The compass within

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Head direction cells have been hypothesized to form representations of an animal's spatial orientation through internal network interactions. New data from mice show the predicted signatures of these internal dynamics.

Have you ever stepped out of the elevator in an office building or hotel and turned down the hallway only to realize that you had turned the wrong way and were headed in the wrong direction? In that moment when something didn't seem right, did the world seem to spin around you as you reoriented to your intended heading? This internal sense of orientation occurs because there are cells in several brain areas that maintain a cognitive representation of your heading. These so-called head direction cells, along with other cells that represent particular locations in an environment, make it possible to know where we are and how to get where we are going. Head direction cells have been hypothesized to maintain a representation of orientation through internal network dynamics, and in an elegant study examining head direction ensembles in mice, Peyrache *et al.*[1] directly reveal these internal network dynamics.

Head direction cells were first reported in a Society for Neuroscience abstract by Ranck in 1984 (Ranck, J.B. Jr., *Soc. Neurosci. Abstr.* **10:599**, 1984), and the first thorough description of them was made by Taube *et al.*[2] in 1990. Head direction cells are found in a number of structures, including the anterior dorsal nucleus of the thalamus (ADN), the postsubiculum (PoS) and the lateral mammillary nuclei[3,4]. A typical head direction cell shows a tight, monotonic tuning to a particular direction, and, as a group, they are thought to represent orientation by the subset of cells that are active at any given time[5].

In the mid-1990s, theoreticians suggested that a mathematical model called an attractor network (now known as a ring attractor) could explain how interactions between head direction cells could generate their directional tuning properties and how the directional representation of heading could be continuously maintained across changing orientations by coherent shifts in the functional interactions in head direction networks[5–8]. This theoretical framework predicted an internal generation of the sense of orientation and explained how sensory cues could keep the representation aligned with the world or could bring it back into register when disoriented[2–5,9–12].

The ring attractor theory proposed that head direction cells that represent nearby directions (with similar tuning curves) would be positively coupled, whereas cells tuned to distal orientations would be negatively coupled[5–8]. This pattern of functional connectivity, local excitation amidst global inhibition, generates a bump or packet of activity. The theory implies that the activity packet should be coherent even in the absence of external input (**Fig. 1**)[5,8,13,14]. The location of the activity packet on the representational ring differentiates one heading from another[5–8]. This internal generation of a heading percept therefore represents a cognitive sense, much like an internal 'neural compass' in which the compass needle corresponds to the packet of active neurons that generate the heading representation. Unlike a compass, which detects an external magnetic field, the head direction system defines its own internal north. Notably, the ring attractor theory predicts that internal neural coordination of the head direction signal is primary[5–9] and that environmental information could become associated with the internal sense to guide navigation[9–12].

The predictions of the ring attractor theory could only be tested with sufficiently large simultaneously recorded neural ensembles. To reveal these attractor dynamics in terms of the functional interactions between neurons, Peyrache *et al.*[1] recorded ensembles of head direction cells from two brain areas, the ADN and the PoS. Notably, pairs of neurons with more similar head direction preferences showed strongly correlated activity in terms of both spike rates and timing, and neuron pairs with very different directional preferences showed negatively correlated activity. Peyrache *et al.*[1] found that the pairwise correlations between head direction cells transitioned from positive to negative correlations at 60 degrees of angular offset, linking the underlying functional network connectivity to the parameters of the tuning curves of individual head direction cells.

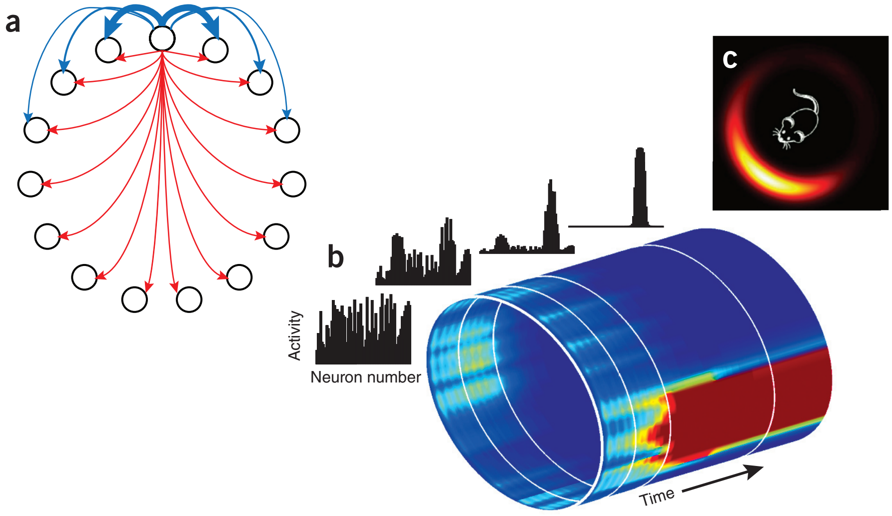

Figure 1 The attractor-network model of the head direction system produces a coherent head direction representation even in the absence of external inputs. (**a**) The ring attractor network. Each cell is positively coupled (blue) to its representational neighbors and negatively coupled (red) to the entire ring, which produces a structure of local excitation amidst global inhibition. (**b**) Even in the absence of external inputs, the internal dynamics of the ring network settles to a 'bump' or 'activity packet' (red, high activity; blue, low activity). This specific simulation was generated using code from ref. 5, but all ring attractor models produce equivalent dynamics. (**c**) An activity packet seen by Peyrache *et al.*[1] during sleep states, showing the 'virtual gaze' of the mouse (reprinted from ref. 1 with permission).

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The ring attractor theory also predicted that the activity packet across the ring attractor should be coherent and self-consistent, even in the absence of external inputs. Peyrache *et al.*[1] evaluated head direction ensemble activity during waking and sleep states, finding coherent, but drifting, representations (what they call the virtual gaze) during sleep. This is clear evidence that functional connectivity in head direction networks is capable of continuously representing adjacent headings in terms of functionally adjacent (overlapping) network states and that the network states that represent different directions are robust across brain states. During slow wave sleep, this coherent representational drift was maintained at a much faster timescale than during waking or REM sleep, which is reminiscent of the temporal compression of hippocampal sequence replay events during slow-wave sleep[15]. Whether the drift in head direction representation during sleep corresponds to any other representations that replay during sleep (such as in hippocampus and neocortex) is a very intriguing, but open, question.

Both of the brain structures that Peyrache *et al.*[1] recorded from exhibited dynamics consistent with attractor theory, but the coordinated activity in ADN exhibited stronger internal coherence than that in PoS. Furthermore, the correlations between ADN-PoS neuron pairs were stronger than the correlations between PoS-PoS neuron pairs. Other researchers have suggested that the ring attractor that underlies the head direction representation occurs upstream of ADN and PoS and is passed down to them[3]. The data from Peyrache *et al.*[1] suggest that the head direction information is passed down from ADN to PoS, but suggest that ADN or its upstream inputs do contain the ring attractor dynamics to generate the internal sense of direction. Further causal manipulations will be required to determine exactly which brain structures internally generate the head direction signal.

The importance of the findings presented by Peyrache *et al.*[1] is that their observation of coherent representations during both waking and sleep states implies an internally generated head direction representation. Their data support the well-developed theory of attractor-based internal generation of the orientation sense in the head direction system. The attractor network framework provides a clear context in which many already established findings regarding the head direction system have been understood. Sometimes, theory suggests incisive experiments that yield results that force us, as researchers, to re-orient the trajectory of our inquiries. In this case, the elegant findings presented by Peyrache *et al.*[1] embody a striking confirmation that these theories have headed us in the right direction.

COMPETING FINANCIAL INTERESTS

The authors declare no competing financial interests.

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Forming artificial memories during sleep

Classical conditioning, such as the association between a tone and an odor, can be induced in sleeping humans. On page 493, de Lavilléon *et al.* report an attempt to create artificial memories in sleeping mice. The authors took advantage of the properties of hippocampal place cells, which are thought to encode specific locations in an animal's environment. Patterns of place cell activity generated during waking are replayed during subsequent sleep. This replay occurs during sharp wave ripples, which are an oscillatory pattern of activity thought to support memory consolidation. Pairing rewarding stimulation with replay of place cell activity, the authors showed that they could indeed induce artificial memories in sleeping mice.

The authors first showed that they could induce false memories in awake mice. They recorded from neurons in area CA1 of the hippocampus as mice explored an arena, analyzing spiking activity online to identify putative place cells. Using a brain-computer interface (BCI), they could pair activity of a particular place cell with stimulation of the medial forebrain bundle (MFB), which is known to be rewarding, with a very short latency (less than 2 ms). Such use of the BCI led mice to linger in the location encoded by the place cell paired with MFB stimulation, and their preference for this location remained even after the BCI was shut off.

In a second cohort of mice, the authors identified place cells while mice explored the arena, but they then allowed the animals to sleep. The BCI was then switched on, again pairing activity of a particular place cell with MFB stimulation, all while the mice slept. When mice were placed back in the arena after they woke up, mice went directly to the location encoded by the place cell whose activity was paired with MFB stimulation, and continued to display a preference for this location throughout the trial.

These results show that it is possible to induce new memories during sleep in mice. While previous studies in humans have shown that classical conditioning and implicit memories can be formed during sleep, this study goes a step further to show that an explicit memory leading to goal-directed behavior can be induced during sleep, and that this can be done using neural recordings and brain stimulation, bypassing sensory inputs. Further, because the memory induced by the authors here relied on activity of place cells that was uncoupled from the animal's actual position, this study provides the strongest evidence yet that place cells have a causal role in spatial memory and navigation.

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