Motivational state influences the content of hippocampal sequences

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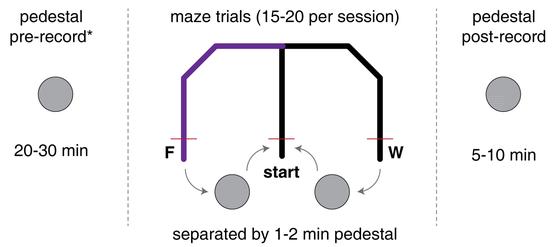
Introduction

Spatial trajectories (paths) traversed by behaving rodents can be accurately decoded from the activity of place cell ensembles. Similar activity patterns can be observed – in compressed form – in the absence of overt behavior during sharp wave-ripple complexes (SWRs). Although this phenomenon was originally referred to as "replay", the content of SWR-associated **hippocampal sequences** is not limited to repeats of previous experience. In particular, hippocampal sequences can include **never-experienced trajectories** [1-3], and are **biased towards goal locations** [4], suggesting a possible role in planning (model-based decision-making).

To develop this idea, we recorded hippocampal SWR sequences during **motivational shifts:** with food and water reward available on different arms of a T-maze, rats were alternately food- and water-restricted. Adaptive behavior under such circumstances is thought to require **model-based prediction** and **evaluation**, and thus provides a test case for proposals regarding the functional role of SWR-associated sequences.

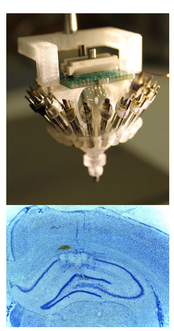
Methods

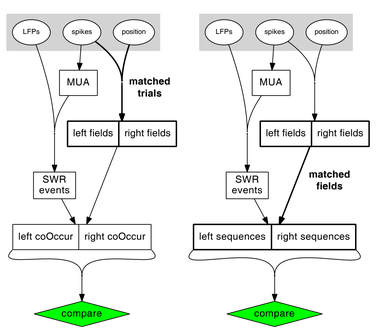


maze pretraining: 4 days
surgery + recovery (7 days)
maze retraining: 2-5 days

days 1, 3, 5: food restriction; days 2, 4, 6: water restriction overnight
(*"reminder" of both rewards prior to each session)

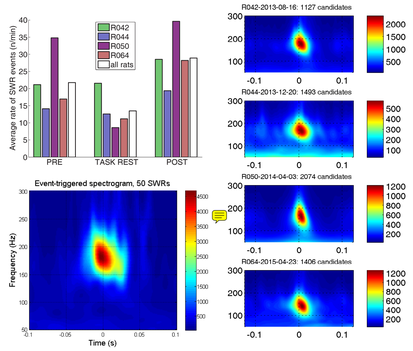
Task: Rats (n = 4) performed a simple T-maze task with food reward (**F**) available at the end of the left arm, and water reward (**W**) at the end of the right arm. During recording (6 daily sessions per rat), rats were alternately food- or water-restricted.





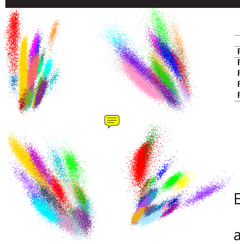
Analysis: Two main analyses comparing place cell activity corresponding to the left and right maze arms were performed: (1) **pairwise co-occurrence** z-scores, normalized to ISI-shuffled controls (middle panel; note we used matched numbers of trials to estimate place fields), and (2) template-based **sequence detection**, using $p < 0.001$ relative to cell identity and within-event spike time shuffles (right panel; note we used matched place fields).

Candidate events



Candidate events were detected using a scoring algorithm which combines (1) spectral similarity of the local field potential to manually selected "gold-standard" events, and (2) multi-unit activity with an adaptive threshold. Figures show the distribution of candidate events over task phases (left, top), an example event-triggered spectrogram for manually selected events (left, bottom) and example event-triggered spectrograms for candidate events (right).

Neural units

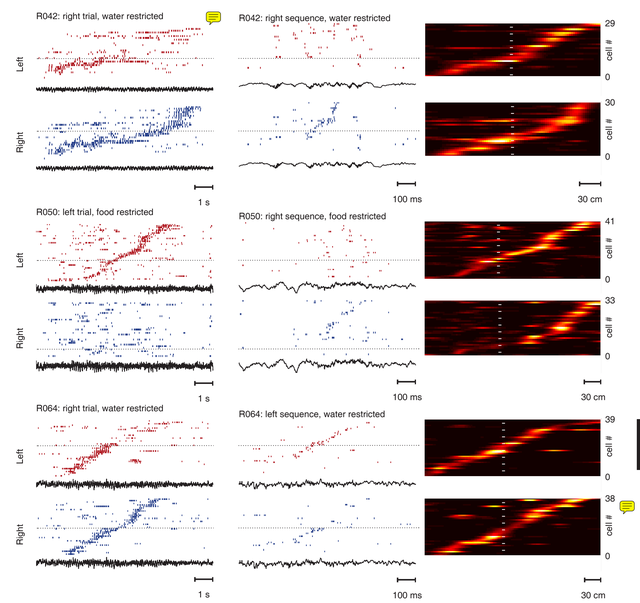


	Session 1		Session 2		Session 3		Session 4		Session 5		Session 6		Total	
Rat ID	L	R	L	R	L	R	L	R	L	R	L	R	L	R
R042	4	3	20	12	26	30	13	6	17	16	21	18	**101**	**85**
R044	8	8	3	6	12	15	13	9	5	9	6	12	**47**	**59**
R050	21	25	32	30	21	27	31	33	40	33	34	30	**179**	**178**
R064	34	33	32	38	36	37	35	50	50	48	39	38	**226**	**244**

Rat ID	Session 1	Session 2	Session 3	Session 4	Session 5	Session 6	Total
R042	22	74	107	64	73	59	**399**
R044	17	13	43	53	50	41	**217**
R050	72	94	72	113	128	112	**591**
R064	121	136	116	162	178	151	**864**

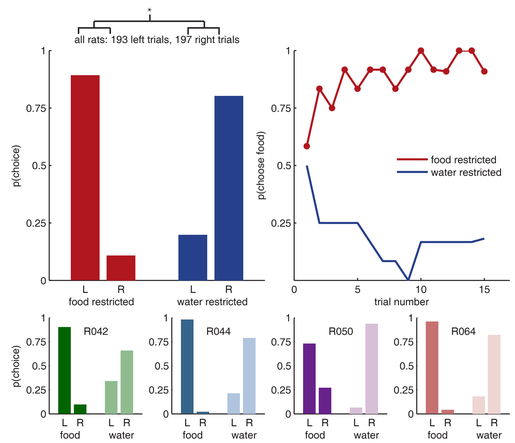
Example clusters (4 tetrodes from same session, left) and numbers of recorded units (above).

Example sequences



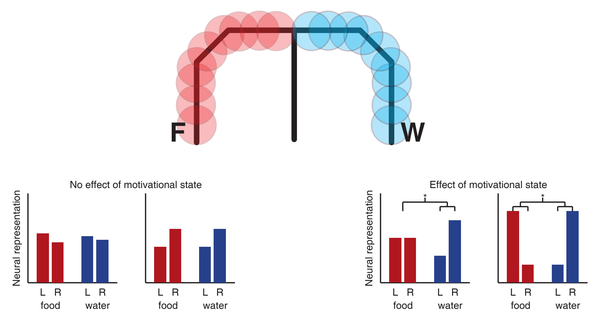
Rasterplots of activity during single trials (left), tuning curves (one row per cell matching rasterplot; middle) and example SWR-associated sequences (right) for three different rats

Behavior



Behavior: Rats reliably preferred the arm containing the restricted food type (top left), although not necessarily on the first trial (top right). In some sessions, for some trials, we blocked one arm to ensure that each session contained a minimum of 5 trials on the non-preferred arm. These blocked trials were not counted in the above data.

Hypothesis



Hypothesis: For those cells with place fields on the left and right arms separately, we used **pairwise co-occurrence** and the **number of significant sequences** to test for effects of motivational state.

Because individual rats and/or sessions may have idiosyncratic biases for the left (food) or right (water) arm, we tested for an **interaction** of motivational state (food/water restriction) and arm (left/right).

We hypothesized that hippocampal sequences would be more likely to occur on the arm corresponding to the currently desired outcome, i.e. hungry rats would (p)replay the food arm more.

References and acknowledgements

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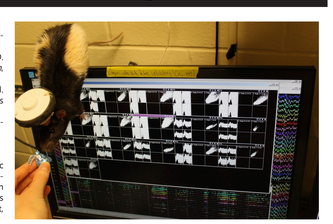
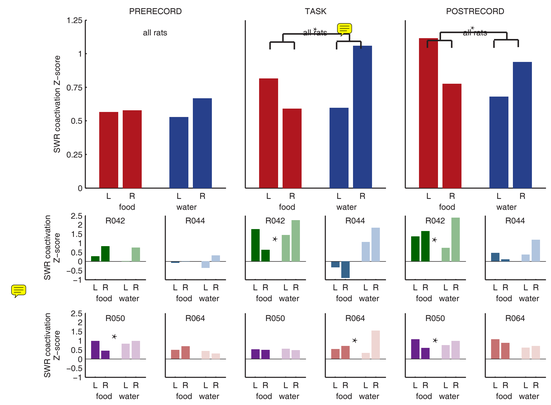
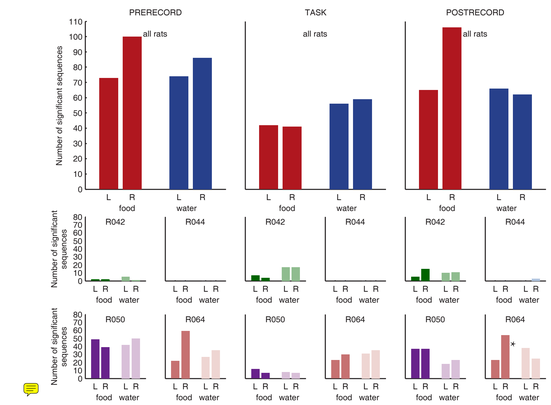


Results



Pairwise co-occurrence: Across all rats, and in 2 out of 4 rats individually, motivational state had a significant effect on the content of hippocampal sequences during TASK and POSTRECORD. During PRERECORD, a significant effect was only detected in one rat (R050).



Sequences: Across all rats, motivational state did not have a significant effect on the content of hippocampal sequences in any phase during the session, or overall. In 1 out of 4 rats (R064) there was a significant effect in POSTRECORD.

Conclusions and caveats

Viewed through the lens of pairwise co-activation, we found evidence that motivational state biases the content of hippocampal sequences towards the favored reward: hungry rats are more likely to activate pairs of cells with fields on the food arm of the maze, and thirsty rats are more likely to activate pairs of cells on the water arm.

However, only for one rat was this effect apparent BEFORE the task, so it remains to be clarified to what extent reactivation of recent experience explains motivational sequence content bias in other rats.

When examining full sequences, different rats show idiosyncratic patterns that can diverge from the co-occurrence results. We are currently investigating the sources of this difference, and the properties of different sequence analysis methods more generally, using generative models of hippocampal sequences.