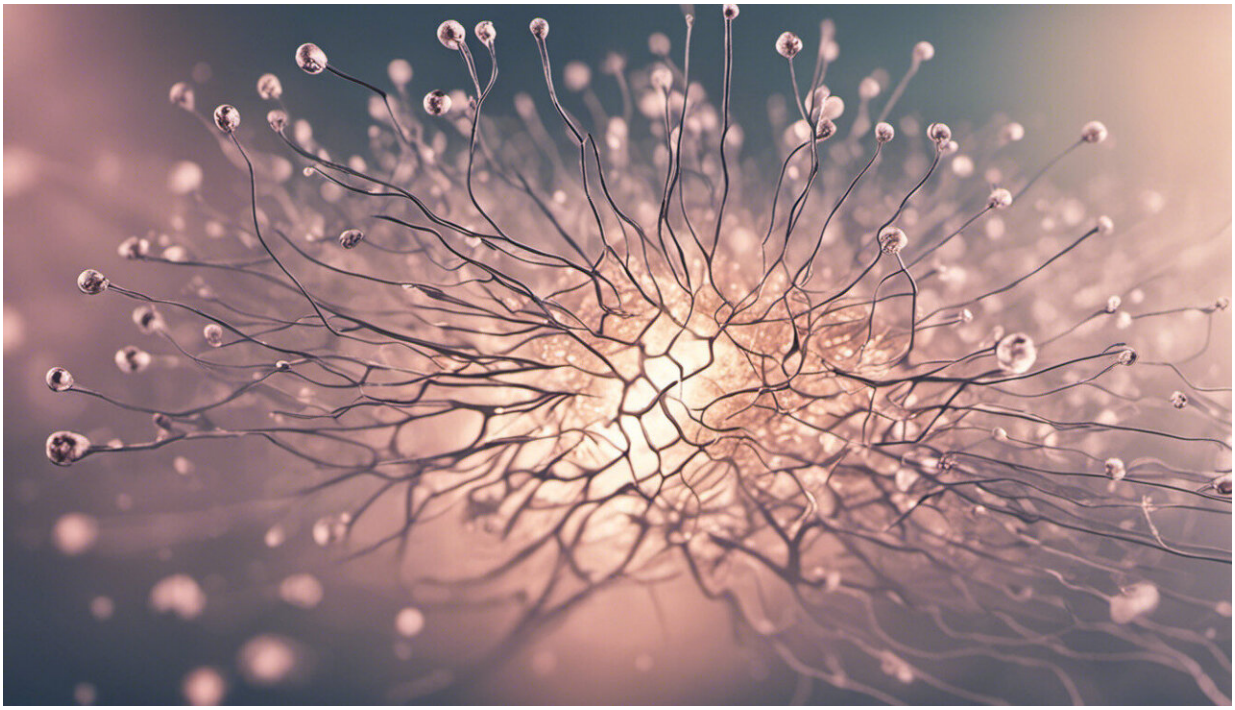
Deciphering how memory works in the brain – at the level of individual cells

September 21 2018, by Andrej Bicanski



Credit: AI-generated image (disclaimer)

Say you meet an old friend at the train station. She is standing about a metre ahead of you, and on the tracks to your right a train has just pulled into the station. Behind your friend you see a bakery. We often remember such scenes in vivid detail. But exactly how we do that by forming mental images has long been a bit of a mystery.

Many researchers liken someone's recall of an episode from their life (episodic memory) to re-experiencing of the original event. What is unclear is how this process could be realised in the brain, at the level of single brain cells (neurons). Now our new study, published in eLife, has come up with a suggestion.

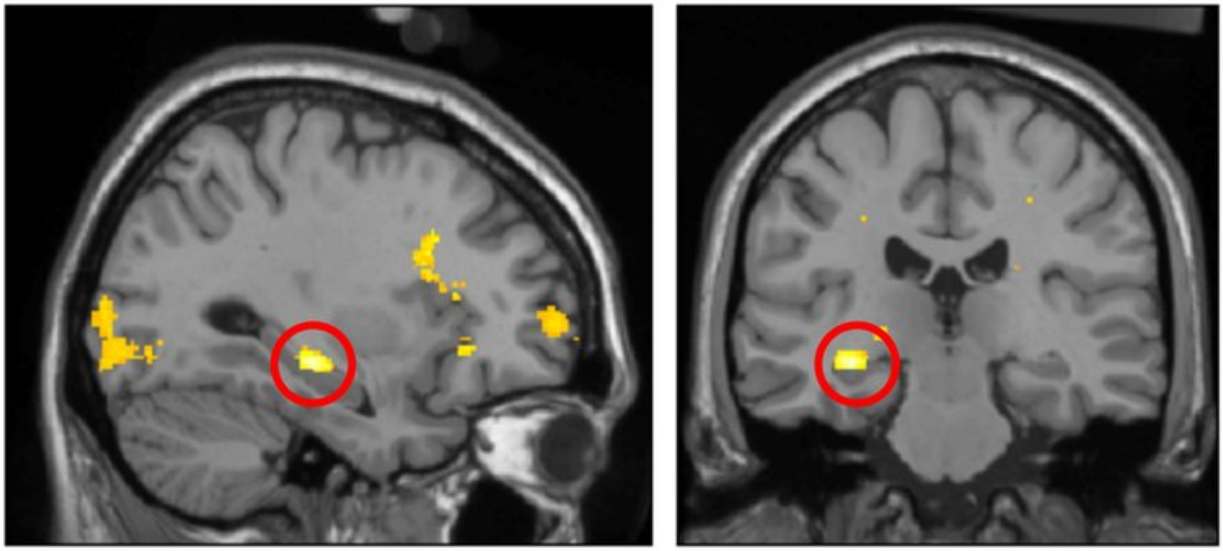
It is possible to measure the activity of single brain cells. Experiments with rodents have shown that certain cells are active whenever an animal is located at a particular spot in the environment. These so-called "place cells" therefore represent an animal's position in a given environment.

Similarly, other brain cells fire whenever there is an environmental boundary –such as the walls of a room – at a certain distance and direction from the animal. Such findings have given us clues as to how spatial relations are represented in the brain. As you meet your friend at the train station, cells in your brain that represent your location relative to the train station should be active. Similarly, other cells would signal the presence of "objects" (like your friend, the bakery and train) at given distances and directions from you. Yet other cells signal the identity of these items. However, it is not known how all these cells might work in concert to realise mental processes involved in perceiving, remembering and even imagining life events.

On a more abstract level, all these elements – your friend, the bakery and the train – and their spatial arrangement collectively form what psychologists refer to as "a scene". The term "scene construction" designates all the mental processes involved in perceiving, remembering and even imagining scenes. So knowing how the different cells work together would allow these abstract notions to be understood at the level of single cells.

The area of the brain known as the hippocampus has long been known to be crucial for memory. However, patients with hippocampal damage

have been reported to also have difficulties imagining coherent spatial scenes – suggesting that imagining spatial experiences is linked to memory. Subsequently, brain scans have shown that imagination of new experiences and recall of memories do engage overlapping brain areas.



Activity in the hippocampus. Author provided

Brain imaging techniques, however, typically identify areas of the brain that can contain millions of cells, comprising many individual networks potentially representing different information. It is therefore difficult to tell how individual networks of cells behave based on brain scans.

Modelling memory

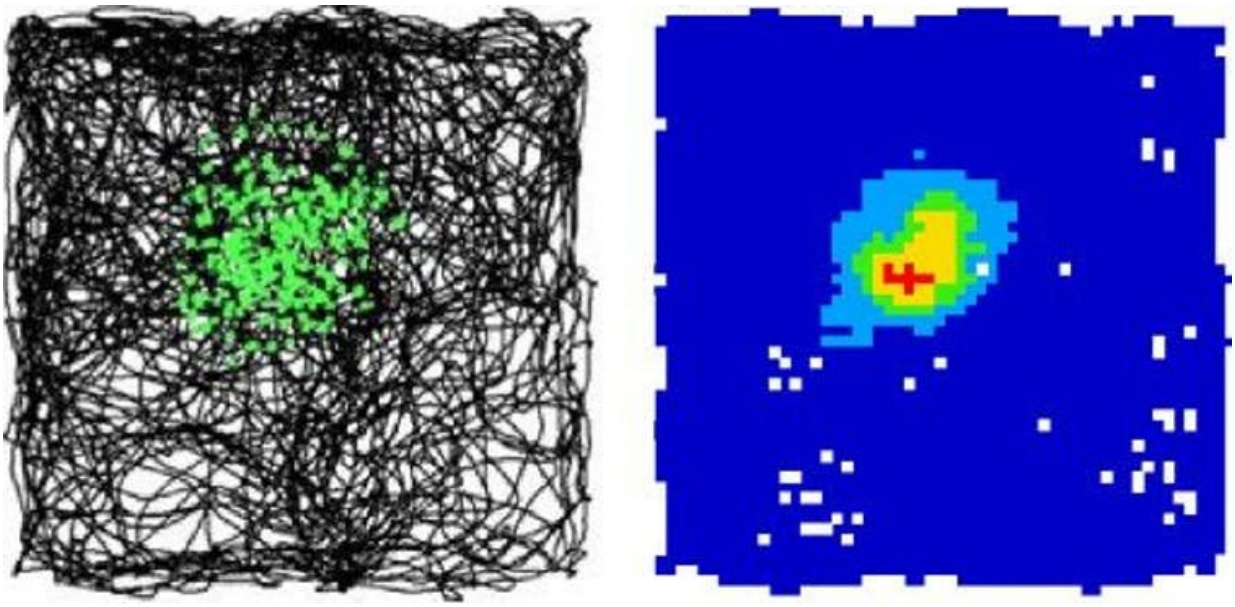
Our goal was to pull together all the evidence at the level of single neurons and use it to model the encoding and recall of scenes which contained meaningful items (for example your friend at the train

station). To do this we assigned specific roles to a large number of spatially selective cells (such as place cells), linking them all together via synaptic connections in the model.

The case that spatially selective brain cells are involved in memory has been made before, but relating them to our experience revealed an interesting discrepancy. Spatially selective cells represent the elements of a scene relative to the scene itself. That is, spatially selective brain cells code for our location and for the locations of scene elements in "world-centered" terms. For simplicity we can liken this reference frame to compass directions – with the train as being south-east of the bakery because this is true, irrespective of our own position and orientation.

However, our direct spatial experience as we perceive a scene is "egocentric" in nature. That is, we perceive the train as being to our right and our friend as being ahead of ourselves. So how do neurons in and near the hippocampus come to represent environmental boundaries and objects in a world-centered format as we memorise a scene?

Memorising the layout of a scene in world-centered terms has the benefit of only needing to memorise one set of related information – such as the train being south-east of the bakery, irrespective of our orientation (the train could be on our right or on our left depending on which way we are facing).



Left: an animal's trajectory (black lines) as it explores a square box. Green dots indicate locations where the place cells was active. Right: colour-coded regions of activity in the square environment (blue means silent, red means maximal activity). Credit: Barry C, Bush D. From A to Z: a potential role for grid cells in spatial navigation. Neural systems & circuits. 2012 Dec;2(1):6., CC BY

Transforming neural representations

Our model shows that this transformation (from egocentric to world-centered) could be performed by another network of spatially selective neurons. Neurons representing the location of objects in the egocentric frame of reference (ahead, left, right) would drive cells in the transformation network, which in turn would activate cells that constitute the world-centered representations. Strengthening connections between these latter cells then corresponds to laying down the memory in long-term storage.

Crucially, this transformation circuit would also act in reverse – neurons

which encode long-term memories could reactivate cells that represented object locations in egocentric terms. In other words, an original event could be re-experienced at a later time. The memory model therefore implements a form of imagery, where the cells which were originally driven by perception at the time of the original event are later reactivated from memory. Importantly the exact content of the reconstruction depends on the imagined heading. If the transformation circuit activated cells representing the train being to your left instead of to your right, we would be imagining facing south and not north.

The model allowed us to simulate brain damage in both humans and rodents, investigating different aspects of amnesia. For instance, a lesion to the transformation circuit can leave us unable to recall a memory. Interestingly our model suggests that the memory is technically still present in and near the hippocampus, but the subject would be unable to reconstruct a mental image of it.

While it is too early to simulate specific diseases such as Alzheimer's, the model may provide a good starting point to deduce how diffuse brain damage – spanning multiple brain areas with distinct functions and containing different spatially selective cells – might affect cognition.

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