Behavioral/Cognitive

Animal-to-Animal Variability in Partial Hippocampal Remapping in Repeated Environments

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Hippocampal place cells form a map of the environment of an animal. Changes in the hippocampal map can be brought about in a number of ways, including changes to the environment, task, internal state of the subject, and the passage of time. These changes in the hippocampal map have been called remapping. In this study, we examine remapping during repeated exposure to the same environment. Different animals can have different remapping responses to the same changes. This variability across animals in remapping behavior is not well understood. In this work, we analyzed electrophysiological recordings from the CA3 region of the hippocampus performed by Alme et al. (2014), in which five male rats were exposed to 11 different environments, including a variety of repetitions of those environments. To compare the hippocampal maps between two experiences, we computed average rate map correlation coefficients. We found changes in the hippocampal maps between different sessions in the same environment. These changes consisted of partial remapping, a form of remapping in which some place cells maintain their place fields, whereas other place cells remap their place fields. Each animal exhibited partial remapping differently. We discovered that the heterogeneity in hippocampal representational changes across animals is structured; individual animals had consistently different levels of partial remapping across a range of independent comparisons. Our findings highlight that partial hippocampal remapping between repeated environments depends on animal-specific factors.

Key words: context; hippocampus; interindividual variability; overdispersion; place cell; remapping

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Significance Statement

Context identification is a difficult problem. Animals are not provided with objective context identity labels, so they must infer which experiences come from which contexts. Different animals may have different strategies for performing this inference. We find that different animals have stereotypically different extents of partial hippocampal remapping, a neural correlate of subjective assessment of context identity.

Introduction

Place cells are hippocampal neurons that fire at specific locations in an environment (O'Keefe and Dostrovsky, 1971), leading the place cell population to collectively form a map of the environment (O'Keefe, 1976). When aspects of the the experience of an animal change, the firing patterns of place cells change unpredictably, leading to a new map across the population (Muller and Kubie, 1987). This phenomenon is referred to as remapping.

Remapping can be triggered by a variety of changes, including changes to the environment, such as minor cue changes (Muller and Kubie, 1987; Sanders et al., 2019) or moving to a different room (Leutgeb et al., 2005), changes in task (Markus et al., 1995), changes in the internal state of the subject (Frank et al., 2000; Wood et al., 2000), and the passage of time (Mankin et al., 2012). On its simplest level, remapping enables place cell firing patterns to be unique for each context, thus providing a potential mechanism for encoding novel experiences and enabling context-dependent learning (Colgin et al., 2008). Remapping takes a variety of forms, including global remapping, rate remapping, and partial remapping. In particular, partial remapping is a commonly observed phenomenon, which involves some fraction of the place cell population remapping its place fields while other place fields stay constant (Muller and Kubie, 1987; Shapiro et al., 1997; Wood et al., 2000; Hargreaves et al., 2007; Kinsky et al., 2018; Fetterhoff et al., 2021). Partial remapping is thought to reflect the

representation of multiple hypotheses about context identity (Jackson and Redish, 2007; Fenton et al., 2010; Sanders et al., 2020).

The context-identification problem is not as simple as it might seem. Animals don't have direct access to objective context labels but instead must infer context identity. Characterizing remapping as hidden state inference (Sanders et al., 2020) captures many of the ways in which remapping does not follow the formula of one room equals one map (Lever et al., 2002; Markus et al., 1995; Law et al., 2016). One particular implication of the lack of access of an animal to objective context labels is that different animals may infer context identity differently when presented with the same experiences. Variability among inference of context identity between animals would be most easily observable in ambiguous situations, such as those that elicit partial remapping. This difference between animals has been observed previously in studies focusing on other aspects of remapping (Lever et al., 2002; Wills et al., 2005) and is consequently widely recognized by experimenters but has not been quantified or directly investigated.

Lack of access of an animal to objective context labels could result in animal-to-animal variability in remapping behavior, as different animals take different approaches to an ambiguous problem. Previous work had shown that factors such as age could cause changes in remapping (Barnes et al., 1997; Lister and Barnes, 2009) and even that variation in remapping among aged animals correlated with other firing phenomena (Hok et al., 2012) or with learning capacity (Wilson et al., 2003). However, previous work did not investigate the variability in remapping behavior across animals during normal cognitive function.

In this study, we reanalyzed electrophysiological data from Alme et al. (2014) in which rats were exposed to 11 different rooms over 28 sessions. To measure the extent of remapping, we calculated average rate map correlations (RMCs). We verified that RMCs are higher for same-environment comparisons than for different-environment comparisons. For same-environment comparisons, all animals exhibited partial remapping. However, there was substantial variability in remapping behavior for same-environment comparisons. We found that variability across animals was consistent for a variety of independent same-environment comparisons, pointing to consistent individual differences in remapping response. We demonstrate that these individual differences in remapping behavior across animals persist when controlling for several different behavioral parameters and differences in cell yield in the recordings for different animals. Overall, we provide evidence for the hypothesis that individual animals have consistently different partial remapping responses to the same set of experiences.

Materials and Methods

The data for this study was collected by Alme et al. (2014), and permission was granted to us to conduct the analyses described below. Detailed descriptions of the animals, surgery, electrode preparation, and implantation can be found in the original publication (Alme et al., 2014). All analysis code can be found at https://github.com/ParsaNilchian/animal-variability.

Experimental design and statistical analyses
All animals were male. The number of cells recorded from each animal is shown in Table 1. We analyzed the data with Python using the NumPy (Harris et al., 2020) and SciPy (Virtanen et al., 2020) libraries. Plots were developed with Matplotlib (Hunter, 2007). The preprocessing

Table 1. Number of place cells recorded from each animal and the color codes of the animals used in the figures in this article

Animal ID	Number of place cells	Color code
18024	25	red
17769	35	purple
19251	38	orange
17894	66	blue
18237	66	green

steps were based on Alme et al. (2014). The analysis was not preregistered.

Behavioral procedures
Seven male Long-Evans rats, ages 4–5 months at implantation, foraged for food in one familiar (F) and 10 novel (N) environments over a two-day period. Ten of the 11 boxes had dimensions of $100 \times 100 \times 50$ cm, and one box was $100 \times 100 \times 80$ cm. A white cue card was placed on the North wall of each box, but its size and position varied across rooms. Each animal was tested over a period of two days with 8 h recording sessions on each day. Electrophysiological recordings in each novel room lasted 30 min (two sessions of 15 min each), followed by 15 min rest blocks (Fig. 1A, schedule of recording day). The familiar room was tested as the first and last session of each day and was preceded and succeeded by a rest period. Five of the 10 novel rooms (N1–N5) were tested on the first day, and the other five novel rooms (N6–N10) were tested on the second day. The animal was recorded twice in each novel room with no rest period in between. In five of the seven animals, N1 and N6, the first novel rooms of day 1 and 2, were tested at the end of each day again. The data of these five animals were used for this study because we were interested in the repetitions of N1 and N6 in particular. One of the animals was only tested once in N1. The data of animal 17769 room F1 and animal 19251 room N4 session 1 (N4) was missing.

Notation of sessions
The familiar room is denoted as F1 and F1* on day 1 and F2 and F2* on day 2. For the familiar room the number following F indicates the day and the asterisk (*) refers to the second session at the end of the day. Novel rooms are described as N followed by the room number (e.g., N3 for novel room 3) and the immediate repetitions are marked with an exclamation mark (!; e.g., N3!). The third and fourth repetitions of rooms N1 and N6 at the end of days 1 and 2 are labeled with an asterisk and an asterisk and an exclamation mark (*!; e.g., N1* and N1*!). In general, * denotes sessions in the same room at a different time of the day, whereas ! denotes sessions that are immediately repeated.

Position data processing
The position data consisted of one-dimensional (1D) arrays of x- and y-coordinates recorded with an approximate frequency of 25 Hz; x- and y-positions were smoothed with a 1D Gaussian filter (sigma = 5 samples ≈ 200 ms).

Behavioral metrics
To quantify the behavior of the animals in each session, we used the smoothed position data to calculate the mean, that is, (1) speed, (2) acceleration, and (3) absolute angular velocity of each animal in each session.

Speed. The change in x- and y-position (the difference between two consecutive smoothed x- or y-positions, respectively) was divided by the time difference between the two position coordinate recordings (~0.04 s). Total speed was the square root of the sum of squares of the x- and y-speed. The speed was then smoothed with a Gaussian filter (sigma = 7 time bins ≈ 0.28 s). Hence, we obtained a 1D speed vector, with each entry describing the speed of the animal between two consecutive position recordings. This smoothed speed was used for all further analyses.

Acceleration. The x- and y-speed 1D vectors were used to calculate the acceleration in x- and y-direction, respectively, across all animals and sessions. To calculate the x-acceleration vector, we calculated the difference in two consecutive x-speed entries to obtain the change in speed in
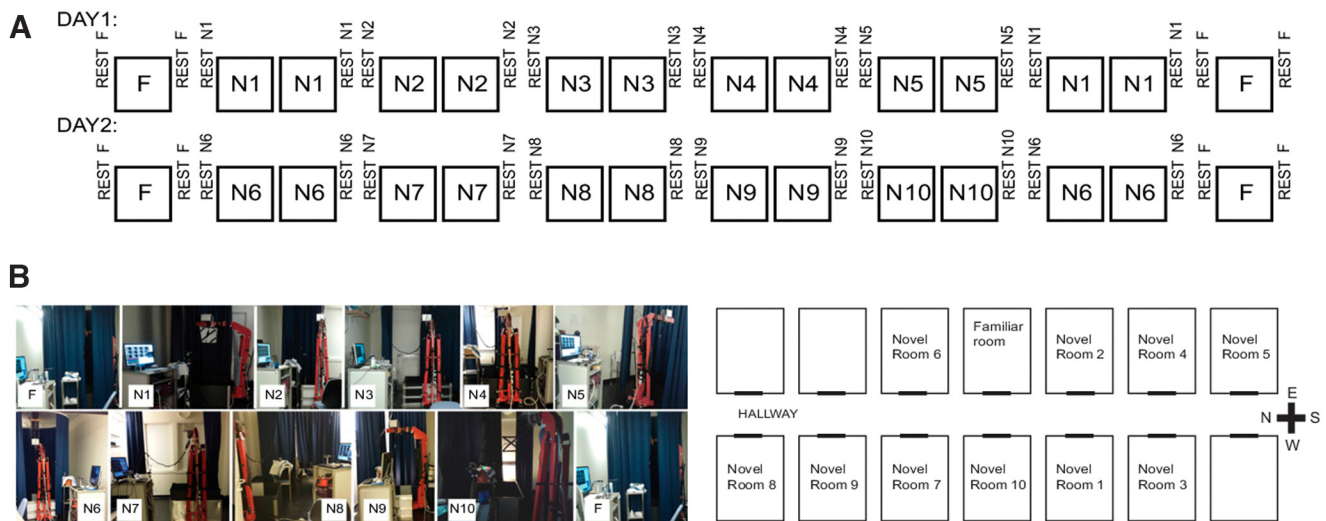
Figure 1. Experimental design. *A*, Experimental protocol. Five male Long-Evans rats were exposed to 11 rooms over 2 d. In each room, the rats foraged for food in a 100 cm × 100 cm box. Animals were pretrained in the F room but did not experience any of the 10 N rooms before testing. Exposure to each novel room was performed over two consecutive 15 min sessions. The animal was not removed from the box between the first and second session. The F room and the first N room of each day, N1 and N6, were tested again at the end of the day. Each rest period lasted 15 min. *B*, Pictures of the familiar and novel rooms. A mobile recording rig along with the red crane allowed continuous recording. The arrangement of the rooms along the hallway did not follow a particular pattern. Adapted from Alme et al. (2014).

the *x*-direction. Subsequently, we divided the change in speed in the *x*-direction by the amount of time that passes between the speed entries to obtain a 1D *x*-acceleration vector. The 1D *y*-acceleration vector was calculated according to the same steps using the *y*-speed vector. We then calculated the total acceleration as the square root of the sum of the *x*-acceleration and *y*-acceleration squared to obtain a 1D acceleration vector. The acceleration vector of the animals was smoothed with Gaussian filters (sigma = 10 time bins ≈ 0.4 s). Last, we computed the mean acceleration for all animals and sessions.

Absolute angular velocity. The mean absolute angular velocity for each animal in each session was calculated using the smoothed position data from the session. The change in *x*- and *y*-position was used to calculate a 1D-vector describing the angle of the movement of the animal between each of the position recording times. Subsequently, we calculated the difference between two consecutive angle entries to obtain a 1D vector describing the angular change in the direction of the animal across the session. The angular change in direction was divided by the time that had passed between the two position entries to obtain a 1D vector describing the angular velocity of the animal across the session. Last, we converted each entry of the 1D angular velocity vector to its absolute value and calculated the mean of the resulting absolute angular velocity vector.

Rate maps
The 100 × 100 cm boxes were divided into 400 (20 × 20) 5 × 5 cm bins. We also performed our analyses with 30 × 30 bins, with substantively similar results (data not shown). As is standard in the field, place fields were only calculated using time points when the animal was moving at least 5 cm/s to limit analyses to periods with engaged behavior. For each cell and each spatial bin, the firing rate of that cell was computed as the ratio of the number of spikes fired by that cell when the animal was in that bin (spike count) divided by the total time spent in that bin (occupancy). Both spike counts and occupancy in each bin were calculated using only time points when the smoothed speed (see above, Behavioral metrics for definition) was above 5 cm/s (Fig. 2). Rate maps were then smoothed with a 2D Gaussian filter (sigma = 1 bin = 5 cm). This value of sigma was chosen to match the firing rates in Figures 3 and S2 in Alme et al. (2014). Bins with no occupancy were replaced with a Gaussian filtered average of surrounding bins with appropriate normalizations. When comparing the place field locations and firing rates of our rate maps to those of Alme et al. (2014), we noticed minor differences in the maximum firing rates (commonly deviations of 1–2 Hz), which may

have been related to differences in the speed filtering and smoothing of the data. Overall, we were able to replicate the rate maps of the original publication well (Fig. 3).

RMC
We calculated RMCs to quantify the amount of remapping between-session pairs. We categorized the cells into three groups for a given session. Cells either had no spikes (silent), <10 spikes (below threshold), or at least 11 spikes (active) in a given session. We did not define the RMC if the cell was below threshold or silent in both sessions. The RMC was defined as zero if the cell was silent in one session and was active in the other. If the cell was active in one session and either active or below threshold in the other, we defined the RMC as follows: We turned the smoothed rate map of each cell in each session into a 1D vector with 400 entries, each corresponding to one bin of the room. We then calculated the Pearson correlation coefficient for each cell between this 1D vector for the two sessions being compared. This correlation coefficient is the RMC.

Average RMC
In addition to calculating the RMC of individual place cells across two sessions, we also averaged across cells for a given session pair to obtain the average RMC.

Population vector dot products (PVDPs)
For each session, the rate maps of each cell are stacked. For a particular bin, the firing rate from the rate map of each cell at that bin forms a vector (length, number of cells) called the population vector. To compare two sessions, we calculated the dot product of corresponding bins between each session [excluding any NaN (invalid) values] and then normalized by the number of cells. We then averaged these normalized dot products across all bins to create an average population vector dot product (PVDP) for that session-pair comparison. We compiled all the session-pair comparisons into a matrix (size: #Sessions × #Sessions). Finally, we scaled each row of the matrix to the maximum value in that row so that all values would be in the range of 0–1.

Animal-to-animal variability
To quantify the animal-to-animal variability in remapping behavior, we performed three general linear models (GLMs). We were interested in identifying relationships among the remapping behavior for the repetitions of the familiar room, the repetitions of N1 and N6 at the end of each day, and the immediate repetitions of the N rooms. We correlated
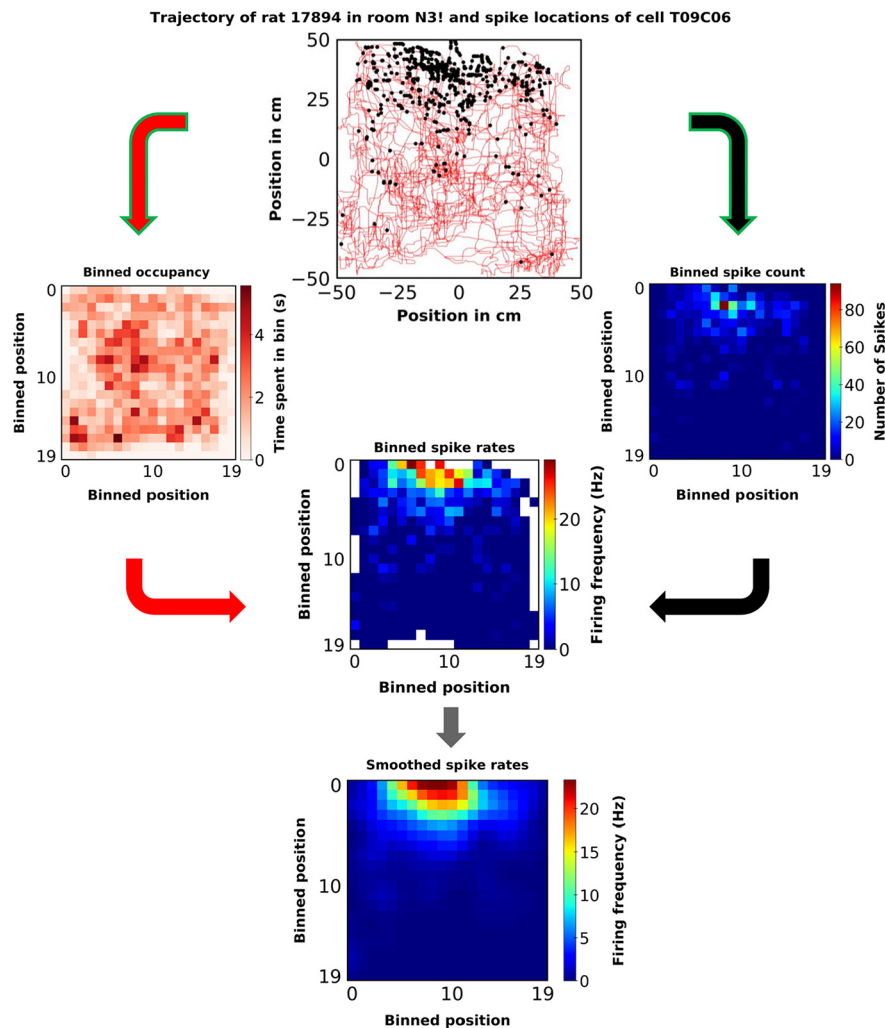
Figure 2. Data processing pipeline. The box in each session was binned using 400 (20 × 20) 5 cm square bins. Using the position data of each animal, we calculated the binned occupancy for each session in seconds (red arrows). Additionally, we counted how many times each place cell spiked in each bin (black arrows). Top, The position data and the spiking data were speed filtered (green line around the arrows). Periods during which the speed of the animal dropped below 5 cm/s were excluded from the binned occupancy, and spikes during these periods were not counted. Binned spiking rates for each place cell were calculated as the ratio of the number of spikes and the time spent in that bin in seconds (bottom, red and black arrows). A Gaussian filter (sigma = 1 bin) was used to smooth the rate maps (gray arrow).

the following: (1) Mean N between-session versus Mean F between-session RMCs, (2) Mean N1 between-session versus Mean N6 between-session RMCs, and (3) Mean N within-session versus Mean N between-session RMCs. Table 2 provides a detailed description of the variables, the respective sessions used, and averaging procedures for this analysis.

Behavioral controls
We used the mean speeds, accelerations, and absolute angular velocities of the animals as behavioral parameters to control the relationship between the neural dependent and independent variables of Figure 7C. The dependent variable in Figure 7C was the Mean N within-session RMC for each animal, and the independent variable was the mean N between-session RMC for each animal, both defined in Table 2. To control the findings of Figure 7C, we reconstructed the GLM six times, each time adding a behavioral control parameter to the model as a second independent variable. A detailed description of the behavioral control variables can be found in Table 3. Initially, we used mean differences in mean speeds, accelerations, and absolute angular velocities (Table 3, method 1, top three rows). Subsequently, we used speed means, acceleration means, and

absolute angular velocity means, as behavioral independent variables (Table 3, method 2, bottom three rows). The results of these controls are reported in Table 4.

Results
We were interested in looking at the changes in hippocampal maps between experiences. In the experiment we analyzed (Alme et al., 2014), electrophysiological recordings were taken from the CA3 region of hippocampi of rats while they foraged for food in 11 different 100 cm x 100 cm boxes over 2 d (Fig. 1; see above, Materials and Methods). According to the experimental protocol, some rooms were repeated immediately (N1–N10), whereas others were repeated at a later time during the same day (F, N1, and N6) or during a different day (F). This experiment allowed us to compare repetitions of a variety of different experiences, immediate repetitions of novel rooms, repetitions of novel rooms later during the day, and repetitions of the familiar room. This experiment also allowed us to compare the hippocampal representation between distinct experiences.

First, we had to quantify maps for each experience. The processing pipeline (Fig. 2) illustrates how we combined the spiking data of the cells with the position data of the animals to create rate maps for each place cell across all sessions (see above, Materials and Methods).

We observed multiple examples of remapping (Fig. 3). We can use RMCs to quantify remapping of individual cells for a particular pair of sessions. High RMCs indicate high similarity in the rate maps of the cell across two sessions and thus less remapping. Low RMCs indicate low similarity in the maps and thus more remapping. In some cases, place fields were conserved but firing frequencies changed, resembling rate remapping (Cell T0505 in sessions N1 and N1*, RMC = 0.69). Global remapping occurred when the place field locations changed across different sessions (T07C02 in animal 19251 between sessions N2 and N3, RMC = −0.14). However, not all place cells remapped across all sessions. In many cases, firing frequencies and place field locations were conserved (T09C06 in animal 17894, sessions N3 and N3!, RMC = 0.82 or T07C02 in animal 19251 between rooms N3 and N3!, RMC = 0.94).

We looked at the RMCs of individual cells across different and repeated sessions to assess the remapping behavior across the place cell population (Fig. 4). For this analysis, we grouped all repeated session pairs together and all different session pairs together. Because it is generally assumed that place cells globally remap when animals move to new rooms, we expected a distribution of RMCs clustered around zero for different room comparisons. This pattern was confirmed for all five animals, indicating that most place cells do indeed globally remap across
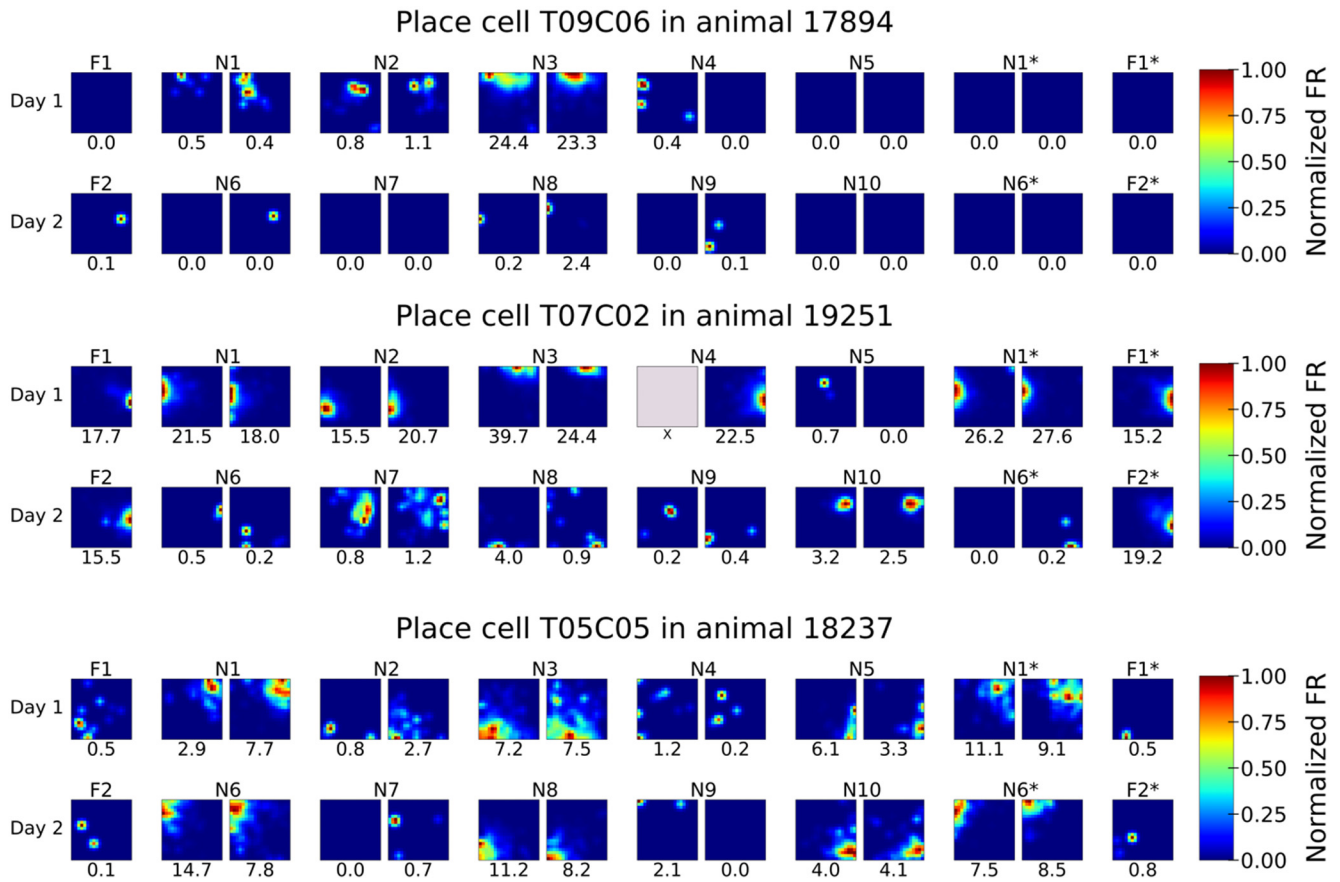
Figure 3. Smoothed firing rates of example place cells. We observed various instances of global and rate remapping. An instance of global remapping is the change of the place field location of place cell T07C02 in animal 19251 between the second session of N2 versus the first session of N3 (RMC = −0.14). The same cell did not remap between the first and second session of N3 (RMC = 0.94). The remapping behavior of place cell T05C05 in animal 18237 between the first session of N1 and the third session of N1 later during the day is an example of rate remapping (RMC = 0.69). The color scale in each session is scaled to the maximum firing frequency displayed below the rate map. Gray boxes indicate unavailable data. F1, F1*, F2, and F2* all refer to the same familiar room. See "Notation of sessions" subsection of the Methods section for more detail.

different rooms in this experiment (Fig. 4). Interestingly, we observed a tendency toward a tail of higher RMCs for the different session comparisons. These relatively high RMCs may correspond to some comparisons between different rooms having limited remapping (clusters of high RMCs in Fig. 5). Given that all boxes have the same shape and dimensions, these place cells could indicate the similarity of the context to the animals despite the changing rooms.

Based on the current understanding of remapping in our field, one would expect only a small number of place cells to remap across repeated sessions (Leutgeb et al., 2005; Colgin et al., 2008), that is, RMCs centered around 0.8–1. Yet, RMCs were relatively evenly distributed between zero and one (Fig. 4). These findings support the notion that partial remapping occurs across repeated sessions. Although some place cells remap (low RMCs), potentially indicating a new context in the same environment, other place cells do not remap (high RMCs), potentially coding for the unchanging spatial information. Interestingly, of the cells that remap in repeated sessions, a large number of cells lose their place field entirely or gain a new place field (Fig. 4, lime green bars). Clearly, however, RMCs are higher for repeated sessions than for different sessions. We performed the KS test and concluded that for each of the five animals, all repeated versus different session comparisons were significant ($p < 0.01$).

To compare different session pairs to each other, we generated a single number that described similarity in hippocampal maps across the session pair by averaging the RMCs across the population (Fig. 5). High average RMCs between two sessions indicate greater similarity in the hippocampal maps of these sessions and thus less remapping, whereas low average RMCs indicate greater dissimilarity and more remapping. Therefore, we expected to observe low average RMCs for comparisons of different rooms and relatively high average RMCs for repetitions of the familiar room (Fig. 5B; purple square near midline), immediate repetition of the novel rooms (Fig. 5B; turquoise squares one off diagonal), and repetitions of N1 and N6 at the end of each day (Fig. 5B; green four squares near midline). Although this pattern was broadly confirmed (Fig. 5), we observed variability among the five animals. Across four of the five animals, repetitions of F had high average RMCs, yet the magnitude of the correlation coefficients and thus the extent of partial remapping varied across animals. Immediate repetitions of the novel rooms showed consistently high average RMCs across all five animals. Yet again the remapping pattern was distinct for each animal, as indicated by the difference in the magnitude of the average RMCs across immediate repetitions of the novel rooms. Likewise, repetitions of N1 and N6 at the end of each day resulted in relatively high average RMCs in four of the five animals. Overall, the comparisons between different rooms led to low average RMCs or slightly negative average RMCs, indicating that global remapping occurs between different rooms (Fig. 5; relatively white background). Indeed, RMCs of repeated rooms were significantly

Table 2. Variables used in GLMs of Figure 7

Variable	Description	Sessions
Mean F between session	The repetitions of the familiar room at the end of days 1 and 2	• F1/F1* • F1/F2 • F1/F2* • F1*/F2 • F1*/F2* • F2/F2*
Mean N1 between session	The repetitions of the novel room N1 at the end of day 1	• N1/N1* • N1/N1*! • N1!/N1* • N1!/N1*!
Mean N6 between session	The repetitions of the novel room N6 at the end of day 2	• N6/N6* • N6/N6*! • N6!/N6* • N6!/N6*!
Mean N between session	The repetitions of the rooms N1 and N6 at the end of days 1 and 2, respectively	• N1/N1* • N1/N1*! • N1!/N1* • N1!/N1*! • N6 / N6* • N6/N6*! • N6!/N6* • N6!/N6*!
Mean N within session	The immediate repetitions of the novel rooms N1 to N10	• N1/N1! • N2/N2! • N3/N3! • N4/N4! • N5/N5! • N6/N6! • N7/N7! • N8/N8! • N9/N9! • N10/N10!

Each row describes how we calculated the value of a variable used in Figure 7. The rows contain the name of the variable in the left column, a verbal description of the session pairs used in the middle column, and the actual list of session pairs in the right column. For a given variable, we calculated the RMC for each cell for the session pairs listed in the right column. We averaged across all cells for each session pair. We then averaged across all session pairs for each animal. In this way, we arrive at a single value of each variable for each animal.

Table 3. Behavioral controls used for the GLMs of Figure 7C

Behavioral control	Description	Sessions
Mean speed difference N between session	Average difference in mean speeds for the sessions of N between session	• |N1–N1*| • |N1–N1*!| • |N1!–N1*| • |N1!–N1*!| • |N6–N6*| • |N6–N6*!| • |N6!–N6*| • |N6!–N6*!|
Mean acceleration difference N between session	Average difference in mean accelerations for the sessions of N between session	• |N1–N1*| • |N1–N1*!| • |N1!–N1*| • |N1!–N1*!| • |N6–N6*| • |N6–N6*!| • |N6!–N6*| • |N6!–N6*!|
Mean absolute angular velocity difference N between session	Average difference in mean absolute angular velocities for the sessions of N between session	• |N1–N1*| • |N1–N1*!| • |N1!–N1*| • |N1!–N1*!| • |N6–N6*| • |N6–N6*!| • |N6!–N6*| • |N6!–N6*!|
Mean speed N between session	Average of average speeds for the sessions of N between session	• N1 • N1! • N1* • N1*! • N6 • N6! • N6* • N6*!
Mean acceleration N between session	Average of average accelerations for the sessions of N between session	• N1 • N1! • N1* • N1*! • N6 • N6! • N6* • N6*!
Mean absolute angular velocity N between session	Average of average mean absolute angular velocities for the sessions of N between session	• N1 • N1! • N1* • N1*! • N6 • N6! • N6* • N6*!

Each row describes how we calculated the value of a control variable used in Figure 7C. The rows contain the name of the variable in the left column, a verbal description of the variable in the middle column, and the session pairs used in the right column. We controlled the relationship between the dependent and independent variables displayed in Figure 7C by reconstructing the GLM with the addition of a behavioral variable to the model. In total, we used six different behavioral controls derived from three behavioral characteristics (speed, acceleration, and absolute angular velocity) and two different methodological approaches (mean differences shown in top three rows and means displayed in bottom three rows). The top three rows describe mean differences (method 1). For each animal, we calculated the average value of a behavioral variable (speed, acceleration, absolute angular velocity) for the sessions of interest. Subsequently, we calculated the absolute difference between the mean values for the sessions of interest and averaged to obtain a single value for a given animal. The bottom three rows (method 2) describe average behavioral parameters. For each animal, we calculated the mean of the behavioral parameter of interest for the listed sessions. Subsequently, we averaged to obtain a single value describing the behavior of a given animal across the listed sessions.

higher than RMCs of different rooms for four of the five animals (t test for unequal variances; 17894, $p^{***} = 1.6 \times 10^{-4}$, DoF (Degrees of Freedom) 352, $t = 5.2$; 18237, $p^{***} = 2.4 \times 10^{-5}$, DoF 352, $t = 4.9$; 19251, $p^{***} = 2.9 \times 10^{-6}$, DoF 326, $t = 5.0$; 17769, $p = 0.20$, DoF 325, $t = 1.2$; 18024, $p^{***} = 7.8 \times 10^{-4}$, DoF 352, $t = 3$). The exact remapping pattern was, however, variable and unique for each animal, as reflected by the uniqueness of each of the matrices. For some animals, we observed clusters of relatively high average RMCs for rooms that were tested close in time to each other (Fig. 5A, Animals 17894 and 19251; light red boxes clustered together near diagonal). This may be an indication that less remapping occurs between rooms that are tested closer to each other, yet more data are needed to validate this claim.

To examine the variability in the partial remapping behavior across animals for repetitions of the same room, we monitored the distribution of average RMCs for repetitions of F versus repetitions of N1 and N6 as described in Table 2 (Fig. 6). We observed a very large range of average RMCs for both, repetitions of the familiar room (range ≈ 0–0.64) and repetitions of N1 and N6 at the end of each day (range ≈ 0–0.47). Overall, we found that the mean RMCs for repetitions of F was higher than the mean RMC for the repetitions of N1 and N6, meaning that less remapping occurs in the familiar room. At the same time, we observed more variability (indicated by a wider distribution) in remapping behavior in the familiar room compared with the novel rooms N1 and N6. Both these findings were borderline significant and varied depending on the arbitrary changes in the parameters of our data analysis pipeline (e.g., speed filtering and smoothing). More data are needed to make definitive conclusions about the remapping behavior of the animals in the
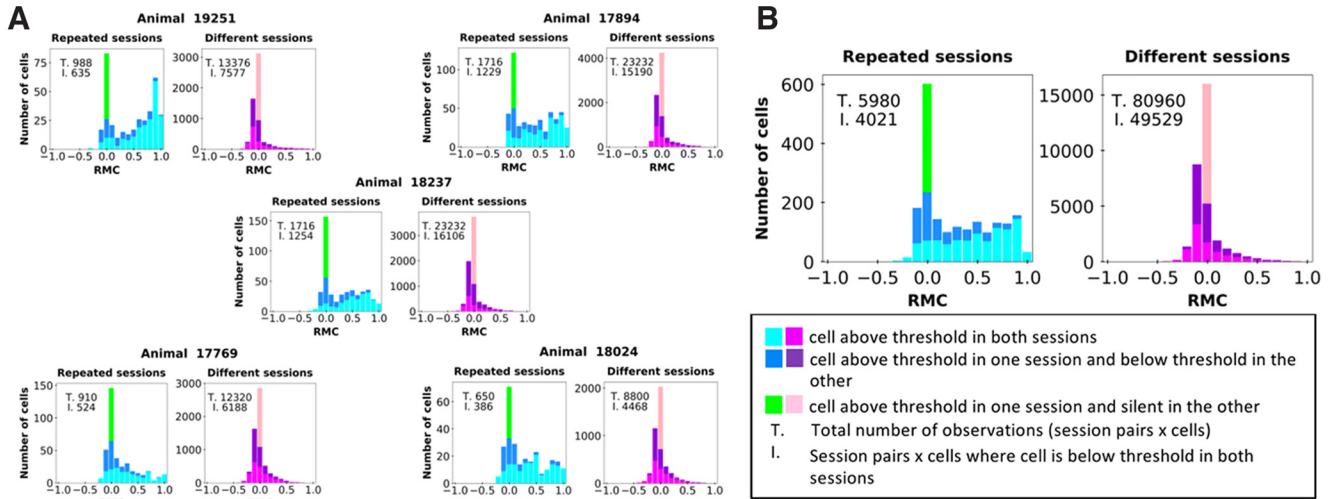
Figure 4. RMCs across repeated and different sessions. Repeated sessions refer to repetitions of F, repetitions of each novel room, and repetitions of N1 and N6 at the end of each day. Different sessions include comparisons across different rooms. T, Total number of observations (number of recorded cells times the number of sessions compared); I, inactive cells. Observations where the cell was either below threshold in both sessions, silent in both sessions, or silent in one and below threshold in the other session, were excluded from the analysis. **A**, RMCs of individual cells for each animal. In repeated sessions, RMCs of individual cells ranged from zero to one, indicating that partial remapping has occurred across the population of cells. This trend was consistent across all five animals. In different sessions, RMCs were clustered around zero indicating that most cells remap. **B**, RMCs of individual cells across all animals. When pooling the data of all five animals, the pattern described in **A** became more apparent.
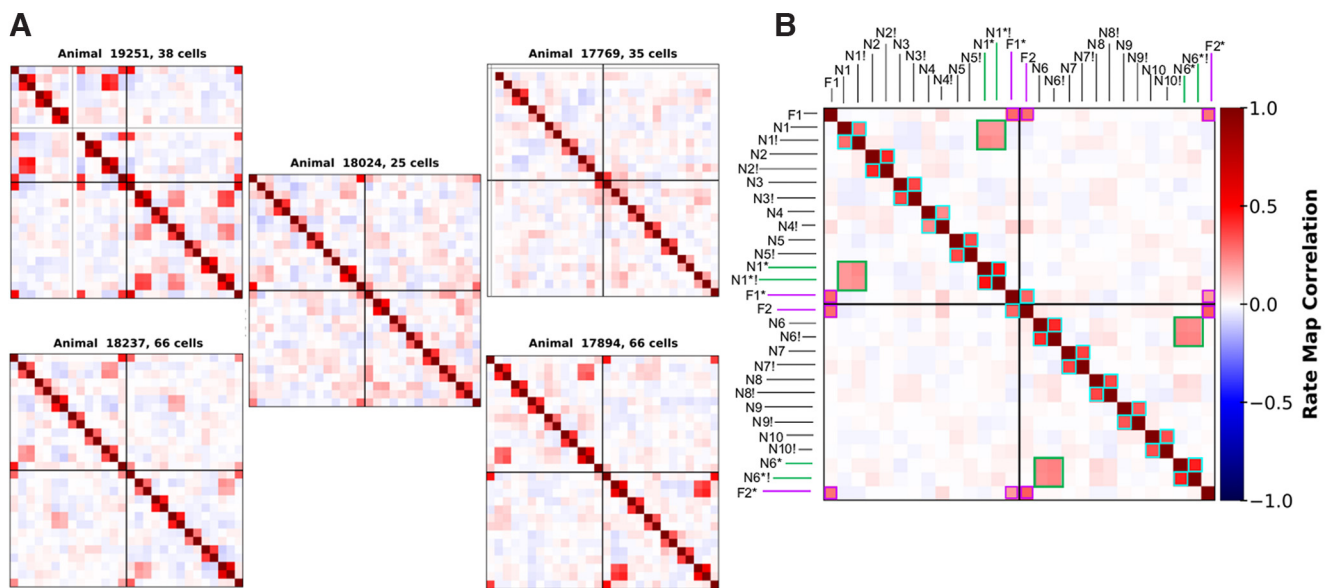

Figure 5. Average RMCs across animals and sessions. This is the population version of Figure 4, illustrating the extent of remapping as a whole. **A**, Average RMCs of each animal individually. Overall, average RMCs were elevated for repetitions of the familiar room, immediate repetitions of the novel rooms, and repetitions of N1 and N6 at the end of each day. Comparisons between different sessions generally showed low average RMCs around zero. However, we observed a remarkable amount of deviation from this pattern across animals. For some animals, the repetitions of N1 and N6 at the end of each day displayed very low average RMCs (animals 17769 and 18024). Additionally, for animal 19251 some comparisons between different rooms revealed relatively high average RMCs (rooms N6 and N8). These findings indicate that remapping behavior is variable across animals. **B**, Average RMCs across all animals. When averaging mean RMCs across animals, the broad pattern described in **A** became more apparent. Although repetitions of novel rooms and the familiar room showed elevated average RMCs, comparisons between different rooms led to relatively low average RMCs. The repetitions of N1 and N6 at the end of each day are marked with green frames, whereas repetitions of the familiar room are marked with a purple frame. Immediate repetitions of the novel rooms adjacent to the diagonal are marked with turquoise frames.

familiar versus the novel rooms. Interestingly, the relative order of average RMCs across animals for repetitions of N rooms was similar to the relative order of average RMCs for repetitions of the F room, raising the question of whether there is a pattern in the remapping behavior of the animals.

To examine the characteristics of partial remapping behavior across the population of animals, we looked at the consistency of RMCs across different repeated session comparisons in each

animal. We found that animals with a higher mean RMC for the repetitions of F displayed higher RMCs for the repetitions of N1 and N6 at the end of each day (Fig. 7A; $r^2 = 0.6$, $p = 0.08$). Likewise, animals with a higher mean RMCs for repetitions of N1 showed higher RMCs for the repetitions of N6 (Fig. 7B; $r^2 = 0.72$, $p^* = 0.04$). Additionally, animals with a higher Mean N within-session RMC, showed a higher Mean N between-session RMC (Fig. 7C; $r^2 = 0.93$, $p^{**} = 0.005$). Together, these findings
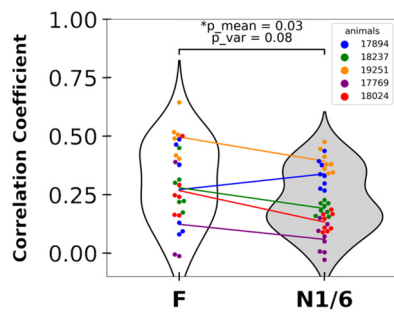
Figure 6. Partial remapping differences between repetitions of familiar and novel rooms. The mean RMC for repetitions of F was higher compared with the mean RMC for the repetitions of N1 and N6 at the end of each day. Furthermore, we observed more variability for RMCs describing repetitions of the familiar room relative to repetitions of N1 and N6 at the end of each day. These findings were borderline significant and shifted slightly based on arbitrary decisions concerning the speed filtering, smoothing, and thresholding of the rate maps. We observed an animal-specific clustering of RMCs. For repetitions of F and repetitions of N1/N6 there seems to be a large variability between animals, as shown by the wide range of RMC distributions. However, the within-animal variability is much smaller, as the RMCs of each animal occupy specific regions within the distribution. This phenomenon resulted in a clustering of RMC for each animal so that the RMCs of the animals seemed to be ordered, with animal 19251 displaying the highest and animal 17769 the lowest RMCs.

indicate that the partial remapping behavior across animals for repeated rooms is structured and not random. Despite only five available data points (for five animals) in these analyses, the correlations described above were relatively high and stable across a variety of values of the parameters of our preprocessing pipeline (e.g., speed filtering, smoothing). Ideally, we would have liked to perform the analysis on a larger dataset, and we hope our findings will be encouragement for others to do so.

In addition to looking at partial remapping behavior across repeated rooms, we also quantified remapping behavior of animals across different rooms. In contrast to repeated rooms, we found no animal-specific remapping behavior across different rooms (data not shown).

RMCs are not the only metric for characterizing remapping. PVDPs have also been used previously (Leutgeb et al., 2005; Alme et al., 2014). RMCs are sensitive to global remapping and measure changes in place field locations of individual cells across two sessions. On the other hand, PVDPs measure changes in relative firing rates of cells across the population at a particular location, and so are more sensitive to rate remapping Leutgeb et al. (2005). We replicated the analyses in Figures 5 and 7 using PVDPs. Repeated rooms generally showed elevated PVDPs, and comparisons between different rooms led to relatively low average PVDPs. The correlations of Figure 7 were largely confirmed, with one comparison being highly significant, one borderline significant, and one nonsignificant (Fig. 8). We also attempted to confirm the results using instantaneous firing rate correlations between corecorded cells (Kubie et al., 2020) but did not have large enough simultaneously recorded cell populations for interpretable results. Because the number of simultaneously recorded cells with overlapping place fields was small on average, we did not observe a statistical difference in average instantaneous firing rate correlations between repeated and different rooms.

The number of recorded cells varied across the five animals (Table 1; range, 25–66 cells). To test whether the size of the recorded place cell population affected animal-to-animal variability, we performed random sampling analyses. We took 100 random samples of 25 cells from one of the animals with the highest number of cells and calculated the average RMC for F1/

F2 for each random sample (Fig. 9A). We compared that distribution of subsampled population average RMCs to the average RMC for F1/F2 calculated with the full population for that animal and for the animal with the smallest population (animal 18024, 25 cells). If variation in recorded population size caused the variation in RMCs, the average F1/F2 RMC of the animal with the lowest number of cells (Fig. 9A; animal 18024, red line) should have fallen within the distribution of the average RMCs of the animal with the highest number of cells after subsampling to the same population size (Fig. 9A; 17894, blue bars). However, the average F1/F2 RMC of animal 18024 was clearly outside the range of the subsampled population RMCs, whereas the average F1/F2 RMC of animal 17894 was in the center of the range of the subsampled population RMCs, indicating that variation between animals in the number of cells sampled did not give rise to the variation between animals in partial remapping behavior. Furthermore, we examined whether sampling bias affected the main finding of the study, shown in Figure 7. Because the animal with the lowest number of cells had 25 recorded units, we reconstructed the correlation shown in Figure 7C 100 times, each time sampling 25 random cells from the other four animals. The subsampled data of each animal was clearly clustered around the original data point, and the variability across animals was preserved (Fig. 9B). Together, these findings suggest that variation across animals in recorded population size is unlikely to explain the structured variability in the partial remapping behavior across animals.

To test whether differences in behavior accounted for the differences in partial remapping shown in Figures 5-7, we quantified average speed, acceleration, and absolute angular velocity of the animals for each session. We wanted to test whether the correlations between the different RMCs for each animal were actually because of correlations of those RMCs or because of some other behavioral variable that was consistent in each animal. To do so, we constructed GLMs that augmented each of the correlations shown in Figure 7C with one of these behavioral variables. For each GLM, there were two independent variables (regressors) and one dependent variable. Exactly like the correlations in Figure 7, the dependent variable was the average RMCs for a particular set of session pairs averaged across all pairs of that class. Like the correlations in Figure 7, one of the independent variables was the average RMCs for a different set of session pairs averaged across all pairs of that class. In addition, the other independent variable was the difference in one of the behavioral variables between sessions in the same session pairs as those used for the dependent variable, averaged across all session pairs in that class. The idea behind structuring the GLMs this way is that we wanted to see whether the variability in the neural data for a given set of session pairs was better predicted by behavioral variability in that same set of session pairs or by variability in the neural data for a completely different set of session pairs. We used two classes of behavioral control variables, constructed as explained in Table 3. One class was the mean differences in the behavioral variables (Table 3, top three rows). The mean differences in a behavioral variable between two sessions reflect the dissimilarity with respect to that behavioral variable, just as RMCs reflect the similarity in hippocampal maps between two rooms. Therefore, using mean differences as a control for RMCs compares the similarity of behavior across two sessions with the similarity of hippocampal maps between those same sessions. The other class was the mean behavioral variables themselves (Table 3,
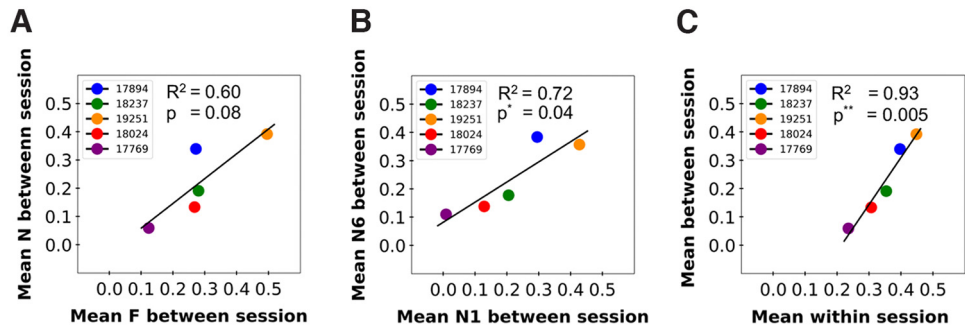
Figure 7. Structured heterogeneity in partial remapping behavior across animals. **A**, Relationship between mean F and mean between-session RMC. Rats with higher RMCs for repetitions of F displayed higher RMCs in the repetitions of N1 and N6 at the end of each day. **B**, Relationship between mean N1 and mean N6 RMCs. Rats with higher RMCs for repetitions of N1 at the end of day 1 displayed higher RMCs for N6 at the end of day 2. **C**, Relationship between mean within-session and mean between-session RMCs. Animals with higher within-session RMC (immediate repetitions) displayed a higher between-session RMC for repetitions of N1 and N6 at the end of each day.
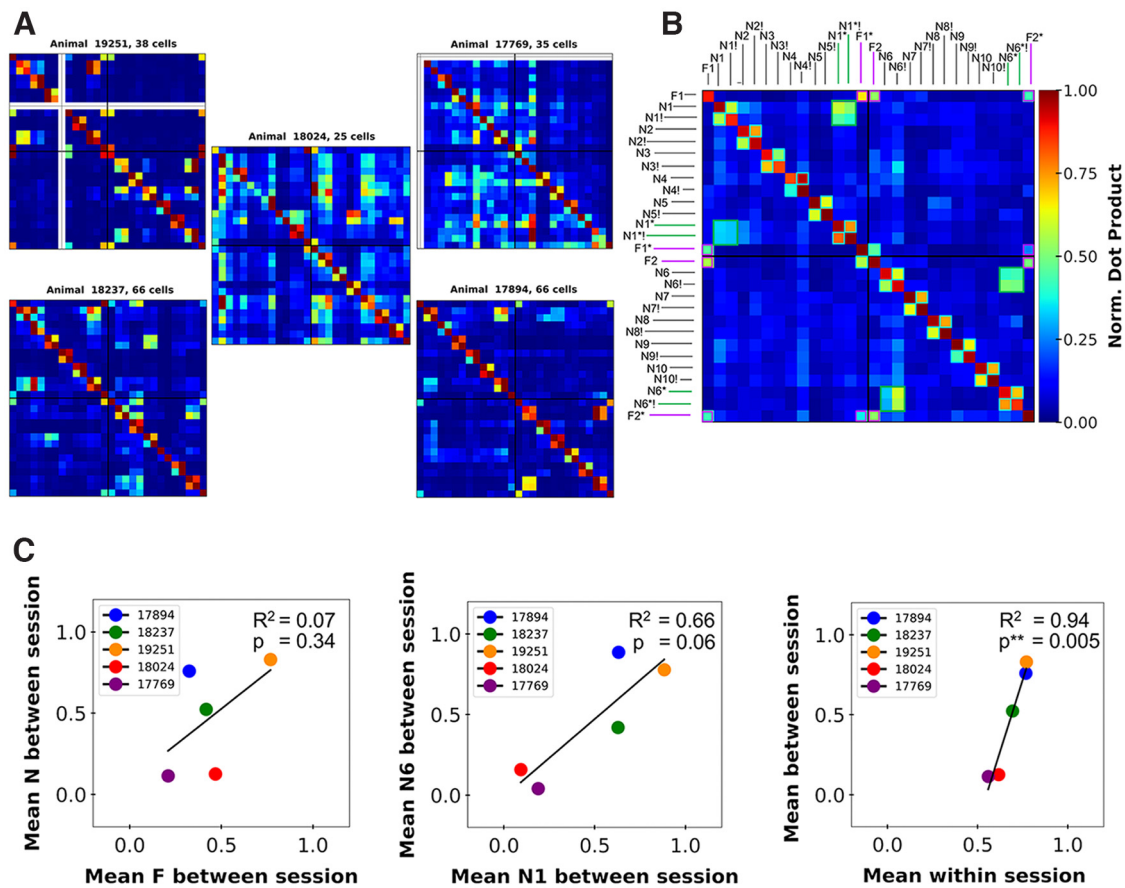

Figure 8. PVDP replicates RMC findings. **A**, PVDP version of Figure 5. Average PVDPs of each animal individually. Overall, PVDPs were elevated for repeated room comparisons. Comparisons between different sessions showed average PVDPs around zero, with more noise than RMCs. The extent of similarity was variable across animals. **B**, When averaging PVDPs across animals, the broad pattern described in **A** became more apparent. Repetitions of novel rooms and the familiar room showed elevated PVDPs, whereas comparisons between different rooms led to relatively low average PVDPs. **C**, PVDP version of Figure 7. The results using PVDPs were less consistent than RMCs but broadly confirmed animal-specific partial remapping behavior. One of the three GLMs remained significant, and a second was borderline significant. Left, Relationship between mean F and mean N between-session PVDPs. Center, Relationship between mean N1 and mean N6 RMCs. Rats with higher RMCs for repetitions of N1 at the end of day 1 displayed higher RMCs for N6 at the end of day 2. Although observable, this trend was weaker when using PVDPs compared with RMCs. Right, Relationship between mean within-session and mean between-session PVDPs. Animals with higher within-session PVDPs (immediate repetitions) displayed a higher between-session PVDP for repetitions of N1 and N6 at the end of each day.

bottom three rows), which allow us to describe the average behavior of the animal across all the sessions that were used to construct the neural variables used for the GLMs in Figure 7C. In this approach, we controlled for the possibility that behavioral characteristics of the animals may directly relate to RMC values, as would be expected, for example, if average speed

and RMCs both related to attentional levels. In each of the six controls of Figure 7C, we observed a high correlation between the neural independent variable and the neural dependent variable along with a low correlation between the behavioral independent variable and the neural dependent variable (Table 4). This finding confirmed that the high correlation
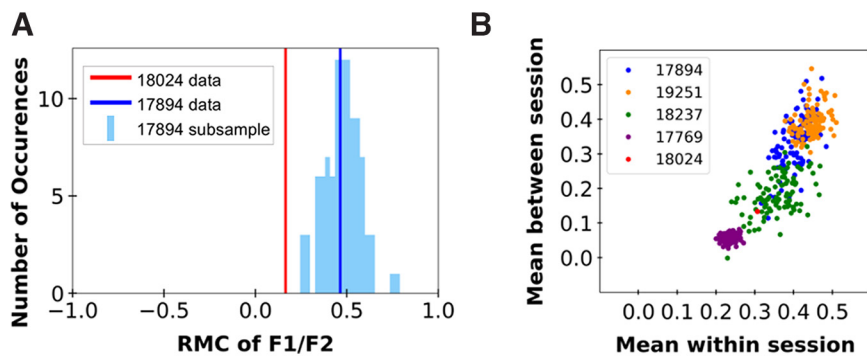
Figure 9. Experimental sampling controls. **A**, We compared the animal with the fewest recorded cells (animal 18024, 25 cells) with 100 random subsamples of 25 cells from one of the animals with the most cells (animal 17894, 66 cells). The bars show the number of occurrences of each average F1/F2 RMC among the 100 subsamples of animal 17894 (blue). The vertical lines are the average RMC for the F1/F2 session pair for the full recorded population for each animal (animal 17894, blue; animal 18024, red). The full population RMC for animal 17894 is at the center of its own subsampled range of RMCs, whereas the full population RMC for animal 18024 is outside the range of subsampled RMCs for animal 17894. **B**, We re-created a subsampled version of Figure 7C, where each dot is the RMC calculated using a subsample of 25 cells from that animal. As evident by the linear arrangement of the data, higher mean within-session RMCs correlated with higher mean between-session RMCs, and the data for each animal maintained the order of Figure 7C.

between Mean N within-session RMCs and Mean N between-session RMCs cannot be explained by the speed, acceleration, and absolute angular velocities of the animal, nor can it be explained by changes in those behavioral variables. The exact structure of the GLMs can be found in Table 3.

Hippocampal representations drift over time (Ziv et al., 2013), in that the more time that has elapsed between exposures to an environment, the more different place field representations are. This drift has been posited to encode time (Mankin et al., 2012). One hypothesis stemming from these results is that different animals may have different rates of representational drift. To test this hypothesis, we looked at all comparisons for repeated sessions. We compared the time elapsed between the sessions with the average RMC for that comparison (Fig. 10A). Surprisingly, we did not observe consistent representational drift. Of the five animals, only one had a significant correlation between time between sessions and average RMC (17894, $r^2 = 0.136, p = 0.091$; 18237, $r^2 = 0.186, p^* = 0.045$; 19251, $r^2 = 0.003, p = 0.809$; 17769, $r^2 = 0.067, p = 0.284$; 18024, $r^2 = 0.050, p = 0.320$).

Indeed, comparisons between the F room had consistently higher RMCs than comparisons between novel rooms N1 and N6 at the beginning and end of the day, although the familiar room comparisons had longer intervals that elapsed between them (Fig. 1). It is possible that representational drift occurs independently for novel and familiar rooms (Fig. 10A, first two and last three intervals, respectively). Overall, we find that animal-to-animal variability in partial remapping is not because of differences in coding of time (speed of representational drift). Even more strikingly, we did not find consistent representational drift at all in this dataset, although this may be because of the fact that this dataset was collected in CA3, which has previously been shown to have less representational drift than CA1 (Mankin et al., 2012). If time is being encoded through representational drift in this dataset, it must be encoded independently for novel and familiar rooms. We then looked specifically at the variability in the speed of drift (speed of decrease in RMCs over time) in representations of novel rooms across animals. It might be possible that animal-specific drift speeds might lead to the animal-specific patterns we saw in partial remapping behavior. For each animal, we

calculated the N1/N1!, N1/N1*, N6/N6!, and N6/N6* RMCs, that is, the RMCs for the immediate repetitions and day-end repetitions of N1 and N6. For each animal, we then calculated the difference between the N1 comparisons and the difference between the N6 comparisons, that is, (N1/N1!–N1/N1*) and (N6/N6!–N6/N6*). This difference characterizes the speed of drift in the representation of each of the novel rooms for each animal. We then plotted these difference values for each room against each other. We did not find a correlation between these values across animals (Fig. 10B; $r^2 = 0.049, p = 0.721$). Overall, it seems that time encoding through representational drift is not consistently occurring in this dataset, and differences in speed of drift do not lead to the animal-to-animal variability in partial remapping that we observe.

Discussion

Hippocampal remapping is a complex and highly variable phenomenon. In this work, we studied the characteristics of cell-to-cell and animal-to-animal variability in partial remapping behavior. We compared the firing patterns of individual cells of five rats across 11 repeated and different rooms. Although most cells remapped across different room comparisons, we observed a large amount of variability across repeated rooms, indicating that partial remapping occurs in the latter type of comparison. We then shifted our focus from individual cells to comparing the changes in the hippocampal maps of the animals across repeated and different sessions, using average RMCs. We discovered extensive remapping across different rooms but much less remapping across repeating sessions, indicating that hippocampal maps are similar yet not identical across repeated sessions. Although this general remapping pattern applied to all five animals, we detected variability across the animals. We quantified the pattern of variability in the partial remapping behavior of the animals by correlating different categories of neural partial remapping data (Fig. 7). Across all comparisons, we discovered a high correlation between the neural variables of the five animals, and the animals stratified along a spectrum that was preserved for each comparison. We concluded that the animal-to-animal variability in partial remapping behavior is structured. Neither the subsampling of place cells (Fig. 9) nor the underlying behavioral characteristics of the animals (Table 4) accounted for the structured variability we observed, raising the question of the origins of this phenomenon.

Definition of remapping

The term hippocampal remapping has a variety of uses in the literature. Sometimes remapping is used to refer to what is now known as global remapping. For example, in a recent comprehensive review of hippocampal remapping, Kubie et al. (2020) use this as their primary definition of remapping. However, partial remapping and rate remapping are forms of remapping that are commonly explored as well, as reviewed toward the end by Kubie et al. (2020). Indeed, the classic studies of remapping

Table 4. Effect of behavioral parameters on the results shown in Fig. 7C

Independent Variable 1	Independent Variable 2	Dependent Variable	r^2 (1)	p (1)	m (1)	p (2)	m (2)
Mean N within session	N/A	Mean N between session	0.93	0.005	1.66	N/A	N/A
Mean N within session	Mean speed difference N between session	Mean N between session	0.97	0.04	1.22	0.15	−0.12
Mean N within session	Mean acceleration difference N between session	Mean N between session	0.95	0.05	1.32	0.30	−0.06
Mean N within session	Mean absolute angular velocity difference N between session	Mean N between session	0.91	0.04	1.76	0.75	0.0013
Mean N within session	Mean speed N between session	Mean N between session	0.92	0.05	1.49	0.57	0.01
Mean N within session	Mean acceleration N between session	Mean N between session	0.93	0.05	1.47	0.49	0.01
Mean N within session	Mean absolute angular velocity N between session	Mean N between session	0.94	0.02	1.66	0.35	−0.0018

We constructed a total of 6 new GLMs (rows 2-7) to control for the findings shown in Fig. 7C (row 1). Each time, we recreated the GLM of Fig. 7C but added a second independent variable to the model to examine whether the behavior of the animals could explain the structured heterogeneity in their partial remapping. Across all 6 controls, the correlation between the two types of neural data (independent variable 1 and dependent variable) was high, as indicated by the non-zero slope values (m1). The relationship between the neural variables remained significant (p(1) < 0.05) even after the incorporation of the behavioral controls. However, we found no correlation between the behavioral data and the neural data (independent variable 2 and dependent variable), as indicated by the negligible slope values (m2). The relationship between the behavioral and neural data was not significant (p(2) > 0.05), confirming that the variability in the animals' remapping characteristics cannot be explained by the variability in these behavioral metrics.

reported partial remapping (remapping of a fraction of the place fields in the environment; Muller and Kubie, 1987; O'Keefe and Speakman, 1987; Markus et al., 1995; Gothard et al., 1996). It seems that the field refers to the study of the difference in hippocampal representations between different experiences as the study of remapping, which can take many forms. As we emphasize in Sanders et al. (2020), differences in hippocampal representations between different experiences fall along a continuum, which we referred to as extent of remapping.

The current study follows the view that remapping occurs on a continuum and explores variability between animals in extent of remapping between different experiences in repeated environments. We did not find animal-to-animal variability in extent of remapping between experiences in different environments, as all animals expressed complete or global remapping between experiences in different environments (Figs. 4, 5, RMCs near zero). However, we did find consistent animal-to-animal variability in extent of partial remapping between different experiences in repeated environments.

Figure 10. Effect of the passage of time on RMCs in repeated rooms. *A*, We compared the amount of time (*x*-axis) between sessions with RMCs for that comparison (*y*-axis). We used immediate repetitions of novel rooms (e.g., N1/N1!, 15 min), repetitions of novel rooms later in the day (e.g., N1/N1*, 285 min), repetitions of the familiar room during the same day (e.g., F1/F1*, 390 min), repetitions of the familiar room at the end of day 1 versus the beginning of day 2 (F1*/F2, 1050 min), repetitions of the familiar room at the beginning of day 1 versus the beginning of day 2 (F1/F2, 1440 min), and the repetition of the familiar room at the beginning of day 1 versus the end of day 2 (F1/F2*, 1830 min) as comparisons. We did not see a consistent relationship between time elapsed between sessions and RMCs. *B*, For each animal, we calculated the N1/N1!, N1/N1*, N6/N6!, and N6/N6* RMCs, that is, the RMCs for the immediate repetitions and day-end repetitions of N1 and N6. For each animal, we then calculated the difference between the N1 comparisons (RMC Diff. N1) and the difference between the N6 comparisons (RMC Diff. N6), that is, (N1/N1!–N1/N1*) and (N6/N6!–N6/N6*). We did not find a correlation between these differences across animals.

Changes in hippocampal activity: remapping, stability, drift?
There are several potential factors that may cause changes in the neural representation of a controlled stimulus, such as an experiment room. One possibility is that the animal is representing uncontrolled changes in the stimulus. Another possibility is that the representation has drifted; the computational content of the representation is the same, but the neurons involved have changed (Ziv et al., 2013; Rule et al., 2019). Earlier literature referred to a similar phenomenon as place field instability (Thompson and Best, 1990; Kentros et al., 2004; Wills et al., 2010), although place field instability can also refer to forgetting, in which the computational content changes as well (Kentros et al., 1998). A final possibility is that the computational categorization of the animals of the stimulus has changed as a result of intervening experience (Sanders et al., 2020). This possibility is especially relevant as place field maps clearly change as a result of experience (Shapiro et al., 1997; Lever et al., 2002; Law et al., 2016). Further work will be necessary to distinguish among these possibilities, both in
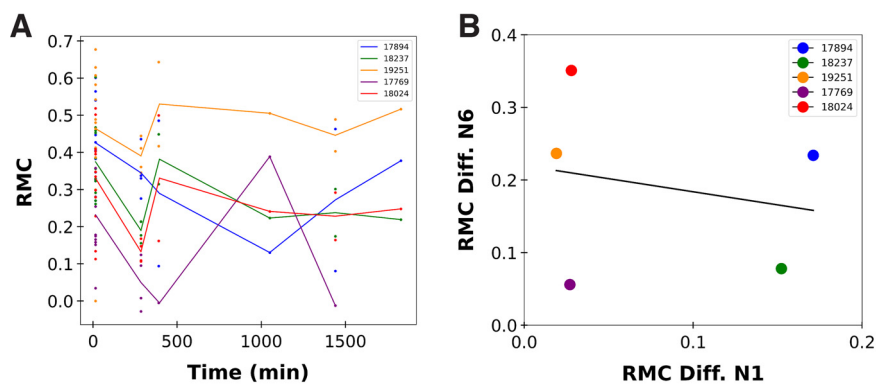
our work and in the field in general. A key question is whether and when coding changes are playing a computational role as opposed to being ancillary to computation. Experiments similar to those proposed below and those proposed by Sanders et al. (2020) can determine the extent to which hippocampal coding changes lead to behavioral and learning changes.

Possible origins of animal-specific remapping behavior
There are several potential explanations for this animal-specific partial remapping behavior that we cannot yet distinguish.

One class of possibilities (strategy variability) is that animals have computational-level differences in how they deal with the inherent ambiguity in context definition. As described in the Introduction, animals do not have direct access to context labels and therefore must infer the hidden context identity, a process characterized as hidden state inference by Sanders et al. (2020). The trade-off between splitting and lumping (increased differentiation vs increased generalization, more vs fewer hidden states) has no a priori solution, which is why populations will have individuals with a variety of tendencies on that axis (Simpson, 1945). Sanders et al. (2020) suggested that differing settings of a parameter of the model, alpha, could underlie variation in remapping

behavior as it controls the tendency of the model to prefer a greater or smaller number of hidden states. Of course, other forms of variation could arise from other parameters of that model or of other models of remapping behavior that explicitly include parameters with no a priori optimal values. In short, this class of possibilities suggests that variability in remapping behavior might correspond to variability in problem-solving strategies.

Another class of possibilities (capability variability) is that animals have differences in cognitive abilities. Learning impairments can cause an animal to be unable to retrieve a memory of an environment. If that occurs, the map would not be reused when the animal re-enters the environment, which would result in global remapping (near-zero average RMC). A previous result interpreted using this perspective is a series of studies on aging rats by Barnes et al. (1997), reviewed by Lister and Barnes (2009), who show that aging animals have a greater tendency to globally remap when presented with the same environment (although it has also been shown that aged animals have a lower tendency to remap when presented with a modified environment; Wilson et al., 2003). Indeed, others showed that among aged animals, tendency to remap correlated with other firing characteristics (Hok et al., 2012). In this way, it could be that the variability across animals observed in our data was the result of learning deficits in some animals. It is unlikely that aging per se is the cause of variability in this dataset, as all animals were 4–5 months at the time of implantation (see above, Materials and Methods), but it is possible that other forms of learning differences could be present among the animals. A related explanation in this class is that remapping can be induced by a lack of attention paid to the cues that differentiate environments. For example, Kentros et al. (2004) show that changing attentional demands changed the tendency of animals to remap. The experimental data we analyzed were recorded during a task with low attentional demands, so intrinsic differences in attention among animals may have given rise to differences in remapping tendencies. This class of possibilities suggests that variability in remapping behavior might correspond to variability in cognitive capabilities.

The key distinction between these classes of hypotheses is how variability in neural responses corresponds to variability in behavior. The strategy variability hypothesis would suggest that different animals would be differentially skilled at different tasks. The capability variability hypothesis would suggest that some animals would be better at all context-dependent tasks.

Unfortunately, it is unclear exactly how remapping relates to behavior. The standard assumption in the field is that hippocampal remapping corresponds to context-specific learning, that animals will generalize behaviors learned between experiences using the same map but not between experiences using different maps (Colgin et al., 2008). This assumption has not been directly proven, and in fact there is limited evidence to the contrary (Jeffery et al., 2003). For the sake of argument, let's accept this assumption, however. Under the capability variability hypothesis, animals that remap more would simply have more difficulty generalizing knowledge past the experience they learned it in as they do not reuse maps. Under the strategy variability hypothesis, something more nuanced occurs. Animals with a greater tendency to remap would be faster at learning tasks that required distinctions, such as a context-specific go/no-go task. This would be because animals that remap less would have a greater tendency to generalize across slightly different experiences. On the other hand, animals with a lower tendency to remap would be faster at learning tasks that required greater levels of generalization. Another potential behavioral prediction of the strategy

variability hypothesis is that the tendency of remapping might correspond to the extent of generalization during fear conditioning. When a shock is only presented a single time, the animal has to infer what extent of generalization of that experience is appropriate. Differences in sensitivity in environmental changes giving rise to remapping would be predicted to correspond to differences in sensitivity to environmental changes that elicit a conditioned fear response.

One final possibility is that differences in the recording locations in different animals may have given rise to the differences in remapping behavior, if different parts of the hippocampus respond characteristically differently. There are reasons to believe that remapping might have different properties along the CA3–CA1 (proximo-distal) axis (Lee et al., 2004; Leutgeb et al., 2004; Guzowski et al., 2004) as well as along the dorsal-ventral (septotemporal) axis (Royer et al., 2010). If these different animals were implanted in characteristically different locations, the remapping behavior of the recorded cells might be consistently different even if the animals in general did not have consistent differences. We do not have access to the recording locations of the animals, so we could not verify this hypothesis.

One result that gives rise to several questions is that of the subsampling done in Figure 9. In addition to the across-animal correlation that is preserved despite subsampling, there is also the within-animal correlation across separate subsamples. This implies that different cells within an animal have different tendencies to remap. This could arise with the previous hypothesis, that different recording locations might have characteristically different remapping behaviors. A related possibility was mentioned in Sanders et al. (2020), namely, that hierarchical hidden state inference could be performed by having a gradient of remapping tendencies within a population.

Finally, this article suggests a poor man's remapping metric—within-session variability. We show that within-session partial remapping correlates with between-session partial remapping (Fig. 7C). If between-session remapping tendency turns out to correlate with learning style (as suggested by the strategy variability hypothesis) or with learning capability (as suggested by the capability variability hypothesis), measures of within-session firing variability such as overdispersion (Olypher et al., 2002; Kelemen and Fenton, 2016) could be used as a proxy for the tendency to notice small differences or with learning speed, respectively. Indeed, remapping has been shown to correlate with overdispersion in aged rats (Hok et al., 2012). The utility of this measure awaits research into its behavioral relevance, but certainly those designing future studies of remapping should keep it in mind.

References

Alme CB, Miao C, Jezek K, Treves A, Moser EI, Moser MB (2014) Place cells in the hippocampus: eleven maps for eleven rooms. Proc Natl Acad Sci U S A 111:18428–18435.

Barnes CA, Suster MS, Shen J, McNaughton BL (1997) Multistability of cognitive maps in the hippocampus of old rats. Nature 388:272–275.

Colgin LL, Moser EI, Moser MB (2008) Understanding memory through hippocampal remapping. Trends Neurosci 31:469–477.

Fenton AA, Lytton WW, Barry JM, Lenck-Santini PP, Zinyuk LE, Kubík S, Bures J, Poucet B, Muller RU, Olypher AV (2010) Attention-like modulation of hippocampus place cell discharge. J Neurosci 30:4613–4625.

Fetterhoff D, Sobolev A, Leibold C (2021) Graded remapping of hippocampal ensembles under sensory conflicts. Cell Rep 36:109661.

Frank LM, Brown EN, Wilson MA (2000) Trajectory encoding in the hippocampus and entorhinal cortex. Neuron 27:169–178.

Gothard KM, Skaggs WE, Moore KM, McNaughton BL (1996) Binding of hippocampal CA1 neural activity to multiple reference frames in a landmark-based navigation task. J Neurosci 16:823–835.

Guzowski JF, Knierim JJ, Moser EI (2004) Ensemble dynamics of hippocampal regions CA3 and CA1. Neuron 44:581–584.

Hargreaves EL, Yoganarasimha D, Knierim JJ (2007) Cohesiveness of spatial and directional representations recorded from neural ensembles in the anterior thalamus, parasubiculum, medial entorhinal cortex, and hippocampus. Hippocampus 17:826–841.

Harris CR, et al. (2020) Array programming with NumPy. Nature 585:357–362.

Hok V, Chah E, Reilly RB, O'Mara SM (2012) Hippocampal dynamics predict interindividual cognitive differences in rats. J Neurosci 32:3540–3551.

Hunter JD (2007) Matplotlib: a 2D graphics environment. Comput Sci Eng 9:90–95.

Jackson JC, Redish AD (2007) Network dynamics of hippocampal cell-assemblies resemble multiple spatial maps within single tasks. Hippocampus 17:1209–1229.

Jeffery KJ, Gilbert A, Burton S, Strudwick A (2003) Preserved performance in a hippocampal-dependent spatial task despite complete place cell remapping. Hippocampus 13:175–189.

Kelemen E, Fenton AA (2016) Coordinating different representations in the hippocampus. Neurobiol Learn Mem 129:50–59.

Kentros C, Hargreaves E, Hawkins RD, Kandel ER, Shapiro ML, Muller RV (1998) Abolition of long-term stability of new hippocampal place cell maps by NMDA receptor blockade. Science 280:2121–2126.

Kentros CG, Agnihotri NT, Streater S, Hawkins RD, Kandel ER (2004) Increased attention to spatial context increases both place field stability and spatial memory. Neuron 42:283–295.

Kinsky NR, Sullivan DW, Mau W, Hasselmo ME, Eichenbaum HB (2018) Hippocampal place fields maintain a coherent and flexible map across long timescales. Curr Biol 28:3578–3588.

Kubie JL, Levy ER, Fenton AA (2020) Is hippocampal remapping the physiological basis for context? Hippocampus 30:851–864.

Law LM, Bulkin DA, Smith DM (2016) Slow stabilization of concurrently acquired hippocampal context representations. Hippocampus 26:1560–1569.

Lee I, Yoganarasimha D, Rao G, Knierim JJ (2004) Comparison of population coherence of place cells in hippocampal subfields CA1 and CA3. Nature 430:456–459.

Leutgeb S, Leutgeb JK, Treves A, Moser MB, Moser EI (2004) Distinct ensemble codes in hippocampal areas CA3 and CA1. Science 305:1295–1298.

Leutgeb S, Leutgeb JK, Barnes CA, Moser EI, McNaughton BL, Moser MB (2005) Independent codes for spatial and episodic memory in hippocampal neuronal ensembles. Science 309:619–623.

Lever C, Wills TJ, Cacucci F, Burgess N, O'Keefe J (2002) Long-term plasticity in hippocampal place-cell representation of environmental geometry. Nature 416:90–94.

Lister JP, Barnes CA (2009) Neurobiological changes in the hippocampus during normative aging. Arch Neurol 66:829–833.

Mankin EA, Sparks F, Slayyeh B, Sutherland R, Leutgeb S, Leutgeb JK (2012) Neuronal code for extended time in the hippocampus. Proc Natl Acad Sci U S A 109:19462–19467.

Markus EJ, Qin YL, Leonard B, Skaggs WE, McNaughton BL, Barnes CA (1995) Interactions between location and task affect the spatial and directional firing of hippocampal neurons. J Neurosci 15:7079–7094.

Muller RU, Kubie JL (1987) The effects of changes in the environment on the spatial firing of hippocampal complex-spike cells. J Neurosci 7:1951–1968.

O'Keefe J (1976) Place units in the hippocampus of the freely moving rat. Exper Neurol 51:78–109.

O'Keefe J, Speakman A (1987) Single unit activity in the rat hippocampus during a spatial memory task. Exp Brain Res 68:1–27.

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

Olypher AV, Lánský P, Fenton AA (2002) Properties of the extra-positional signal in hippocampal place cell discharge derived from the overdispersion in location-specific firing. Neuroscience 111:553–566.

Royer S, Sirota A, Patel J, Buzsáki G (2010) Distinct representations and theta dynamics in dorsal and ventral hippocampus. J Neurosci 30:1777–1787.

Rule ME, O'Leary T, Harvey CD, O'Leary T, Harvey CD (2019) Causes and consequences of representational drift. Curr Opin Neurobiol 58:141–147.

Sanders H, Ji D, Sasaki T, Leutgeb JK, Wilson MA, Lisman JE (2019) Temporal coding and rate remapping: representation of nonspatial information in the hippocampus. Hippocampus 29:111–127.

Sanders H, Wilson MA, Gershman SJ (2020) Hippocampal remapping as hidden state inference. Elife 9:e51140.

Shapiro ML, Tanila H, Eichenbaum H (1997) Cues that hippocampal place cells encode: dynamic and hierarchical representation of local and distal stimuli. Hippocampus 7:624–642.

Simpson GG (1945) The principles of classification and a classification of mammals. New York: American Museum of Natural History.

Thompson LT, Best PJ (1990) Long-term stability of the place-field activity of single units recorded from the dorsal hippocampus of freely behaving rats. Brain Res 509:299–308.

Virtanen P, et al. (2020) SciPy 1.0: fundamental algorithms for scientific computing in Python. Nat Methods 17:261–272.

Wills TJ, Lever C, Cacucci F, Burgess N, O'Keefe J (2005) Attractor dynamics in the hippocampal representation of the local environment. Science 308:873–876.

Wills TJ, Cacucci F, Burgess N, O'Keefe J (2010) Development of the hippocampal cognitive map in preweanling rats. Science 328:1573–1576.

Wilson IA, Ikonen S, McMahan RW, Gallagher M, Eichenbaum H, Tanila H (2003) Place cell rigidity correlates with impaired spatial learning in aged rats. Neurobiol Aging 24:297–305.

Wood ER, Dudchenko PA, Robitsek RJ, Eichenbaum H (2000) Hippocampal neurons encode information about different types of memory episodes occurring in the same location. Neuron 27:623–633.

Ziv Y, Burns LD, Cocker ED, Hamel EO, Ghosh KK, Kitch LJ, Gamal AE, Schnitzer MJ (2013) Long-term dynamics of CA1 hippocampal place codes. Nat Neurosci 16:264–266.