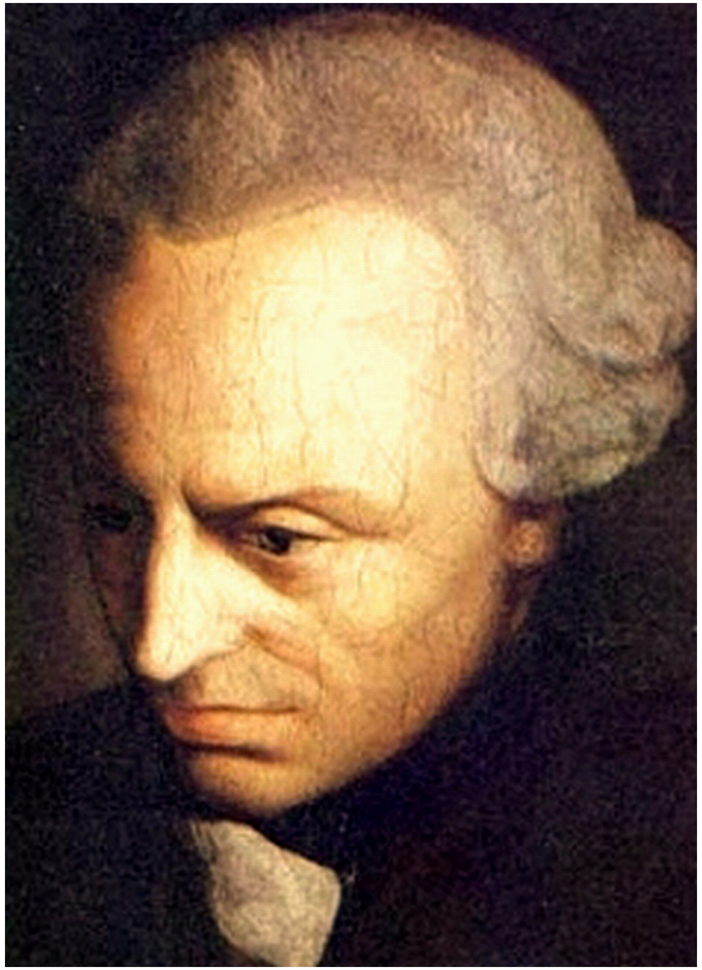
DAVID HUME



Immanuel Kant

http://plato.stanford.edu/entries/kant-spacetime/

Space is not a discursive, or as one says, general concept of relations of things in general, but a pure intuition…It follows from this that an *a priori* intuition (which is not empirical) underlies all concepts of space. Similarly, geometrical propositions, that, for instance, in a triangle two sides together are greater than the third, can never be derived from the general concepts of line and triangle, but only from intuition and indeed *a priori* with apodictic certainty.

Kant's suggestion in the passage above appears to be that intuition must somehow have its seat in the subject—it must somehow be a “form” of the mind…

OR:

“intuition” must be a group of neurons with special computational properties.

Questions about place and navigation have engaged philosophers and scientists for a long time. More than 200 years ago, the German philosopher Immanuel Kant argued that some mental abilities exist as a priori knowledge, independent of experience. He considered the concept of space as an inbuilt principle of the mind, one through which the world is and must be perceived.

In 1971, John O'Keefe (Nobel Prize 2014) discovered the first component of this positioning system. He found that a type of nerve cell in an area of the brain called the hippocampus that was always activated when a rat was at a certain place in a room. Other nerve cells were activated when the rat was at other places. O'Keefe concluded that these "place cells" formed a map of the room.

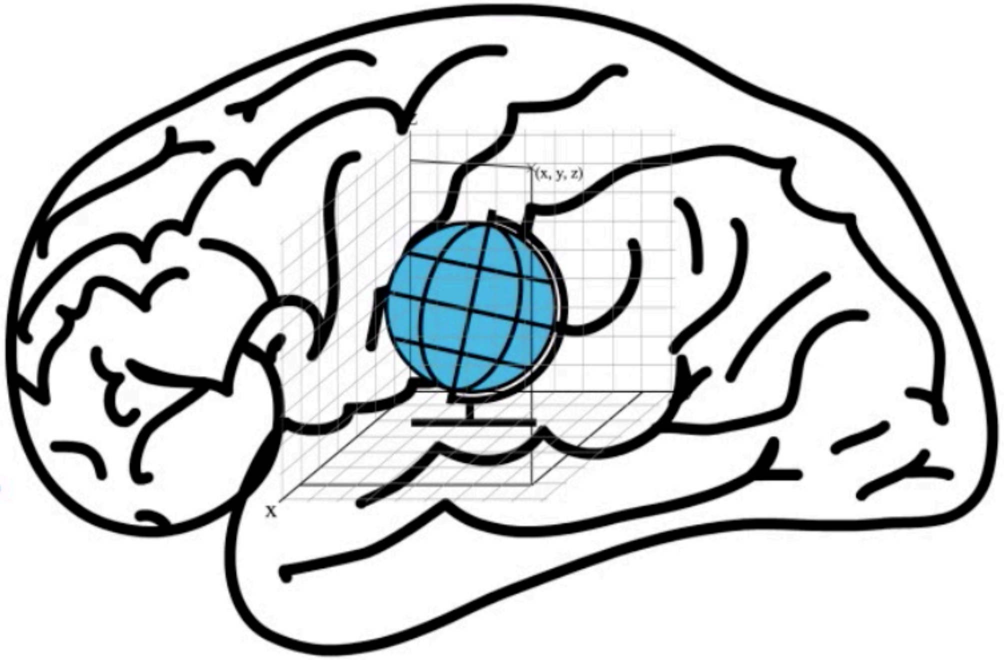
May-Britt and Edvard Moser (Nobel Prize 2014) , working at the Norwegian University of Science and Technology in Trondheim, found that these locations formed a hexagonal grid, with each "grid cell" within the entorhinal cortex reacting in a unique spatial pattern — collectively the grid cells form a pattern — collectively the grid cells form a coordinated system that allowed spatial navigation through a complex maze.

SPACE IS MERELY A FORM
OF OUR INTUITION, THAT IS,
JUST A STRUCTURE OUR OWN
MINDS IMPOSE ON TO OUR
REPRESENTATIONS, AND
SPACE IS NOT A PROPERTY
OF THINGS IN THEMSELVES.
THAT IS, IT'S NOT A PROPERTY
OF THINGS AS THEY EXIST INDEPENDENTLY
OF OUR MINDS AND OF
OUR KNOWLEDGE OF THEM.

A COMPLETELY DIFFERENT PICTURE

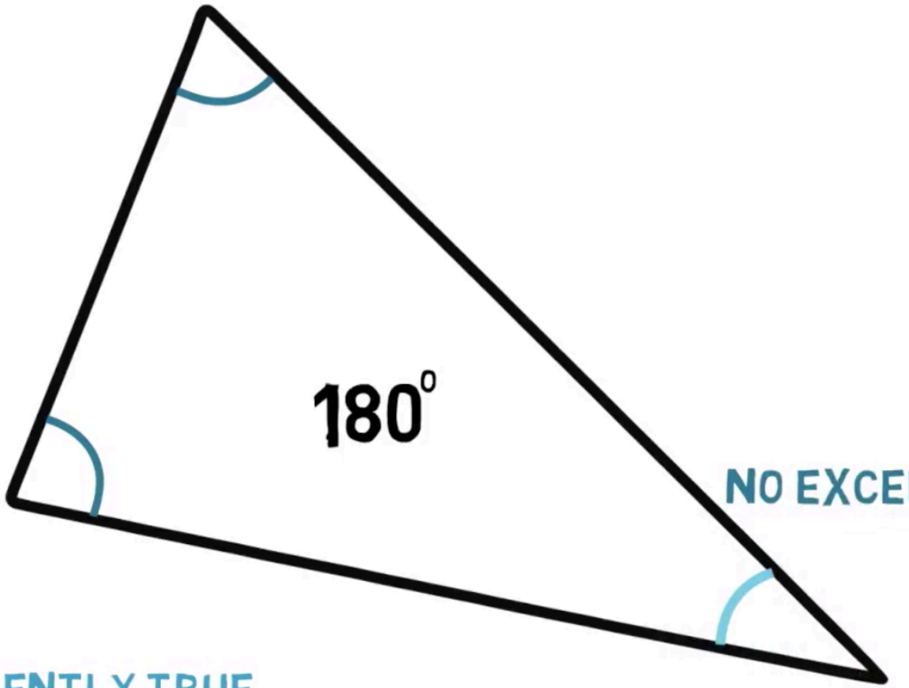
THE TRANSCENDENTAL
IDEALITY OF SPACE

TRANSCENDENTAL
IDEALISM



IMPOSES SPACIAL STRUCTURE ON TO
OUR REPRESENTATIONS OF THE WORLD

PREMISE 1: GEOMETRICAL KNOWLEDGE IS SYNTHETIC A PRIORI.

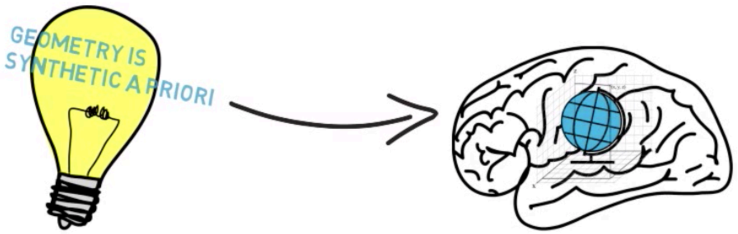


NO EXCEPTIONS

NOT CONTINGENTLY TRUE

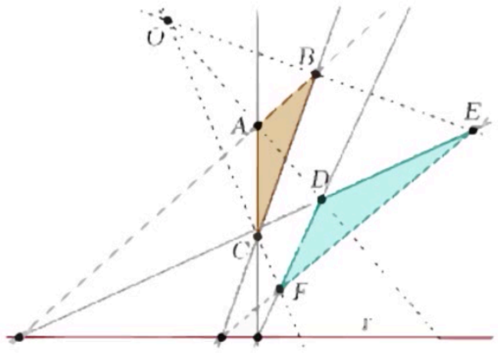
PREMISE 2:

SYNTHETIC A PRIORI KNOWLEDGE IS POSSIBLE ONLY IF SPACE IS MERELY A FORM OF OUR INTUITION AND NOT A PROPERTY OF THINGS IN THEMSELVES



WHY SHOULD WE THINK THAT PREMISE IS TRUE?

KNOWLEDGE OF GEOMETRY



SYNTHETIC A PRIORI

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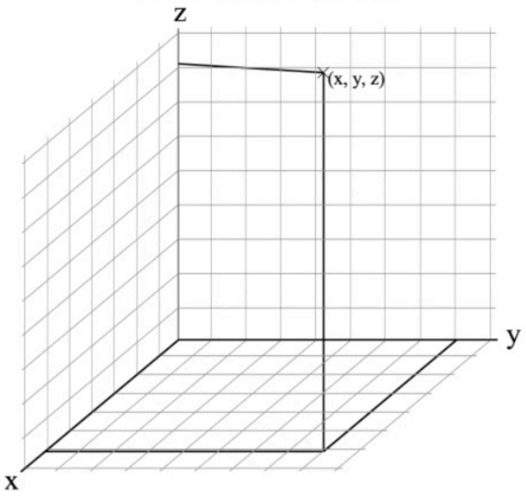
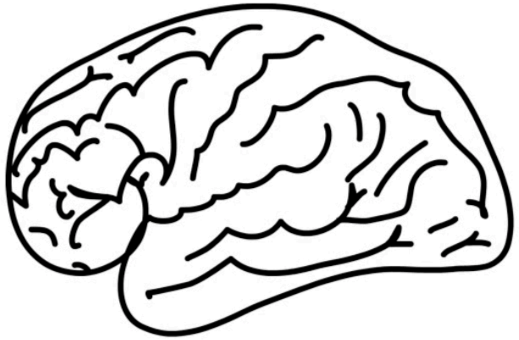
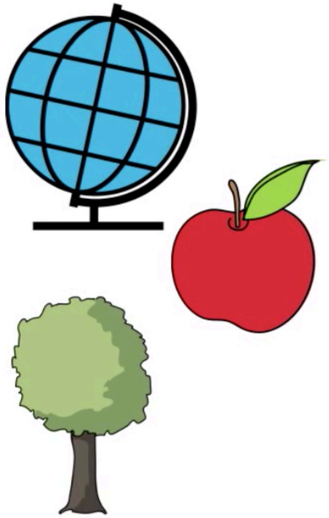
KNOWLEDGE OF SPACE



SYNTHETIC A PRIORI



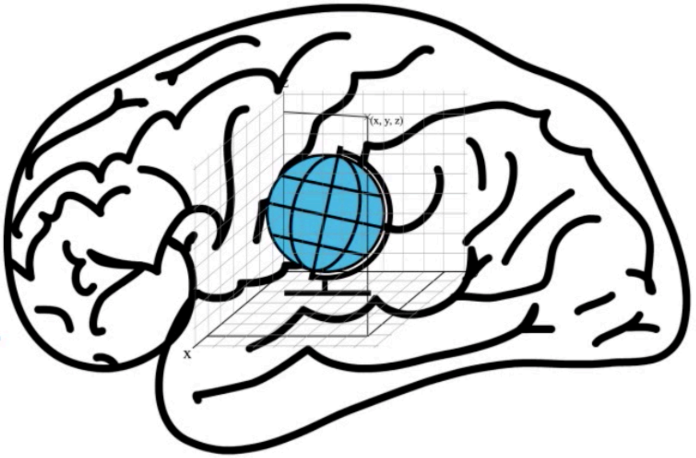
INDEPENDENT OF



A COMPLETELY DIFFERENT PICTURE

THE TRANSCENDENTAL IDEALITY OF SPACE

TRANSCENDENTAL IDEALISM



IMPOSES SPACIAL STRUCTURE ON TO OUR REPRESENTATIONS OF THE WORLD

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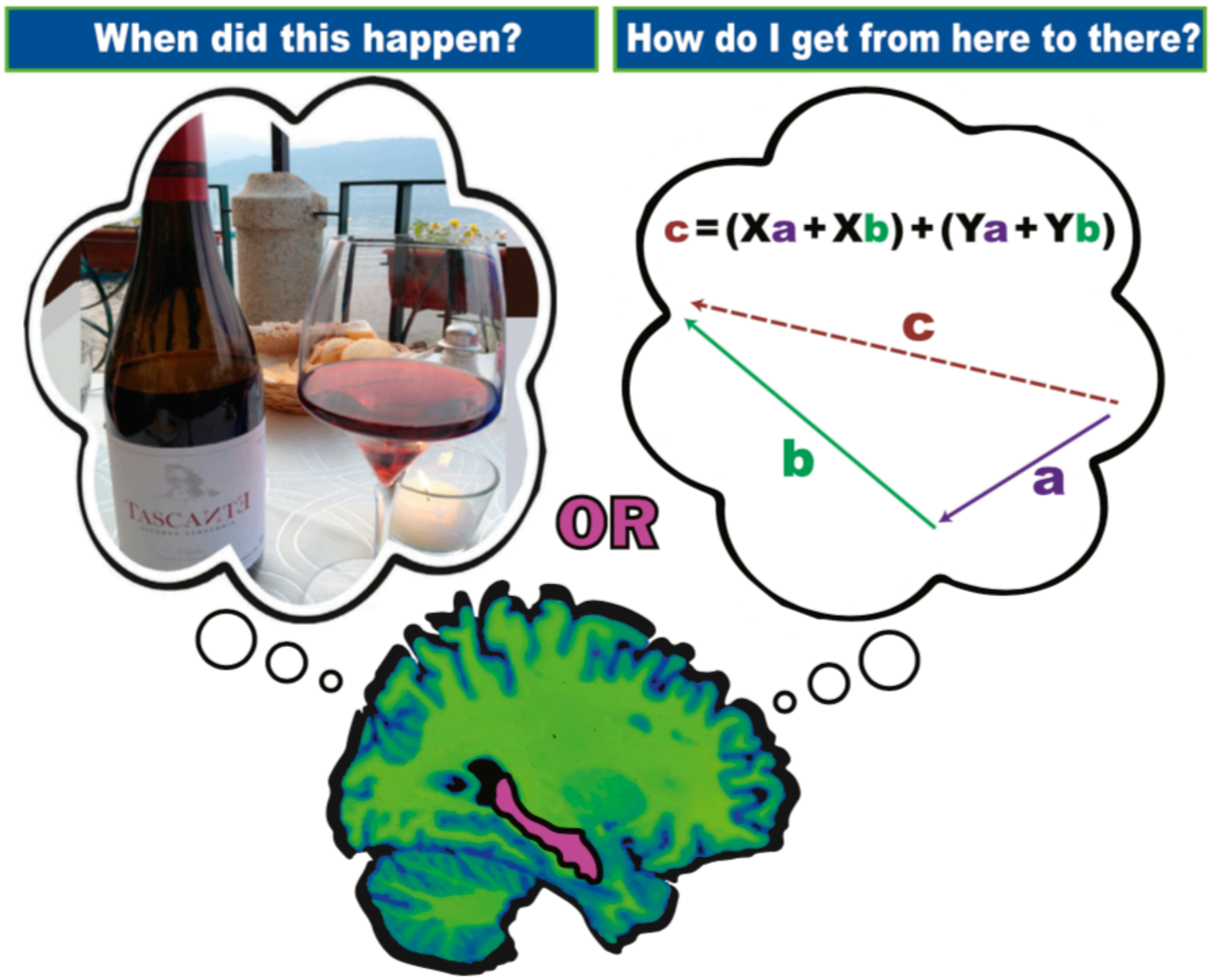
PREMISE 1: GEOMETRICAL KNOWLEDGE IS SYNTHETIC A PRIORI.

PREMISE 2: SYNTHETIC A PRIORI KNOWLEDGE IS POSSIBLE ONLY IF SPACE IS MERELY A FORM OF OUR INTUITION AND NOT A PROPERTY OF THINGS IN THEMSELVES.

CONCLUSION: SPACE IS A FORM OF INTUITION AND A STRUCTURE OUR OWN MINDS IMPOSE ONTO OUR REPRESENTATIONS OF THE WORLD.

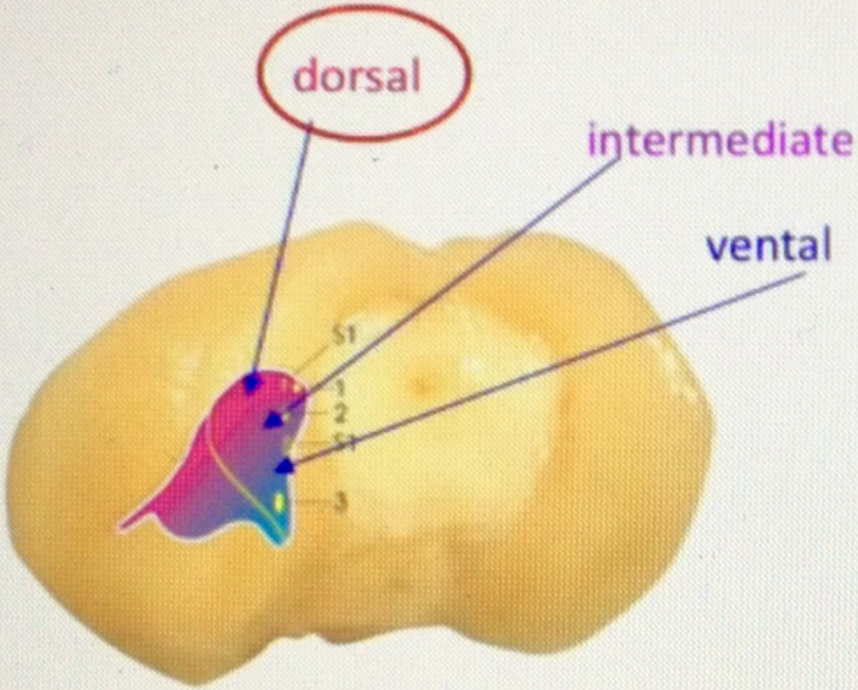


Two Popular Views on Hippocampal Function

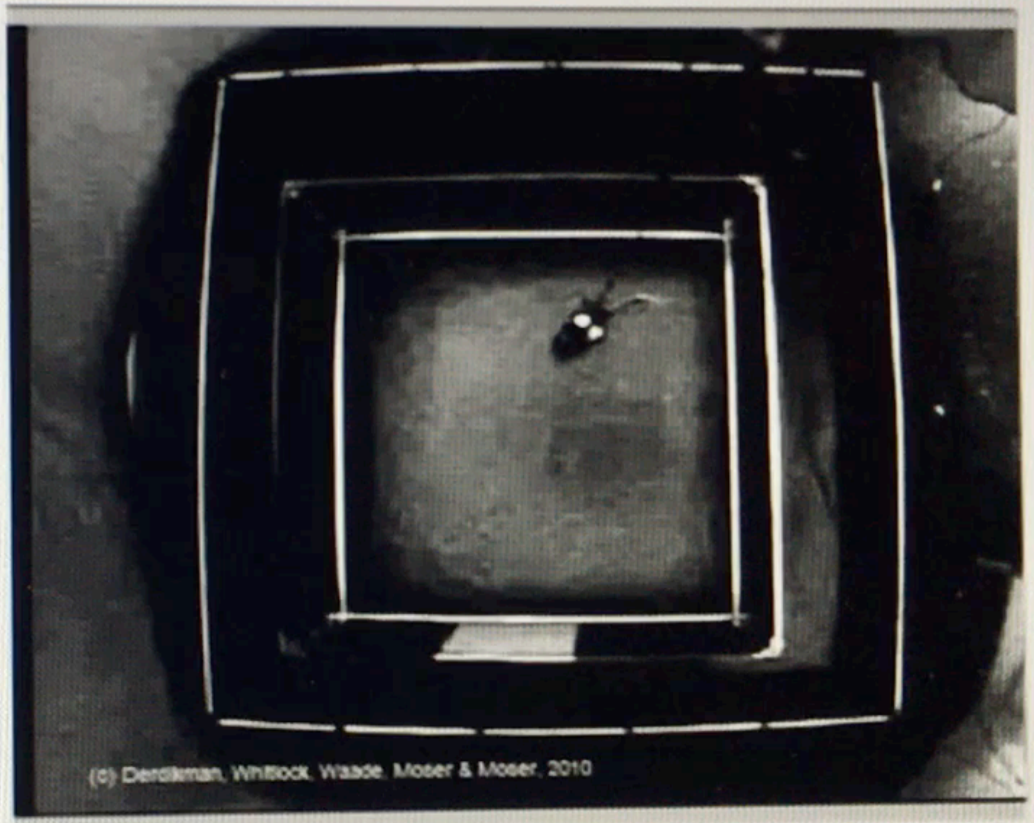
Does the hippocampus represent the relations among elements of memories in spatial and temporal context (e.g., the events of a mealtime occasion), or does it support spatial navigation by path integration (a vector summation problem)?

Could the Kantian microchip be in the hippocampus?

Entorhinal cortex of a rat
brain (seen from behind):

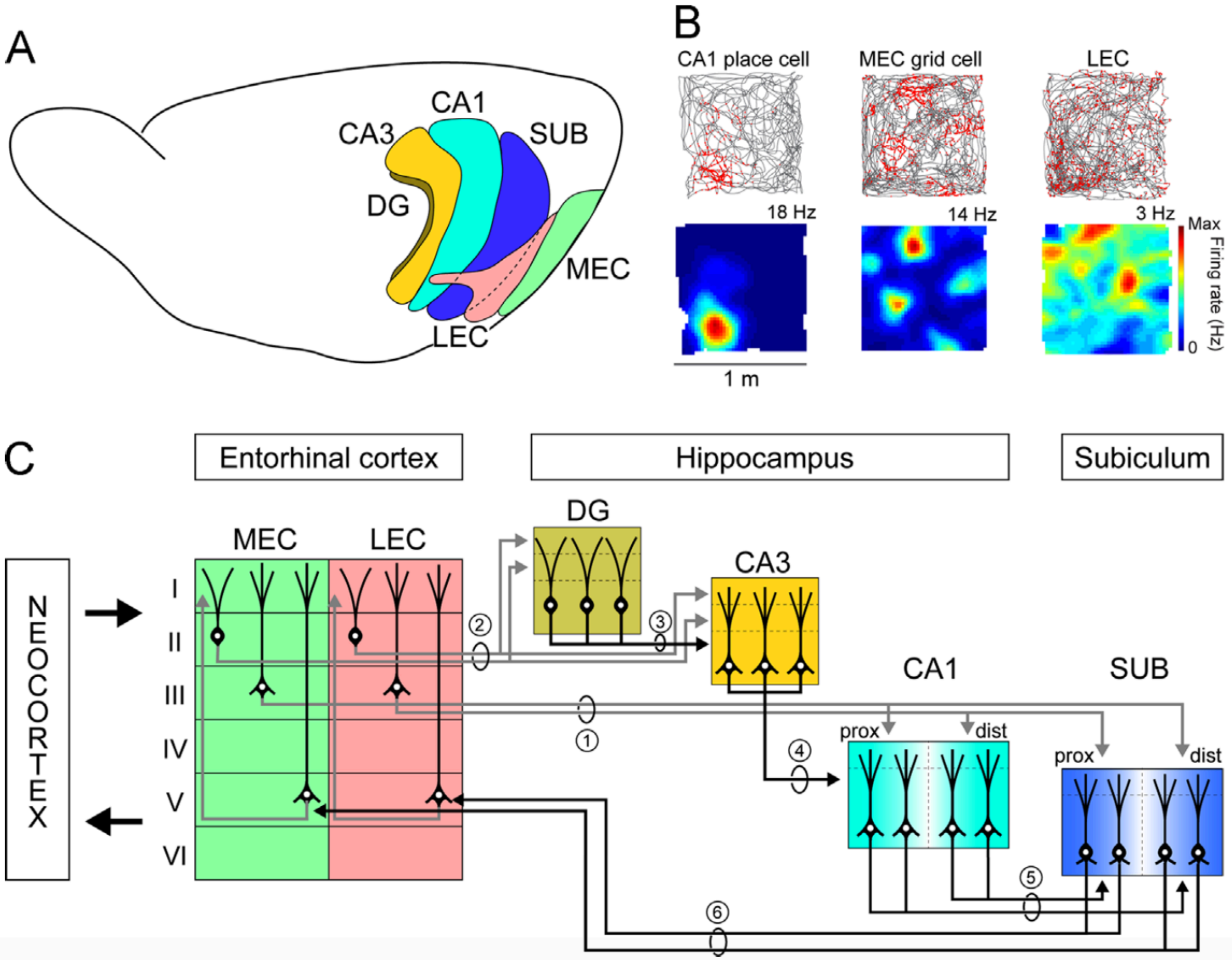


Fyhn et al. (2004). *Science* 305:1258-1264


(c) Derdikman, Whitlock, Waade, Moser & Moser, 2010

Entorhinal cells had multiple fields and the fields exhibited a regular pattern. But what was the pattern?

Place Cells and Neural Maps for Space



Architecture of the rat hippocampal regions.

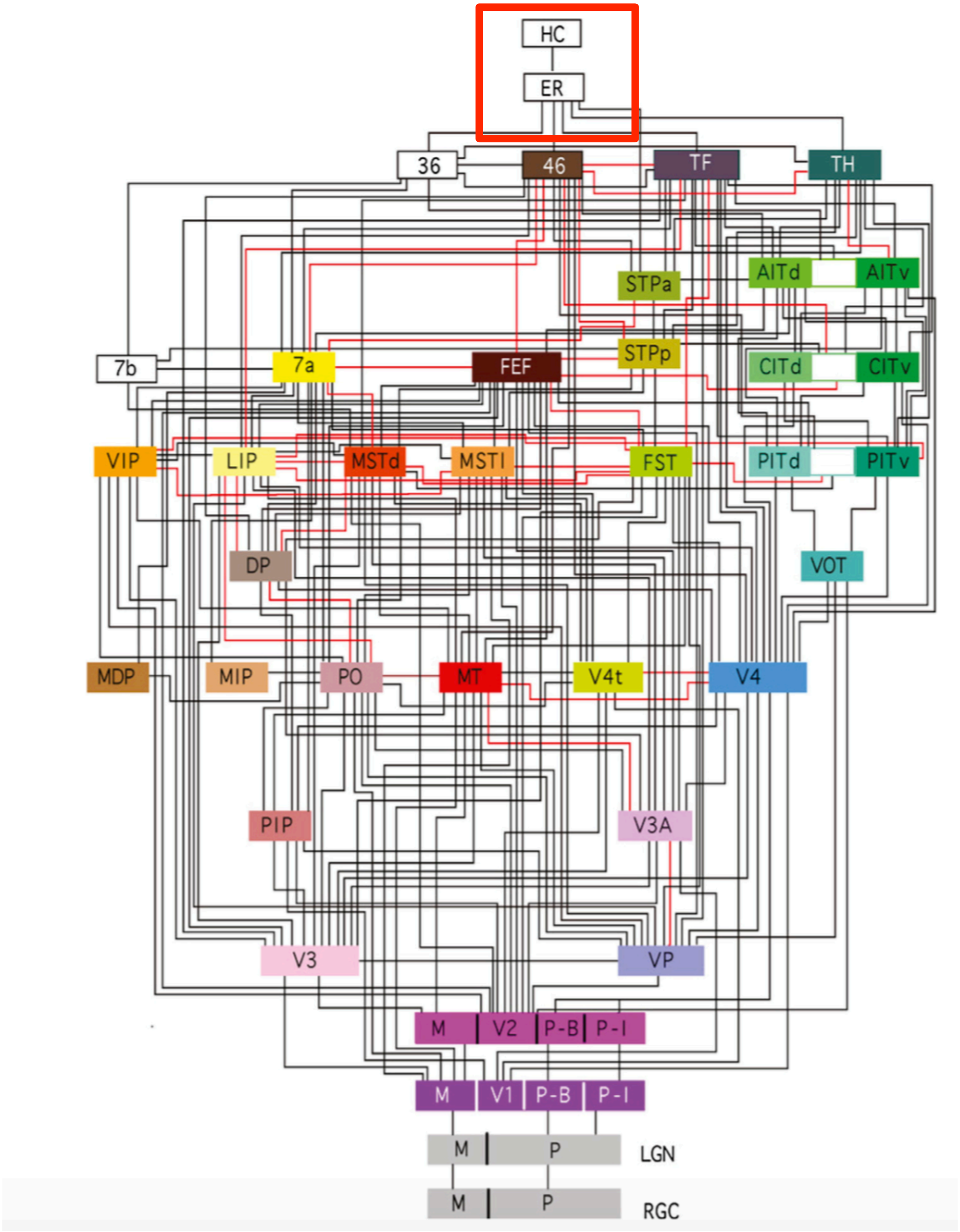
(A) Schematic showing lateral view of key hippocampal regions in the rat brain. The regions include hippocampal subfields CA1, CA3 and dentate gyrus (DG), as well as the subiculum, **medial entorhinal cortex (MEC)** and the **lateral entorhinal cortex (LEC)..**

(B) An example place cell in the CA1 (left), an example grid cell in the MEC (middle), and a representative cell with low spatial information in the LEC. Firing rate maps of spikes recorded in 1m square box are shown. Top, trajectory of animal (gray) with spike positions superimposed (red).

Bottom, color-coded rate maps. Color scale to the right. Peak firing rates (Hz) are indicated on top right and shown in red color.

(C) Diagram of the major connections of the rat hippocampal formation. The hippocampus receives and sends information from the neocortex via entorhinal cortex. MEC and LEC project to CA1 through direct and indirect pathways. In the direct pathway , layer III cells in MEC largely project to proximal CA1 (prox), whereas layer III cells in LEC project to distal CA1 (dist). By contrast, in the indirect pathway, axons of layer II cells in MEC and LEC converge on the same population of cells in the dentate gyrus (DG) and CA3. This mixed information in DG and CA3 is conveyed to CA1 via mossy fibers and Schaffer collaterals . Output form CA1 is conveyed to entorhinal cortex mainly via the subiculum (SUB). In this output, information from proximal CA1 is conveyed to MEC via the distal part of subiculum, whereas distal CA1 projects to LEC via the proximal part of the subiculum.

Igarashi, K. (2016). The entorhinal map of space. Brain Research,1637, 177–187



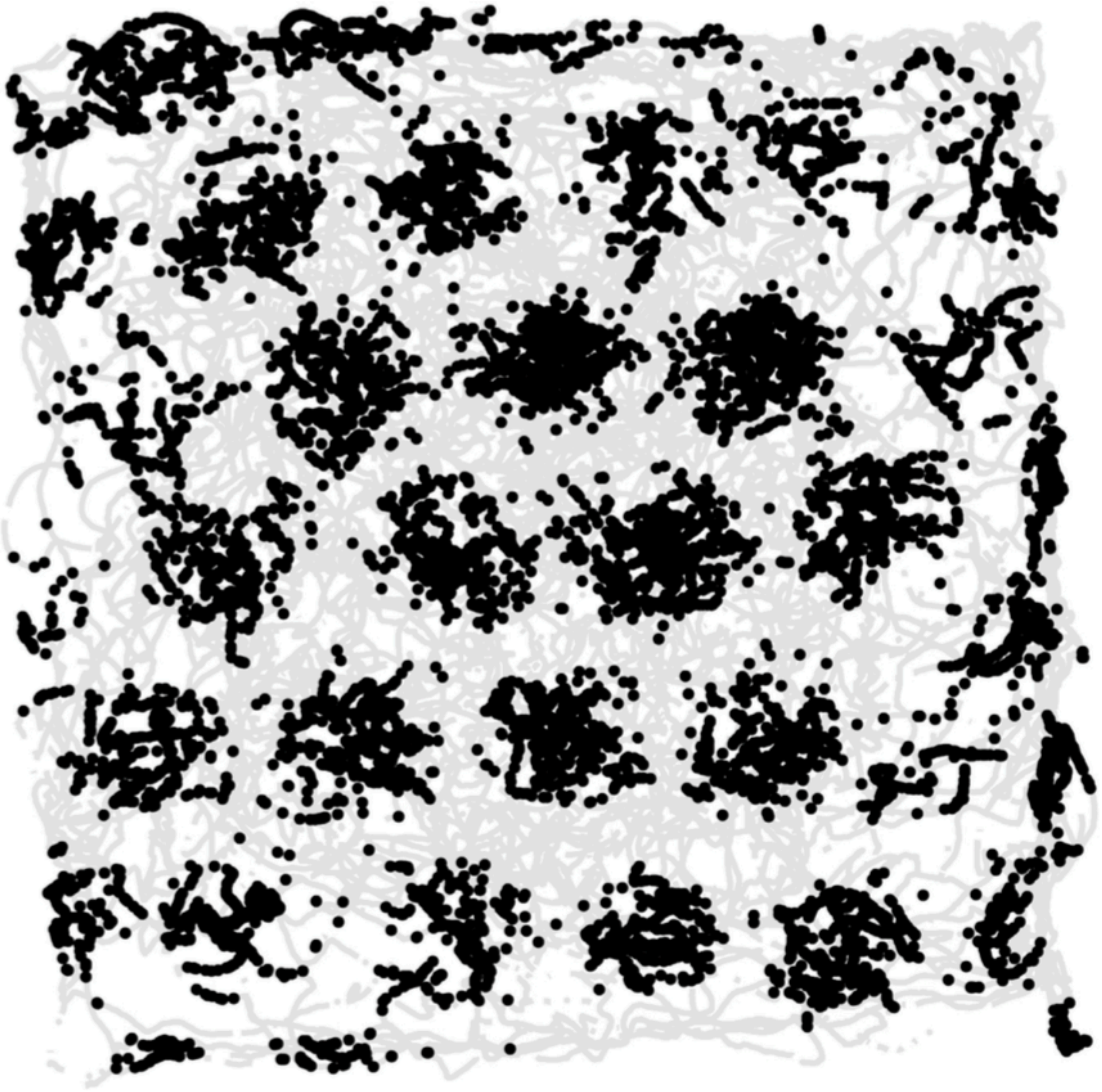
It is possible to decipher neural-circuit mechanisms in the deepest parts of the cortex, far away from sensory receptors and motor neurons.

Hierarchical Connectivity Map of the Cortex

Visual input is shown at the bottom (RGC, retinal ganglion cells; LGN, lateral geniculate nucleus) and entorhinal cortex (ER) and hippocampus (HC) at the top. One of the goals of modern neuro- science is to understand pattern formation in high- end cortices such as the entorhinal cortex and the hippocampus.

Felleman and Van Essen (1991).

Felleman, D.J., and Van Essen, D.C. (1991). Distributed hierarchical processing in the primate cerebral cortex. Cereb. Cortex 1, 1–47.

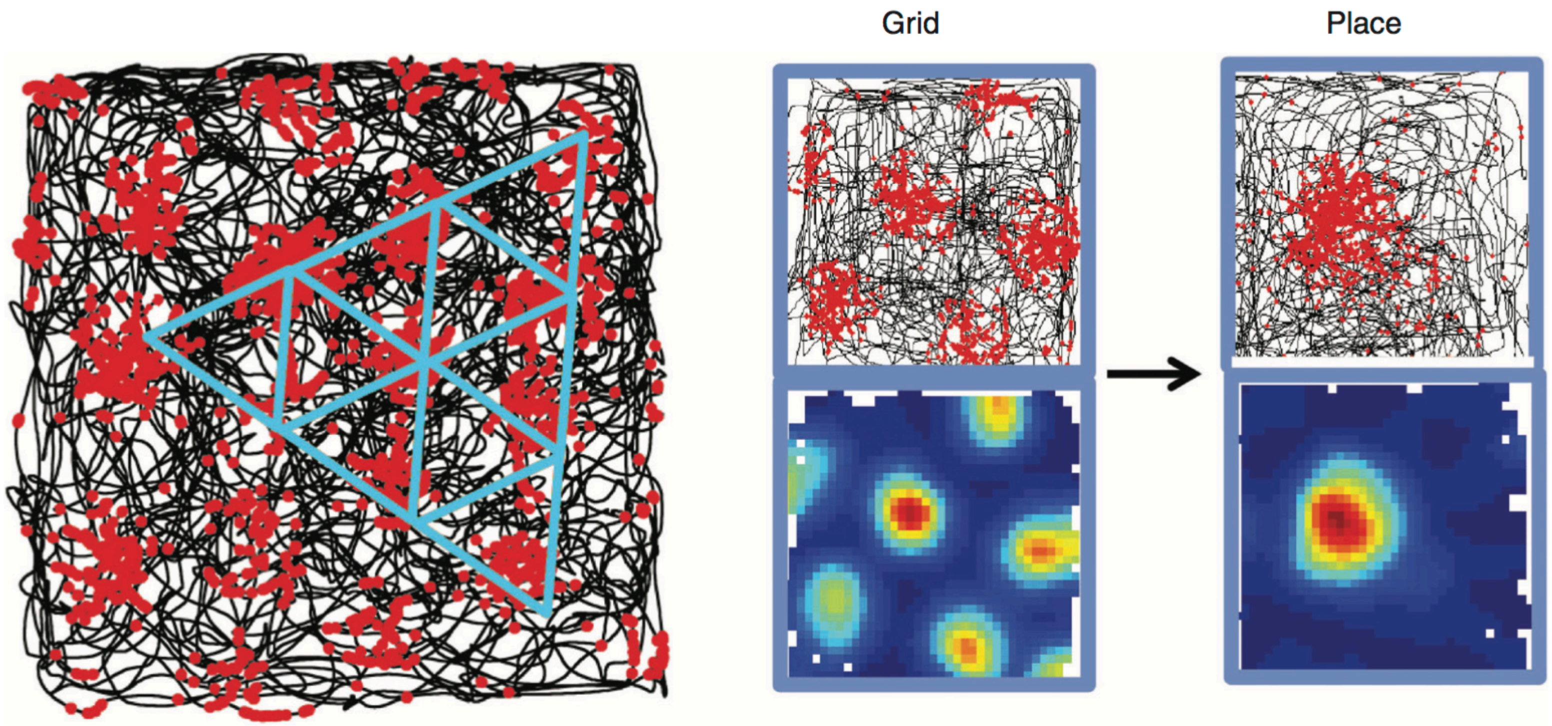


A Grid Cell from the Medial Entorhinal Cortex of the Rat Brain

(Grid cells were discovered in 2005)

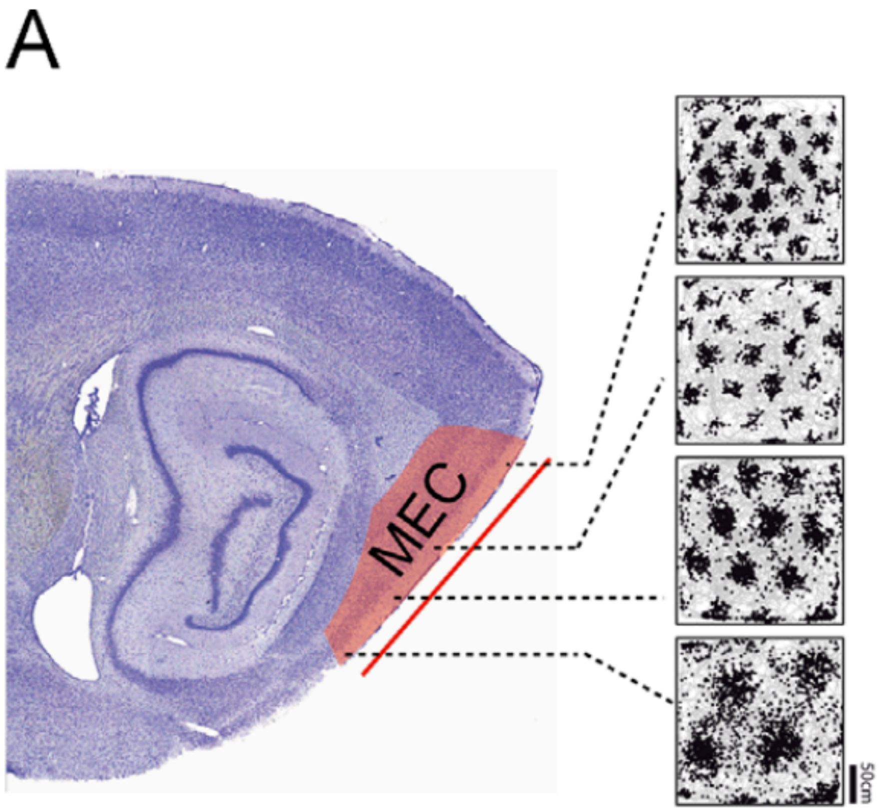
The gray trace is the trajectory of a rat that is foraging in a 2.2 m wide enclosure. Spike locations of the grid cell are superimposed on the track. Each black dot corresponds to one spike. Data were recorded by Kristian Frøland.

Moser, E. I., & Moser, M.-B. (2013). Grid Cells and Neural Coding in High-End Cortices. Neuron, 80(3), 765–774



Grid cells and place cells. (Left) A grid cell from the entorhinal cortex of the rat brain. The black trace shows the trajectory of a foraging rat in part of a 1.5-m-diameter-wide square enclosure. Spike locations of the grid cell are superimposed in red on the trajectory. Each red dot corresponds to one spike**. Blue equilateral triangles have been drawn on top of the spike distribution to illustrate the regular hexagonal structure of the grid pattern**. (Right) Grid cell and place cell. (Top) Trajectory with spike locations, as in the left part. (Bottom) Color- coded rate map with red showing high activity and blue showing low activity. Grid cells are thought to provide much, but not all, of the entorhinal spatial input to place cells.

Moser, M.-B., Rowland, D., & Moser, E. (2015). Place Cells, Grid Cells, and Memory. Cold Spring Harbor Perspectives in Biology, 7(2), a021808. doi:10.1101/cshperspect.a021808



Recording position for grid cells illustrated on a sagittal section of brain through the MEC. Each panel on the right shows the grid fields of one layer II cell. Note the increase of grid cell scale from dorsal to ventral portions of the MEC.

Igarashi, K. (2016). The entorhinal map of space. Brain Research, 1637, 177–187

Grid cell firing provides a spectacular example of internally generated structure, both individually and in the almost crystalline organization of the firing patterns of different grid cells. A similarly strong organization is seen in the relative tuning of head-direction cells. ***This strong internal structure is reminiscent of Kantian ideas regarding the necessity of an innate spatial structure with which to understand the spatial organization of the world.***

Perhaps the most intriguing aspect of the structure manifested by grid cell firing is its obvious potential power as a coding scheme—almost as if it were designed by a mathematician or engineer.
Together a relatively small number of modules have a potentially exponential coding capacity representing a neural code of unprecedented power and efficiency.

Burgess, N. (2014). The 2014 Nobel Prize in Physiology or Medicine: A Spatial Model for Cognitive Neuroscience. Neuron 84: 1120–1125

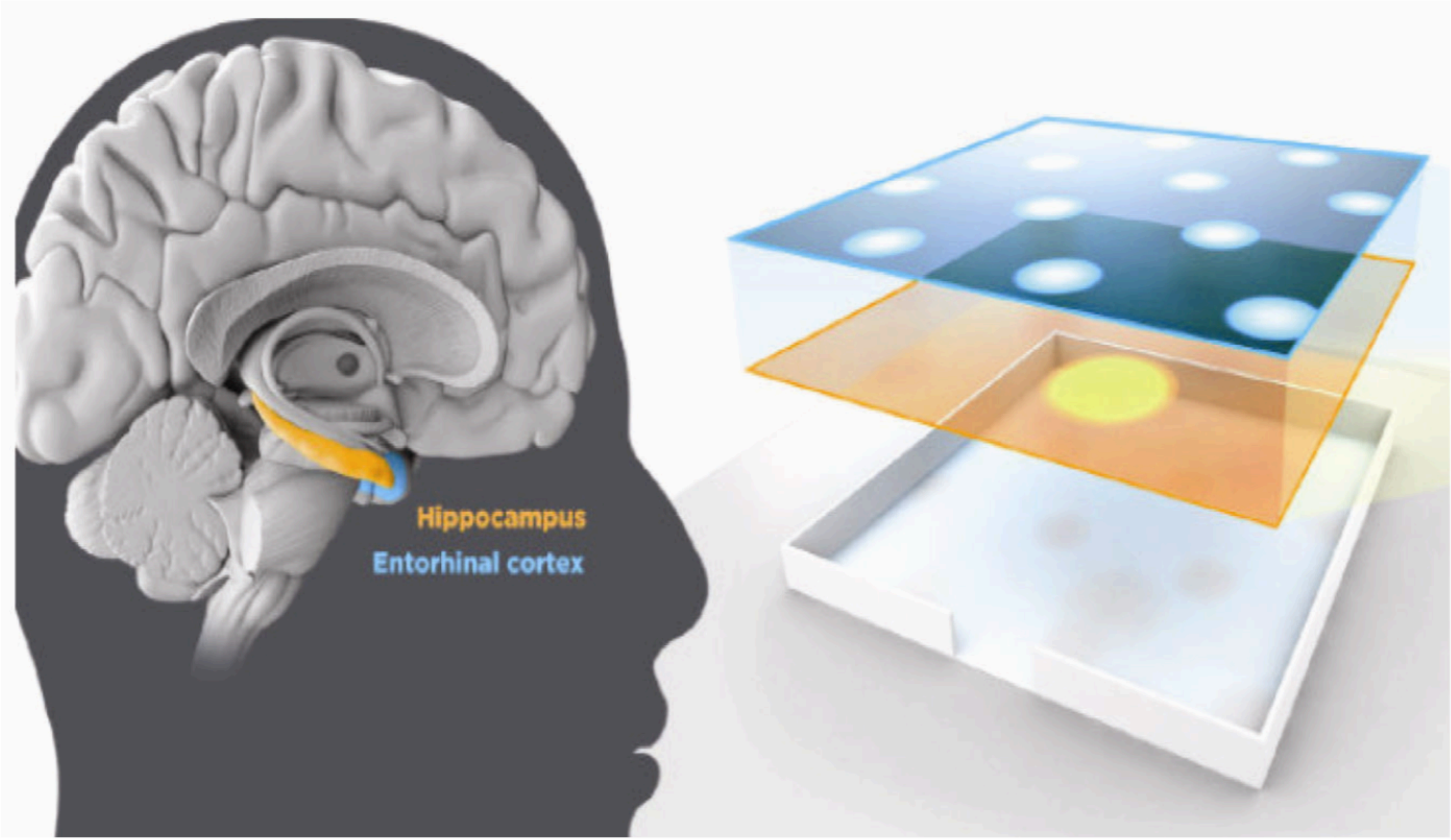


Figure 1. Grid cells, together with other cells in the entorhinal cortex that recognize the direction of the head of the animal and the border of the room, form networks with the place cells in the hippocampus. This circuitry constitutes a comprehensive positioning system, an inner GPS, in the brain. The positioning system in the human brain appears to have similar components as those of the rat brain. [Credits: Illustration and layout by Mattias Karlén/© 2014 The Nobel Committee for Physiology or Medicine.]

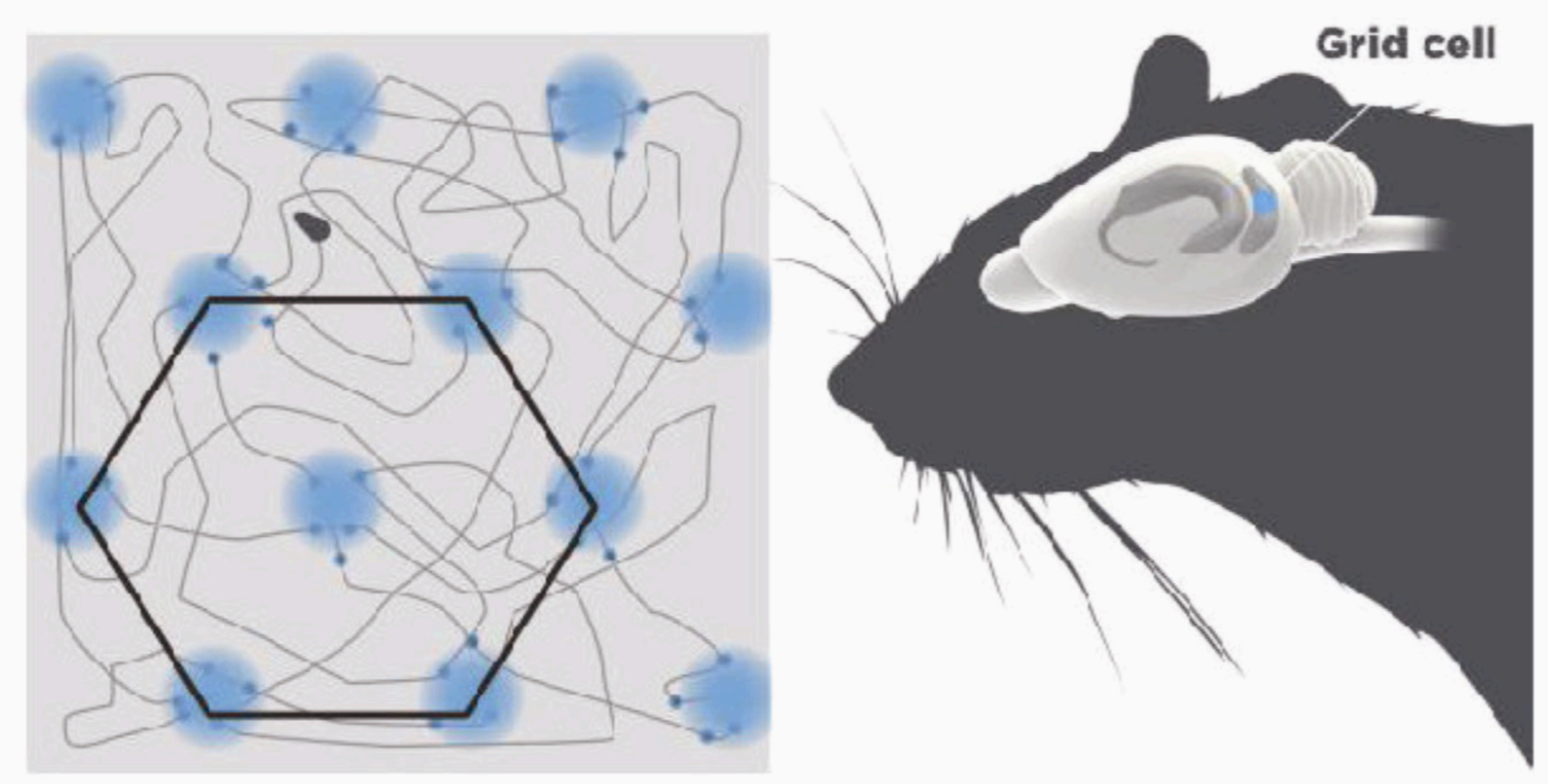


Figure 2. The grid cells are located in the entorhinal cortex depicted in blue. A single grid cell fires when the animal reaches particular locations in the arena. These locations are arranged in a hexagonal pattern. [Credits: Illustration and layout by Mattias Karlén/ © 2014 The Nobel Committee for Physiology or Medicine.]

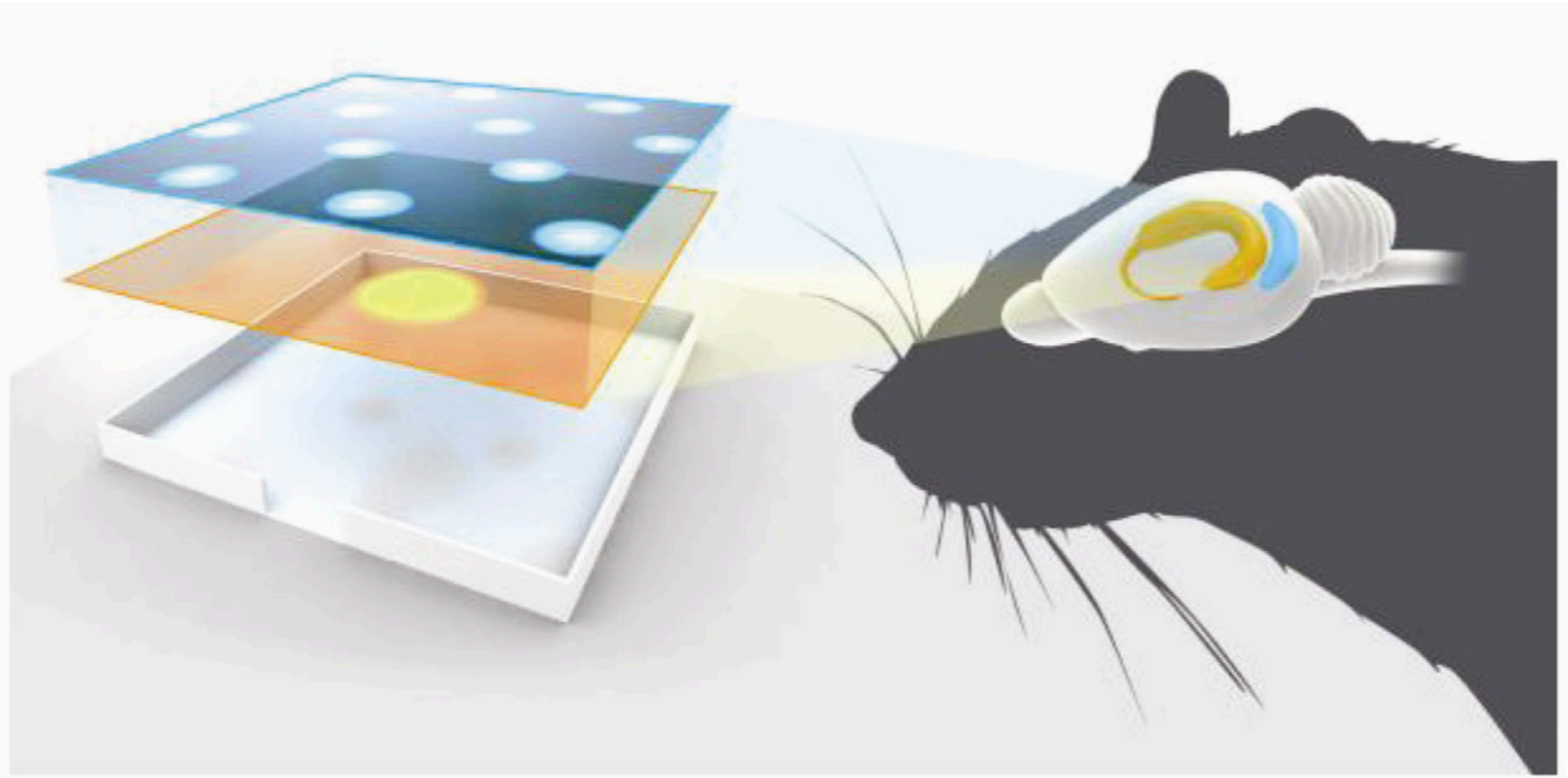
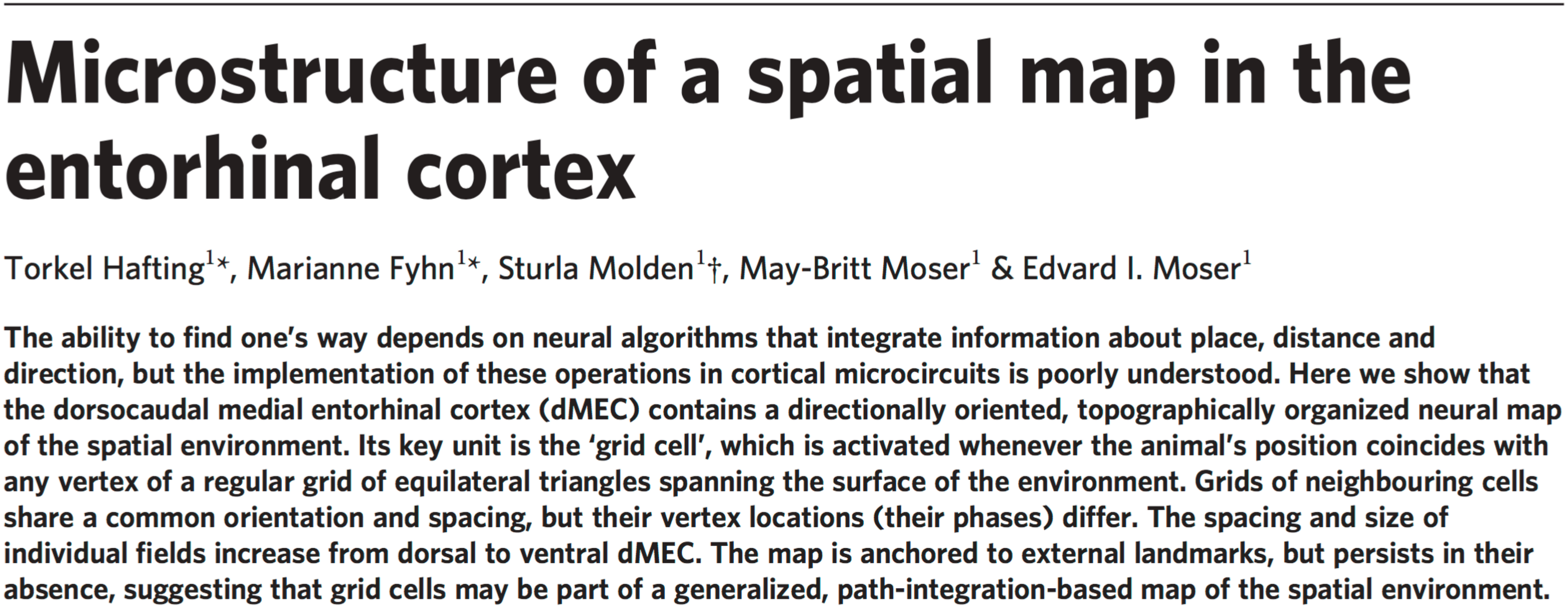


Figure 3. A schematic diagram showing grid cells (blue) and place cells (yellow) in the entorhinal cortex and hippocampus respectively. [Credits: Illustration and layout by Mattias Karlén/© 2014 The Nobel Committee for Physiology or Medicine.]



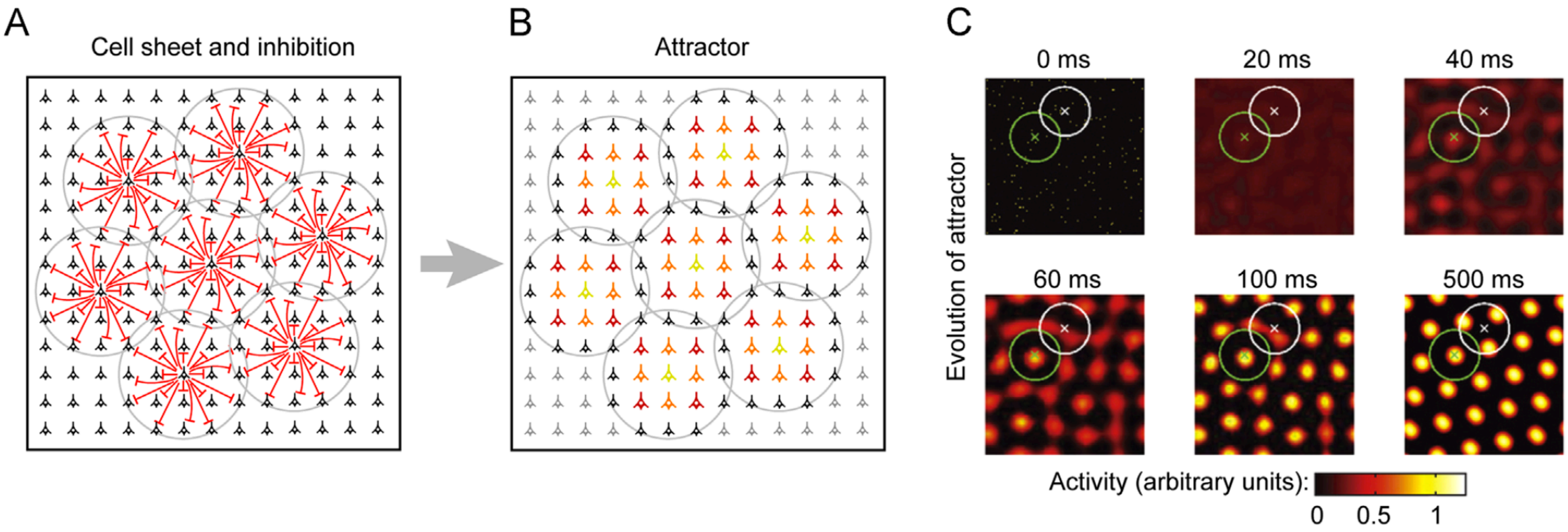
Microstructure of a spatial map in the entorhinal cortex

Torkel Hafting[1]*, Marianne Fyhn[1]*, Sturla Molden[1]†, May-Britt Moser[1] & Edvard I. Moser[1]

The ability to find one's way depends on neural algorithms that integrate information about place, distance and direction, but the implementation of these operations in cortical microcircuits is poorly understood. Here we show that the dorsocaudal medial entorhinal cortex (dMEC) contains a directionally oriented, topographically organized neural map of the spatial environment. Its key unit is the 'grid cell', which is activated whenever the animal's position coincides with any vertex of a regular grid of equilateral triangles spanning the surface of the environment. Grids of neighbouring cells share a common orientation and spacing, but their vertex locations (their phases) differ. The spacing and size of individual fields increase from dorsal to ventral dMEC. The map is anchored to external landmarks, but persists in their absence, suggesting that grid cells may be part of a generalized, path-integration-based map of the spatial environment.

It was shown that the grid formation did not arise out of a simple transformation of sensory or motor signals, but out of complex network activity.

Hafting, T., Fyhn, M., Molden, S., Moser, M.-B., & Moser, E. (2005). Microstructure of a spatial map in the entorhinal cortex. Nature 436(7052), 801–6.



Schematic illustration of grid cell formation in an attractor network model. (A). Virtual sheet of MEC neurons arranged conceptually according to relative proximity of anatomical connections. Each cell sends recurrent inhibitory input to neighboring cells located within a given distance of itself (red lines). Note that inhibition is illustrated only for seven cells in this figure, although every cell has inhibitory connections to the surround. (B) Competition between inhibitory influences will cause activity to evolve towards a stable attractor state where the cluster of active cells is arranged in a close-packed hexagonal pattern. Highly active cells (yellow) inhibit neighboring cells. Cells that receive inhibition from multiple yellow cells (black, along the circumference of each circle) become inactive. This pattern of activity leads to a hexagonal arrangement of firing rates across the layer. (C) Spontaneous emergence of hexagonally patterned activity in the cell sheet in (A) and (B) as predicted by computational modeling. In this figure, ‘hotter’ colors represent high activity rates of individual cells. Inhibitory connection radii of two example neurons are shown as white and green circles. A hexagonal pattern emerges after inhibitory competition starts.

Igarashi, K. (2016). The entorhinal map of space. Brain Research,1637, 177–187

Direct recordings of grid-like neuronal activity in human spatial navigation

Joshua Jacobs[1], Christoph T Weidemann[2], Jonathan F Miller[1], Alec Solway[3], John F Burke[4], Xue-Xin Wei[4], Nanthia Suthana[5], Michael R Sperling[6], Ashwini D Sharan[7], Itzhak Fried[5,8,9] & Michael J Kahana[4,9]

Jacobs, J., Weidemann, C.T., Miller, J.F., Solway, A., Burke, J.F., Wei, X.X., Suthana, N., Sperling, M.R., Sharan, A.D., Fried, I., and Kahana, M.J. (2013). Direct recordings of grid-like neuronal activity in human spatial navigation. Nat. Neurosci. 16, 1188–1190.

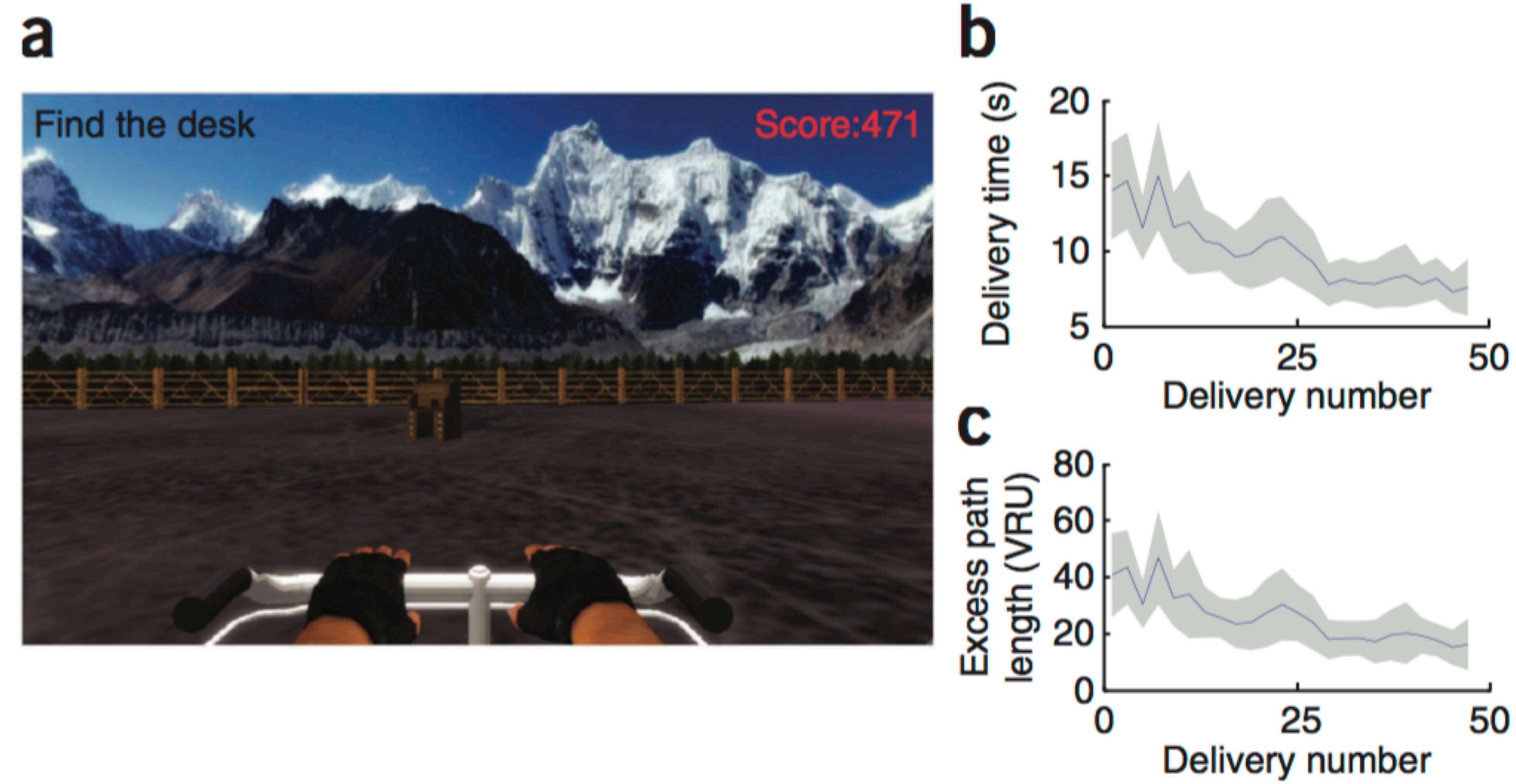
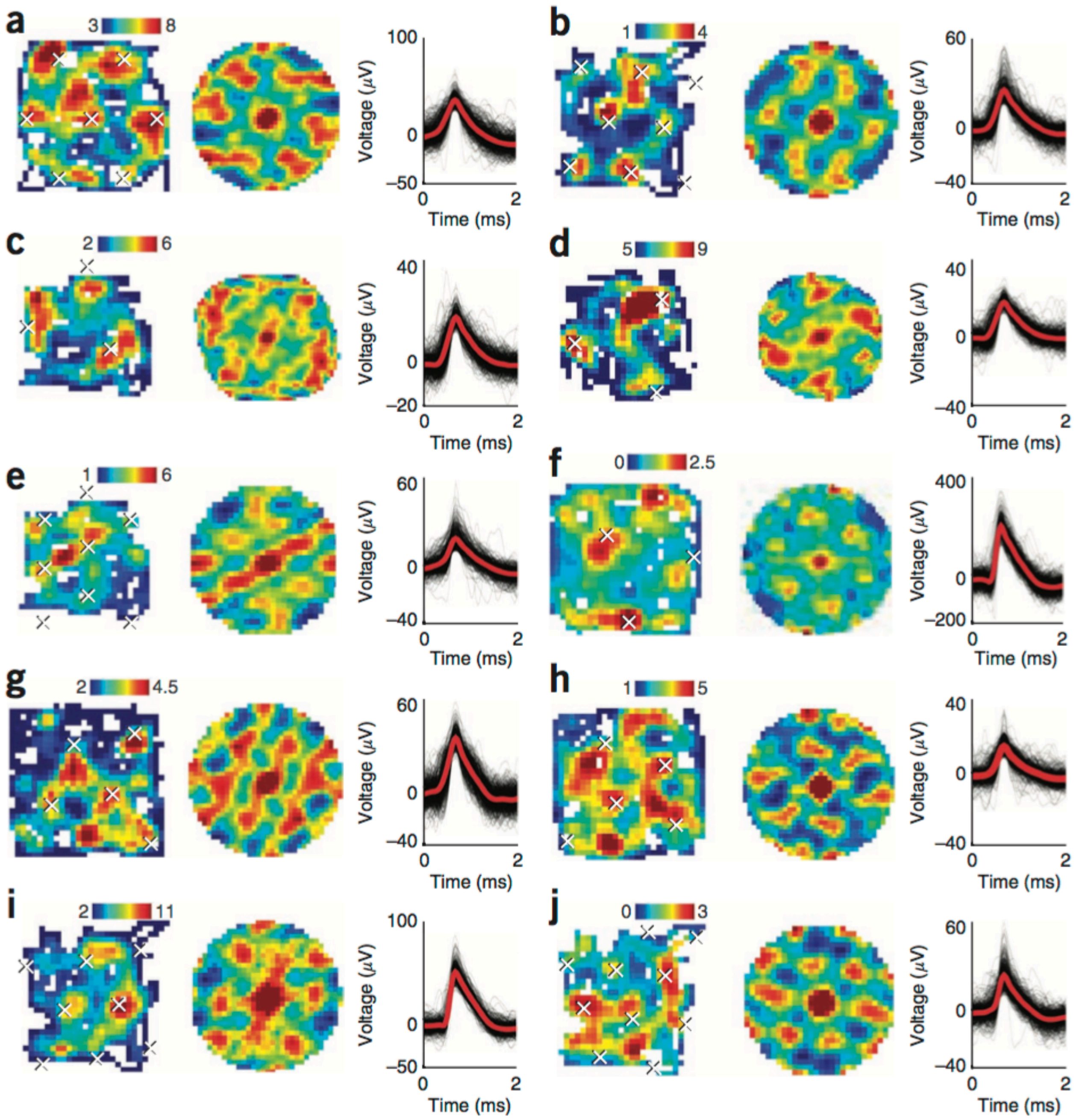


Figure 1 Virtual navigation task. (**a**) Participant's view of the experiment. (**b**) Mean duration of successive deliveries in the task, averaged across consecutive pairs of deliveries. (**c**) Mean excess path length. VRU is a measure of virtual distance. Error shading denotes 95% confidence intervals.

Jacobs, J., Weidemann, C.T., Miller, J.F., Solway, A., Burke, J.F., Wei, X.X., Suthana, N., Sperling, M.R., Sharan, A.D., Fried, I., and Kahana, M.J. (2013). Direct recordings of grid-like neuronal activity in human spatial navigation. Nat. Neurosci. 16, 1188–1190.



Examples of grid-like spatial firing.
(**a**) The activity of a cell from participant 6's left entorhinal cortex. Left, overhead view of the environment, with color representing the firing rate (in Hz) at each virtual location. Middle, two-dimensional autocorrelation of the cell's activity. Peaks in the autocorrelation function determined the spacing and angle of the fitted **c** grid, which was then used to plot the estimated grid peaks (white ×) across the entire environment.
Right, cell spike waveform; red denotes mean. This cell had a gridness score of 0.51.
(**b**) The firing of a cell from participant 10's right entorhinal cortex (gridness score = 0.63).
(**c**,**d**) The firing of a different cell from participant 10's right entorhinal cortex in two consecutive **e** sessions (gridness scores = 0.60 and 0.74).
(**e**) The activity of a different cell from participant 10's right entorhinal cortex (gridness score = 0.63).
(**f**) The activity of a cell from participant 11's right cingulate cortex (gridness score = 0.67).
(**g**) The activity of a cell from participant 7's **g** right cingulate cortex (gridness score = 0.51).
(**h**) The activity of a different cell from participant 7's right cingulate cortex (gridness score = 0.8).
(**i**) The activity of a cell from participant 10's right hippocampus (gridness score = 0.46).
(**j**) The activity of a cell from participant 10's right parahippocampal gyrus (gridness score = 0.72).

Results demonstrate the existence of cells with grid-like spatial firing in the human brain and suggest that the human grid-cell network includes both entorhinal cortex and cingulate cortex.

Jacobs, J., Weidemann, C.T., Miller, J.F., Solway, A., Burke, J.F., Wei, X.X., Suthana, N., Sperling, M.R., Sharan, A.D., Fried, I., and Kahana, M.J. (2013). Direct recordings of grid-like neuronal activity in human spatial navigation. Nat. Neurosci. 16, 1188–1190.

Organizing conceptual knowledge in humans with a gridlike code

Alexandra O. Constantinescu,[1*]† Jill X. O'Reilly,[1,2,3]† Timothy E. J. Behrens[1,4*]

Constantinescu, Alexandra O. O'Reilly, Jill X. Behrens, Timothy EJ (2016) Organizing conceptual knowledge in humans with a gridlike code Science 352:1464-1468 *(2016)*

It has been hypothesized that the brain organizes concepts into a mental map, allowing conceptual relationships to be navigated in a manner similar to that of space. Grid cells use a hexagonally symmetric code to organize spatial representations and are the likely source of a precise hexagonal symmetry in the functional magnetic resonance imaging signal. Humans navigating conceptual two-dimensional knowledge showed the same hexagonal signal in a set of brain regions markedly similar to those activated during spatial navigation. This gridlike signal is consistent across sessions acquired within an hour and more than a week apart. Our findings suggest that global relational codes may be used to organize nonspatial conceptual representations and that these codes may have a hexagonal gridlike pattern when conceptual knowledge is laid out in two continuous dimensions.

***Constantinescu, Alexandra O. O'Reilly, Jill X. Behrens, Timothy EJ (2016) Organizing conceptual knowledge in humans with a gridlike code* Science 352:1464-1468 (2016)**

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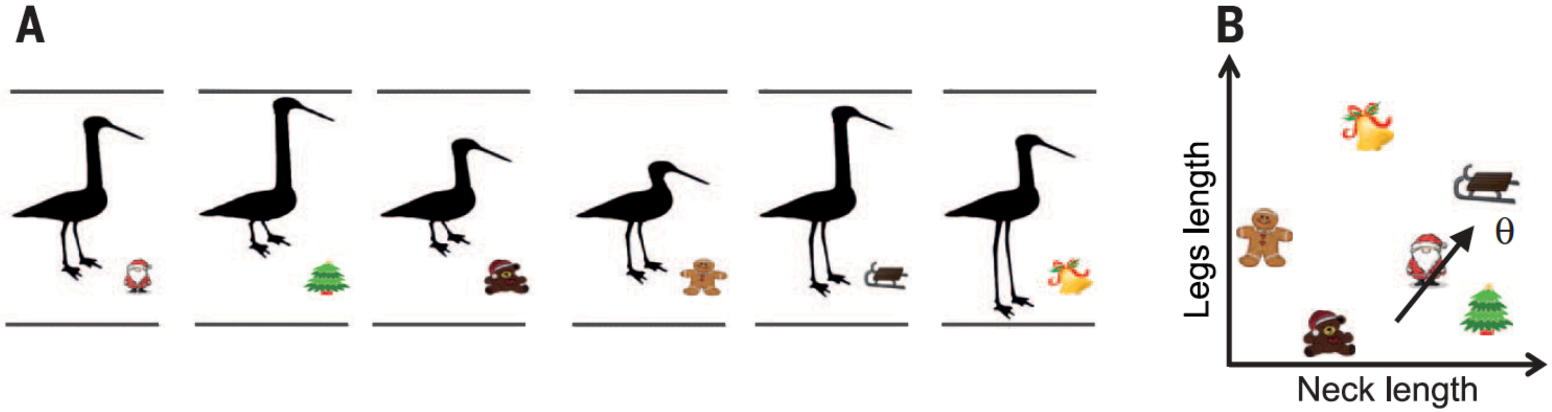
We used fMRI to test if humans use a hexagonally symmetric code when navigating through abstract conceptual representations. We designed a task analogous to the one used for navigation in physical space (C. F. Doeller, C. Barry, N. Burgess, Nature 463, 657–661 (2010).),with the notable difference that our dimensions were organized in an abstract, rather than physical, space.

Constantinescu, Alexandra O. O'Reilly, Jill X. Behrens, Timothy EJ (2016) Organizing conceptual knowledge in humans with a gridlike code Science 352:1464-1468 (2016)



Twenty-eight healthy subjects performed a stimulus-outcome (S-O) learning task in which they learned that bird stimuli (25) were associated with different Christmas symbols (Fig. 1A). The study therefore resembles other S-O learning tasks except that here, the bird stimuli were not independent fractals or symbols but, instead, they varied according to two continuous dimensions: the lengths of the neck and legs. Each stimulus could therefore be described within a two-dimensional conceptual "bird space" (Fig. 1B).

Even though the features of this bird space were lengths as in physical maps, here they had to be extracted from a one-dimensional (vertical) visual space where different stimuli did not form any angles (Fig. 1A) and transformed into a two-dimensional conceptual map (Fig. 1B).

***Constantinescu, Alexandra O. O'Reilly, Jill X. Behrens, Timothy EJ (2016) Organizing conceptual knowledge in humans with a gridlike code** Science 352:1464-1468 (2016)*

We periodically
tested their knowledge of the bird space by
asking them to find specific outcomes from arbitrary
start positions, by correctly choosing the
appropriate neck:legs ratio

http://science.sciencemag.org/content/sci/suppl/2016/06/15/352.6292.1464.DC1/aaf0941s1.mov

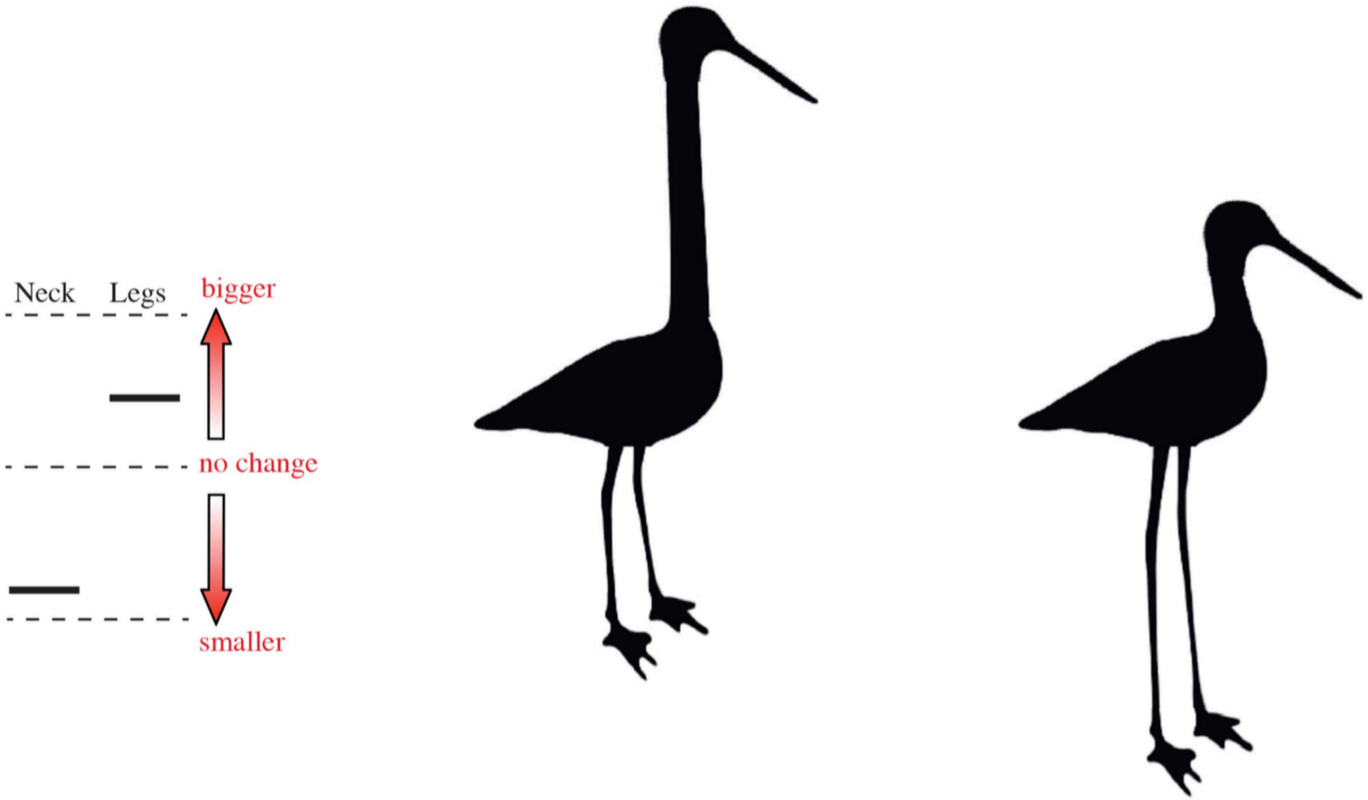


Fig. S1.

Example screenshot of the match task. Here, to morph the bird on the left into the one on the right, the neck needed to decrease more than the legs needed to increase. The correct neck:legs ratio to achieve this is shown on the controller on the left side of the screen (notice the position of the two black bars).

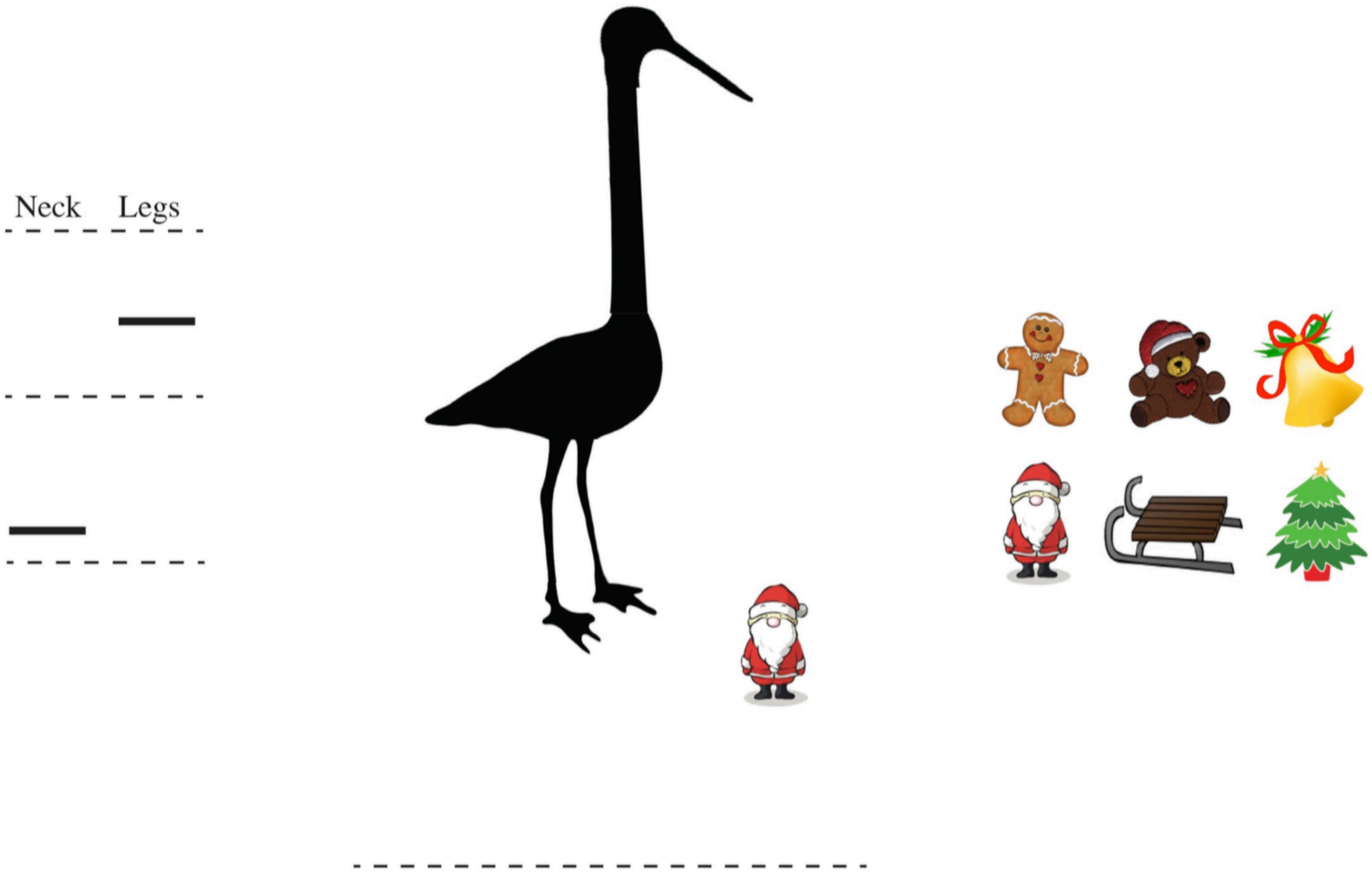
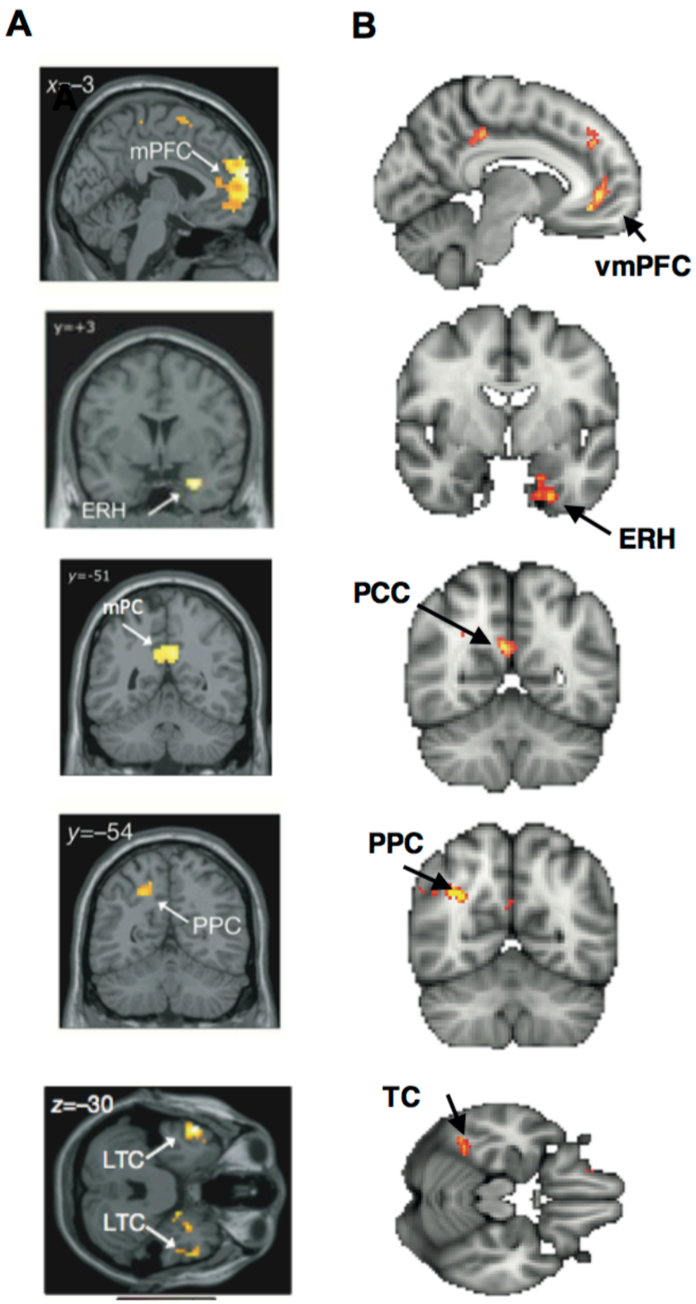


Fig. S2

Example screenshot in the explore task where the subject found Santa Claus.



Evidence for grid cells in a human memory network
(**B**). Abbreviations: ventromedial prefrontal cortex (vmPFC), entorhinal cortex (ERH), posterior cingulate cortex (PCC), posterior parietal cortex (PCC), temporal cortex (TC). A is adapted by permission from Nature, Doeller et al, 2010.

Doeller, C., Barry, C., & Burgess, N. (2010). Evidence for grid cells in a human memory network. Nature, 463(7281), 657–61