

# Erasing, Tracing, and Harnessing long-term memory storage

André Fenton, PhD  
Professor of Neural Science  
Neurobiology of Cognition Laboratory  
Center for Neural Science

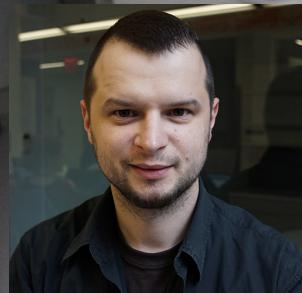
“What we think we become.”  
Gautama Siddharta



# Neurobiology of Cognition Laboratory



Fraser  
Sparks



Dino  
Dvorak



Zoe  
Talbot



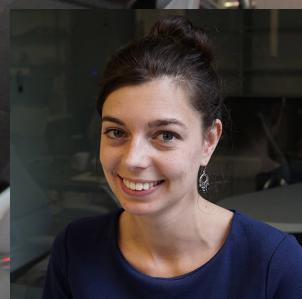
Hsin-Yi  
Kao



Edith  
Lesburgueres



EunHye  
Park



Milenna  
van Dijk



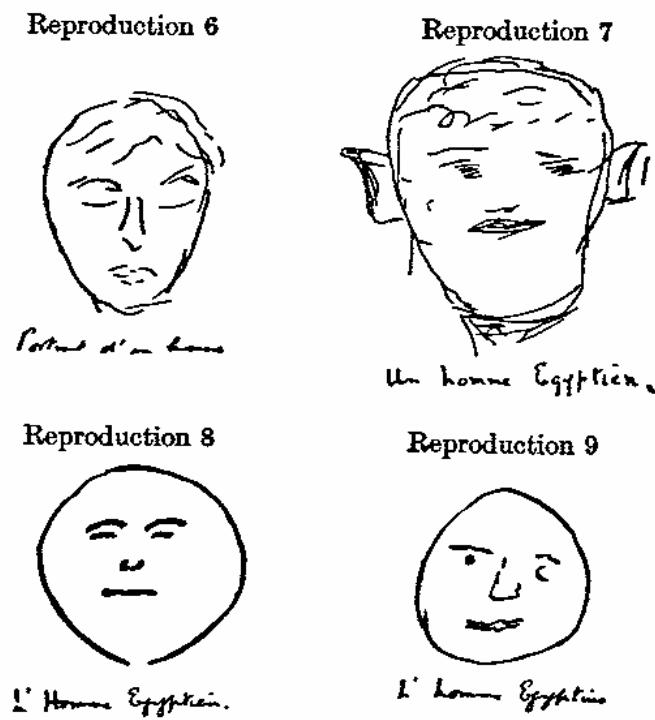
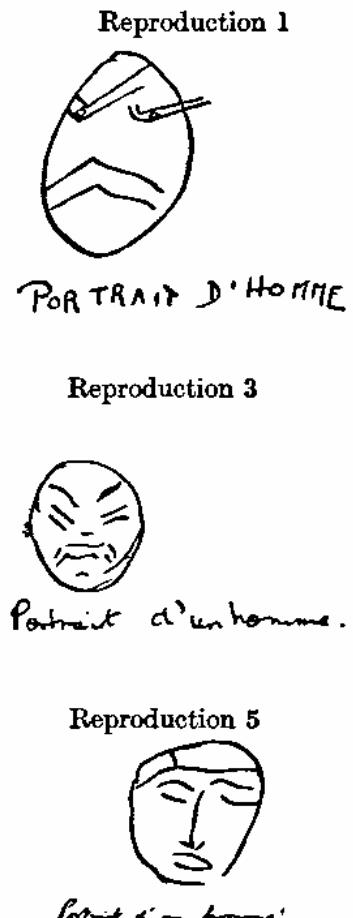
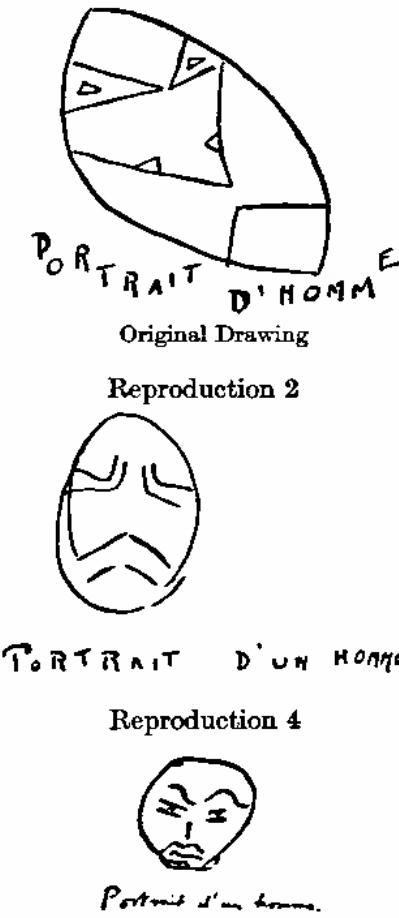
Kally  
O'Reilly



Ain Chung

- The truthiness of memory
- Cognitive experience leaves a major imprint within the synaptic organization of the brain
- Learning-related local field potentials create an infrastructure that organizes neural activity

We make up stories...  
Memory is reconstructive not reproductive



Bartlett, 1932

We remember events that never happened

The Deese–Roediger–McDermott paradigm

SODA

**HEART**

TOOTH

TART

**TASTE**

SOUR

**BITTER**

**SAUCE**

JELLY

GOOD

SUGAR

CANDY

NICE

CAKE

PIE

CHOCOLATE

HONEY

SODA  
HEART  
SPICE  
TOOTH  
TART  
TASTE  
SOUR  
SWEET  
BITTER  
SAUCE  
JELLY  
GOOD  
SUGAR  
CANDY  
NICE  
CAKE  
PIE  
CHOCOLATE  
HONEY

How does memory in the brain work?

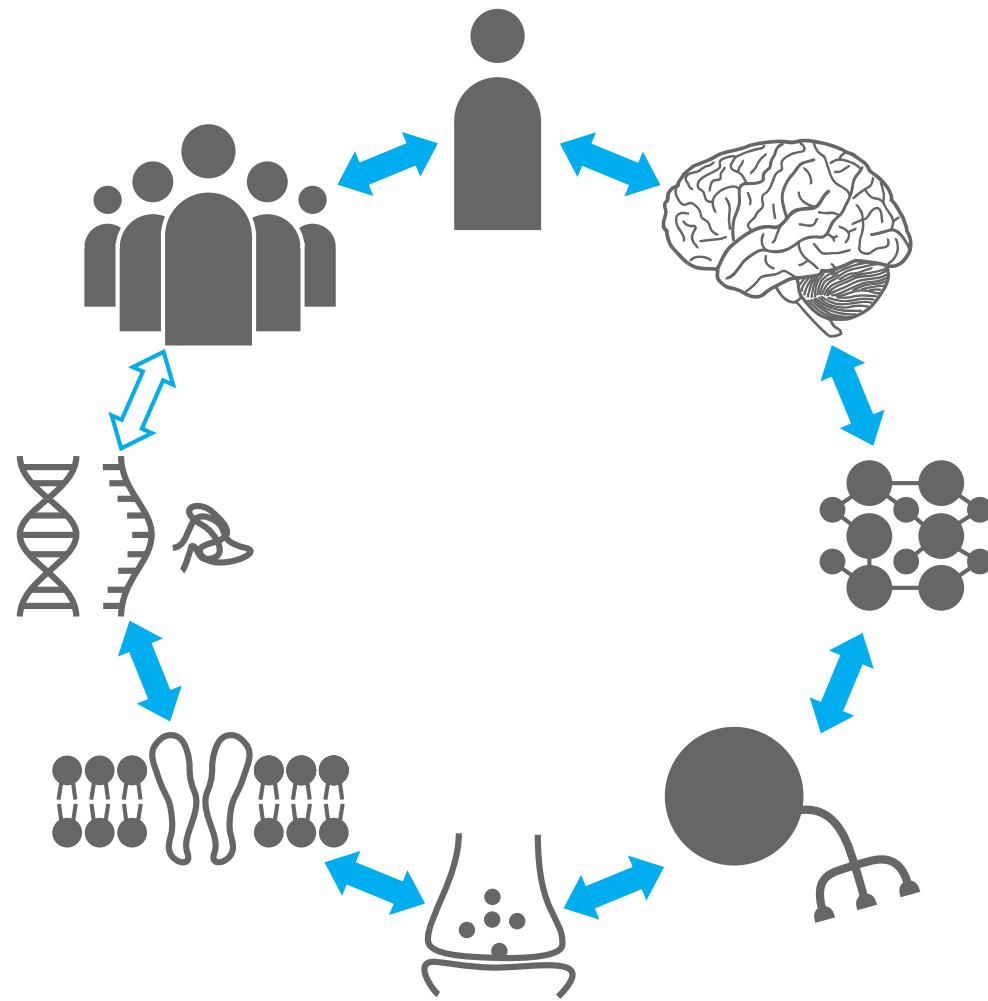
...where to start?

Multi-level complexity

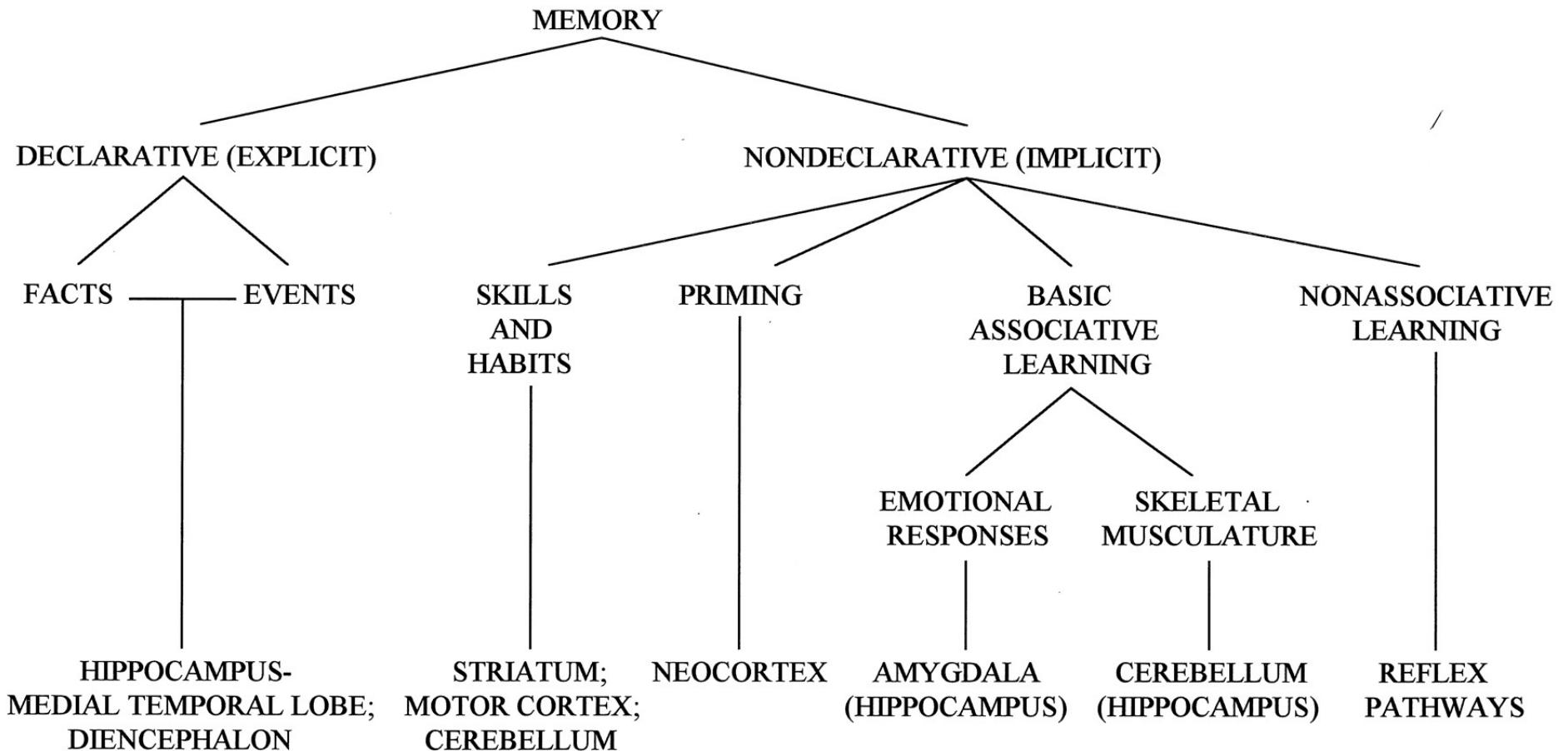


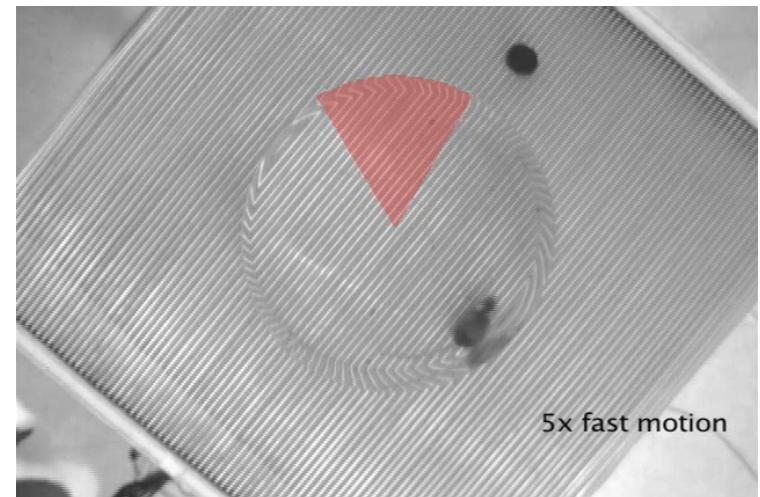
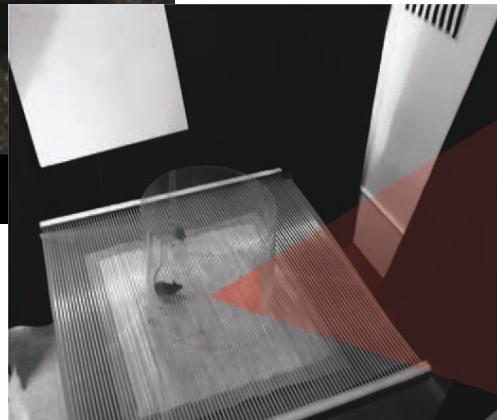
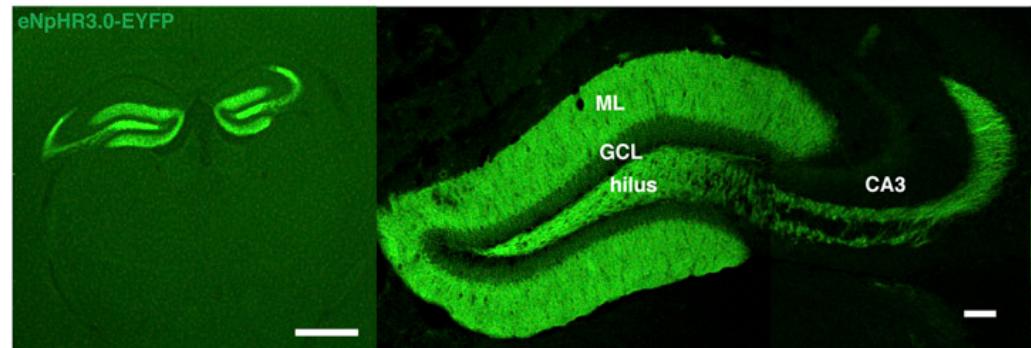
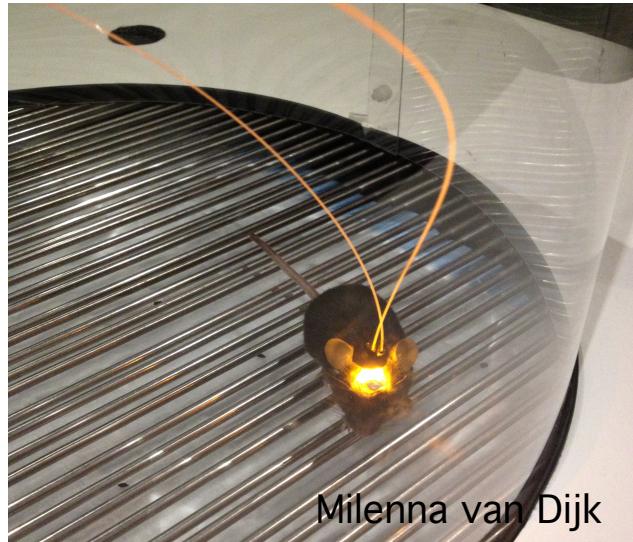
Courtesy UCLA

# “Circle of Biological Being”



# There are multiple (competing) memory systems

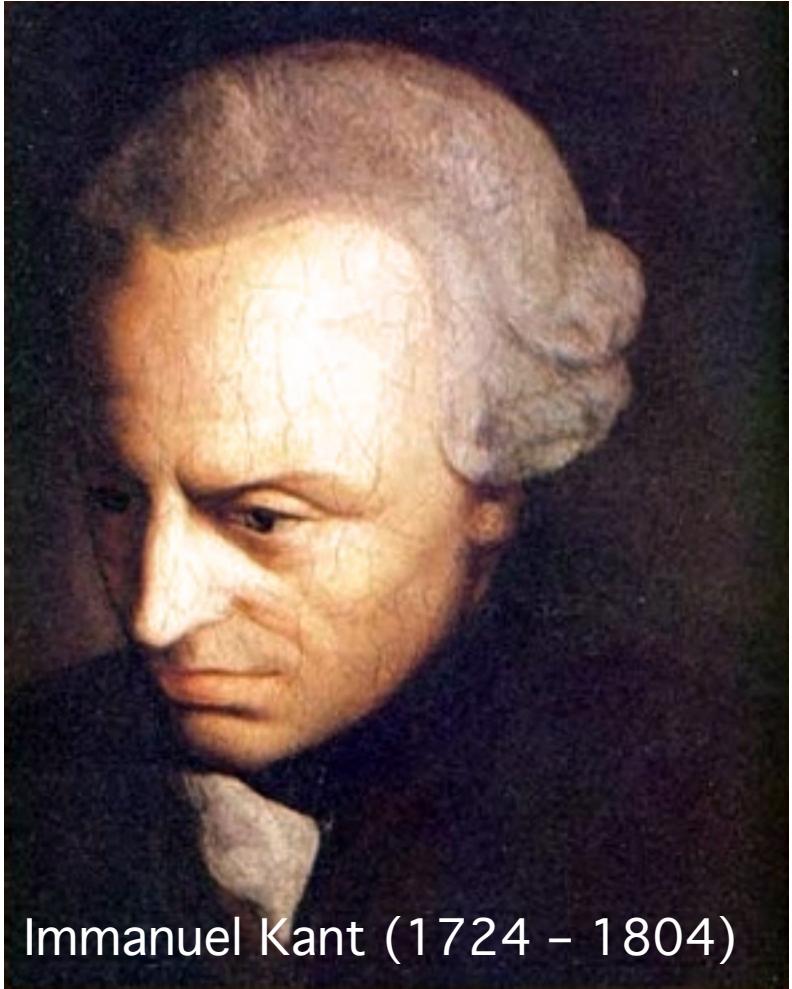




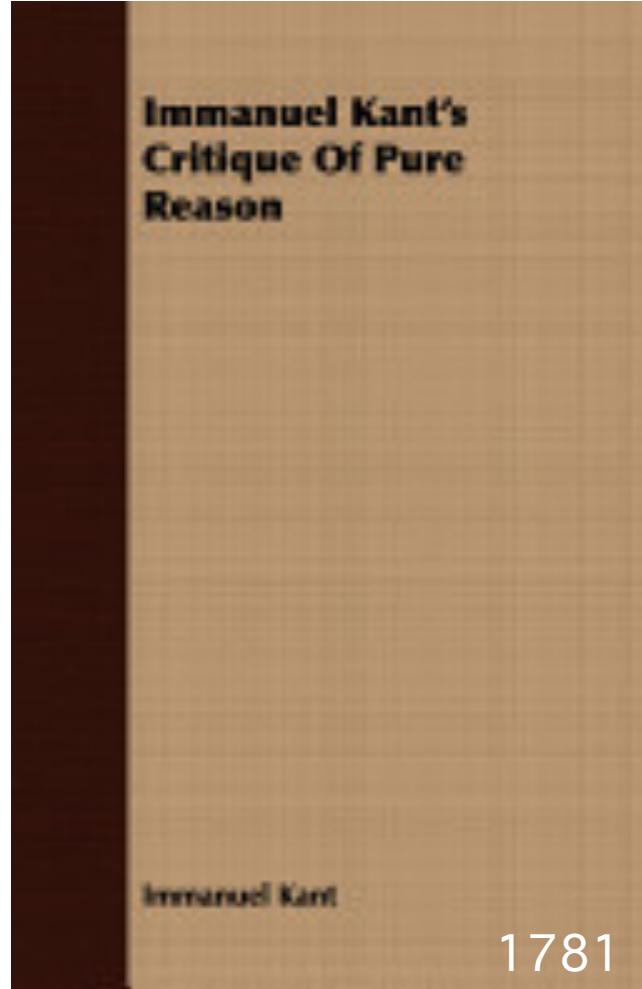
- The truthiness of memory
- Cognitive experience leaves a major imprint within the synaptic organization of the brain
- Learning-related local field potentials create an infrastructure that organizes neural activity

# Electrical activity in the (human) brain

H. Gelbard-Sagiv, R. Mukamel, M. Harel, R. Malach, I. Fried, *Science* (2008)



Immanuel Kant (1724 – 1804)



- Our experiences are structured by necessary features of our minds.

# The Nobel Prize in Physiology or Medicine 2014

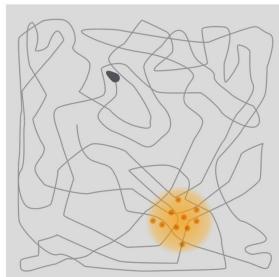


Fig. 1



John O'Keefe

**John O'Keefe** discovered, in 1971, that certain nerve cells in the brain were activated when a rat assumed a particular place in the environment. Other nerve cells were activated at other places. He proposed that these "place cells" build up an inner map of the environment. Place cells are located in a part of the brain called the hippocampus.

May-Britt Moser and  
Edvard I. Moser



**May-Britt och Edvard I. Moser** discovered in 2005 that other nerve cells in a nearby part of the brain, the entorhinal cortex, were activated when the rat passed certain locations. Together, these locations formed a hexagonal grid, each "grid cell" reacting in a unique spatial pattern. Collectively, these grid cells form a coordinate system that allows for spatial navigation.

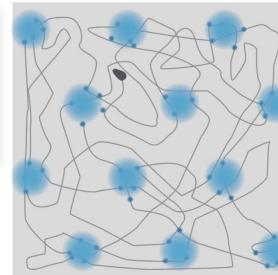


Fig. 2

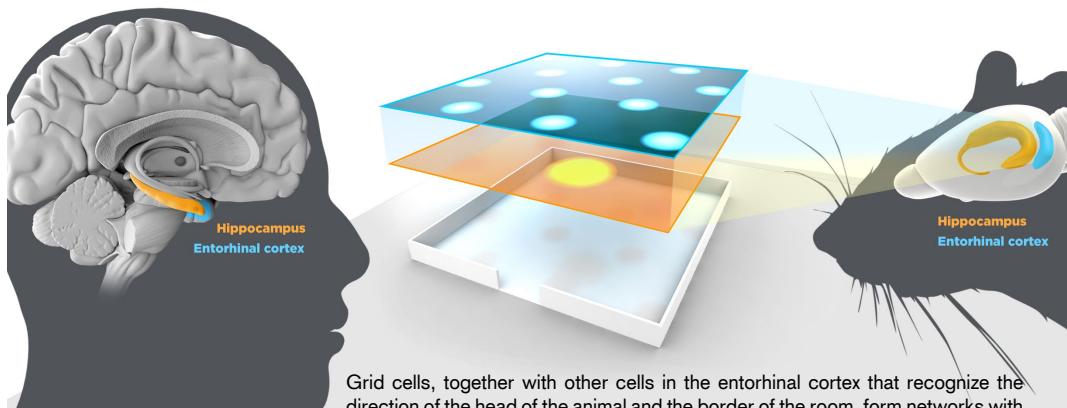
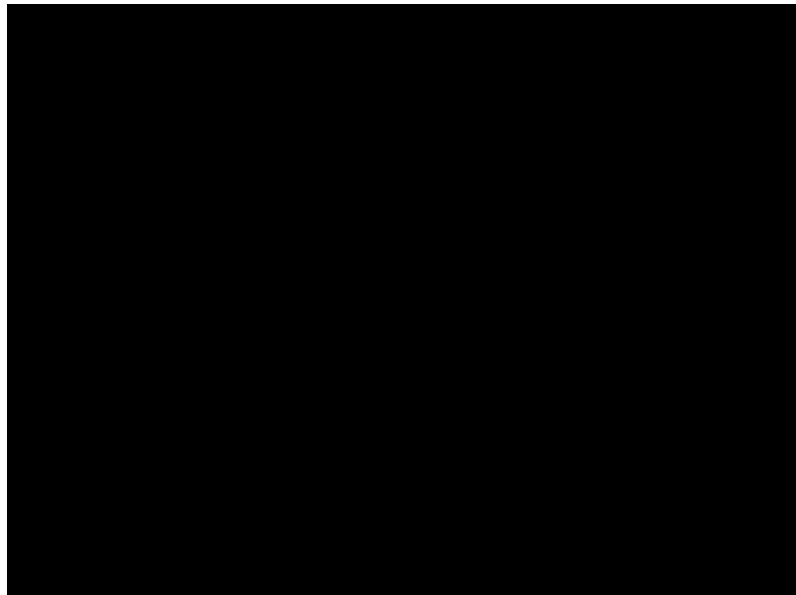


Fig. 3

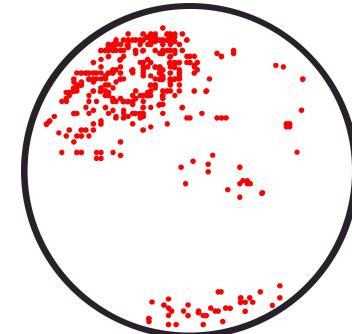
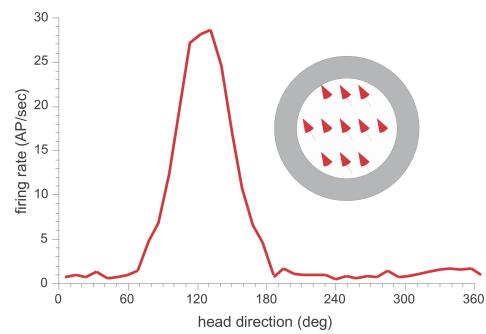
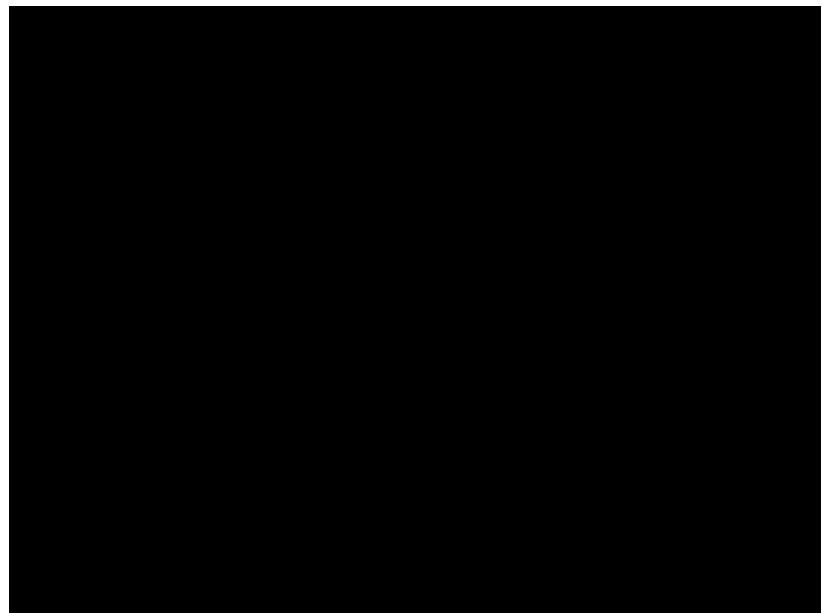
Grid cells, together with other cells in the entorhinal cortex that recognize the direction of the head of the animal and the border of the room, form networks with the place cells in the hippocampus. This circuitry constitutes a comprehensive positioning system, an inner GPS, in the brain. The positioning system in the human brain appears to have similar components as those of the rat brain.

# Electrical activity in the (rodent) brain

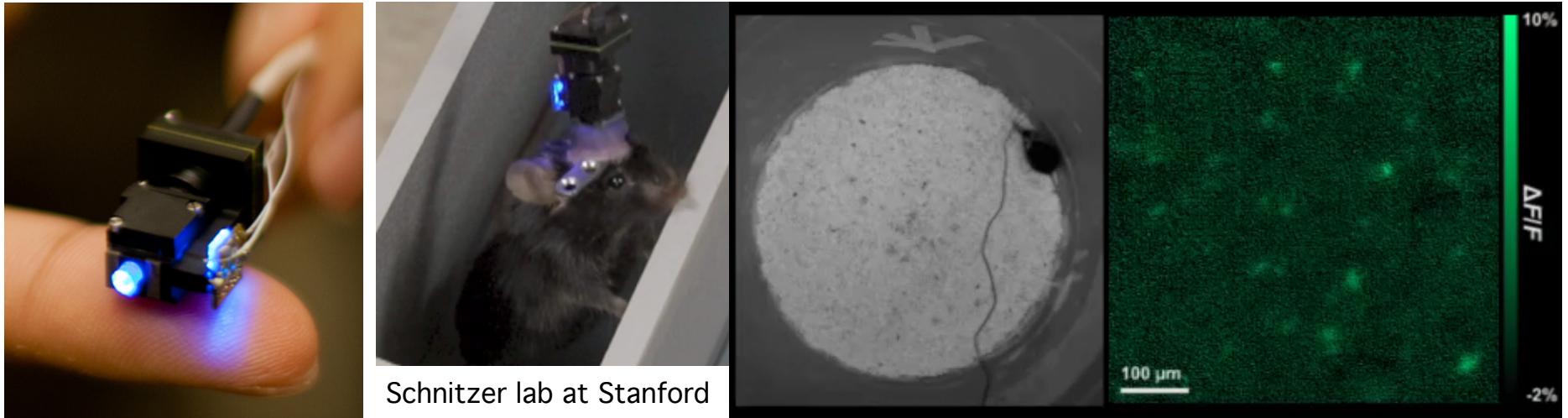
A Head-direction Cell



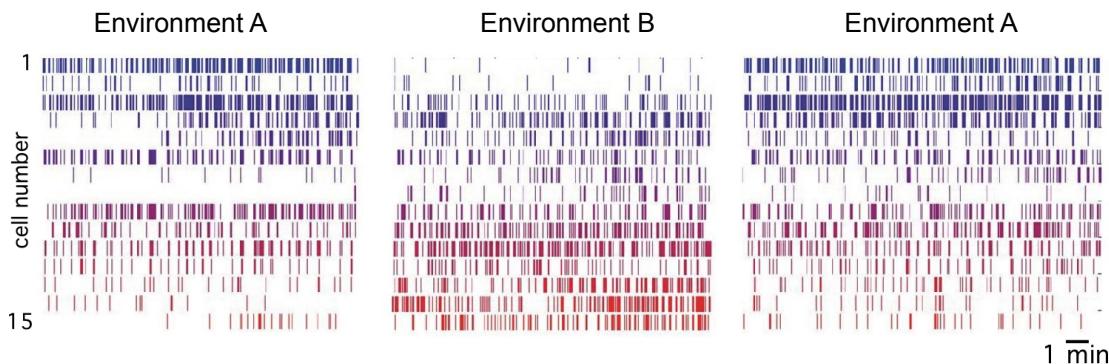
A Place Cell



# How does memory in the brain work?



...synapses are key

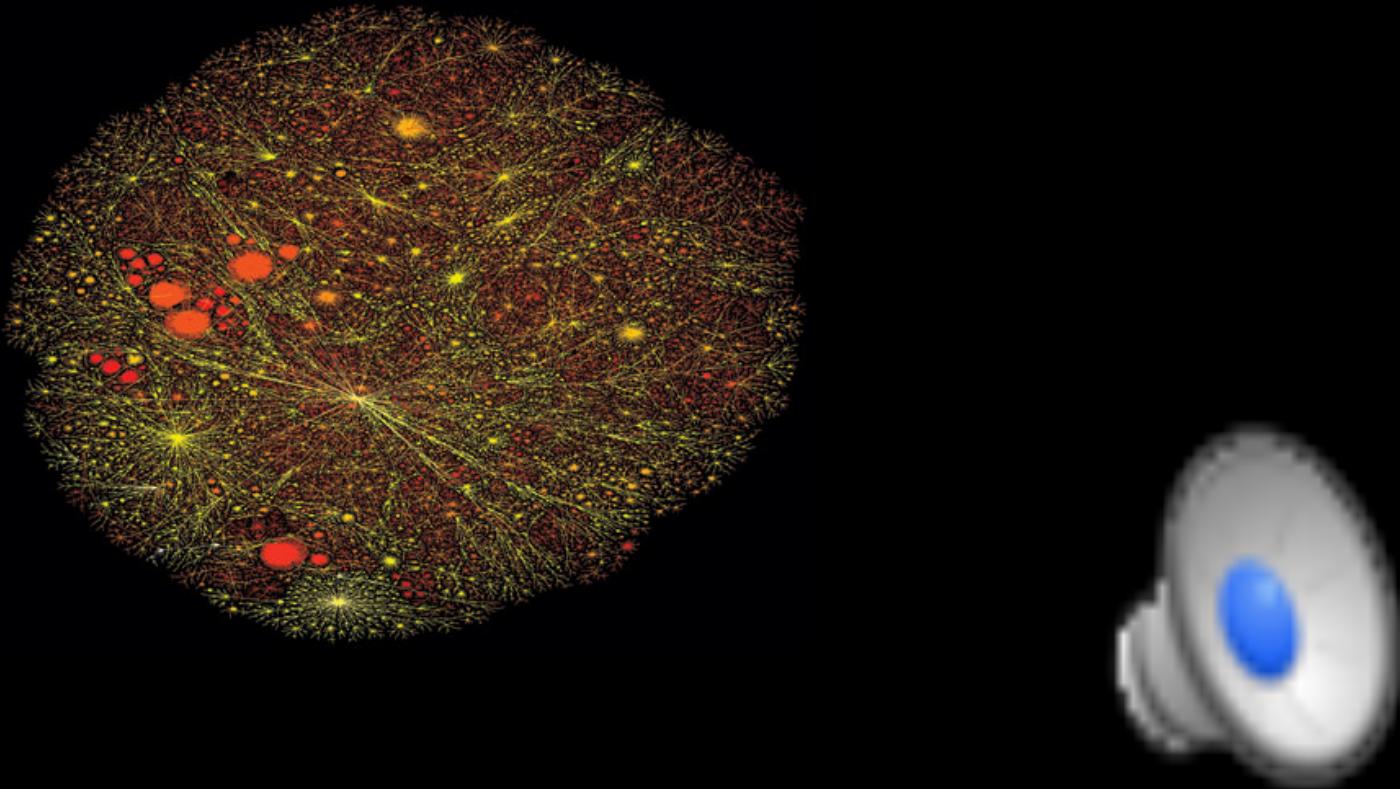


Synaptic connections are a fundamental property of neurons



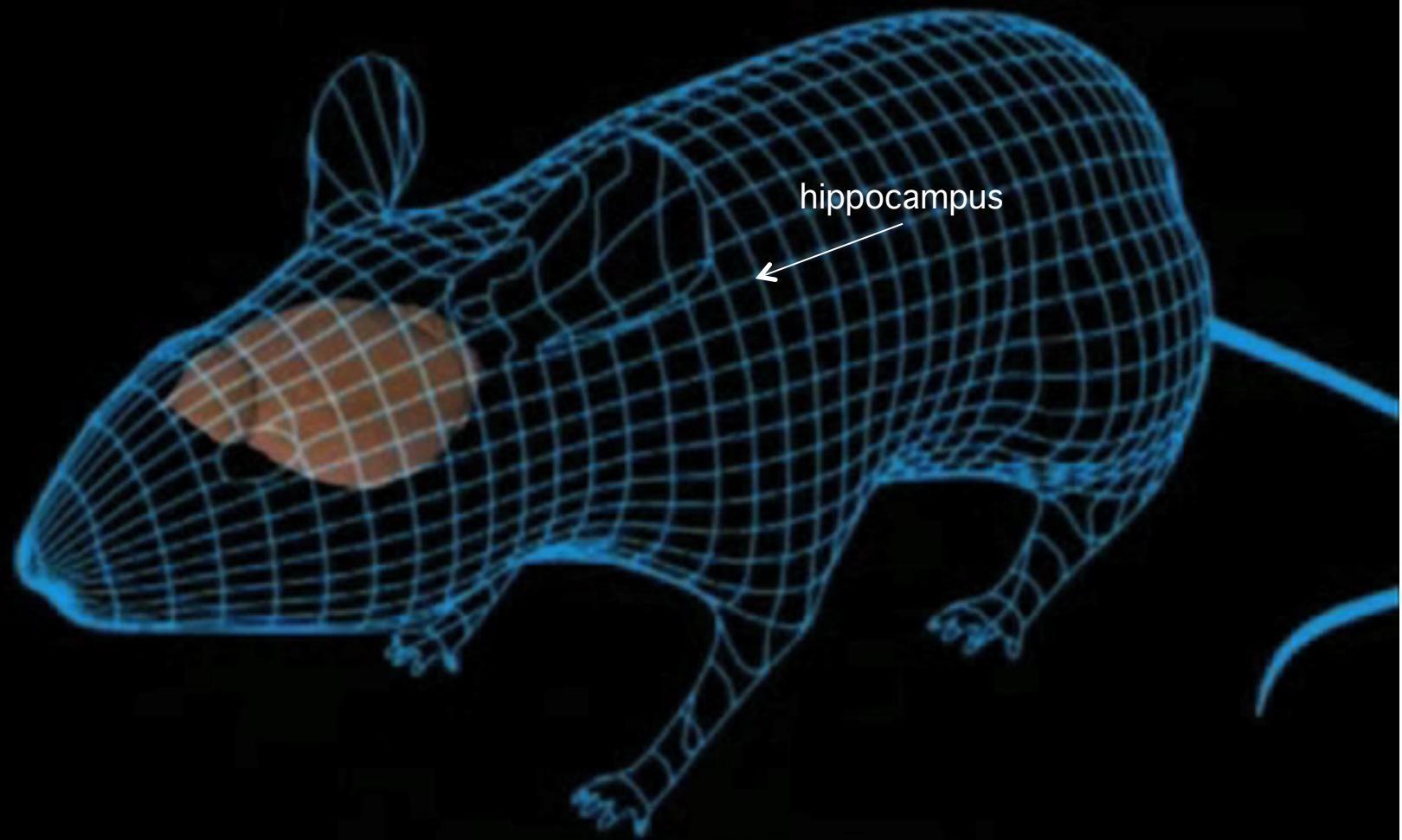
Tuning and maintaining the strength of specific synapses is a fundamental function of a neuron.

Traffic and the internet offer conceptual frameworks to think about information communication within networks of neurons



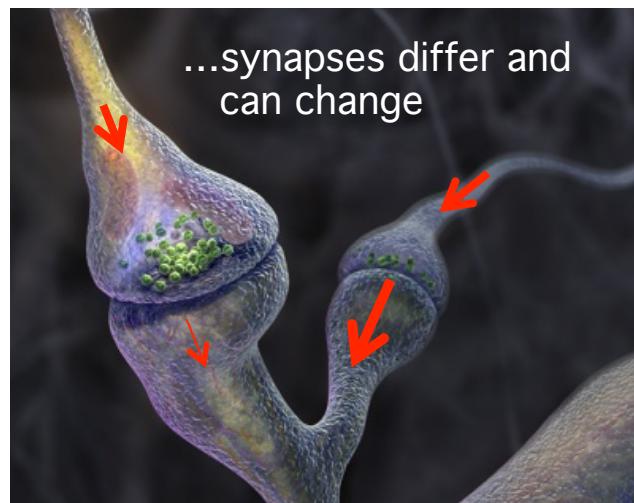
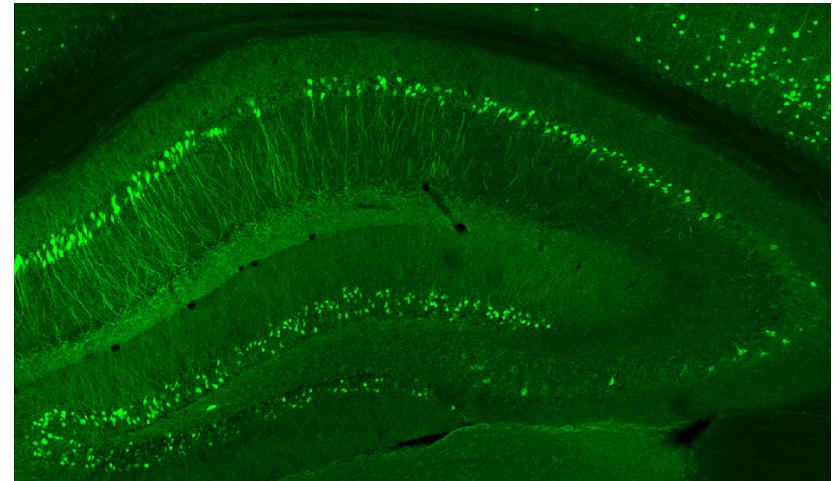
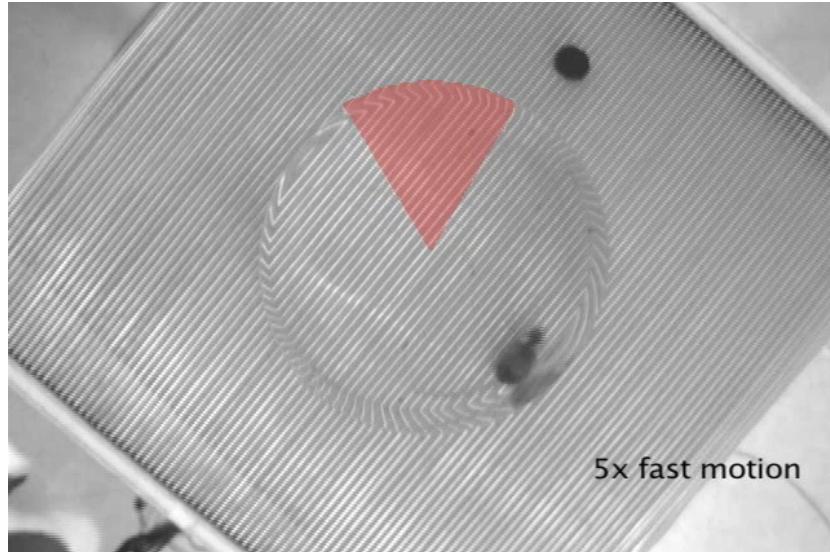
Godfrey Reggio's Koyaanisqatsi

The hippocampus is a critical neuronal circuit “hub” for the formation, storage and processing of memory

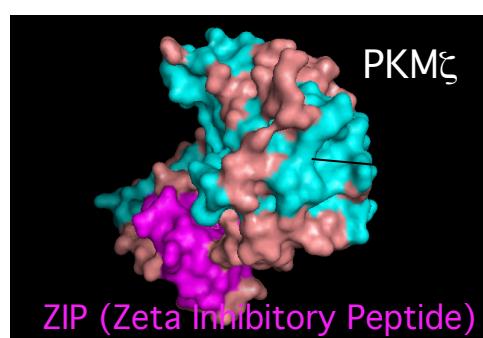


HHMI

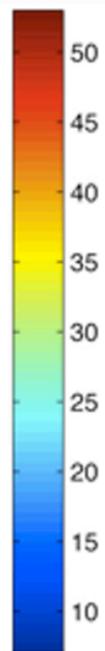
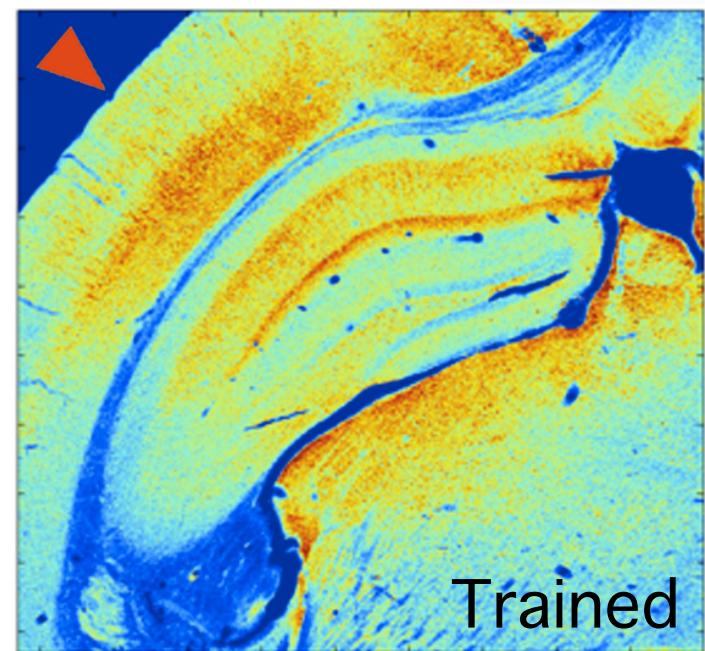
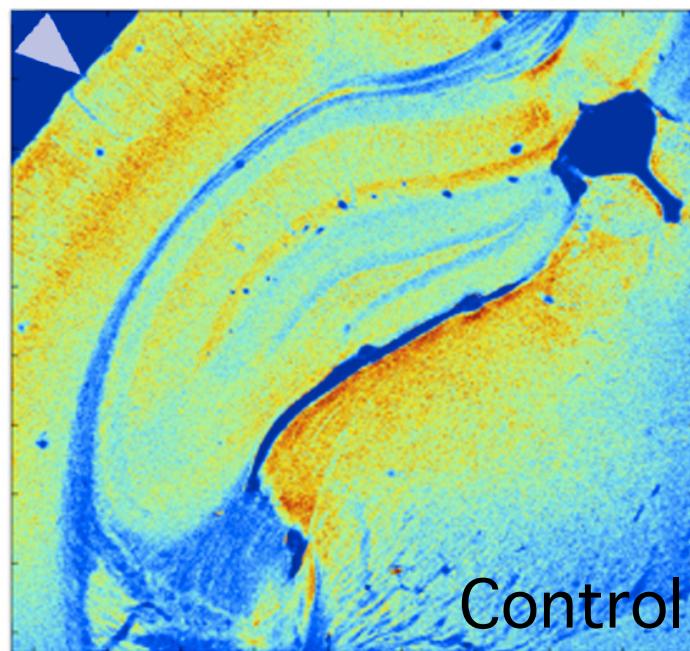
But how do neurons “remember” whether or not and when to be active?



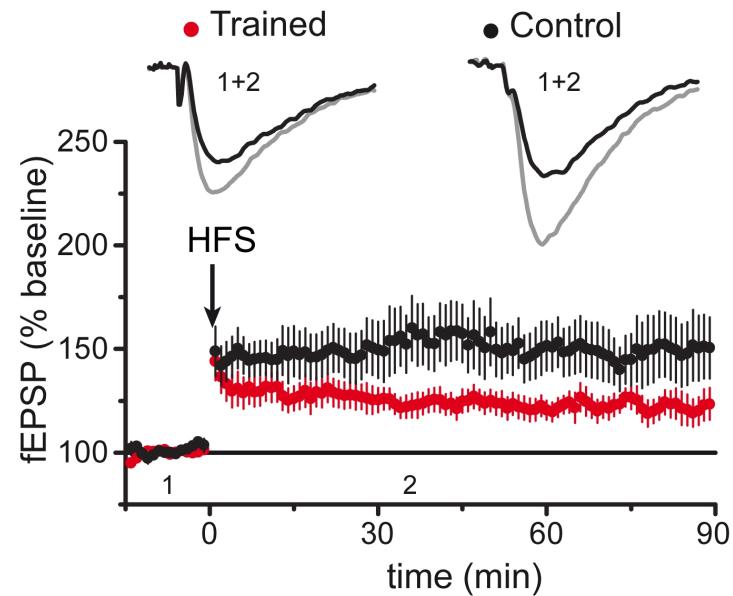
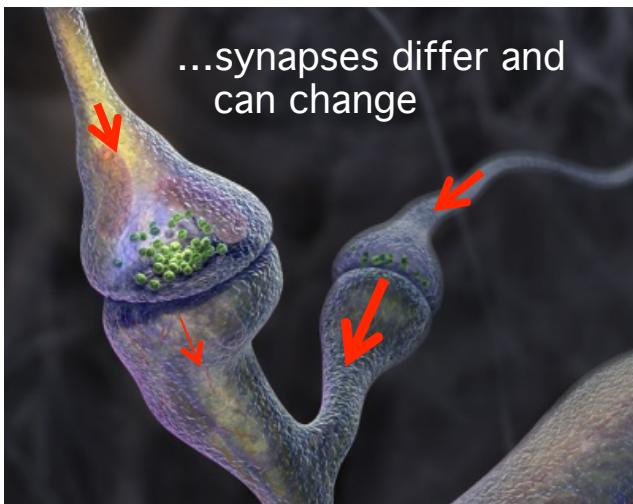
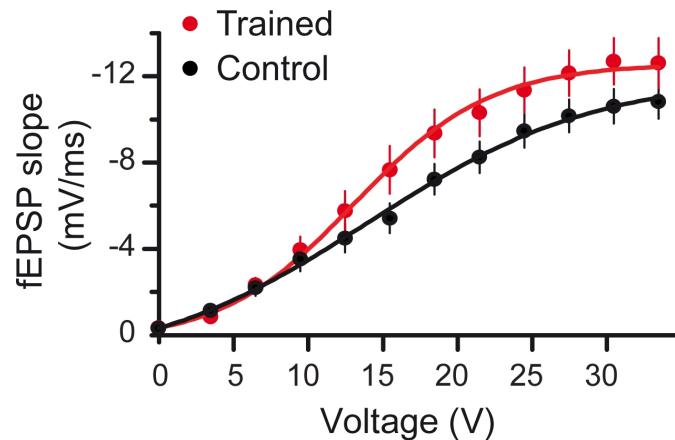
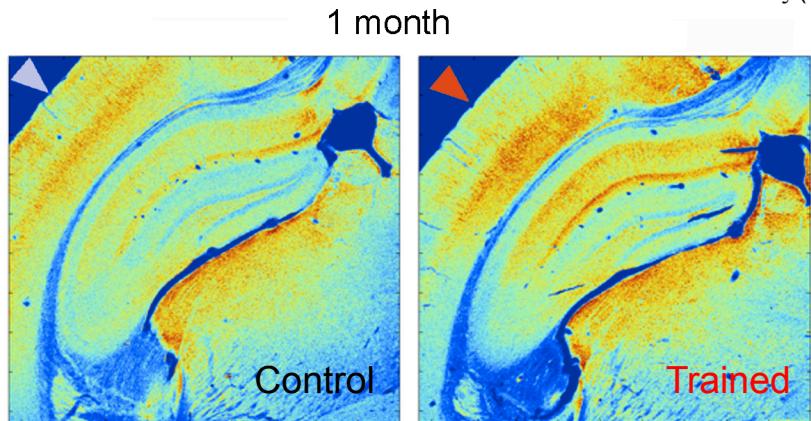
# PKM $\zeta$ forms a long-lasting trace of experience (“long-term memory”) in brain



1 month

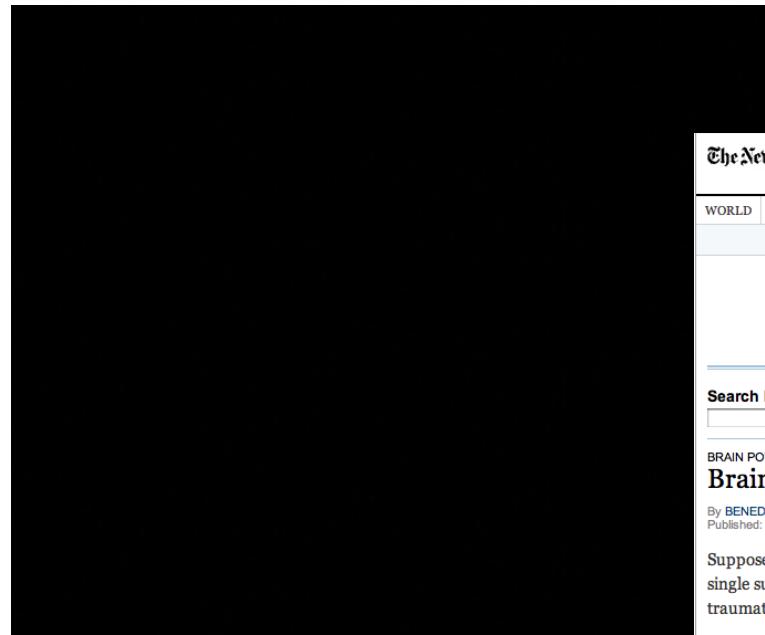


# Memory persistence changes synaptic functioning



# “Storage of information by the maintenance mechanism of LTP”

Pastalkova et al., 2006



(memories can be erased)

The New York Times

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BRAIN POWER

**Brain Researchers Open Door to Editing Memory**

By BENEDICT CAREY  
Published: April 5, 2009

Suppose scientists could erase certain memories by tinkering with a single substance in the brain. Could make you forget a chronic fear, a traumatic loss, even a bad habit.

Enlarge This Image

Researchers in Brooklyn have recently accomplished comparable feats, with a single dose of an experimental drug delivered to areas of the brain critical for holding specific types of [memory](#), like emotional associations, spatial knowledge or motor skills.

The drug blocks the activity of a substance that the brain apparently needs to retain much of its learned information. And if enhanced, the substance could help ward off dementias and other memory problems.

Fred R. Conrad/The New York Times

André A. Fenton studies spatial memory in mice and rats.

TWITTER

COMMENTS (188)

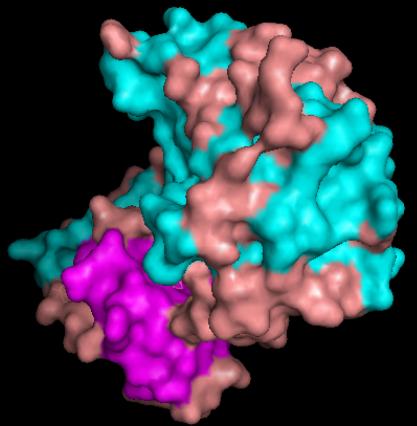
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...but memory is not everything.  
It's a lot about how you use it

# Cognitive control (a.k.a. executive function)

The ability to coordinate the use of information from multiple sources, typically for optimizing actions

Cognitive control is impaired in mental illness

- Depression
- Addiction
- Autism Spectrum Disorders
- Attention Deficit Hyperactivity Disorder
- Post Traumatic Stress Disorder
- Anxiety Disorders
- Schizophrenia

Say the color ignore the  
meaning

**WHITE**

**Ready?**

**Go!**

**Green**

**Blue**

**Yellow**

**Green**

**Red**

**Blue**

**Green**

**Red**

**Yellow**

**Blue**

Blue

**Green**

**Green**

**Yellow**

**Red**

**Green**

**Red**

**Yellow**

**Yellow**

**Blue**

**Green**

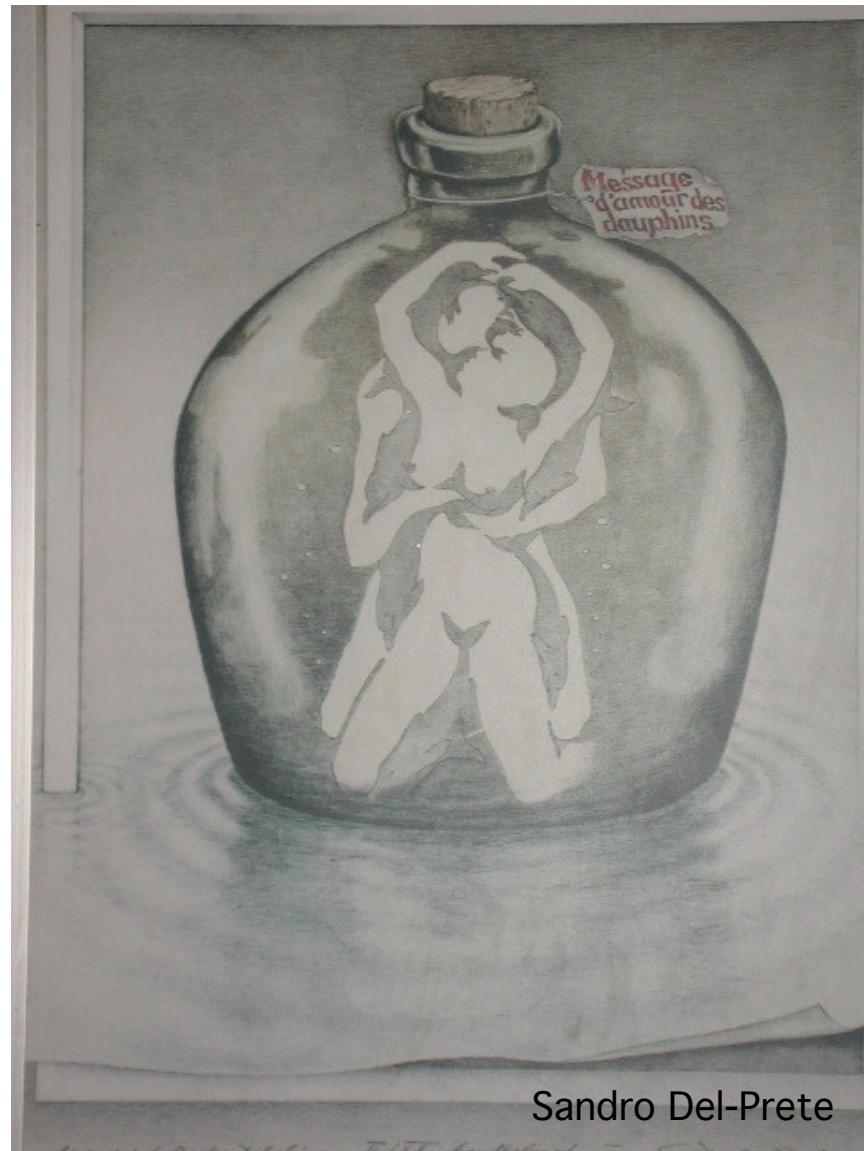
**Blue**

**Blue**

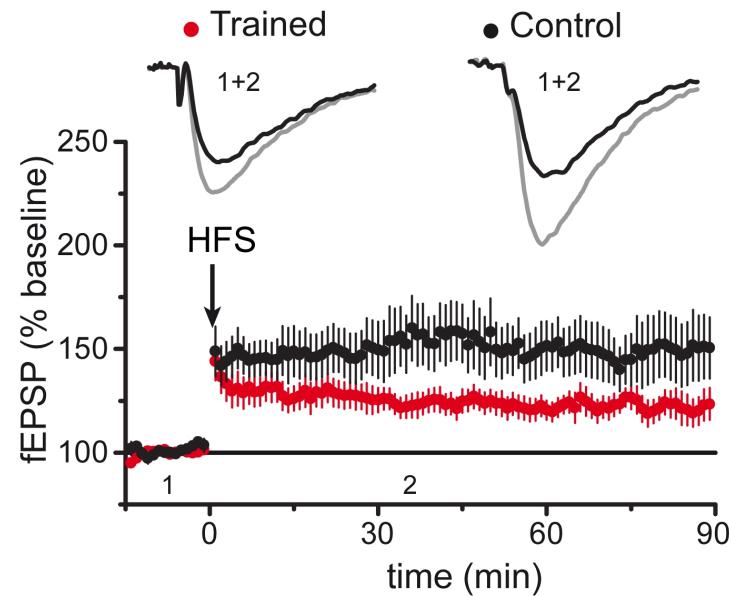
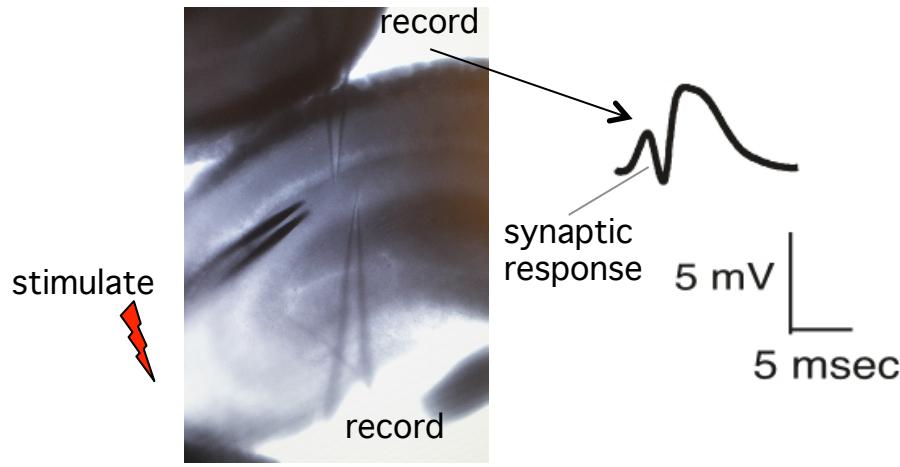
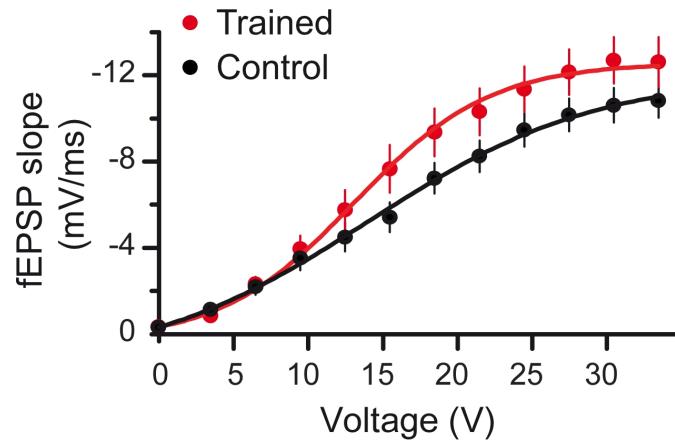
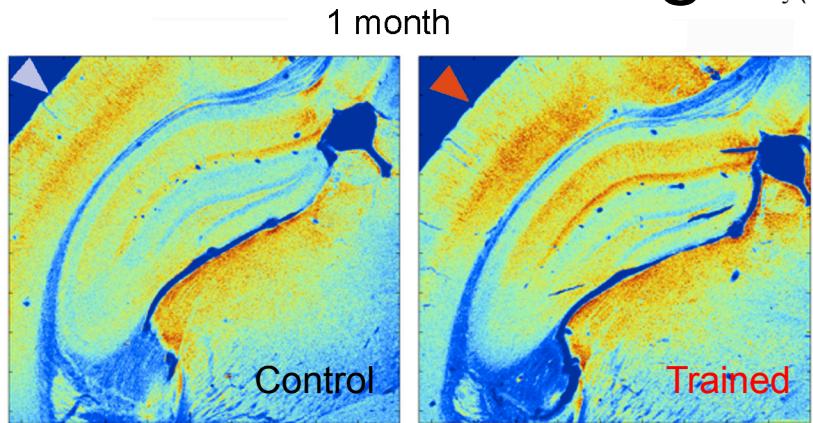
A basic challenge in psychiatry is to improve cognitive control in patients

... our memory research suggests there may be a new (ancient), powerful way forward

Prior experience (memory) often changes how and what we subsequently experience, comprehend and learn



# What happens to the function of a neural circuit when long-term memory is stored?



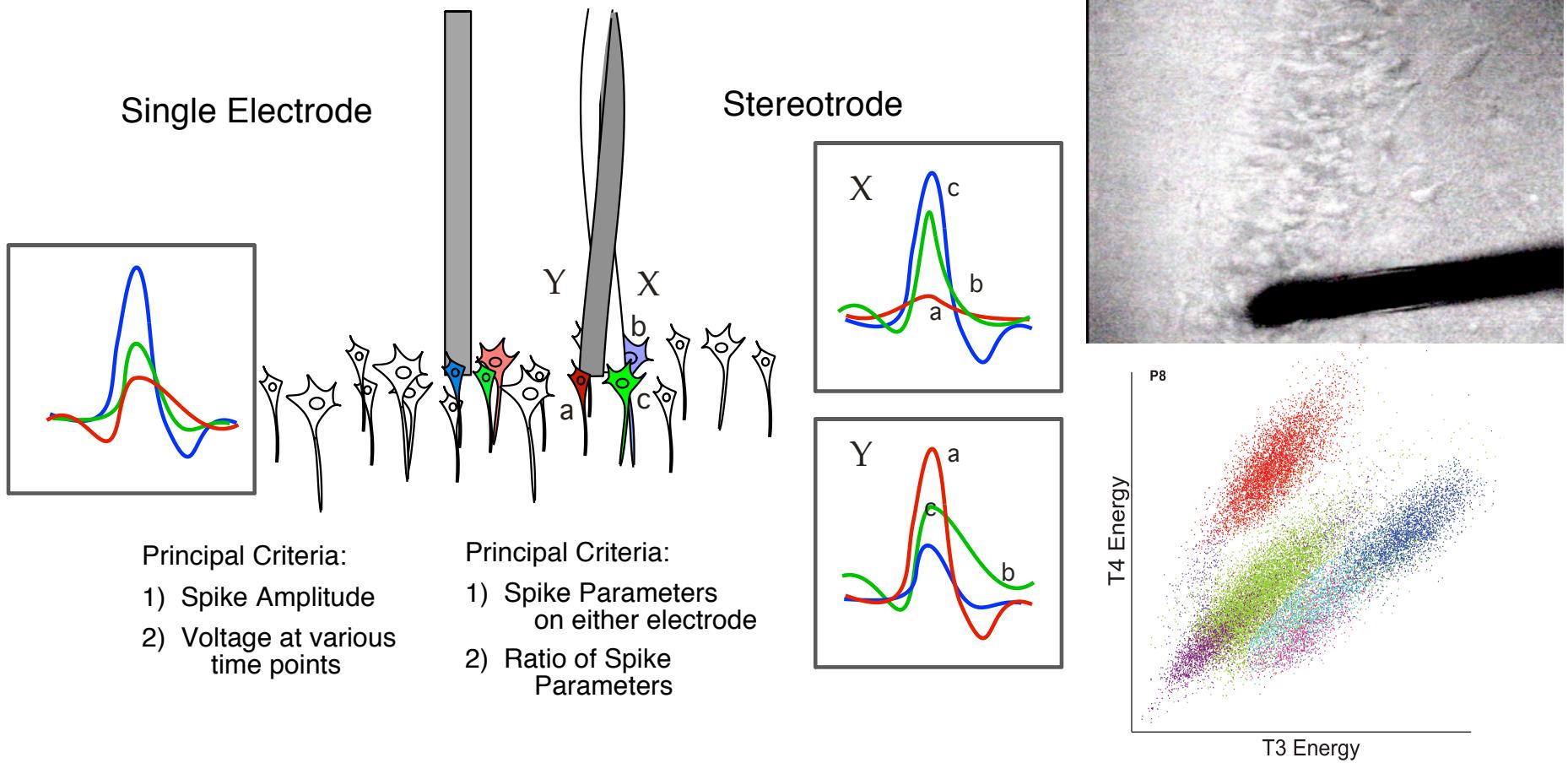
Storing long-term memory from cognitive experience causes persistent changes of synaptic and neural circuit function.

These experience-driven changes are surprisingly large.

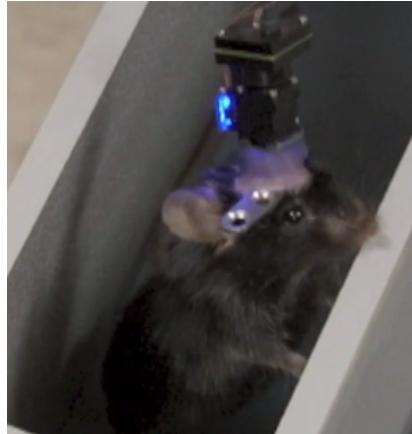
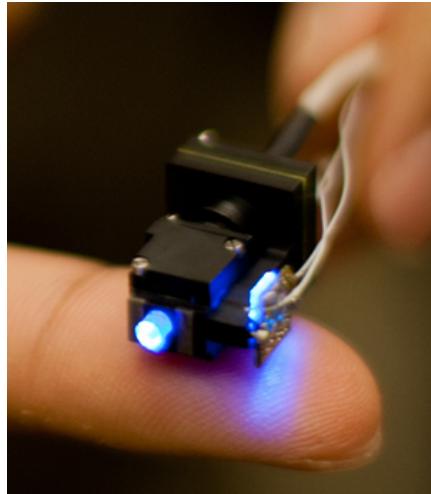
They are so large that they are unlikely to reflect the memorized information itself, and rather indicate a functional tuning (reorganization) of neural circuitry.

- The truthiness of memory
- Cognitive experience leaves a major imprint within the synaptic organization of the brain
- Learning-related local field potentials create an infrastructure that organizes neural activity

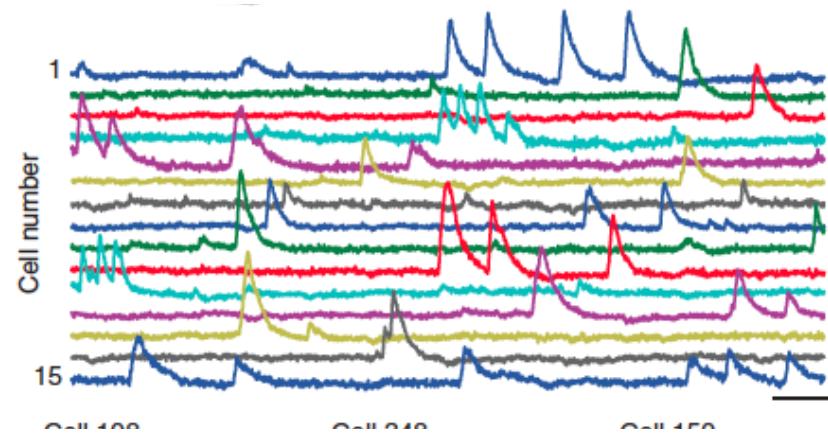
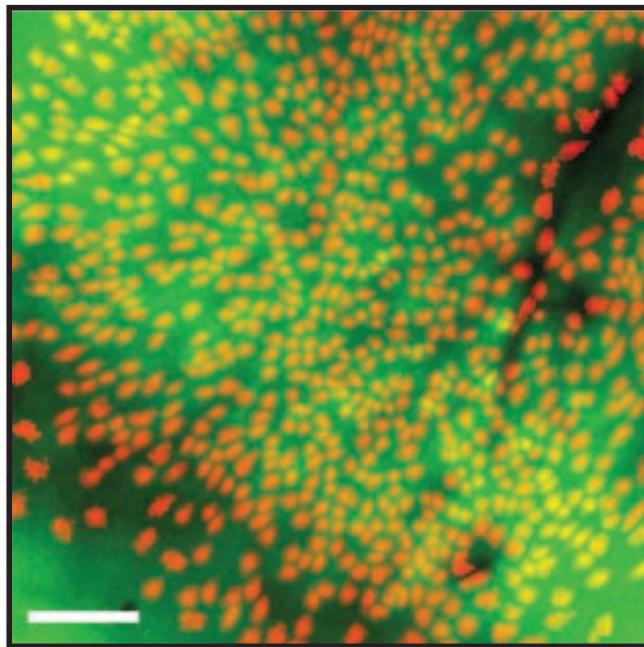
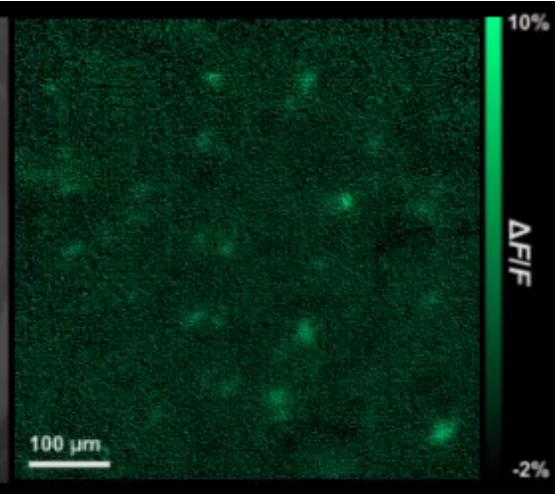
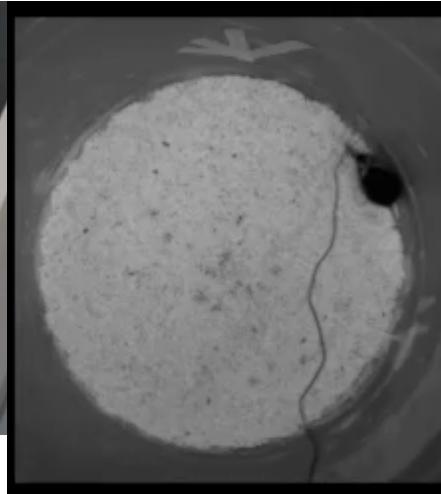
# How we record electrical activity



# How we are starting to record electrical activity

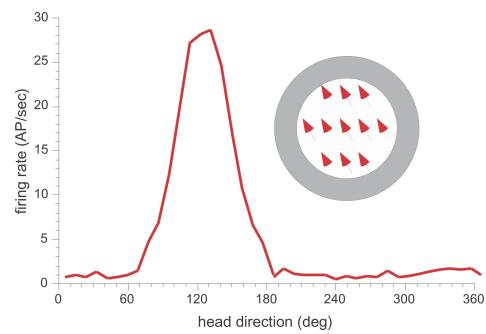
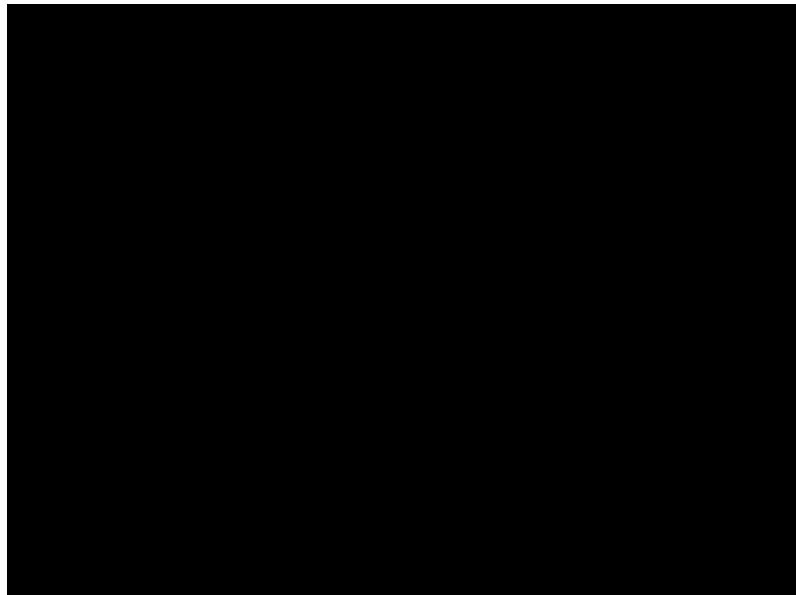


Schnitzer lab at Stanford

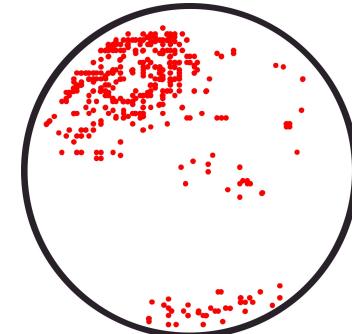
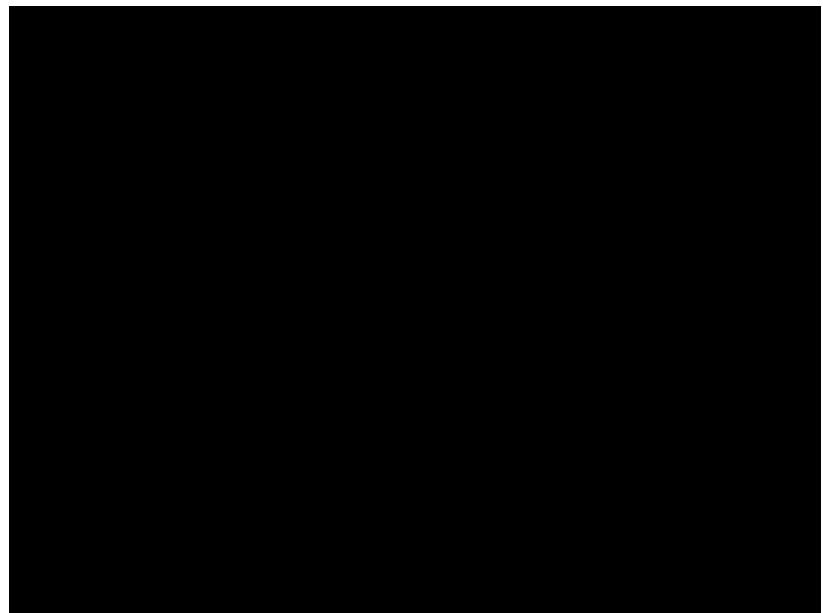


# Electrical activity in the (rodent) brain

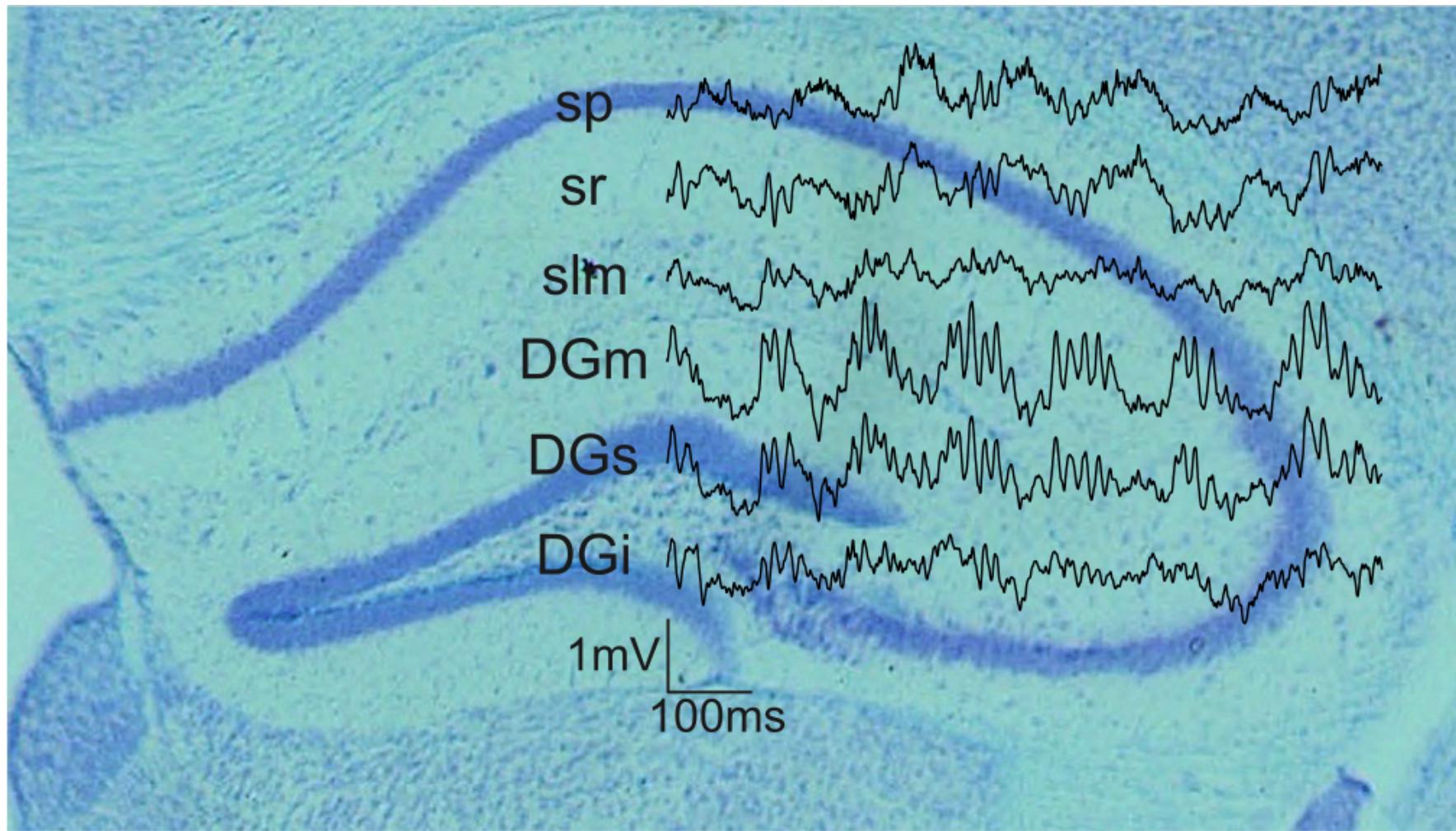
A Head-direction Cell



A Place Cell



# Local Field Potentials (LFP) create an temporal neural infrastructure



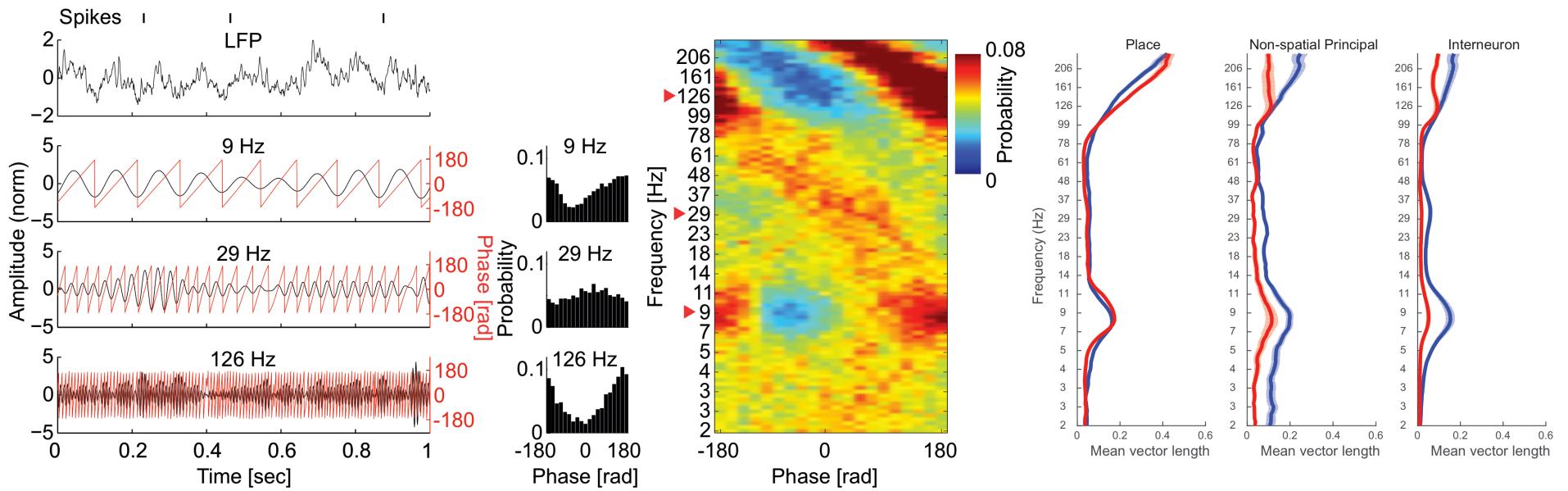
## The importance of timing: Phase synchrony



<https://www.youtube.com/watch?v=QgMCZphTXCA>

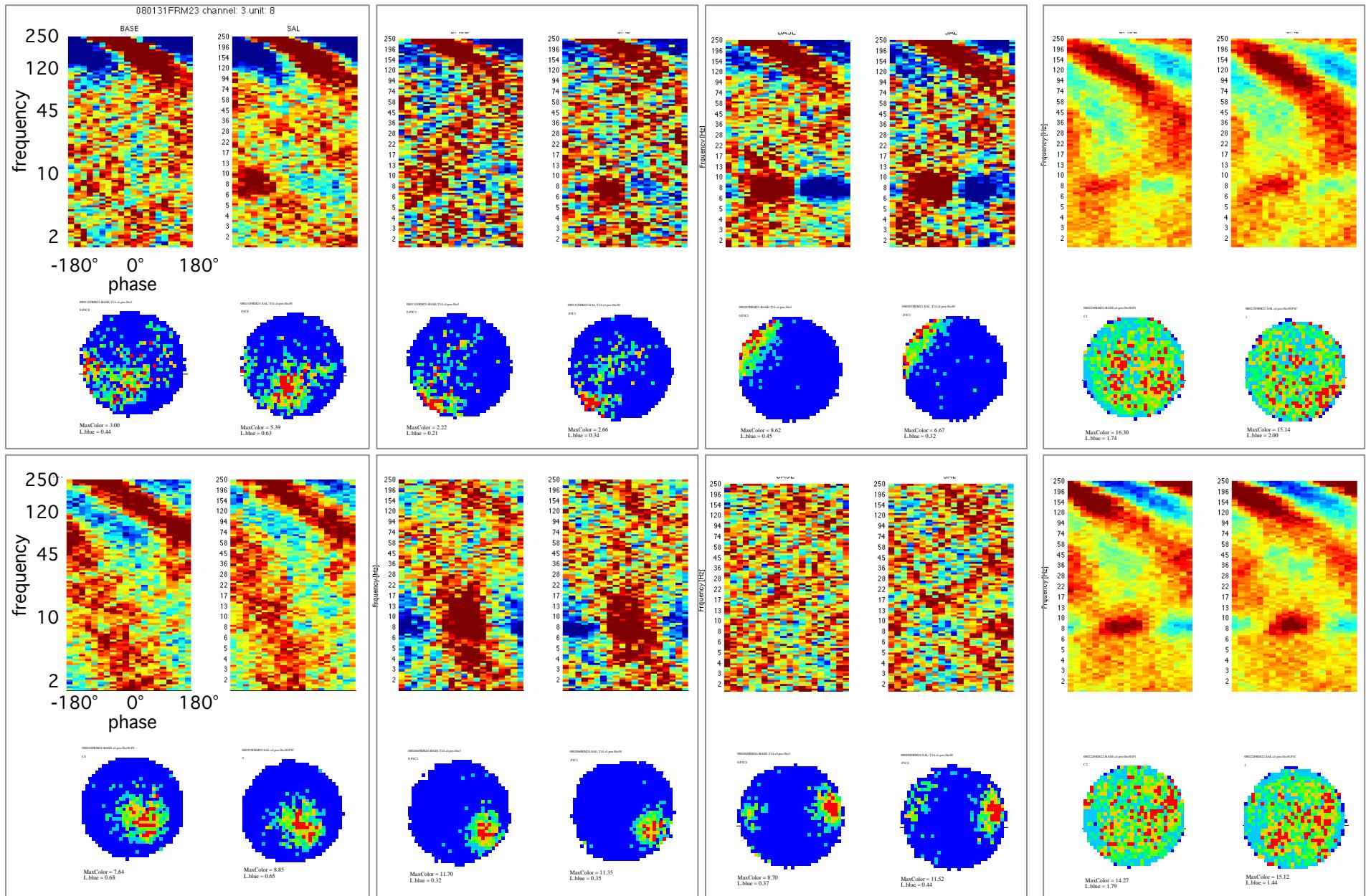
# Phase-frequency spike-field coupling

- a temporal infrastructure that organizes spike discharge

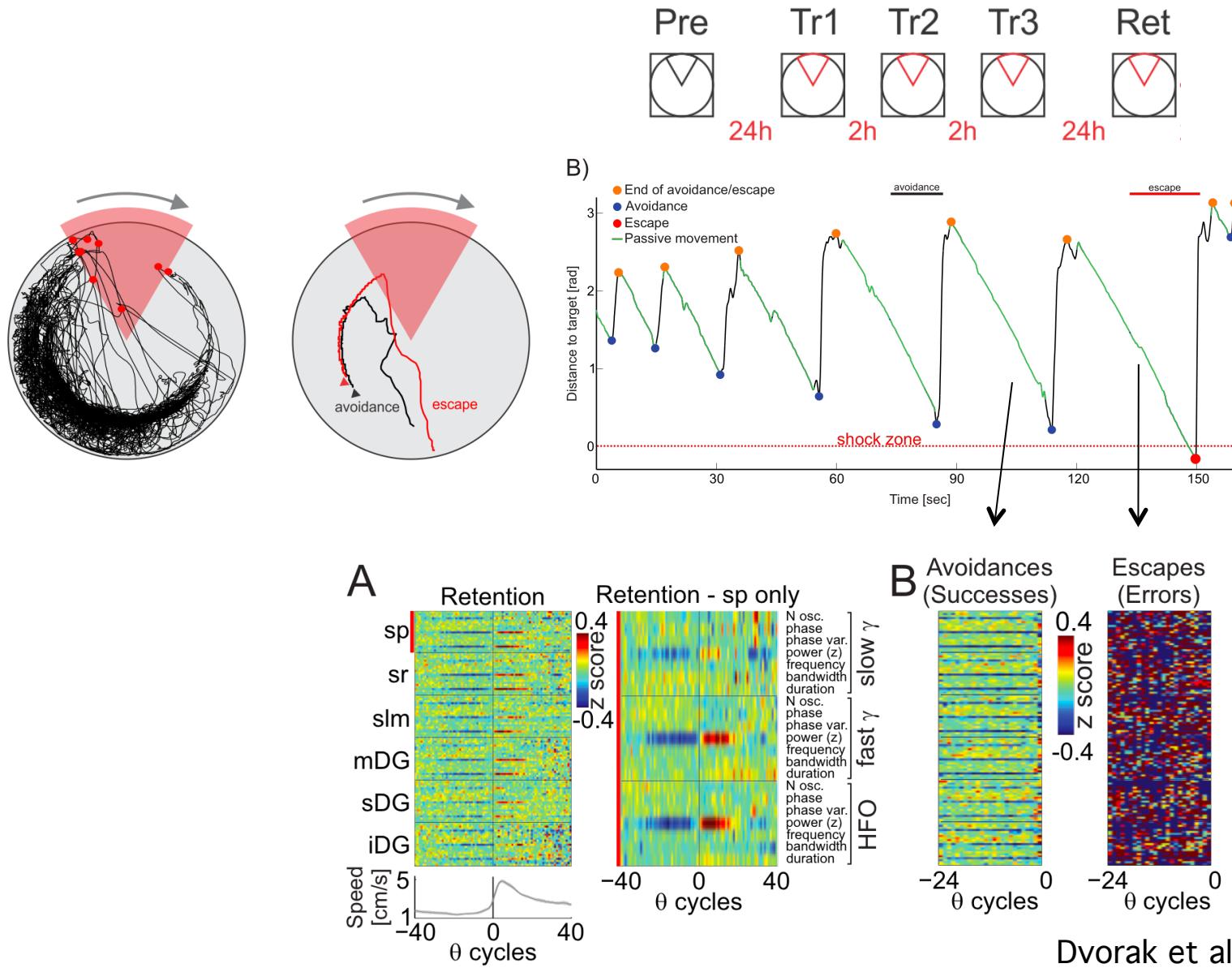


Dvorak, Sparks et al (in preparation)

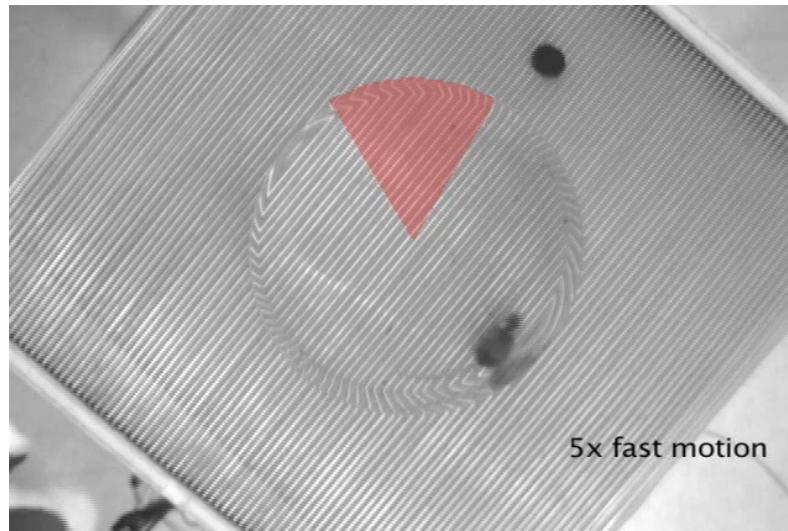
# If space was time – the LFP oscillation phase-frequency space



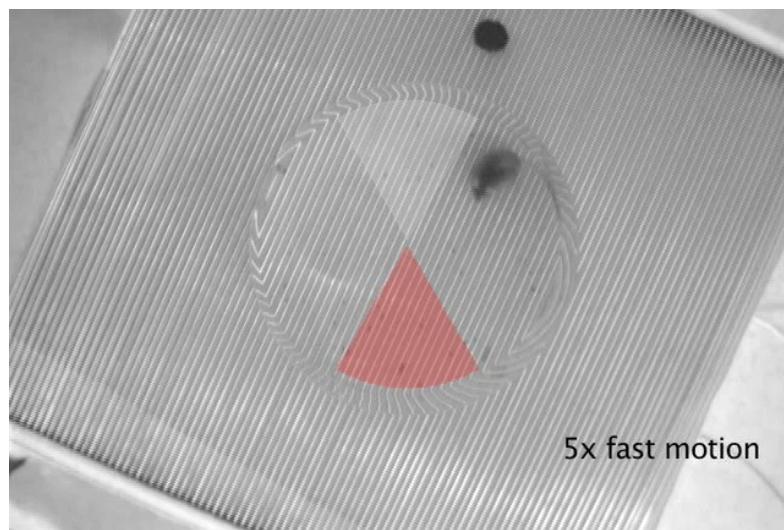
# Oscillatory events in the hippocampal LFPs predict place avoidance success and failure



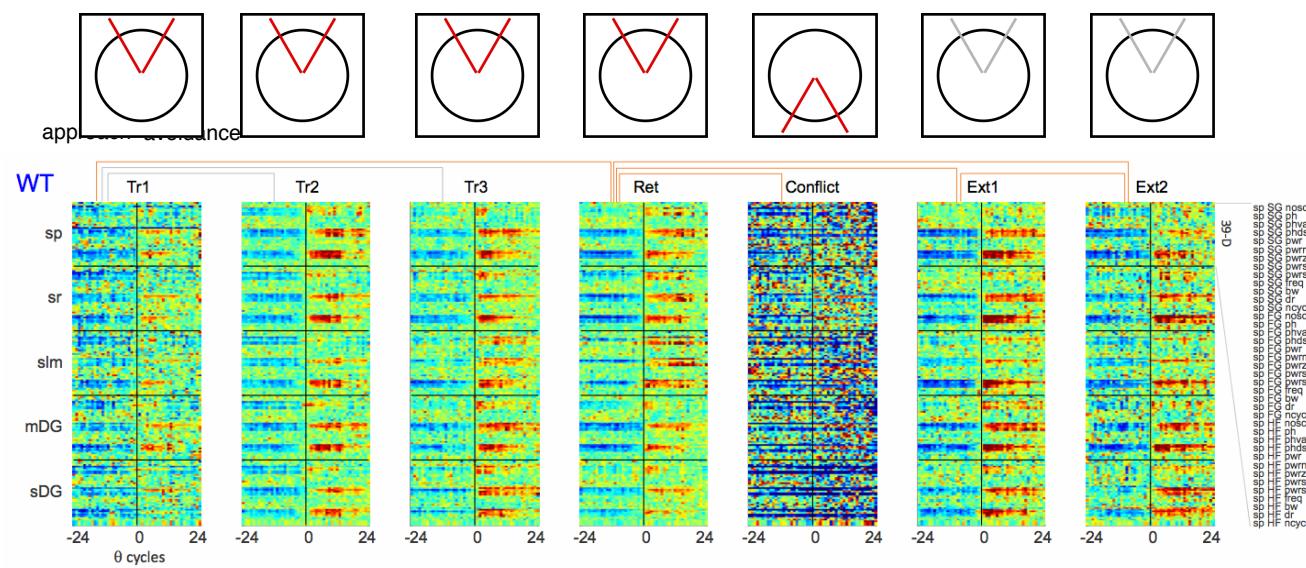
Training



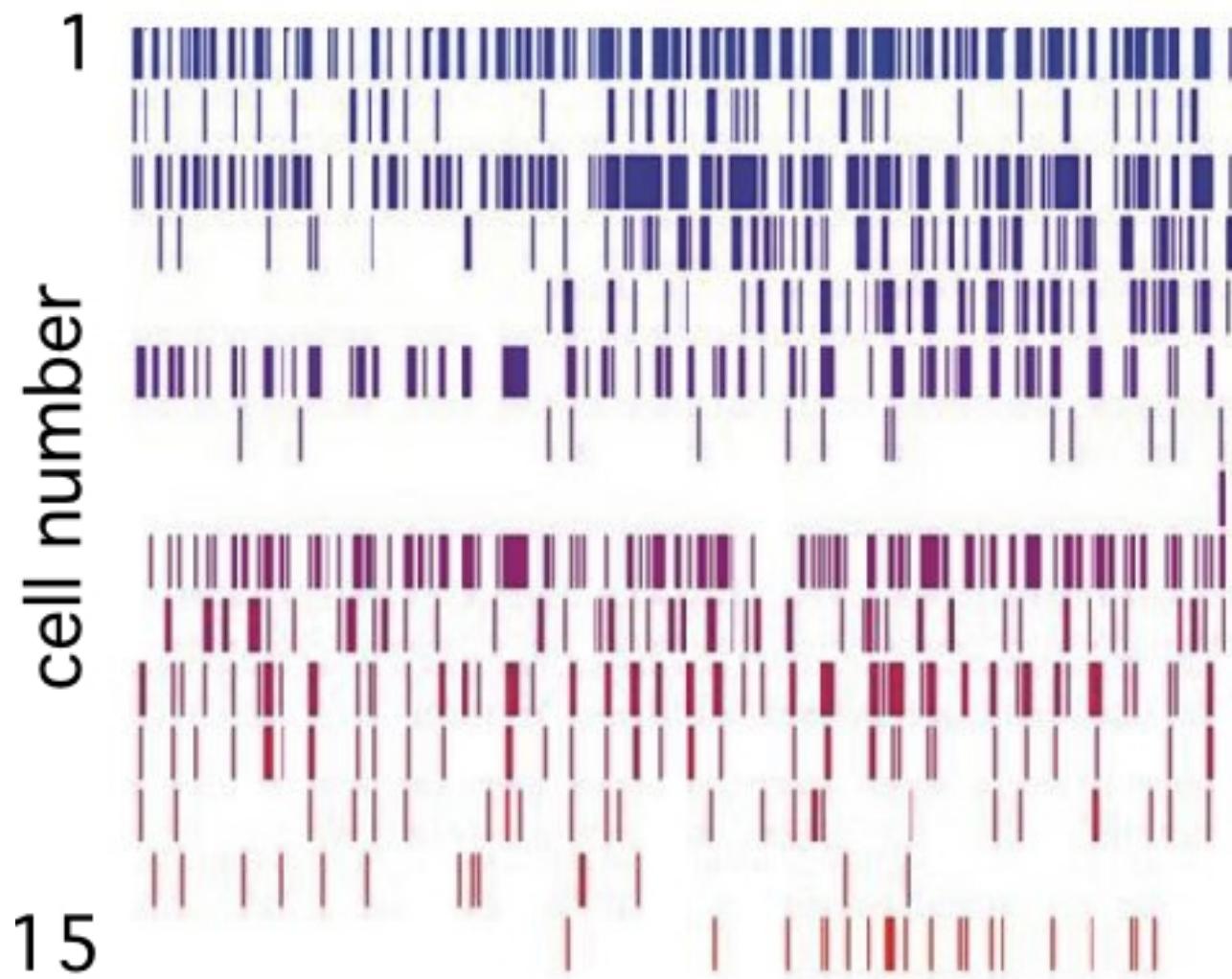
Conflict

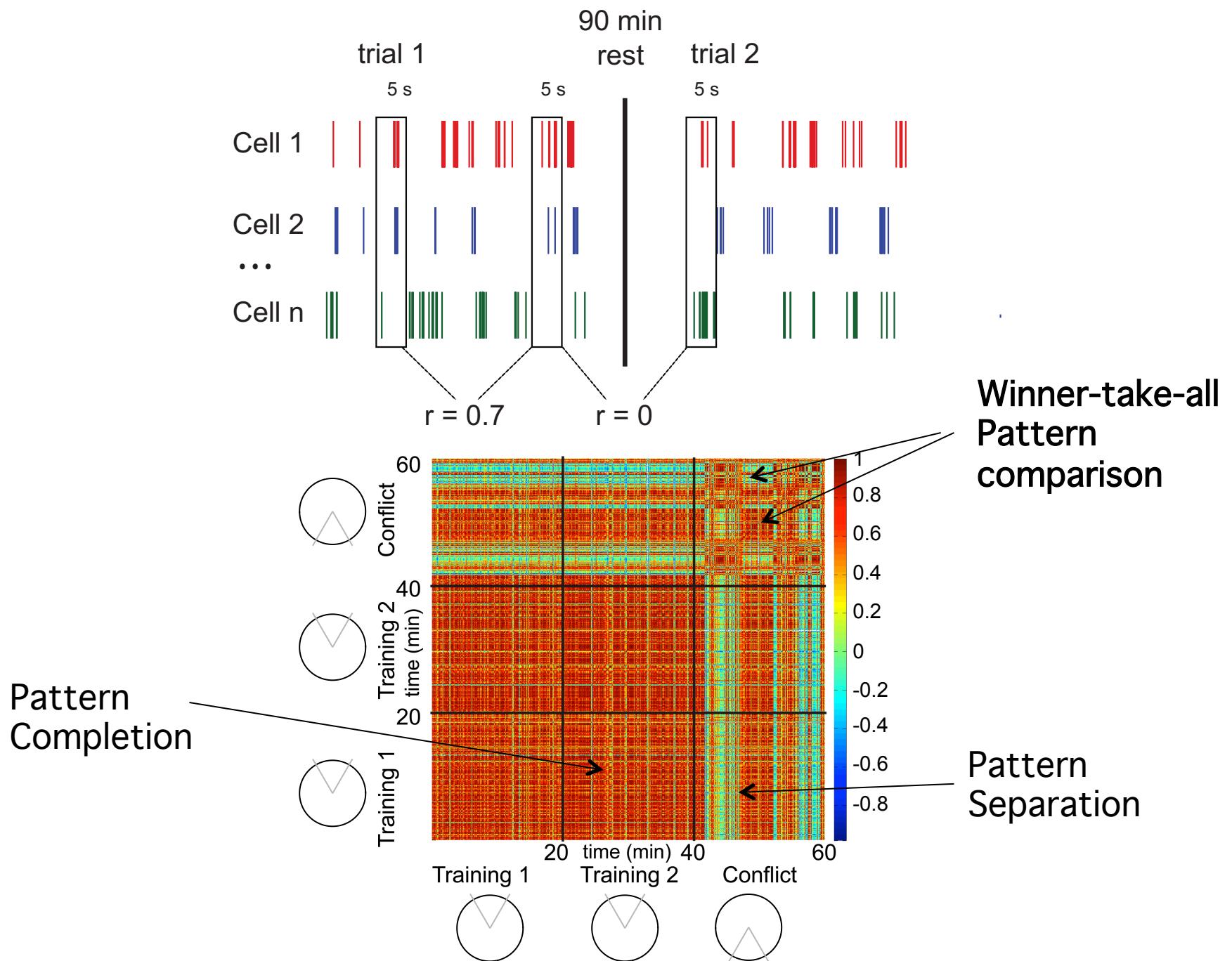


# Hippocampal oscillatory events change with learning and differ with cognitive effort



Let's now integrate the neural discharge





**COGNITIVE EXPERIENCE** tunes synaptic communication pathways to create and control information flow through the brain ... this is the stuff of MEMORY

**COGNITIVE CONTROL** itself may be a therapeutic opportunity for experience-driven tuning of cognitive networks

“What we think we become.”

Gautama Siddharta

# NEUROBIOLOGY OF COGNITION LABORATORY

## PRESENT MEMBERS

Alice Berners-Lee  
**Dino Dvorak**  
Hussam Jourdi  
**Hsin-Yi Kao**  
Stephen Keeley  
Benjamin Lee  
**Edith Lesburgueres**  
Kally O'Reilly  
Albert Park  
Eunhye Park  
Basma Radwan  
Fraser Sparks  
**Milenna van Dijk**  
Emma Wallace

**PAST MEMBERS**  
Samah Abdel-Baki  
Karel Jezek  
Eduard Kelemen  
**Heekyung Lee**  
Sam Neymotin  
Andrey Olypher  
**Eva Pastalkova**  
Jun Zhong

## RECENT/ACTIVE COLLABORATORS

**Juan Marcos Alarcon**  
Jeremy Barry  
Peter Bergold  
Nesha Burghardt  
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Lila Davachi  
René Hen  
Cliff Kentros  
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Stroke (NINDS)  
**National Institute of  
Mental Health (NIMH)**  
National Institute of  
Nursing Research (NINR)  
National Science  
Foundation

- The truthiness of memory
- Cognitive experience leaves a major imprint within the synaptic organization of the brain
- Preemptive cognitive experience: experience has the power to change brain and cognitive function