Neural sequences: Hippocampal representation of spatial trajectories in flying bats

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By recording large populations of neurons in flying bats, two recent studies have observed sequential activities in the hippocampus that represent ongoing spatial trajectories during movement and recently experienced trajectories during rest, analogous to 'theta sweeps' and 'replay' previously described in rodents.

The sequential activation of neural populations that encode different actions or stimuli can be used to represent specific sequences of behaviour. In rodents, for example, hippocampal place cells are active only in restricted regions of an environment[1], such that sequences of place cell activity can simulate specific spatial trajectories through that environment. These dynamics are observed both during movement, where the current sequence of locations being traversed is represented by 'sweeps' of place cell firing repeated in each cycle of the 6–12 Hz theta rhythm[2,3], and during rest, where longer trajectories are 'replayed' during sharp-wave ripples — concomitant large amplitude deflections and high frequency oscillations in the local field potential[4]. Although some evidence for theta phase coding and hippocampal reactivation has been found in other mammalian species, including humans[5,6], dynamic sequences of single cell activity during active behaviour and rest have not previously been reported outside of the rodent. Now, two new studies by Forli *et al.*[7] and Eliav, Maimon *et al.*[8] describe hippocampal replay and theta sweeps in Egyptian fruit bats.

In the first study, Forli *et al.*[7] wirelessly recorded large populations of single cells and multi-site local field potentials bilaterally from the dorsal hippocampi of six freely flying bats using high density 'Neuropixels' probes, alongside three-dimensional position, accelerometer data, and echolocation calls. Over the course of each 1–2 hour session, these animals flew between landing platforms in indoor and outdoor enclosures for food rewards. Consistent with previous reports[9], a large proportion of hippocampal units were found to be place cells, with isotropic three-dimensional firing fields that spanned each flight trajectory. Importantly, the authors found that the same sequences of place cell firing observed during flight were recapitulated during waking rest periods at each feeding platform on a compressed timescale of several hundred milliseconds. As in rodents, these events involved a significant fraction of hippocampal place cells (~50% of flight-active neurons on average); tended to co-occur with sharp-wave ripples, which were previously described in local field potential recordings from crawling bats[10]; could replay previous trajectories in both the forward and reverse direction[11]; and represented both local and nonlocal trajectories that had been experienced recently or remotely[12]. Intriguingly, the authors also found that replay events tended not to occur during echolocation, which is consistent with the observation that sharp-wave ripples in other species are reduced during active engagement with the environment.

In the second study, Eliav, Maimon *et al.*[8] carried out wireless tetrode recordings from the dorsal hippocampus of seven bats flying freely between two landing points at the end of very long (130 m or 200 m) tunnels, as well as during sleep periods before and after. Consistent with the results described by Forli *et al.*[7], they also found that sequences of place cell firing corresponding to coherent spatial trajectories were recapitulated during rest — in this case, both in wake and sleep. Again, these replay events could encode both local and nonlocal trajectories in the forward or reverse direction, and were accompanied by increased population firing rate and sharp-wave ripples. Interestingly, however, the lengths of simulated trajectories were much smaller than behavioural trajectories through the environment (~8 m on average), suggesting that the hippocampus might 'chunk' longer experiences into shorter packets that are replayed independently (or sometimes successively, across several consecutive sharp-wave ripples[13]).

Next, Forli *et al.*[7] examined place cell dynamics during flight to look for evidence of theta sweeps, which may be essential to encode ongoing experience for subsequent replay[14]. While they found little evidence for theta band activity in the hippocampal local field potential, the spike trains of a large proportion of place cells (326/875, or 37%) were significantly modulated by the 8 Hz wing-beat frequency. Moreover, spike train rhythmicity was slightly but persistently faster in many of those place cells (147/326, or 45%), such that they fired at progressively earlier phases of each wingbeat cycle as their firing fields were traversed, consistent with observations of theta phase precession in rodents[15]. This resulted in 'theta sweeps' during flight: sequences of neural activity in each wingbeat cycle that encoded the ongoing movement trajectory[2,3]. Interestingly, the authors found that theta sweeps — like replay events — were also disrupted during echolocation. This may account for the previous observation that place fields are smaller during these periods[16], because they incorporate less prospective or retrospective firing.

The results presented by Forli *et al.*[7] and Eliav, Maimon *et al.*[8] are the

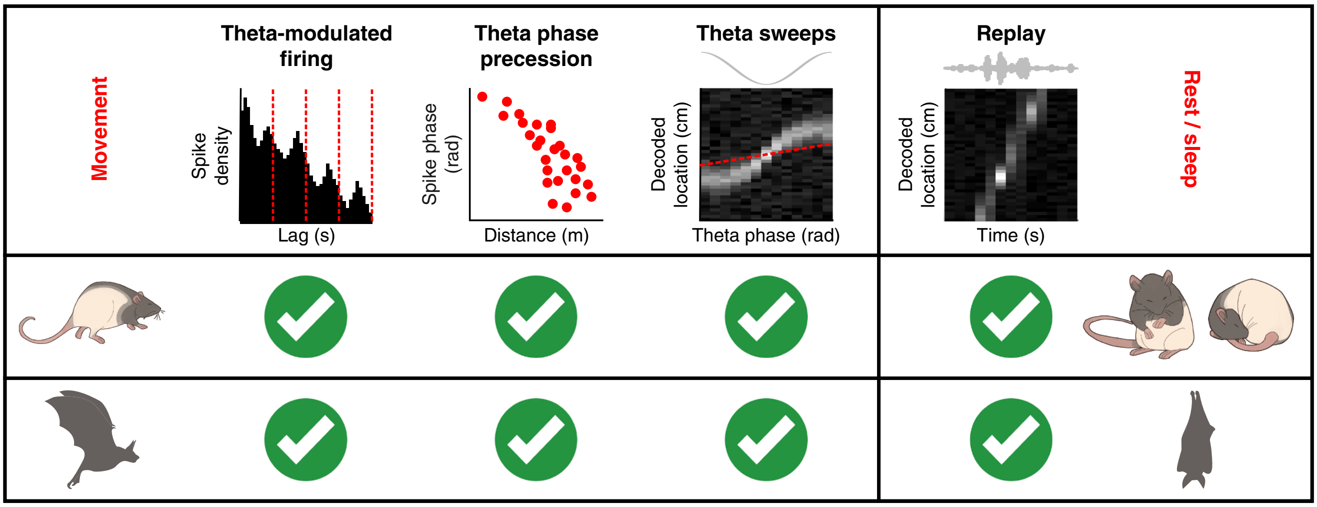

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Figure 1. Hippocampal neural sequences during movement and rest in rodents and flying bats.
During active translational movement (left), recordings of hippocampal single unit activity in both rodents and flying bats show: theta modulated firing, whereby the firing rate (or 'spike density') of a significant proportion of cells is higher at specific theta phases (red dashed vertical lines demarcate individual theta cycles); theta phase precession, whereby the preferred firing phase in each oscillatory cycle becomes progressively earlier as the firing field is traversed; and theta sweeps, whereby the location decoded from place cell population activity sweeps from immediately behind to immediately in front of the animal's current location (red dashed line) along its current movement direction within each theta cycle (grey line). During periods of waking rest or sleep (right), place cell population activity recapitulates spatial trajectories that have previously been experienced on a compressed timescale, typically during sharp-wave ripples (grey line). (Rats by Can Liu and Yu Kang; flying bat by Tiago Branco and Gil Costa from SciDraw (CC BY 4.0).)

first demonstration of neural sequences outside the rodent brain, the observation of which requires the simultaneous recording of large populations of neurons. The close correspondence between theta sweeps and replay in bats and rodents suggests conserved neural mechanisms of hippocampal processing across mammalian species — although some important differences also remain. For example, replay events in bats appear to last longer than in the rodent (with median durations of 358 ms and 210 ms in Forli *et al.*[7] and Eliav, Maimon *et al.*[8], respectively, compared to ∼100 ms in rats[4,11–14]). Moreover, the duration of replay events in bats did not scale with the length of the represented trajectory, such that longer trajectories were replayed more rapidly, unlike in rodent data[13]. As a result, the speed of simulated trajectories was faster in bats, although their movement speed is also much faster, such that they exhibited a lower 'compression ratio' (the ratio between replayed and real trajectory speeds) compared to rodents.

These results[7,8] from flying bats also contrast with the absence of spike train theta rhythmicity in the same species during crawling[17,18], possibly reflecting the fact that flying is the more natural mode of translational movement. Instead, the same authors have previously identified single cell phase precession against 'non-oscillatory' local field potential signals whose frequency varied dynamically over a wide (1–10 Hz) range in crawling bats[18]. This suggests that sequential representations of the current movement trajectory may also have been present, although insufficient cells were recorded to test that hypothesis. Hippocampal theta oscillations are similarly disrupted in rodents during passive movement through an environment, even though place cell firing remains stable[14]. The absence of local field potential theta rhythmicity during flight is puzzling, however, given the relatively high proportion of cells with theta modulated firing rates. In addition, previous wireless recordings from the same species during flight found that very few hippocampal cells (<3%) exhibited spike train theta rhythmicity[9], in contrast to the results of Forli *et al.*[7].

In summary, these new results[7,8] suggest that bats exhibit theta sweeps and phase coding that closely resemble rodent data during their most natural form of movement — free flying — together with the replay of longer trajectories during periods of waking rest and sleep (Figure 1). Although the absence of local field potential theta oscillations in bats is unexpected, the relationship between rhythmic hippocampal activity and wing beats has some parallels in rodent studies, where paw movements during memory guided locomotion can exhibit theta phase locking[19]. It is also worth noting that theta oscillations typically occur in short bouts in human hippocampal local field potential recordings, even during active walking[20]. Future studies that make use of new technologies to record large populations of neurons in other species, including humans actively navigating in ethologically valid contexts, should aim to establish whether neural sequences during theta sweeps and replay events are a canonical mechanism of hippocampal information processing.

DECLARATION OF INTERESTS

The authors declare no competing interests.

REFERENCES

1. O'Keefe, J., and Dostrovsky, J. (1971). The hippocampus as a spatial map. Preliminary evidence from unit activity in the freely-moving rat. Brain Res. *34*, 171–175.

2. Burgess, N., Recce, M., and O'Keefe, J. (1994). A model of hippocampal function. Neural Networks *7*, 1065–1081.

3. Skaggs, W.E., McNaughton, B.L., Wilson, M.A., and Barnes, C.A. (1996). Theta phase precession in hippocampal neuronal populations and the compression of temporal sequences. Hippocampus *6*, 149–172.

4. Lee, A.K., and Wilson, M.A. (2002). Memory of sequential experience in the hippocampus during slow wave sleep. Neuron *36*, 1183–1194.

5. Qasim, S.E., Fried, I., and Jacobs, J. (2021). Phase precession in the human hippocampus and entorhinal cortex. Cell *184*, 3242–3255.

6. Zheng, J., Yebra, M., Schjetnan, A.G.P., Patel, K., Katz, C.N., Kyzar, M., Mosher, C.P., Kalia, S.K., Chung, J.M., Reed, C.M., *et al*. (2024). Theta phase precession supports memory formation and retrieval of naturalistic experience in humans. Nat. Hum. Behav. *8*, 2423–2436.

7. Forli, A., Fan, W., Qi, K.K., and Yartsev, M.M. (2025). Replay and representation dynamics in the hippocampus of freely flying bats. Nature, https://doi.org/10.1038/s41586-025-09341-z.

8. Eliav, T., Maimon, S.R., Sarel, A., Palgi, S., Las, L., and Ulanovsky, N. (2025). Fragmented replay of very large environments in the hippocampus of bats. Cell *188*, 4091–4105.e16.

9. Yartsev, M.M., and Ulanovsky, N. (2013). Representation of three-dimensional space in the hippocampus of flying bats. Science *340*, 367–372.

10. Ulanovsky, N., and Moss, C.F. (2007). Hippocampal cellular and network activity in freely moving echolocating bats. Nat. Neurosci. *10*, 224–233.

11. Foster, D.J., and Wilson, M.A. (2006). Reverse replay of behavioural sequences in hippocampal place cells during the awake state. Nature *440*, 680–683.

12. Karlsson, M.P., and Frank, L.M. (2009). Awake replay of remote experiences in the hippocampus. Nat. Neurosci. *12*, 913–918.

13. Davidson, T.J., Kloosterman, F., and Wilson, M.A. (2009). Hippocampal replay of extended experience. Neuron *63*, 497–507.

14. Drieu, C., Todorova, R., and Zugaro, M. (2018). Nested sequences of hippocampal assemblies during behavior support subsequent sleep replay. Science *362*, 675–679.

15. O'Keefe, J., and Recce, M.L. (1993). Phase relationship between hippocampal place units and the EEG theta rhythm. Hippocampus *3*, 317–330.

16. Ulanovsky, N., and Moss, C.F. (2011). Dynamics of hippocampal spatial representation in echolocating bats. Hippocampus *21*, 150–161.

17. Yartsev, M.M., Witter, M.P., and Ulanovsky, N. (2011). Grid cells without theta oscillations in the entorhinal cortex of bats. Nature *479*, 103–107.

18. Eliav, T., Geva-Sagiv, M., Yartsev, M.M., Finkelstein, A., Rubin, A., Las, L., and Ulanovsky, N. (2018). Non-oscillatory phase coding and synchronization in the bat hippocampal formation. Cell *175*, 1119–1130.

19. Joshi, A., Denovellis, E.L., Mankili, A., Meneksedag, Y., Davidson, T.J., Gillespie, A. K., Guidera, J.A., Roumis, D., and Frank, L.M. (2023). Dynamic synchronization between hippocampal representations and stepping. Nature *617*, 125–131.

20. Aghajan, Z., Schuette, P., Fields, T.A., Tran, M.E., Siddiqui, S.M., Hasulak, N.R., Tcheng, T.K., Eliashiv, D., Mankin, E.A., Stern, J., *et al*. (2017). Theta oscillations in the human medial temporal lobe during real-world ambulatory movement. Curr. Biol. *27*, 3743–3751.

Cell migration: How animal cells run and tumble

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Animal cells migrating up chemotactic gradients often show speed oscillations. A new study describes a molecular circuit that switches zebrafish germ cells between phases of straight runs, tumbling and directional reorientation.

When a bacterium swims up a chemotactic gradient, it uses the famous 'run and tumble' strategy, one of the most thoroughly investigated paradigms in molecular biology. The bacterium measures the concentration of the attractant and, whenever it is higher than that previously encountered, it keeps swimming on in the same direction. While it does so, it continuously adapts its sensory system to the increasing concentrations, allowing it to maintain this migration. If the concentration decreases, the bacterium transiently reverses the direction of its flagellar motor, which makes the cell body tumble for a moment, and then the bacterium swims off in another — random — direction. Repeating this process guides the bacterium along a 'biased random walk' towards the attractant[1] (Figure 1). For an organism that is small and fast, such a temporal sensing regime is the most efficient way to detect differences in attractant concentrations. Larger and slower cells have another option: they can spatially sense differences in attractant concentrations across their cell body. Chemoattractant receptors are randomly distributed on the cell surface of amoebae and animal cells. The receptors located on the region of the cell closest to the higher levels of attractant bind more attractant than those on other parts of the cell. In response to this signal asymmetry, the cell triggers the polymerization of its actin cytoskeleton accordingly, and the resulting flow of actin moves the cell towards the higher levels of attractant[2].

Like the bacterium, the animal cell has to fulfill two tasks: turn the signal asymmetry of the gradient into a clear front–back polarization (which causes movement), and adapt the sensory system to the ambient concentrations of chemoattractant. While both polarity and adaptation could in principle be continuous, a landmark study in neuronal growth cones showed that adaptation is associated with a transient arrest in migration that goes along with a partial

