Neural mechanisms of spatial memory

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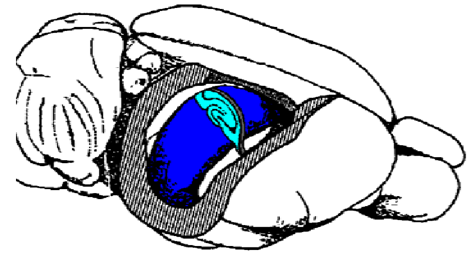
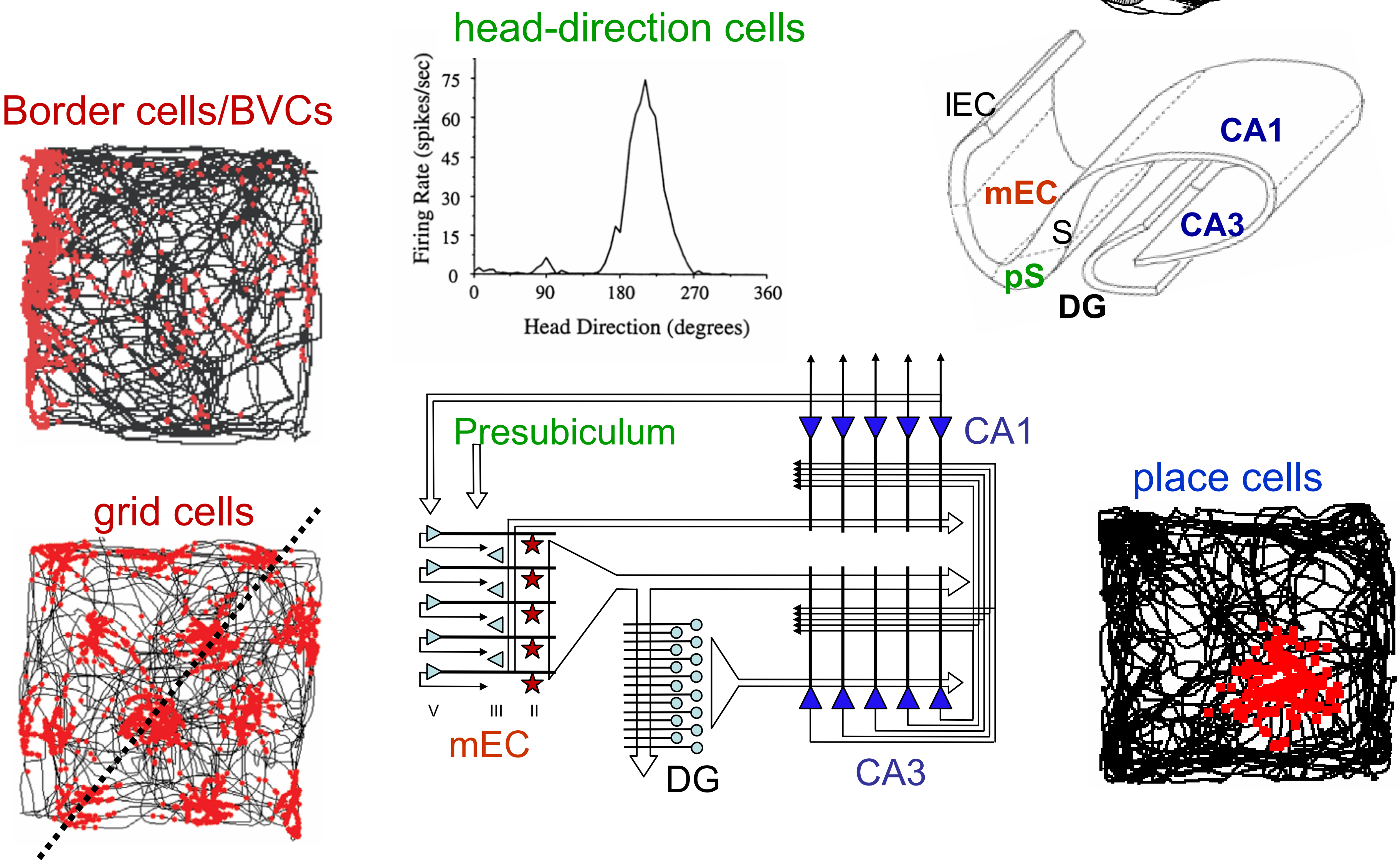
"Principles of memory"
Hippocampal dependence of memory reflects the *content* to-be-remembered, not only LTM vs STM; how 'declarative'; recollection vs familiarity etc etc.
E.g. layout vs appearance of scenes; scenes vs faces; words vs faces; known vs unknown faces.
Hartley et al *Hippocampus* 2007;
Bird and Burgess *Nat Rev Neurosci* 2008;
Bird and Burgess *Curr Biol* 2008
Trinkler et al *Hippocampus* 2009

Focus on spatial memory where we know a lot about the representations..

A neural circuit for navigation in & around the hippocampus



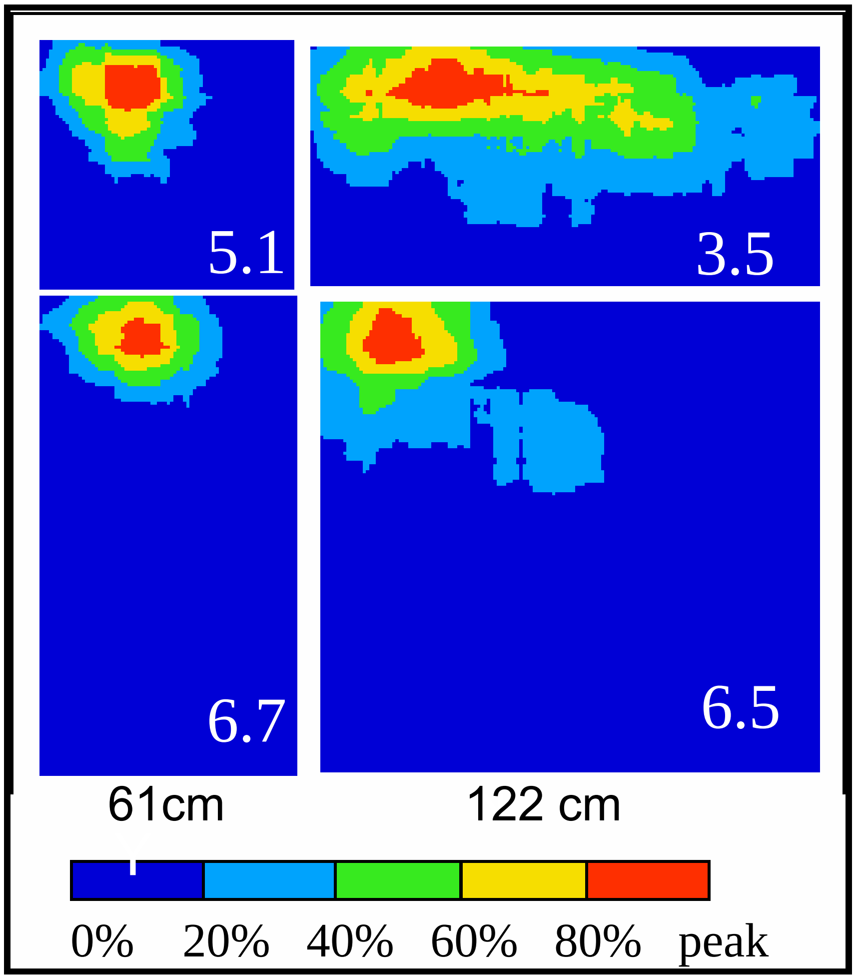


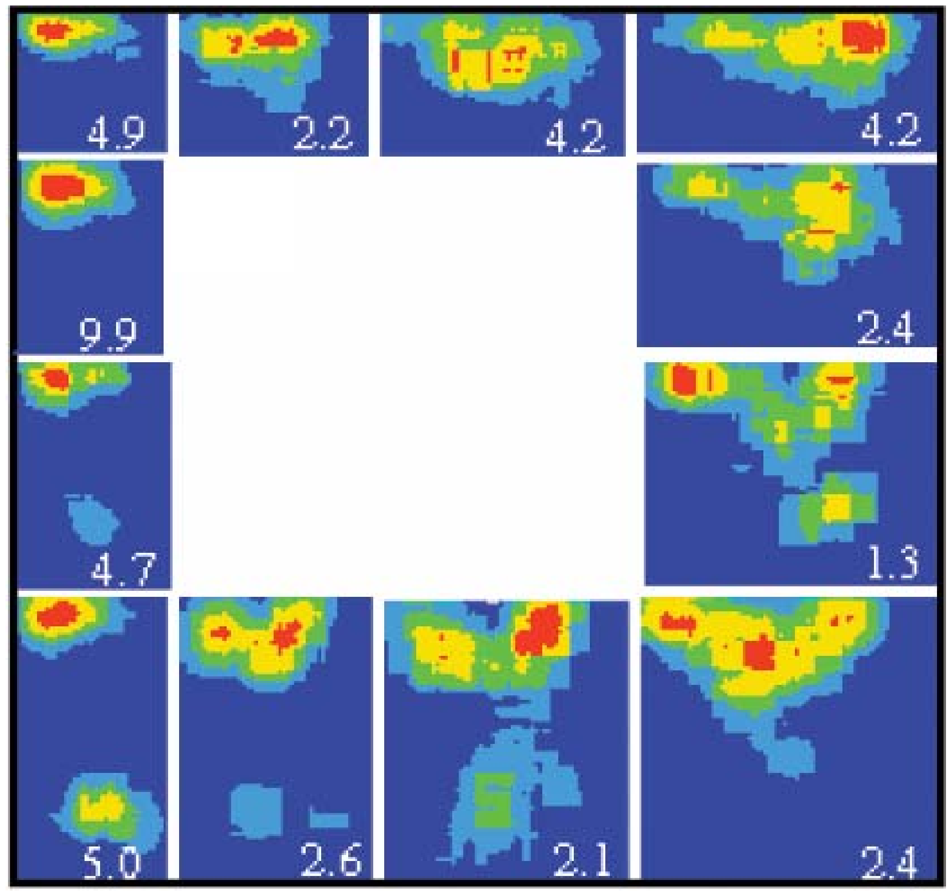
Outline

- Neural mechanisms of self-location in the rat
  - Environmental info: Boundary Vector Cells and Place Cells
  - Path Integration: Oscillatory interference and Grid Cells
  - Interaction of environment & PI, novelty and theta
- Human spatial memory
  - Hippocampo-parietal LTM, WM, imagery
  - Boundary Vector Cells/Place Cells

What are the environmental inputs to place cells?

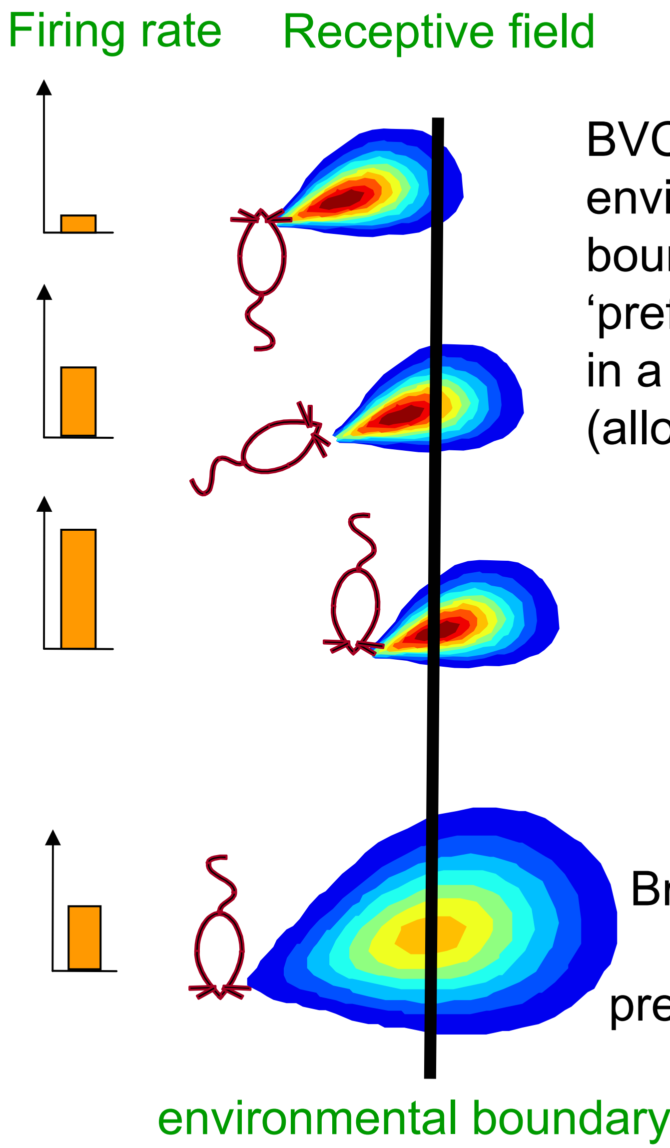
When recorded in a deformable box, place cell firing fields deform:





O'Keefe & Burgess, Nature (1996)

Proposed place cell inputs: “boundary vector cells” (BVCs)

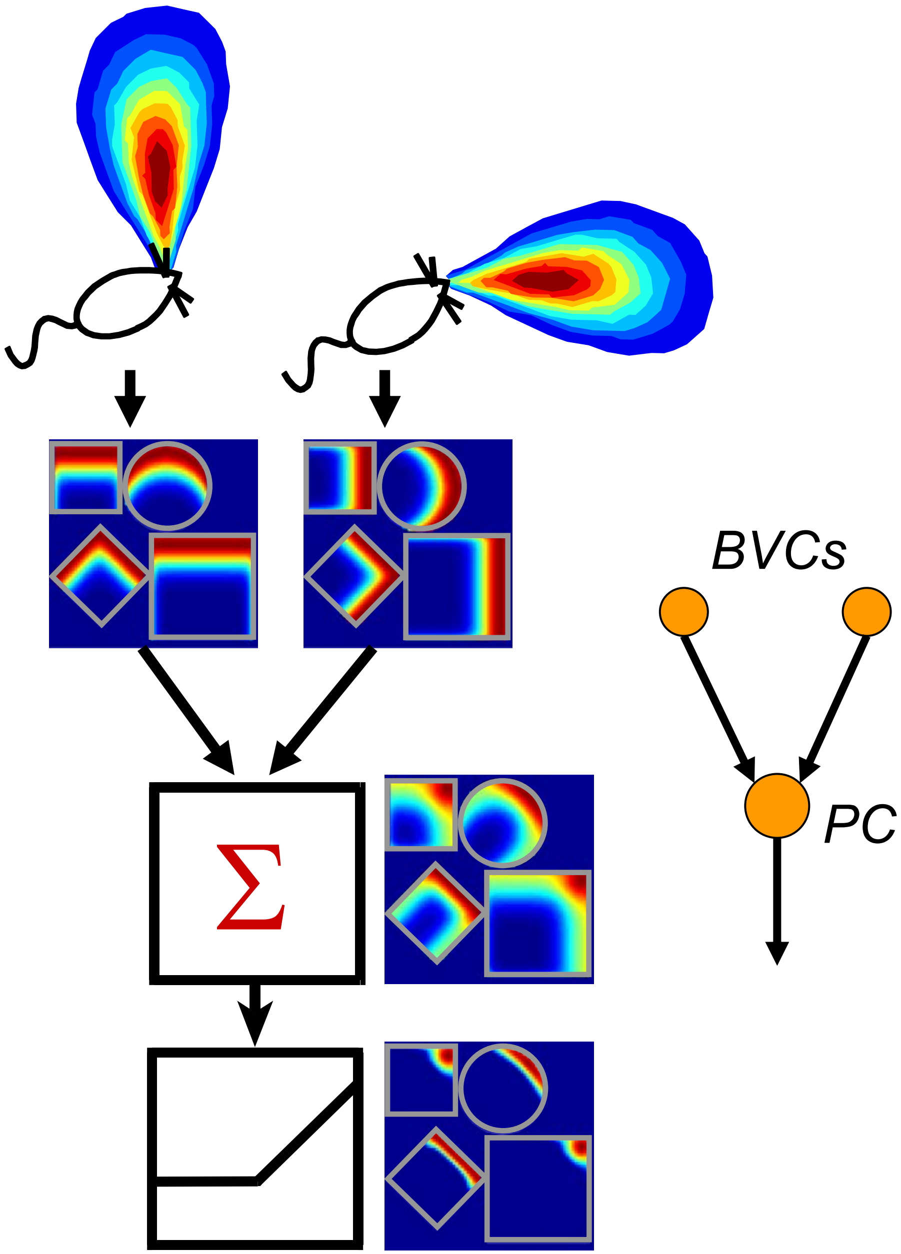


BVC responds to an environmental boundary at a ‘preferred’ distance in a ‘preferred’ (allocentric) direction

Broader tuning to more distant preferred distances

Burgess et al., Biol. Cyb. (2000); Hartley et al., Hippocampus (2000)

Place cell firing is the thresholded sum of the firing of its BVC inputs



Random selection of BVC inputs (short ranges over-represented) => correct number, shape, size, firing rate of place fields in the 4 boxes

Hartley et al., Hippocampus (2000); Burgess et al., Biol. Cyb. (2000)

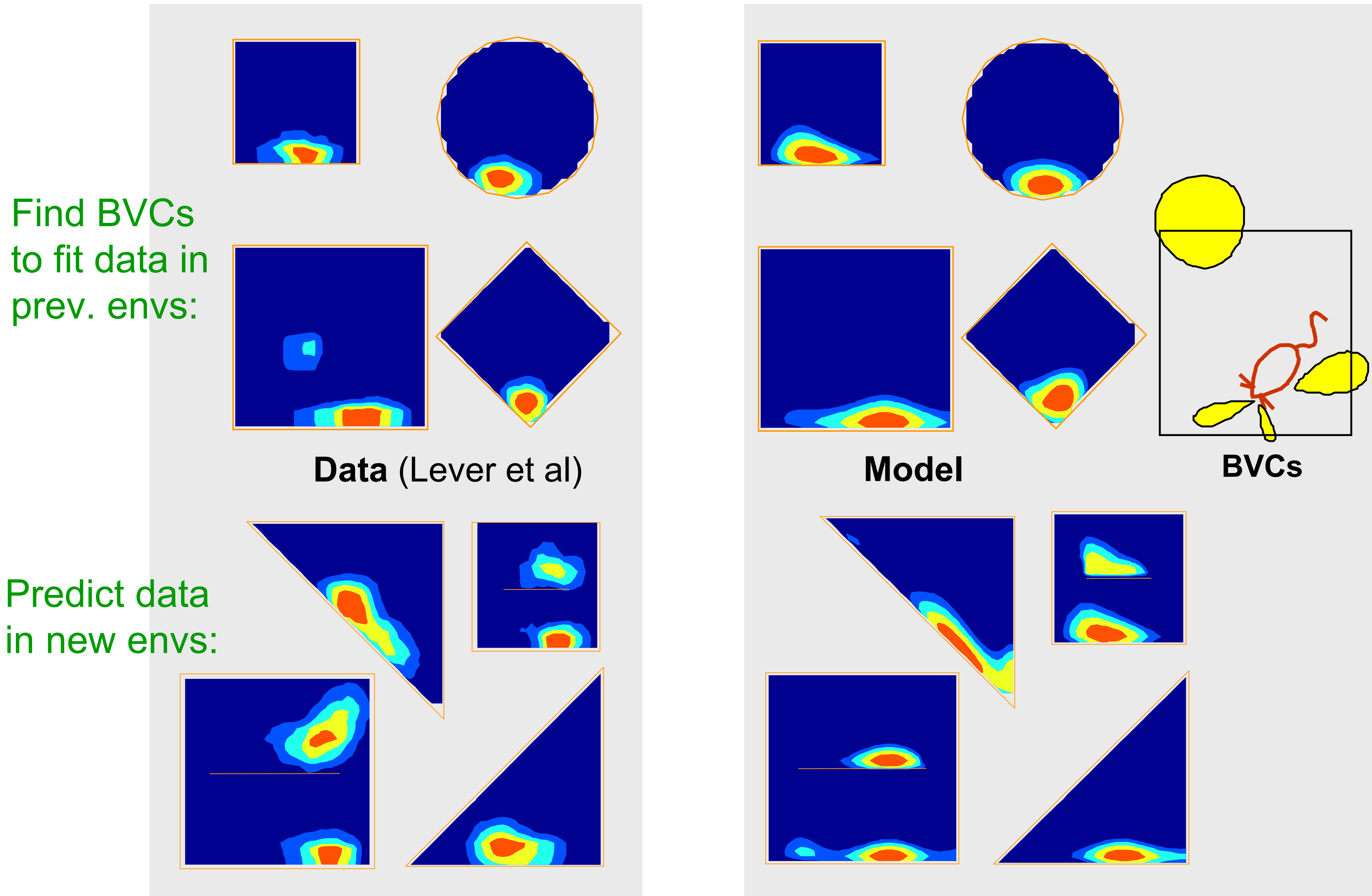
BVC model predicts human search after env. manipulations

Hartley et al Cognition (2004)

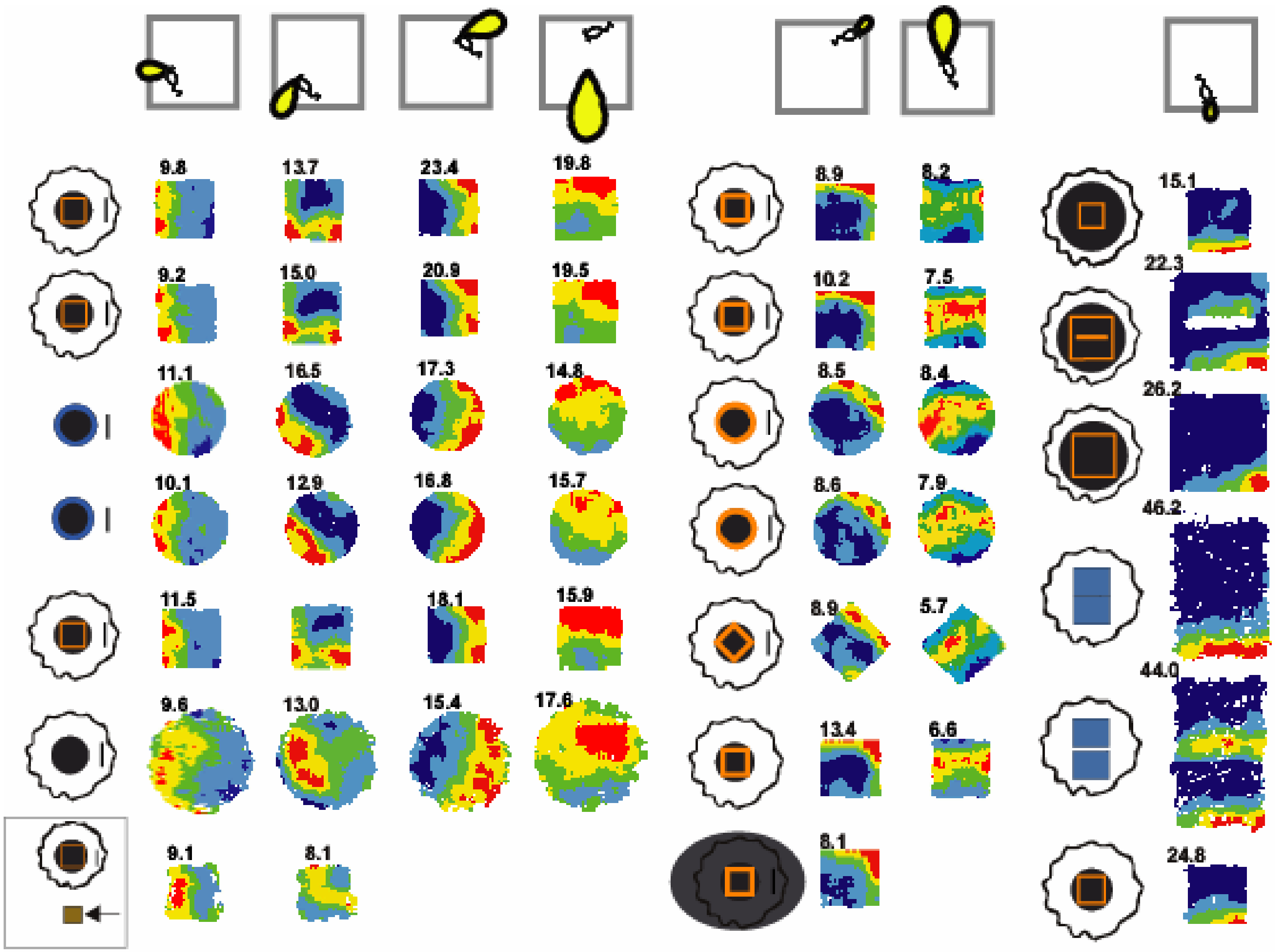
BCM learning rule => correct 'tidying up' of multiple fields.

Barry & Burgess Hippocampus (2007)

Place cell firing in new environments predicted from that in previous environments



BVCs subsequently found in entorhinal cortex & subiculum



Barry et al., 2006; Solstad et al., (2008); Savelli et al., (2008); Lever et al., in prep.

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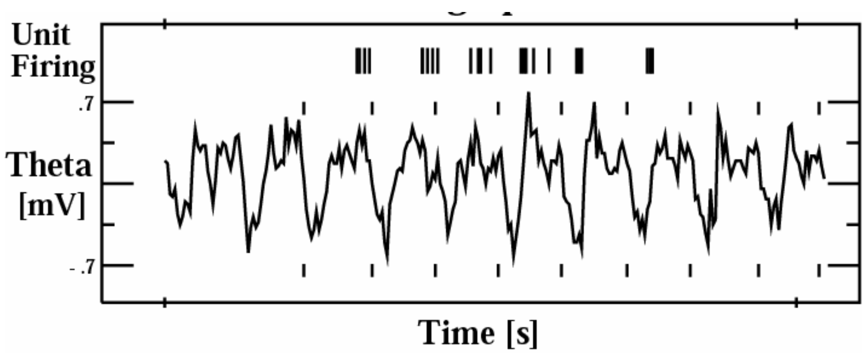
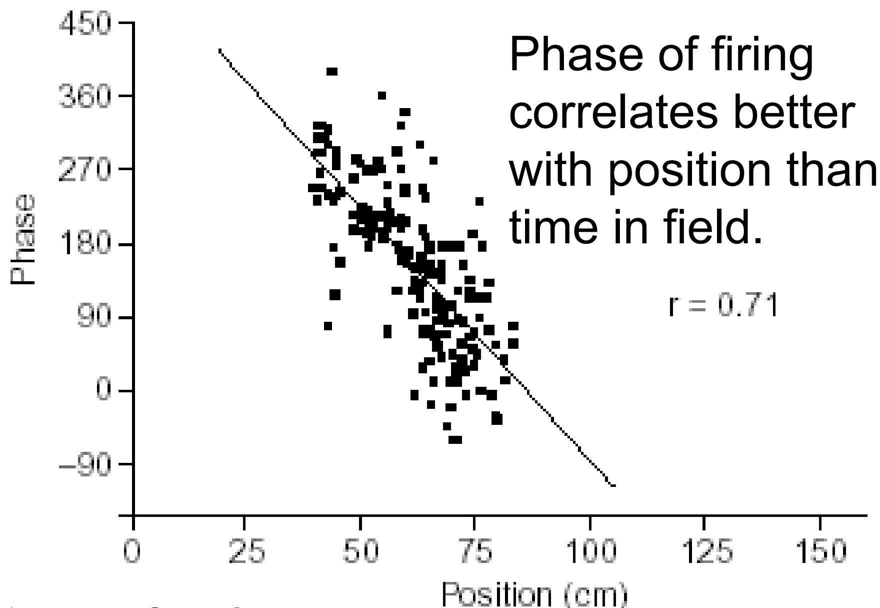
Temporal coding: theta-phase ‘precession’ of place cell firing

firing shifts from *late* to *early* phase
as rat runs through the place field:



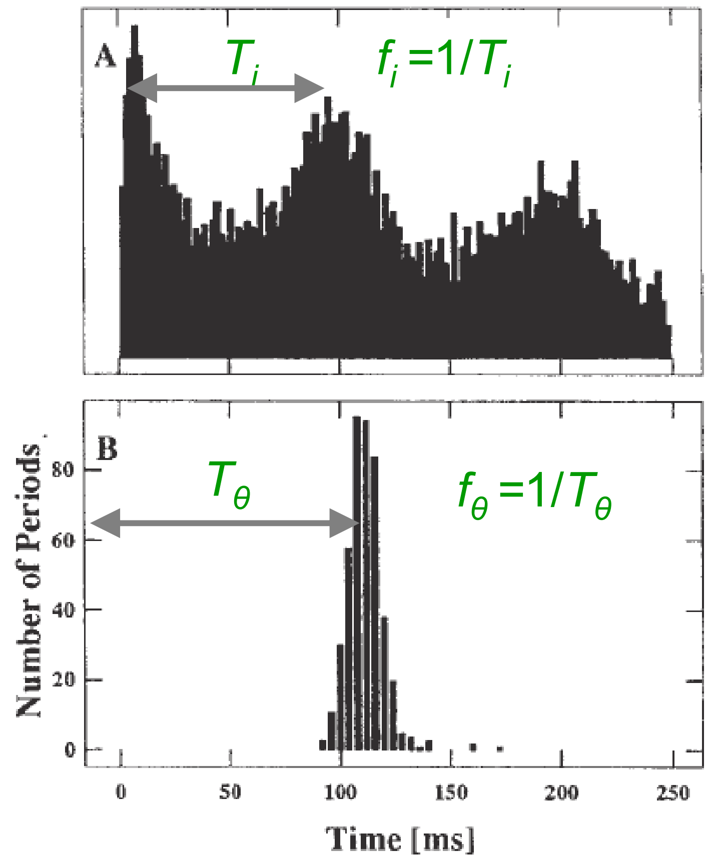


Phase of firing correlates better with position than time in field.

‘place field’

Firing rate:

Intrinsic firing frequency f_i exceeds theta frequency f_θ



O’Keefe & Recce, Hippocampus, 1993

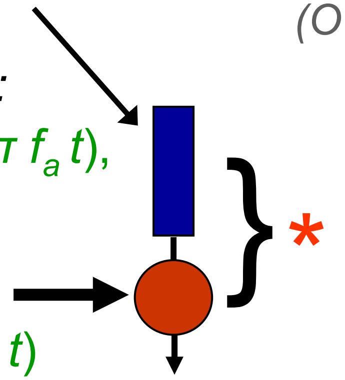
Oscillatory interference model of phase precession

input ~ running speed s   from 'speed cell' *(O'Keefe et al., 1998)*

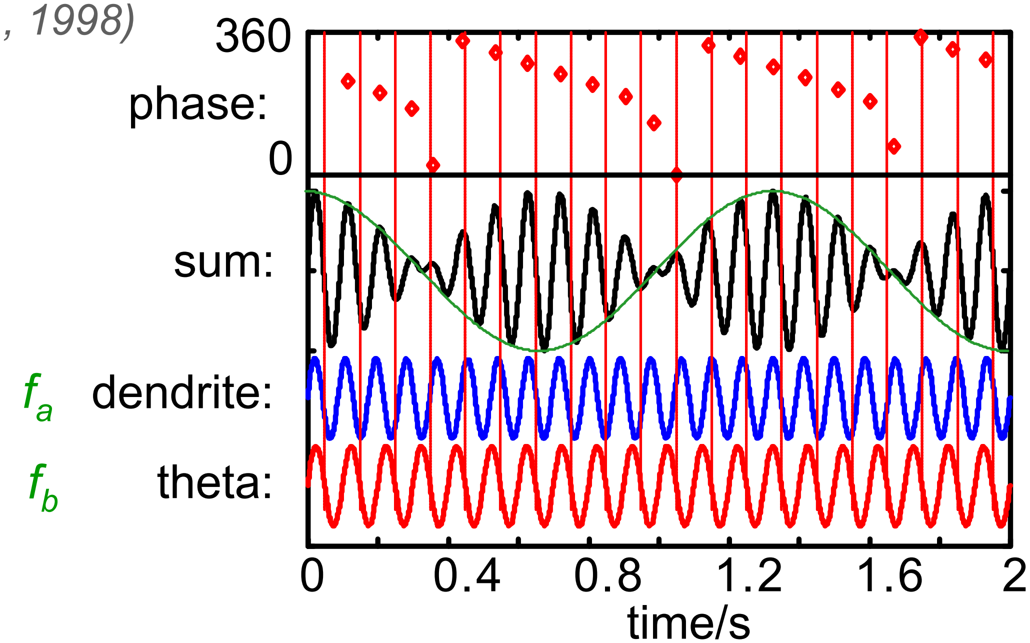
V Con MPO:

$v_a = \cos(2\pi f_a t)$,
$f_a = f_b + \beta s$

theta rhythm
$v_b = \cos(2\pi f_b t)$



$f = \Theta(v_a + v_b)$



* amplitude of interference pattern ~ phase difference

$= \int 2\pi(f_a - f_b)dt$

$= 2\pi\beta \int s(t)\, dt$

$= 2\pi\beta$ x distance travelled

Phase of "speed-controlled oscillator" integrates speed to give distance

But place cells have single firing field & distance ≠ position..

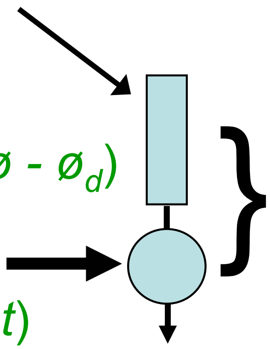
O'Keefe & Recce, 1993; Lengyel et al., 2003; Geisler et al., 2007; Burgess et al 2007.

Velocity controlled oscillators could integrate velocity to give distance travelled in a ‘preferred’ direction

Head-direction cell,
preferred direction $\varnothing_d$
$s\cos(\varnothing - \varnothing_d)$

s = speed
$\varnothing$ = heading

$v_a = \cos(2\pi f_a t)$
$f_a = f_b + \beta s \cos(\varnothing - \varnothing_d)$



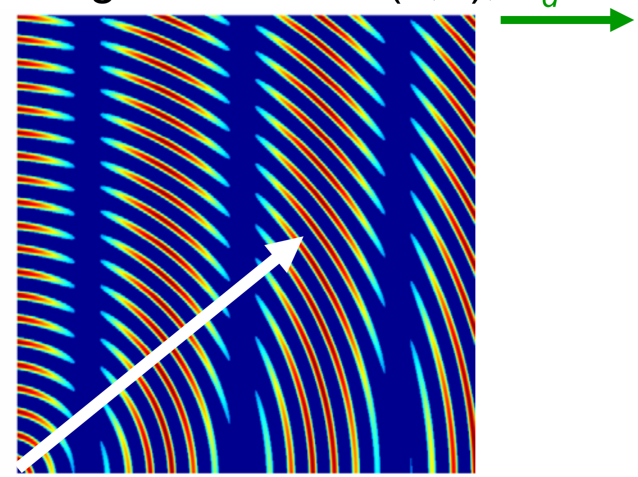
phase difference ~ distance travelled in preferred direction $\varnothing_d$

theta rhythm
$v_b = \cos(2\pi f_b t)$

$f = \Theta(v_a + v_b)$

β *sets spatial scale*

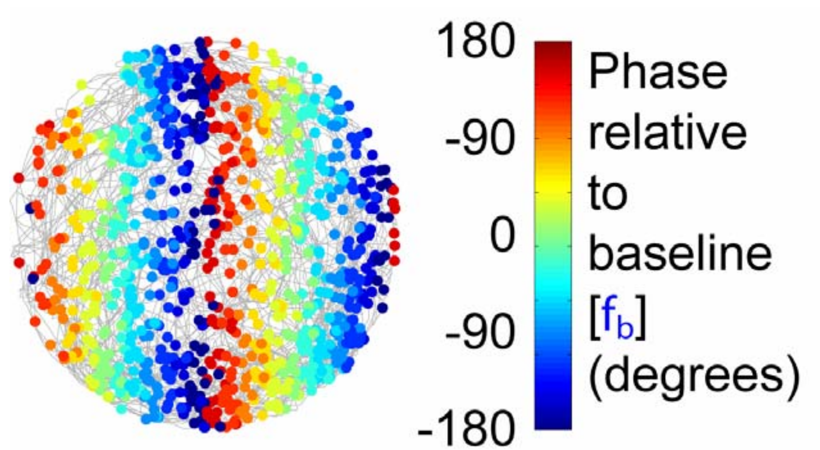
Straight runs from (0,0), $\varnothing_d$=0



MPO interference

Burgess, Barry, O’Keefe, 2007

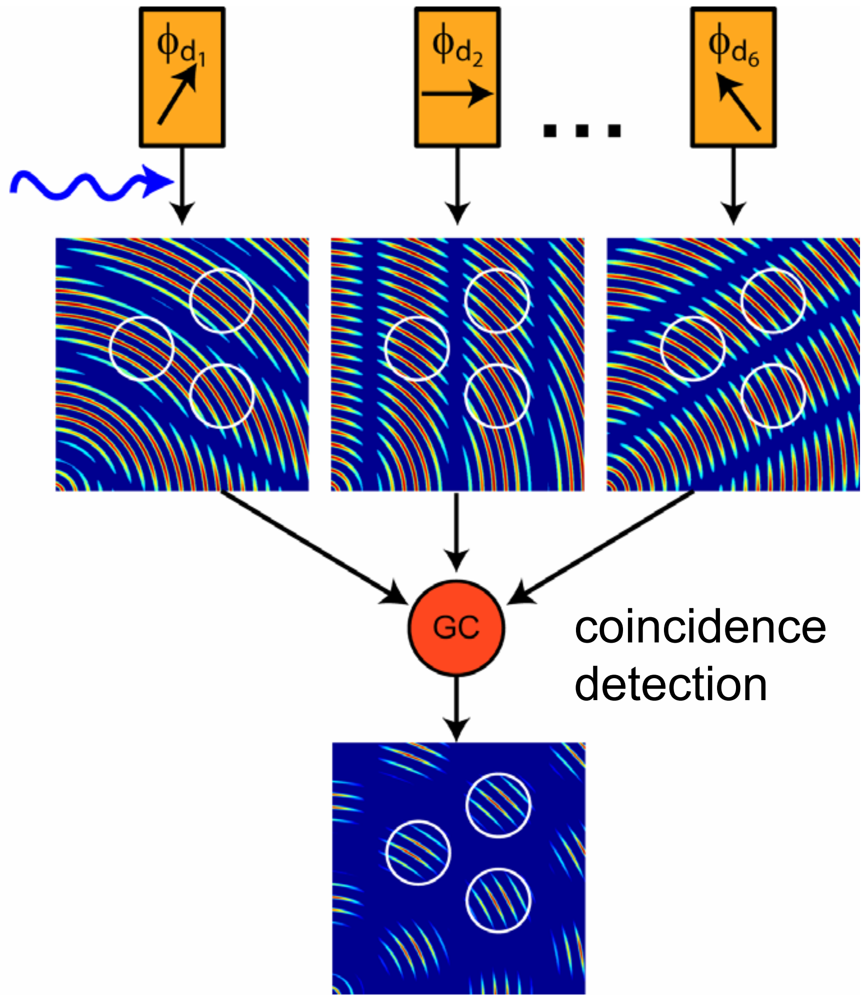
‘Velocity controlled oscillator’
could be dendritic MPO,
or firing of another neuron:



Burgess, Hippocampus, 2008
see also Hasselmo, 2008

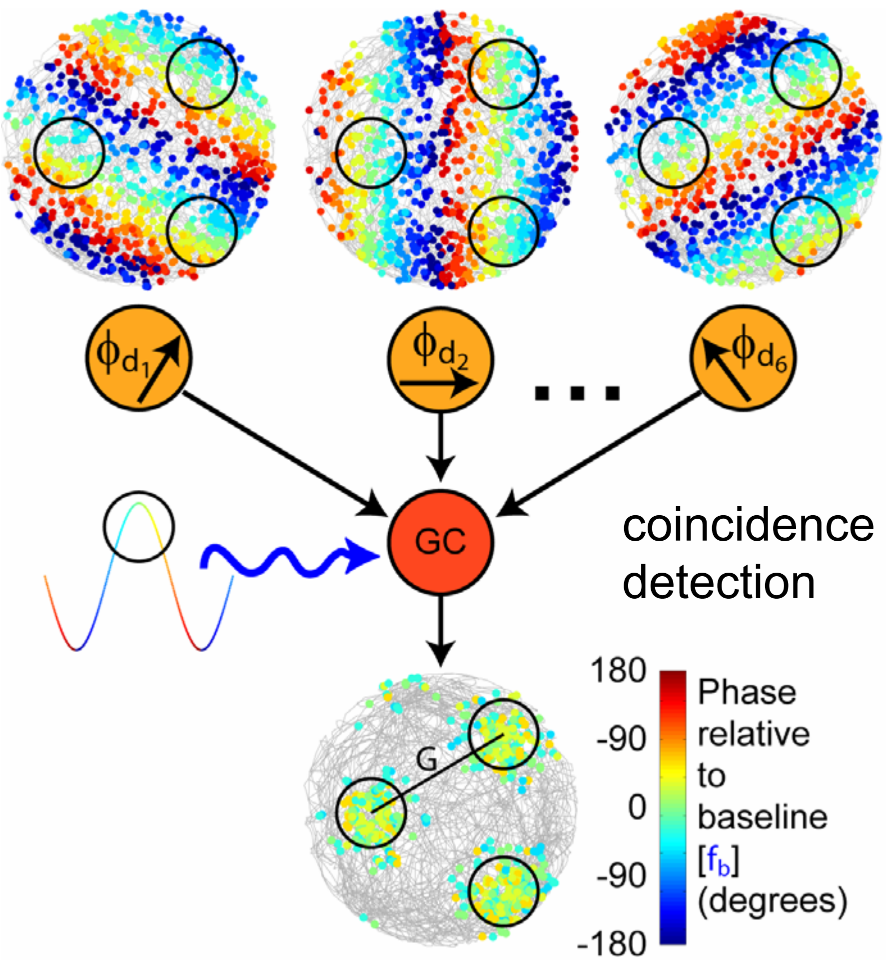
Multiple velocity controlled oscillators combine to form grids

multiple dendritic oscillators..



Burgess, et al., Hippocampus, 2007

..or neuronal oscillators..



Burgess, Hippocampus, 2008
see also Hasselmo, 2008

Implementation & predictions

Basic eqn:

$$f_a(t) = f_b(t) + \beta s(t)\cos(\phi(t) - \phi_d)$$

phase integrates distance in preferred direction,
β sets scale $L(\phi\text{-}\phi_d) = s(t)/|f_a(t)\text{-}f_b(t)| = 1/\beta|\cos(\phi\text{-}\phi_d)|$
$G = 2/\sqrt{3}\beta$

Implement f_a as a VCO with +ve only input:

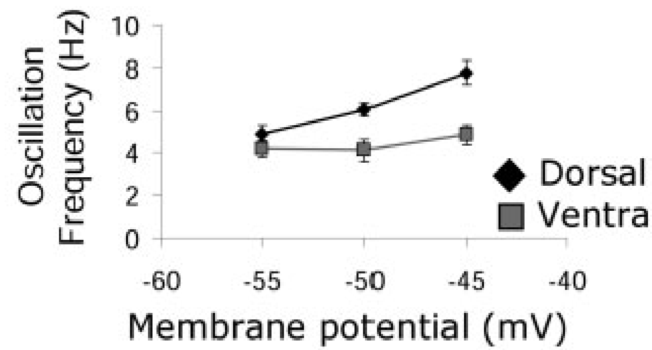
$f_a(V(t)) = f_0 + \beta V(t)$,

$V(t) = s(t)(1+\cos\{\phi(t)\text{-}\phi_d\})$

$\Rightarrow f_a(t) = f_0 + \beta s(t)(1+\cos\{\phi(t)\text{-}\phi_d\})$

Implement f_b as local average of f_a's over all preferred directions ϕ_d

$f_b(t) = \langle f_a(t)\rangle_{\phi d} = f_0 + \beta s(t)$



+ β varies dorsoventrally like $1/G$

Giocomo & Hasselmo, 2008

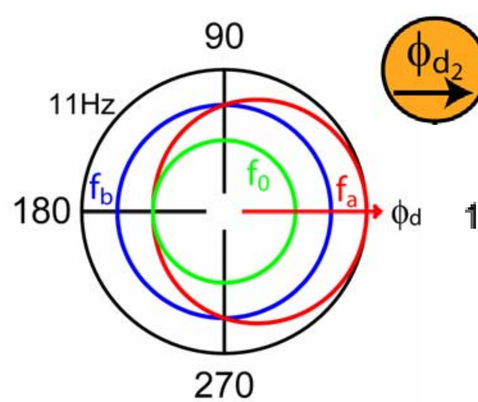
If *directionally modulated* VCO firing (layer II)
& $f_i = (f_a + f_b)/2$

$$\langle f_i(t)\rangle_{\phi(t)} = f_b(t) + \frac{\beta s(t)}{\pi} = f_0 + \frac{2(\pi+1)}{\sqrt{3}\pi G}s(t)$$

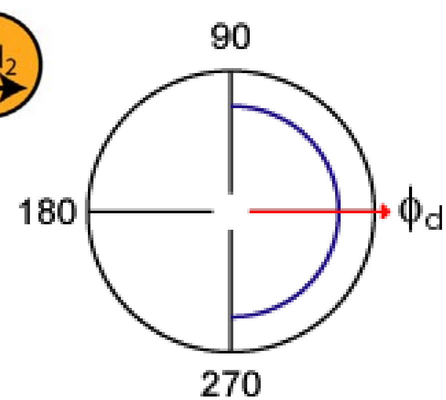
Assume f_θ is global average of f_a's or f_b's

$f_\theta(t) = \langle f_b(t)\rangle_\beta = f_0 + \langle\beta\rangle s(t)$

Burgess, Hippocampus, 2008

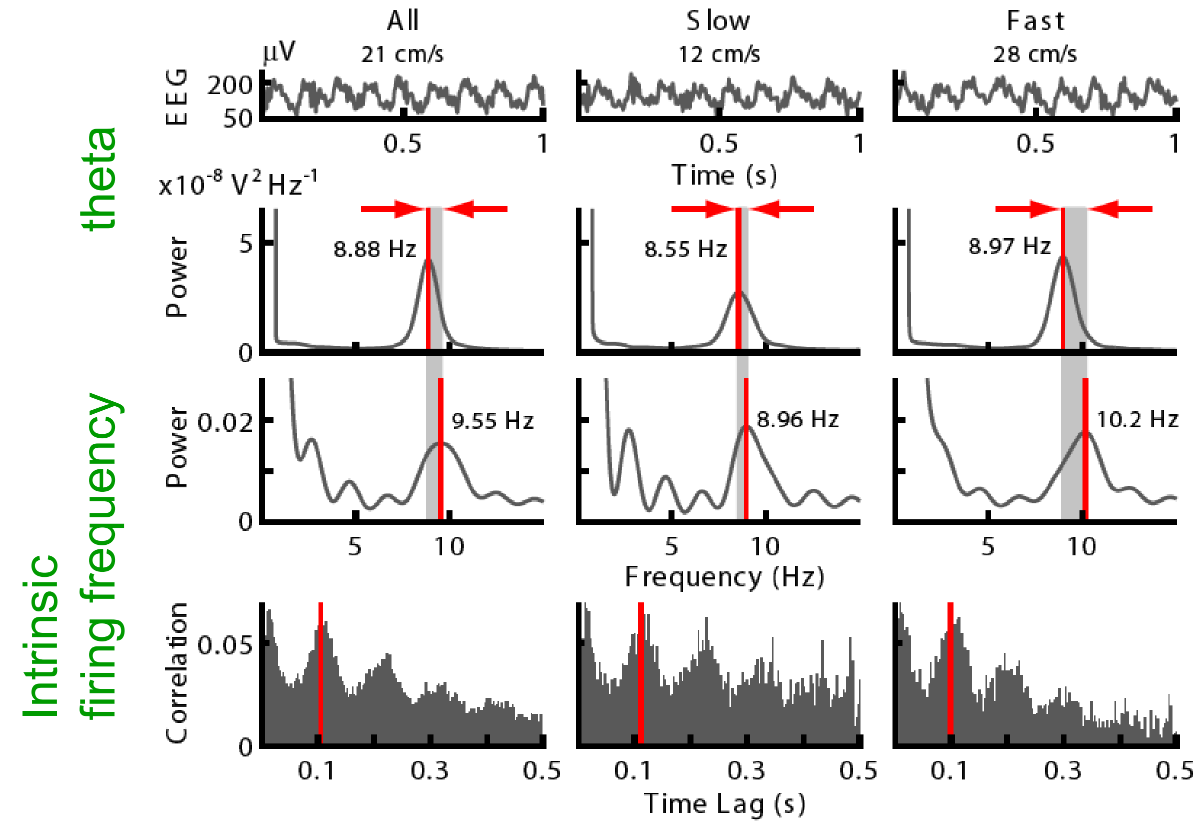


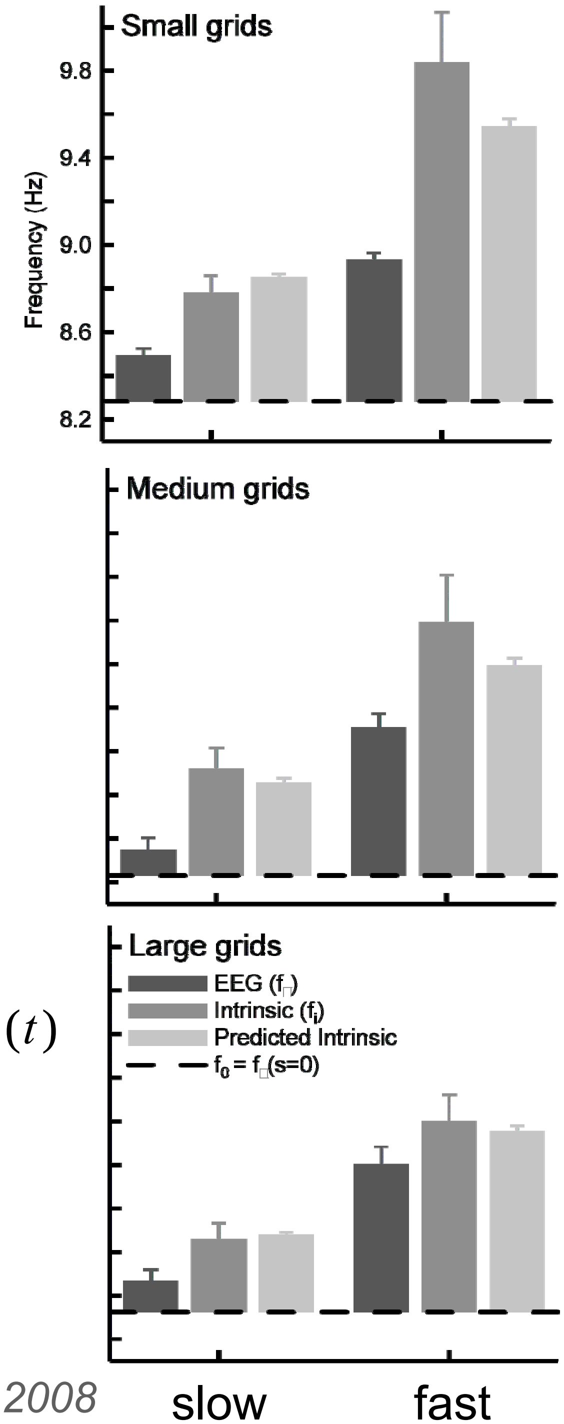
MPOs vs $\phi(t)$

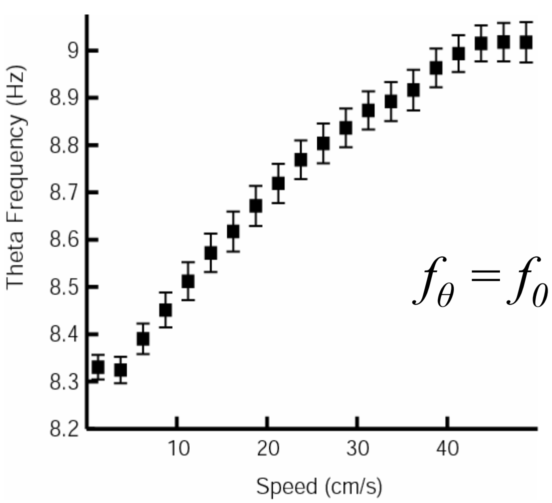


firing rate vs $\phi(t)$

Intrinsic firing frequency & theta







$$< f_i(t) >_{\phi(t)} = f_0 + \frac{2(\pi+1)}{\sqrt{3}\pi G} s(t)$$

$$f_\theta = f_0 + <\beta> s(t)$$

Jeewajee, Barry, O'Keefe, Burgess, 2008

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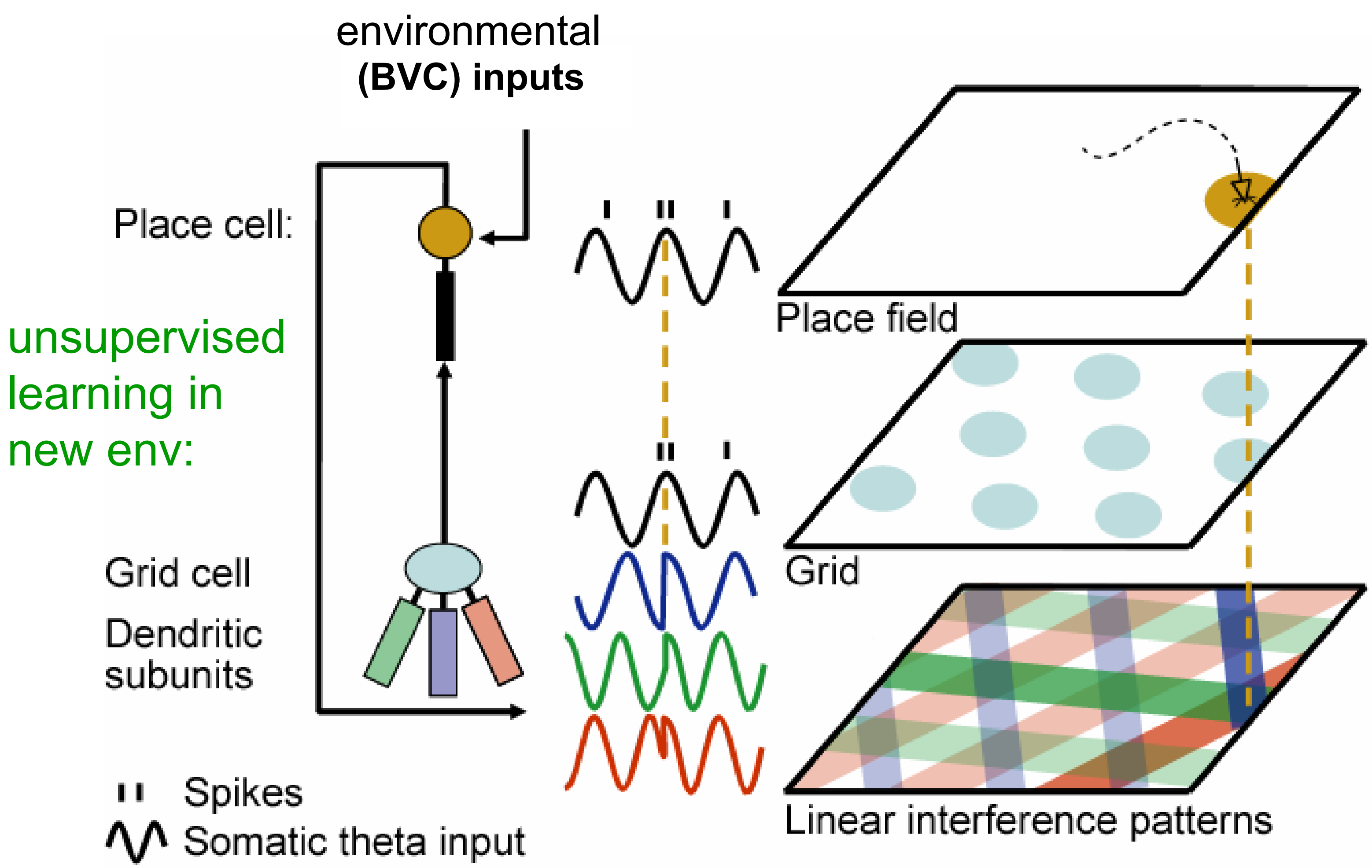
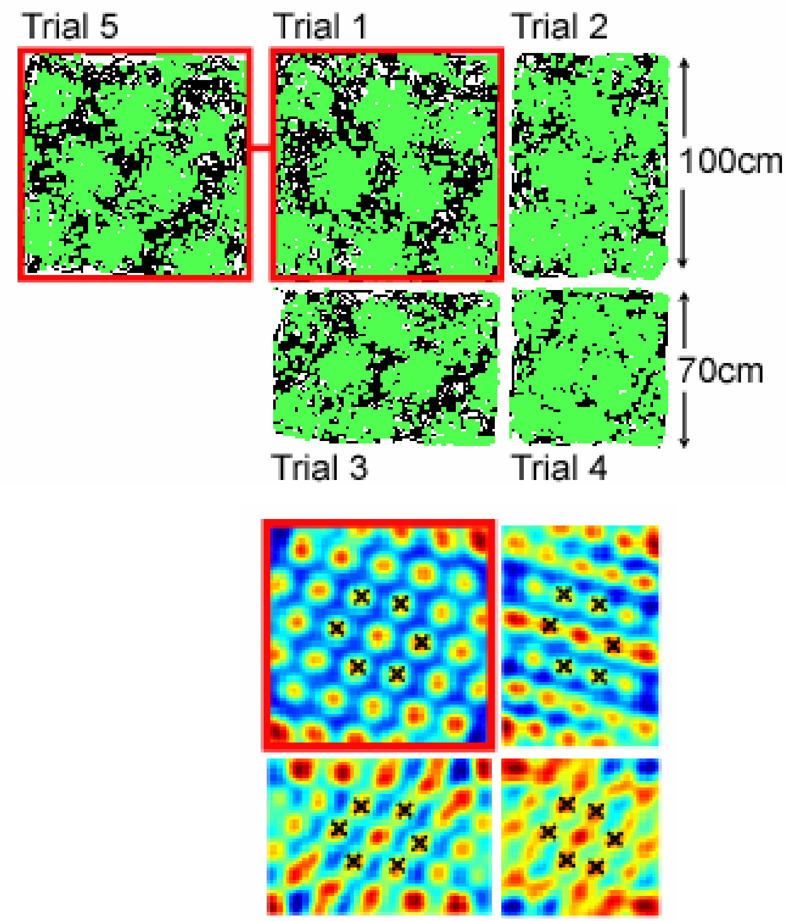
Interaction between place cells and grid cells.

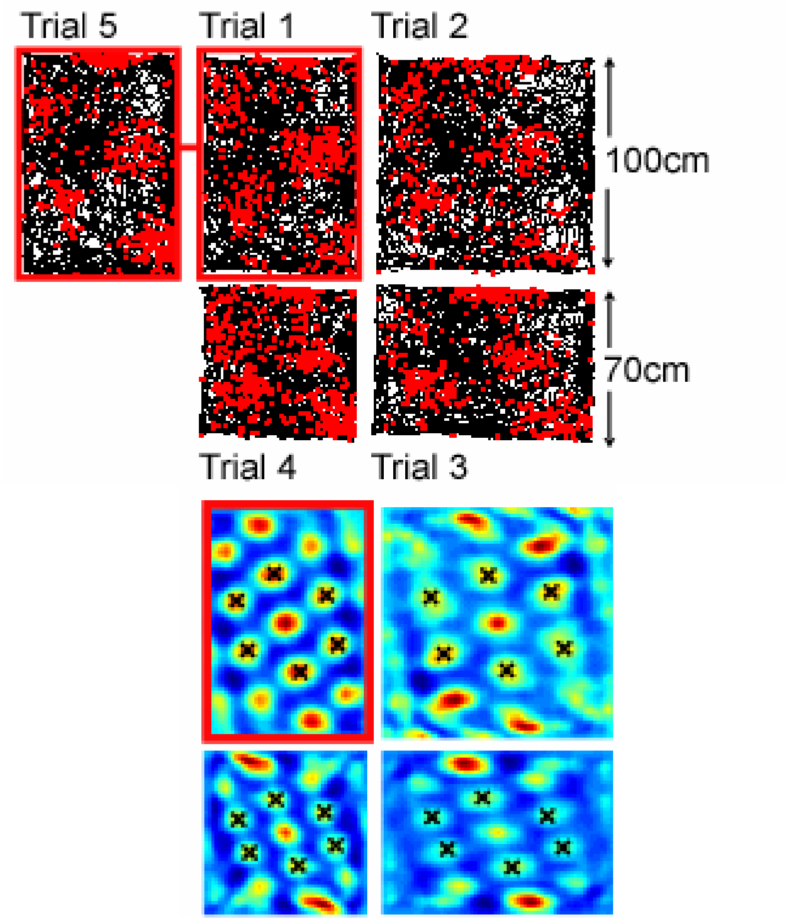
Self-location as a compromise between environmental and path integrative information.



O'Keefe & Burgess, 2005; Burgess et al, 2007

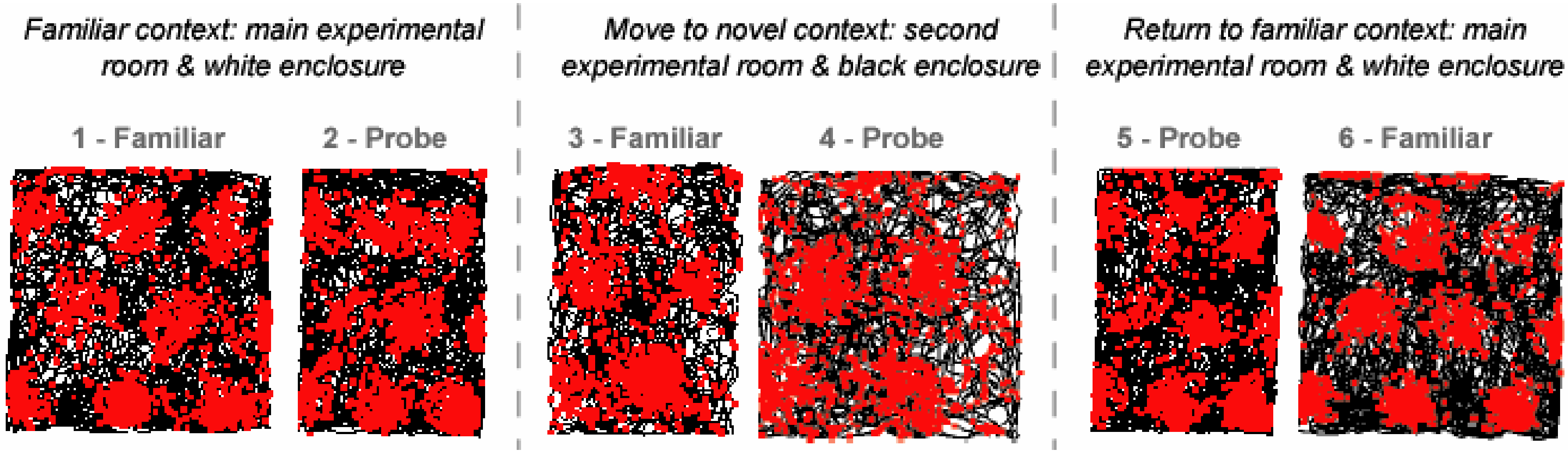
PC-GC associations => deformation of a *familiar* environment should deform grids..





Barry, Hayman, Burgess, Jeffery Nature Neurosci (2007)

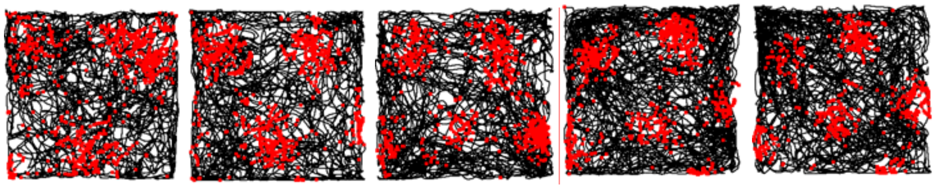
Grid rescaling depends on context & experience



Barry et al (2007) SI

Novelty => grid expansion

Barry, Jeewajee, O'Keefe, Burgess (in prep)

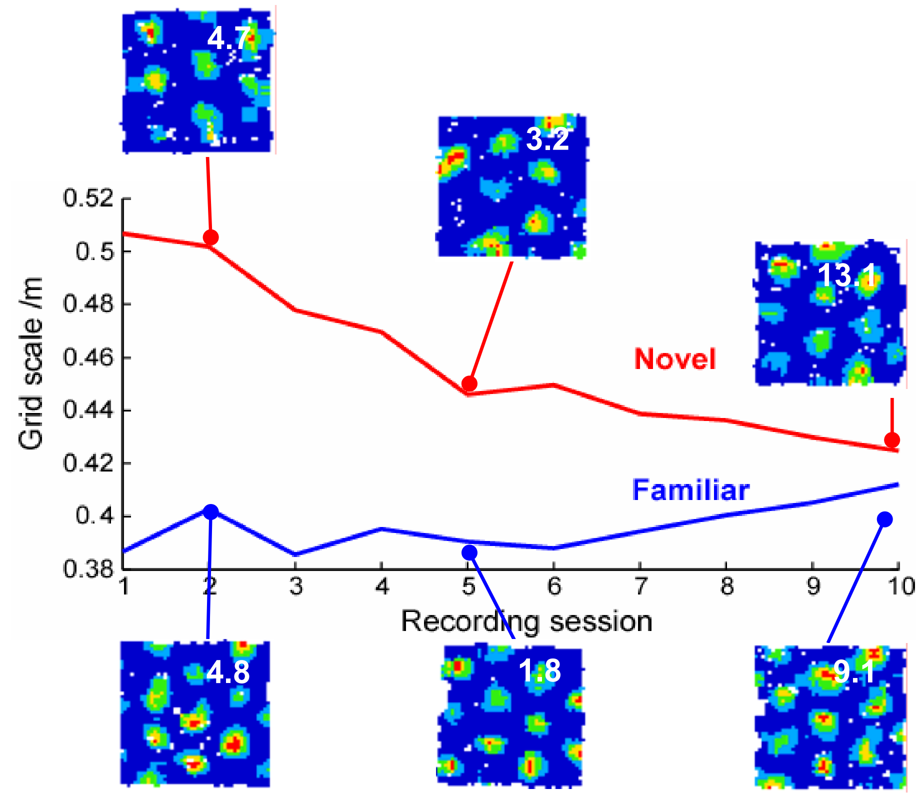


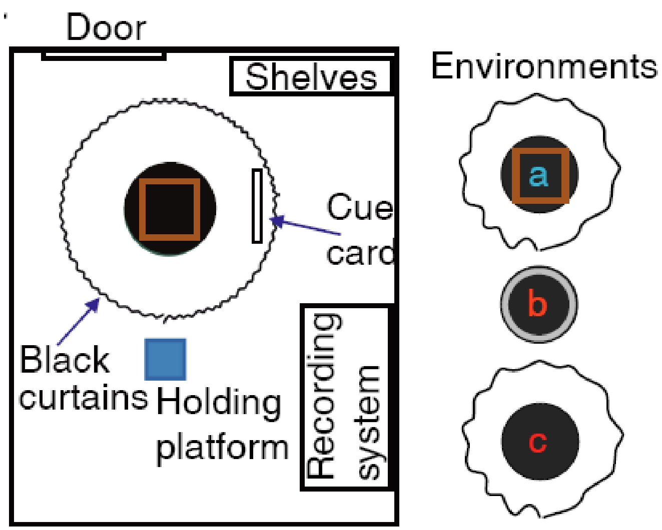
first trial per day (dark, novel)

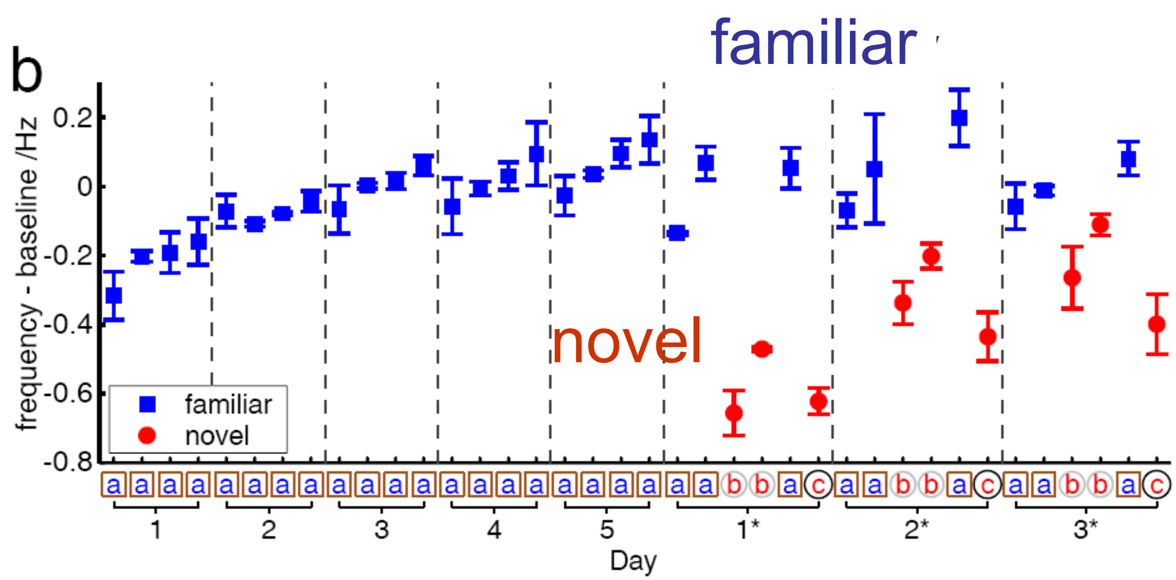
=> reduced $<\beta>$ as $\beta=2/\sqrt{3}G$

=> reduced theta frequency

as $f_\theta = f_0 + <\beta> s(t)$







Jeewajee, Lever et al (2008)

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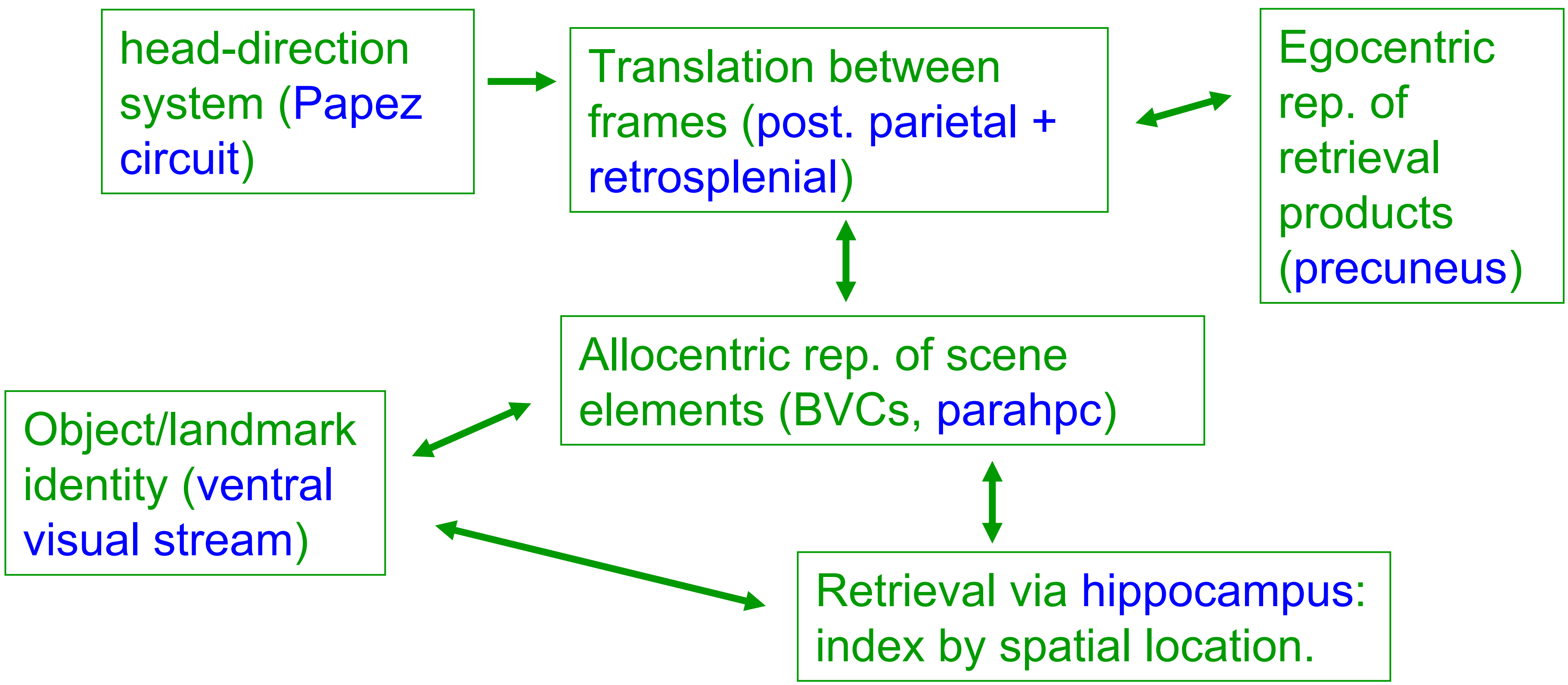
A model of memory & imagery for spatial scenes

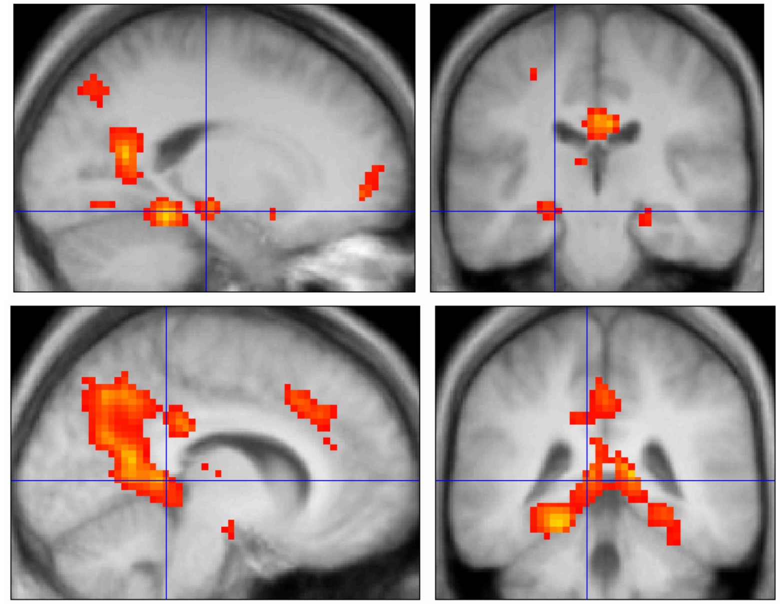
MTL *allocentric* memory interacts with (parietal) *egocentric* working memory at encoding & retrieval.

=> role of head-direction circuit in rats (Papez's circuit) in recollection (e.g. Aggelton & Brown, Gaffan)



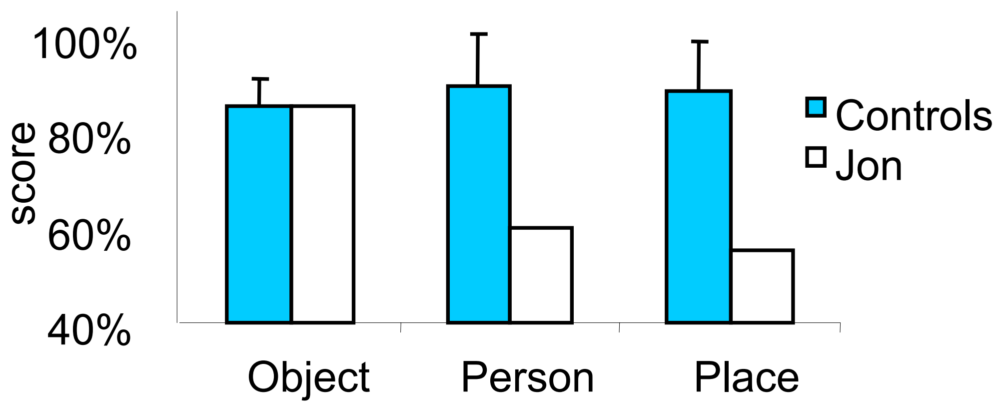
Becker & Burgess NIPS (2001) A temporoparietal model of spatial memory, imagery & neglect; Burgess et al., Phil Trans Roy Soc (2001); Byrne, Becker, Burgess, Psych Rev. (2007)

Areas activated in memory for the spatial context of an event



Burgess, Maguire, Spiers, O'Keefe, NeuroImage 2001.

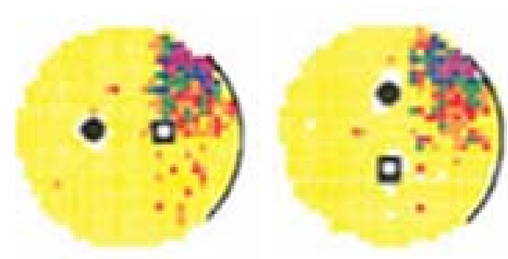
Memory for context is hippocampal dependent



King, Trinkler, Hartley, Vargha-Khadem, Burgess, Neuropsychology, 2004
Spiers et al 2001a,b

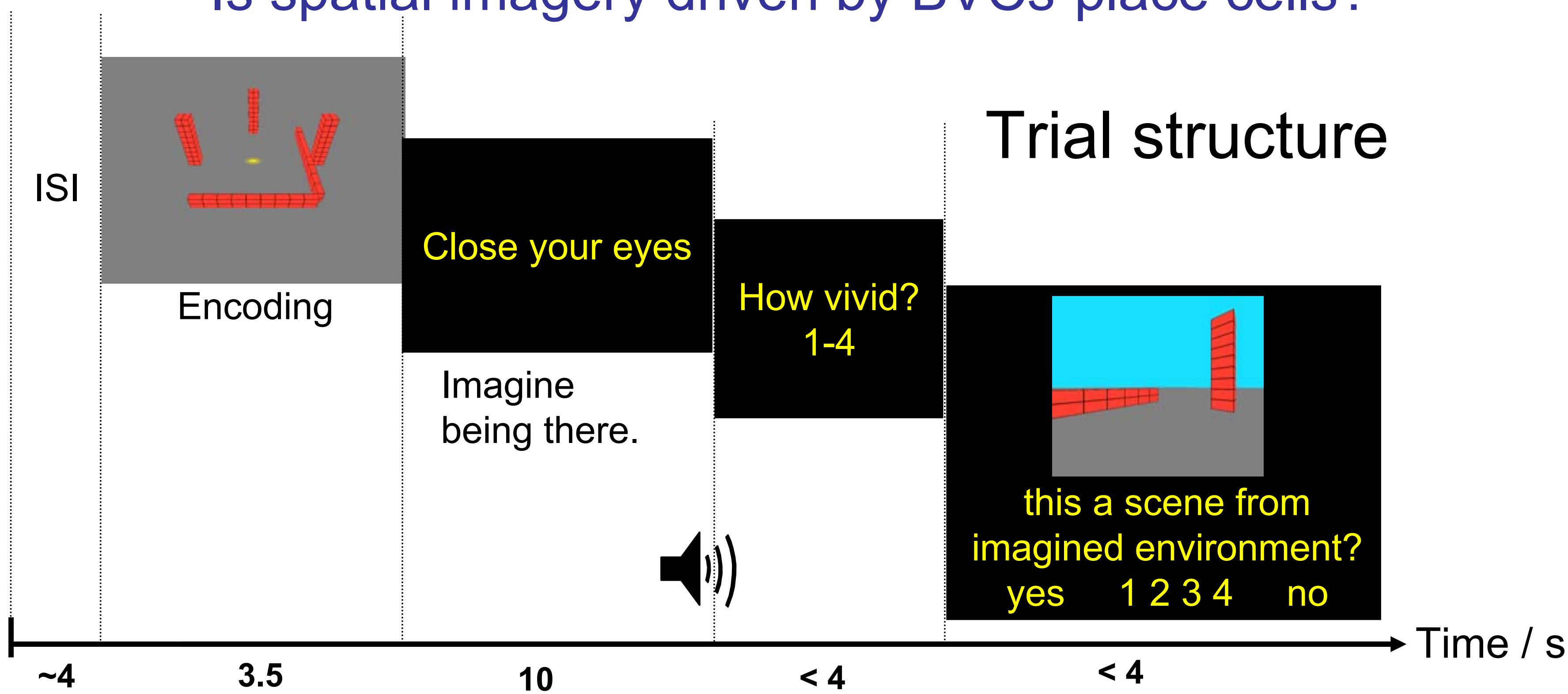
Place cells really are driven by boundaries.

Hayman & Jeffey in Barry et al., 2006

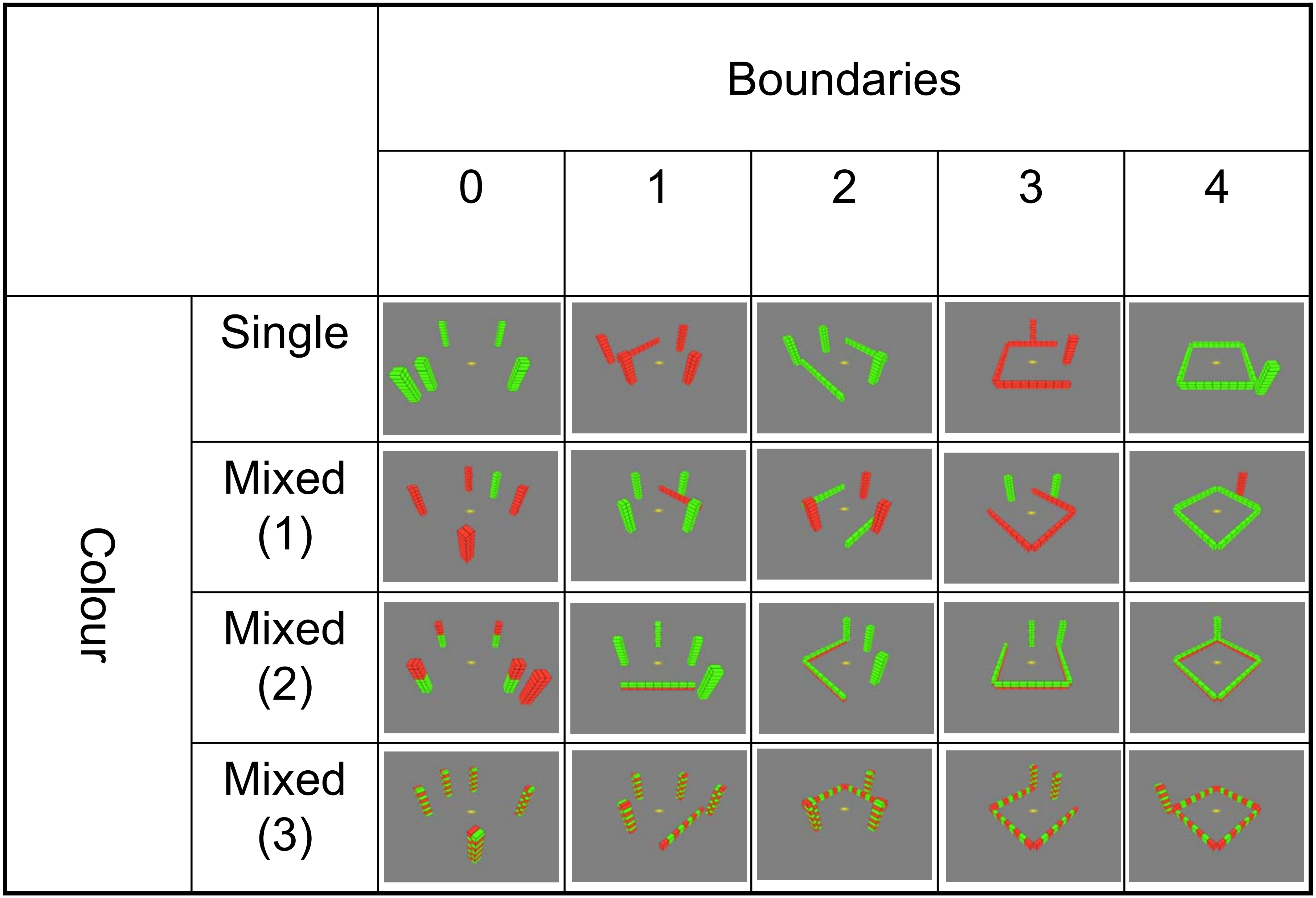


Cressant et al., 1997

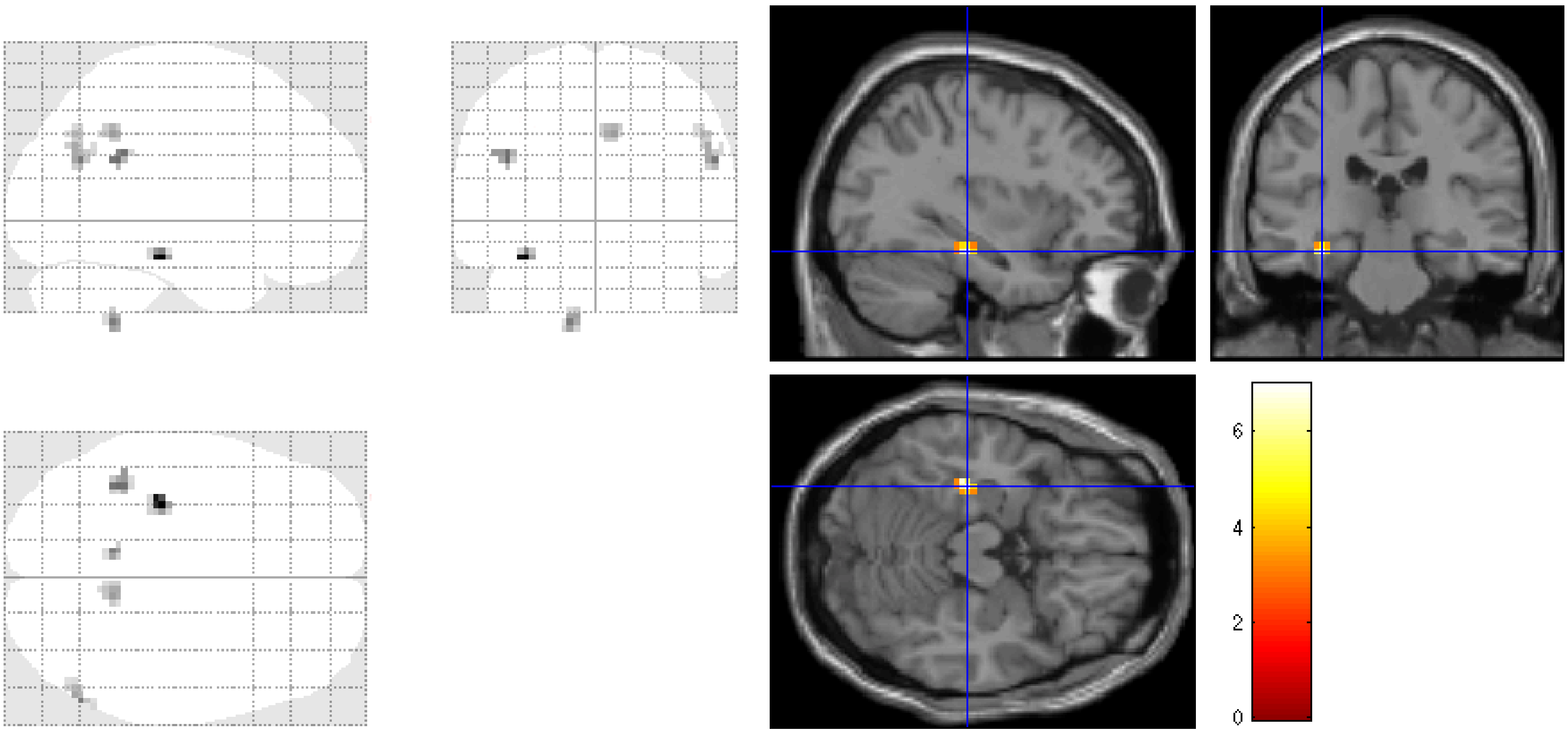
Is spatial imagery driven by BVCs-place cells?



Bird, Caponi, Doeller, Burgess, in prep.


Boundaries
0
1
2
3
4
Colour
Single
Mixed (1)
Mixed (2)
Mixed (3)

Parametric effect of number of boundaries in hippocampus during imagination phase



Bird, Caponi, Doeller, Burgess, in prep.

Conclusions

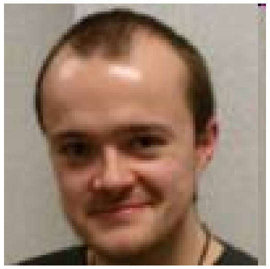
- The nature of the stored representations matters.
- We know what some of the spatial ones are, and different representations and learning rules exist in different areas.
- Self location likely a compromise between path integration (via oscillatory interference/grid cells) and environmental info (via BVCs/place cells)
- Hippocampus supports “spatial context” in imagery & retrieval = (re)activation of BVCs consistent with being in a single location

Thanks to..

VR tests & fMRI
Christian Doeller
Tom Hartley
John King

Single unit recording
Caswell Barry
Ali Jeewajee
Colin Lever
Kate Jeffery
John O'Keefe

Modelling
Caswell Barry
Ali Jeewajee
Tom Hartley
Sue Becker
Patrick Byrne



Caswell Barry

Chris Bird

Christian Doeller

Ali Jeewajee