Learning produces a hippocampal cognitive map in the form of an orthogonalized state machine

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ABSTRACT

Cognitive maps confer animals with flexible intelligence by representing spatial, temporal, and abstract relationships that can be used to shape thought, planning, and behavior. Cognitive maps have been observed in the hippocampus, but their algorithmic form and the processes by which they are learned remain obscure. Here, we employed large-scale, longitudinal two-photon calcium imaging to record activity from thousands of neurons in the CA1 region of the hippocampus while mice learned to efficiently collect rewards from two subtly different versions of linear tracks in virtual reality. The results provide a detailed view of the formation of a cognitive map in the hippocampus. Throughout learning, both the animal behavior and hippocampal neural activity progressed through multiple intermediate stages, gradually revealing improved task understanding and behavioral efficiency. The learning process led to progressive decorrelations in initially similar hippocampal neural activity within and across tracks, ultimately resulting in orthogonalized representations resembling a state machine capturing the inherent structure of the task. We show that a Hidden Markov Model (HMM) and a biologically plausible recurrent neural network trained using Hebbian learning can both capture core aspects of the learning dynamics and the orthogonalized representational structure in neural activity. In contrast, we show that gradient-based learning of sequence models such as Long Short-Term Memory networks (LSTMs) and Transformers do not naturally produce such representations. We further demonstrate that mice exhibited adaptive behavior in novel task settings, with neural activity reflecting flexible deployment of the state machine. These findings shed light on the mathematical form of cognitive maps, the learning rules that sculpt them, and the algorithms that promote adaptive behavior in animals. The work thus charts a course toward a deeper understanding of biological intelligence and offers insights toward developing more robust learning algorithms in artificial intelligence.

INTRODUCTION

Intelligence, at its core, manifests in an organism's or an agent's ability to engage dynamically with its environment, interpret information, adjust to unfamiliar situations, and implement complex tasks. A central concept in the study of natural and artificial intelligence (AI) is the notion of 'internal models'. These models convert external world observations into a well-organized representation, thereby enabling adaptive behavior. In neuroscience, a notable example for such internal models is the concept of 'cognitive maps'. Conceptualized early in the twentieth century, cognitive maps are believed to be neural constructs that enable animals to comprehend their environment and understand the interactions between their bodies and the external world, which supports efficient navigation, even in novel circumstances[1]. This concept gained momentum with the discovery of 'place cells' in the hippocampus, neurons that fire selectively at specific positions in the environments[2–4]. Since then, the neural underpinnings of cognitive maps have been studied extensively, revealing a vast body of knowledge about the firing properties of neurons that comprise cognitive maps in the brains of rodents[5], primates (including humans)[6–17], and other animals[18,19].

These foundational studies indicate that the hippocampus not only captures features of the environment, but also the relationships between them and the animal's actions within it. For example, many hippocampal neurons carry information in the form of activity that is greatest at a particular location in the environment (the cell's 'place field')[2], while others store information not only about place, but also about contextual features such as the animal's movement direction[20,21], running speed[20], or movement history[22,23]. Hippocampal neurons can also learn to represent more abstract spaces, such as the position in a sound landscape[24], accumulated evidence[25], arbitrary relationships between objects or events[26,27], and social factors[28–30].

Despite an extensive body of knowledge about the neuronal firing properties constituting hippocampal cognitive maps, and recent ideas concerning their algorithmic structure[31–35], we are still yet to fully characterize the formation process of whole cognitive maps during the entire learning phase of moderately complex tasks. Acquiring such empirical data is crucial, as it facilitates identification of the learning principles that drive the creation of cognitive maps. While cognitive maps have been shown to form rapidly in novel environments and modify rapidly in response to changes in familiar environments[36–38], technical limitations such as the limited number of total recorded neurons (hundreds) and short durations (days) of longitudinal tracking of

individual neurons have impeded the ability to study the formation of cognitive maps representing more complex relationships that require extensive exploration and learning. Here, we leveraged technological advances that allowed us to follow neural activity in thousands of hippocampal neurons in each mouse, stably for many days or weeks, as they learned to perform a task requiring them to form cognitive maps representing spatial, temporal, and abstract relationships as they interacted with a complex but predictable environment.

Our results show that during learning, mice proceed through a stereotypical series of behavioral changes that are mirrored by structured changes in neural activity. Specifically, hippocampal activity undergoes a series of decorrelation steps that orthogonalize neural activity in regions of the environment where sensory stimuli are similar, but task demands differ. We analyzed the representational structure of the task, visualized the low-dimensional geometry of the neural activity, and compared neural activity in the hippocampus to unit activity in a variety of cognitive models and artificial neural networks trained using the same task structure. We show that day-to-day dynamics of hippocampal activity are consistent with the formation of a state machine, consisting of orthogonalized latent representations of task-specific features. The transitions between these latent states, each encoding specific task features or segments, are learned to predict the dynamics of the animal's interaction with the environment. Remarkably, orthogonal states can represent similar sensory stimuli, highlighting latent task structure as the driver of state orthogonalization.

We show further that this orthogonalized state machine (OSM) can be reproduced by a Hidden-Markov-Model (HMM)-based model called a Clone-Structured Causal Graph (CSCG)[33,39] or by a biologically plausible recurrent neural network (RNN) trained using Hebbian learning[40], an unsupervised local learning rule that does not require backpropagation of error[41]. Despite their effectiveness in sequence modeling, we show that gradient-based learning of models such as LSTMs[42] or Transformers[43] do not naturally generate representational geometries that mirror those observed during animal learning. We further demonstrate that neural activity shows flexible usage of the OSM in altered tasks conditions such as the introduction of new visual cues and adjustment in the lengths of track segments. In sum, these findings shed light on the architecture and learning principles governing the formation of cognitive maps and provide potential guides for the design of future artificial systems.

RESULTS

Learning the linear 2-alternative choice task

We trained transgenic mice expressing GCaMP6f in hippocampal neurons to navigate in a virtual reality (VR) environment while head-fixed to enable imaging of neural activity as they learned the relationship between visual cues and the future location of water reward delivery (Fig. 1a; see Methods for details). On each trial, water was delivered at one of two reward zones, either near or far from the beginning of the track, which we call R1 and R2, respectively. Prior to these rewarded locations, a visually distinct indicator cue (Ind) perfectly predicted the rewarded location (Fig. 1a, bottom). Efficient execution of this linear 2-alternative choice task (L2AC) requires mice to form and use long-term memory of the relationship between the indicator cues and reward locations and short-term memory of the indicator cue after it disappears and before the rewarded location.

Mice were initially trained for 5 days (one-hour session each day) to run on a spherical treadmill and collect randomly delivered water rewards in the dark. Subsequently, screens were turned on to display the VR environment. In each subsequent one-hour daily session, mice performed ~80-200 trials (124 ± 43 trials, n = 11 mice), with the reward location depending on the trial type. Both *Near* and *Far* trial types were presented sequentially in a randomized manner (Methods). To initiate a new trial, mice had to run to the end of the corridor, which was decorated by a 'brick wall' cue, and a 2-second period of dark screens ('teleportation') preceded the next trial. The two trial types shared identical visual cues at all locations other than the indicator region. Outside of the indicator region and the reward regions, the walls of the virtual corridor were decorated with relatively featureless gray wood grain ('gray' regions). This sensory ambiguity within trials (four gray regions) and across trials (both gray regions and reward-zone cues are visually identical) is a key feature of the task. For the first 1-3 days of training, water rewards were delivered even if the mouse did not lick in the rewarded zone, until consistent anticipatory licking was observed. On all subsequent days, mice were rewarded with a drop of water on any trial only if they licked in the correct reward zone. No penalty was imposed for licking in other locations. Thus, mice learned the task through exploration, presumably motivated to slow down and lick only when rewards were expected.

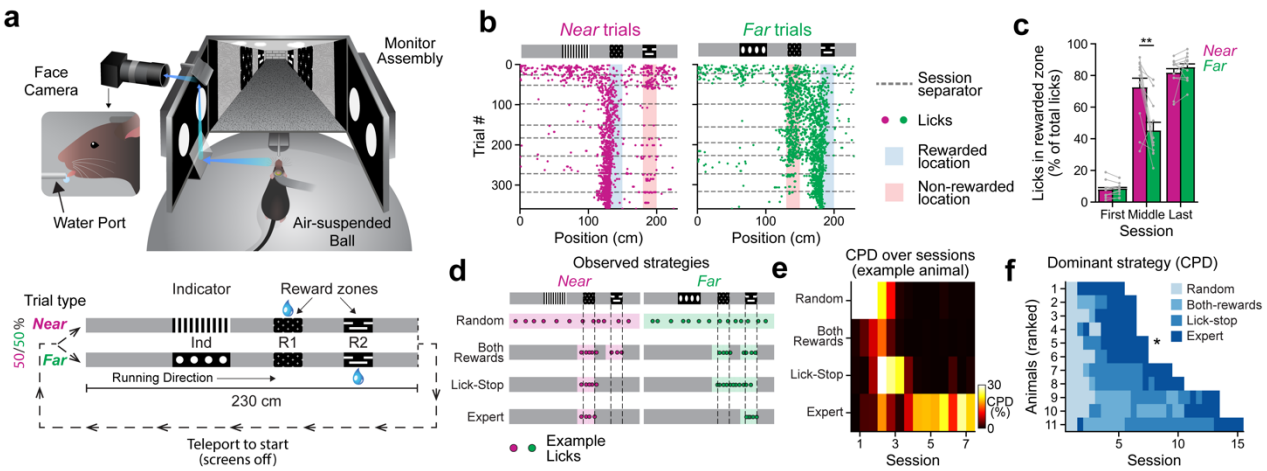

Figure 1. Animals exhibit stage-wise behaviors when learning the linear 2-alternative choice task. **(a)** Diagram of the virtual reality behavior setup (top) and illustration of the task (bottom). Ind: Indicator regions, R1: Near reward zones, R2: Far reward zones. **b)** Example lick patterns of a single animal across sessions for both the *Near* and *Far* trial types. Each dot represents a single lick within a trial and dashed lines indicate separation between sessions. **(c)** Percentage of licks at the correct reward locations for both the *Near* and *Far* trial types for the first session, an intermediate session, and the last session in which the animals show expert performance (n = 11 mice; P <0.01**, dependent samples t-test). **(d)** Illustration of four different behavior strategies animals exhibit during learning. Colored shadings denote the non-zero regions within the basis functions for regression against licking density across track locations. **(e)** Coefficients of Partial Determination for the four behavior strategies for one example animal. **(f)** Dominant strategy for all animals over sessions (ranked by learning speed). Asterisk denotes the animal shown in e. Values in e and f are calculated by splitting each session into two parts of equal duration (start/end). Number of sessions per strategy, Random: 1.9 ± 0.7, Both-rewards: 2.0 ± 2.5, Lick-stop: 3.3 ± 2.8, Expert: 3.6 ± 0.5.

We assessed learning by plotting licking behavior as a function of position for all trials across several days of training on the L2AC task (Fig. 1b). Initially, mice licked throughout the entire track, but they quickly learned to restrict licking to portions of the track near the two reward zones in both trial types. This change in behavior occurred within 2-3 sessions in all animals (Suppl. Fig. 1) Around the same time, mice developed an intermediate strategy and learned to suppress licking after receiving a reward. As a result, licking behavior was near optimal for the *Near* trial type (not licking at the far reward zone), but remained suboptimal for the *Far* trial type (Fig. 1c, middle session), because licking began at the near reward zone and was often sustained until the reward delivery at the far reward zone. With additional training, mice eventually learned to suppress licking in the near reward zone on the *Far* trial type, thus achieving near optimal performance on both trial types (Fig. 1c, last session). Thus, licking behavior appears to evolve in

stages, marked with distinct behavioral strategies (Fig. 1d): (1) random licking, (2) licking in both reward locations, (3) licking in reward locations and stop licking until a reward is collected ('lick-stop'), and (4) only licking near the correct reward locations ('expert'). We used a statistical method called Coefficient of Partial Determination (CPD) to assess the contribution of each of the four behavior strategies to the overall behavior of the animals. Using these four behavior strategies as regressors accounted for 36.5 ± 5.9 % of variance in licking behavior averaged across all sessions (n = 9 ± 3 sessions per mouse). This explained variance percentage is within the expected range for behavioral studies involving complex tasks[44]. By removing a regressor corresponding to each behavior strategy one at a time, we were able to determine its unique contribution to the behavior. CPD analysis demonstrated that these four strategies emerged in successive waves at different points during the learning process (Fig. 1e), which was mirrored by gradual changes in the profile of animals' running speed (Suppl. Fig. 2). Despite variations in the number of sessions required for different animals to reach expert performance, the progression through these dominant behavior strategies was remarkably consistent (Fig. 1f).

Longitudinal imaging of hippocampal activity during learning

Prior to training, all mice were implanted with a cranial window to enable imaging of neural activity using GCaMP6f expressed in pyramidal neurons in area CA1 of the dorsal hippocampus (Fig. 2a; see Methods). Activity was imaged using a two-photon random access mesoscope (2P-RAM)[45]. The 3-mm cranial window was readily imaged with the 2P-RAM, which has a 5-mm field of view (FOV). Thousands of cells (within single sessions: 4682 ± 827 on average per animal across all sessions, range: 3813 - 6490; maximum single session cell count: 5545 ± 848 on average per animal, range 4266 – 7309. n = 11 mice) mostly near the center of the FOV, were readily resolved and reidentified in each session across several weeks of training and imaging (cells tracked across sessions: 3954 ± 661 on average per animal, range 3034 - 5354; see Methods. Fig. 2b; Suppl. Fig. 3, 4).

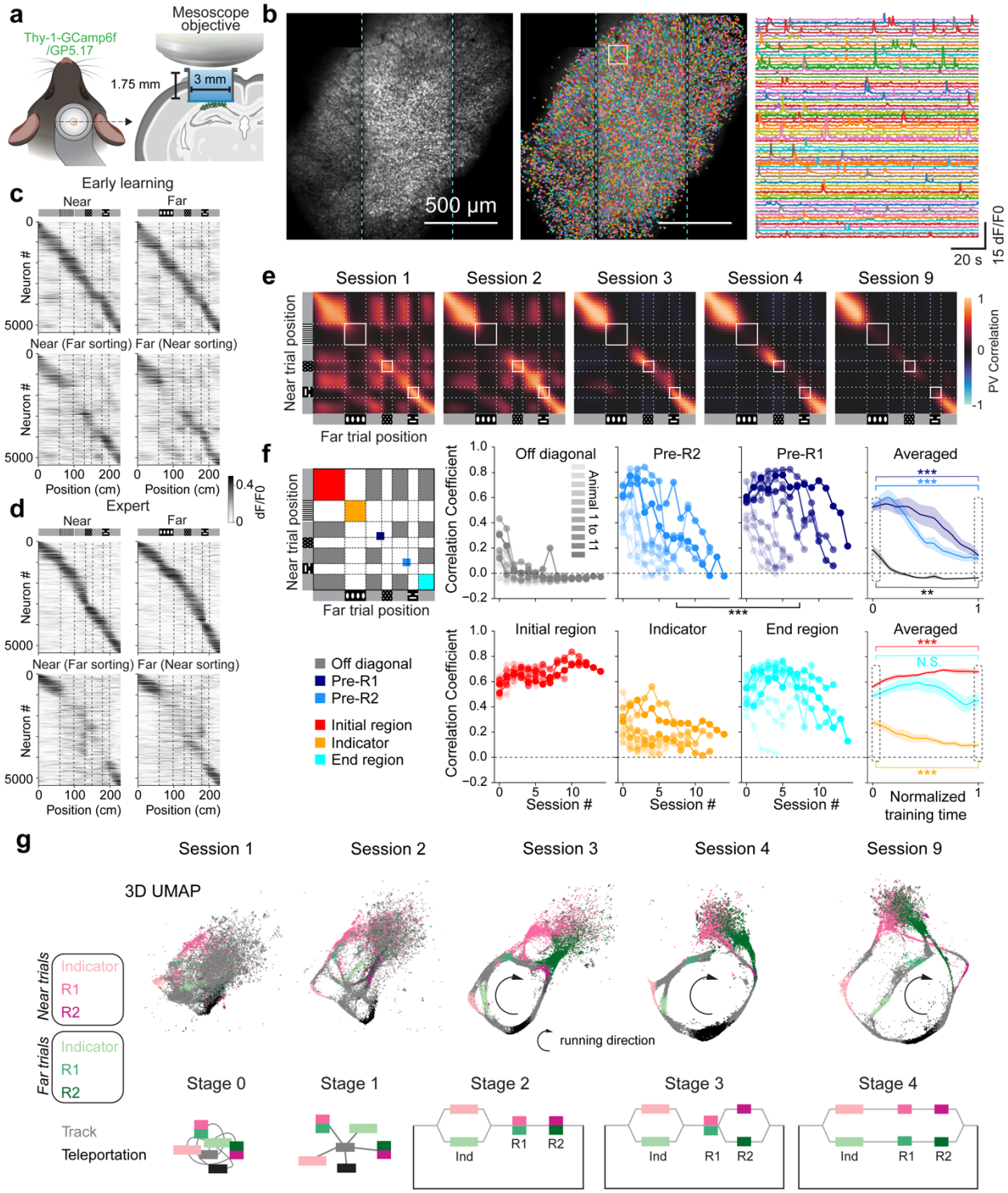

Figure 2. Progressive decorrelation of neural activity during learning.
(a) Diagram of the window implant for CA1 imaging. **(b)** Example field of view, cell segmentations, and example extracted fluorescent signals. Cyan dashed lines mark the boundary between vertical scanning stripes of the 2P-RAM microscope. **(c)** Trial-averaged neural activity versus track position for both the *Near* and *Far* trial types on session 2 in a representative animal (Animal 7 in Fig. 1f). Top row: cells ordered

by the center of mass (COM) of the largest place field by indicated trial type. Bottom row: cells ordered by opposite trial type. **(d)** Similar to **c**, but for session 9 of the same animal. **(e)** *Near*-versus-*Far* PV Cross-correlation matrices along all track positions for sessions 1, 2, 3, 4, 9 for the same example animal. **(f)** PV correlation averaged for different regions on the cross-correlation matrix across sessions, for the off-diagonal gray region correlations (gray), Pre-R2 region (light blue), and Pre-R1 region (dark blue), Initial region (red), Indicator region (orange), End region (cyan) shown for each animal separately and averaged across all of them. Comparing all sessions, a significant difference was observed between the Pre-R1 and Pre-R2 regions (Wilcoxon signed-rank test, $P < 0.001$***). Comparisons between the first and last session revealed significant changes in the Pre-R2, Pre-R1, Indicator (decreasing over sessions), and Initial region (increasing over sessions) with $P < 0.001$***. For the off-diagonal region, a significant decrease in correlation was also observed with $P < 0.01$**. In contrast, changes in the End region were not significant (N.S.). **(g)** 3D UMAPs and corresponding state diagrams of the neural manifold for 5 different sessions across learning from the same example animal in e, the 2D views of the UMAP are shown here were chosen to best illustrate the learning dynamics captured by the 3D structure.

By the second session, many cells exhibited elevated activity at well resolved positions along the track. Ordering cells according to the position of the peak activity revealed a clearly resolvable diagonal band of spatial responses tiling the whole virtual track in both trial types (Fig. 2c). Ordering cells according to their spatial activity pattern for the opposite trial type also showed a diagonal spatial band indicating many cells are active at similar locations in both trial types. However, activity differed between trial types most prominently at the indicator cue position (Fig. 2c), indicating that sensory information dominates the neural activity at this early stage. Indeed, cells that were most active in one of the four gray regions also showed moderate activity in other gray regions (Fig. 2c). After several more days of training, these neural activity-based 'maps' of the L2AC task increasingly differentiated within single trial types (among multiple gray regions) and between the two trial types (Fig. 2d).

Stage-wise changes of hippocampal activity during learning

The representational structure of the *Near* and *Far* trial types was compared by computing a population vector (PV) correlation for the two trial types (Methods), which decreased systematically in selected positions during training. Analysis of the cross-correlation between trial types across all regions of the track indicated that the indicator cue region had the smallest correlation, as expected from the differences in visual stimuli at this location (Fig. 2e, f). Both within and between trial types, the four gray regions of the track were moderately correlated on the first session for all animals but by the third session, the correlation had significantly reduced (Fig. 2e, f & Suppl. Fig. 5 showing PV angles also approaching 90°), suggesting that the

hippocampus had orthogonalized its representations of these visually similar regions. Between-trial-type correlations, decreased in an ordered, stage-like fashion, with the neural activity at the track region right before the far rewarded zone (Pre-R2) decorrelating generally earlier than the region before the near rewarded zone (Pre-R1; Fig. 2e, f). Neural activity corresponding to the indicator cue, while low from the onset, decorrelated further with increased exposure to the two trial types (Fig. 2e, f). While most track regions underwent complete decorrelation into near orthogonal representations, the beginning and end of the track remained correlated throughout training for most animals (Suppl. Fig. 6). This suggests that the decorrelation process is shaped by the task structure, as after collecting the reward, the animal has no information on which trial type it will be in next until it sees the next indicator.

Taken together, the initial decorrelation of gray regions suggests that the hippocampus first learns the sequential structure of the two linear environments by learning to differentiate each of the four visually similar gray regions within the linear tracks. During training, the hippocampus learns to further differentiate the similar visual cues between the two trial types, following a highly consistent sequential order, as indicated by the progressive decorrelation towards orthogonalization of neural activity across specific track locations: Initially, based presumably on whether the animal successfully collected reward at the near reward zone (rewarded in *Near*, but not yet rewarded in *Far*), neural activity decorrelates immediately after the animal has passed the first reward region. As training progresses, the remaining correlated activity prior to the first reward region eventually undergoes orthogonalization.

The hippocampal representation has properties of an orthogonalized state machine

We further visualized the day-to-day dynamics of neural activity utilizing a non-linear dimensionality reduction technique, specifically Uniform Manifold Approximation and Projection (UMAP)[46]. A single embedding space was used to reduce the activities of thousands of cells to points in a low-dimensional (3D) UMAP space, using longitudinally registered data gathered across all days of imaging, where each point represents the activity of all cells in a single imaging frame (see Methods, Fig. 2g). Notably, this UMAP representation not only echoed the gradual decorrelation and orthogonalization we previously described (Suppl. Fig. 5, 6), but it also allowed us to intuitively observe the overall topological changes of the neural manifold during learning.

Here we describe the UMAP from a representative animal, exhibiting all learning stages. The UMAP representation from the initial session distinctively clusters the neural activity associated with each sensory cue. Despite this differentiation, the overall neural manifold appears relatively unstructured at this stage (Fig. 2g, Stage 0). By the second day, the UMAP adopts a 'hub-and-spoke' appearance (Fig. 2g, Stage 1), with the hub corresponding to all gray regions and the spokes corresponding to activity trajectories between a gray region and all other cues (i.e., indicator cue, near and far reward cues, and the dark teleportation region). This structure hints that the neural activity associated with the concept of 'linear tracks' may not be fully developed at this point. An additional point cloud near the reward-zone embeddings corresponds to periods of water-reward licks and a post-reward period where the mouse was not running. By the third session, the UMAP adopts a ring-like structure that is closed by activity during the 2-second dark teleportation period linking the end of one trial and the start of the next trial (Fig. 2g, Stage 2). As training progresses, the activity trajectories for the two trial types become increasingly distinct, eventually resembling a split-shank wedding ring, consisting of a band that splits into two strands with a diamond in the center. Here, the splitting band corresponds to the principal manifold of neural activity while the mouse is running and the diamond corresponds to the point cloud when the animal is stationary, mostly during and right after reward consumption. We speculate that this reward-associated point cloud, observable in the UMAP representations at all stages (Suppl. Fig. 7), may be related to replay of neural activity and may contribute to synaptic plasticity in the hippocampus as well as its downstream targets[47]. The gradual appearance of a split-shank ring UMAP mirrors the dynamics of trial-type decorrelation described above (Fig. 2e, f).

The observed progressive changes in the representational structure reflected by both the correlation matrices and UMAPs resemble a gradually evolving state machine undergoing several meaningful intermediate stages and finally reaching a structure capturing the essence of the task (Fig. 1a, bottom and Fig. 2g, state diagrams below the UMAPs). This process involves several stages of disambiguation of similar sensory inputs at different regions along the two trial types in the populational activity level, eventually producing orthogonalized state representations for previously latent states of the task. We call this learned manifold an "orthogonalized state machine" (OSM).

The orthogonalization process of neural representations, as described earlier, reflects changes in the firing properties of individual neurons that occur together with the changes in an

animal's behavior. As training progresses, the firing properties of numerous neurons undergo modifications. One prominent change in the early stages of learning involves neurons tuned for multiple gray regions becoming more selective, firing at fewer gray regions and in many cases a single one (Fig. 3a). As learning continued, neurons displayed increasingly distinct tuning across the *Near* and *Far* trial types in regions including the pre-reward track regions ("pre-R1" and "pre-R2"). This encompassed neurons that were initially silent but later became active in specific regions for one trial type and not the other, as well as neurons that started as active on both trial types but eventually became trial-type-specific by decreasing the activity in the other trial type (Fig. 3b, c). We found that such 'splitter cells'[22,23,48] were generated at every stage of learning (Fig. 2e, Fig. 3). In summary, these single-cell tuning changes described above can be understood from the perspective of the hippocampus progressively extracting the latent task structure from ambiguous sensory experiences.

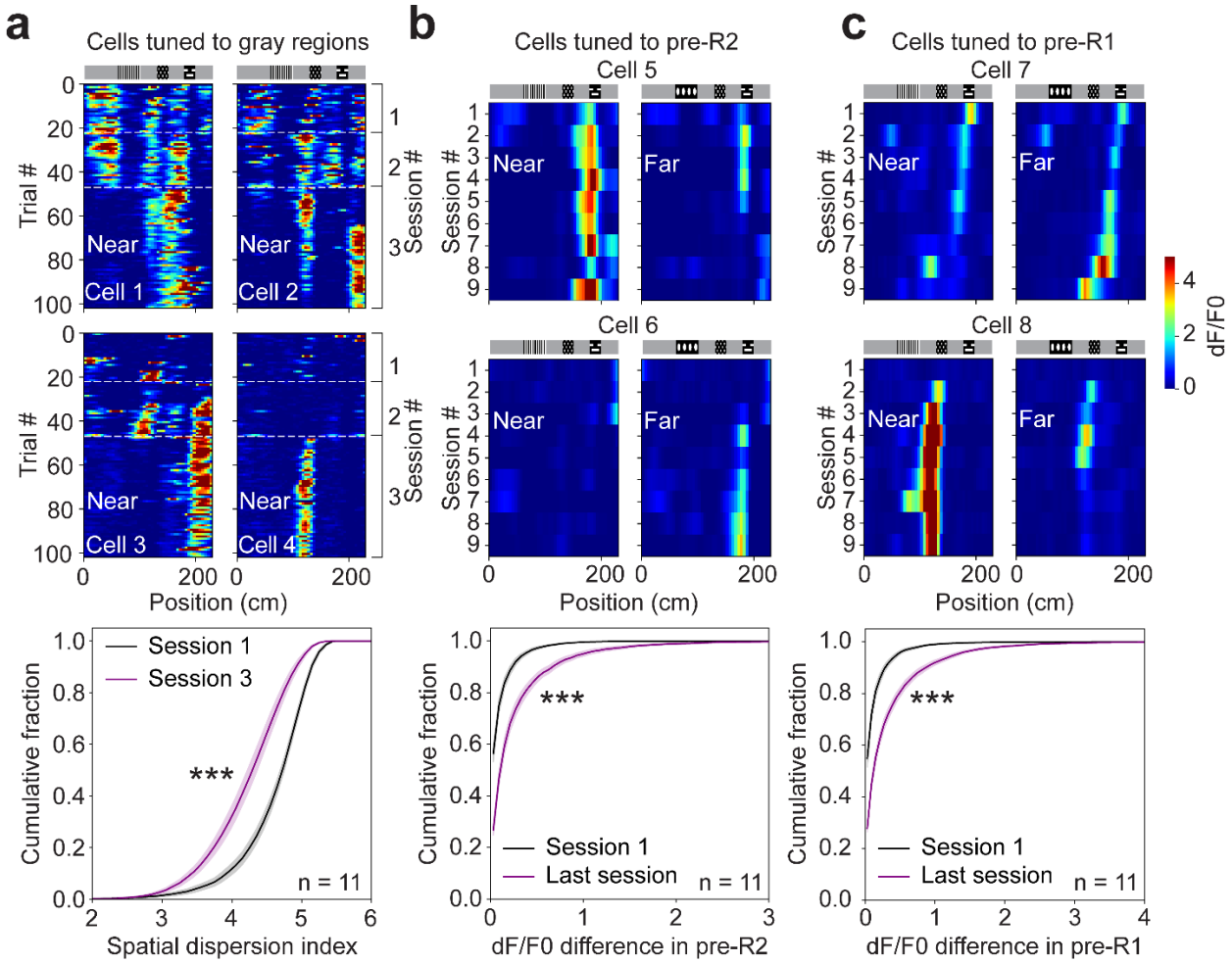

Figure 3. Single-cell tuning changes during learning.
(a) Top: positional tuning for 4 example cells tuned to gray regions from one animal across *Near* trials for stage 1 to 2 transition (first 3 sessions for this example animal). Bottom: cumulative percentage plot of the spatial dispersion index (entropy of normalized spatial tuning, see Methods) for all cells with gray region tuning within the first 3 sessions in the *Near* trial for session 1 and session 3 (Wilcoxon rank-sum test, $P < 0.001$***). **(b)** Top: session-averaged positional activity for the *Near* and *Far* trials across 9 sessions for two example cells tuned to pre-R2 region for either *Near* or *Far* trials. Bottom: cumulative percentage of the dF/F0 difference in pre-R2 between *Near* and *Far* trial types for all cells with significant tuning in pre-R2, for session 1 and last session (session 9) (Wilcoxon rank-sum test, $P < 0.001$***). **(c)** Similar to **b**, but for the pre-R1 region (Wilcoxon rank-sum test, $P < 0.001$***).

Comparing the structure of hippocampal maps to mathematical and computational models

The large number of neurons we recorded over many days of training presents a unique opportunity to probe the learning algorithms that can lead to the gradual emergence and the final representational structure of cognitive map of the L2AC task. Aligned with previous work[32,33,35,39,49–55], we conceptualize the problem as learning the underlying structure of the world by learning to predict sequences of sensory inputs.

To explore the class of models that can recapitulate animal's learning process, we first used an HMM-based model called the 'clone-structured causal graph' (CSCG)[33]. Fundamentally, HMMs and their variants like CSCGs aim to uncover hidden structures from sequential data, capturing meaningful latent states and their temporal dependencies. CSCGs consist of 'clones' that correspond to states with occupancy probabilities that are influenced by current and past sensory stimuli that are experienced sequentially. The model is constructed using the Expectation Maximization (EM) algorithm[56] to predict the sequence of sensory symbols representing different track regions and reward delivery (as a sensory cue) in the L2AC task (Fig. 4b, Methods, Suppl. Fig. 8, 9; Methods). The resulting clones and their occupancy probabilities can be compared to neural activity in the hippocampus by conceptualizing them as units and activity. Consistent with previous work[33], we found that units in the CSCG trained using sequences from the L2AC task progressed through stages of orthogonalization that closely mirrored what we observed in the hippocampus (Fig. 4b, Suppl. Fig. 8). For example, the CSCG gradually learns to use different clones to represent visual cues with similar sensory features arriving in different contexts (e.g., gray cue following the indicator cue or the first reward cue). In addition, the CSCG generated using the learned transition matrix progressed through various stages during its training that bear a striking resemblance to the representations of neural activity we observed in mice (Fig. 2e, g;

Suppl. Fig. 8d). The finding that CSCG, a cloned HMM, can recapitulate significant aspects of animal learning indicates that extracting meaningful latent states from potentially ambiguous, ongoing sequential sensory experiences is a key feature of hippocampal learning.

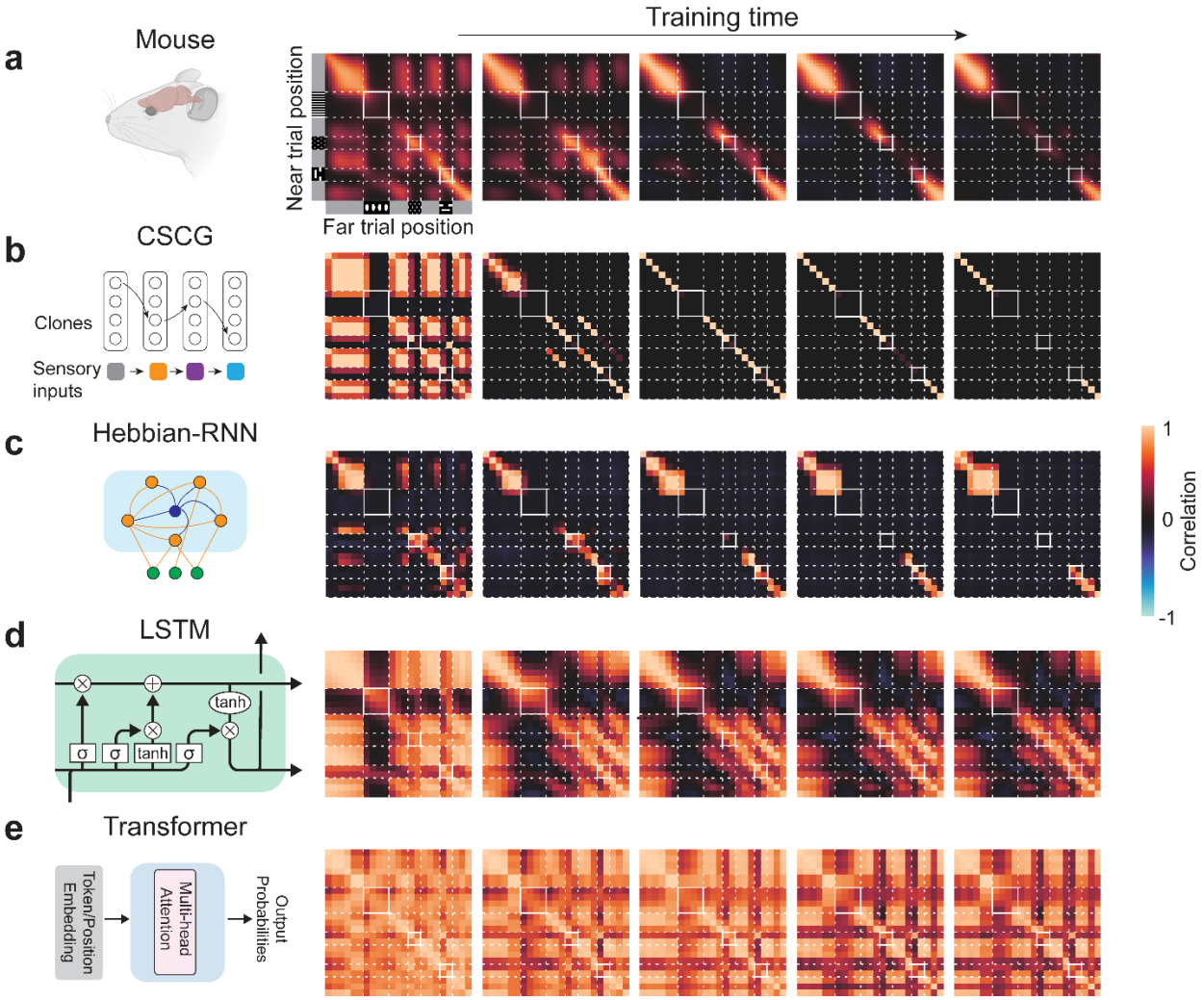

Figure 4. Representational structure during learning for mice and different models.
(a) CA1 PV cross-correlation between *Near* and *Far* trials in an example mouse over 5 different sessions (Sessions 1, 2, 3, 4, 9, from left to right, same data from Fig. 2e). **(b-e)** Cross-correlation matrices for different models trained to learn from sensory sequences sampled from a structurally similar task to L2AC: (b) CSCG, (c) RNN with Hebbian plasticity (Hebbian-RNN), (d) LSTM, (e) Transformer. CSCG and Hebbian-RNN are trained until convergence; LSTM and Transformer start with random performance and trained until expert performance (Suppl. Fig. 11).

Prior work has suggested that Hebbian plasticity such as spike-timing-dependent plasticity (STDP)[57,58] can result in attractors that stably encode sequences[59,60] in a manner that is robust to noise[61], form predictive maps[62–64], and approximate HMM learning[49,65]. To test this idea further, we built a spiking RNN model that included a soft winner-take-all (WTA) mechanism, which leverages the principle of feedback inhibition to ensure that only the highest firing neurons remain active within the network. Using only a timing-based Hebbian plasticity rule[49] based on local activity (i.e., no end-to-end training), the model (Hebbian-RNN) progressed through stages of decorrelation to result in an orthogonalized representation of the L2AC task that is qualitatively similar to the CSCG trained using expectation maximization (Fig. 4c). However, in Hebbian-RNN, pre-R1 decorrelated before pre-R2, whereas in CSCG, and in the hippocampus, pre-R2 decorrelates before pre-R1. These results suggest that Hebbian plasticity and feedback inhibition in a RNN are sufficient to reproduce various aspects of single cell tuning changes (Suppl. Fig. 10) and a final representation of the L2AC task with features like the OSM representation we observed in the hippocampus, but that additional mechanisms will be required to fully mimic the learning dynamics (see Discussion).

Artificial neural networks such as LSTMs[42] and Transformers[43] are powerful models for sequence learning. Using gradient descent via backpropagation of error, we trained an LSTM model to predict the next input in a sensory sequence (reward delivery also as a sensory cue) in a L2AC task (Fig. 4d; see Methods). Although the LSTM model could learn to perform perfectly on the task (Suppl. Fig. 11), unit activity in the well-trained model differed strikingly from the properties of neural activity we observed in the mouse hippocampus. Specifically, most of the activity corresponding to the same sensory input in different latent states remain highly correlated (Fig. 4d) and trial-type differences in activity in the well-trained agent were minor compared to the activity levels (Suppl. Fig. 11). Using a similar approach, we used gradient descent to train a decoder-only Transformer to learn to predict the next input in the L2AC task. Again, while the trained model accurately predicted future states in the L2AC task, unit activity in the model differed markedly from what we observed in mice, with properties like those of the LSTM model (Suppl. Fig. 11).

Next, we examined if adding various regularization schemes could help LSTMs to produce representational structures that more closely resembled those observed in the brain. Our findings suggested that commonly employed regularization techniques — those that promote sparseness or

introduce noise during the training phase — were unsuccessful in capturing the orthogonal representational structure in the fully trained model (Suppl. Fig. 11). Notably, however, we could coerce the model into generating an orthogonalized representational structure by using a cost function that specifically penalized non-zero values in the correlation matrix between hidden states for both *Near* and *Far* trials. This is consistent with the recognized capability of approximating complicated functions in neural networks[66,67] (Suppl. Fig. 11f).

Novel task features lead to adaptation of the existing hippocampal state machine

To investigate how the hippocampal state machine, once learned by a mouse, can be utilized when new elements are introduced, we expanded and later modified the structure of the task. First, after mice learned the task with the original indicator cues (cue pair A) we replaced them with two unfamiliar visual patterns. To do this we developed four unique indicator pairs (cue pair B, C, D, and E) and presented them to mice that had already learned the original cue pair (Fig. 5a). Every day, the mice were initially exposed to cue pair A for a duration of 5 to 10 minutes, after which the indicators for the task were replaced with one of the novel pairs. This change enabled us to collect neural activity data for both the original and new cue pairs. Training on the new cue pair continued until the mouse could proficiently execute the task, demonstrated by restricting its licking to the rewarded location and just before it on 75% of the trials for three successive sessions. Mice were then sequentially trained on each subsequent novel indicator pair on the following days in the same manner. Through this training process mice learned the new cue sets in significantly fewer trials (147 ± 39 trials for the new cue sets compared to 483 ± 70 trials for the original cue set; n = 3 mice; $P < 0.05$*, unpaired *t*-test. Fig. 5b).

Comparing PV correlations of the neural activity for trials with novel indicators versus the original indicators revealed high similarities in neural representations between the old and new tasks in all track regions except the indicator region (Fig. 5c). In other words, the neural activity in the presence of new indicators mirrored the common task structure while maintaining information about the visual identities of the novel indicator cues. In terms of the state machine framework, this shows that once a state machine is established in the hippocampus, it can be effectively utilized and reused for new task variants. New task elements can be integrated into the existing state machine, either through the creation of new states or linking new sensory inputs to existing states (Fig. 5d). This flexible adaptation and integration, in turn, expedites learning.

In a second variation of the task, we extended the length of the gray zones following the indicator cue and after the first reward cue, thus requiring animals to travel longer distances to reach the reward zones (Fig. 5e, f; Methods). These 'stretched trials' were introduced every 5-6 trials, to evaluate how well-trained animals for the original task respond to the altered environment without extensively training them to adjust to these task modifications (Methods). In both stretched *Near* (*Near'*) and stretched *Far* (*Far'*) trial types, mice displayed a tendency to lick towards the beginning of the usual reward location, even though the reward cue was not yet encountered (Suppl. Fig. 12a). A comparison of the tuning location for each cell during normal and stretched trials of the same type (i.e., *Near-Near'* or *Far-Far'*) provided insights into how the animals might perceive the modified task (Fig. 5e, f). As expected, for the initial part of the tracks (ranging from the start of the track to the gray region just prior to the stretched region), which are identical to the original trials, the place fields were tuned to similar locations between the regular and stretched trials (Fig. 5d). As the animal enters the first stretched region in the *Near* trials, which is the first deviation from the normal trial, many cells tuned for the gray region before the first reward location (pre-R1) were active throughout the stretched region (Fig. 5e, n = 3 mice). This potentially indicates that the animal may believe it remains in the same patch of gray zone right before the first reward region. Interestingly, during *Far* trials, the difference in reward location expectation drives a different pattern to emerge. When the animal enters the first stretched region in far trials, the place cells didn't persistently extend their activity. Instead, they rapidly shifted their tuning to align with the region just before the second reward area (pre-R2), as if the animal is anticipating the second reward location (Fig. 5f). However, when the animal eventually sees the first reward cue, the representation quickly resets and anchors to the representation reflecting the first reward region in the original task. These results imply that, when the animals encounter modified components of the task, the neural representations can settle into discrete states to mirror inferred latent states under conditions of uncertainty (Fig. 5e, f). In conclusion, these discoveries substantiate the idea that the learned manifold exhibits the properties of a state machine that can potentially infer and flexibly use learned states in novel situations.

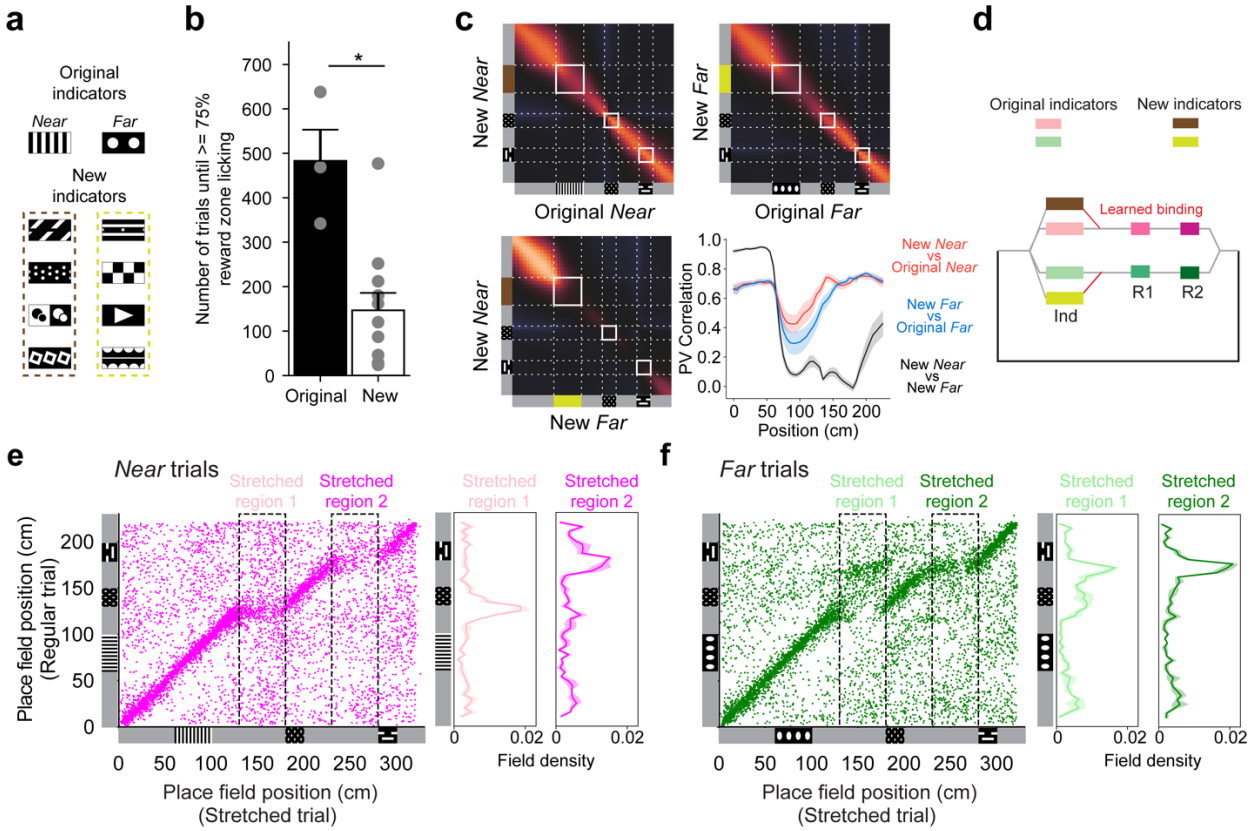

Figure 5. State machines can be flexibly used in novel settings.
(a) Original and novel indicator pairs. **(b)** Number of trials before high performance (restricting licking to the rewarded location and just before it on 75% of the trials) for each indicator pair (bar graph showing mean ± s.e.m, p = 0.039, unpaired *t*-test). Dots represent data from a single animal for one indicator pair. **(c)** PV cross-correlation between the neural activity for trials with the original and new indicators for the same trial type (*Near*, top left; *Far*, top right); between *Near* and *Far* trials for the new indicators (bottom left). Bottom right: quantification of the diagonal cross-correlations in 3 cross-correlation matrices. **(d)** Conceptual diagram for the incorporation of new indicator states into an existing state machine. **(e)** Place field locations in the stretched *Near* trials plotted against those in the regular *Near* trials (n = 3 mice, data pooled together). The histograms of field locations in the two stretched regions are plotted to the right. **(f)** Similar to **e** but for the *Far* trials.

DISCUSSION

Cognitive maps evolved to allow animals to exhibit flexible behaviors in complex and rapidly changing environments. They allow animals to navigate and forage efficiently, and more recently, it has been suggested these maps may permit the understanding and use of complex relationships such as concepts[11], stimulus relations[26], and other non-spatial dimensions[24,68,69,25,70,71,30].

The work described here builds on a long history of experimental and theoretical research on cognitive maps in the hippocampal-entorhinal system. Pioneering studies ranging from the early lesioning experiments demonstrating the causal roles of the hippocampus in memory formation[72] to the discovery of place cells[2], grid cells[73], and other spatially selective response properties[74], as well as modulation of these firing properties by factors such as running speed[20] and direction[20,21], highlight the central role of this system in the formation of cognitive maps.

Many studies have examined the dynamics of hippocampal cognitive maps as a function of time in static or changing environments[75–77]. Most of these studies have been performed using electrodes implanted in freely moving rats or mice. While the stability of these recordings places limits on the duration of longitudinal studies and makes it difficult to distinguish between all-or-none changes in neuronal firing properties and electrode movement artifacts, a few studies have attempted to solve this problem using imaging[78–81,52]. This approach has facilitated the investigation of longitudinal properties of neural activity, including place field formation and long-term dynamics, revealing key mechanisms for experience-dependent changes in place fields[82–86]. Additionally, it has uncovered time-dependent changes in hippocampal firing patterns occurring over weeks to months, a phenomenon called 'representational drift'[79,80,87,88].

Earlier imaging studies primarily focused on the temporal stability of the hippocampal code in simple task settings such as open arenas or linear tracks with fixed reward locations[79,81,87], without fully monitoring cognitive map formation in naïve animals learning to navigate more cognitively demanding tasks. Furthermore, these studies also limited longitudinal cell tracking up to a few hundred cells[79,86]. By ensuring stable functional imaging from thousands of neurons over several weeks, our study significantly increases the density and duration of sampled neural activity. This increase enhances the signal-to-noise ratio, aiding in accurate estimation of the underlying neural manifold[89–91]. We were also able to monitor the formation of cognitive maps throughout

the entire learning process of a moderately complex task that includes sensory cues that must be interpreted in context to guide effective behavior, thus providing single-cell and population-level data from which to infer the principles underpinning cognitive map formation.

Our results reveal that the hippocampus constructs an orthogonalized state machine during learning, with distinct, mutually orthogonal states corresponding to latent states of specific task features. With increasing task exposure, these states exhibit progressive differentiation and form precise inter-state transitions, accurately mapping the task's inherent structure. Importantly, the hippocampal representational structure and the exact trajectory of the learning dynamics, marked by the evolution of these state machines, offers empirical constraints to understand learning principles underlying hippocampal cognitive map formation.

Our findings are related to and expand upon many previous studies, including those describing the concepts of partial remapping[92] (only some neurons change their spatial firing patterns while other neurons remain unchanged upon specific modifications of the environment), rate remapping[93] (the location cells' tuning remains unchanged but the firing rate varies), and global remapping[76,93,94] (the activity patterns in two different environments are not correlated), which refer to subtle and more extensive changes in the hippocampal code when the animal's environment changes subtly or dramatically[95]. Our study indicates that learning the L2AC task can gradually induce partial remapping, with cells tuned to specific track segments, such as the reward cues, showing progressively decorrelated neural activity, while other cell populations, specifically those tuned to the beginning or end of the track, sustain highly correlated activity across trial types. Our results also suggest that rate remapping and partial remapping could be an intermediate stage for the gradual orthogonalization process of two contexts[96,97], as the PV correlation for various parts of the track decrease from highly correlated to near orthogonal representations as learning progresses. Additionally, we observed that the visually distinct indicators for both trial types show highly decorrelated neural activity from the very beginning of task exposure, which further deepens and approaches orthogonalization as learning progresses. This suggests that even representations of distinct sensory cues could be further orthogonalized if they represent different task states. Therefore, some forms of global remapping might result from a gradual orthogonalization process.

Our work is also related to the concept of pattern separation[98–102], as we show that mice can learn to decorrelate and produce orthogonal representations for subtly differing sequences of

sensory stimuli. While our work shows qualitatively similar observations of decorrelation, we find that hippocampal representations were driven to decorrelate towards capturing the underlying task structure. We also propose learning mechanisms that might support such gradual decorrelation. Pattern separation can be enabled by expansion recoding[103] or neuronal nonlinearities in recurrent networks (without weight changes)[104]. While our Hebbian-RNN modeling relies on both local weight updates through STDP and recurrent dynamics to generate decorrelation trajectories towards discovering task structure, it remains possible that all these mechanisms could work in tandem to reduce sensory interference and build robust models of the environment.

We also demonstrate that neural activity corresponding to gray regions of the corridor with similar sensory stimuli are decorrelated as they are interspersed in the context of reliably repeating cue sequences. This is reminiscent of other studies showing that identical locations or sensory stimuli can be distinctly represented when experienced in different contexts[22,23,69,105,106]. Splitter cells, which fire differentially on the overlapping segment of a maze that differ in their past and/or future, for example, closely relates the core phenomenon of the orthogonalization process we observed. Our study extends this idea from differential neuronal tuning of specific locations to a systematic orthogonalization process that generates cells matching the core features of splitter cells at each stage of the learning process (e.g., gray regions, and two separate reward zones). The emergence of such generalized splitter cells suggests that an important learning mechanism and computation performed by the hippocampus are intrinsically linked to the separation of similar sensory experiences based on their different task implications[22,32,33,38,69,106]. Such computations allow the hippocampus to approximate the environment's generative process through the creation of hippocampal 'state cells' representing the gradually discovered task-related latent states during each learning stage[33,35,107–110].

Based on the similarity of the hippocampal cognitive map to a CSCG, as well as our evidence that the cognitive map is used to shape flexible behavior when task conditions change, we posit that hippocampal cognitive maps constitute sparse, orthogonalized state machines. A classical concept in computer science, a state machine is a computational structure consisting of a finite set of states with the transitions between these states based on defined inputs or conditions[111]. States reflect current sensory input from the environment and the animal's own body, as well as latent information such as the recent history of sequential observations. Transitions are constrained by the current state and transition probabilities to other states and are driven by the animal's own

movements as well as changes in the environment. We posit that neural activity in the hippocampal OSM could shape behavior, such as speeding up, slowing down, or licking. These behaviors in turn influence neural activity, and thus transitions to new states in the hippocampal OSM, both by changing the animal's external and internal sensory experience and by changing the stimuli coming from the environment. The hippocampal OSM operates in closed loop with the rest of the brain, the animal's body, and its environment to produce the properties of a state machine.

We found that the orthogonalized representation structure of the hippocampal cognitive map was reproduced by a recurrent neural network model based entirely on a local Hebbian learning rule. Recurrent networks using Hebbian learning rules are often used to model the hippocampus[61,112–114], which exhibits attractor dynamics[115–117], especially within the recurrent CA3 region. This result underscores the potential of unsupervised local learning rules, which operate without the necessity for error backpropagation, to mimic biological learning mechanisms, and to do so in a way that resembles the EM algorithm used to construct HMM models[49].

Sparse orthogonal representations have long been proposed by others to constitute a powerful mechanism for memory and intelligence[118–127]. However, we find that traditional AI systems trained with backpropagation of error—specifically LSTMs and Transformers—do not naturally produce the sparse orthogonalized geometry. We found that this key property of the hippocampal OSM was only observed in LSTM when the cost function explicitly penalized activity correlation between the two trial types. Orthogonalized representations might also be produced via other mechanisms such as compression [34]. Influential work in AI has shown that the enforced-orthogonalization approach is a powerful tool in self-supervised learning systems[128]. In addition, the ability to tailor LSTMs to exhibit orthogonalized states has implications for uncovering mechanisms that implement error backpropagation in the brain[129].

Other frameworks for modeling hippocampal function include predictive coding and representations[130–132,31,35,51], statistical learning[125,133], latent states inference[32,33,108,134–136], compression[34,50,137,138], and hippocampal models tasked with generalization such as the Tolman Eichenbaum Machine[107] and spatial memory pipeline[139]. These varied approaches reflect the rich complexity of the hippocampal system, and each offers distinctive insights into our understanding of cognitive maps and the broader mechanisms of learning and memory in the brain.

Several aspects of our study warrant further investigation. While both CSCG and the online Hebbian-RNN can capture the orthogonalized representational structure, they differ in how they

mirror the process by which this orthogonalization unfolds in animals. Specifically, the Hebbian-RNN model accurately reproduces the end-stage representation but deviates in the exact sequence of orthogonalization when compared to CSCG and observed neural dynamics of the animal. This discrepancy highlights an opportunity for future research to develop more refined and biologically realistic models of hippocampal cognitive maps, for example by incorporating plasticity mediated by forward and backward replay mechanisms[140,141]. Future work is also needed to identify the brain regions and plasticity mechanisms responsible for the formation of a cognitive map. Although we observed the map in CA1, the changes we observed likely result not only from synaptic plasticity in CA1, but also plasticity in other brain regions, which produced altered activity in CA1. For example, pattern separation has been shown to occur in the dentate gyrus (DG) and proximal parts of CA3[101,102], while more distal regions of CA3, which are extensively recurrent, likely contribute to the pattern completion attractor dynamics associated with orthogonalized representations[142].

In summary, we provide detailed, high-resolution, longitudinal data on the formation of a cognitive map in the hippocampus during learning of a moderately complex task, which progresses in stages over the course of several training sessions. The excellent match between CSCGs, Hebbian-RNNs, and hippocampal data, suggest that state machines with sparse, orthogonalized representations are likely to provide a powerful framework for neural computation[121], memory[122,143], and intelligence[144]. These results also underscore the need to understand how different learning rules such as local Hebbian learning and gradient descent-based learning might synergistically function to promote a more effective and efficient learning process in both natural and artificial learning systems[145–147].

METHODS

All procedures were performed in accordance with the Janelia Research Campus Institutional Animal Care and Use Committee guidelines. Both male and female GCaMP6f (Thy1-GCaMP6f[148]) transgenic mice were used, 3 to 6 months old at the time of surgery (3 to 8 months old at the beginning of imaging studies).

Surgery

Mice were anesthetized with 1.5 - 2.0% isoflurane. A craniotomy on the right hemisphere was performed, centered at 1.8 mm AP and 2.0 mm ML from the bregma using a 3 mm diameter trephine drill bit. The overlying cortex of the dorsal hippocampus was then gently aspirated with a 25-gauge blunt-tip needle under cold saline. A 3 mm glass coverslip previously attached to a stainless-steel cannula using optical glue was implanted over the dorsal CA1 region. The upper part of the cannula and a custom titanium headbar were finally secured to the skull with dental cement. Animals were allowed to recover for a minimum of 2 days before being put under water-restriction (1.0-1.5ml/day), in a reversed dark-light cycle room (12-hour light-dark cycle).

Behavior

VR setup

The VR behavior setup was based on a design previously described in Cohen et al. 2017[149]. The cylindrical treadmill consisted of a hollowed-out Styrofoam ball (diameter = 16 inches, 65g) air-suspended on a bed of 10 air-cushioned ping-pong balls in an acrylic frame. Animals were head-fixed on top of the treadmill using a motorized holder (Zaber T-RSW60A; Optics Focus MOG-130-10 and MOZ-200-25) with their eyes approximately 20 mm above the surface. To translate the movement of the treadmill into VR, two cameras separated at 90 degrees were focused on 4 mm^2 regions of the equator of the ball under infrared light[149]. Three axis movement of the ball was captured by comparing the movement between consecutive frames at 4kHz and readout at 200 Hz[149]. A stainless-steel tube (Inner diameter= 0.046 inches), attached to a three-axis motorized stage assembly (Zaber NA11B30-T4A-MC03, TSB28E14, LSA25A-T4A, and X-MCB2-KX15B), was positioned in front of the animal's mouth for delivery of water rewards. The animal was shown a perspective corrected view of the VR environment through 3 screens (LG LP097QX1 with Adafruit Qualia bare driver board) placed roughly 13 cm away from the animal

(Fig. 1a). This screen assembly could be swiveled into position using a fixed support beam. All rendering, task logic and logging was handled by a custom software package called Gimbl (https://github.com/winnubstj/Gimbl) for the Unity game engine (https://unity.com/). All inter-device communication was handled by a MQTT messaging broker hosted on the VR computer. Synchronization of the VR state with the calcium imaging was achieved by overlaying the frame trigger signal of the microscope with timing information from inbuild Unity frame event functions. To observe the mouse during the task without blocking its field-of-view, we integrated a periscope design into the monitor assembly. Crucially, this included a 45° hot-mirror mounted at the base of a side monitor that passed through visible light but reflected IR light (Edmund optics #62-630). A camera (Flea3-FL3-U3-13Y3M) aimed at a secondary mirror on top of the monitor assembly could hereby image a clear side view of the face of the animal. Using this camera, a custom Bonsai script[150] monitored the area around the tip of the lickport and detected licks of the animal in real time that were used in the VR task as described below.

Head fixation training

After recovering from surgery, mice were placed on water restriction (1.0 -1.5 ml per day) for at least 2 weeks before starting any training. Body weight and overall health indicators were checked every day to ensure animals remained healthy during the training process. Mice were acclimated to experimenter handling for 3 days by hand delivering water using a syringe. For the next 3 sessions, with the VR screens turned off, mice were head-fixed on the spherical treadmill while water was randomly dispensed from the lick-port (10 ± 3 sec interval; 5 µl per reward). These sessions lasted until animals acquired their daily allotment of water or until 1 hour had passed. We observed that during this period most mice started to run on their own volition. Next, we linked water rewards to bouts of persistent running and increased this duration across sessions till the animal would run for at least 2 seconds straight (~5 sessions). During this time, we also slowly increased the height of the animal with respect to the treadmill surface across sessions to improve performance. Animals that did not show sufficient running behavior to acquire their daily allotment of water were discarded in further experiments.

Linear 2 alternative choice (L2AC) task

At the beginning of each trial mice were placed at the start of a virtual 230 cm corridor. The appearance of the walls was uniform except at the location of three visual cues that represented

the indicator cue (40 cm long) and the two reward cues (near/far; 20cm long). Depending on the trial type, a water reward (5 µl) could be obtained at either the near, or far reward cue (near and far reward trials). The only visual signifier for the current trial type was the identity of the indicator cue at the start of the corridor. For the first 2-3 sessions the animal only had to run past the correct reward cue in order to trigger reward delivery ('Guided' sessions). On all subsequent sessions mice had to lick at the correct reward cue ('Operant' sessions). No penalty was given for licking at the incorrect reward cue. In other words, if the animal licked at the 'near' reward cue during a 'far' trial type then the animal could still receive a reward at the later 'far' reward cue. Upon reaching the end of the corridor the VR screen would slowly dim to black, and mice would be teleported to the start of the corridor to begin the next semi-randomly chosen trial with a 2-second duration. The probability of each trial type was 50% but in order to prevent bias formation caused by very long stretches of the same trial type, sets of near/far trials were interleaved with their number of repeats set by a random limited Poisson sampling (lambda= 0.7, max repeats=3). The identity of the indicator cue was kept hidden for the first 20 cm of the trial and was rendered when the animals pass the 20cm position. To internally track the learning progress of the animal we utilized a binarized accuracy score for each trial depending on whether the animal only licked at the correct reward cue. Once the animal had 3 sessions where the average accuracy was above 75%, we considered the animal to have learned that cue set.

L2AC task with novel indicators

For 3 mice out of the 11 well-trained animals on the original L2AC task, we subsequently trained them to perform the L2AC task novel indicator cues. After reaching 3 consecutive sessions with >75% task accuracy for the original L2AC task, the novel task was introduced the following session, but with the original task shown for the first 5 to 10 minutes at the beginning of each session before switching completely to the new task. When the animal can perform the new task for 3 consecutive days > 75%, we move on to the next novel indicator pair until the last one is finished (4 novel indicator pairs in total).

L2AC task with extended gray regions

As another modification to the original task design, the gray regions were extended in certain trials which we call the "stretched trials". In the stretched trials, the linear track was extended from 230 cm to 330 cm, and the reward positions were moved from [130, 150] cm to

[180, 200] cm (the 1st rewarding (Near) object), and [180, 200] cm to [280, 300] cm (the 2nd rewarding (Far) object). Note that the distance between the indicator cue and the Near object in the stretch trial is equal to the one between the indicator cues and the Far object in the normal trial. During a session with stretch trials, following a 5-minute warm-up using only the normal L2AC trial, the stretch trial was adopted at intervals of every 5 or 6 trials, lasting 40 minutes.

Calcium Imaging

Neural activity was recorded using a custom-made 2p-RAM mesoscope[45] and data acquired through ScanImage software[151]. GCaMP6f was excited at 920 nm (Chameleon Ultra II, Coherent). 3 adjacent ROIs (each 650 µm wide) were used to image dorsal CA1 neurons. The size of the ROIs was adjusted to ensure a scanning frequency at 10 Hz. Calcium imaging data were saved into tiff files and were processed using the Suite2p toolbox (https://www.suite2p.org/). This included motion correction, cell ROIs, neuropil correction, and spike deconvolution as described elsewhere[152].

Multiday alignment

To image the same cells across subsequent days, we utilized a combination of mechanical, optical, and computational alignment steps (Suppl. Fig. 3). First, mice were head fixed using a motorized head bar holder (see above) allowing precise control along three axes (roll, pitch, and height) with submicron precision. Coordinates were carefully chosen at the start of training to allow for unimpeded movement and reused across subsequent sessions. The 2p-RAM microscope was mounted on a motorized gantry, allowing for an additional three axis of alignment (anterior/posterior, medial/lateral, and roll). Next, we utilized an optical alignment procedure consisting of a 'guide' led light that was projected through the imaging path, reflected off the cannula cover glass and picked up by a separate CCD camera (Suppl. Fig. 2b). Using fine movement of both the microscope and the head bar, the location of the resulting intensity spot on the camera sensor could be used to ensure exact parallel alignment of the imaging plane with respect to the cover glass.

To correct for smaller shifts in the brain tissue across multiple sessions, we took a high-resolution reference z-stack at the start of the first imaging session (25 µm, 1 µm interval; Suppl. Fig. 2c). The imaging plane on each subsequent session was then compared to this reference stack by calculating a cross correlation in the frequency domain for each imaging stripe along all depth

positions. By adjusting the scanning parameters on the remote focusing unit of the 2p-ram microscope we finely adjusted the tip/tilt angles of the imaging plane to achieve optimal alignment with the reference stack. We used a custom online Z-correction module (developed by Marius Pachitariu[153], now in ScanImage), to correct for Z and XY drift online during the recording within each session, using a newly acquired z-stack for that specific session.

To find cells that could be consistently imaged across sessions we first performed a post hoc, non-rigid, image registration step using an averaged image of each imaging session (Diffeomorphic demon registration; python image registration toolkit) to remove smaller local deformations (Suppl. Fig. 2g-f). Next, we performed hierarchical clustering of detected cells across all sessions (jaccard distance; Suppl. Fig. 3). Only putative cells that were detected in 50% of the imaging sessions were included for further consideration. We then generated a template consensus mask for each cell based on pixels that were associated with this cell on at least 50% of the sessions. These template masks were then backwards transformed to the spatial reference space of each imaging session to extract fluorescence traces using Suite2p.

Data analysis

Coefficient of Partial Determination

To assess the unique contribution of each behavioral strategy (random licking, licking in both reward locations, lick-stop, and expert) to overall animal behavior, we used the coefficient of partial determination (CPD). In this analysis, a multivariable linear regression model was first fitted using all behavioral strategies as regressors, providing the sum of squares error (SSE) of the full model ($SSE_{fullmodel}$). Each regressor was then sequentially removed, the model refitted, and the SSE without that regressor ($SSE_{\sim i}$) was computed. The CPD for each regressor, denoted as CPD_i, was then calculated as $CPD_i = (SSE_{\sim i} - SSE_{fullmodel}) / SSE_{\sim i}$, revealing the unique contribution of each behavioral strategy to the overall variance in licking behavior.

Place field detection

To identify significant place cells, we utilized an approach based on Dombeck et. Al. 2010[78] (but see also Grijseels et al., 2021[154] for overall caveats with such approaches). Place fields were determined during active trials, indicated by active licking within reward zones, and at running speeds greater than 5cm/s. For detecting activity changes related to position we first calculated a demixed calcium signal by subtracting the fluorescence of each cell mask with the

activity in the surrounding neuropil using suite2p. Next, the baseline fluorescence activity for each cell was calculated by first applying gaussian filter (5 secs) followed by calculating the rolling max of the rolling min ('maximin' filter, see suite2p documentation). This baseline fluorescence activity (F0) was used to calculate the differential fluorescence (dF/F0), defined as the difference between fluorescent and baseline activity divided by F0. Next, we identified significant calcium transient event in each trace as events that started when fluorescence deviated 5σ from baseline and ended when it returned to within 1σ of baseline. Here, baseline σ was calculated by binning the fluorescent trace in short periods of 5 seconds and considering only frames with fluorescence in the lower 25th percentile.

Initially, putative place fields were identified by spatially binning the resulting ΔF/F0 activity (bin size: 5 cm) as continuous regions where all dF/F0 values exceeded 25% of the difference between the trial's peak and the baseline 25th percentile dF/F0 values. We imposed additional criteria: the field width should be between 15-120 cm in virtual reality, the average ΔF/F0 inside the field should be at least four times greater than outside; and significant calcium transients should occur at least 20% of the time when the mouse was active within the field (see above). To verify that these putative place fields were not caused by spurious activity we calculated a shuffled bootstrap distribution for each cell. Here, we shuffled blocks of 10 secs calcium activity with respect to the animal's position and repeated the same analysis procedure described above. By repeating this process 1000 times per cell we considered a cell to have a significant place field if putative place fields were detected in less than 5% of the shuffles.

Population vector (PV) analysis

For the analysis of similarity of representation between *Near* vs *Far* trial types, we performed population vector correlation on the fluorescence dF/F0 data. Each 5cm spatial bin, we define the population vector as the mean dF/F0 value for each neuron. Fluorescence data were included only when the animal's speed exceeded 5cm/sec. The cross-correlation matrix was generated by calculating the Pearson correlation coefficient between all location pairs across the two trial types.

Spatial dispersion index

To evaluate the extent of spatial dispersion in place tuning across single cells – such as distinguishing between tuning to single positions versus multiple positions, we take the single cell

tuning curve over track positions and normalize it so the area under the curve is 1. The spatial dispersion index is defined as the entropy of this normalized dF/F0 signal by: Entropy = - ∑ [p(i) * log2 p(i)], where p(i) denotes the probability associated with each position bin index.

Uniform Manifold Approximation and Projection (UMAP)

To visually interpret the dynamics of high-dimensional neural activity during learning, we utilized UMAP on our deconvolved calcium imaging data. The UMAP model was parameterized with 100 nearest neighbors, 3 components for a three-dimensional representation, and a minimum distance of 0.1. The 'correlation' metric was used for distance calculation. The data, a multidimensional array representing the activity of thousands of cells concatenated from several imaging sessions, was fitted into a single UMAP model. This resulted in a three-dimensional embedding, where each point characterizes the activity of the neuron ensemble at a single imaging frame.

Modeling

CSCG

In the L2AC task, the combination of position along the track and trial type defines a state of the world (z). Although this state is not directly observable to the animal, it influences the sensory observation (x) that the animal perceives (Suppl. Fig. 8a). The sequence of states in the environment obeys the Markovian property, whereby the probability distribution of the next state (i.e. next position and trial type) depends only on the current state, and not all the previous states, assuming the animal always travels at a fixed speed. When an animal learns the structure of the environment and builds a map, it tries to learn which states (position, trial type) are followed by which states, and what sensory experience they generate. This can be viewed as a Markov learning problem. A Hidden Markov model (HMM) consists of a transition matrix whose elements constitute $p(z_{n+1} \mid z_n)$ i.e., the probability of going from state z_n at time n to z_{n+1} at time $n+1$, an emission matrix whose elements constitute $p(x_n \mid z_n)$, ie. the probability of observing $x_n$when the hidden state is z_n, and the initial probabilities of being in a particular hidden state $p(z_1)$.

CSCG (Cloned Structured Causal Graph) is an HMM with a structured emission matrix where multiple hidden states, referred to as clones, deterministically map to the same observation.

In other words, $p(x_n = j|z_n = i) = 0$ if $i \notin C(j)$ and $p(x_n = j|z_n = i) = 1$ if $i \in C(j)$, where $C(j)$ refers to the clones of observation j [33] (Suppl. Fig. 8b). The emission matrix is fixed and CSCG learns the task structure by only modifying the transition probabilities (Suppl. Fig. 8b), making the learning process more efficient. Baum Welch expectation maximization algorithm was used to update the transition probabilities such that it maximizes the probability of observing a given sequence of sensory observations[155–157].

We trained CSCG on sequences of discrete sensory symbols mimicking the sequence of patterns shown to the animals in the 2 tracks. Each 10 cm segment of the track was represented by a single sensory symbol. Additionally, the teleportation region was represented by a distinct symbol repeated thrice, spanning 30cm. In the rewarded region, the animals could receive both visual input and a water reward simultaneously. However, our model could only process a single discrete stimulus at a time. Thus, we divided the rewarded region into two parts. We presented the visual cue first, mimicking the animals' ability to see the rewarded region ahead before reaching it. Subsequently, we presented a symbol representing the water stimulus, which was shared across the two trials. The near trial sequence, denoted as [1,1,1,1,1,1,2,2,2,2,1,1,1,4,6,1,1,1,5,5,1,1,7,0,0,0], and the far trial sequence, denoted as [1,1,1,1,1,1,3,3,3,3,1,1,1,4,4,1,1,1,5,6,1,1,7,0,0,0]', were used. Where 1 represented the gray regions, 2 and 3 the indicators for near and far tracks respectively, 4 the visual observation associated with the first reward zone, 5 denoted the visual stimulus associated with the far reward zone, 6 represented the common water reward received in both tracks, 7 the brick wall at the end of each trial, and 0 indicated the teleportation region (Suppl. Fig. 8c).

We initialized the model with 100 clones for each sensory observation symbol and performed 20 iterations of the expectation-maximization process at each training step with sequences from 20 randomly selected trials, comprising both near and far trial types. We extracted the transition matrix at different stages of learning and used Viterbi training algorithm to refine the solution[33] and then plotted the transition matrix as a graph, showing only the clones that were used in the representation of the 2 trials (Suppl. Fig. 8d). We ran multiple simulations and compared how correlation between the two trial types changed over learning for different positions along the track (Suppl. Fig. 8e).

We also explored alternate sequences of sensory stimuli. In one variant, we provided the water symbol prior to the visual symbol of the reward zone (for ex. […1,1,1,6,4,1,1,1…] where 6

represents the water and 4 the visual symbol). Additionally, we introduced a symbol that conjunctively encoded the simultaneous water reward and visual symbol (for ex. and […111,4,6,111…] in the near trial and […111,5,8,111…] in the far trial, where 6 denotes a combined code for water and visual R1, and 8 represents a combined code for water and visual R2) (Suppl. Fig. 9a). While the final learned transition graphs matched for all the 4 sequence variants, the exact sequence of learning differed. Specifically, reward cue followed by a visual cue for reward zone often led to decorrelation of Pre-R1 followed by Pre-R2 (Suppl. Fig. 9b, c), contrary to what is often observed during learning in animals. Therefore, for further analysis, we utilized the visual followed by common reward sequence, as it led to a learning trajectory that closely matched the learning observed in animals.

Hebbian-RNN

Work by Kappel et al. (2014)[49] showed that a local Hebbian learning rule in a recurrent neural network (RNN) can approximate an online version of HMM learning. We used an RNN consisting of $K = 100$ recurrently connected neurons and $N = 96$ feedforward input neurons. The feedforward input neurons carried orthogonal inputs for each of the 8 sensory stimuli, with 12 different neurons firing for each stimulus (Suppl. Fig. 10a). The recurrent weights V and feedforward weights W were initialized from a normal distribution with 0 mean and standard deviation 2.5 and 3.5 respectively. The membrane potential of the kth neuron at time t is given by $u_k^t = \sum_i^N w_{ki}\, x_i^t + \sum_j^K v_{kj}\, y_j^{(t-\Delta t)}$, where w_{ki} is the feedforward weight from input neuron i to RNN neuron k, v_{kj} is the recurrent weight from neuron j to neuron k, $\Delta t = 1ms$ is the update time, and x_i^t and $y_j^{t-\Delta t}$ are exponentially filtered spike trains of the feedforward and recurrent neurons respectively (exponential kernel time constant, 20ms). The probability of neuron k firing in Δt was computed by exponentiating the membrane potential and normalizing it through a global inhibition, $f_k = \frac{e^{u_k}}{\sum_l^K e^{u_l}}$. For each neuron k, spikes were generated with a probability of f_k by a Poisson process, with a refractory period of 10 ms during which the neuron cannot spike again. When the post-synaptic neuron k spiked, then the weights onto neuron k were updated as $\Delta w_{ki}(t) = \alpha(e^{-w_{ki}} x_i(t) - 0.1)$ and $\Delta v_{kj}(t) = \alpha\left(e^{-v_{kj}} y_j(t) - 0.1\right)$, where α is the learning rate (0.1) and $y_j(t)$ is exponentially filtered spike train. Both weights V and W were kept excitatory. We computed the correlation between the RNN representation of different positions in

the near and far trial types at different stages during learning and compared it with cross-correlation matrices for animals.

LSTM

In our study, we utilized LSTMs for predicting the next sensory symbol in sensory sequences in a L2AC task. Task sequences incorporated numerical symbols with unique meanings: '1' denoted the gray region; '2' and '3' represented near and far cues respectively; '4' and '5' indicated near and far reward cues; '6' symbolized reward; and '0' denoted teleportation. An example of a near trial followed the structure: 1,1,1,1,1,1,2,2,2,2,1,1,1,4,6,1,1,1,5,5,1,1,0, and far trial follows the structure: 1,1,1,1,1,1,3,3,3,3,1,1,1,4,4,1,1,1,5,6,1,1,0. We converted these numerical symbols into one-hot encodings to represent these categories. The LSTM model was constructed with PyTorch, having 128 neurons in the single hidden layer and eight neurons in the output layer. For optimization, we used Adam with a learning rate of 3e-4 with a Cross Entropy Loss. Initially, the model was trained without any regularization to establish a baseline performance. Later, we implemented different regularization techniques, namely L1, L2, dropout[158], and correlation penalization (akin to Barlow Twins[128]), in distinct simulation versions (Suppl. Fig. 11).

Transformers

We implemented a Transformer architecture based on the minGPT repository (https://github.com/karpathy/minGPT). We designed trials that represent sequences in an environment with each symbol denoting a specific meaning similar to the LSTM simulations. We created sequences of trials with random starts for a total of 3000 batches. The trials were randomly assembled in a sequence length of 10 trials. We then generated sequences of 'near' and 'far' trials and selected random 100-element chunks to form our input sequences. The vocabulary size and block size were set according to our dataset. The Transformer model was trained using a learning rate of 3e-4 for a total of 600 iterations. During test time, 4-symbol sequences were used to test the trained model's next-input prediction accuracy.

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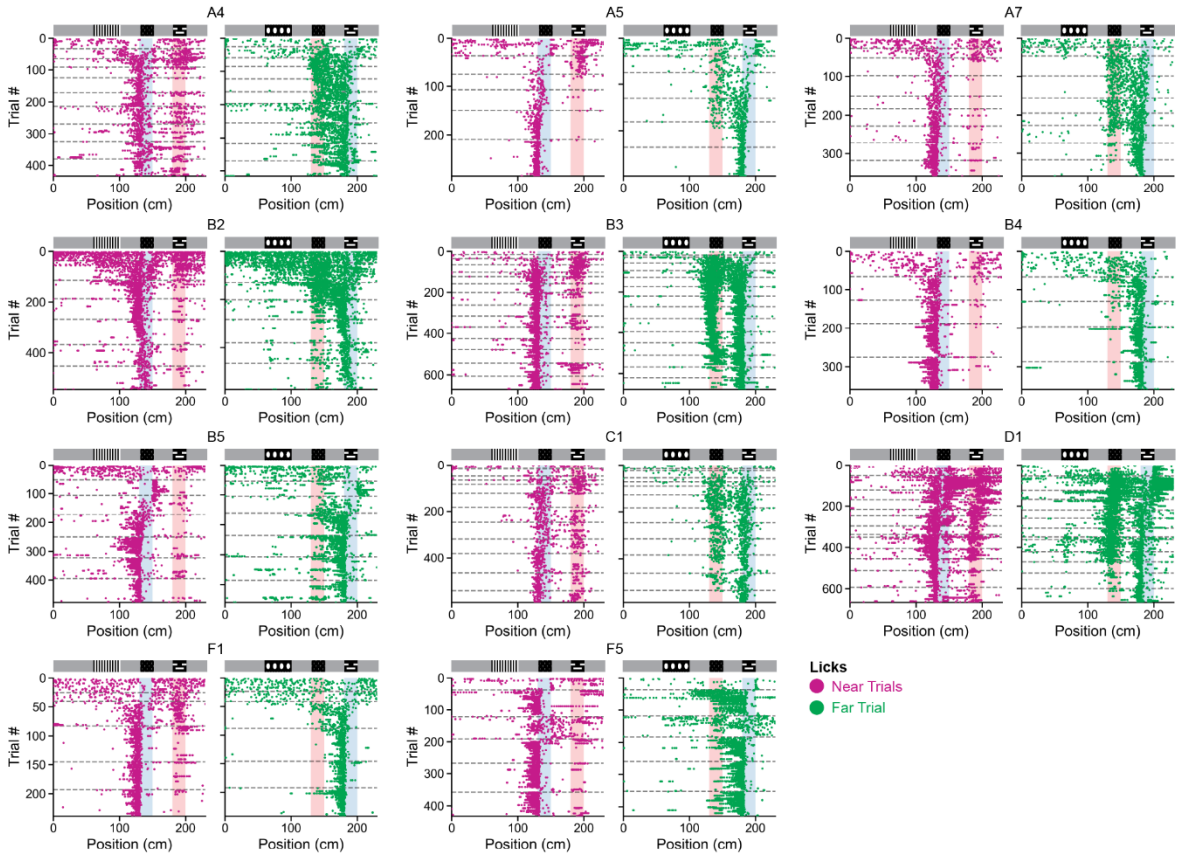
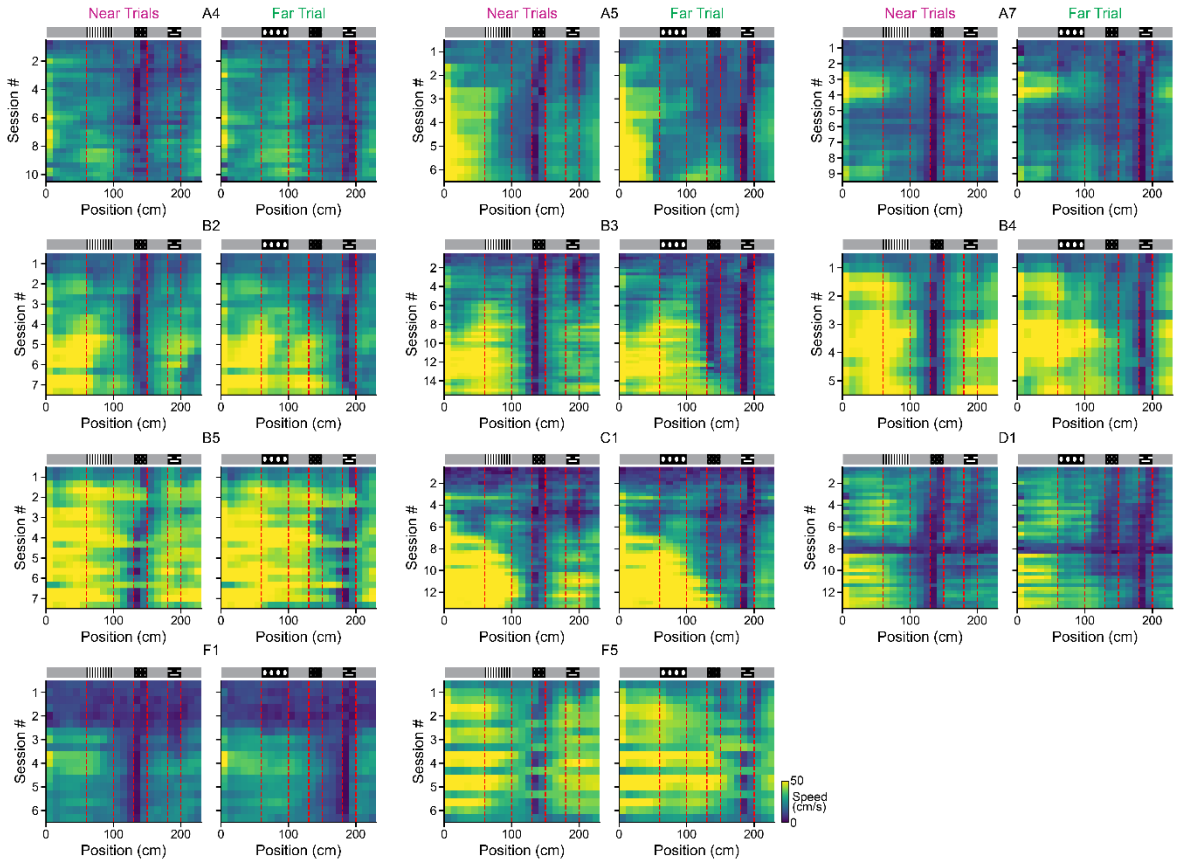
SUPPLEMENTARY FIGURES



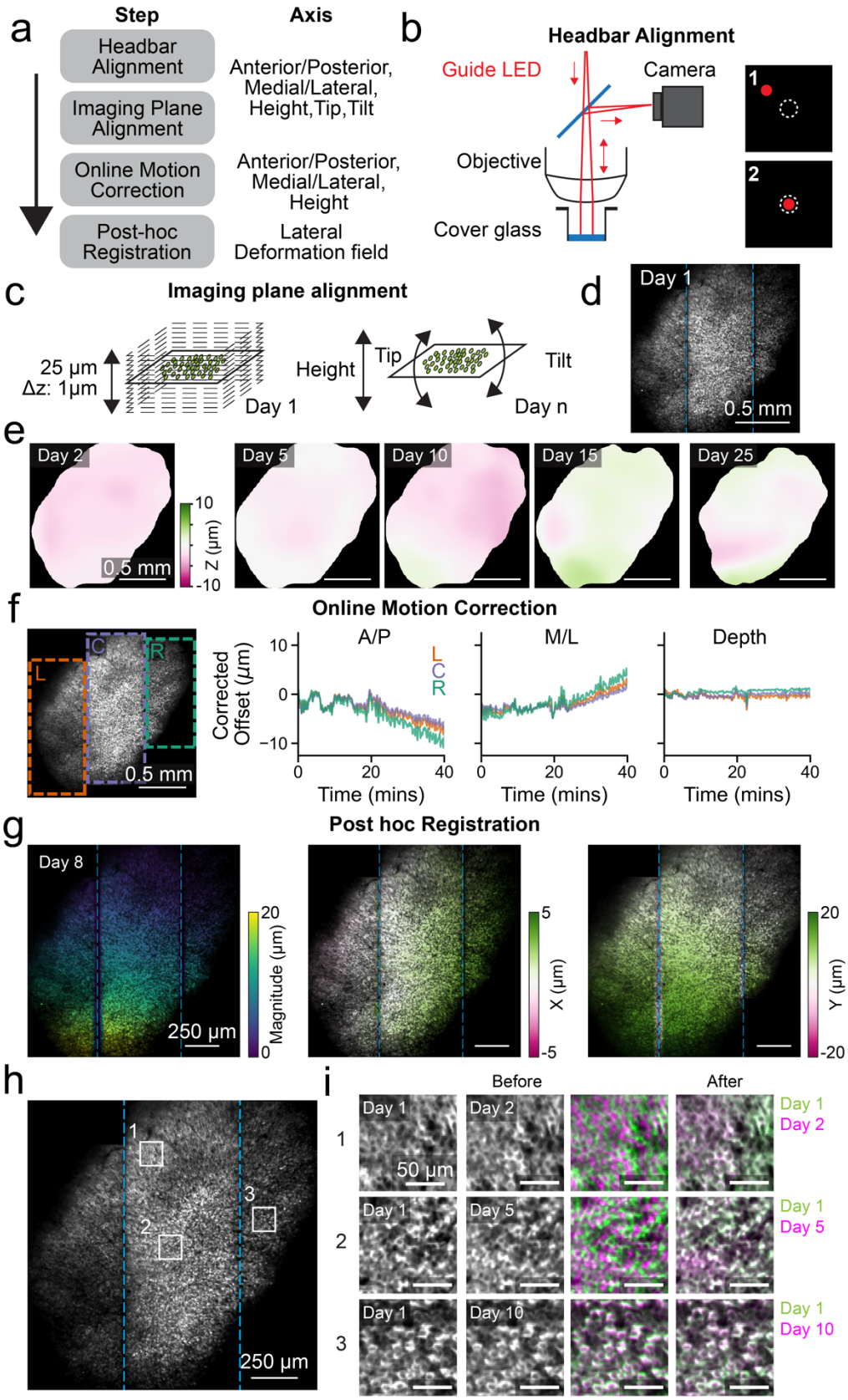
Supplementary figure 1

Changes in licking behavior during learning across all animals. Each dot indicates a single lick made by an animal relative to its position on the track in either a 'near' (magenta) or 'far' trial type (green). Dashed lines indicate the end of a session.



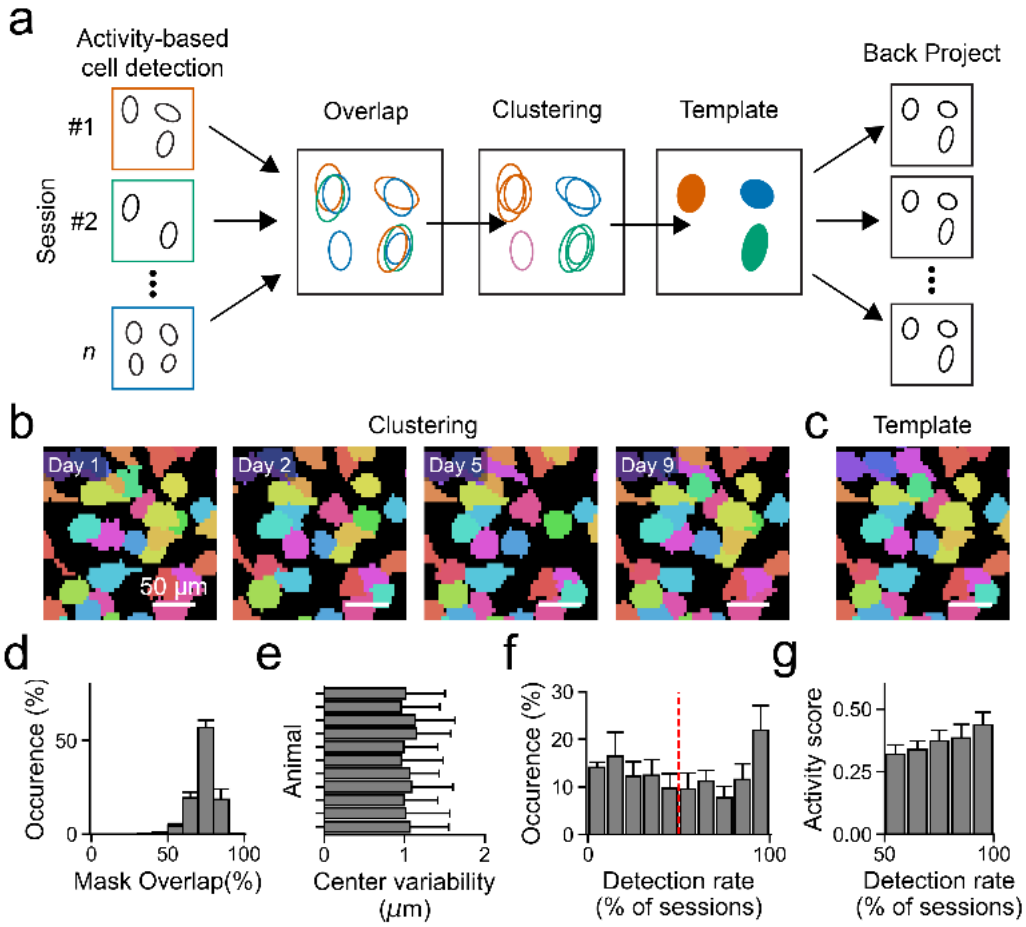
Supplementary figure 2

Changes in running speed during learning across all animals.
Spatially binned speed profiles of all animals across training sessions during 'Near' and 'Far' trial types. Dashed red lines indicate the location of the indicator and reward cues. 'A4', 'A5'… denote animal nicknames.


a
Step
Axis
Headbar Alignment
Anterior/Posterior, Medial/Lateral, Height, Tip, Tilt
Imaging Plane Alignment
Online Motion Correction
Anterior/Posterior, Medial/Lateral, Height
Post-hoc Registration
Lateral Deformation field
b
Headbar Alignment
Guide LED
Camera
Objective
Cover glass
1
2
c
Imaging plane alignment
25 µm
Δz: 1µm
Day 1
Height
Tip
Tilt
Day n
d
Day 1
0.5 mm
e
Day 2
Day 5
Day 10
Day 15
Day 25
0.5 mm
10
Z (µm)
-10
f
Online Motion Correction
L
C
R
0.5 mm
Corrected Offset (µm)
A/P
M/L
Depth
Time (mins)
g
Post hoc Registration
Day 8
250 µm
Magnitude (µm)
X (µm)
Y (µm)
h
1
2
3
250 µm
i
Before
After
Day 1
Day 2
50 µm
Day 5
Day 10

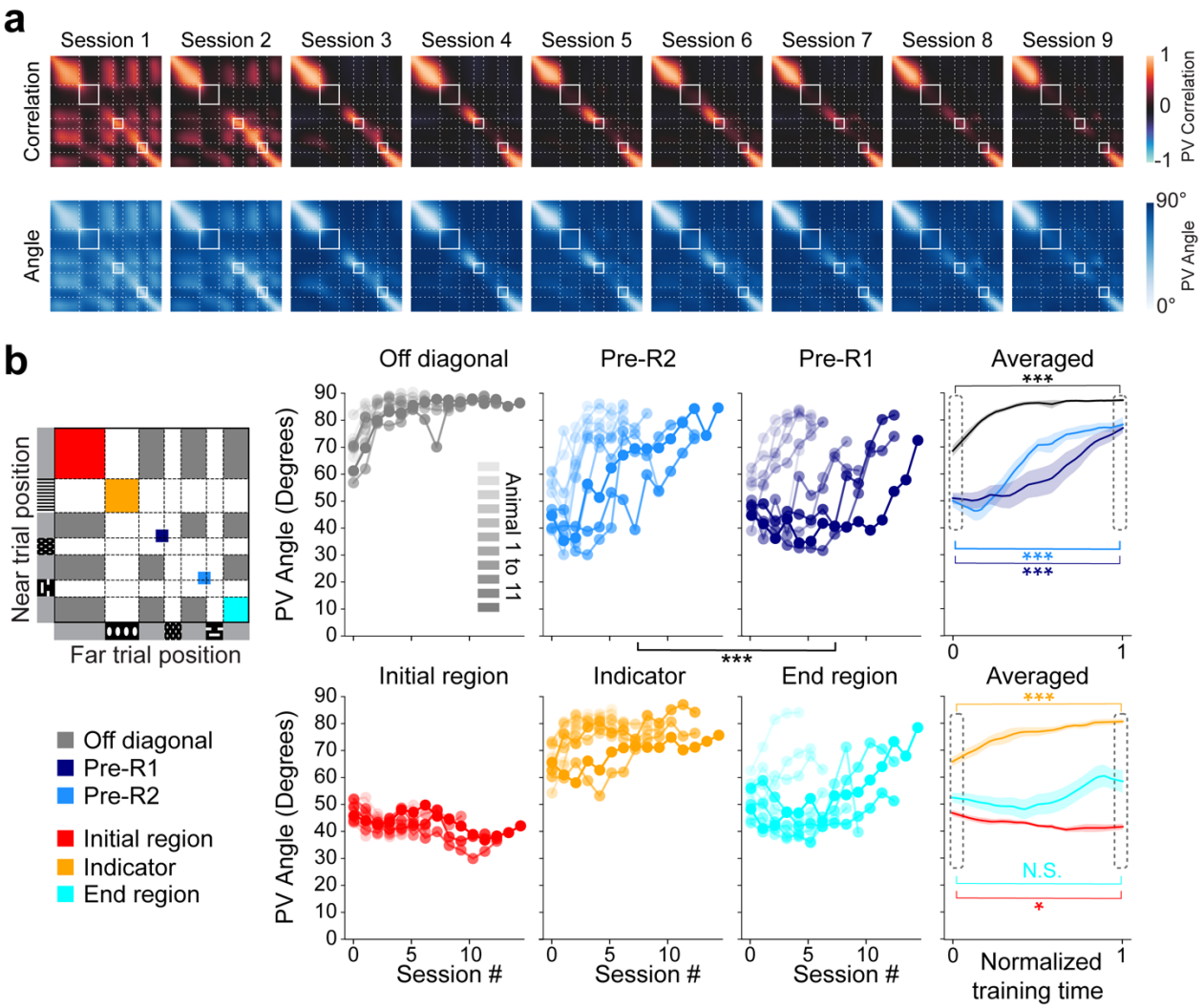
Supplementary figure 3

Overview of imaging alignment across sessions. (a) Left, schematic view of the alignment steps for registering the field-of-view across imaging sessions. Right, the axis that can be controlled in each alignment step. (b) Headbar alignment, focused light from a guide LED was projected through the optical path and reflected of the cover glass in the implanted canula. The position of the resulting spot on the camera sensor was used to ensure consistent alignment relative to the cover glass. (c) Image plane alignment. (left) A reference image z-stack was taken on day 1 of training. (right) The heigh, tip, and tilt of the imaging surface was adjusted on each day to achieve optimal alignment to the reference stack. (d) Example image of the field-of-view on day 1 from same animal shown in e. Dashed lines indicate the location of the imaging stripes (see Methods). (e) Heatmap of the remaining z error after alignment. (f) Online motion correction. (left) Locations of the left (orange), center (purple), and right (green) imaging stripes. (right) Online adjustment of individual imaging stripe positions during an example recording. (g) Example of post hoc registration. (left) Magnitude of elastic, non-rigid, deformation across the field-of-view. (right) Amount of deformation in x and y. (h) Location of ROIs shown in i. (i) Result of post hoc registration step. Each row shows a single ROI comparing the image on day 1 to that of day 2,5, or 10. Third and fourth column shows the overlay of the two images with day 1 in green and the comparison day in magenta both before and after registration. Note that the outline of the cells now overlap (white pixels) indicating that the same cells can be monitored across days.



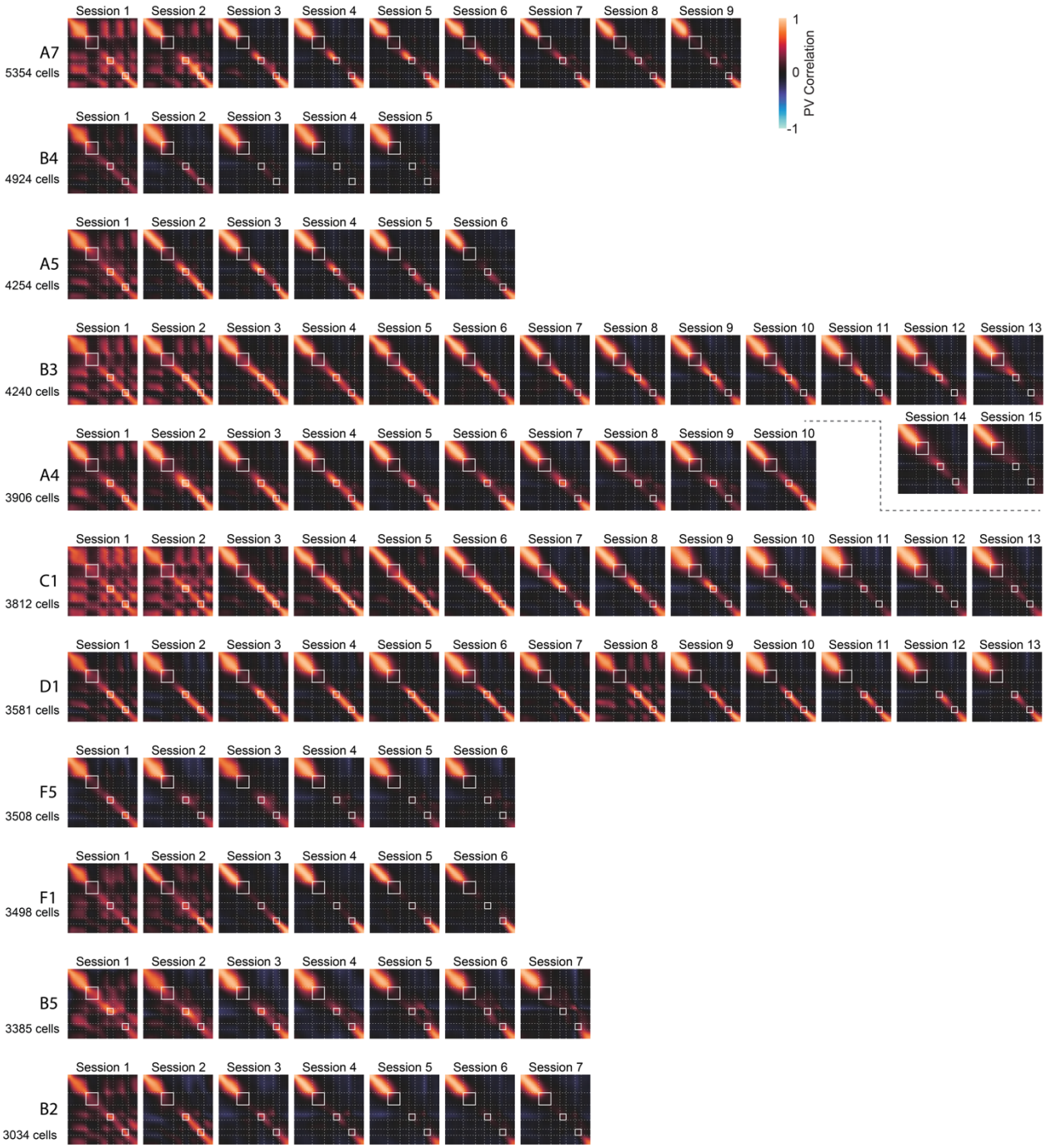
Supplementary figure 4

Identification of consistent cell masks across imaging sessions. (a) Schematic of computational pipeline. (left) Activity-based cell mask extraction is performed for each individual session using Suite2p (see methods). (center) The overlap between identified cell masks across all imaging sessions after registration was calculated and used to perform hierarchical clustering. The resulting clusters are used to calculate a single 'template' cell mask based on the median of present pixels across all sessions. Cell mask clusters that were not detected in the majority of sessions, or whose template mask was too small, were discarded (see methods for additional details). (right) The template masks were projected back to the spatial reference frame of each individual imaging session and used for calcium trace extraction. (b) Example of clustered cell masks across imaging sessions. (c) Resulting cell mask templates of the same cells shown in b. (d) Histogram of the percentage of spatial overlap of clustered cell masks with their resulting template mask averaged across animal€(e) Average variability in the center of clustered cell masks for all animals. (f) Histogram of observed detection rates of clustered cell masks as percentage of all sessions averaged across animals. Red line indicates the used inclusion threshold detection rate (50%) for all further analysis. (g) Relationship between cell detection rate and a cells activity score determined as the averaged deconvolved fluorescence signal across all sessions. Histogram values are averaged across all animals.



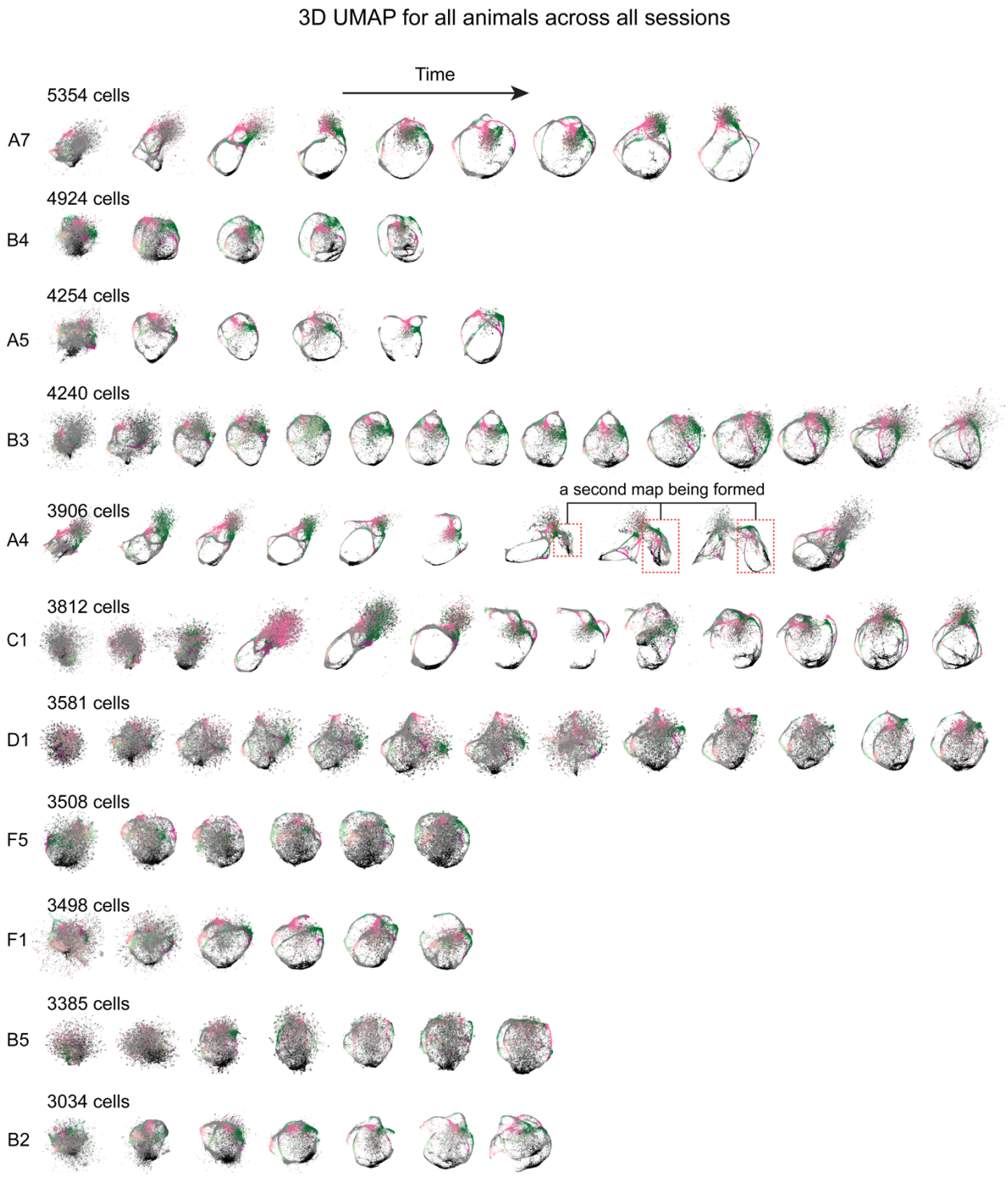
Supplementary figure 5

Changes in PV angle mirror the progressive decorrelation dynamics. (a) Top: *Near*-versus-*Far* PV Cross-correlation matrices along all track positions for sessions 1, 2, 3, 4, 9 for an example animal. Bottom: *Near*-versus-*Far* PV angle matrices along all track positions for the same animal. (b) PV angle averaged for different regions on the angle matrix across sessions, for the off-diagonal gray region correlations (gray), Pre-R2 region (light blue), and Pre-R1 region (dark blue), Initial region (red), Indicator region (orange), End region (cyan) shown for each animal separately and averaged across all of them. Comparing all sessions, a significant difference was observed between the Pre-R1 and Pre-R2 regions (Wilcoxon signed-rank test, $P < 0.001$***). Comparisons between the first and last session revealed significant changes in Off-diagonal gray regions, Pre-R2, Pre-R1, Indicator (angle increasing over sessions), and Initial region (angle decreasing over sessions) with $P < 0.05$*. In contrast, changes in the End region were not significant (N.S.). These results qualitatively mirror those in Fig. 2f.



Supplementary figure 6

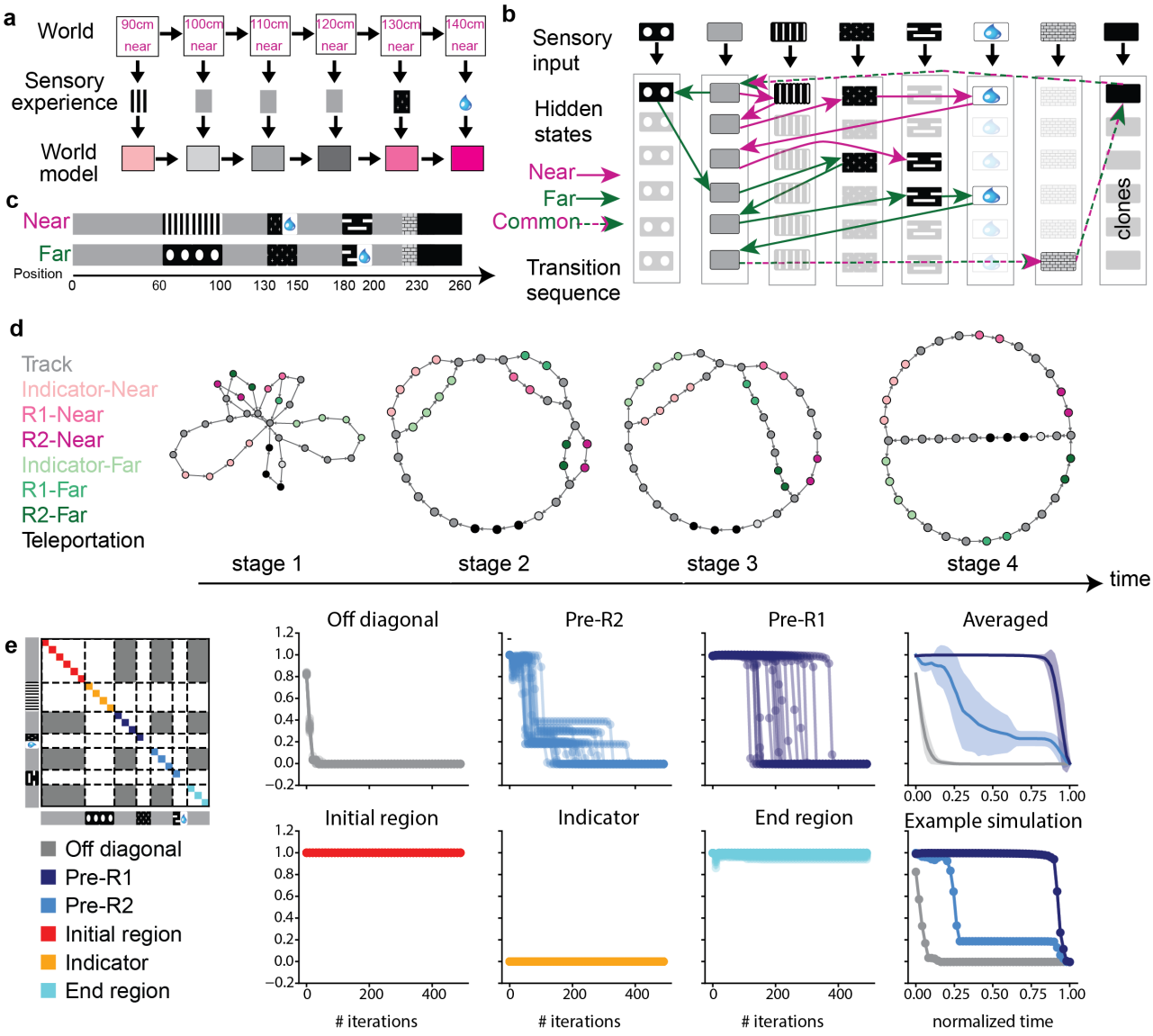
***Near* vs *Far* trial cross-correlation matrices for all 11 animals through all training sessions.** Animals are ordered by the number of cells registered across sessions.



Supplementary figure 7

UMAP for all 11 animals through all training sessions. Animals are ordered by the number of cells registered across sessions. Note that while UMAPs shed light on the dynamics of neural activity, our conclusions are primarily driven by the representational structure reflected by the PV angles and PV correlations (Suppl. Fig. 5, 6). The utility of UMAP, influenced by the choice of

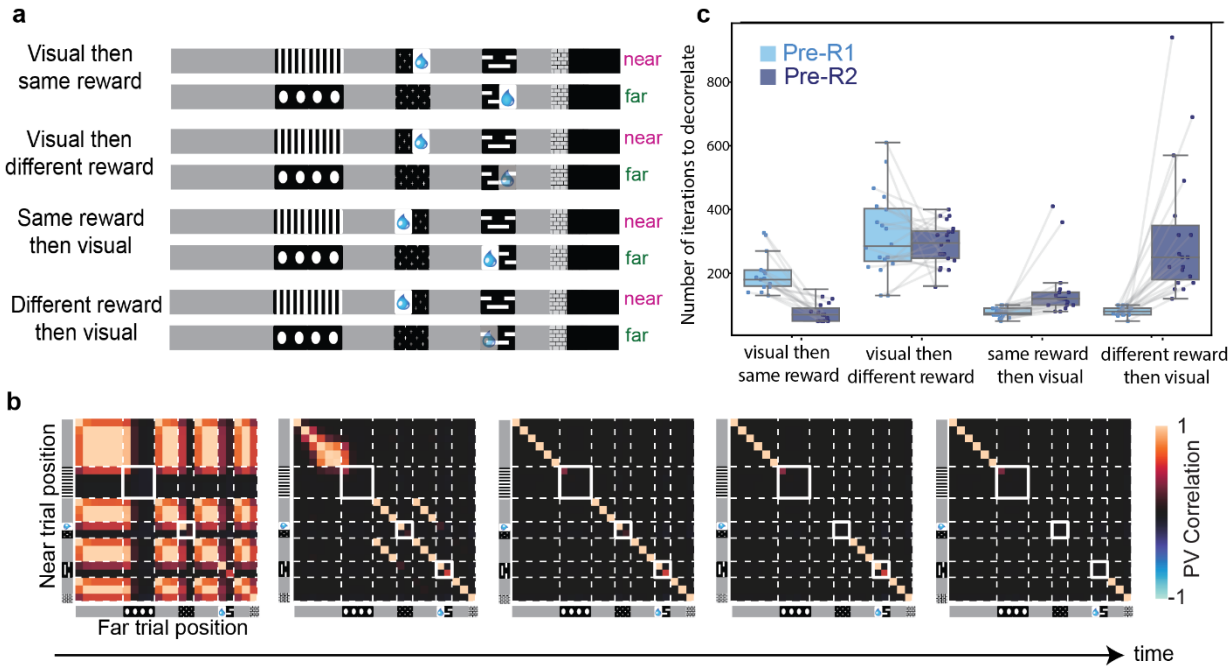
hyperparameters and cell count, can yield a range of representations. Some may appear visually streamlined while others might seem noisy or fragmented. Even though their visual presentation may differ, these manifolds can offer potential insights into underlying neural dynamics. For example, the discovered manifolds can help reveal individual variability. In some animals, UMAP and correlation matrices both indicated lack of decorrelation at the track's end (Suppl. Fig. 6). In other cases, UMAP revealed otherwise less visible aspects, such as error trials showing single trial UMAP trajectory jumping between the embeddings of correct *Near* and *Far* trial types and a novel map appearing during learning (animal A4, this form of 'remapping' in an unchanging environment has also been observed and modeled in the entorhinal cortex[159,160]).



Supplementary figure 8

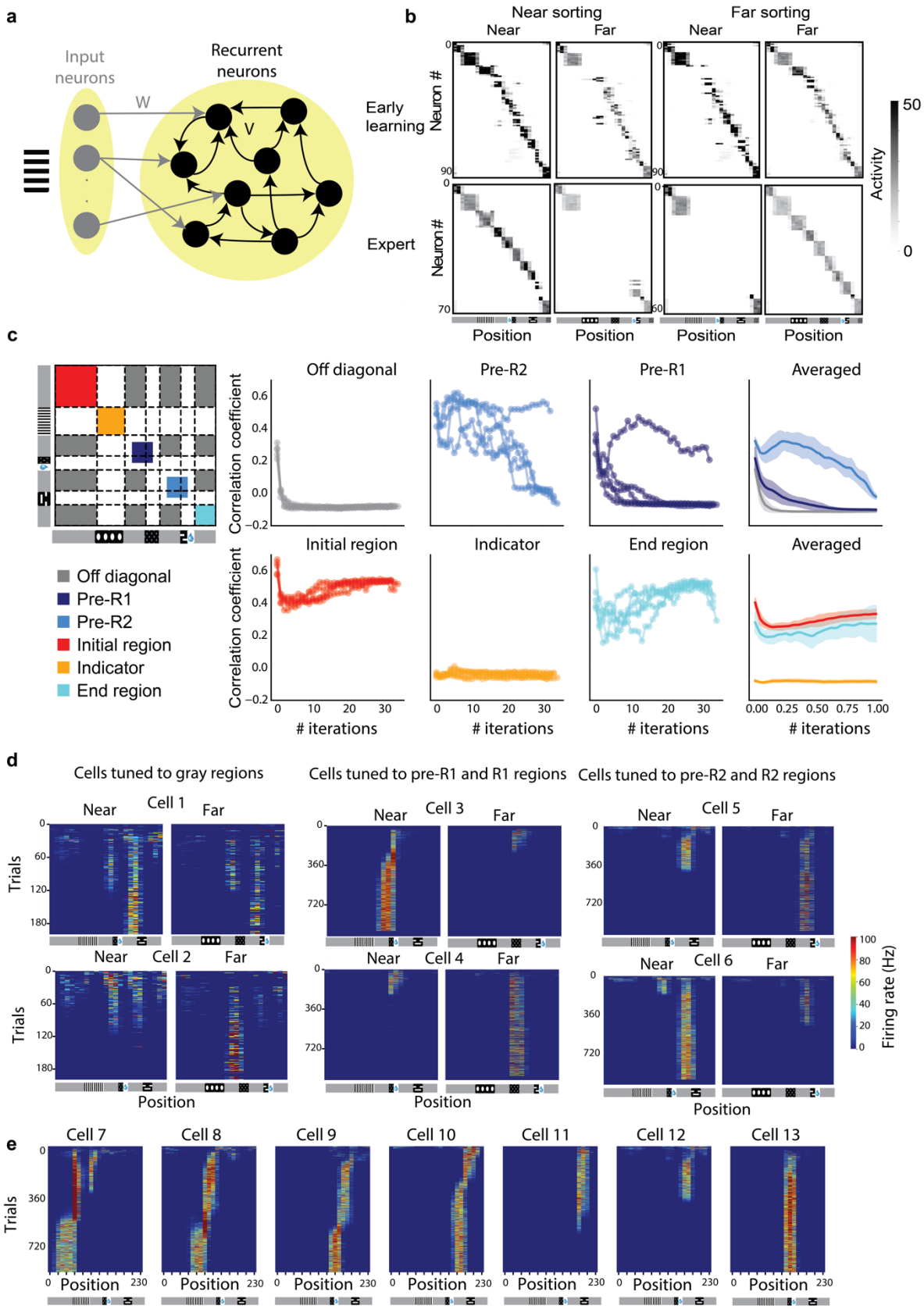
Hidden Markov learning using Clone-Structured Causal Graph recapitulates animal's learning process. (a) The world state, determined by the position and trial type, is not directly accessible to the model. Instead, the system can access sensory experiences generated based on the world state, which is used to learn a world model that accurately predicts the next sensory experience. (b) Schematic of the CSCG and the learned transition sequence. Each sensory stimulus is associated with a set of clones, which determine the hidden state. The system learns transition probabilities between these clones to generate a world model. Gray sensory stimuli are observed at distinct locations on the near and far trials, and different clones representing the gray stimulus learn to represent distinct locations. For less ambiguous stimuli, such as the indicator, most clones remain unused. (c) Schematic representation of the sequence of sensory stimuli presented to the model for near and far trial types. The rewarded region R1 of near trial and R2 of far trial are

divided into an initial visual symbol common to both trial types, followed by a shared reward symbol. The end of track symbol simulates the wall observed by the animal before teleportation. (d) The transition graph of CSCG during different learning stages recapitulates the low-dimensional neural manifolds observed in animals during learning. (e) Matrix depicting the correlation of probabilities over clones averaged for different regions over time during learning. The off-diagonal gray region (gray) decorrelates first, followed by the Pre-R2 region (sky blue), which decorrelates to a non-zero value, and then when the Pre-R1 region (navy blue) decorrelates, it is accompanied by complete decorrelation of the Pre-R2 region. The initial and end regions remain correlated. Simulations that did not fully decorrelate both Pre-R1 and Pre-R2 were excluded.



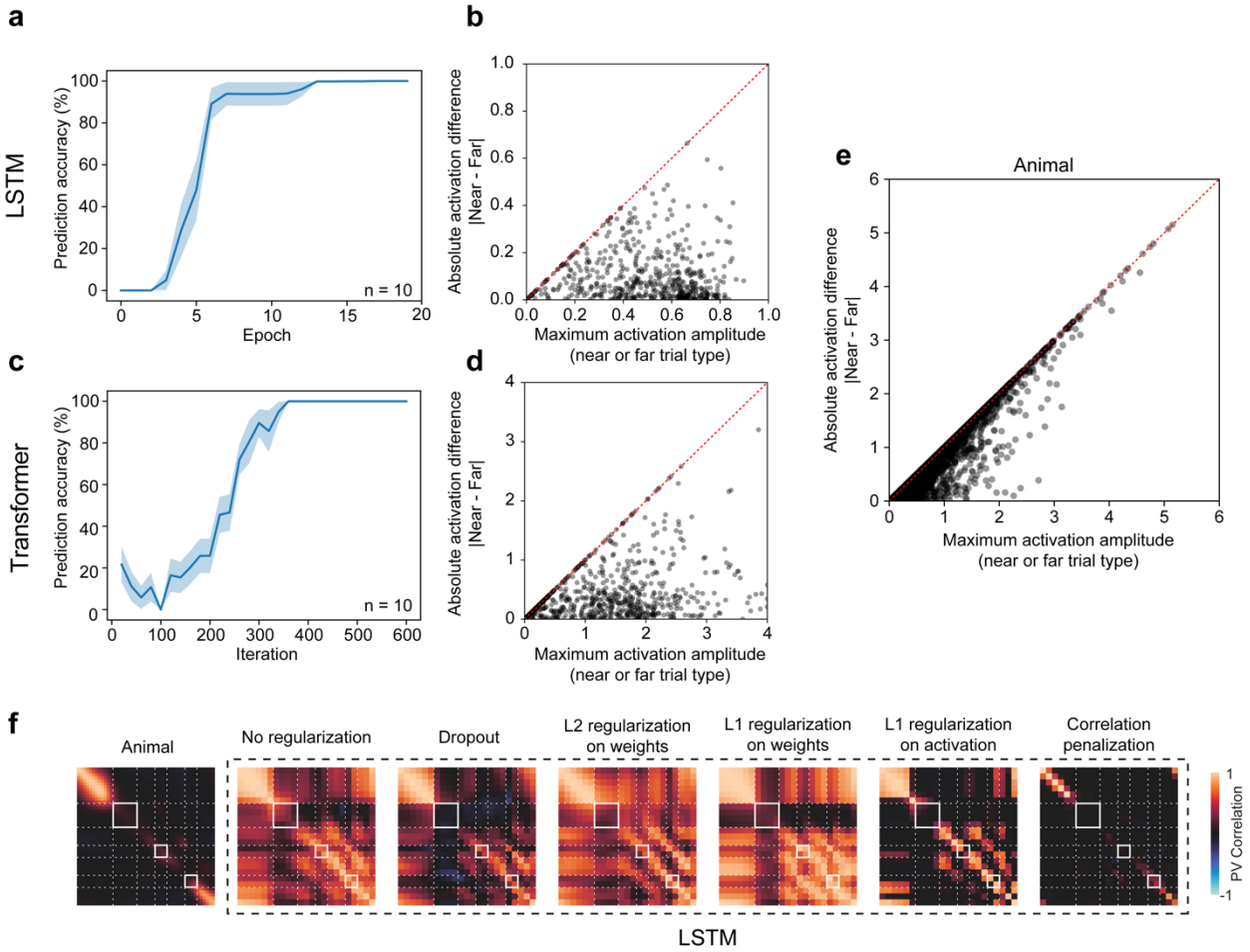
Supplementary figure 9

Sequence of learning/decorrelation depends on the exact sequence of sensory stimuli used in training CSCG. (a) Schematic representation of different possible sensory symbol sequences mimicking the animal's experience, including different orders of visual and reward experiences, and a separate reward or a combined code for reward and visual symbol. (b) Cross-correlation matrices illustrating the near-versus-far probability over clones along all track positions for the reward followed by visual sequence, showing a different learning trajectory with Pre-R1 decorrelating first, followed by Pre-R2. (c) Time taken for the correlation between vectors of probability over clones (of Pre-R1 and Pre-R2 regions) between the near and far trial types to drop below 0.5. An asymmetry between Pre-R1 and Pre-R2 regions is created when the reward is followed by a visual symbol, as the system needs to decorrelate 1 R1 visual and 3 gray zones Pre-R2, whereas only 3 gray zones Pre-R1 need to be decorrelated, thus leading to decorrelation of Pre-R1 first. A visual symbol followed by reward suggests an equal probability of either Pre-R1 or Pre-R2 decorrelation occurring first, but a shared reward symbol makes it more likely for Pre-R2 to decorrelate first, mimicking animal's learning trajectory.


a
Input neurons
Recurrent neurons
W
V
b
Near sorting
Far sorting
Near
Far
Early learning
Expert
Neuron #
Activity
50
0
Position
c
Off diagonal
Pre-R1
Pre-R2
Initial region
Indicator
End region
Correlation coefficient
iterations
Averaged
d
Cells tuned to gray regions
Cells tuned to pre-R1 and R1 regions
Cells tuned to pre-R2 and R2 regions
Cell 1
Cell 2
Cell 3
Cell 4
Cell 5
Cell 6
Trials
Firing rate (Hz)
e
Cell 7
Cell 8
Cell 9
Cell 10
Cell 11
Cell 12
Cell 13

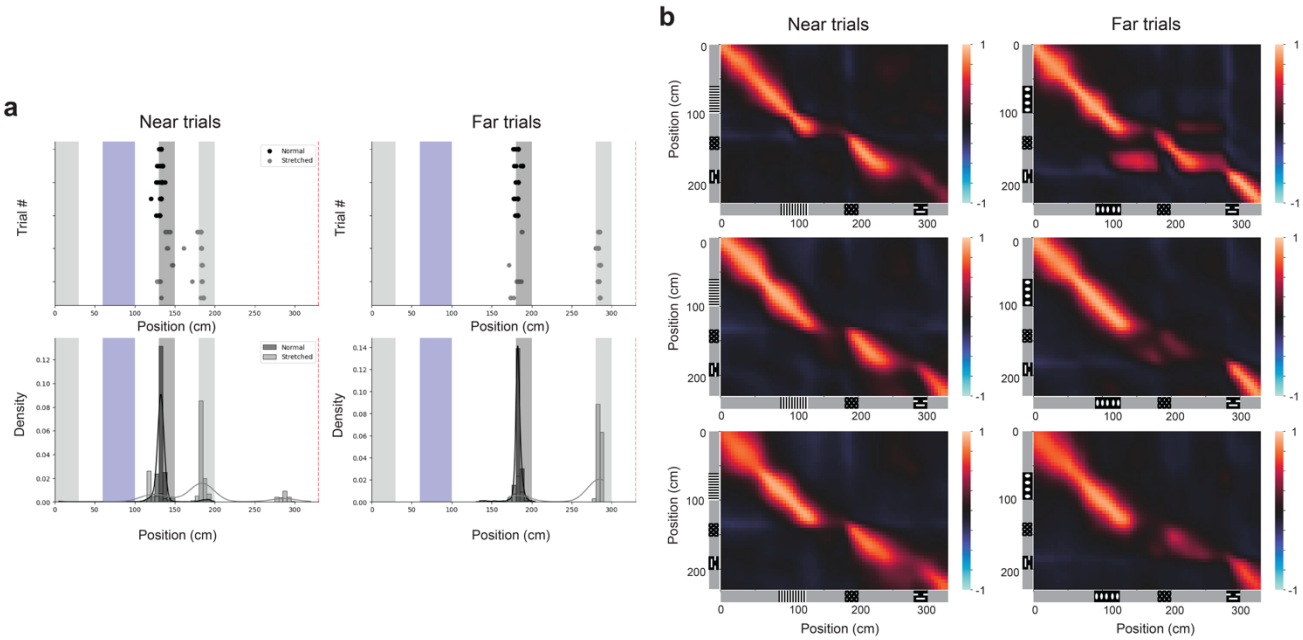
Supplementary figure 10

Hebbian-RNN recapitulates learned representations of animals at the population and single-cell level, though the precise learning trajectory differs between animals and RNN. (a) Schematic representation of a recurrent neural network (RNN) used to model the hippocampus. (b) Trial-averaged neural activity plotted against track position for both near and far trial types, at early and late stages of learning. Left: Cells ordered by their activity in the near trial type. Right: Cells ordered by their activity in the far trial type. Initially, the same cells encode both trial types (except the indicator region), but as learning progresses, cells coding for regions from the indicator to R2 become trial type specific. (c) Near vs far PV (Population Vector) Matrix depicting the correlation of probabilities over clones averaged for different regions over time during learning. The off-diagonal gray region (gray) decorrelates first, followed by the pre-R1 region (navy blue), and then pre-R2 region (sky blue). This suggests an order different from that observed in most animals. The initial and end regions show a slight decrease and subsequent slight increase in correlation, while the indicator region remains uncorrelated. (d) Dynamics of positional tuning for RNN cells replicate aspects of the single-cell dynamics observed in animals. Left: Example cells involved in the transition from stage 1 to stage 2, where neurons tuned to multiple gray regions become selective to one. Middle: Example cells tuned to pre-R1 and R1 regions for both trial types become selective to one trial type. Right: Example cells tuned to pre-R2 and R2 regions for both trial types become selective to one trial type. (e) Example cells exhibiting selective firing at various locations along the track in the near trial type. This includes a backward shift in cells 7 to 10, loss of selectivity in cells 11 and 12, and a stable field in cell 13.



Supplementary figure 11

Training LSTM and Transformer on L2AC task. Prediction accuracy for reward regions in both *Near* and *Far* trials for LSTM (a), and Transformer (c), both shown average of 10 independent runs, shading indicates ± s.e.m. Prediction accuracy is defined as the percentage of correct reward region predictions (for both *Far* and *Near* trial types) out of all reward region predictions during test trials. (b) Maximum unit activation in *Near* and *Far* trials at a particular location plotted against the absolute activation difference between *Near* and *Far* trials, for all units and pooled across all positions from the beginning of R1 to end of R2. (d) Similar in b, but for transformer pre-logit layer activations. (e) Similar to b, but for animal neuronal activations. (f) Final model representational structure using different regularizations applied to LSTM. Regularization strength was incremented progressively; the final level was selected when subsequent increase began to degrade test performance. Correlation penalization involved storing hidden state activations for both a *Near* and a *Far* trial. The sum of all entries within the cross-correlation matrix between the two trial types was then added to the training loss.



Supplementary figure 12

Behavior and neural activity in stretched trials. (a) Example licking patterns (top row) and the licking position distribution over a single session (bottom row) in both near and far trials for normal (black) and stretched (gray) trials. (b) PV Correlation between the average neural population activity in normal and in stretched trials for both near (left column) and far (right column) trials. Each row corresponds to a single animal.