

Article

Moving bar of light evokes vectorial spatial selectivity in the immobile rat hippocampus

<https://doi.org/10.1038/s41586-022-04404-x>

Received: 1 May 2020

Accepted: 4 January 2022

Published online: 9 February 2022

 Check for updates

Chinmay S. Purandare^{1,2,5}, Shonali Dhingra^{1,5}, Rodrigo Rios¹, Cliff Vuong¹, Thuc To¹, Ayaka Hachisuka¹, Krishna Choudhary¹ & Mayank R. Mehta^{1,3,4} 

Visual cortical neurons encode the position and motion direction of specific stimuli retrospectively, without any locomotion or task demand¹. The hippocampus, which is a part of the visual system, is hypothesized to require self-motion or a cognitive task to generate allocentric spatial selectivity that is scalar, abstract^{2,3} and prospective^{4–7}. Here we measured rodent hippocampal selectivity to a moving bar of light in a body-fixed rat to bridge these seeming disparities. About 70% of dorsal CA1 neurons showed stable activity modulation as a function of the angular position of the bar, independent of behaviour and rewards. One-third of tuned cells also encoded the direction of revolution. In other experiments, neurons encoded the distance of the bar, with preference for approaching motion. Collectively, these demonstrate visually evoked vectorial selectivity (VEVS). Unlike place cells, VEVS was retrospective. Changes in the visual stimulus or its predictability did not cause remapping but only caused gradual changes. Most VEVS-tuned neurons behaved like place cells during spatial exploration and the two selectivities were correlated. Thus, VEVS could form the basic building block of hippocampal activity. When combined with self-motion, reward or multisensory stimuli⁸, it can generate the complexity of prospective representations including allocentric space⁹, time^{10,11} and episodes¹².

Sensory cortical neurons generate selective responses to specific stimuli, in an egocentric (for example, retinotopic) coordinate frame, without any locomotion, memory or rewards¹. By contrast, the hippocampus is thought to contain a visually evoked, abstract, allocentric cognitive map, supported by spatially selective place cells², grid cells¹³ and head direction cells¹⁴. These responses are thought to arise from not only visual³ but also self-motion cues^{9,15}, for example, via path integration¹⁶. Recent studies have demonstrated hippocampal activity modulation by auditory^{17–19} or social stimuli^{20,21}. However, to elicit these responses, additional behavioural, cognitive or reward variables were required, whose removal nearly eliminated hippocampal selectivity^{17,18,22–25}. To our knowledge, no study has yet demonstrated hippocampal neural selectivity to a moving visual stimulus, without self-motion or rewards, similar to that found in visual cortices, even though they provide a major input to the hippocampus, and are thought to be crucial for hippocampal function. Hence, we investigated whether place cells encode the angular and linear position as well as motion direction of a simple stimulus, regardless of self-motion, memory or reward.

Rats were gently held in place on a large spherical treadmill, surrounded by a cylindrical screen²⁶. They could move their heads around the body by a small amount but could not turn their body. To keep them motivated, they were given random rewards, similar to typical place cell experiments, and were pretrained to do a virtual navigation task in the same apparatus (Methods). The only salient visual stimulus during the experiments was a vertical bar of light that was 74 cm tall, 7.5 cm wide and 33 cm away from

the rat, thus subtending a 13° solid angle. In the first set of experiments, the bar revolved around the rat at a constant speed (36° s⁻¹), without any change in shape or size (Fig. 1a, b). The revolution direction of the bar switched between clockwise (CW) and counterclockwise (CCW; or ‘anticlockwise’) every four revolutions. In subsequent experiments, we varied the colour, pattern, movement direction and trajectory of the bar. A majority of neurons showed selective responses in all cases.

Most CA1 neurons encode stimulus angle

We measured the activity of 1,191 putative pyramidal neurons (with a firing rate above 0.2 Hz during the experiment) from the dorsal CA1 of eight Long-Evans rats in 149 sessions using tetrodes (Methods)⁸. Many neurons showed clear modulation of firing rate as a function of the angular position of the bar, that is, angle VEVS (aVEVS) (Fig. 1c), with elevated firing rates in a limited region of visual angles. Across the ensemble of neurons, 464 (39%) showed significant (sparsity (z) > 2, corresponding to $P < 0.023$) (Methods, Extended Data Fig. 1) tuning in either the CW or CCW direction (Fig. 1d). These were classified as tuned cells, in contrast with untuned cells with $z < 2$.

Similar to the visual cortical neurons and hippocampal place cells, most tuning curves were unimodal (Extended Data Fig. 2) with a single preferred angle where the firing rate was the highest. Off responses (a significant decrease in firing rate) were virtually nonexistent. The preferred angles spanned the entire range, including angles behind the rat

¹W.M. Keck Center for Neurophysics, Department of Physics and Astronomy, UCLA, Los Angeles, CA, USA. ²Department of Bioengineering, UCLA, Los Angeles, CA, USA. ³Department of Neurology, UCLA, Los Angeles, CA, USA. ⁴Department of Electrical and Computer Engineering, UCLA, Los Angeles, CA, USA. ⁵These authors contributed equally: Chinmay S. Purandare, Shonali Dhingra.  e-mail: MayankMehta@ucla.edu

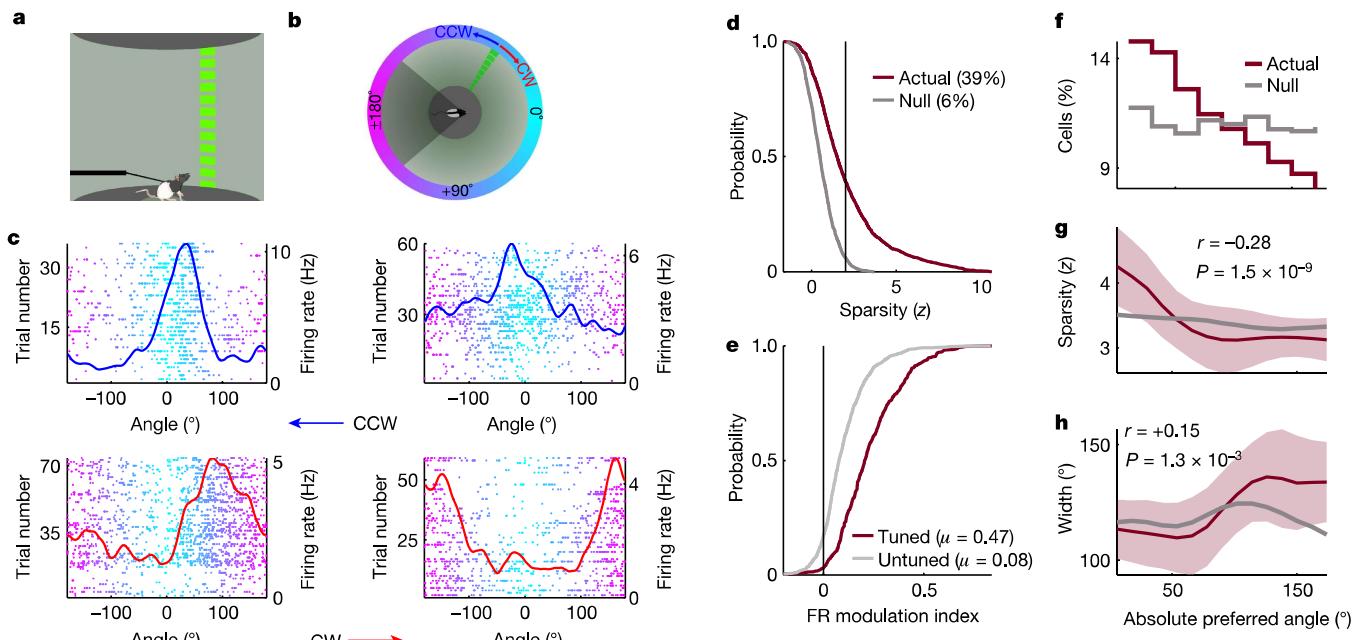


Fig. 1 | Hippocampal response to a revolving bar of light. **a, b**, Schematic of the experimental setup (**a**) and its top-down view (**b**). The field of view is 270° for the rat. The region behind the rat (dark grey) is invisible to him. CCW, counterclockwise; CW, clockwise. **c**, Trial number (yaxis on the left) and firing rates (yaxis on the right) of four CA1 neurons as a function of the angular position of the bar (front is 0°; behind is ±180°). Revolution direction of the bar: CCW is in blue (top); CW is in red (bottom). **d**, Cumulative distribution function of the strength of tuning (z-scored sparsity; Methods); response with higher tuning was chosen between CCW and CW (**d–f**). The measured data (maroon line) show significantly greater ($P=1.26 \times 10^{-89}$, Kolmogorov–Smirnov test here

and in **e**) tuning than the shuffled data (grey line). 39% of neurons showed significant ($z > 2$) tuning. **e**, Cumulative distribution function of the firing rate (FR) modulation index within versus outside the preferred zone (Methods) for tuned cells ($z > 2$) was significantly different ($P=1.9 \times 10^{-50}$) than untuned ($z < 2$) cells. **f**, Twice as many tuned cells (y axis) had their preferred angles (angle of maximal firing; x axis) in the front than behind. **g**, z -scored sparsity (the solid line is the median and the shaded area is the s.e.m. here and in **h**) of tuned cells decreased as a function of their preferred angle (Pearson correlation coefficient, here and in **h**, is also included). **h**, Full-width at quarter maxima of tuned responses increased with the preferred angle.

that he could not see barring rare occasions (Fig. 1f). These responses resembled striate cortical neurons in many ways^{1,27}. More neurons encoded the positions in front of the rat (0°) and there was a gradual twofold decline in the number of tuned cells for angles behind (±180°). The strength of aVEVS (Fig. 1g, Methods) was much larger near 0° than near 180°. The tuning curve width increased gradually (from 114° to 144°) (Fig. 1h) as a function of the absolute preferred angle from 0° to 180°. However, the widths were quite variable at every angle, spanning about one-third of the visual field, similar to place cells on linear tracks^{28,29}.

Hippocampal place cells on one-dimensional tracks have high firing rates within the field with little spiking outside²⁸. By contrast, most neurons with significant aVEVS spiked considerably outside the preferred zone, as evidenced by modest values of the firing rate modulation index (Fig. 1e, Methods). These broad aVEVS tuning curves resembled the angular tuning of CA1 neurons recently reported in the real world and in virtual reality³⁰, with a comparable fraction of neurons showing significant angular tuning. The trial-to-trial variability of aVEVS was comparable to recent experiments in visual cortex of mice under similar conditions³¹. Notably, the variability in the mean firing rate across trials was small and unrelated to the degree of aVEVS. However, the trial-to-trial variability of the preferred angle was quite large and predictive of the degree of aVEVS of a neuron (Extended Data Fig. 3).

inspected the selectivity, directionality and stability (Methods) of the aVEVS. The firing rates were comparable for most neurons in two directions of revolution (see below). The degree of tuning varied continuously across neurons with no clear boundary between tuned and untuned neurons (Extended Data Fig. 4). Some neurons were bidirectional, that is, significant ($z > 2$) aVEVS in both directions of revolution (Fig. 2a, Extended Data Fig. 4). However, a larger subset of neurons was unidirectional, with significant ($z > 2$) aVEVS in only one movement direction (Fig. 2b, Extended Data Fig. 4). There were many untuned stable neurons, which were deemed untuned based on the standard, z -scored sparsity criteria ($z < 2$) but showed consistent, significantly stable (stability Kolmogorov–Smirnov test $P < 0.05$; Methods) spiking across trials (Fig. 2c, Extended Data Fig. 4). Across the ensemble, 13% (154) of neurons were bidirectional, 26% (310) were unidirectional, and the majority, 35% (421), were untuned stable (Fig. 2d, Extended Data Fig. 4). Thus, the vast majority (74%, 885) of hippocampal pyramidal neurons were consistently modulated by the angular position and direction of the revolving bar. However, unlike the visual cortex, far more aVEVS neurons were unidirectional, and unlike hippocampal place cells and the visual cortex, a far greater number of neurons showed untuned but stable responses. The preferred tuning angle was around 0°, that is, in front of the rat for most neurons (Extended Data Fig. 5), and this bias was greater for the bidirectional cells.

The highest (and significant) correlation between CCW and CW tuning curves was seen for bidirectional cells, followed by unidirectional cells and then untuned stable cells, but not for the untuned unstable cells (Extended Data Fig. 5). The mean rates were comparable in two directions, but were significantly larger in the direction with better aVEVS, largely because of an increase in firing within the preferred zone (±90° around the preferred angle) in the tuned direction. Higher rate cells were more likely to be bidirectional than unidirectional, even after accounting for the differences in firing rate (Extended Data Fig. 6).

Revolution direction selectivity of aVEVS

In the primary visual cortex, the majority of neurons respond selectively to the angular position of a stimulus, regardless of its movement direction¹. However, the majority of hippocampal neurons on linear tracks are directional, with far greater firing rate in one direction of journey^{8,28}. Furthermore, in both areas, neurons that are active in both directions, show significant and stable selectivity in both directions too. Hence, we

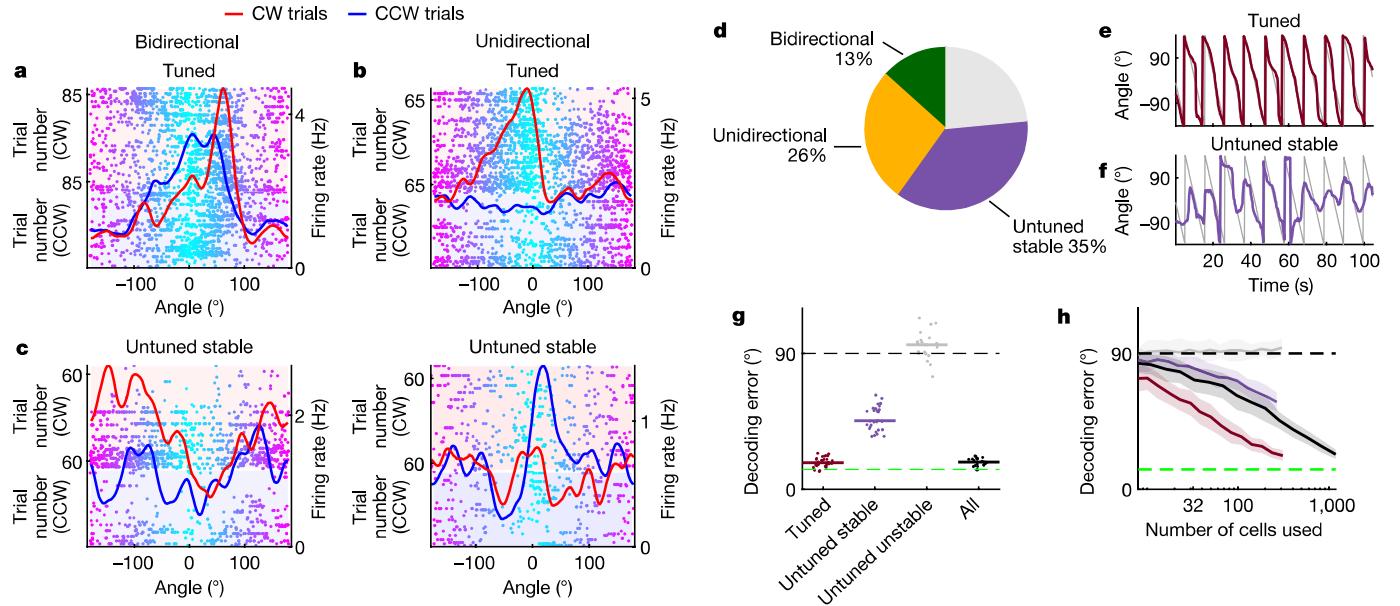


Fig. 2 | Directionality, stability and ensemble decoding of aVEVS. **a**, A bidirectional cell, with significant ($z > 2$) tuning in both CCW and CW directions. **b**, Similar to **a**, but for a unidirectional cell, with significant tuning in only one direction (CW). **c**, Cells with multi-peaked, stable responses that did not have significant sparsity or tuning ($z < 2$) (bidirectional stable is shown on the left; unidirectional stable (CCW) is shown on the right). **d**, Distribution of selectivity. **e**, Decoded angle using only tuned cells in the CCW direction (maroon). **f**, Same as **e** but using only the untuned stable cells (lavender). **g**, Median error between stimulus angle and decoded angle over 30 instantiations

of 10 trials each for actual and shuffled data (not shown). The decoding errors for tuned ($\mu \pm \text{s.e.m.} = 17.6 \pm 0.6^\circ$) and untuned stable ($45.2 \pm 1.4^\circ$) were significantly less than that of shuffles (Kolmogorov–Smirnov test $P = 1.8 \times 10^{-14}$ for both). **h**, Decoding error (median $\pm \text{s.e.m.}$) decreases with increasing population size for all (black), tuned (maroon) and untuned stable (lavender) cells, but not for untuned unstable cells (grey). Grey shading denotes s.e.m. In **g** and **h**, the green dashed line indicates the width of the visual cue, and the black dashed line indicates the median error expected by chance.

Population vector decoding of aVEVS

In addition to individual cells, the population responses were also coherent for tuned and untuned stable populations (Methods, Extended Data Fig. 7). During spatial exploration, the ensemble of a few hundred place cells was sufficient to decode the position of the rat using population vector decoding³². Using similar methods, we decoded the angular position of the bar (Methods).

The ensemble of 310 tuned cells (CCW), with a short temporal window of 250 ms, could decode the angular position of the bar with a median accuracy of 17.6° (Fig. 2e, g), comparable to the bar width (13°) and similar to position decoding with place cells^{7,32}. In addition, the 266 untuned stable cells (CCW shown) could also decode the position of the bar significantly better than chance. Although the median error of 45.2° (Fig. 2f, g) was larger than that for the tuned cells, it was much smaller than chance (90°), further demonstrating significant aVEVS in untuned stable cells. Decoding performance improved when using a larger number of tuned or untuned stable cells (Fig. 2h). Thus the ensemble of untuned stable cells contained significant stimulus angle information, even though these individual cells did not³³. This was not the case for the untuned unstable cells.

aVEVS is retrospective

Under most conditions, visual cortical neurons respond to the stimulus with a short latency, that is, retrospectively, whereas most hippocampal bidirectional cells on linear tracks are prospective³, that is, they fire before the rat reaches a given position from the opposite movement directions^{6–8}. However, the converse was true for the bidirectional aVEVS (Extended Data Fig. 8). The preferred angle in the CCW direction lagged behind that in the CW direction (example cell) (Fig. 3c), that is, in both directions, the neuron responded to the bar after it had gone past a specific angle, which is a retrospective response. The circular difference

between the preferred angle between the CW and CCW directions (bidirectional population response) (Fig. 3a, b) was predominantly positive. We next asked whether only the peaks of aVEVS are retrospective or if the entire tuning curves show lagged responses. The cross-correlation between the entire tuning curves between the CW and CCW directions (Fig. 3d) of the majority (80%) of neurons showed maximum correlation at positive latency. Thus, most neurons responded to the moving bar retrospectively, that is, with a lag.

The median latency to response was 276.4 ms, which translates to a 19.9° median shift in cross-correlation (Fig. 3e). This retrospective coding was evident across the entire ensemble of bidirectional cells, such that the overlap of the population vector between the two directions was highest at values slightly above the diagonal (Fig. 3f, Methods).

Unidirectional cells also showed retrospective tuning, with a cross-correlation latency (19.9° , or 276.4 ms) comparable to bidirectional cells (Extended Data Fig. 9). Thus, the retrospective coding does not arise due to difference in tuning strengths. Small but significant retrospective bias was also observed in the untuned stable cells but not for the unstable cells (Extended Data Fig. 9). Additional experiments using a photodiode showed that this lag could not be explained by the latencies in the recording equipment (Extended Data Fig. 10).

Gradual change in aVEVS with stimuli and time

Change in distal visual cues causes remapping in place cells, that is, large changes in firing rate, degree of spatial selectivity and the preferred location^{34,35}. Conversely, primate hippocampal neurons show selectivity to a visual stimulus³⁶. To address this, we measured the responses of the same set of neurons, on the same day, to bars of light with gradual changes in their visual features (Methods), without any other changes. First, we changed the stimulus minimally (pattern change; row 1 in Fig. 3g, Fig. 3h–j). Neural firing rates, preferred tuning location and tuning curve profiles were largely invariant and comparable to intra-session

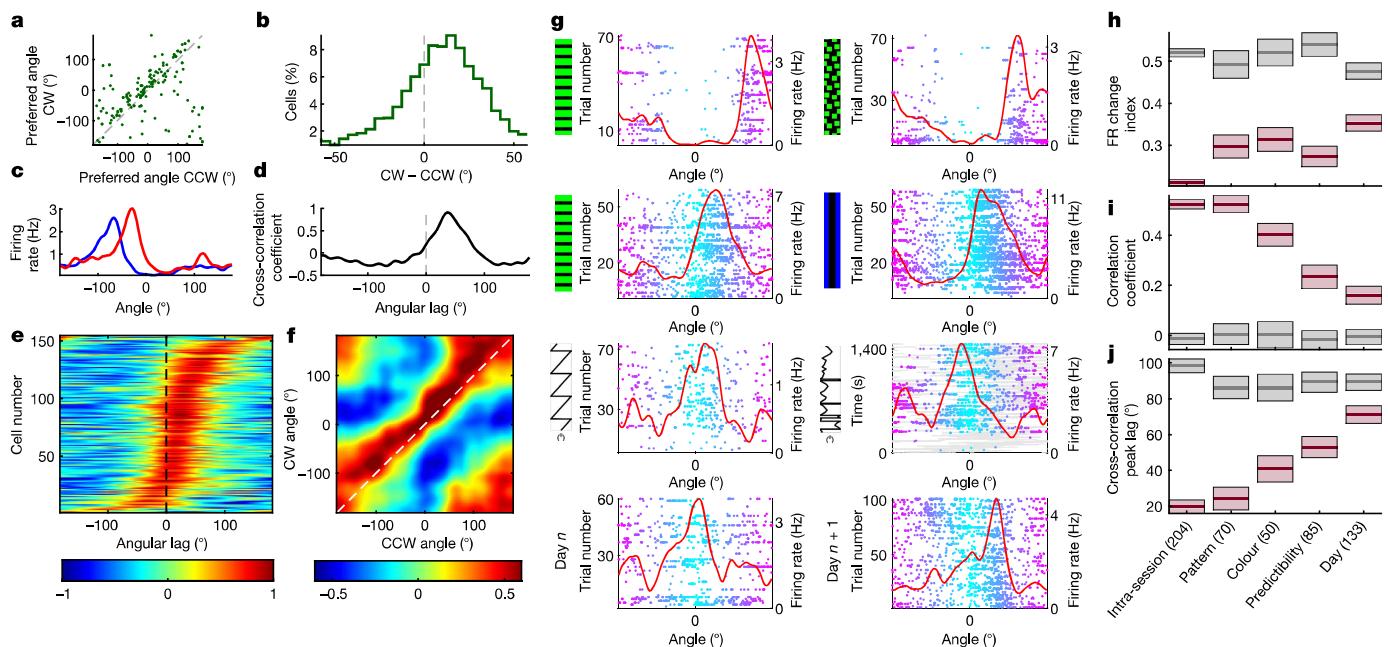


Fig. 3 | aVEVS is retrospective and changes gradually with stimulus pattern, colour, motion predictability and time. **a**, For bidirectional tuned cells, the preferred angle in the CW (y axis) direction was greater than that in the CCW (x axis) direction. **b**, Histogram of difference (CW–CCW, restricted to $\pm 50^\circ$) was significantly (t -test at $0^\circ, P = 0.003$) positive, indicating a retrospective shift. **c**, Retrospective latency between the CCW (blue) and CW (red) tuning curves for a bidirectional cell. **d**, Cross-correlation between the CW and CCW responses was maximum at positive latency (+27°). **e**, Such cross-correlations were performed for each bidirectional cell and sorted according to their peak lag. The majority (80%) of lags were positive (median $+19.9 \pm 49.8^\circ$, circular median t -test at $0^\circ, P = 4.8 \times 10^{-16}$). **f**, Population vector overlap of aVEVS had a significant (circular median t -test, $P = 1.5 \times 10^{-36}$) peak at a positive lag (median $+54.3 \pm 25.3^\circ$). **g**, Change in pattern (green-striped (left) versus green-checkered (right)) caused the smallest change in aVEVS (row 1). Changes in colour (green versus blue; row 2) and pattern (horizontal versus vertical

stripes) caused gradually greater change in aVEVS. Changes in predictability of the stimulus motion (row 3) or mere passage of time (1 day) caused the greatest changes (row 4). Only CW example cells are shown here. **h**, Firing rate remapping, quantified by the firing rate change index, was significantly (Kolmogorov–Smirnov test, P value range 1.2×10^{-90} to 1.4×10^{-5}) smaller for the actual data (dark pink) than for the shuffled data (grey) for all conditions. **i**, Similar to **e**, the correlation coefficient between the tuning curves across different conditions was significantly greater than shuffle (Kolmogorov–Smirnov test P value range 2.6×10^{-58} to 3.8×10^{-6}). **j**, Same as **e**, the angular lag in cross-correlation to quantify the amount of shift between tuning curves across the two conditions. All were significantly lesser than shuffle (Kolmogorov–Smirnov test P value range 4×10^{-46} to 1.3×10^{-3}). n is shown in parentheses and indicates the number of responses measured. In **h–j**, the thick line indicates the median and the box represents the s.e.m.

variation (Fig. 3h–j, Methods). Next, we introduced larger change in the bar appearance by changing both colour and pattern. This resulted in significantly more changes in all measures of aVEVS, although this too was far less than expected by chance.

Sequential tasks can influence neural selectivity in the hippocampus^{9,10} and the visual cortex³⁷. Hippocampal neurons also show selectivity in sequential, non-spatial tasks^{19–21}. Sequential versus random goal-directed paths induce place field remapping in the real world³⁸ and large change in selectivity in virtual reality. To compute the contribution of the sequential movement of the bar of light to aVEVS, we designed a randomly moving bar paradigm (row 3 in Fig. 3g). The bar moved only 56.7° in one direction on average, and then abruptly changed speed and direction. This was called the ‘randomly’ moving bar experiment. Here, 26% of neurons showed significant aVEVS, which was far greater than chance, although lesser than the systematic condition (Extended Data Fig. 11). The percentage of unidirectional, bidirectional and untuned stable cells were qualitatively similar to the systematic stimulus experiments (Extended Data Fig. 11). Thus, the aVEVS cannot arise entirely from sequential movement of the bar. The retrospective latencies were also unaffected (Extended Data Fig. 9). To directly ascertain the effect of predictability on aVEVS, we separately analysed the randomly moving bar data in the first 1 s after flip of the stimulus direction, and an equivalent subsample of data from later (Methods, Extended Data Fig. 11). aVEVS was similar in these two conditions. Furthermore, aVEVS was not systematically biased by the angular movement speed of the stimulus, nor did hippocampal firing encode stimulus speed beyond chance levels (Extended Data Fig. 11).

Recent studies have reported representational drift, that is, slow remapping of place cells over several days³⁹. We measured the activity of the same cells for more than 1 day, and measured changes in aVEVS without any changes in stimuli for the predictably moving, systematic bar of light. There was a large remapping of aVEVS across 2 days, evidenced by a very low correlation between the tuning curves of the same neuron across 2 days (Fig. 3i). This was not due to difference in novelty, because rats had experienced this stimulus for at least 1 week.

Thus, unlike all-or-none changes in place cells that show complete remapping with large, but not small, changes in visual cues⁴⁰, aVEVS responses were largely invariant as measured by the correlation coefficient of the tuning curves (Fig. 3i). They showed gradually larger change in aVEVS with progressively greater changes in the visual cues, ranging from pattern, then colour, then predictability but largest with the passage of time. These results were partly mediated by the change in preferred angle under different conditions. However, even when this contribution was factored out, a similar pattern of changes was observed (Extended Data Fig. 11).

Most VEVS neurons are place cells

During spatial exploration, the majority of rodent hippocampal neurons show spatially selective responses, that is, place cells. Thus, we investigated the relationship between aVEVS and spatial selectivity of neurons. We measured the activity of the same set of CA1 neurons, on the same day, during the aVEVS protocol and while rats freely foraged

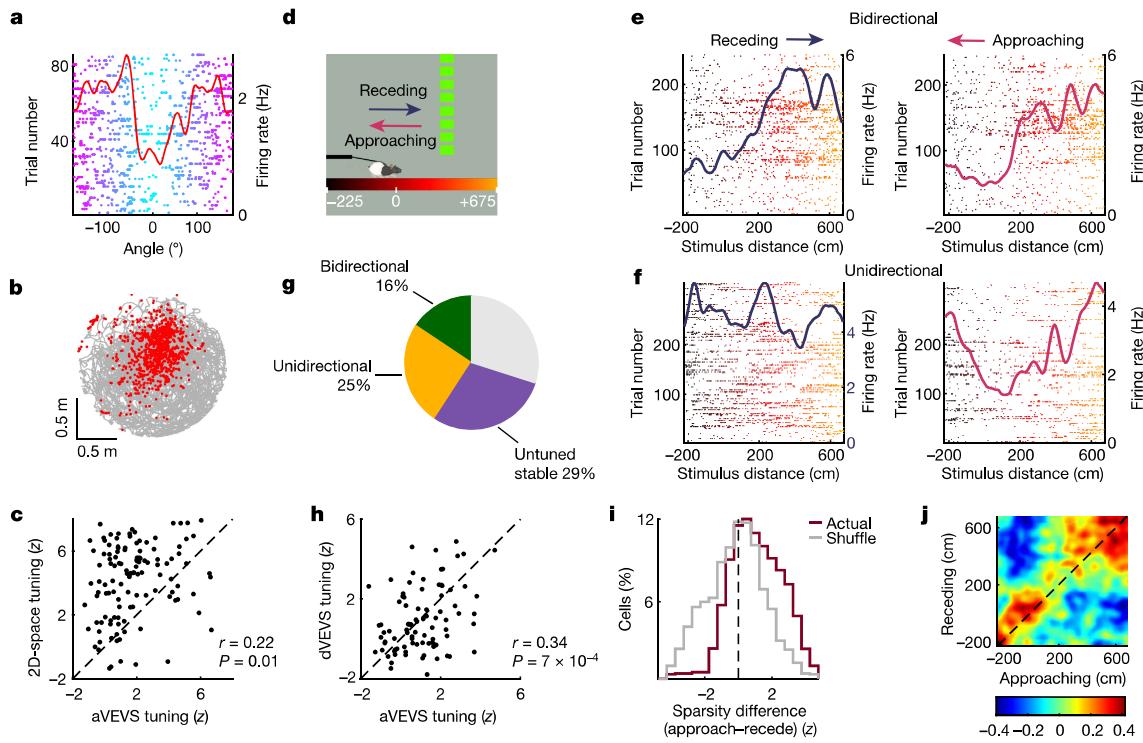


Fig. 4 | aVEVS cells are place cells and stimulus distance-encoding cells.

a, b, A cell recorded on the same day showing significant aVEVS in the revolving bar of the experiment (**a**) and allocentric spatial selectivity during free foraging on a circular table (**b**). The position of the rat (grey) and spikes (red) are shown. **c**, Strength of aVEVS and spatial selectivity measured by z-scored sparsity were significantly correlated (Pearson correlation is also indicated). **d**, Schematic of the stimulus distance experiment. The bar of light moved towards and away from the rat at a fixed angle (0°). **e**, Raster plots and firing rates of a bidirectional cell with significant tuning to the approaching (pink) as well as the receding (dark blue) bar of light. The trial number (y axis on the left) and firing rates (y axis on the right) are shown. **f**, Same as **e**, but for a unidirectional

cell, tuned for stimulus distance only during movement of the approaching stimulus. **g**, Relative percentages of cells, similar to Fig. 2d. **h**, Angular and linear stimulus distance tuning was positively correlated (Pearson correlation is also indicated). **i**, Stimulus distance tuning is larger during approaching epochs, even after down sampling spikes to have the same firing rate (Kolmogorov-Smirnov test actual $P = 4.6 \times 10^{-4}$, shuffle $P = 0.06$). **j**, Population vector overlap between responses in approaching and receding stimulus movement shows retrospective response, with maxima at values above the black diagonal dashed line, similar to Fig. 3f, corresponding to a median latency of 70.6 cm or 196.1 ms (± 377.6 ms).

for randomly scattered rewards in two-dimensional environments (Fig. 4a, b, Methods). Of the neurons that were active in the bar of light experiment, 79% (184 out of 234) were also active during spatial exploration. This is far greater than the fraction (approximately 20%) of place cells that are active in two different environments during spatial exploration. Furthermore, the firing rates during exploration and moving bar experiments were strongly correlated (Extended Data Fig. 12). Among cells that showed significant aVEVS, 90% (70 out of 78) showed significant spatial selectivity. Notably, the strength of tuning was also significantly correlated between these two experiments (Fig. 4c). Thus, despite very different experimental conditions and behaviour, the majority of aVEVS cells were also place cells, with similar activity and tuning.

Spatial exploration involves not only angular optic flow but also looming signals. Hence, in the same apparatus, we measured 147 cells when the stimulus moved towards or away from the rat, at a fixed angle of 0°, completing one lap in 10 s (Fig. 4d). Similar to the revolving bar experiments, the animal was body-restricted, and the movements of the rat had no effect on the motion of the bar or rewards (Fig. 1). The firing rates of 41% of neurons showed significant modulation as a function of the stimulus distance, that is, distance VEVS (dVEVS) (Fig. 4g), and 29% of cells had untuned but stable responses. Neurons not only encoded distance but also direction of movement, with 17% and 8% of neurons showing significant tuning to only the approaching (moving towards) or receding (moving away) bar of light, respectively. For cells recorded in both stimulus distance and angle experiments (Methods), firing rates (Extended Data Fig. 12) as well as the strength of tuning were correlated, suggesting that the same population of neurons can

encode both distance and angle (Fig. 4h). The preferred distance (that is, the position of maximal firing) for the bidirectional cells was not uniform but bimodal, with over-representation near the rat (0 cm) or the locations farthest away (500 cm) (Extended Data Fig. 12). Neural firing rates were quite similar for approaching and receding stimuli, but coding of the stimulus distance was much stronger for approaching movements (Fig. 4i). Retrospective response was also seen in distance VEVS (Fig. 4j), with the population overlap between approaching and receding responses shifted to values above the diagonal (Fig. 4j). This corresponds to a retrospective shift of 70.6 cm or 196.1 ms.

Discussion

These results demonstrate that a moving bar of light can reliably generate selectivity to distance, angle and direction of motion in hippocampal place cells, without any task demand, memory, reward contingency or locomotion requirements. Selectivity to these three spatial variables demonstrates VEVS, which is unlikely to arise due to non-specific variables (Extended Data Fig. 13 for reward-related controls, Extended Data Fig. 14 for behaviour-related controls, Extended Data Fig. 15 for generalized linear model estimates, Extended Data Fig. 16 for simultaneously recorded neurons showing diverse aVEVS and Extended Data Fig. 17 for quantification of co-fluctuation of firing responses). Similar to place cells, only a few hundred aVEVS neurons were sufficient to accurately decode the angular position of the stimulus. Positions in front of and near the rat were over-represented, similar to the visual cortices. The majority of neurons that encoded the bar position were also spatially selective during

Article

real-world exploration, and the strength of VEVS and spatial tuning were correlated. However, unlike place cells that shut down completely outside the place field, VEVS showed significant activity outside the preferred zone. Whereas place cells remap when the behaviour is sequential rather than random³⁸, aVEVS was relatively unchanged when the predictability or sequential nature of the stimuli was altered.

Whereas VEVS was retrospective, hippocampal place cells during spatial exploration^{5–8,41} and head direction cells in related areas^{42–44}, including in the virtual reality setup similar to that used here⁸, show prospective or predictive responses (Extended Data Fig. 8). Thus, self-motion signals may be required to turn the retrospective VEVS into prospective coding, necessary for navigational maps¹². Indeed, robust responses and prospective coding were seen in virtual reality, but for relative distance, not absolute position, as only the optic flow and locomotion cues were correlated at identical distance⁸.

These results show that during passive viewing, rodent hippocampal activity patterns fit the visual hierarchy⁴⁵. For example, aVEVS shows similar but smaller nasal-temporal magnification as the visual cortex, for example, a larger width of the tuning curve for more peripheral stimuli, and over-representation of the nasal compared with temporal positions²⁷. aVEVS is weaker but not absent for stimulus locations behind the rat, suggesting history dependence or other downstream processing providing stimulus information when it is not directly visible. History dependence could also explain the unidirectional responses in our experiments, also seen in the primary visual cortex⁴⁶, perhaps arising from similar plasticity mechanisms⁴⁷. Furthermore, similar to the visual cortex, hippocampal neurons too showed retrospective responses, but with larger response latency, suggesting that visual cortical inputs reached the hippocampus to generate VEVS. The larger latency is remarkably similar to that in the human hippocampus⁴⁸, and in the rodent cortico–entorhinal–hippocampal circuit during up–down states^{49–51}. However, there were no off responses in the VEVS and the tuning curves were broader and more unidirectional than in the primary visual cortex. This could arise due to processing in the cortico–hippocampal circuit, especially in the entorhinal cortex⁵¹, or due to the contribution of alternate pathways from the retina to the hippocampus⁵².

Hippocampal spatial maps are thought to rely on the visual cues². Rats can not only navigate using only vision in virtual reality but they also preferentially rely on vision²⁶. Furthermore, rats can navigate in virtual reality without robust vestibular cues, and neurons show robust selectivity to distance travelled and the direction of the hidden reward location that predicts behavioural performance¹². Consistent with the multisensory pairing hypothesis^{9,30}, these multiplexed responses could arise when visual cue-evoked VEVS is paired with locomotion and reward cues during the navigation task. In the absence of any correlation between multisensory stimuli, hippocampal neurons generate invariant, non-abstract and retrospective VEVS, which are less robust than place cells. In real-world navigation tasks, the greatly enhanced correlations between all of the internal and external multisensory cues could be encoded more robustly via Hebbian plasticity to generate anticipatory or prospective coding of absolute position^{12,28,53}. Thus, the hippocampus can be driven reliably by a moving visual cue, similar to the visual cortex, to generate a vectorial representation of space in a polar coordinate frame centred on the head of the rat. When combined with self-motion, rewards and multisensory cues, this could elicit not only allocentric place cells² but also task-related hippocampal complexity¹².

Online content

Any methods, additional references, Nature Research reporting summaries, source data, extended data, supplementary information, acknowledgements, peer review information; details of author contributions and competing interests; and statements of data and code availability are available at <https://doi.org/10.1038/s41586-022-04404-x>.

- Hubel, D. H. & Wiesel, T. N. Receptive fields, binocular interaction and functional architecture in the cat's visual cortex. *J. Physiol.* **160**, 106–154 (1962).
- O'Keefe, J. & Dostrovsky, J. The hippocampus as a spatial map. Preliminary evidence from unit activity in the freely-moving rat. *Brain Res.* **34**, 171–175 (1971).
- O'Keefe, J. & Nadel, L. *The Hippocampus as a Cognitive Map* (Clarendon Press, 1978).
- Muller, R. U. & Kubie, J. L. The firing of hippocampal place cells predicts the future position of freely moving rats. *J. Neurosci.* **9**, 4101–4110 (1989).
- Mehta, M. R. Neuronal dynamics of predictive coding. *Neuroscience* **7**, 490–495 (2001).
- Battaglia, F. P., Sutherland, G. R. & McNaughton, B. L. Local sensory cues and place cell directionality: additional evidence of prospective coding in the hippocampus. *J. Neurosci.* **24**, 4541–4550 (2004).
- Resnik, E., McFarland, J. M., Sprengel, R., Sakmann, B. & Mehta, M. R. The effects of GluA1 deletion on the hippocampal population code for position. *J. Neurosci.* **32**, 8952–8968 (2012).
- Ravassard, P. et al. Multisensory control of hippocampal spatiotemporal selectivity. *Science* **340**, 1342–1346 (2013).
- Aghajan, Z. M. et al. Impaired spatial selectivity and intact phase precession in two-dimensional virtual reality. *Nat. Neurosci.* **18**, 121–128 (2015).
- Pastalkova, E., Itskov, V., Amarasingham, A., Buzsaki, G. & Buzsáki, G. Internally generated cell assembly sequences in the rat hippocampus. *Science* **321**, 1322–1327 (2008).
- MacDonald, C. J., Lepage, K. Q., Eden, U. T. & Eichenbaum, H. Hippocampal 'time cells' bridge the gap in memory for discontiguous events. *Neuron* **71**, 737–749 (2011).
- Moore, J. J., Cushman, J. D., Acharya, L., Popeney, B. & Mehta, M. R. Linking hippocampal multiplexed tuning, Hebbian plasticity and navigation. *Nature* **599**, 442–448 (2021).
- Fyhn, M., Molden, S., Witter, M. P., Moser, E. I. & Moser, M. B. Spatial representation in the entorhinal cortex. *Science* **305**, 1258–1264 (2004).
- Taube, J. S., Müller, R. U. & Ranck, J. B. Head-direction cells recorded from the postsubiculum in freely moving rats. II. Effects of environmental manipulations. *J. Neurosci.* **10**, 436–447 (1990).
- Foster, T. C., Castro, C. A. & McNaughton, B. L. Spatial selectivity of rat hippocampal neurons: dependence on preparedness for movement. *Science* **244**, 1580–1582 (1989).
- McNaughton, B. L. et al. Deciphering the hippocampal polyglot: the hippocampus as a path integration system. *J. Exp. Biol.* **199**, 173–185 (1996).
- Sakurai, Y. Involvement of auditory cortical and hippocampal neurons in auditory working memory and reference memory in the rat. *J. Neurosci.* **14**, 2606–2623 (1994).
- Itskov, P. M. et al. Sound sensitivity of neurons in rat hippocampus during performance of a sound-guided task sound sensitivity of neurons in rat hippocampus during performance of a sound-guided task. *J. Neurophysiol.* **107**, 1822–1834 (2012).
- Aronov, D., Nevers, R. & Tank, D. W. Mapping of a non-spatial dimension by the hippocampal–entorhinal circuit. *Nature* **543**, 719–722 (2017).
- Omer, D. B., Maimon, S. R., Las, L. & Ulanovsky, N. Social place-cells in the bat hippocampus. *Science* **359**, 218–224 (2018).
- Danjo, T., Toyoizumi, T. & Fujisawa, S. Spatial representations of self and other in the hippocampus. *Science* **359**, 213–218 (2018).
- von Heimendahl, M., Rao, R. P. & Brecht, M. Weak and nondiscriminative responses to conspecifics in the rat hippocampus. *J. Neurosci.* **32**, 2129–2141 (2012).
- Mou, X. & Ji, D. Social observation enhances cross-environment activation of hippocampal place cell patterns. *eLife* **5**, 1–26 (2016).
- Dotson, N. M. & Yartsev, M. M. Nonlocal spatiotemporal representation in the hippocampus of freely flying bats. *Science* **373**, 242–247 (2021).
- Sakurai, Y. Coding of auditory temporal and pitch information by hippocampal individual cells and cell assemblies in the rat. *Neuroscience* **115**, 1153–1163 (2002).
- Cushman, J. D. et al. Multisensory control of multimodal behavior: do the legs know what the tongue is doing? *PLoS ONE* **8**, e08465 (2013).
- Malpel, J. G. & Baker, F. H. The representation of the visual field in the lateral geniculate nucleus of *Macaca mulatta*. *J. Comp. Neurol.* **161**, 569–594 (1975).
- Mehta, M. R., Quirk, M. C. & Wilson, M. A. Experience-dependent asymmetric shape of hippocampal receptive fields. *Neuron* **25**, 707–715 (2000).
- Ahmed, O. J. & Mehta, M. R. The hippocampal rate code: anatomy, physiology and theory. *Trends Neurosci.* **32**, 329–338 (2009).
- Acharya, L., Aghajan, Z. M., Vuong, C., Moore, J. J. & Mehta, M. R. Causal influence of visual cues on hippocampal directional selectivity. *Cell* **164**, 197–207 (2016).
- de Vries, S. E. J. et al. A large-scale standardized physiological survey reveals functional organization of the mouse visual cortex. *Nat. Neurosci.* **23**, 138–151 (2020).
- Wilson, M. A. & McNaughton, B. L. Dynamics of the hippocampal ensemble code for space. *Science* **261**, 1055–1058 (1993).
- Stefanini, F. et al. A distributed neural code in the dentate gyrus and in CA1. *Neuron* **107**, 703–716.e4 (2020).
- Muller, R. U., Kubie, J. L., Bostock, E. M., Taube, J. S. & Quirk, G. J. in *Brain and Space* (ed. Paillard, J.) 296–333 (Oxford Univ. Press, 1991).
- Colgin, L. L., Moser, E. I. & Moser, M. B. Understanding memory through hippocampal remapping. *Trends Neurosci.* **31**, 469–477 (2008).
- Suzuki, W. A., Miller, E. K. & Desimone, R. Object and place memory in the macaque entorhinal cortex. *J. Neurophysiol.* **78**, 1062–1081 (1997).
- Saleem, A. B., Diamanti, E. M., Fournier, J., Harris, K. D. & Carandini, M. Coherent encoding of subjective spatial position in visual cortex and hippocampus. *Nature* **562**, 124–127 (2018).
- Markus, E. J. et al. Interactions between location and task affect the spatial and directional firing of hippocampal neurons. *J. Neurosci.* **15**, 7079–7094 (1995).
- Ziv, Y. et al. Long-term dynamics of CA1 hippocampal place codes. *Nat. Neurosci.* **16**, 264–266 (2013).
- Nakazawa, K. et al. Requirement for hippocampal CA3 NMDA receptors in associative memory recall. *Science* **297**, 211–218 (2002).
- Geiller, T., Fattah, M., Choi, J.-S. S. & Royer, S. Place cells are more strongly tied to landmarks in deep than in superficial CA1. *Nat. Commun.* **8**, 14531 (2017).
- Taube, J. S. & Müller, R. U. Comparisons of head direction cell activity in the postsubiculum and anterior thalamus of freely moving rats. *Hippocampus* **8**, 87–108 (1998).

43. Deacon, T. W., Eichenbaum, H., Rosenberg, P. & Eckmann, K. W. Afferent connections of the perirhinal cortex in the rat. *J. Comp. Neurol.* **220**, 168–190 (1983).
44. Lozano, Y. R. et al. Retrosplenial and postsubiculum head direction cells compared during visual landmark discrimination. *Brain Neurosci. Adv.* **1**, 2398212817721859 (2017).
45. Felleman, D. J. & Van Essen, D. C. Distributed hierarchical processing in the primate cerebral cortex. *Cereb. Cortex* **1**, 1–47 (1991).
46. Hubel, D. H. & Wiesel, T. N. Receptive fields of single neurones in the cat's striate cortex. *J. Physiol.* **148**, 574–591 (1959).
47. Mehta, M. R. & Wilson, M. A. From hippocampus to V1: effect of LTP on spatio-temporal dynamics of receptive fields. *Neurocomputing* **32–33**, 905–911 (2000).
48. Quiroga, R. Q., Reddy, L., Kreiman, G., Koch, C. & Fried, I. Invariant visual representation by single neurons in the human brain. *Nature* **435**, 1102–1107 (2005).
49. Hahn, T. T., Sakmann, B. & Mehta, M. R. Phase-locking of hippocampal interneurons' membrane potential to neocortical up-down states. *Nat. Neurosci.* **9**, 1359–1361 (2006).
50. Hahn, T. T., Sakmann, B. & Mehta, M. R. Differential responses of hippocampal subfields to cortical up-down states. *Proc. Natl Acad. Sci. USA* **104**, 5169–5174 (2007).
51. Hahn, T. T. G., McFarland, J. M., Berberich, S., Sakmann, B. & Mehta, M. R. Spontaneous persistent activity in entorhinal cortex modulates cortico-hippocampal interaction *in vivo*. *Nat. Neurosci.* **15**, 1531–1538 (2012).
52. Beltramo, R. & Scanziani, M. A collicular visual cortex: neocortical space for an ancient midbrain visual structure. *Science* **363**, 64–69 (2019).
53. Mehta, M. R., Barnes, C. A. & McNaughton, B. L. Experience-dependent, asymmetric expansion of hippocampal place fields. *Proc. Natl Acad. Sci. USA* **94**, 8918–8921 (1997).

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

© The Author(s), under exclusive licence to Springer Nature Limited 2022