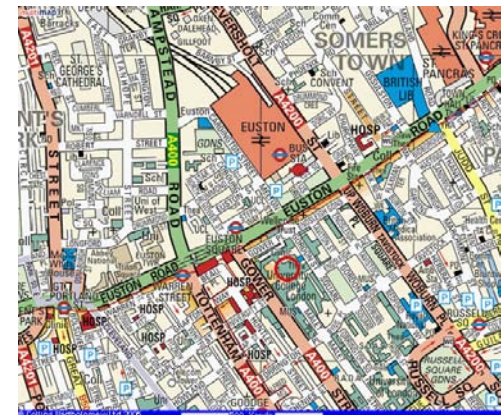


# Spatial Cells in the Hippocampal Formation

John O'Keefe  
University College London

Nobel Prize Lecture  
Stockholm  
7 December 2014





Henry Molaison

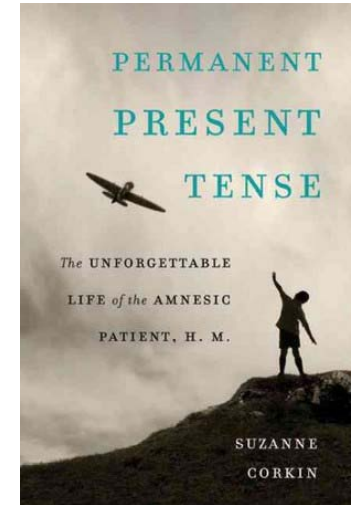
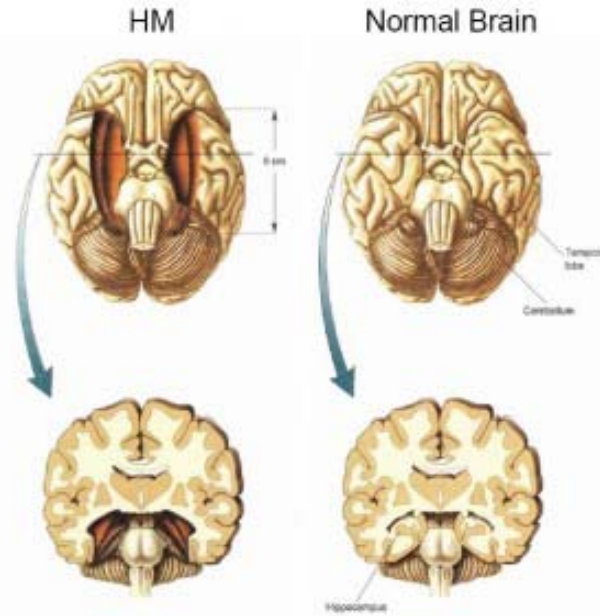
1926-2008



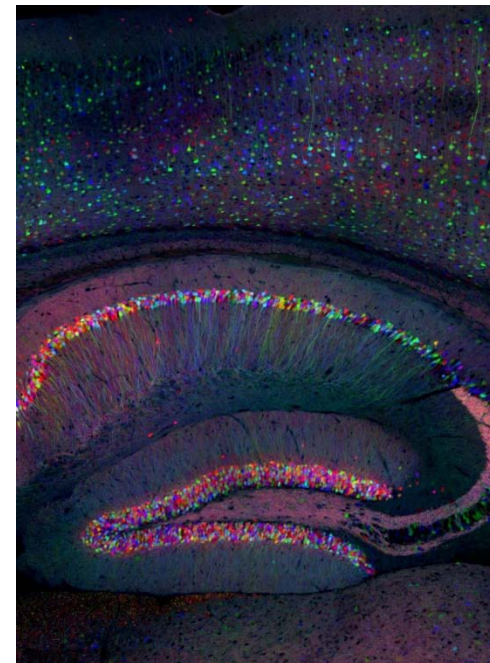
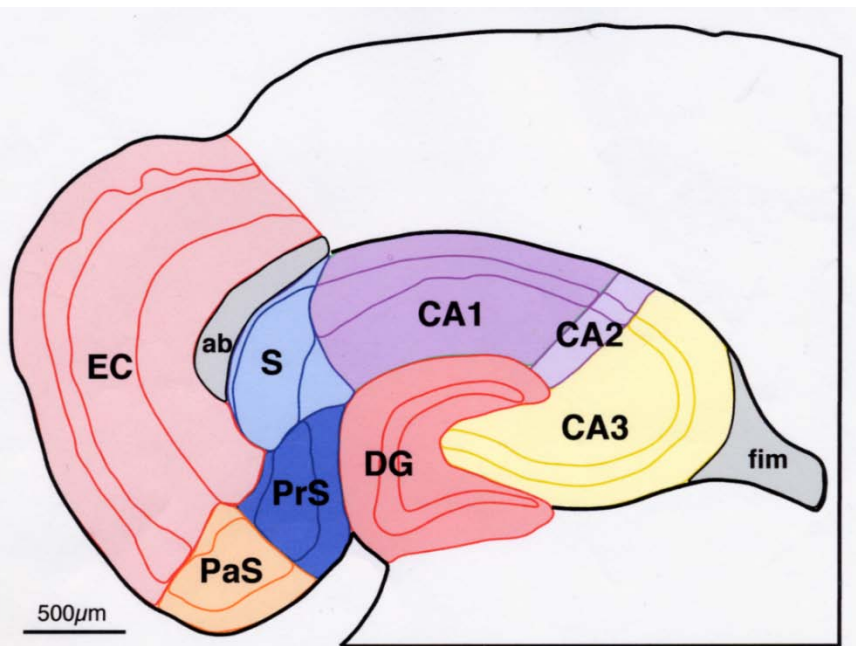
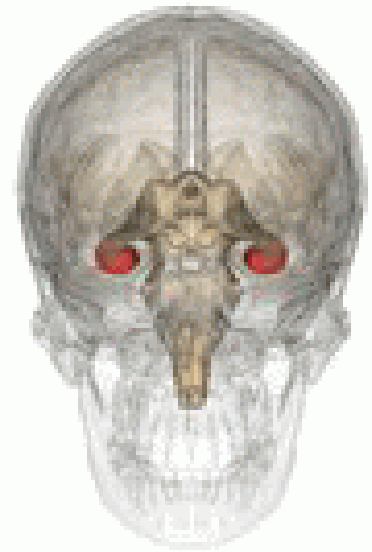
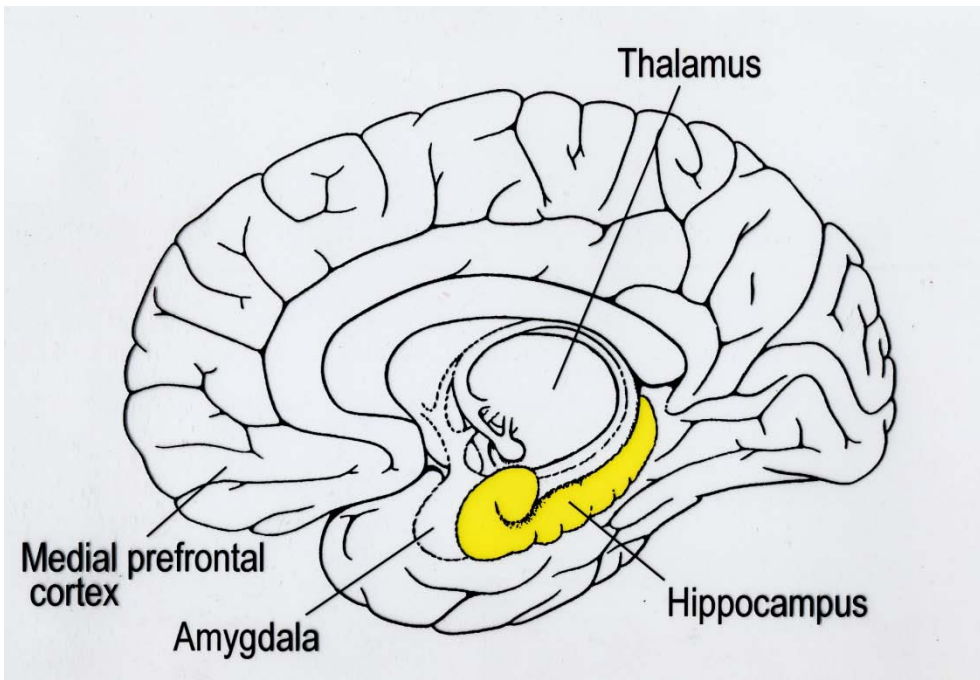
Suzanne Corkin



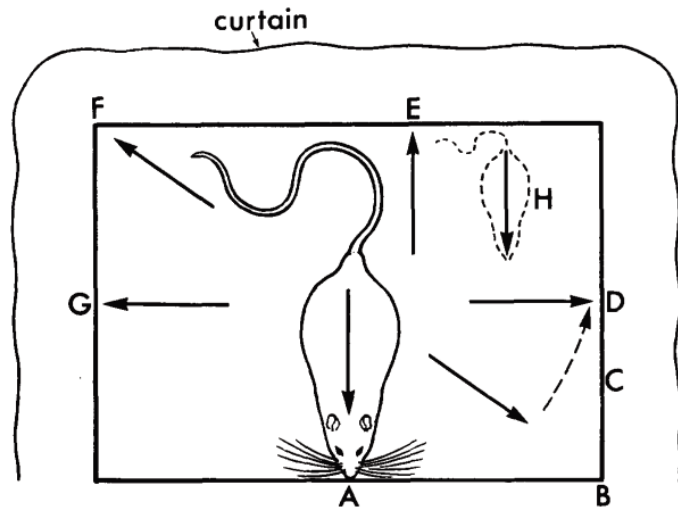
Brenda Milner



“... He ... cannot recall anything that relied on personal experience, such as a specific Christmas gift this father had given him. He retained only the gist of personally experienced events, plain facts but no recollection of specific episodes.” Corkin, p 219

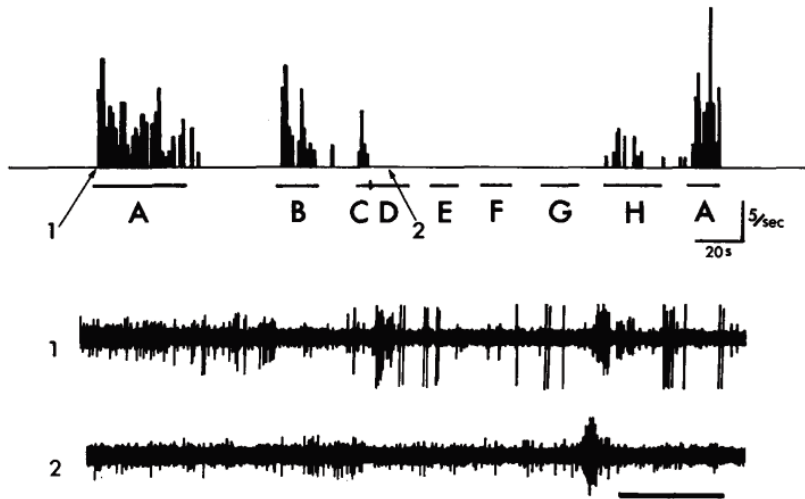


*J Lichtman,  
J Sanes et al*



The hippocampus as a spatial map.  
 Preliminary evidence from unit activity  
 in the freely-moving rat

*O'Keefe & Dostrovsky 1971*



“These findings suggest that the hippocampus provides the rest of the brain with a **spatial reference map**. Deprived of this map.... it could not learn to go from where it happened to be in the environment to a particular place independently of any particular route (as in **Tolman's experiments** )....”

# COGNITIVE MAPS IN RATS AND MEN

E. C. Tolman 1948

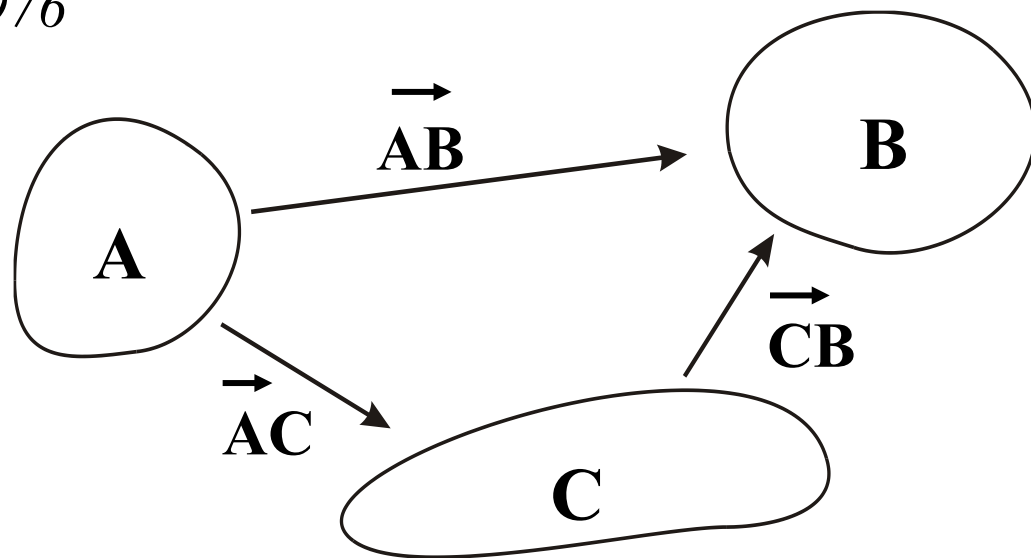
“We believe that in the course of learning, something like a **field map** of the environment gets established in the rat's brain... The stimuli ... are usually worked over ... into a tentative, **cognitive-like map** of the environment. And it is this tentative map, indicating **routes and paths and environmental relationships**, which finally determines what responses, if any, the animal will finally release.” p192



Each **place cell** receives **two** different inputs, one conveying information about a large number of environmental stimuli or events, and the other from a navigational system which calculates where an animal is in an environment independently of the stimuli impinging on it at that moment.....

When an animal had located itself in an environment (using environmental stimuli) the hippocampus could calculate subsequent positions in that environment on the basis of **how far** and **in what direction** the animal had moved in the interim.....

*O'Keefe 1976*

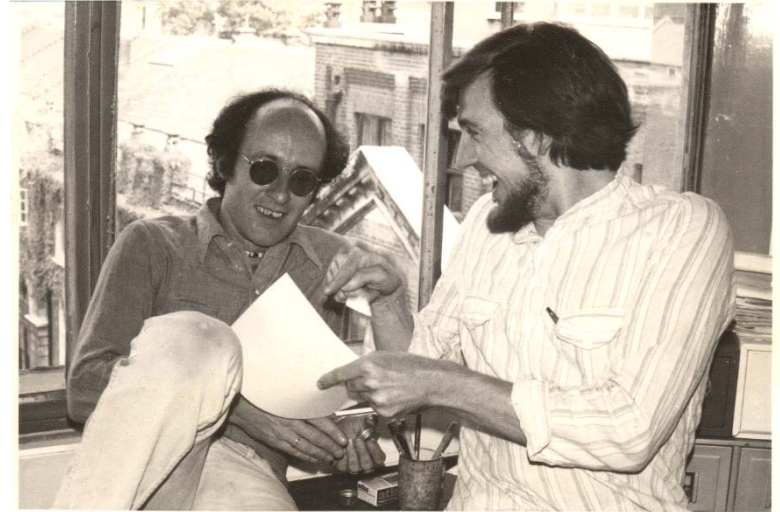


# THE HIPPOCAMPUS AS A COGNITIVE MAP

JOHN O'KEEFE  
AND  
LYNN NADEL



CLARENDON PRESS · OXFORD



## SPACE

plays a role in all our behaviour.

We live in it, move through it, explore it, defend it.

We find it easy enough to point to bits of it:

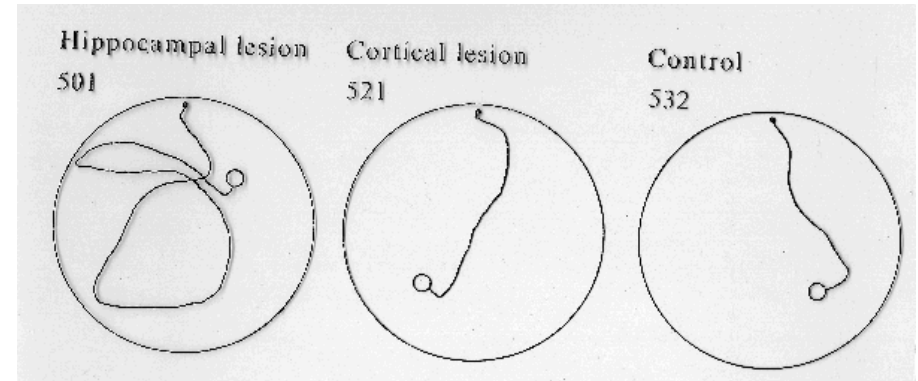
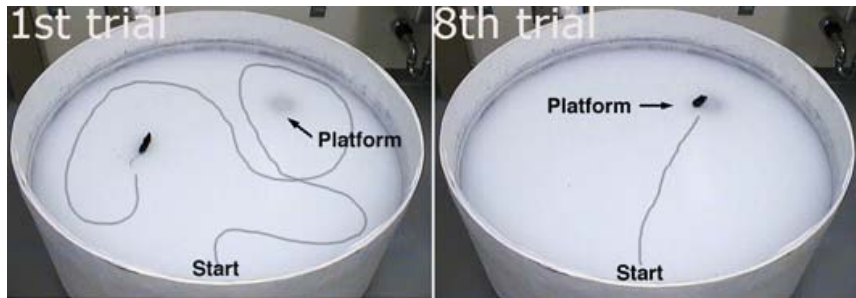
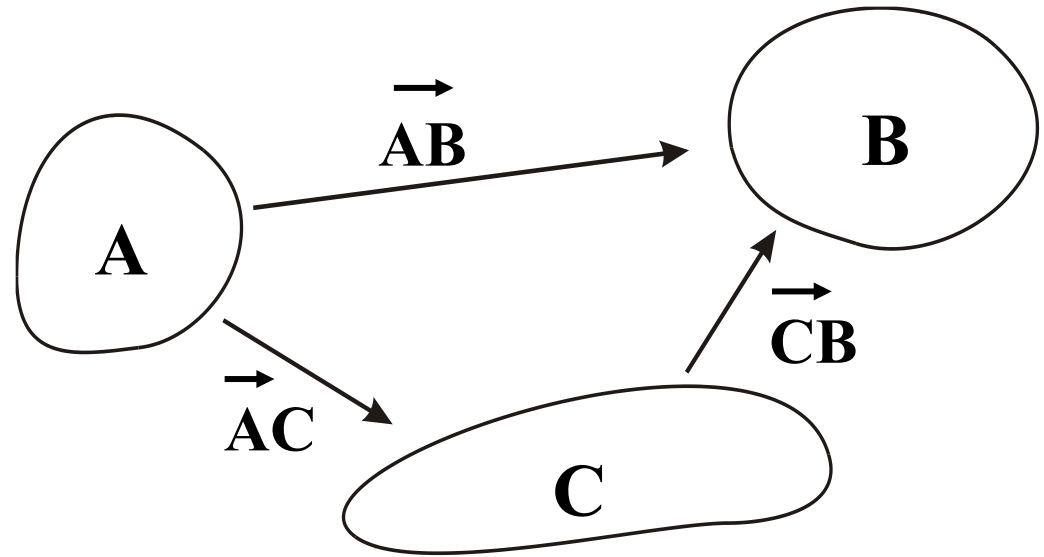
the room,  
the mantle of the heavens,  
the gap between two fingers,  
the place left behind when the piano  
finally gets moved.

Existence of hippocampal signals  
coding direction, distance and  
speed of movement

Deficits in place learning,  
navigation, and exploration

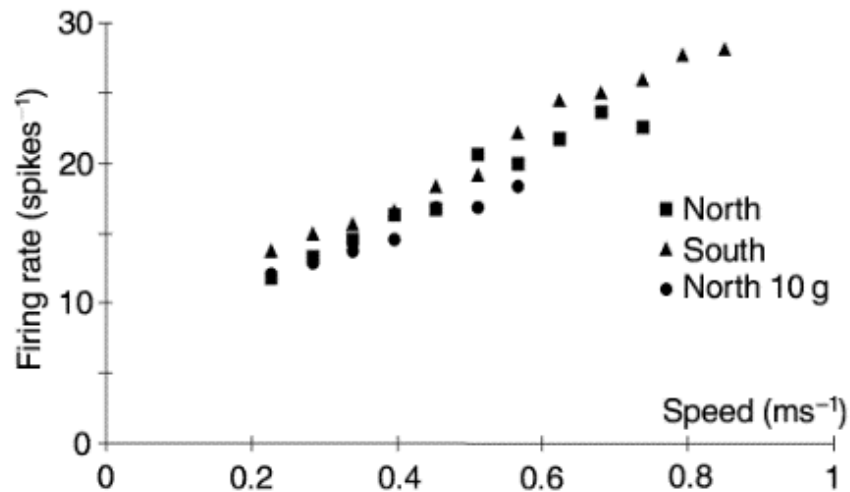
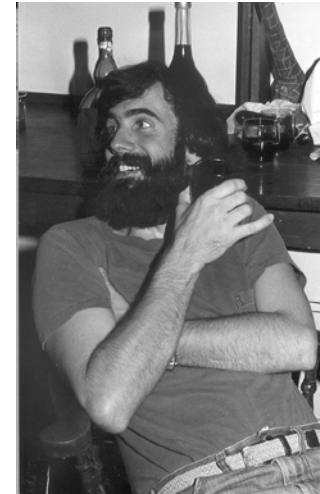
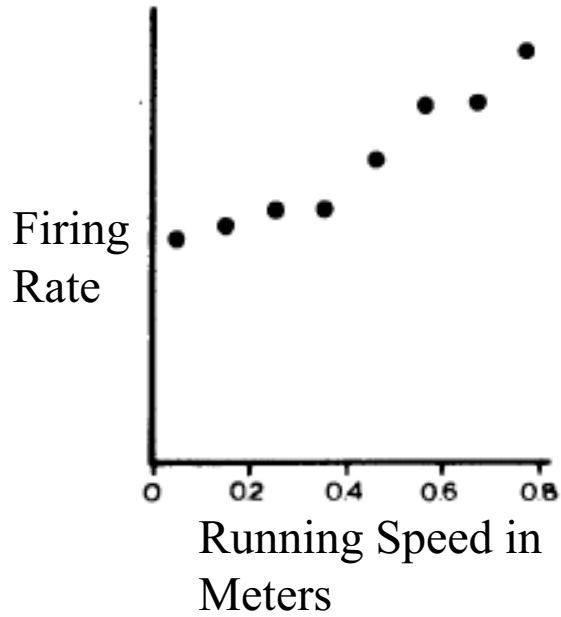


# Morris Water Maze



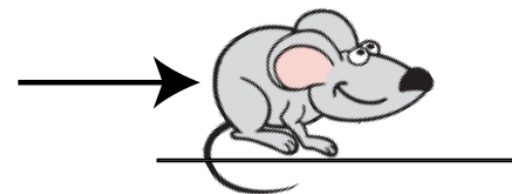


# Place Cell Firing Rate Modulated with Speed

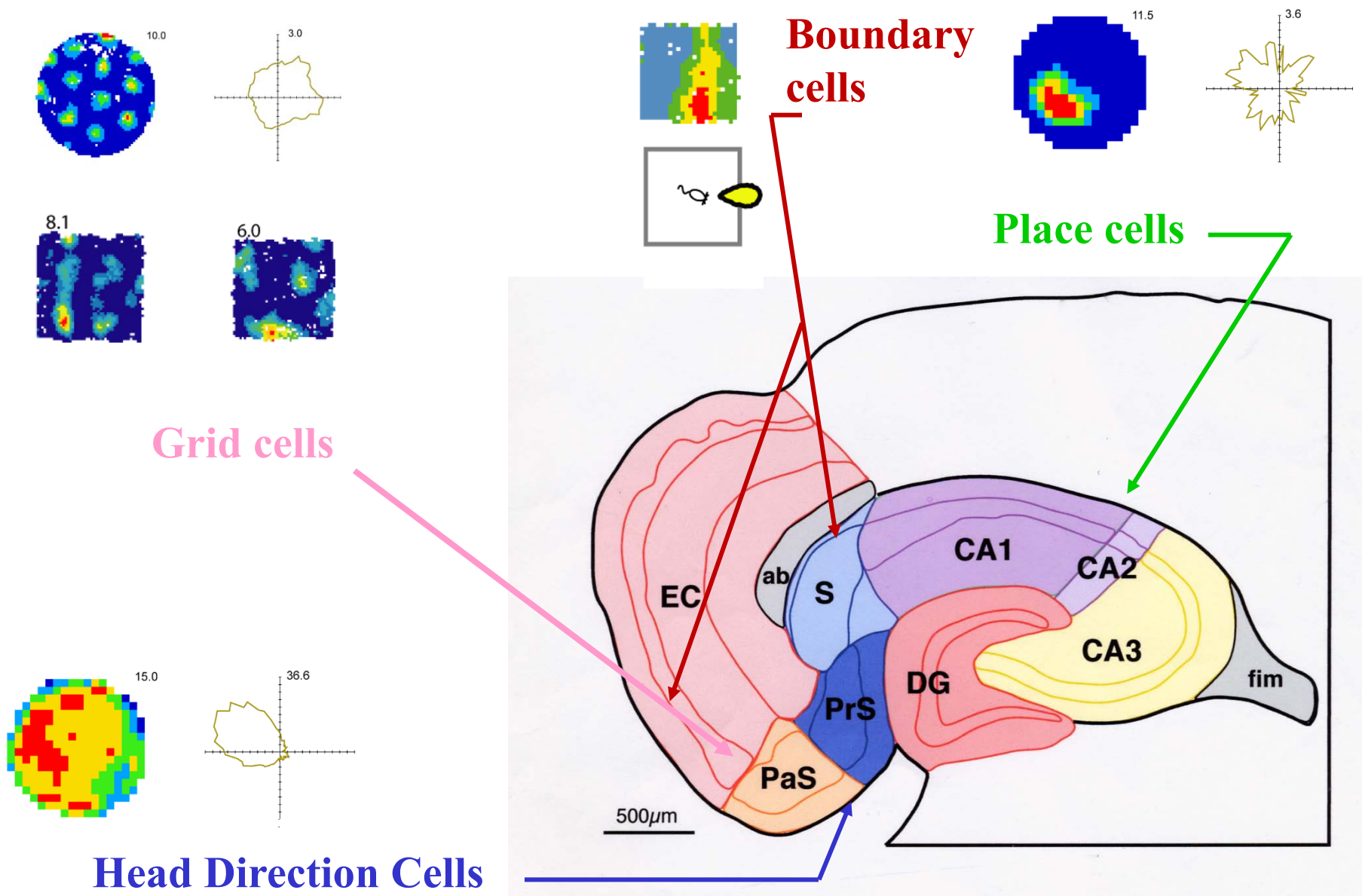


Bruce  
McNaughton

Carol Barnes  
1983



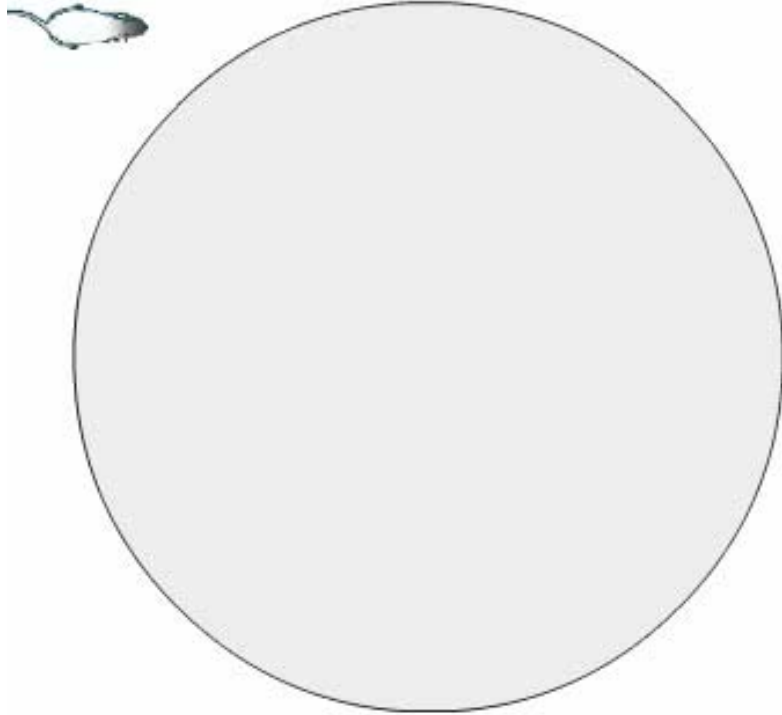
# Spatial cells in the hippocampal formation



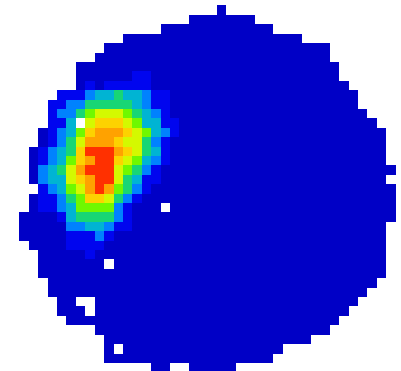
# Place Cell

Usually only one field-  
omnidirectional

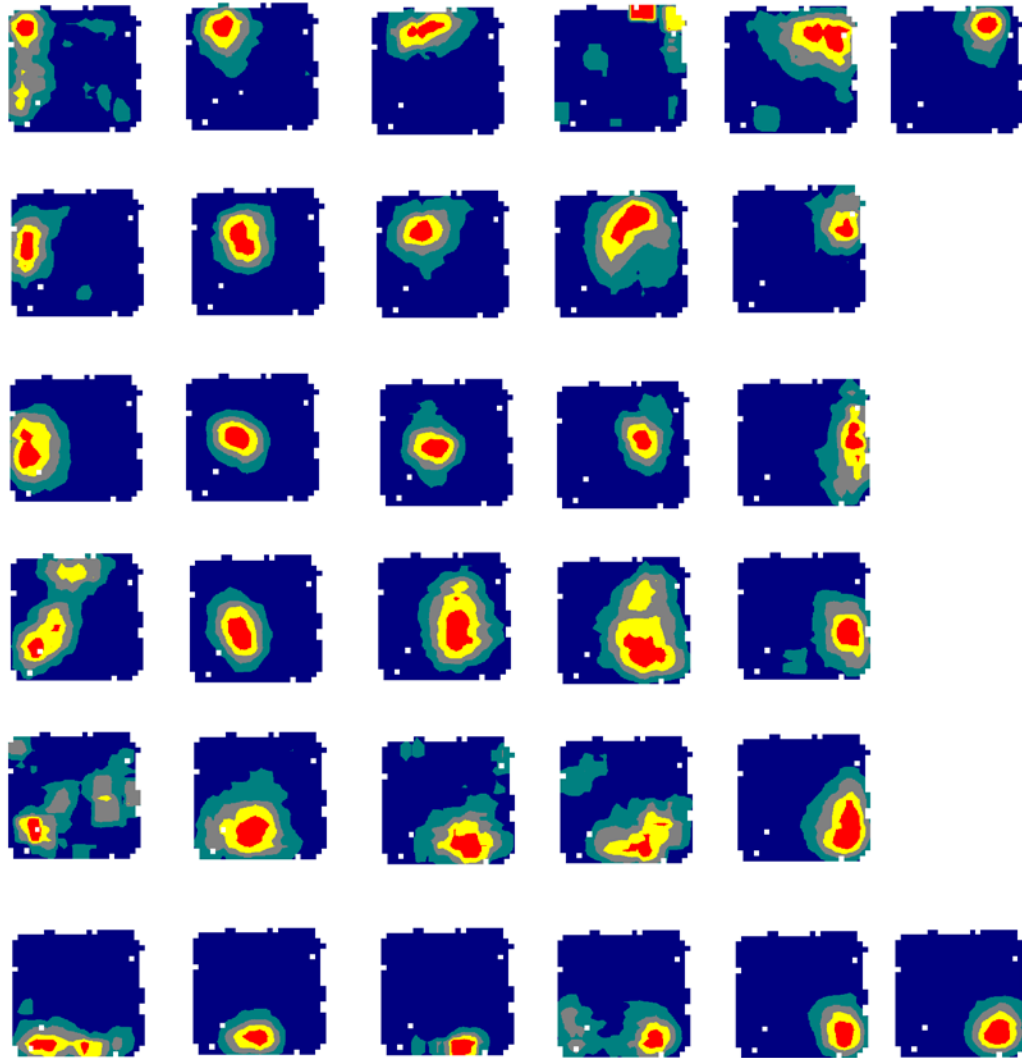
Omni Directional in  
open environments



7.0



# Place cells and cognitive maps

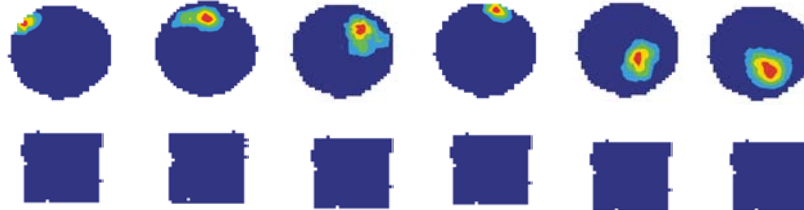


Different cells become active in different **places**

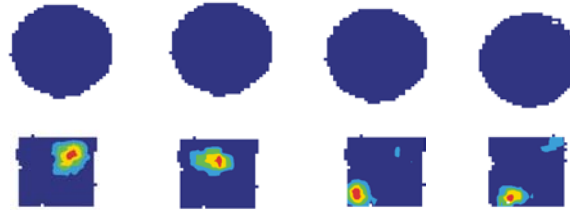


# Place cells differentiate between 2 environments

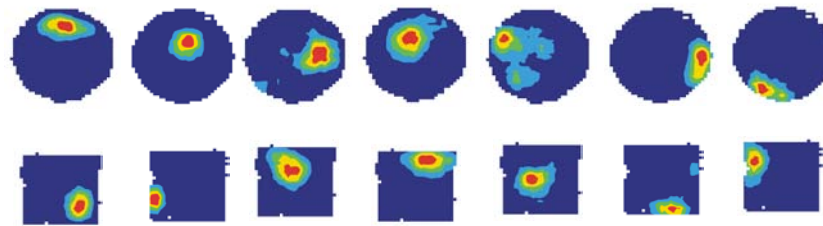
Circle only



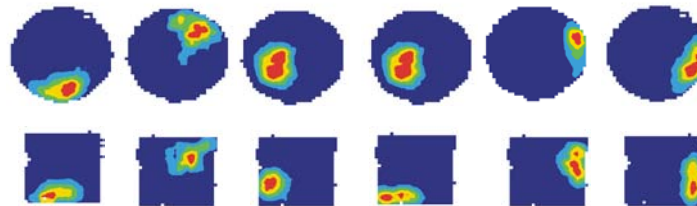
Square only



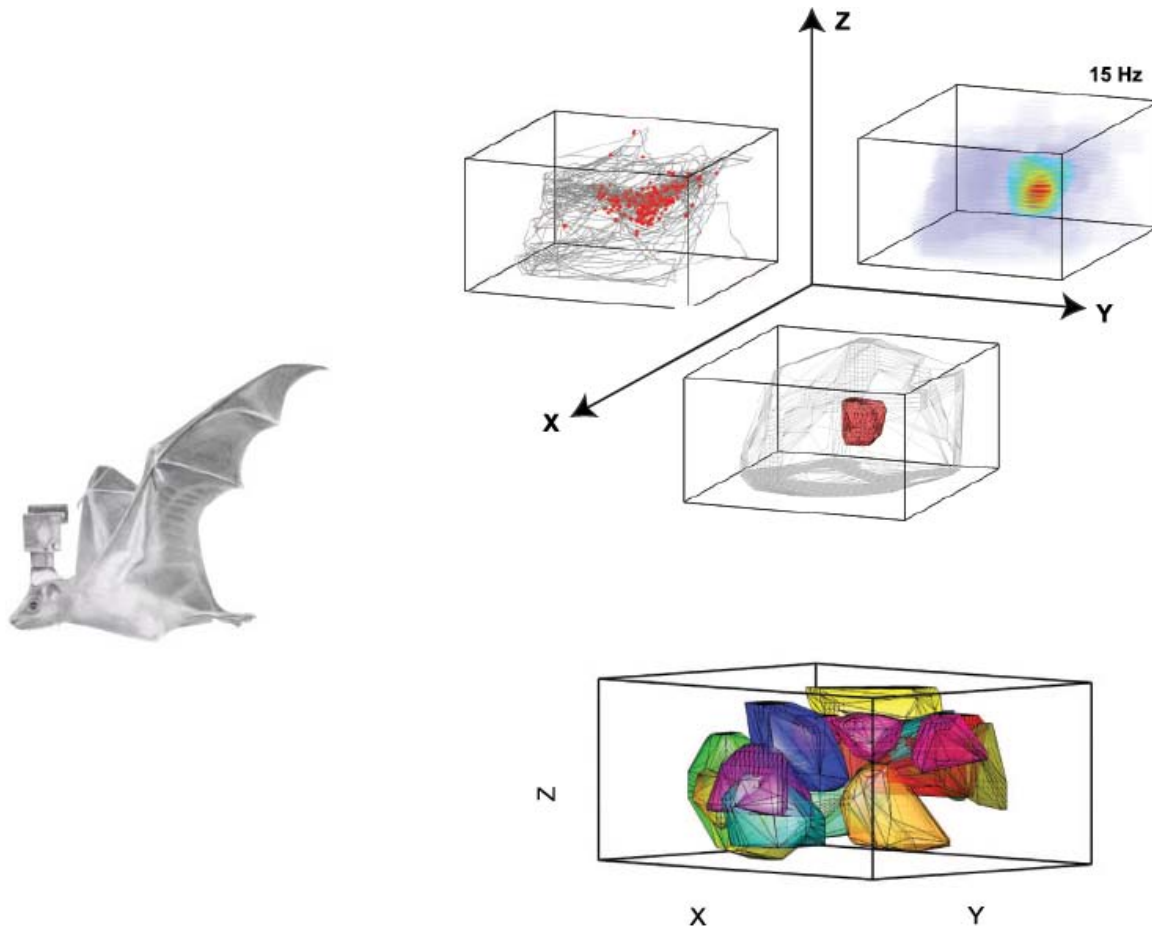
Different locations



Same place

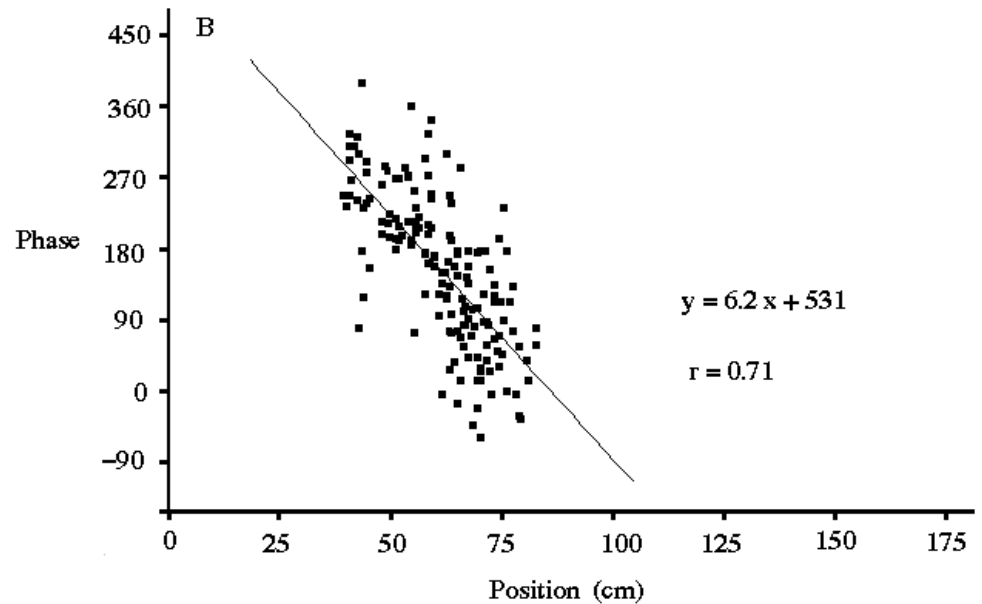
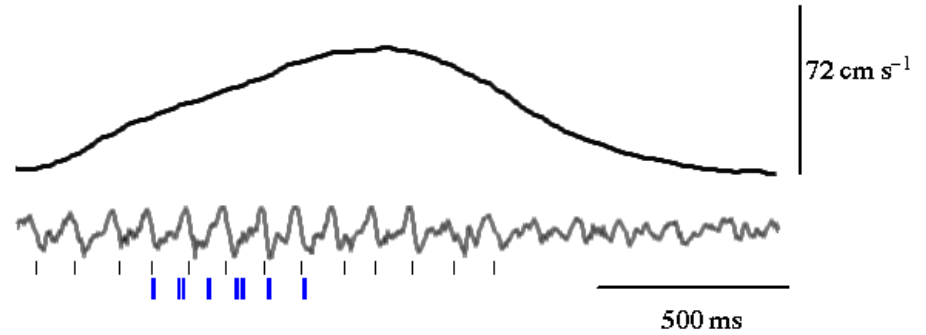
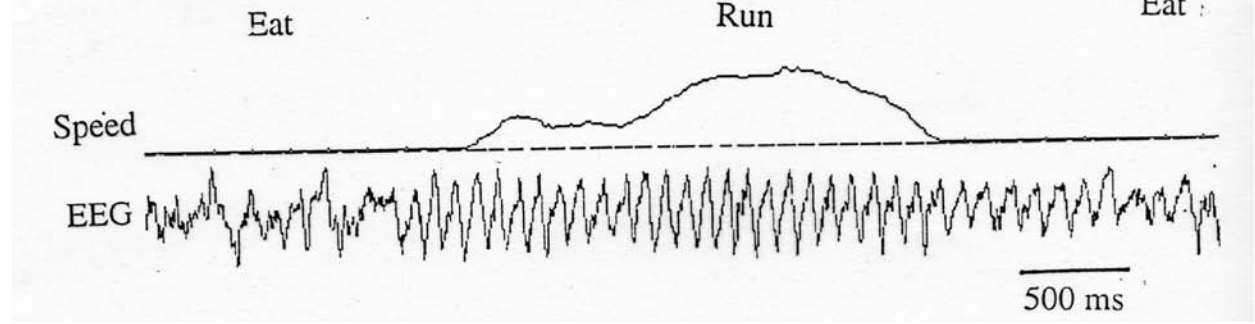
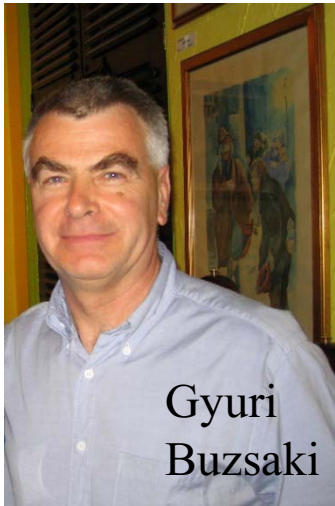


# 3-Dimensional Place Fields



10 place fields

# Temporal Coding of Location



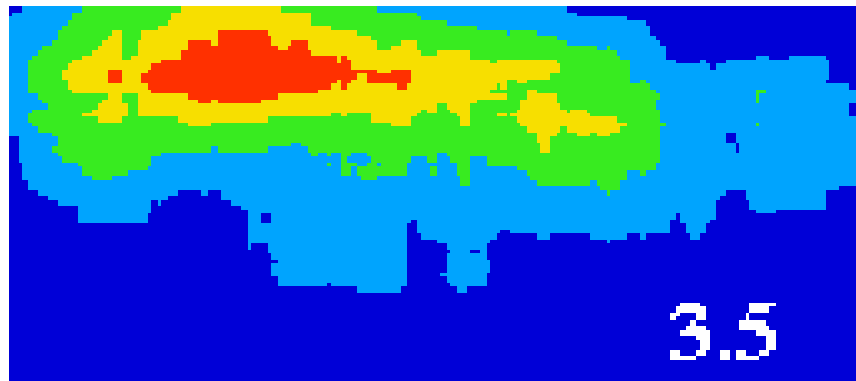
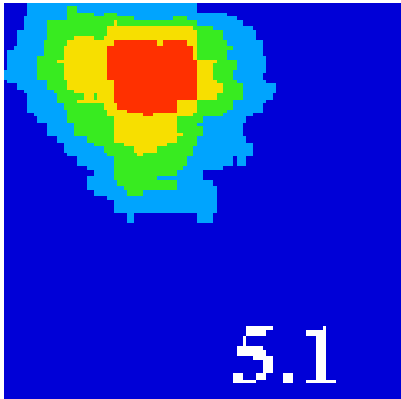
C

*O'Keefe and Recce 1993*



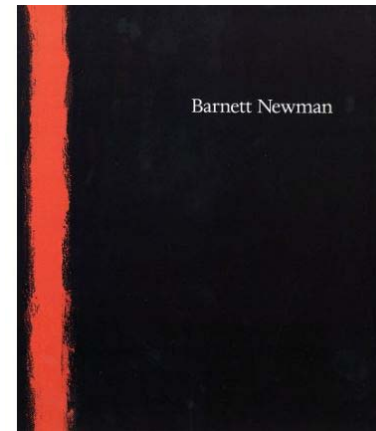
# Boundary Cells provide the Environmental Inputs

Some Place Fields scale with the Distance  
between Sides of the Box

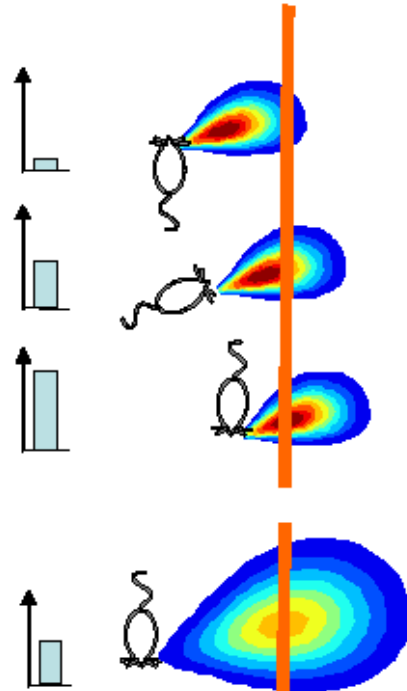




# Boundary Cells: Theory

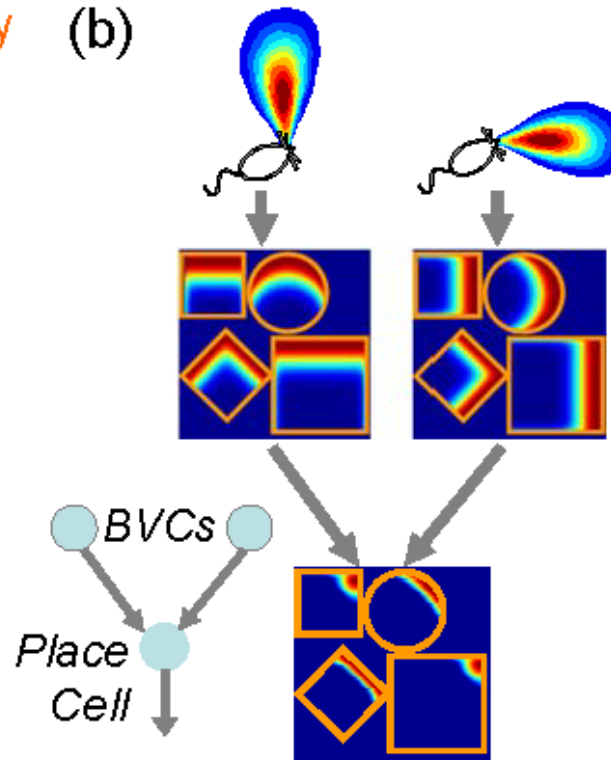


(a) environmental boundary

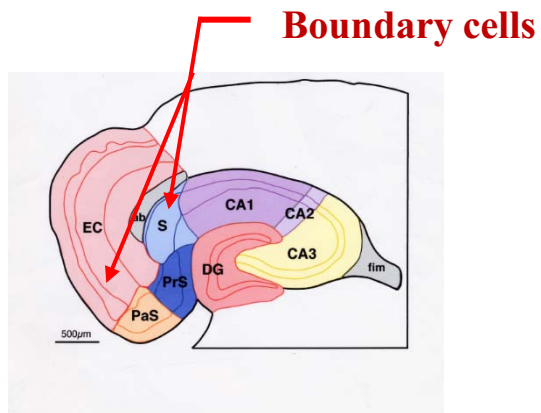
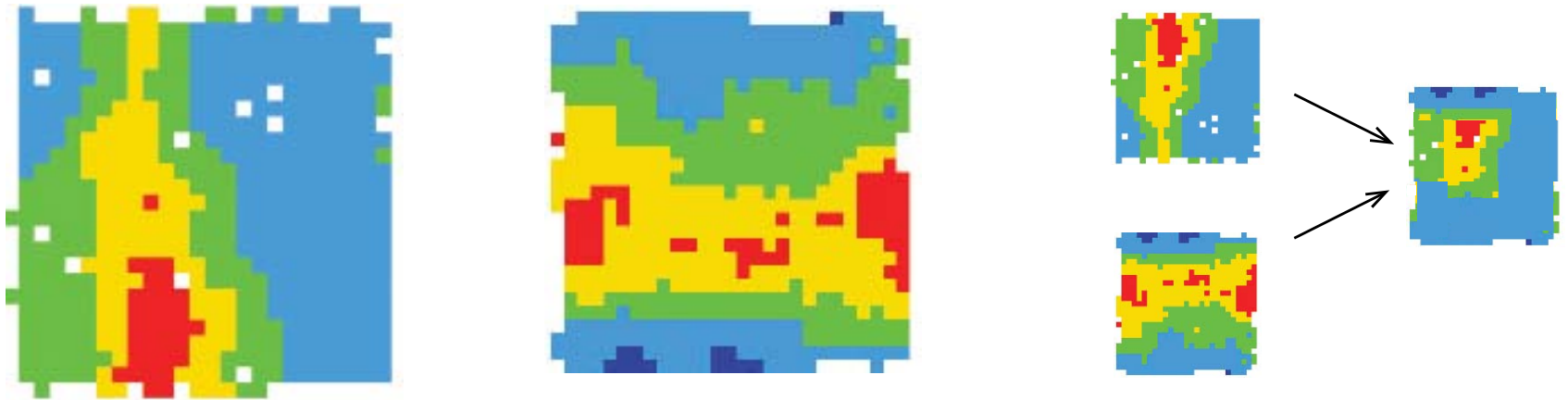


firing rate    receptive field

(b)

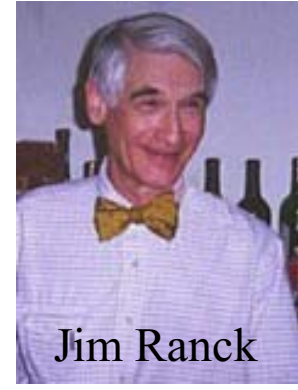
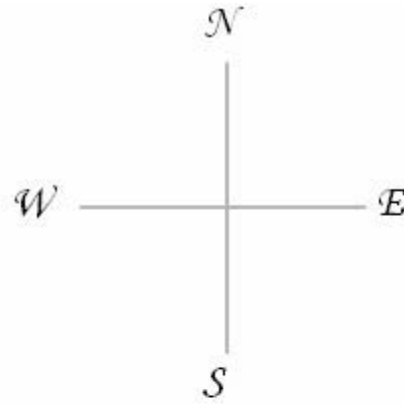
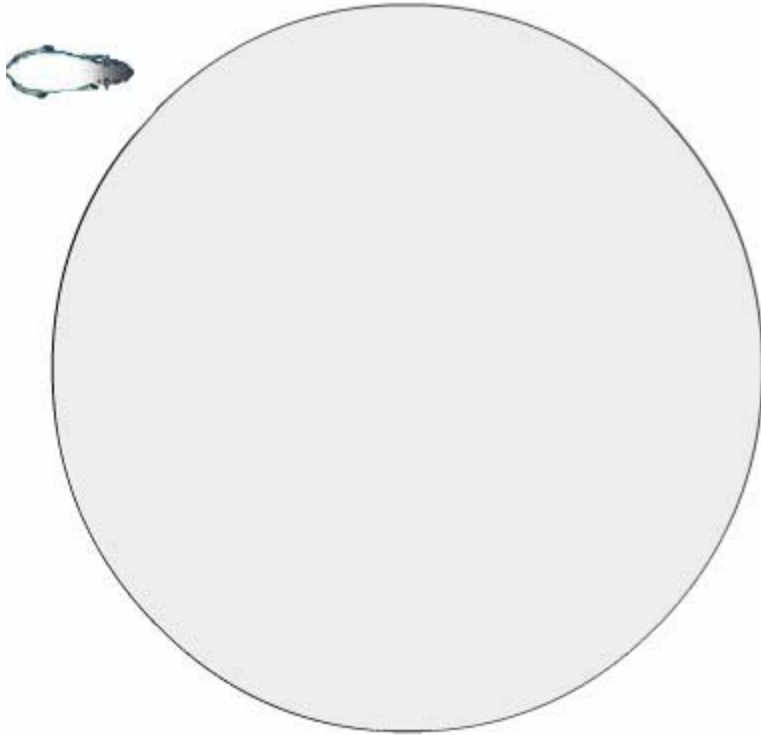


# Boundary Cells in the Subiculum



*Lever et al (2009); Solstad et al (2008)*

# Head Direction Cells

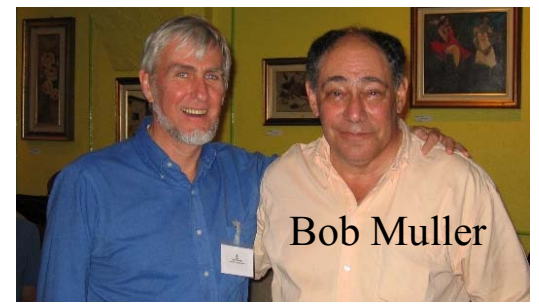
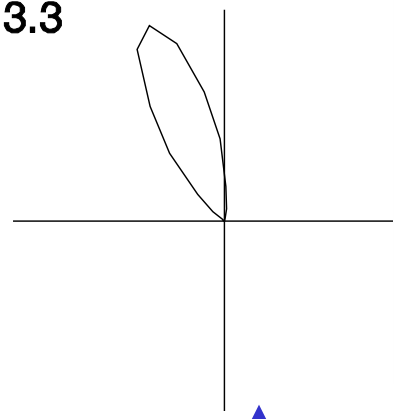


Jim Ranck

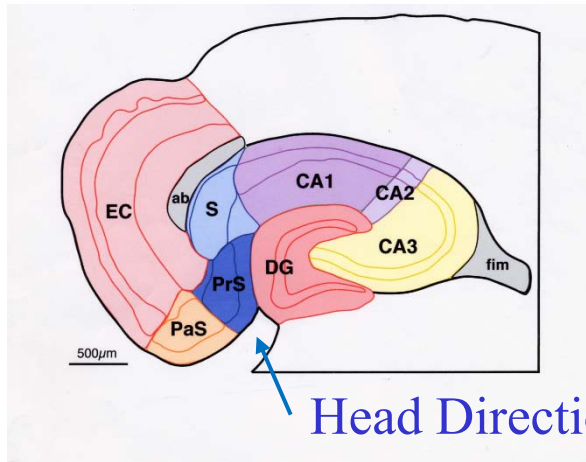


Jeff Taube

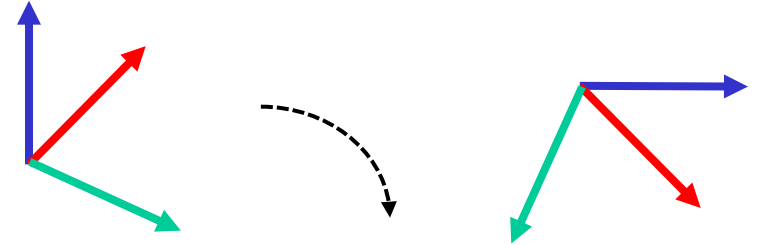
3.3



Bob Muller

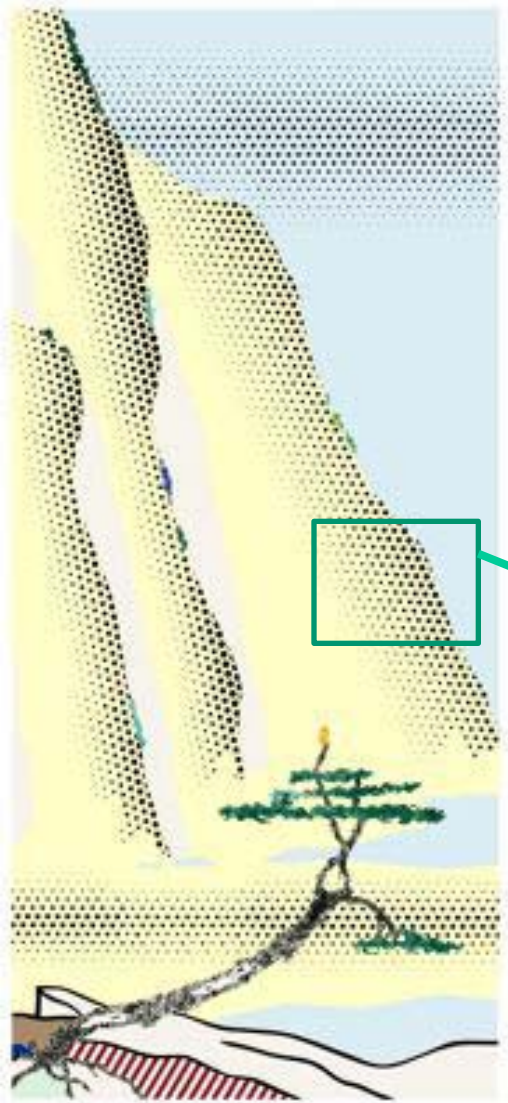


Head Direction Cells

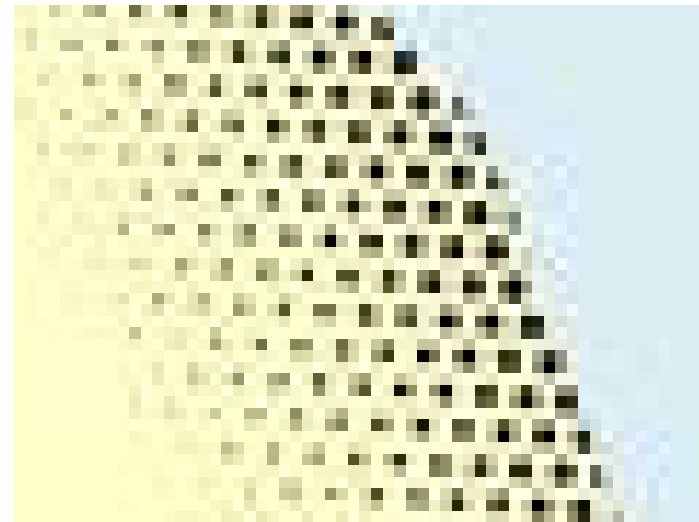


Taube, Muller & Ranck 1990

# How is distance measured?



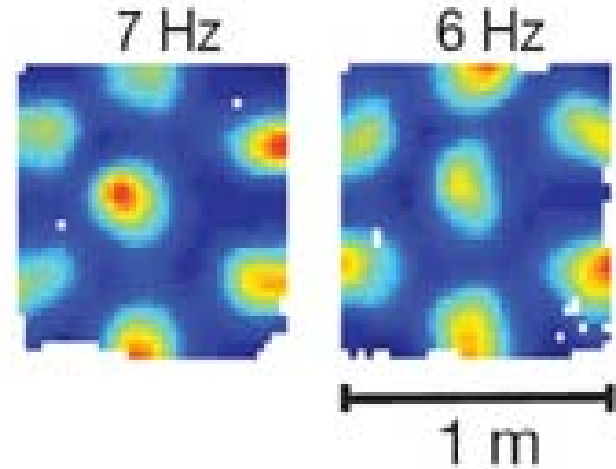
Wm  
Blake



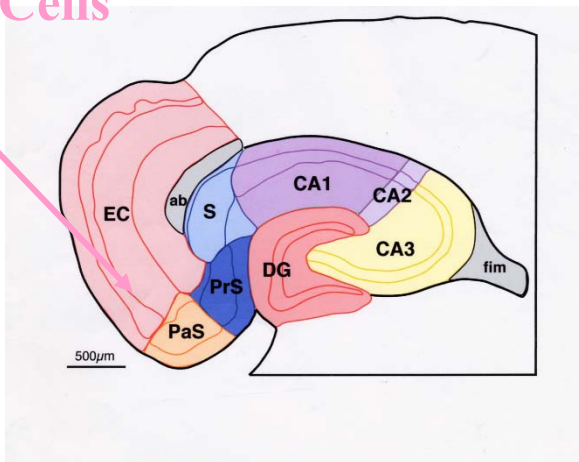
Roy Lichtenstein

**Grid Cells:** the universal metric in the entorhinal cortex?

Firing fields lay out a regular series of equally-spaced fields in every familiar environment



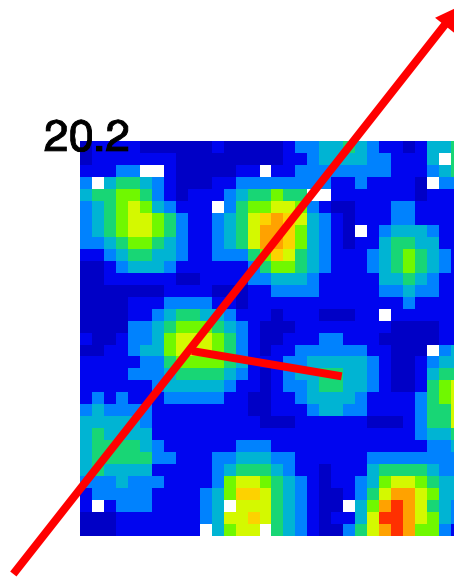
**Grid Cells**



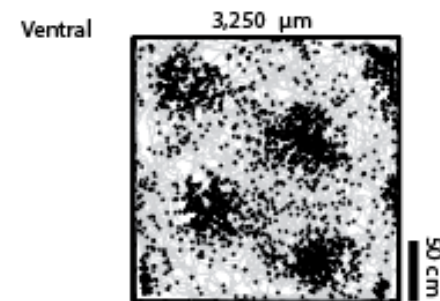
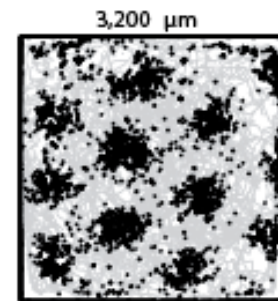
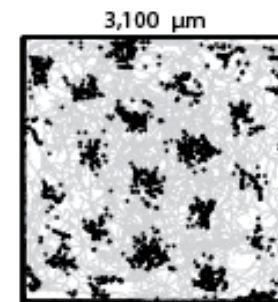
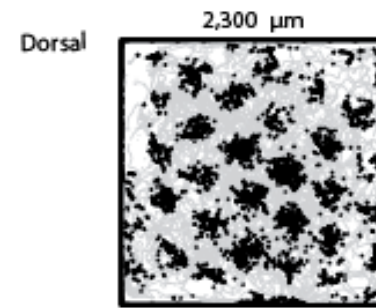
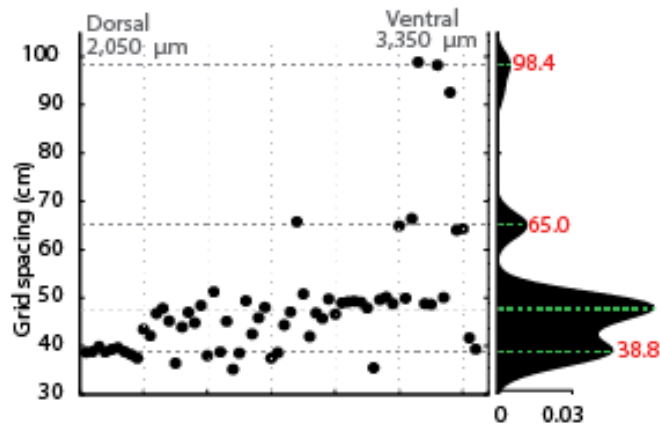
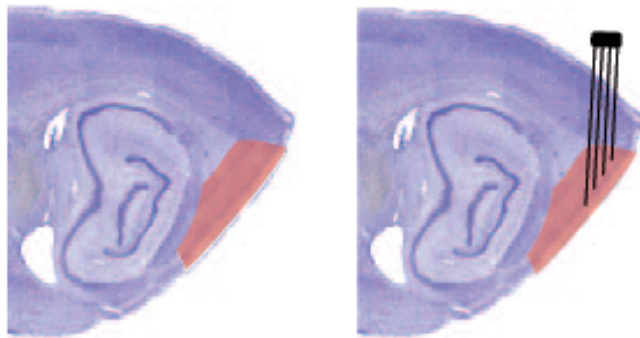
May-Britt & Edvard Moser



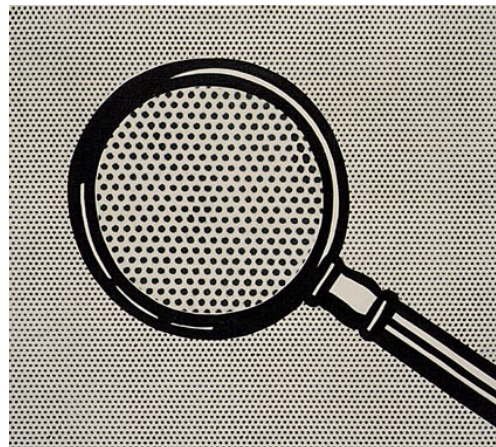
# Grid Cell



# Grid Spacings are Quantised

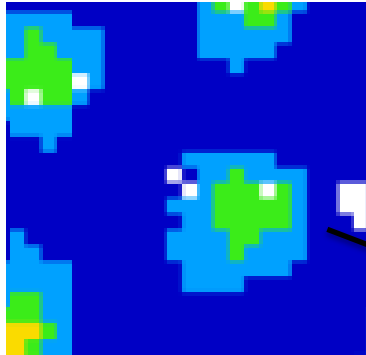


*Stensola et al Nature  
2013*

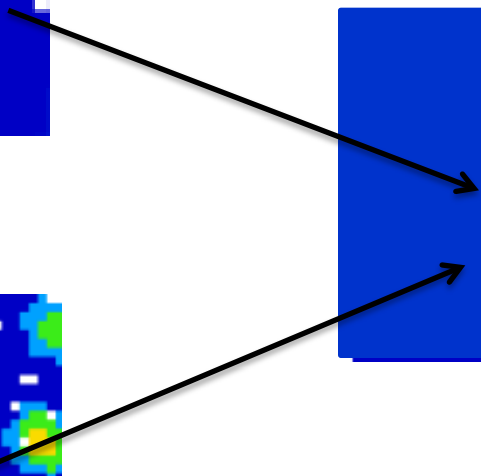
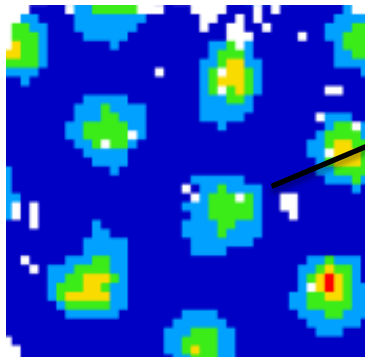
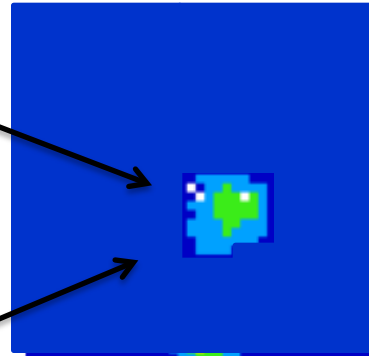


# Grid Fields can add to produce a Place Cell Field

Grid cells

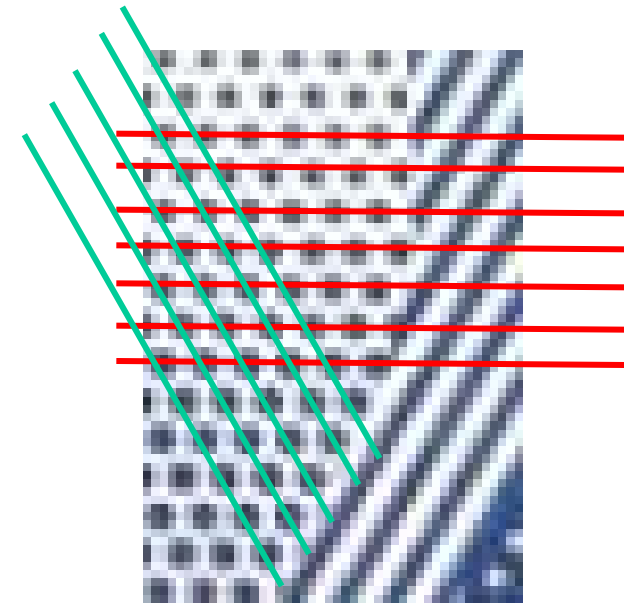
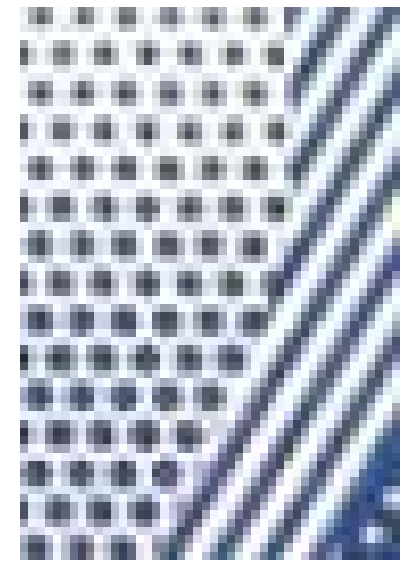
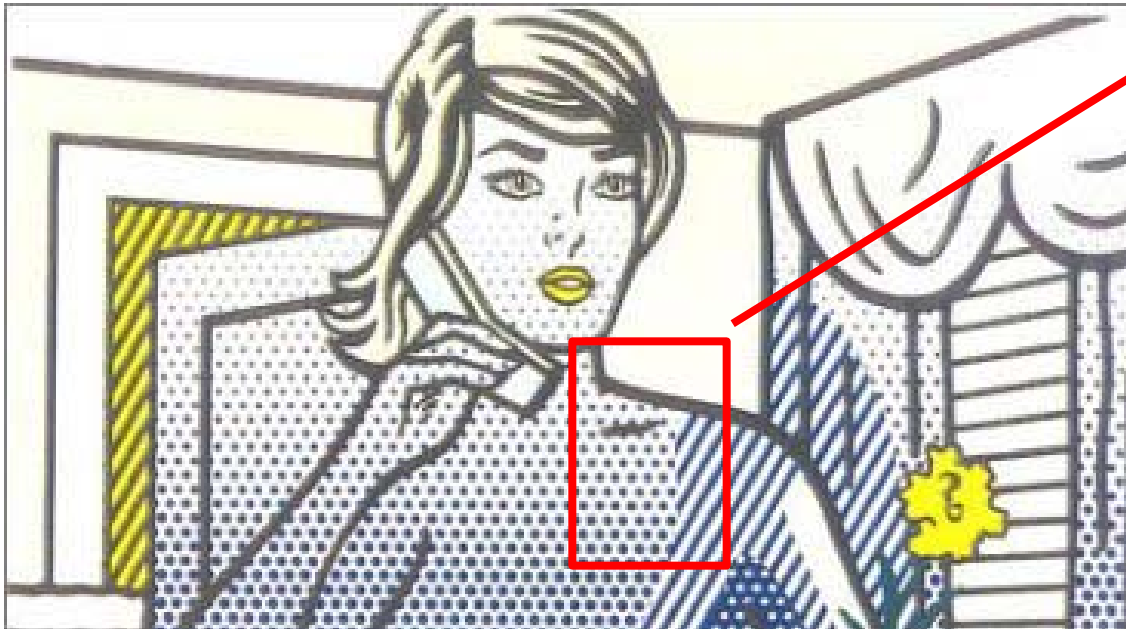


Place Cell



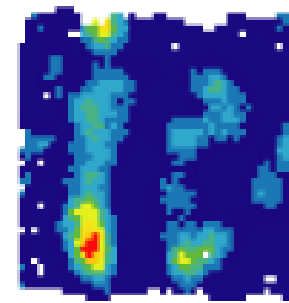
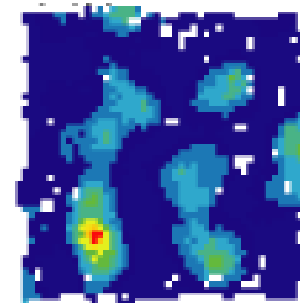
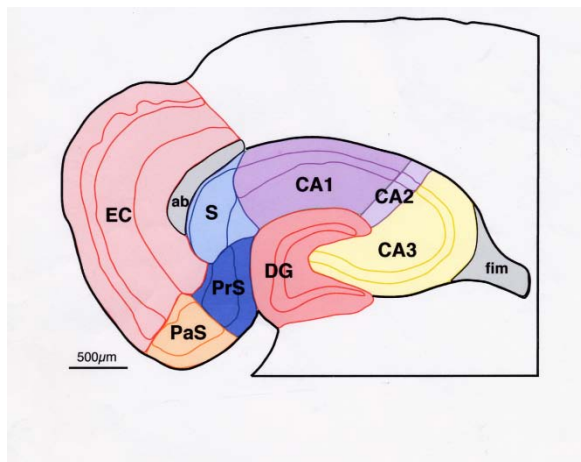
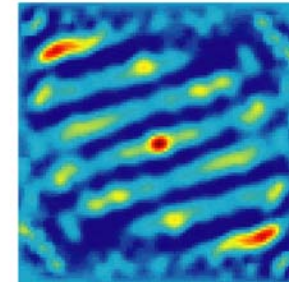
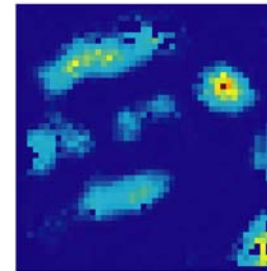
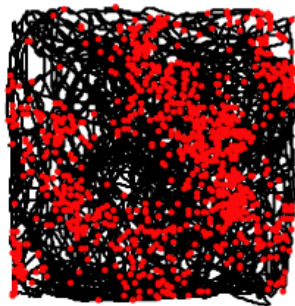
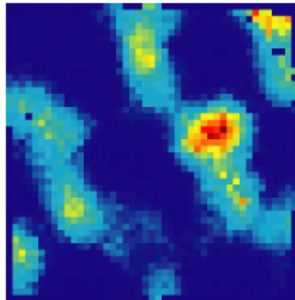


# Relationship between Grids and Stripes



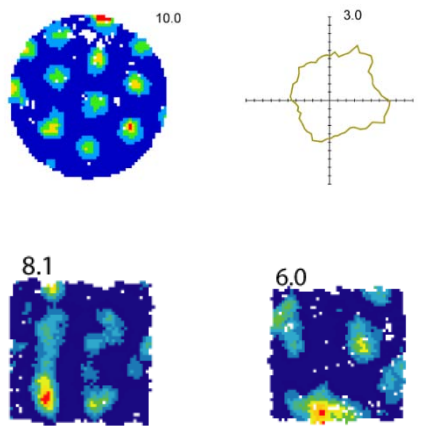
Roy Lichtenstein

# Band-like Cells in the Parasubiculum

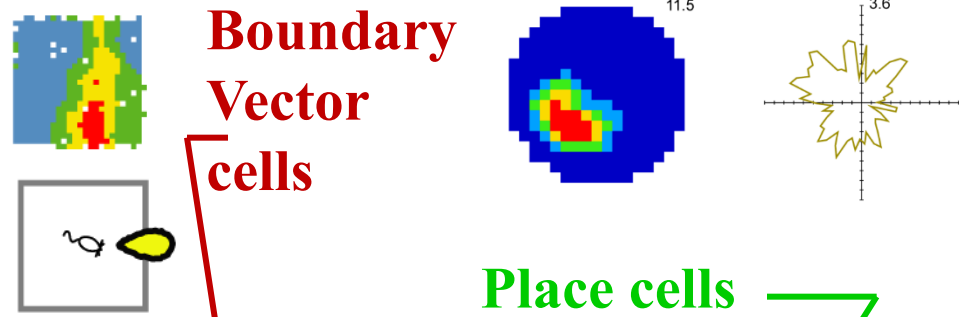


*Krupic, Burgess & O'Keefe Science 2012*

# Spatial cells in the hippocampal formation

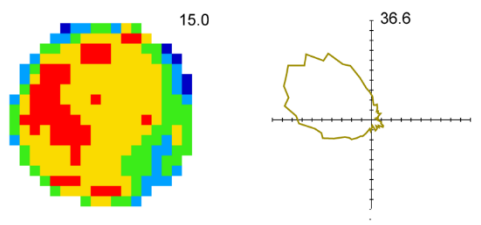


Grid & Spatially Periodic Non-grid cells

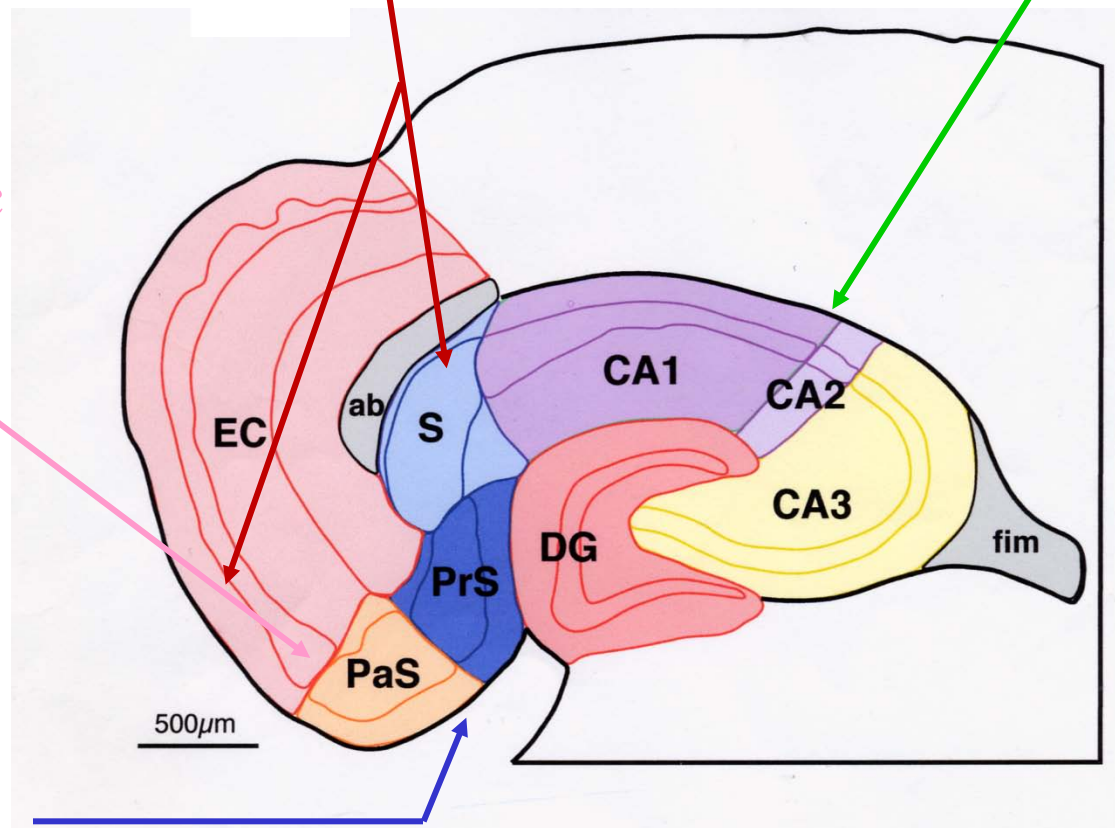


Boundary Vector cells

Place cells



Head Direction Cells



Kant:

'Space is nothing but the form of all appearances of outer sense..... can be given prior to all actual perceptions, and so exist in the mind *a priori*, and .... can contain, prior to all experience, principles which determine the relations of these objects' (*Critique of Pure Reason*, p. 71).

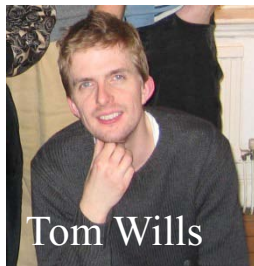
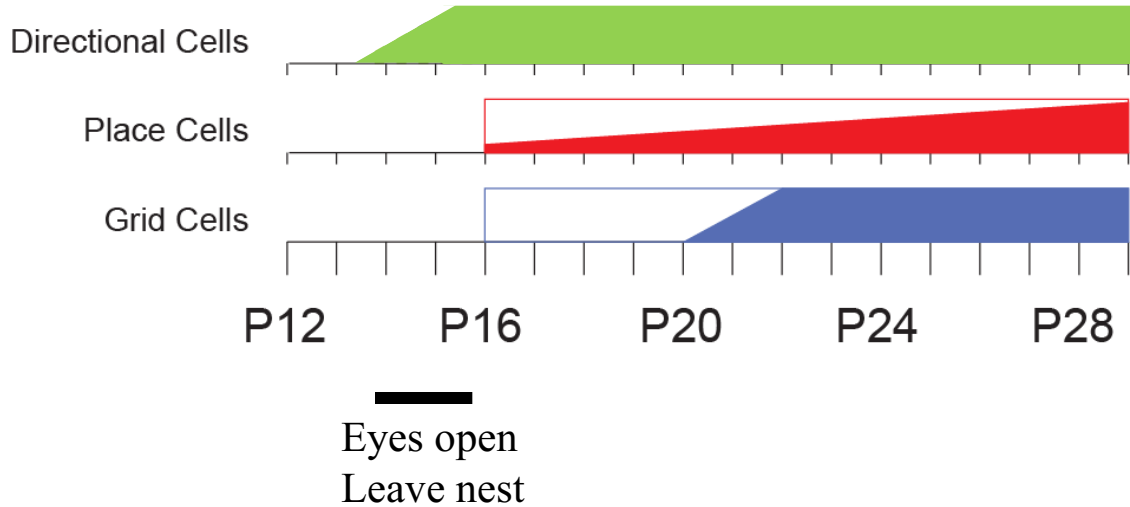


As it is this neo-Kantian position which we shall be adopting in this book, it is worth restating two main features of the argument:

1. Three-dimensional Euclidean space is a form imposed on experience by the mind.
2. This unitary framework, conveying the notion of an all-embracing, continuous space, is a prerequisite to the experiencing of objects and their motions.

*O'Keefe and Nadel 1978 p 23-4*

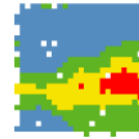
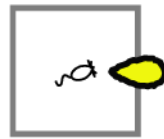
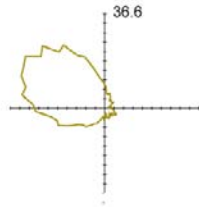
# Ontogeny of spatial cells



*Wills, Cacucci, Burgess & O'Keefe Science 2010, Hui Min Tan et al unpublished; Langston, Ainge et al Science 2010*

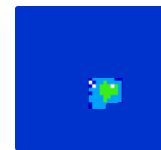
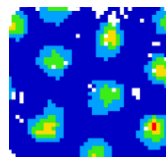
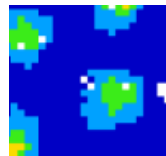
# Grid cells and Boundary Vector cells may provide 2 independent pathways into Place Representations

**Head  
Direction  
Cells**

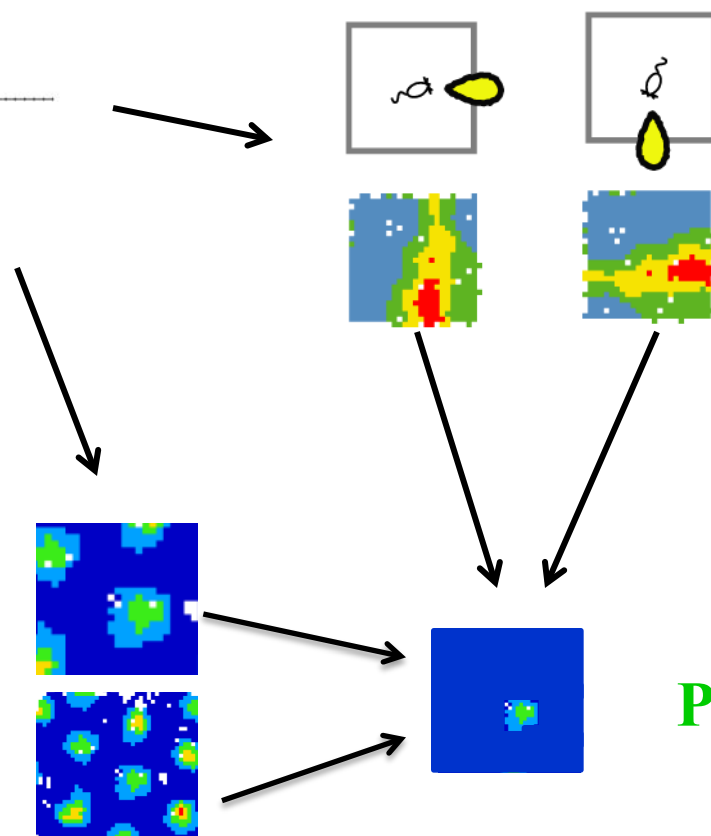


**Boundary  
Vector cells**

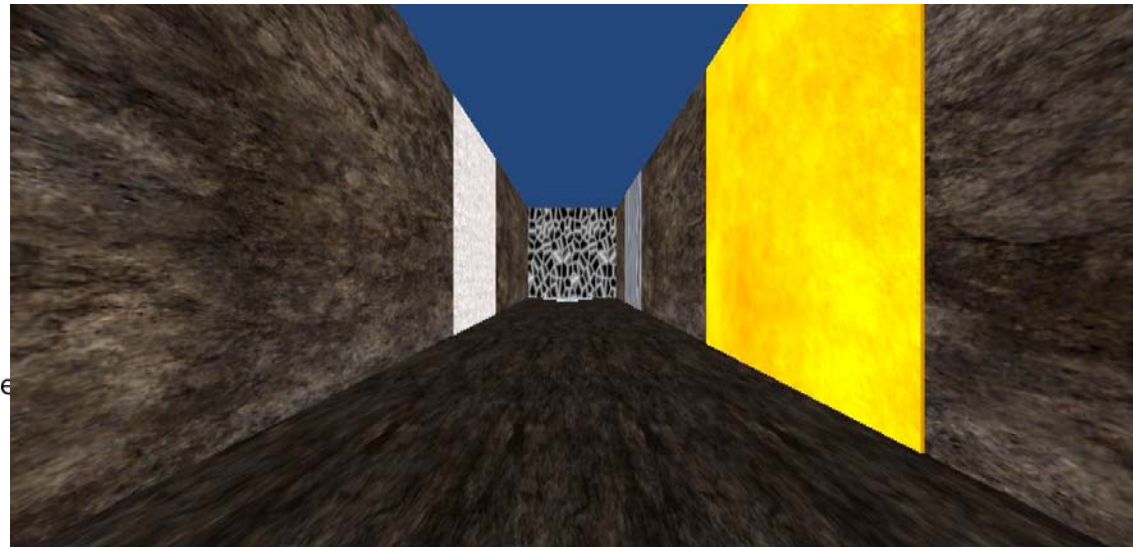
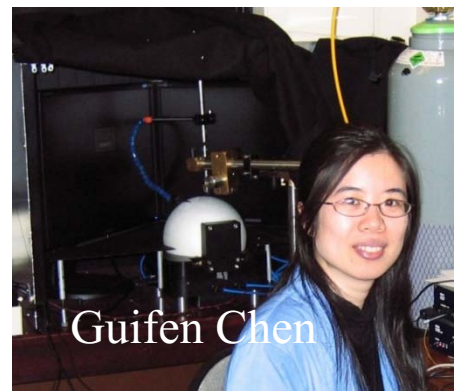
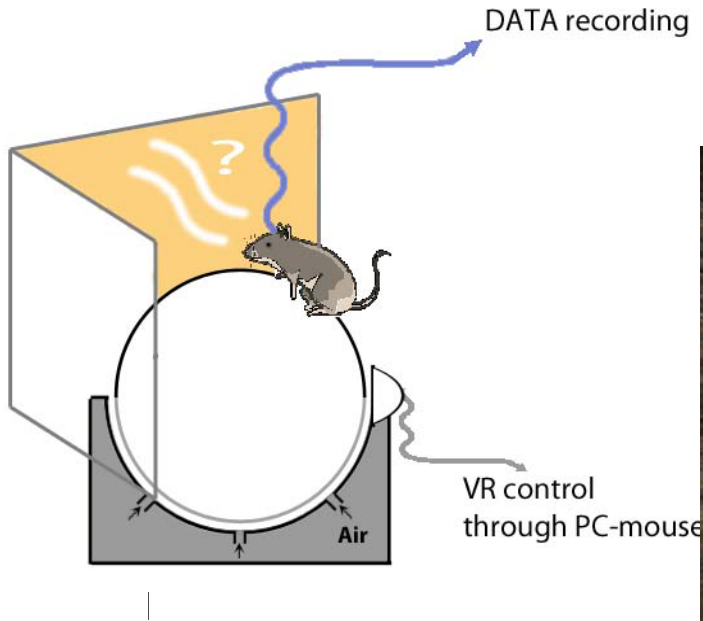
**Grid  
Cells**



**Place cells**

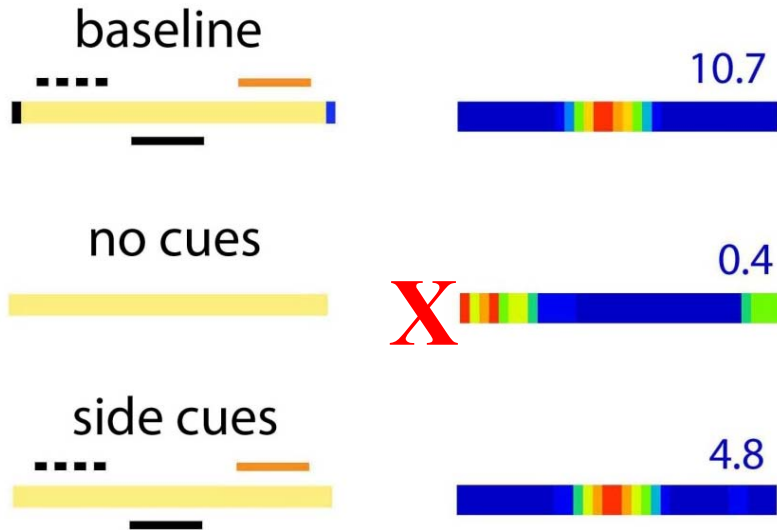


# Virtual Reality environment

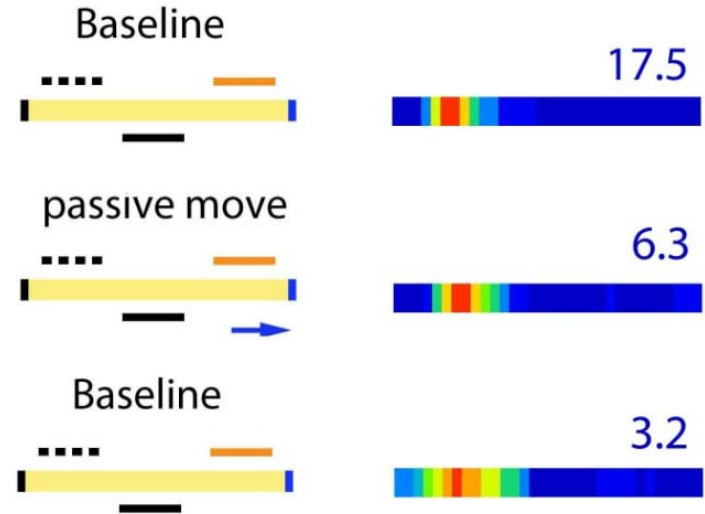


*Harvey et al, 2009; Hölscher et al, 2005; Chen, King, Burgess & O'Keefe 2013*

# Control by visual cues on the side wall



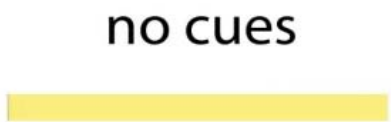
80 % Fields disrupted  
by cue removal



25 % Fields maintained  
in passive probe

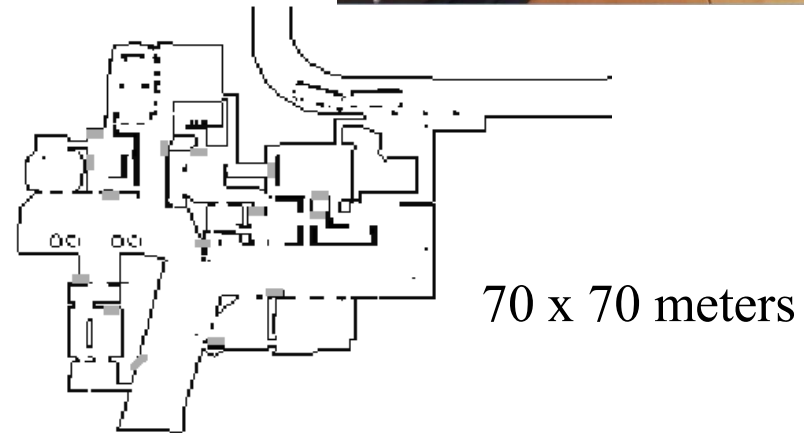
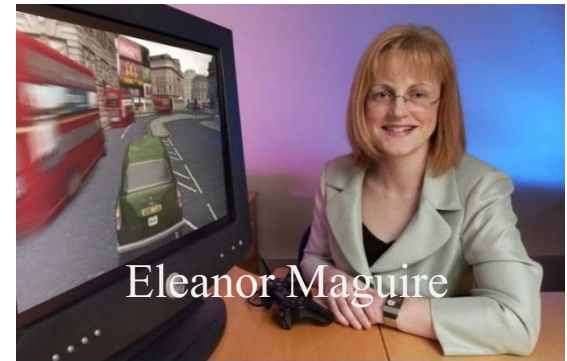
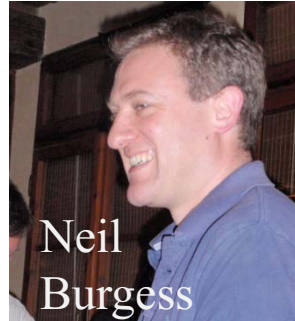


# Path integration (light off trial)

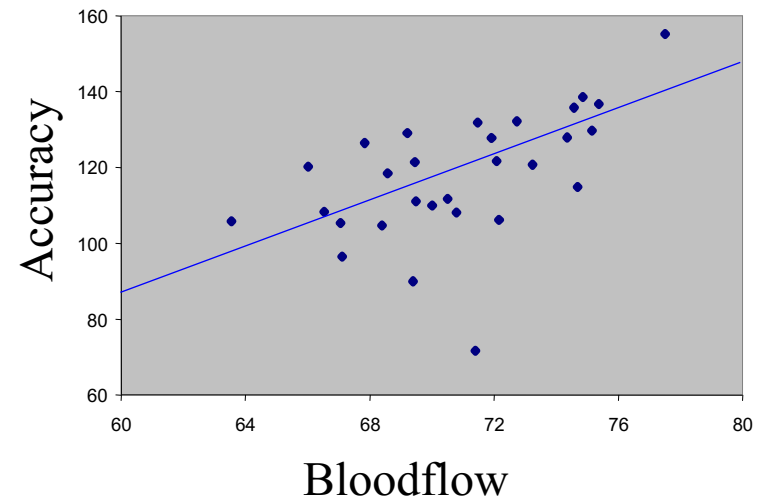
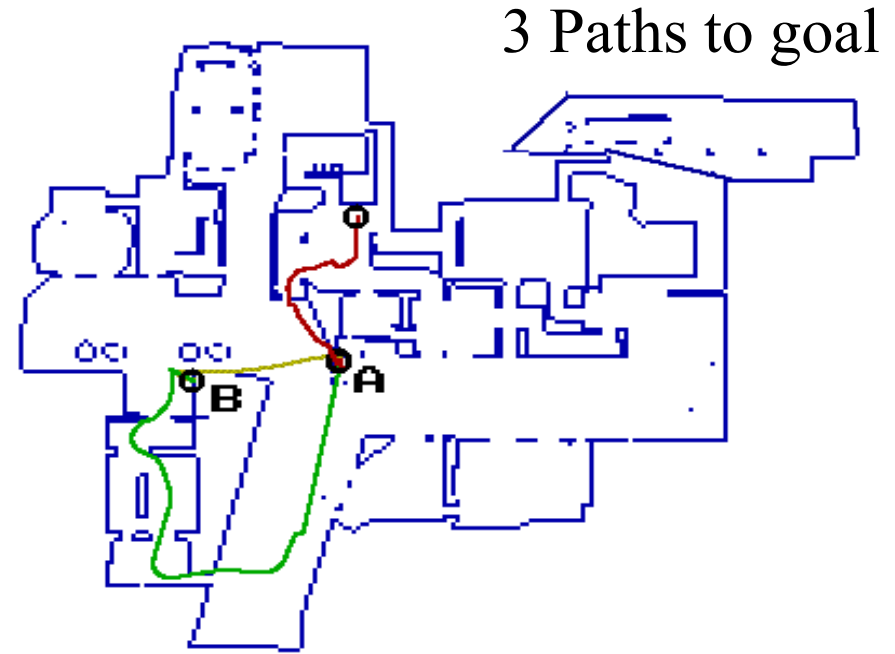
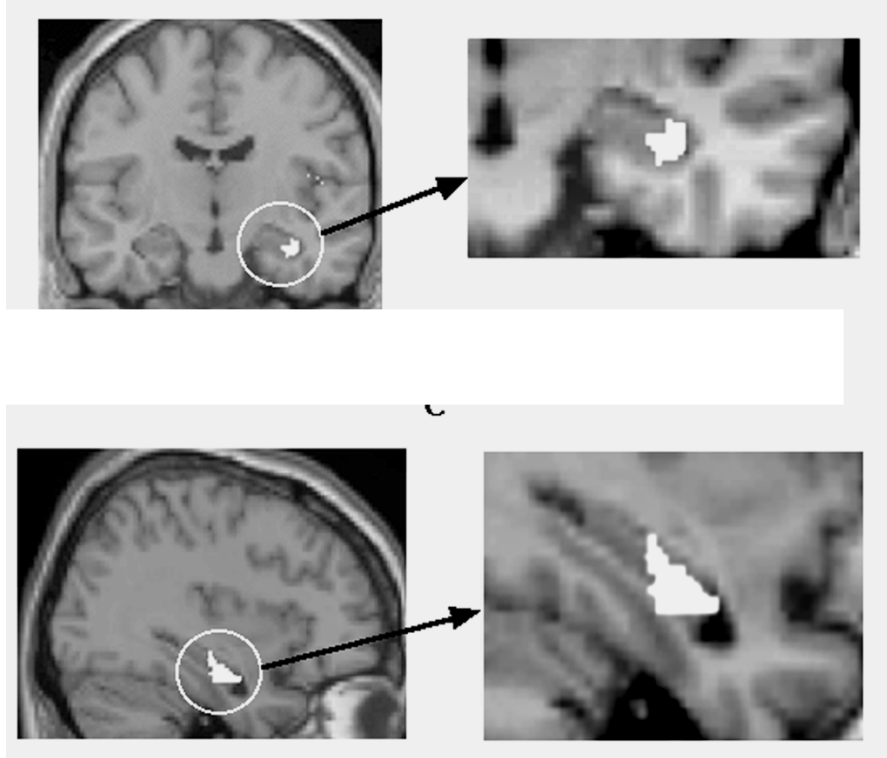


49% maintain fields in lights off PI trials

# The Virtual Town

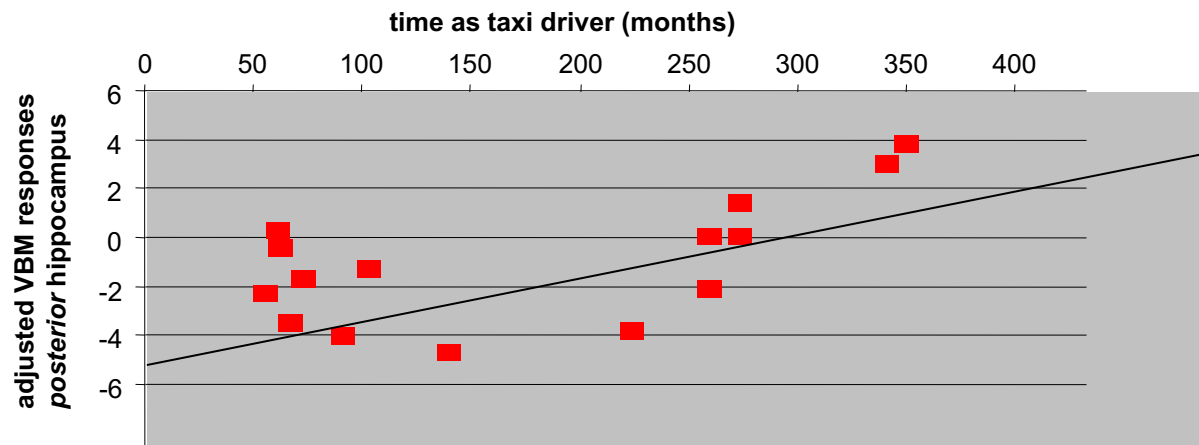
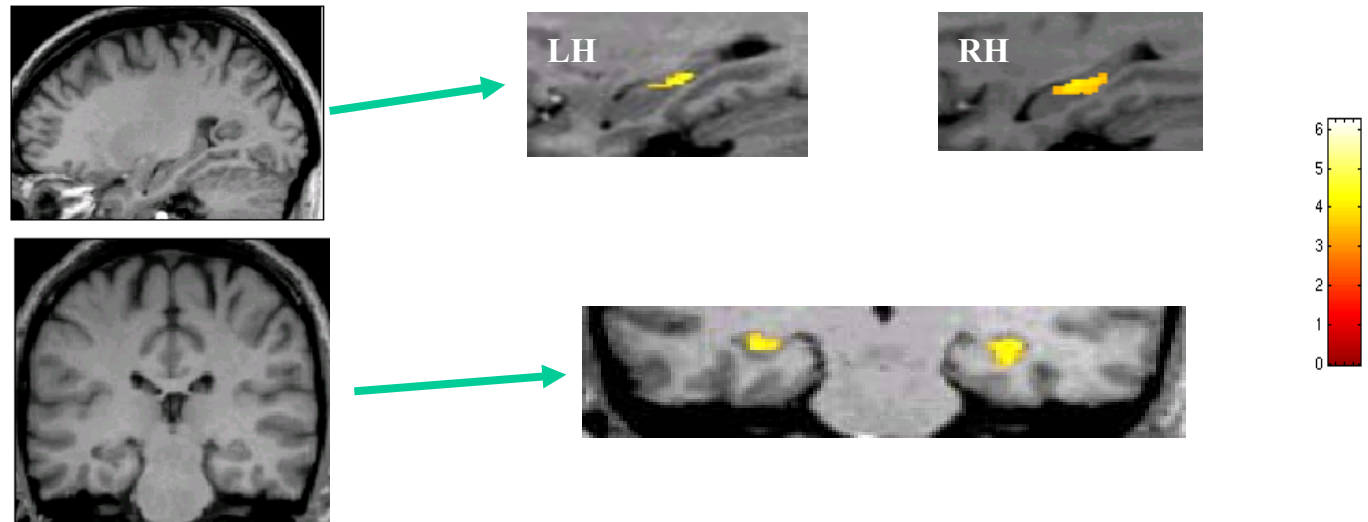


# Hippocampal Activation in Map-Based navigation



*Maguire, Burgess, Donnett, Frackowiak, Frith, & O'Keefe. Science 1998*

# Posterior Hippocampus is LARGER in taxicab drivers and increases with experience



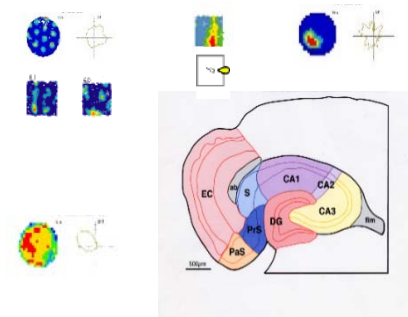
*Maguire et al. (2000) PNAS*

# Summary

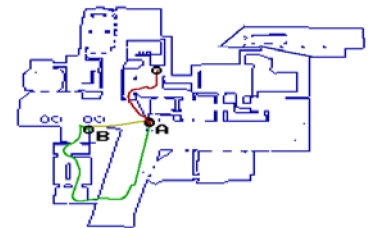
The Hippocampal Formation provides a cognitive map of a familiar environment which can be used to identify the animal's current location and to navigate from one place to another.



The Mapping system provides 2 independent strategies for locating places, one based on environmental landmarks and the other on a path integration system which uses information about distances travelled in particular directions.



A similar spatial system exists in humans which additionally provides the basis for human episodic memory





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