slice of its current trajectory.

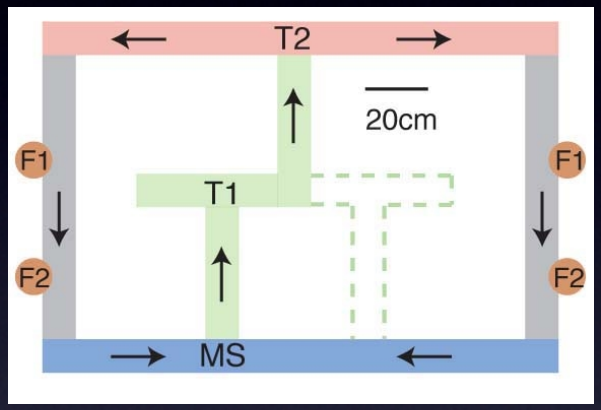
Hippocampal EEG



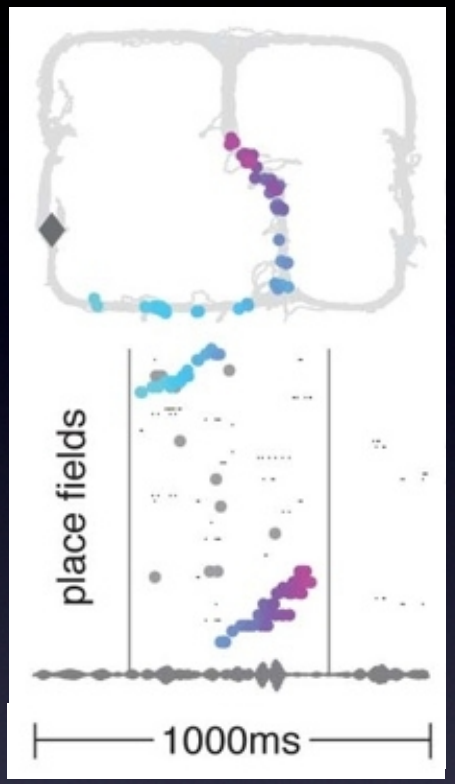
Theta vs Replay Sequences

Theta





Replay



Occur during attentive behavior
Theta oscillation is present
Tied to the animal's location
Forward sequence
Few neurons are active
Relatively short paths represented
Experience encoding and recall

Occur during awake rest
Sharp wave ripples present
Not always tied to the animal's location
Forward or backward sequence
Many neurons are often active
Highly variable path lengths represented
Memory consolidation, learning of cognitive maps

Slide courtesy of Anoopum Gupta

Lisman & Idiart (1995): Working Memory

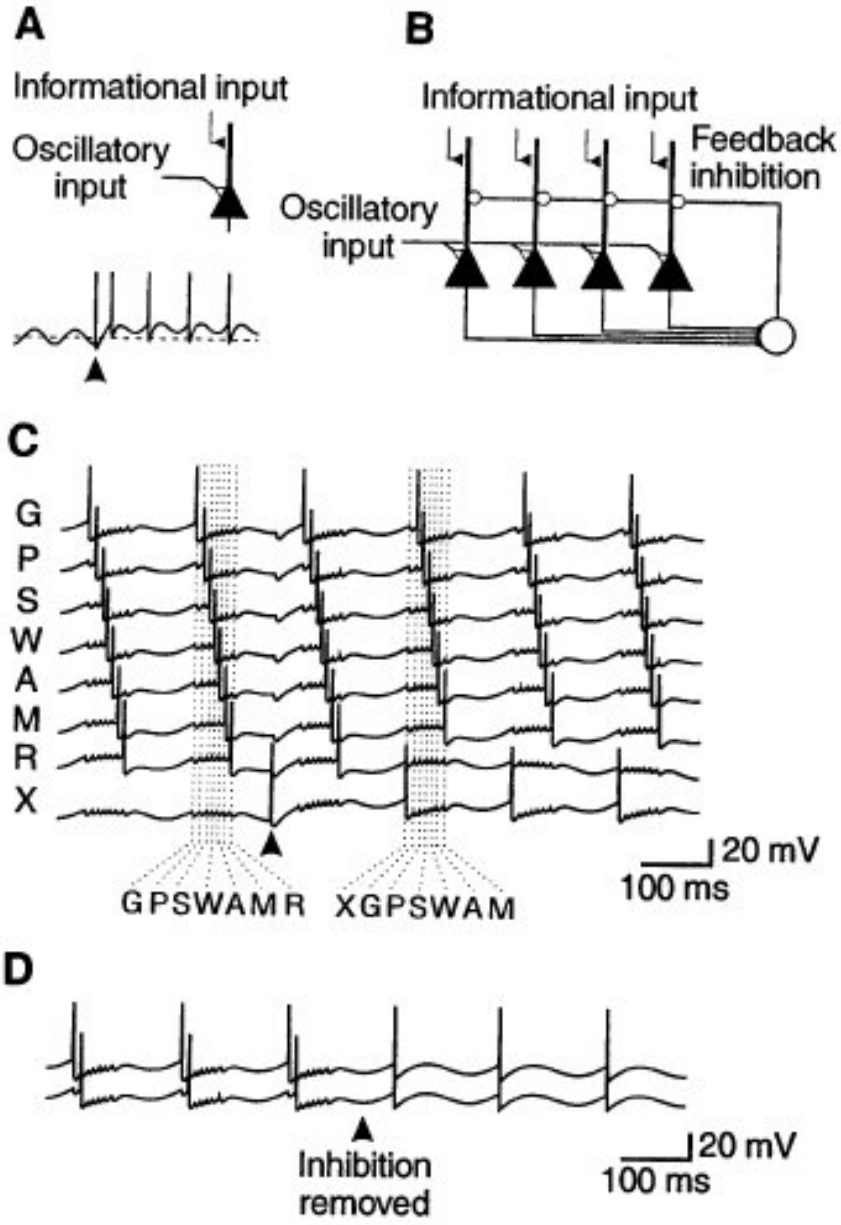
- Hippocampal cells undergo a gradually increasing afterdepolarization (ADP) that re-excites the cell after firing.

- Could this be the basis of a working memory mechanism?
- Sternberg: reaction time on list search task goes up by 38 ms per list item; hypothesize serial scan process.
- Assume true scan time is 25 ms/item (plus 13 ms/item for other "costs", yielding observed 38 ms/item). Can fit seven 25 ms gamma cycles into one theta cycle.

How It Works

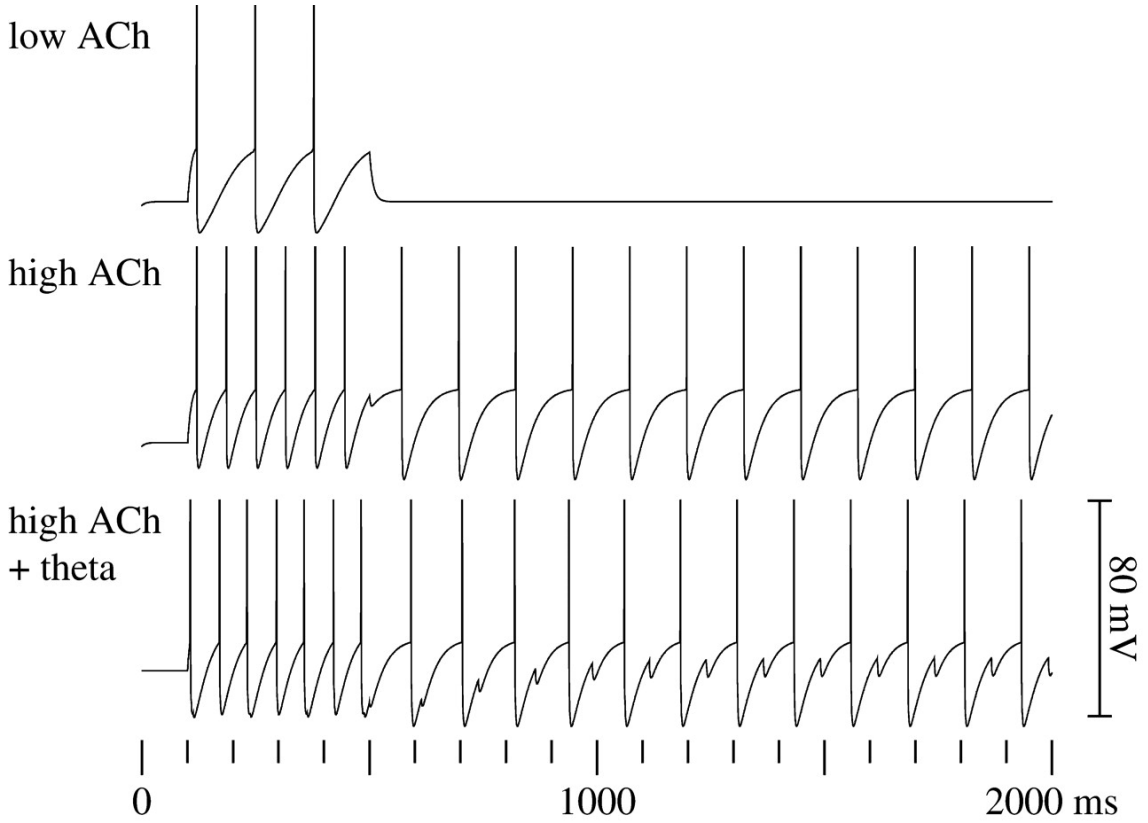
- Each cell receives sub-threshold oscillatory input at the theta frequency.
- Cells that are above threshold due to oscillator plus ADP fire.
- Rapid inhibitory feedback prevents less active cells from firing right afterward; divides up the theta cycle into a set of discrete gamma slots.
- 7 gamma cycles = 175 ms = 5.7 Hz = time for one theta cycle
- So memory capacity is 7 items.

Lisman & Idiart Working Memory Model



Persistent Activity in EC Neurons

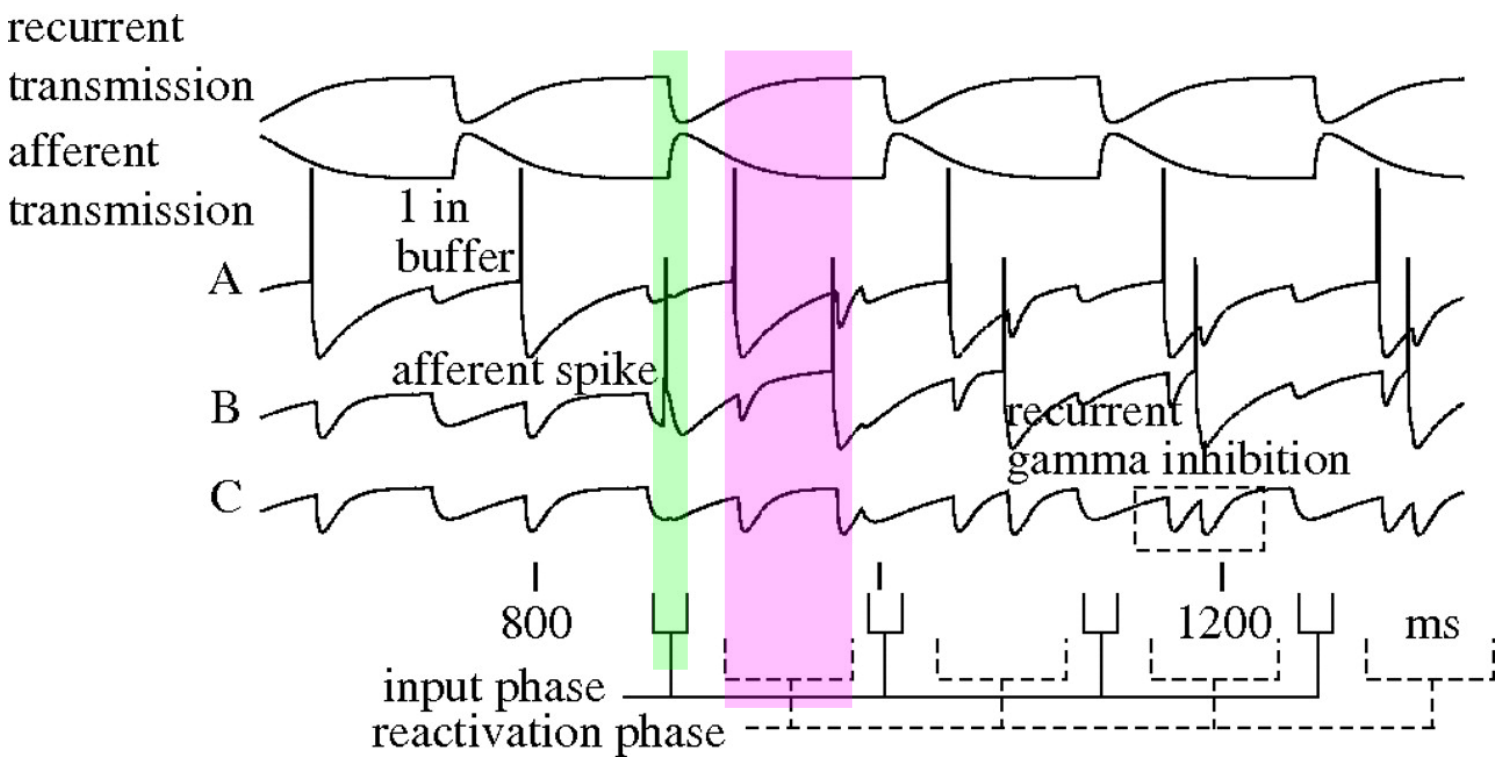
- Pyramidal cells in EC layer II exhibit ADP and persistent firing in the presence of the neuromodulator ACh.



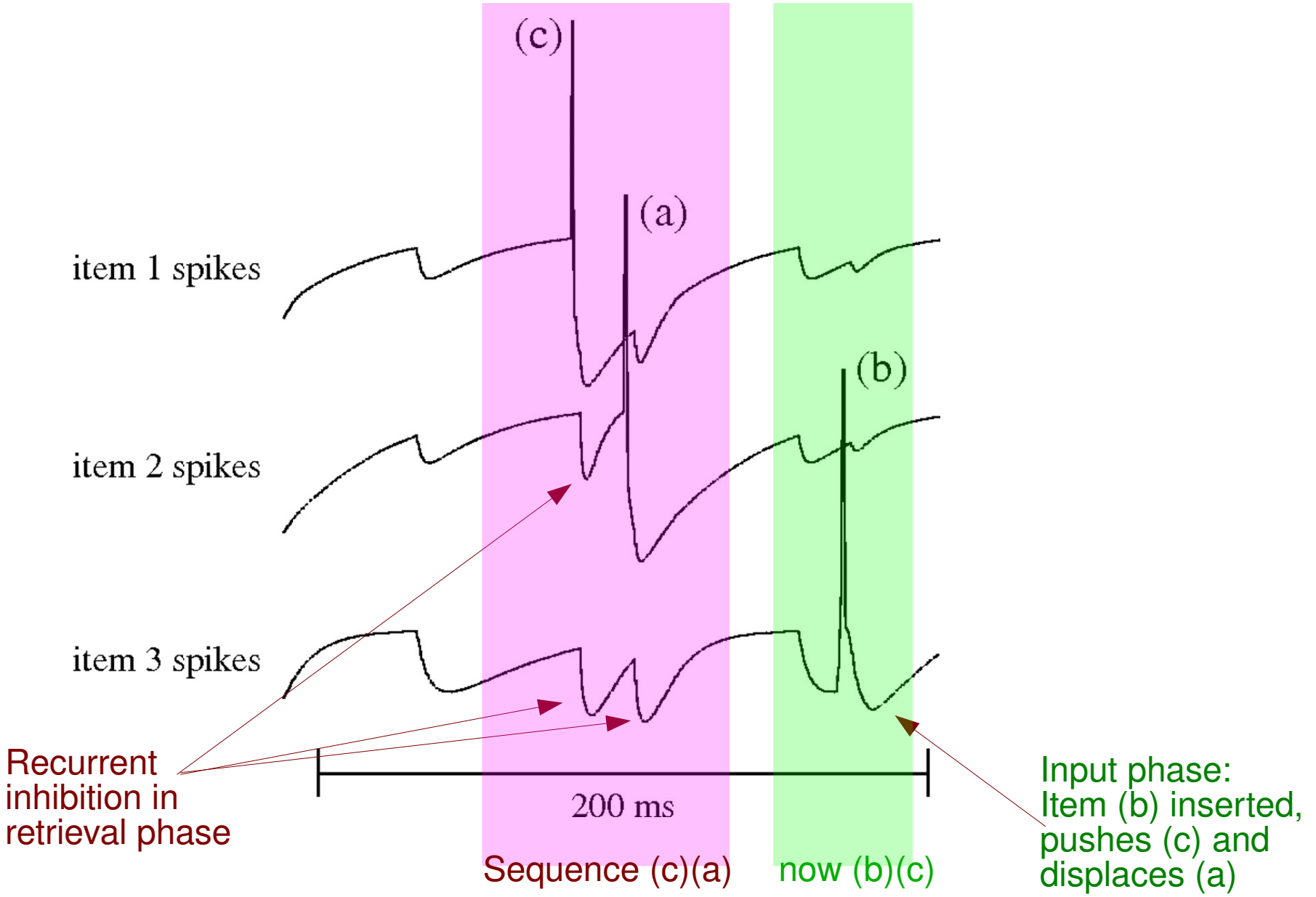
Koene & Hasselmo
Cerebral Cortex 2007

Koene & Hasselmo Buffer Model

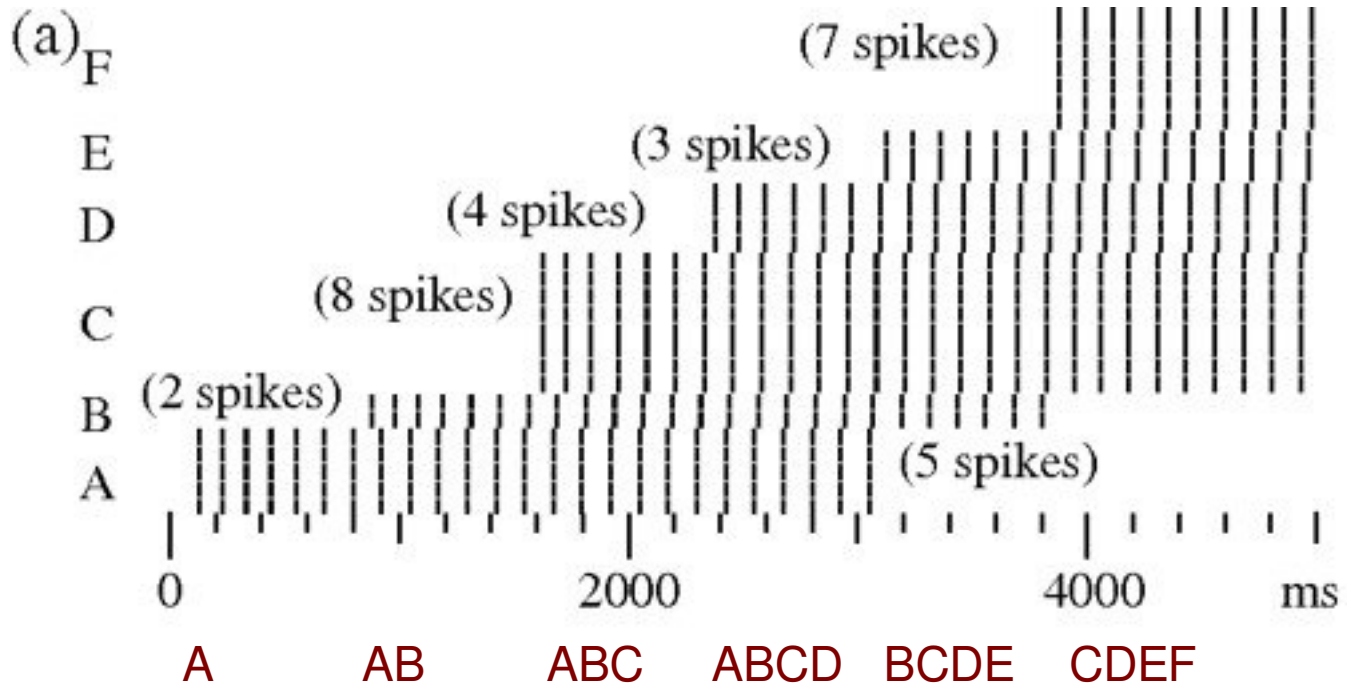
- Input phase plus reactivation phase of theta cycle



Limited Number of Memory Slots (e.g., 2)

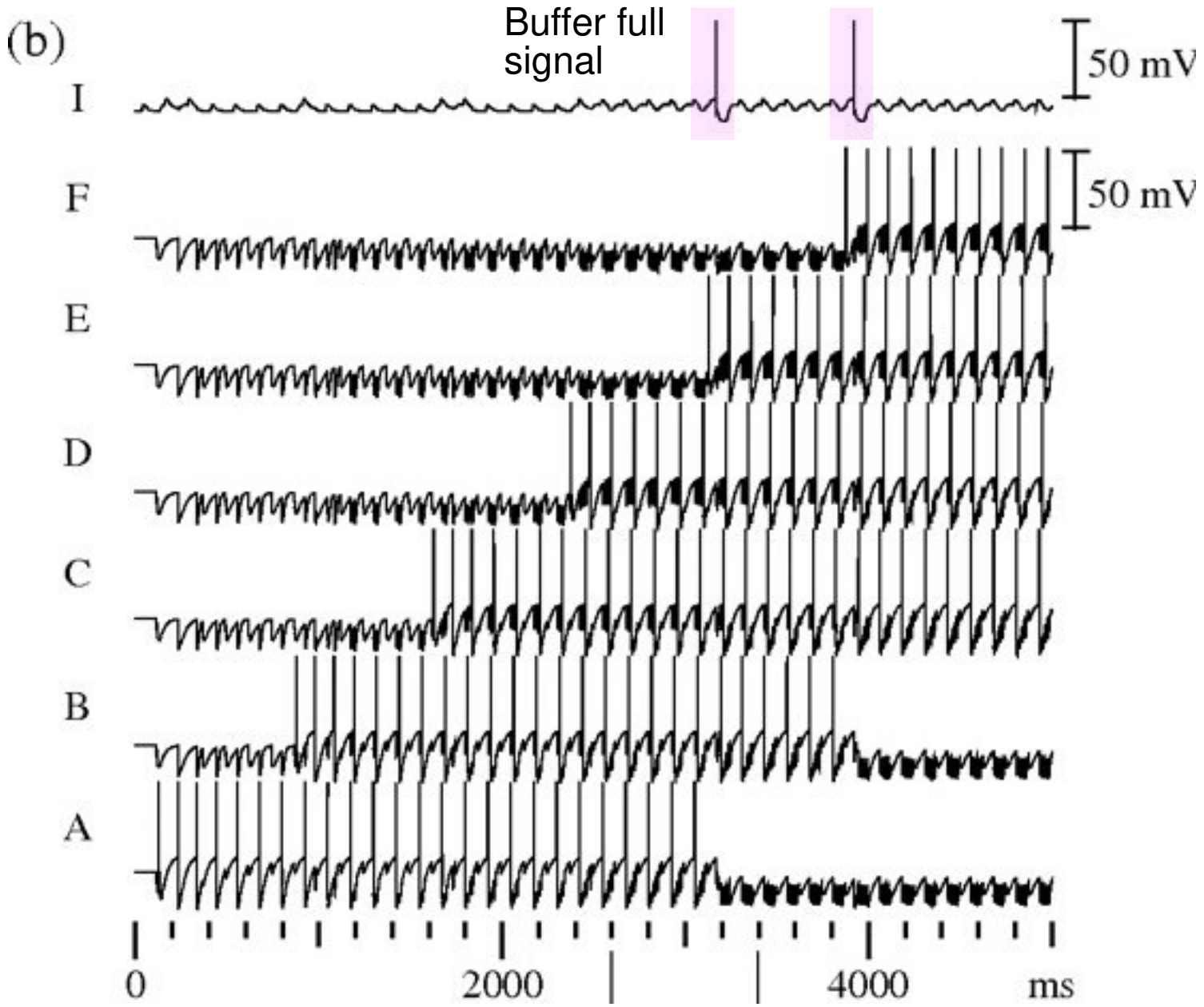


FIFO Replacement; Capacity = 4 Items
Variable Item Size

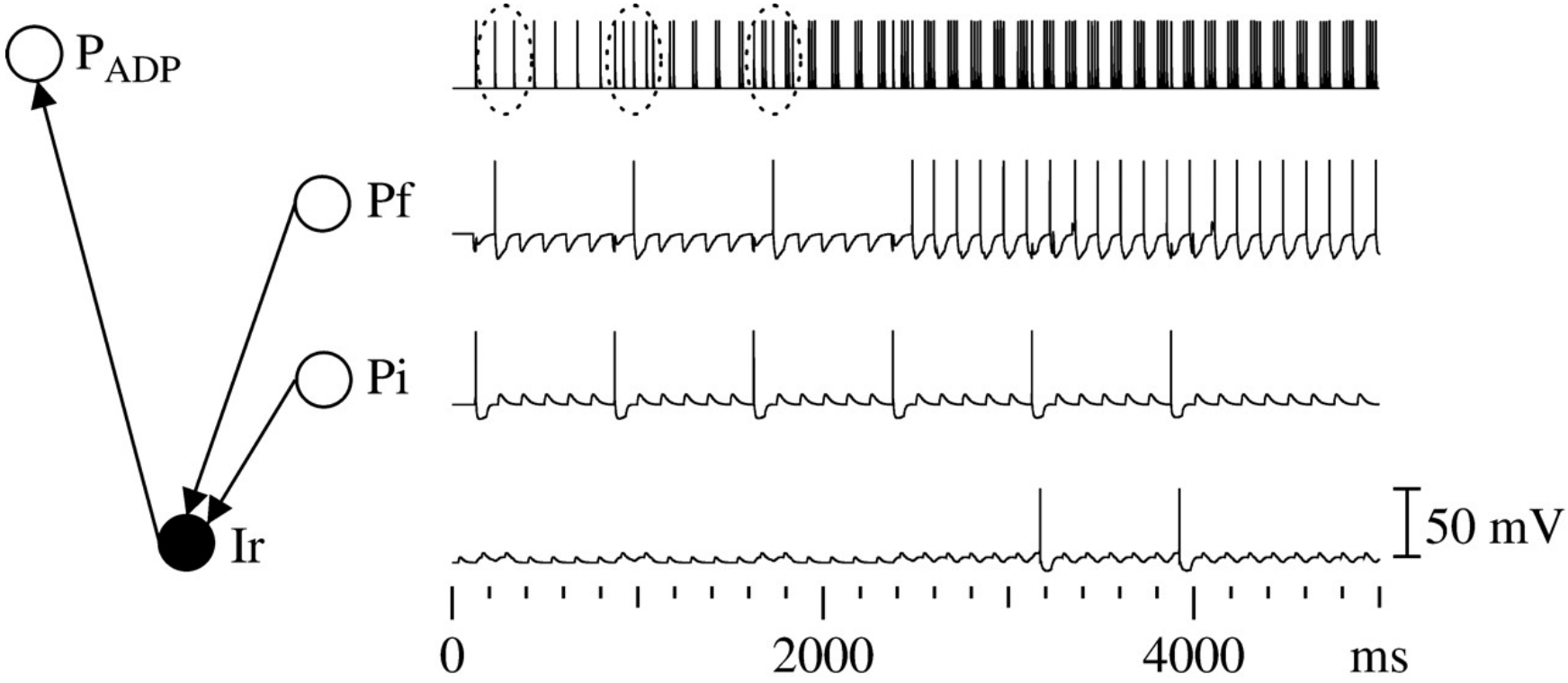


FIFO = First In, First Out
LIFO = Last In, First Out

Membrane Potential

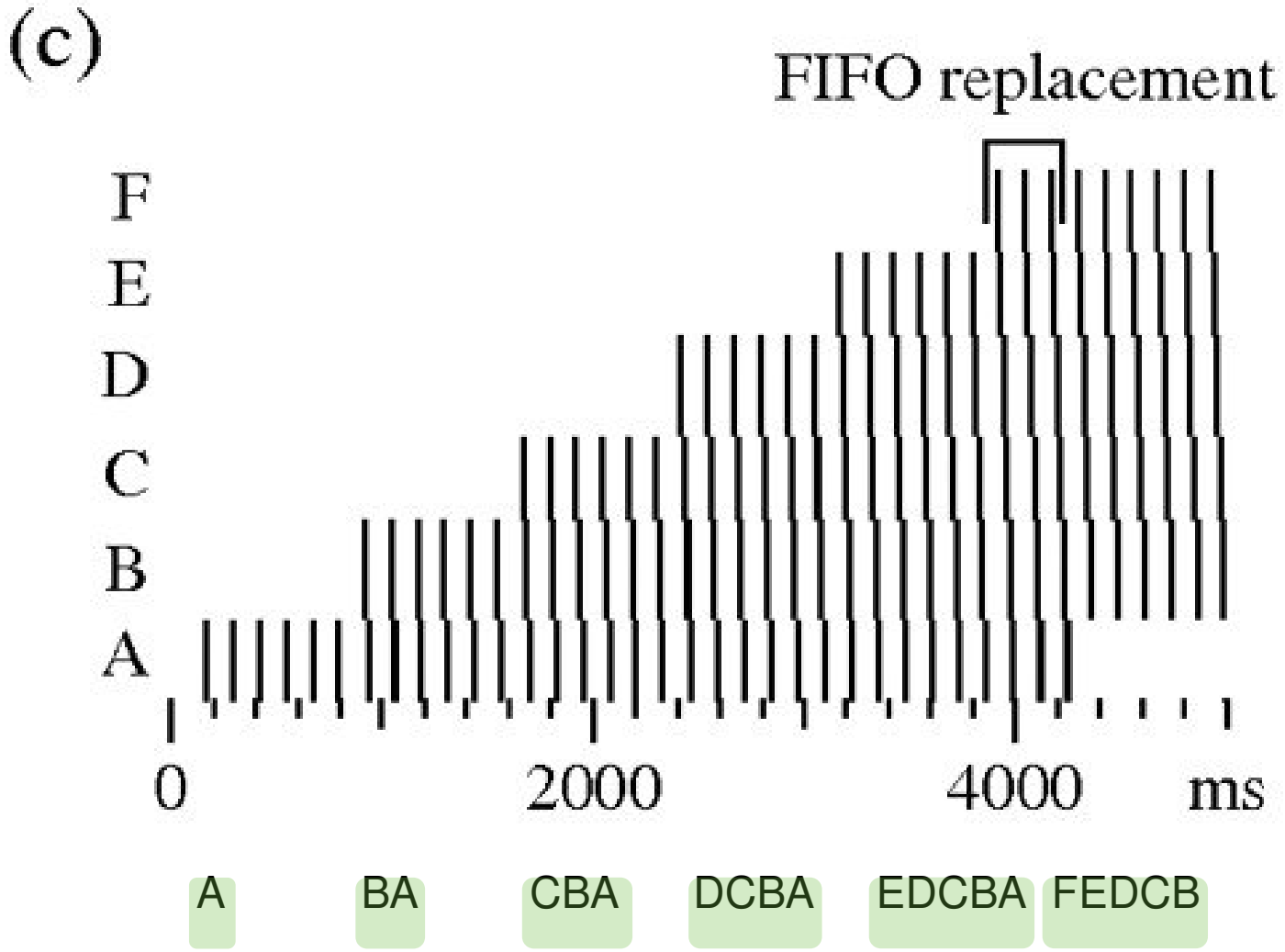


Inhibitory Interneuron Deletes First Item Before Inserting New Item Into a Full Buffer

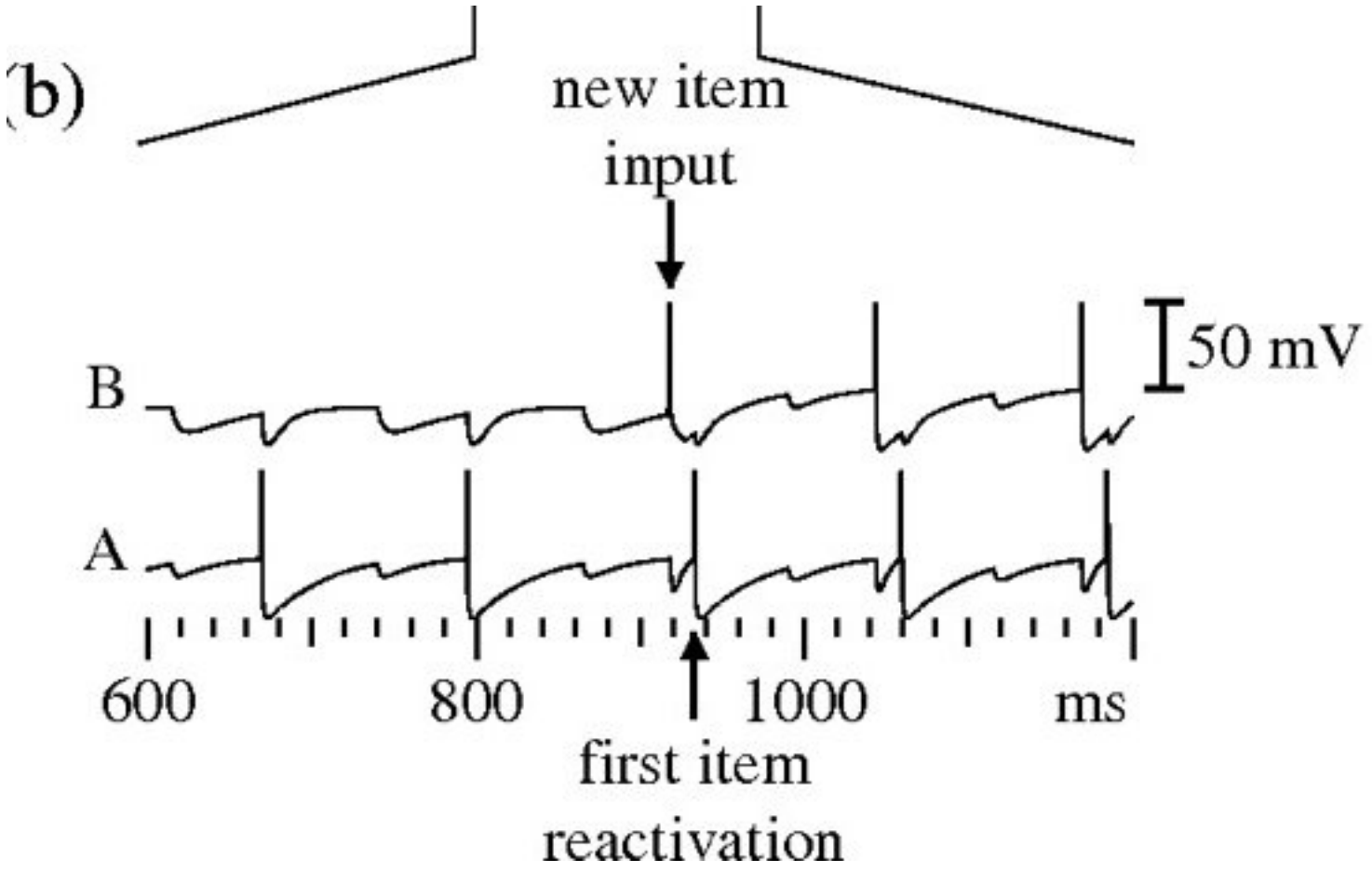


Pf = buffer full
Pi = input arriving
Ir = inhibition for replacement

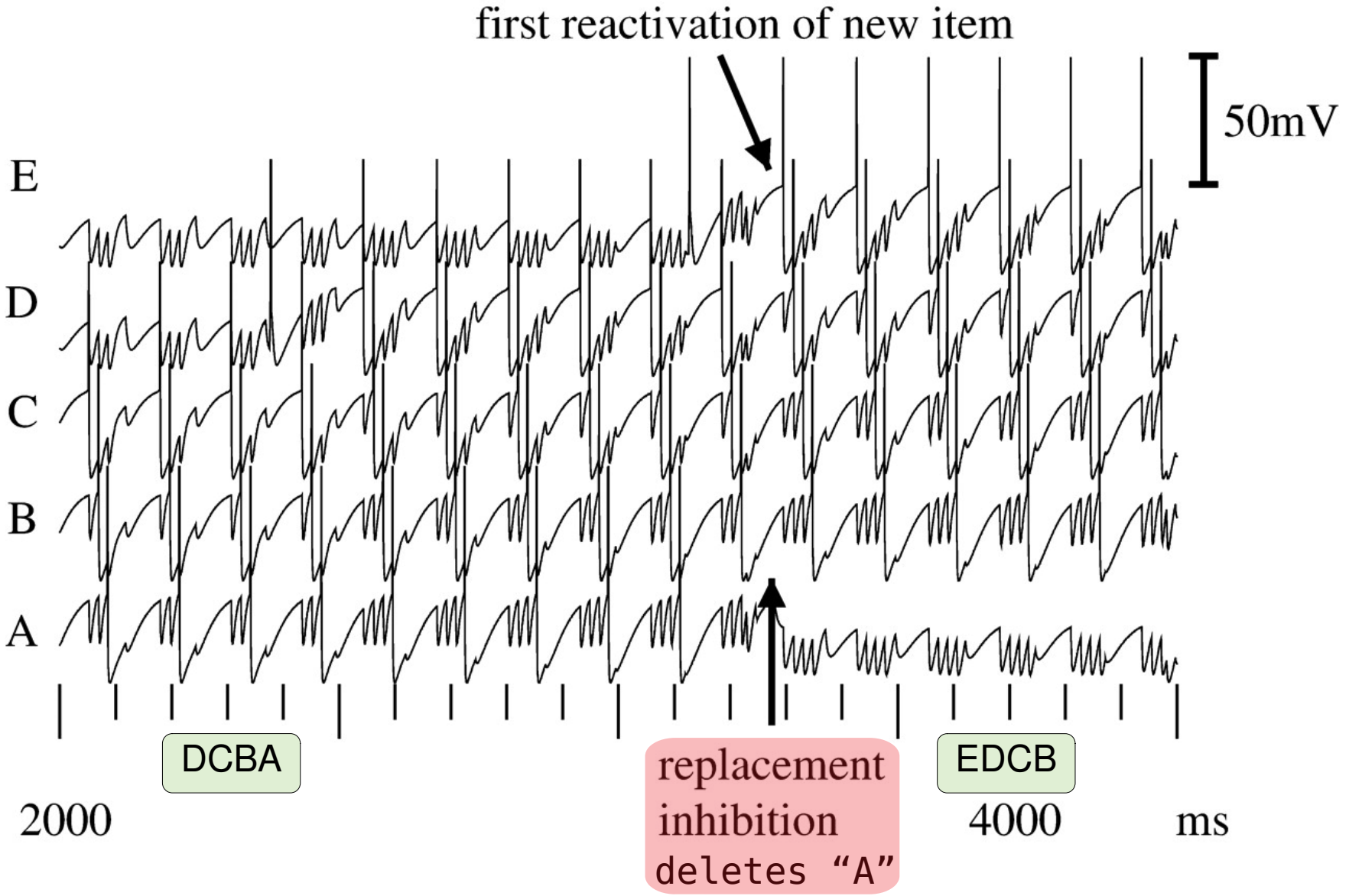
A Reverse-Order (LIFO) Readout Buffer Inserts at the Beginning of the Theta Cycle



Inserting At the Front of the Buffer



Reverse FIFO Buffer With Replacement



Summary

- The theta rhythm introduces temporal structure to hippocampal activity patterns.
- Theta phase precession of place cell firing encodes spatial information in the temporal pattern.
- ADP could allow cells in hippocampus or EC to serve a working memory function.
- The Koene & Hasselmo model can store items with different numbers of active units; only phase matters.
- Is the gamma cycle really a discretization of theta into multiple working memory “slots” for storing discrete items?
- Is the somato-dendritic interference model compatible with the theta/gamma working memory model?