receptive fields, tuning curves, mutual information etc. can relate neural activity to **external variables** (orientation of a bar of light, reaching direction, etc)

but what about **cognition**? (internally generated, covert processes)
M1 cells encode direction of movement

electrophysiology experiments by Apostolos Georgopoulos and others have shown that M1 cells fire before/during a movement and are tuned to movement direction.

Georgopoulos et al (1982), J Neurosci
Population coding in M1

Primary motor cortex cells are broadly tuned to motion direction. So, precise representation of movement direction requires summation of the signals of a population of motor cortex cells. Such coding requires simultaneous activity over an array of cells and is referred to as "vector" or "population" coding.
In this task, a monkey had to make a movement 90 degrees from a cued direction.

Under these conditions, the movement vector initially points in the direction of the cue then rotates to the direction of the actual movement.

Georgopoulos et al. (1989) Science
receptive fields, tuning curves, mutual information etc. can relate neural activity to **external variables** (orientation of a bar, reaching direction, etc)

but what about **cognition**? (internally generated, covert processes)
receptive fields, tuning curves, mutual information etc. can relate neural activity to **external variables**
(orientation of a bar, reaching direction, etc)

but what about **cognition**?
(internally generated, covert processes)

purely sensory and purely motor activity regimes are rare in mammalian brains!
hippocampus as a case study for decoding cognitive processes

first: the 3 big themes of hippocampal function
1957 – Patient H. M.
Original

Direct Copy

Delayed

Try Recall.
No recall of even drawing it.

---

Day 1

Day 2

Day 3

Errors

Trial Within Session
1973 – Bliss and Lomo
Long term potentiation

J. Physiol. (1973), 232, pp. 331–356
With 12 text-figures
Printed in Great Britain

LONG-LASTING POTENTIATION
OF SYNAPTIC TRANSMISSION IN THE DENTATE AREA
OF THE ANAESTHETIZED RABBIT FOLLOWING
STIMULATION OF THE PERFORANT PATH

BY T. V. P. BLISS AND T. LØMO
From the National Institute for Medical Research, Mill Hill,
London NW7 1AA and the Institute of Neurophysiology,
University of Oslo, Norway

(Received 12 February 1973)
1973 – O’Keefe and Dostrovsky
1976 – O’Keefe
Place cells
Different place fields fire at different locations in the environment … and are generally stable

Barnes, Suster, Shen, McNaughton (1997) Nature
Place cells “remap” in different environments

Quirk et al, 1992
“We shall argue that the hippocampus is the core of a neural memory system providing an objective spatial framework within which the items and events of an organism’s experience are located and interrelated.”
Blocking synaptic plasticity in the hippocampus disrupts spatial learning

Intrahippocampal infusion of AP5 (NMDAR antagonist) impairs acquisition of spatial reference memory in a water maze task.

Selective impairment of learning and blockade of long-term potentiation by an N-methyl-D-aspartate receptor antagonist, AP5

R. G. M. Morris*, E. Anderson*, G. S. Lynch†
& M. Baudry†

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![Graphs showing latency over time](image-url)
Figure 4. Hierarchy of visual areas. This hierarchy shows 32 visual cortical areas, shaded according to the same scheme as in Figure 2. 2 subcortical visual stages (the retinal ganglion cell layer and the LGN), plus several nonvisual areas (area 7b of somatosensory cortex, parietal area 36, the ER, and the hippocampal complex). These areas are connected by 187 linkages, most of which have been demonstrated to be reciprocal pathways.
Decoding cognitive processes in the rat hippocampus

Matthijs (Matt) van der Meer

Assistant Professor & Canada Research Chair
Department of Biology, University of Waterloo, Canada

*Psychological and Brain Sciences, Dartmouth College (Jan 2015)

http://www.vandermeerlab.org
the hippocampus is important for the rapid (one-trial) learning of spatiotemporal “episodes”

1. the hippocampus receives highly processed sensory input

2. spatiotemporal input sequences are **encoded** and **stored** as a “continuous record of attended experience” (Morris, 2005)

3. the record can be accessed online (**recall**) and is **consolidated** offline into extrahippocampal areas
raw data
voltage trace

1-475 Hz filter

field potentials

600 Hz - 6 kHz filter

action potentials
(single neuron spikes)

illustration from Buzsaki et al. 2004
“place cell”

place field →
theta (6-10Hz)

local field potential
figures from Malhotra et al. 2012; see also Schmidt et al. 2009, O'Keefe and Recce 1993
figure from Malhotra et al. 2012; see also Skaggs & McNaughton 1996, ...
**SIMULATION**

- **place cell 2 tuning curve (field)**
- **place cell 1 tuning curve (field)**

**WITHOUT PHASE PRECESSION**

- **theta LFP**

**CCG**

(histogram of blue spike times relative to red spike at t = 0)
Possible functional roles for hippocampal phase precession

1. Lookahead. Phase precession implies that, within each theta cycle, a compressed sequence of place cells appears. This sequence moves faster than the animal itself, potentially giving a decoder access to upcoming locations. This requires that the decoder ignores theta phase (see the next panel).
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2. Phase code for position. In contrast to the scenario in panel 1 (left), a decoder can estimate position more accurately when taking theta phase into account (Jensen & Lisman, 2000). No phase-driven lookahead would be decoded in this case.

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3. Rapid encoding of sequences. Phase precession implies specific cross-correlations in sequentially activated place cells conducive to STDP.

Without phase precession. While on average, the first place cell spikes before the second, the cross-correlation in the STDP range is only mildly asymmetric, so $\Delta w$ will be small.

With phase precession. Now, the cross-correlation is strongly asymmetric (the first place cell reliably spikes before the second), so $\Delta w$ will be large, enabling rapid learning.
Poisson assumption
Independence assumption

\[ P(x|n)P(n) = P(n|x)P(x) \]

\[ P(n|x) = \prod_{i=1}^{N} P(n_i|x) = \prod_{i=1}^{N} \left( \frac{\tau f_i(x)^{n_i}}{n_i!} \right) \exp(-\tau f_i(x)) \]


Figure from van der Meer et al. *Neuron* 2010
theta sequences are diverse

R042-2013-08-18
(RIGHT laps)

Carey & van der Meer, in preparation
$Z = p(x|s)$ for times at location $x$; image shows $Z^2$. 

Gupta, van der Meer et al. (2012)
slow (low) and high (fast) gamma in CA1 are associated with CA3 and MEC input respectively.
the hippocampus is important for the rapid (one-trial) learning of spatiotemporal “episodes”

1. the hippocampus receives highly processed sensory input

2. spatiotemporal input sequences are **encoded** and **stored** as a “continuous record of attended experience” (Morris, 2005)

   the hippocampus packages ongoing experience into temporally compressed, repeating “theta packets”

3. the record can be accessed online (**recall**) and is **consolidated** offline into extrahippocampal areas
reduced phase precession in intact place fields

A

Control

Drug

Recovery

$r=-0.61$

$r=-0.27$

$r=-0.48$

Robbe & Buzsaki, J Neurosci 2009
reduced phase precession in intact place fields…is associated with impaired memory for the previous trial.

Robbe & Buzsaki, J Neurosci 2009
“vicarious trial-and-error”
Johnson and Redish, *J Neurosci* 2007
van der Meer et al. (2010), Neuron
van der Meer et al. (2010), *Neuron*
the hippocampus is important for the rapid (one-trial) learning of spatiotemporal “episodes”

1. the hippocampus receives highly processed sensory input

2. spatiotemporal input sequences are **encoded** and **stored** as a “continuous record of attended experience” (Morris, 2005)

   the hippocampus packages ongoing experience into temporally compressed, repeating theta sequences

   content of theta sequences is dynamically modulated

3. the record can be accessed online (**recall**) and is **consolidated** offline into extrahippocampal areas
The hippocampus is important for the rapid (one-trial) learning of spatiotemporal “episodes”

1. The hippocampus receives highly processed sensory input

2. Spatiotemporal input sequences are encoded and stored as a “continuous record of attended experience” (Morris, 2005)

3. The record can be accessed online (recall) and is consolidated offline into extrahippocampal areas
hippocampal sharp wave-ripple complexes (SWRs)

slow depolarization (“sharp wave”) and 140-200Hz fast oscillation in (“ripple”) in CA1 LFP, initiated by CA3 input

occur primarily during slow-wave sleep and “quiet wakefulness”

Stark et al. Neuron 2014
SWR disruption during sleep slows learning

Girardeau et al. Nat Neurosci 2009
SWRs precede reactivation of firing patterns in the prefrontal cortex

Peyrache et al. Nat Neurosci 2009
so far so good...
so far so good...

but what about the content of SWR sequences?
LEFT rewarded

contingency switch

RIGHT rewarded
“same-side”

place fields

1000ms

“opposite-side”

LEFT rewarded

contingency switch

RIGHT rewarded

start  end
“same-side”

place fields

1000ms

“opposite-side”

start end
Gupta, van der Meer et al. (2010)
Gupta, van der Meer et al. (2010)
awake SWRs include never-experienced shortcuts
awake SWRs are preferentially directed at the goal location
disruption of awake SWRs impairs spatial working memory performance

the hippocampus is important for the rapid (one-trial) learning of spatiotemporal “episodes”

1. the hippocampus receives highly processed sensory input

2. spatiotemporal input sequences are encoded and stored as a “continuous record of attended experience” (Morris, 2005)

   the hippocampus packages ongoing experience into temporally compressed, repeating theta sequences

functional relevance unclear, but evidence suggests a role in recall

3. the record can be accessed online (recall) and is consolidated offline into extrahippocampal areas

   but the content of hippocampal “replay” is not tied to experience

   disruption of hippocampal SWR sequences affects spatial choice performance
decoding ensemble spiking activity gives us a window into internal representations – a necessary concept when connecting circuitry to complex behaviors

Rat

“surely one of the least promising organisms in which to investigate intellectual accomplishments”

(Miller et al., Plans and the Structure of Behavior, 1960)