Hippocampal Place-Cell Firing During Movement in Three-Dimensional Space

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Knierim, James J. and Bruce L. McNaughton. Hippocampal place-cell firing during movement in three-dimensional space. *J Neurophysiol* 85: 105–116, 2001. "Place" cells of the rat hippocampus are coupled to "head direction" cells of the thalamus and limbic cortex. Head direction cells are sensitive to head direction in the horizontal plane only, which leads to the question of whether place cells similarly encode locations in the horizontal plane only, ignoring the *z* axis, or whether they encode locations in three dimensions. This question was addressed by recording from ensembles of CA1 pyramidal cells while rats traversed a rectangular track that could be tilted and rotated to different three-dimensional orientations. Cells were analyzed to determine whether their firing was bound to the external, three-dimensional cues of the environment, to the two-dimensional rectangular surface, or to some combination of these cues. Tilting the track 45° generally provoked a partial remapping of the rectangular surface in that some cells maintained their place fields, whereas other cells either gained new place fields, lost existing fields, or changed their firing locations arbitrarily. When the tilted track was rotated relative to the distal landmarks, most place fields remapped, but a number of cells maintained the same place field relative to the *x-y* coordinate frame of the laboratory, ignoring the *z* axis. No more cells were bound to the local reference frame of the recording apparatus than would be predicted by chance. The partial remapping demonstrated that the place cell system was sensitive to the three-dimensional manipulations of the recording apparatus. Nonetheless the results were not consistent with an explicit three-dimensional tuning of individual hippocampal neurons nor were they consistent with a model in which different sets of cells are tightly coupled to different sets of environmental cues. The results are most consistent with the statement that hippocampal neurons can change their "tuning functions" in arbitrary ways when features of the sensory input or behavioral context are altered. Understanding the rules that govern the remapping phenomenon holds promise for deciphering the neural circuitry underlying hippocampal function.

INTRODUCTION

Two types of neurons in the rodent brain have been implicated in spatial learning and navigation processes: "place" cells of the hippocampus and "head direction" (HD) cells of the thalamus and postsubiculum (O'Keefe and Dostrovsky 1971; Taube et al. 1990a). These two brain systems are coupled in that manipulations that cause HD cells to rotate their preferred firing directions in an environment will cause the ensemble of place cells that represent that environment to either rotate their place fields by the same amount or to "remap" the environment (Blair and Sharp 1996; Bostock et al. 1991; Knierim et al. 1995; Sharp et al. 1995; Tanila et al. 1997). A situation has never been reported in which the hippocampal ensemble representation maintains its internal coherency (i.e., does not remap) but changes its orientation relative to that of the HD system, and it has thus been postulated that one role of the HD cell system is to set the orientation of the hippocampal "cognitive map" (Muller et al. 1996; O'Keefe and Nadel 1978).

Nonetheless there are key differences between the properties of place and HD cells. The tuning curves of HD cells are inherently one dimensional. These cells are sensitive to head direction in the yaw axis only; changes in direction in the pitch and roll axes ($\pm 90°$) have no effect on their firing (Stackman et al. 2000; Taube 1998). Under normal conditions, a HD cell will have a preferred firing direction in all environments, and the relative directions between pairs of HD cells will remain constant in all environments (Taube 1998).

Place cells have certain properties that are fundamentally different from these properties of HD cells (Muller et al. 1996). The spatial selectivity of place cells on a flat surface is (at a minimum) two dimensional. Place cells typically change their firing properties unpredictably between two distinct environments, and the spatial relationships between the fields of different place cells do not remain consistent from environment to environment (Kubie and Ranck 1983; O'Keefe and Conway 1978). Finally, only a fraction of place cells are typically active in any given environment; the remaining cells are virtually silent (Guzowski et al. 1999; O'Keefe and Conway 1978; Thompson and Best 1989; Wilson and McNaughton 1993).

Most studies of place cells have been restricted to essentially two-dimensional environments, leaving unanswered the question of whether place cells (like HD cells) are insensitive to changes in the *z* axis. The answer would have strong implications for models that attempt to define the mechanisms by which place cells acquire their spatial specificity. One class of models postulates that place cells encode unique configurations of sensory and internal input ("local views") (McNaughton 1989; McNaughton et al. 1983a) that are available to an animal at a given spatial location (e.g., Shapiro and Hetherington

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1993; Sharp 1991; Zipser 1985). According to a strict interpretation of this view, place fields should be three dimensional as changes in position along the *z* axis result in equivalent modifications of the sensory input as changes in the *x* or *y* axes. A recent model has emphasized the role of the hippocampus in path integration (McNaughton et al. 1996; Samsonovich and McNaughton 1997; see also Whishaw et al. 1997). In this model, place cells use primarily self-motion (idiothetic) cues to encode the animal's distance and bearing relative to some starting location. As the animal moves forward in a certain direction, inputs from idiothetic cues and from the HD cell system update the network to represent the new location. Modifiable inputs from external landmarks allow for the correction of cumulative error after the animal gains familiarity in an environment. Because HD cells are sensitive to changes only in the yaw axis, this model postulates that the path integration mechanisms in the hippocampus would be unable to distinguish forward motion in the horizontal plane from forward motion in an oblique plane and that place cells would thus be insensitive to the animal's location in the *z* axis.

The present study was designed to test this prediction. Ideally one would record from place cells as an animal navigates in a stable, three-dimensional volume. Rats are constrained to navigate along surfaces, however. Thus to address this question, ensembles of place cells were recorded as rats traversed a rectangular track that could be tilted and rotated to different three-dimensional orientations. Although most studies of place cells demonstrate that distal cues have precedence over local surface cues in controlling the firing locations of place cells, recent studies (e.g., Shapiro et al. 1997; Tanila et al. 1997) have shown that more salient local cues can exert an influence over these cells and trigger remapping. It was not known whether changes in the three-dimensional orientation of a local surface would be a cue that is salient enough to exert a similar influence. Thus the place fields were analyzed to determine whether they were bound to the distal cues of the environment, whether they were bound to the two-dimensional rectangular surface, or whether the manipulations caused an unpredictable remapping of the surface. The results demonstrate that such three-dimensional manipulations of the local surface can cause a partial remapping of the hippocampal representation as a majority of cells changed their place fields unpredictably while a minority maintained the same field relative to the *x*-*y* coordinates of the room, ignoring the *z* axis. These results contribute to our understanding of the nature of the interaction between distal landmarks and local cues in the firing of place cells and of the network dynamics of the hippocampal representation of an environment.

METHODS

Subjects

The experiments were performed on two groups of four rats. *Group 1* comprised four male retired breeder Fischer-344 rats obtained from the National Institute on Aging colony at Harlan Laboratories at ~9 mo old. They were ~14 mo old at the time of recording. *Group 2* comprised four specific-pathogen-free male Fischer-344 rats obtained from Taconic Farms at a~ 4 mo old; they were ~9 mo old at the time of recording. All animals were put on a controlled feeding schedule to maintain their weights at 80–90% of their ad libitum weights. The rats had free access to water. During the experiment, they were handled and weighed daily. The rats were housed individually and maintained on a 12:12 h reversed light:dark cycle (lights off 10 AM to 10 PM). Recording was done during the dark portion of the cycle. Animal care, surgical procedures, and euthanasia were carried out according to National Institutes of Health guidelines.

Training

Group 1 was trained initially to shuttle back and forth for combinations of food reward (45-mg pellets or a wet mash of moistened rat chow) or electrical stimulation of the medial forebrain bundle (MFB; 30–150 μA current, 300-μs pulses at 100 Hz for 0.5 s) at each end of a 91 × 13 cm alley. This training, which lasted 3–17 days, was used to ascertain the proper levels of MFB stimulation adequate to promote good behavioral performance for each rat. The rats were then trained to run clockwise for food and MFB stimulation on a rectangular track (38 × 62 cm) that could be tilted up to a 45° angle along its long axis (Fig. 1). The surface of each side of the track was 8.5 cm wide. Hinges connected the four sides and allowed the long sides of the track to be tilted while the short sides of the track remained horizontal. The short side at the north was supported by two stationary wooden blocks (12.7 cm high) attached to a wooden base (76 × 51 cm). The short side at the south was supported by a hinged arm that allowed it to be raised and lowered. The number of rewards per lap was gradually reduced until the rat was receiving rewards only at the middle of each short side of the rectangular track. When the rat was performing this task reliably, the south side of the track was gradually raised in increments of 5° until the rat was running reliably at a track angle of 40−45°. The final stage of training was to acclimate the rat to run 10–15 laps on the flat track, followed by 10–15 laps at the 40−45° tilt angle, and then a final set of 10–15 laps on the flat track. Total training on the rectangle for these rats covered 17–23 sessions over 25–43 days; thus by the time recording commenced, the rats were highly familiar with the tilted track, having spent the majority of training time with some degree of tilt to the track (although they never experienced the track rotations described in the following text before the start of recording).

The rats of *group 2* had a richer set of training experiences prior to this experiment. The rats received ~40 days of presurgery training to shuttle for food on the alley track (described in the preceding text) prior to surgery. After surgical implant of recording electrodes and MFB stimulation electrodes (see following text), they were also trained to perform two more tasks for MFB stimulation: to run clockwise around the tilted rectangular track and to run clockwise around a small plus maze (20 cm per arm). Training sessions occurred

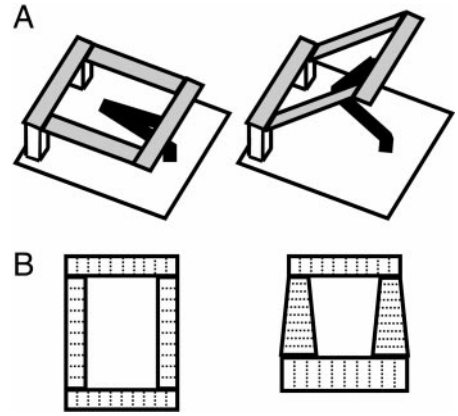

FIG. 1. Projection of maze surface onto overhead camera. *A*: the flat rectangle (*left*) could be tilted in increments of 5° to a maximum tilt angle of 45° (*right*). *B*: the surfaces of the flat and tilted rectangles were projected onto the overhead video camera for tracking of the animal's position. The track was converted into a 40-bin one-dimensional array, where each side of the track was partitioned into 10 equal bins, for the quantitative analysis of the similarity of place fields between the 2 conditions.

for ~30 min for 14 days. The animals then took part in two unrelated experiments involving foraging for food pellets in a cylindrical chamber (Knierim et al. 1998) or along a circular track. At the end of these experiments, they received 5 days of training on the rectangular track described in Fig. 1, including 2 days of acclimation to the interleaved flat/tilted/flat sessions. Three of the rats ran for MFB stimulation, whereas the fourth ran for food reward.

Surgery

Surgeries for these rats were performed according to NIH guidelines using techniques described in detail elsewhere (Gothard et al. 1996). Briefly, rats were anesthetized with pentobarbital sodium (Nembutal, 40 mg/kg ip), supplemented with methoxyflurane (Metofane) inhalation as necessary. Intramuscular penicillin (30,000 U of Bicillin in each hindlimb) was administered as a prophylactic antibiotic. A recording device ("Neuro-hyperdrive," Kopf Instruments, Tujunga, CA) that allowed the independent manipulation of 14 recording probes was implanted over the right hemisphere of each rat (3.8 mm P, 2.0 mm L from Bregma). Twelve of the probes were tetrodes made of four lengths of fine nichrome wire (13-μm diam; H. P. Reid, Palm Coast, FL) twisted together (McNaughton et al. 1983b; Recce and O'Keefe 1989; Wilson and McNaughton 1993). The other two were single-channel probes for recording electroencephalographic (EEG) and reference signals. In addition, each rat was implanted bilaterally with a bipolar stimulating electrode in each hemisphere aimed at the MFB (0.25 mm A, 1.9 mm L from Bregma, 8.5 mm V from brain surface, angled 19.5° posteriorly in the sagittal plane). The stimulating electrode was made of two lengths of 0.003-in diameter, Teflon-insulated, stainless steel wire (Medwire, Mount Vernon, NY) twisted together with ~1 mm spacing between the two electrode tips. After surgery, rats from all groups recovered from anesthesia in an incubator, and they were administered 26 mg of acetaminophen (Children's Tylenol) orally for analgesia. They also received 2.7 mg/ml acetaminophen in their drinking water for 1–3 days after surgery.

Recording electronics

After 2–7 days postsurgical recovery, the electrodes were advanced gradually over the course of many days. Neuronal signals were passed through a headstage of low-noise, unity gain, CMOS operational amplifiers (Neuralynx, Tucson, AZ) that could be attached to the hyperdrive. Also mounted on the front of the headstage was an array of infrared light-emitting diodes (LEDs), and attached to the back was an arm with a single LED on the end (16 cm from the front LEDs) to track the animal's position and head direction during the recording trials. The LED signals were sampled at 20 Hz (SA-2 Dragon Tracker, Boulder, CO) and stored on disk. Electrical signals were amplified between 2,500 and 10,000 times and filtered between 600 Hz and 6 kHz, before being digitized at 32 kHz and stored in a 25-MHz IBM 80486-based workstation. (See Gothard et al. 1996, for a description of the multiunit recording system.) Activity also was monitored through an audio monitor (Grass Instruments, West Warwick, Rhode Island).

Experimental protocol

Three experiments were performed on the rats. All eight rats were tested in *experiment 1*, whereas only the four rats from *group 2* were tested in *experiments 2* and *3*. For each experiment, the rat was brought into the recording room and was placed in a holding dish near the track. Tetrodes were monitored for units, and adjustments were made as necessary to optimize the signal quality. Because the implants on these rats were relatively old (2–3 mo since surgery), many tetrodes were no longer functional, but each rat had at least two functional tetrodes (range 2–9). Baseline data were recorded from each rat for 15–30 min while it sat quietly in the holding dish before the first experimental session and after the last session of the day. Comparison of the firing patterns in these baseline sessions helped in the determination of recording stability during the sessions.

EXPERIMENT 1. For *group 1*, the experiment took place in a corner alcove (3.2 × 2.25 m) of an open laboratory with many visual landmarks (e.g., curtains, bench tops, computers, lights, and electronic equipment). The rectangular track was located approximately 0.5 m from two walls of the alcove and ~2 m from the third wall. The recording system was located next to the track. For *group 2*, the experiment took place in a sound-attenuated recording room illuminated by four dim lights spaced symmetrically around the center of the room. A circle of black curtains that hung from the ceiling to the floor surrounded the perimeter of the room (3.5 m diam). The rectangle apparatus was centered in this curtained area on top of a wooden circular table (1.67 m diam). Nine large salient objects of various dimensions, placed on the floor (a roll of bubble wrap, a wooden triangular apparatus, a large square piece of plywood, a coat rack, a white card, and a large gray ring), attached to the curtains (a white card with black diagonal stripes), or suspended from the ceiling (a white, inverted cone and a striped post) provided distinct visual landmarks in all three dimensions. In addition, the door to the adjacent computer room, which housed the recording electronics, was left ajar, allowing the sounds of the recording equipment and audio monitor into the room. Both groups of rats were taken from the holding dish after the first baseline period and placed in the middle of the north side of the track, facing clockwise. The track used for recording was made of four rectangular pieces of plastic (51 × 8.5 cm) covered with gray foam rubber; it was slightly larger (51 × 68 cm) than that used during training. The rats were run for 10–15 laps around the track for food or MFB stimulation at the middle of each short side of the track with occasional extra rewards given at different locations on the track as necessary to promote good behavioral performance. The rats were placed back in the holding dish, and the south side of the track was raised such that the long sides were tilted at 40−45°; the north side of the track remained in the exact same position in three-dimensional space (see Fig. 2). (For 1 rat, the sides were tilted at only 30° on 1 day because the rat would not perform at the steeper angles; only 2 cells from that session contributed to the analysis and they did not differ from the overall pattern of results.) The rat was placed back on the track at the usual starting location and was run for 10–15 laps on the tilted track. It was removed from the track, the track was returned to its original flat configuration, and a final set of 10–15 laps was run. After a baseline period was recorded in the dish, the rat was returned to the colony room. This procedure was performed two to four times for the rats in *group 1* and only once for each rat in *group 2*.

EXPERIMENT 2. Only the four rats from *group 2* took place in this experiment, which was run in the sound-attenuated room described in the preceding text. After the initial baseline period, the rats ran 12–15 laps on the flat track, after which they were removed and the track was rotated 180° (see Fig. 5). The rats were placed on the north arm of the track (i.e., in the same location relative to the external room but 180° opposite relative to the track) and were run for another 12–15 laps. The track was rotated back to its original position, and the south side was raised to the 40° tilt position for another session. The rat was removed, and the tilted rectangle was rotated 180° such that the high side occupied the same location in *x-y* coordinates that had been occupied by the low side and vice-versa. The rat was placed on the track on the high side (i.e., in the same *x-y* coordinates relative to the room as before) and was run for 12–15 laps. Finally, the track was returned to the standard, flat configuration for a final session of 12–15 laps. After this session, a second baseline period ensued.

EXPERIMENT 3. The four rats from *group 2* took place in this experiment. The protocol was the same as for *experiment 2* except that the track was rotated only 90° in the second and fourth sessions rather than 180° (see Fig. 9). The track was rotated around the vertical line through the center of the rectangle such that none of the arms occu-

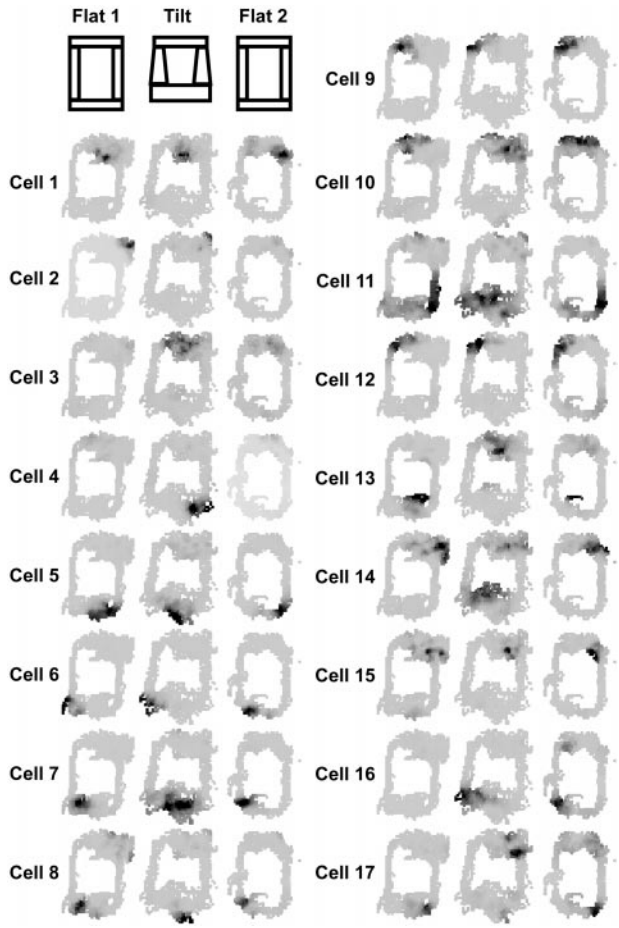

FIG. 2. Place fields from 17 simultaneously recorded cells from *rat 109* in *experiment 1*. Although some cells maintained similar firing fields between the flat and tilted track sessions (e.g., cells 6, 9, and 15), other cells changed their firing properties (e.g., cells 3, 4, and 11).

pied the exact same location in *x-y* coordinates in both the normal and 90° rotated conditions. In these sessions, the rat was placed on the track on the same side relative to the track (i.e., 90° rotated relative to the room) so as to avoid placing the rat on the tilted part of the track in the rotated/tilted session. For two of the rats, *sessions 1, 2,* and *5* were flat and *sessions 3* and *4* were tilted, whereas for the other two rats, *sessions 1, 2,* and *5* were tilted and *sessions 3* and *4* were flat.

Data analysis

OFF-LINE UNIT ISOLATION. The tetrode (McNaughton et al. 1983b; Recce and O'Keefe 1989; Wilson and McNaughton 1993) allows the isolation of single units based primarily on the relative amplitudes of signals recorded simultaneously at four slightly different locations. Additional waveform characteristics, such as spike width, also are used. Waveform characteristics were plotted as a scatter plot of one of the electrodes versus another. Individual units formed clusters of points on such scatter plots, and the boundaries of these plots were defined with the use of a custom interactive program (*Xclust*, M. Wilson) running on a Sun Sparcstation. The spike times of individual units then were combined with the position and direction information provided by the tracker to generate firing rate maps.

FIRING-RATE MAPS. Firing-rate maps were constructed by dividing the behavioral apparatus into 2.4-cm square bins for *group 1* and 1.5-cm square bins for *group 2*. The firing rate for each bin was calculated with an "adaptive binning" formula, which optimizes the tradeoff between sampling error and spatial resolution (Skaggs et al. 1996). The results were plotted as a grayscale rate map. The specificity of spatial tuning for each cell was calculated as the amount of information about the rat's position conveyed by the firing of a single spike from the cell (Skaggs et al. 1993). It was defined as

$$I = \sum p_j \frac{\lambda_j}{\lambda} \log_2 \frac{\lambda_j}{\lambda}$$

where, if the cylinder is divided into square bins, I is the information in bits per spike, p_j is the probability of the rat occupying bin j, λ_j is the mean firing rate for bin j, and λ is the mean firing rate for the whole cylinder. The information score is a good measure of whether a cell has a statistically significant spatial firing bias, and it correlates well with the experimenter's subjective judgments of the quality of a place field. Only cells that had a statistically significant ($P < 0.01$) information score >0.99 and that fired >50 spikes in at least one of the sessions on a given day were included in the analysis. In addition, cells that were judged to be of poor or unstable isolation quality were dropped from analysis. Judgments of unit isolation and stability were made independently of the spatial firing characteristics of the cells.

SPATIAL CORRELATION ANALYSIS. To quantify the similarity in place fields between different sessions, a spatial correlation score was measured for each cell. Each side of the track was divided into 10 bins, and a firing rate for each bin was calculated by dividing the number of spikes fired by the cell while the rat occupied that bin by the total amount of time spent by the rat in the bin, thus generating a one-dimensional, topologically circular array of 40 firing-rate bins (Fig. 1*B*). This analysis was performed on the raw data (rather than the adaptively binned data; see preceding text) and the bins were smoothed by recalculating the firing rate of each bin as the average of itself and its two adjacent bins. For each cell, the similarity in its place fields between two sessions was measured as the Pearson product-moment correlation between its firing-rate arrays in each session. For *experiments 2* and *3*, these correlations were performed in both a track-based reference frame and a room-based reference frame. Because the 40-bin firing rate arrays were anchored to the track itself (i.e., each bin was always at the same location on the track, regardless of the position or orientation of the track in the room), an analysis in the track-based reference frame entailed simply a correlation between corresponding bins. To analyze the results in a room-based reference frame, the data in one array were shifted (by 20 bins for the 180° rotations of *experiment 2* and by 10 bins for the 90° rotations of *experiment 3*) relative to the other array and the correlation was performed between the original array of the first session and the shifted array of the second session. A comparison of the correlation coefficients between the room- and track-based correlations enabled a determination of whether the place fields were bound more strongly to the external room cues or to the cues local to the track. Correlations between a particular pair of sessions for each cell were calculated only if the cell met the inclusion criteria for at least one session of the pair.

RESULTS

Experiment 1: effects of tilting the track

The effects of tilting the rectangular track were analyzed for 82 cells from the eight rats of *groups 1* and *2*. The set of analyzed cells includes only those cells that had a significant place field in at least one of the three sessions and does not include the many cells that were silent or fired weakly on the track. These cells were all recorded from the CA1 field of the hippocampus. This experiment was performed two to four times on each rat of *group 1*. To avoid possible double-counting, cells were included in the analysis for only 1 day of recordings for each tetrode, based on the first day that stable unit isolation was obtained for that tetrode. The analyzed cells

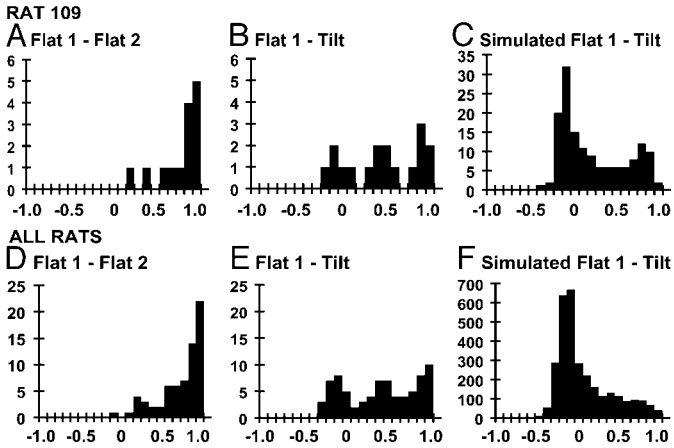

FIG. 3. *A*: for *rat 109*, most cells had a high correlation between the 1st and last flat rectangle sessions. *B*: the correlations were on average much lower between the 1st flat and the tilted sessions, although 1/3 of the cells had a very high correlation. This suggests that there was a partial remapping of the track when it was tilted. *C*: to assess whether the cells that maintained their fields did so by chance, each place field from the 1st flat session was correlated with the place fields of the tilted session for all other cells, thus producing a simulated distribution for complete remapping. A Mann-Whitney test demonstrated that this simulated distribution was significantly different from the experimental distribution ($P \leq 0.014$). *D–F*: the same analyses were performed on 82 cells pooled from all 8 rats. The examples from *rat 109* are representative of the test sample as a whole. The trimodal distributions in *B* and *E* result from some cells remapping completely (low correlation), other cells maintaining 1 subfield but in addition gaining or losing a subfield (medium correlation), and other cells maintaining the same place fields (high correlation).

came from no more than two data sets in each rat. The experiment was performed only once on the rats of *group 2*. The results from 17 of 18 simultaneously recorded cells from *rat 109* are shown in Fig. 2. When the flat track was tilted by ~45°, some cells maintained similar firing fields (e.g., cells 6, 9, and 15), whereas other cells changed their firing fields (e.g., cells 3, 4, and 11). A histogram of correlations between the spatial firing distributions on the flat rectangle versus the tilted rectangle of all cells for this recording session is shown in Fig. 3*B*. The correlations were significantly smaller than the correlations between the first and second flat sessions (Fig. 3*A*; Mann-Whitney *U* test $P \leq 0.024$), although ~1/3 of the cells had a high correlation between the flat and tilted sessions. This distribution suggests that the representation of the track was partially remapped as a result of the 45° tilt, as many cells changed their firing fields on the track, whereas other cells maintained the same field. It is possible, however, that the tilt manipulation caused the hippocampus to remap the track completely and that those cells that maintained a high correlation between the tilted and flat rectangles did so as a result of chance. That is, two hippocampal representations that are completely independent and orthogonal will contain purely by chance a certain proportion of cells with similar place fields in each representation. The expected distribution of such random place field duplications is an unknown function of place field size, shape, and the probability of a cell having a place field in a given environment and/or behavioral task. To estimate this distribution, the spatial firing pattern of each place cell on the flat track was correlated with the place fields of all other cells in the sample on the tilted track. This simulation gives an estimate of what the distribution of correlations would be if the two representations were completely independent. The real distribution of place field correlations was then compared with this simulated distribution to test for the statistical significance of any difference.

Figure 3*C* shows the expected distribution of correlations if the firing fields between the two sessions were completely uncorrelated, and the actual distribution shown in Fig. 3*B* is significantly different from this predicted distribution (Mann-Whitney, $P \leq 0.014$). These results indicate that some place cells maintained their firing fields relative to the track in the tilted and flat tracks, whereas other cells changed their fields. The results from this rat were representative of the population as a whole as the same analyses performed on the 82 cells pooled from all eight rats showed an identical pattern of results (Fig. 3, *D–F*). It is not known whether all eight rats demonstrated partial remapping as there were usually not enough cells recorded in each data set to generate the statistical power to test this question. For the two rats with the greatest number of active place cells recorded in a single session (*rat 109* with 18 cells, described in the preceding text, and *rat 117* with 21 cells), the distributions of correlations between the flat and tilted tracks were each significantly different from those produced by the simulation of completely independent remapping ($P < 0.02$). Thus the partial remapping effect can be seen at the level of individual data sets as well as at the population level (see also Skaggs and McNaughton 1998).

One interpretation of this partial remapping might be that it reflects a three-dimensional tuning profiles of place cells. If place fields are three dimensional, one would predict that the cells that were highly correlated between the tilted and flat rectangles would have fields at the north side of the track (which did not change location in the *z* axis when the flat track was tilted) and that the cells that were uncorrelated between the two tracks would have fields at the south side of the track (the raised side). There was no significant difference, however, between the correlations between the flat and tilted rectangles for those cells that had place fields on the south half (Fig. 4*A*) or the north half (Fig. 4*B*) of the flat rectangle (Mann-Whitney, $P \leq 0.26$). In general, cells on the south half of the track were just as likely to maintain the same firing field on the track as were cells on the north half. Similarly, cells on the north half were as likely to change their firing properties as were cells on the south half. For example, cells 3 and 13 of Fig. 2 had place fields on the north section of the track only during the tilted session (although, interestingly, they both maintained weak remnants of the new field in the *flat 2* session), whereas cell 6

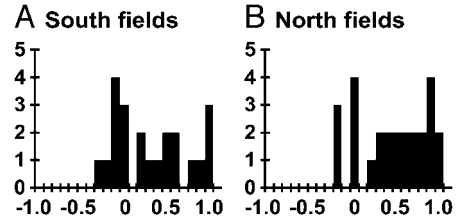

FIG. 4. The partial remapping was not the result of cells on the north (bottom) part of the track maintaining their fields while cells on the south (raised) half changed their fields. Cells on the south half of the track (*A*) were no more likely to change their firing fields than cells on the north half (*B*; Mann-Whitney, $P \leq 0.26$). For example, cell 3 (Fig. 2) had a field on the north side during the tilted session but was silent on the 1st flat session, whereas cell 6 had a field on the south side in all 3 sessions. In addition, the distribution of cells that had fields on the middle of the tilted sides of the track was not different from the fields on the north or south arms (data not shown).

had an identical place field at the south side of the track in all three sessions. It is thus more likely that the change in place fields reflects a remapping of the rectangular surface rather than an inherent three-dimensional structure to place fields.

When the flat track was tilted to the 45° angle, the raised side of the track was no longer in exactly the same *x-y* coordinates in the frame of reference of the room; rather, the south side was moved closer to the north side (although in the track frame of reference, of course, the 2 sides were as far apart as when the track was flat). Another possible interpretation of the data, therefore, is that the correlations between fields in the flat and tilted tracks were reduced because the place fields were bound to the precise *x-y* coordinate frame of the room rather than to the local coordinate frame of the track. It was not possible to answer this question quantitatively, however, due to the small number of cells that did not remap on the long sides of the track. Nonetheless, visual inspection of the data suggests that such an interpretation would not adequately describe the results.

Stackman et al. (2000) demonstrated that 11/13 head direction cells increased their peak firing rates when the animal moved around an elevated annulus compared with when the animal moved around the floor of an apparatus. To determine if place cells changed firing similarly in response to the elevation of the track, the peak firing rates of the nine cells with similar place fields on the south (raised) side of the track on both the *flat 1* and *tilt* sessions were analyzed. Of these cells, four increased their peak firing rate (by a factor of 1.23–6.33) when the south side was raised and five decreased their peak firing rate (by a factor of 1.26–10.2). Thus no consistent effect of raising the platform on the peak firing rates of individual place fields was observed.

Experiment 2: 180° rotations

Many previous studies have indicated that place cells tend to be more strongly influenced by distal cues than by intramaze cues (Cressant et al. 1997; O'Keefe and Conway 1978; O'Keefe and Speakman 1987; but see Shapiro et al. 1997). The four rats of *group 2* were tested under conditions in which the flat and tilted rectangles were rotated 180° to test whether the three-dimensional orientation of the track would affect how strongly the fields were bound to the distal cues.

Figure 5 shows the results from 12 of 23 neurons recorded from *rat 109* during this set of manipulations. When the flat rectangle was rotated 180° between sessions, most cells had similar fields bound to the room cues, corresponding to previous reports, even though the track had salient local cues that broke the symmetry (the most prominent being the support-arm that raised the track to the tilted positions, which the rats often investigated during the sessions). When the tilted rectangle was rotated, the results were very different. A number of cells maintained their place fields relative to the room cues, ignoring the *z* axis (Fig. 5*A*). For example, cell 1 fired on the southeast corner of the track regardless of whether this was the raised corner or the lower corner in the rotated condition. Other cells appeared to maintain the same fields relative to a track-based coordinate frame, in that the fields rotated 180° with the track (Fig. 5*B*). For most cells, the place fields changed unpredictably between the two conditions (Fig. 5*C*). Note that, similar to

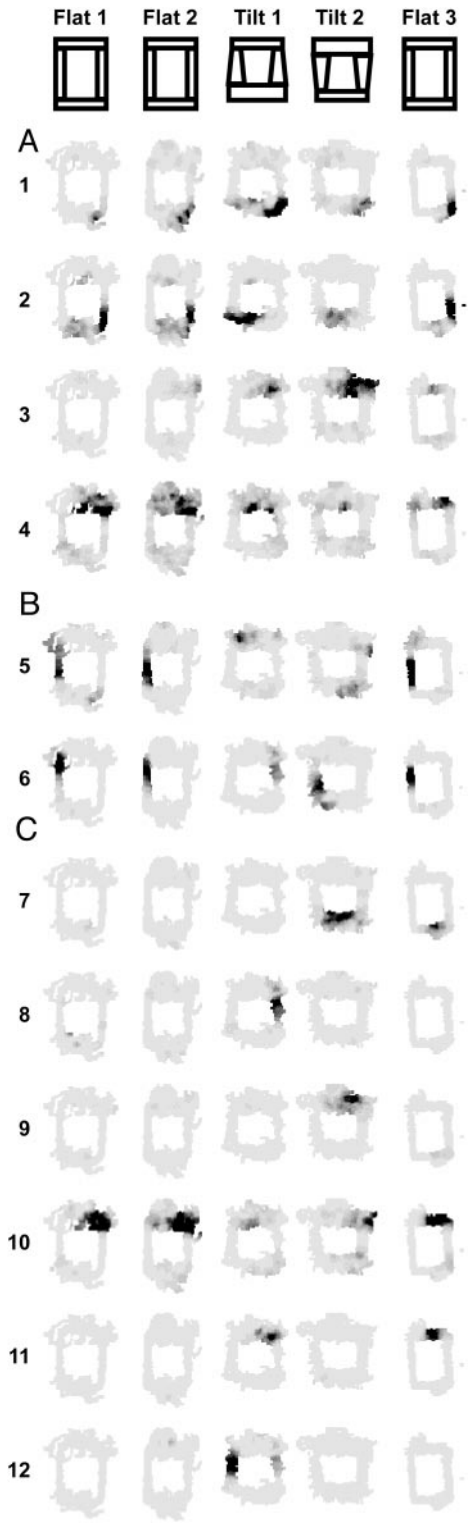

FIG. 5. Place fields from 12 of the 23 simultaneously recorded cells from *rat 109* in *experiment 2*. Almost all cells maintained the same field in the room-based reference frame when the flat rectangle was rotated. When the tilted rectangle was rotated, some cells remained bound to the *x-y* room coordinates (*A*), other cells were apparently bound to the track coordinate frame (*B*), and other cells changed their firing fields (*C*). Subsequent analysis suggested that the cells in *B* maintained the same place fields relative to the track purely by chance. Not shown are cells that had fields on the flat rectangle but that were silent on the tilted rectangle.

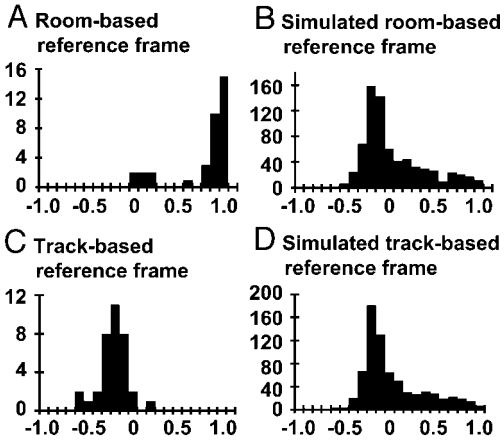

FIG. 6. Correlations between the *flat 1* and *flat 2* sessions in room-based coordinates (*A*) and track-based coordinates (*C*) for all 4 rats. The corresponding simulated distributions for complete remapping are shown in *B* and *D*. The experimental distributions for both room- and track-based coordinates were significantly different from the simulated distributions (Mann-Whitney, $P < 0.000001$).

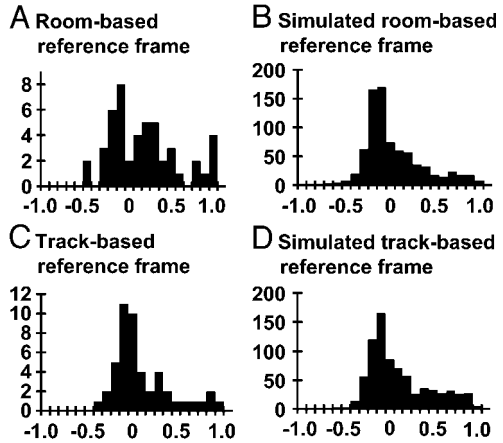

FIG. 7. Correlations between the *tilt 1* and *tilt 2* sessions in room-based coordinates (*A*) and track-based coordinates (*C*) for all 4 rats. The corresponding simulated distributions for complete remapping are shown in *B* and *D*. The experimental distribution for room-based coordinates was significantly different from the simulated distribution (Mann-Whitney, $P \leq 0.026$). The experimental distribution for track-based coordinates did not differ from the simulated distribution ($P \leq 0.77$), suggesting that the cells in Fig. 5*B* appeared to rotate with the track by chance.

experiment 1, some cells maintained vestiges of the remapped fields from the tilted track when the rat was returned to the flat track for the final session (see also Muller and Kubie 1987; Sharp et al. 1990). This was not due to poor isolation of the units as care was taken to exclude those cells that were poorly isolated or had unstable spike waveforms, and such effects were seen in some of the most well-isolated cells in the sample. Thus the changes in the place fields caused by the partial remapping of the tilted track caused changes to the subsequent representation of the flat track, although the representations of the *flat 1* and *flat 3* tracks were still highly correlated [mean correlation *flat 1-flat 2* = 0.74 ± 0.06 (SE); *flat 1-flat 3* = 0.62 ± 0.06; Mann-Whitney U, $P \leq 0.051$].

Figure 6 shows the sample distributions (*left*) and the simulated distributions (*right*) for the correlations between the first and second flat rectangle sessions in the room-based coordinate frame (Fig. 6, *A* and *B*) and in the track-based coordinate frame (Fig. 6, *C* and *D*). The sample distributions for both flat rectangles were highly significantly different from the simulated population distributions (Mann-Whitney, $P < 0.000001$ for both). Because the great majority of cells maintained the same field relative to the distal laboratory cues, almost all correlations were high in the room-based comparison and uniformly low in the track-based comparison. Figure 7 shows the same analysis for the tilted rectangle. For the room-based correlations (Fig. 7, *A* and *B*), the sample distribution was significantly different from the simulated population (Mann-Whitney, $P \leq 0.026$). Although most cells in the sample had low correlations between the tilted rectangle and the 180° rotated tilted rectangle, there were more cells with high correlations than expected by chance if the two maps were completely independent. Thus it is likely that there was a partial remapping of the tilted rectangle in the room-based coordinate frame. There was no difference between the sample distribution and the simulated population distribution for the track-based correlations (Fig. 7, *C* and *D*; Mann-Whitney, $P \leq 0.77$), indicating that the number of cells with apparent track-based firing (e.g., Fig. 5*B*) did not exceed that predicted by completely random remapping.

Because the preceding analysis was performed with the combined cells from four rats (1 recording sequence per rat), it is possible that no individual rat created a partially independent map between the two tilted rectangles; rather, some rats might have remapped the tilted rectangle completely while other rats maintained the same map in room coordinates. To test for partial remapping in individual rats, the same analysis was performed on the cells from each data set. No rat demonstrated a statistically significant difference from the expected distribution for complete remapping for either the room-based or the track-based correlations for the tilted rectangle (Fig. 8). It is clear from Fig. 8, however, that all of the rats displayed remapping in that the majority of cells from each data set had low correlations. Because the larger, pooled sample was significantly different from an independent remapping, partial remapping must have occurred in at least one of the four rats

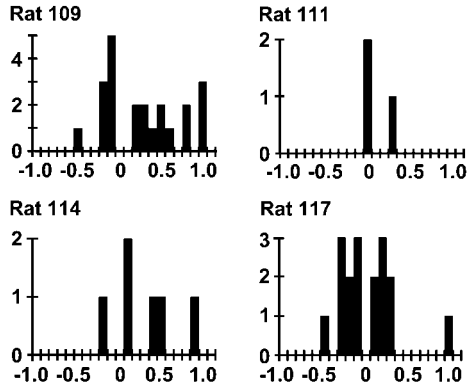

FIG. 8. Correlations between the *tilt 1* and *tilt 2* sessions in room-based coordinates for individual data sets from each rat. Although none of these data sets were statistically different from the simulated distributions (based on the same individual data sets for each rat), all rats show evidence of remapping. Because the combined results from all 4 rats were significantly different from a simulated distribution of complete remapping (Fig. 7, *A* and *B*), ≥1 of the rats must have undergone true partial remapping in an individual data set. The results suggest that *rats 109* and *114* were likely to have remapped partially, whereas *rats 111* and *117* may have undergone complete remapping.

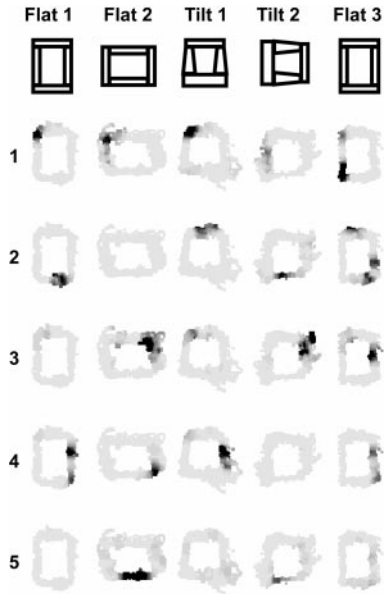

FIG. 9. Place fields from 5 of the 16 cells from *rat 111* in *experiment 3*. When the flat rectangle was rotated 90°, some cells maintained the same firing field in room-based coordinates (cell 1), whereas other cells changed their firing properties (cells 2, 3, 4, 5). When the tilted rectangle was rotated, some cells apparently maintained their fields in the track-based coordinate frame (cell 3), whereas other cells changed their firing properties (cells 1, 2, 4, 5).

(most likely *rats 109* and *114*), and the lack of significance in the individual data sets was most likely due to the small sample size of each individual data set.

Experiment 3: 90° rotations

Figure 9 shows the firing patterns of 5 of 16 cells from *rat 111* when the flat and tilted rectangles were rotated 90°. When the flat rectangle was rotated, most cells changed their firing properties by either becoming silent, gaining a field, or changing a field (e.g., cells 2–5). Some cells, however, maintained the same location in the room-based coordinate frame (e.g., cell 1 and 1 of the fields of cell 4); that is, cells that fired on the long arm of the track in the standard condition fired in approximately the same location on the short arm in the rotated condition (note that, because of the rotation of the anisotropic rectangular track, these place fields were not in precisely the same location in the room-based coordinate frame). When the tilted track was rotated, some cells changed their firing fields unpredictably (e.g., cells 1, 2, 4, and 5), whereas other cells maintained the same field either in the track-based reference frame (e.g., cell 3) or in the room-based reference frame (no examples from this particular data set). To test for the significance of those cells that maintained their firing fields, the same analysis of partial remapping that was performed on the 180° rotation results was performed on these data (Figs. 10 and 11). Notice that the effects of the 90° rotation of the flat rectangle (Fig. 10) were rather different from those of the 180° rotation of the flat rectangle (Fig. 6). The correlations between the standard and the 90° rotated flat rectangles were on average low in both room- and track-based coordinates. Thus the 90° rotation, which approximately swapped the locations of the short and long sides of the rectangle, caused a remapping of the rectangle. Figure 10, *A* and *B*, shows that the remapping was

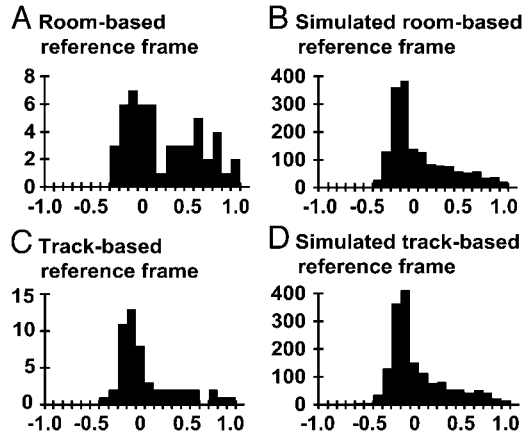

FIG. 10. Correlations between the *flat 1* and *flat 2* sessions in room-based coordinates (*A*) and track-based coordinates (*C*) for all 4 rats. The corresponding simulated distributions for complete remapping are shown in *B* and *D*. The experimental distribution for room-based coordinates was significantly different from the simulated distribution (Mann-Whitney, $P < 0.001$). The experimental distribution for track-based coordinates did not differ from the simulated distribution ($P \leq 0.28$).

partial in the room-based reference frame as more cells have a high correlation in this frame than expected by chance for a full remapping. For the track-based reference frame, the distribution of correlations was not different from the simulated distribution, suggesting that any cell that apparently maintained the same field in track-based coordinates did so by chance. For the tilted rectangle, there was a trend toward partial remapping in the track-based reference frame (Fig. 11, *C* and *D*), although this missed statistical significance ($P \leq 0.07$). There was no evidence for partial remapping in the room-based reference frame (Fig. 11, *A* and *B*). Overall it appears that the hippocampus tended to partially remap the flat rectangle when it was rotated 90° with a small but significant fraction of the cells maintaining their fields in approximately room-based coordinates. (Note that in the 90°-rotated sessions, the starting point of the rat was on the same location in the track reference frame but 90° rotated in the room reference frame in contrast to the

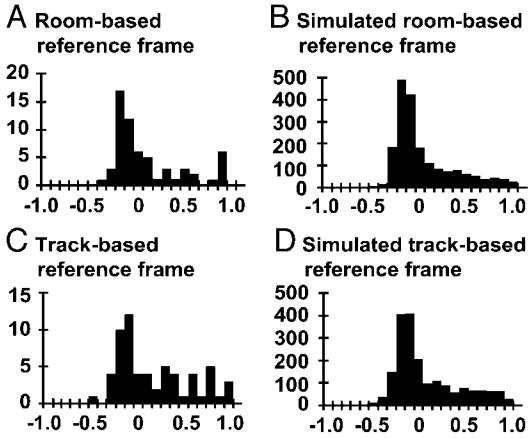

FIG. 11. Correlations between the *tilt 1* and *tilt 2* sessions in room-based coordinates (*A*) and track-based coordinates (*C*) for the same cells as in Fig. 10. The corresponding simulated distributions for complete remapping are shown in *B* and *D*. The experimental distribution for room-based coordinates did not differ from the simulated distribution (Mann-Whitney, $P \leq 0.36$). The difference between the experimental distribution for track-based coordinates and the simulated distribution approached statistical significance ($P \leq 0.07$).

180° rotation experiment; see METHODS.) Additionally, there was another partial remapping of these representations when the normal and 90°-rotated rectangles were tilted (as in *experiment 1*), as many cells maintained these fields on the track, whereas other cells changed their spatial tuning properties. For example, cell 1 of Fig. 9 had the same field in both *flat 1* and *tilt 1*, whereas cell 2 had different fields. Similarly, cell 3 had the same field in both *flat 2* and *tilt 2*, whereas cell 2 had different fields.

DISCUSSION

Place cells are sensitive to the three-dimensional geometry of surfaces

HD cells reflect head direction in the yaw axis and are insensitive to changes in direction in the pitch and roll axes (Stackman et al. 2000; Taube et al. 1990b). The present study was designed to test whether the spatial tuning of place cells extended into the *z* axis or whether place cells (like HD cells) were insensitive to a change in position in this axis. A recent model (Samsonovich and McNaughton 1997; see also Zhang 1996) proposed that self-motion information about speed and distance traveled, coupled with heading direction from HD cells, were the primary inputs that updated place cells; external landmarks acquired, through learning, a role in correcting for the cumulative error that is inherent in such a system. Because the HD cells cannot distinguish between forward motion in the horizontal plane from forward motion in an oblique plane, it was possible that place cells would remain bound to the surface of the track when it was tilted 45°. Alternatively, because the three-dimensional manipulations of the track placed the rat in different locations in three-dimensional space, it was possible that the concomitant changes in the sensory input available at each location on the track would cause the cells to change firing in predictable ways. Because of the partial remapping phenomenon that occurred, however, the results do not fit cleanly with either possibility. Although this study demonstrates for the first time that the representation of an environment in area CA1 is sensitive to three-dimensional manipulations of the recording track (unlike HD cells) (Stackman et al. 2000), the results provide no evidence that individual place fields are inherently three dimensional as the changes in the place fields were not consistent with any of the predictions based on a three-dimensional model of individual place fields. Nonetheless the partial remapping makes it unwarranted to conclude that the place fields on the track were two dimensional. Rather the environmental manipulation of tilting the track may have caused changes to the input into the hippocampus (e.g., changes in the sensory input, in the rat's behavior, or in internal states such as stress level), and attractor dynamics of the hippocampal network may have caused the cells to respond to the altered input in a complex, nonlinear fashion.

It is possible that these cells would have demonstrated the predicted effects of a two- or three-dimensional model of individual place fields had the remapping phenomenon not occurred. Although changes in certain local cues have been demonstrated to cause remapping (Shapiro et al. 1997; Tanila et al. 1997), not all environmental changes do so, and it was not obvious a priori whether the three-dimensional manipulations of the track would provoke the remapping phenomenon. A convincing answer to the question may require a well-explored environment where the animal can move in a three-dimensional volume without the need for experimental manipulation (e.g., a jungle-gym apparatus) (Grobety and Schenk 1992). Logistical concerns, such as the tangling of a recording cable, would make such an experiment difficult to execute, although the development of multi-channel telemetry systems would make this feasible (Hawley et al. 1999). Other situations, in which an animal moves along different surfaces in the *z* axis, might be subject to ambiguous interpretations similar to the present study. For example, the hippocampus may encode each plane of a three-dimensional "stacked" maze as independent two-dimensional surfaces; thus a cell that fires on a single plane would not necessarily demonstrate that the individual place fields are three dimensional. It appears that a number of experiments producing converging evidence will be required to answer this question satisfactorily. Nevertheless although our initial attempt to address this question is incomplete, the results demonstrate a sensitivity to three-dimensional manipulations at the level of population representations, and they reveal a number of important observations on the nature of hippocampal representations in terms of the relative influences of local versus distal cues and the remapping phenomenon.

Local cues versus distal landmarks

Just as the Morris water maze task demonstrated that animals can solve spatial tasks without the use of local markers (Morris et al. 1982), most early experiments on place cells reinforced the notion of the predominance of distal landmarks over local surface cues. In these experiments, if the set of distal landmarks and the recording apparatus were rotated relative to each other, the place fields of hippocampal neurons would usually remain bound to the distal landmarks (Kubie and Ranck 1983; O'Keefe 1976; O'Keefe and Speakman 1987). Similarly, rotation of a salient cue card on the wall of a recording apparatus controlled place field location preferentially over local cues on the floor (Muller and Kubie 1987). Although the cue card can be considered a local apparatus cue, its salience in the otherwise sensory-poor environment and its location at the edge of the apparatus may have endowed it with strong control over the place cells. Support for the influence of both of these factors comes from a number of studies. In the absence of visual input, subtle surface cues (such as olfactory markings) are the most salient cues available, and rotation of the apparatus will often cause the fields to rotate (Hill and Best 1981; see also Young et al. 1994). It is likely that these local cues play a role in the ability of place cells (Markus et al. 1994; Quirk et al. 1990) and HD cells (Knierim et al. 1998; Taube et al. 1990b) to maintain stable place fields/direction preferences for many minutes in complete darkness. The importance of the controlling cue being at the edge of the apparatus was demonstrated by Cressant et al. (1997), who showed that rotation of a set of objects located near the middle of a recording apparatus had little effect on the firing locations of place cells, whereas rotation of the same objects located at the walls of the apparatus caused the place fields to rotate by the same amount.

An important set of studies by Shapiro, Tanila, and Eichenbaum (Shapiro et al. 1997; Tanila et al. 1997) demonstrated recently that local surface cues can have a much greater influence over place cells than previously appreciated even in the

presence of salient distal landmarks. Distinctive textures and odors were placed on each arm of a four-arm maze in an attempt to match the salience of the local cues to that of the distal cues. Under these conditions, when the local cues were rotated relative to the distal cues, some cells followed the local cues, some followed the distal cues, and some completely changed their firing properties (remapped). The present results are very similar, showing that the three-dimensional orientation of a behavioral apparatus is a salient local cue that is strong enough to have a profound influence over place cells in the presence of salient distal cues. Regardless of whether the difference between rotations of the flat and tilted rectangles (Figs. 6 and 7) is due to changes in the visual input caused by the three-dimensional reorientation of the track, changes in behavior (e.g., different locomotor patterns), or other factors, these results demonstrate clearly how a change in the local cue environment can affect place cells.

One difference between the present study and that of Tanila et al. (1997) relates to the question of whether the intramaze cues can actually control the firing of one subset of place cells at the same time that another subset is controlled by the distal cues. Although a casual visual inspection of the place fields in the present study suggested that this dual control occurred, statistical analyses could not rule out the possibility that the apparent examples of track-based control of the fields were the results of random chance. In addition, in the one experiment in which the binding of the place fields to track-based cues approached significance (the 90° rotation of the tilted track), the number of cells bound to the room cues was not significant (Fig. 11). Two data sets from young adult rats of the Tanila et al. (1997) study had fields that rotated with the local cues while simultaneously recorded fields rotated with the distal cues. Because of this low number, it is not known whether the difference between the two studies is due to chance duplication of apparently local-cue-bound fields in the Tanila et al. study or to a lack of statistical power to reveal small but significant binding to local cues in the present study. This issue has important implications as to whether hippocampus circuitry displays attractor dynamics that would tend to suppress such split-control of the place cells. In support of the conclusions of Tanila et al. (1997), a greater number of their data sets (7) contained place fields that did not change their spatial locations after the double rotation of the local and distal cues (i.e., they were bound either to uncontrolled background cues or to idiothetic cues) while simultaneously recorded fields were controlled by local or distal cues. This increased number supports the possibility that this dual control can occur at a level greater than expected by chance, but it is important for future studies to test statistically whether this dual control occurs.

It is also interesting that a number of the cells that appeared bound to the room-based reference frame in the present study (e.g., Fig. 5, cell 1) fired in slightly different locations in *x-y* room coordinates because of the varying two- and three-dimensional orientations of the track. This result, similar to the hysteresis of place fields demonstrated by Rettenmaier et al. (1999) on a three-arm maze, suggests that the distal cues may be involved in setting the global orientation of the hippocampal representation of an environment, but that salient local cues, idiothetic cues, or behavioral variables may be equally or more important for determining the precise location of individual place fields (O'Keefe and Nadel 1978).

Local cues, distal cues, and partial remapping

Early studies of the hippocampal remapping phenomenon were based on recording sessions in which typically one neuron was recorded at a time, thus making it impossible to determine whether remapping was an "all-or-none" phenomenon or whether it could be partial (e.g., Muller and Kubie 1987; see also following text). Based on recordings over multiple sessions, Bostock et al. (1991) suggested that the process was always all or none. Subsequent studies suggested that remapping may be partial (Knierim et al. 1995; Markus et al. 1995; Tanila et al. 1997; see also O'Keefe and Speakman 1987), but the limited number of simultaneously recorded cells made this suggestion difficult to test statistically. The simultaneous recording in one study of head direction cells that remained bound to the stable place fields, while other place cells remapped, suggested strongly that remapping could be partial (Knierim et al. 1995), but this was not verified statistically. By recording many place cells simultaneously and comparing the results of individual recording sessions with a simulated distribution of complete remapping, Skaggs and McNaughton (1998) proved that remapping can be partial. The results of the present experiment provide another strong demonstration of partial remapping.

Muller and Kubie (1987) described a phenomenon in which placing a barrier in the middle of a place field caused the field to be altered, whereas placing the barrier in another part of the environment had no effect on the field. Muller et al. (1996) later referred to this effect as partial remapping. This result, in which a local perturbation of the environment apparently affected only place fields in that local area, is similar in flavor to the description of "misplace" cells by O'Keefe (1976). The partial remapping described in the present and previous studies (Knierim et al. 1995; Skaggs and McNaughton 1998; Tanila et al. 1997) is more global in nature as the remapping occurs in all parts of the environment. It may be useful to distinguish these types of remapping by the use of the term *local remapping* to refer to effects similar to that seen by Muller and Kubie and the term *partial remapping* to refer to the graded nature of incomplete global remapping demonstrated here.

The causes and functional significance of hippocampal remapping are not known. Remapping may be the result of an orthogonalization operation on the input into the hippocampus, such that the subsequent representations stored in the CA3 and CA1 fields are less subject to errors in storage or retrieval (Marr 1971; McNaughton 1989; Rolls 1989). The hypothesized pattern completion functions of the CA3 network cause this orthogonalization function to be sigmoidal (McClelland and Goddard 1996). That is, when two input patterns differ only slightly, the CA3 network will tend to generalize the inputs and make the output patterns more similar than the inputs. As the input patterns become more dissimilar, however, the outputs are made even more independent (orthogonal) than the inputs. Partial remapping may reflect the rising portion of the sigmoidal curve between input pattern overlap and output pattern overlap (McClelland and Goddard 1996) where a moderate amount of input pattern similarity causes the output patterns to be only partially orthogonal.

Another view of partial remapping, not necessarily inconsistent with the preceding view, is that partial remapping reflects the differential sensitivity of place cells to different

subsets of cues in the environment. In this view, cells that do not remap but instead are bound to one set of cues (e.g., distal cues) are interpreted as encoding those cues, whereas cells that remap are interpreted as having encoded a unique combination of cues that has been disrupted by the manipulation that provoked the remapping. Shapiro et al. (1997) have suggested further that a change in control from distal to local cues may reflect a dynamic switching of the inputs into the hippocampus as one set of inputs actively inhibits the other set in a winner-take-all type of mechanism.

Because the strongest input onto individual place cells most likely comes from many other place cells, rather than from any cell that directly represents sensory input, another possibility is that place cells are always influenced by some combination of multiple cues, distal, local, or internal, to the animal. These inputs are presumably modifiable and differ in their relative strengths, but changes in the control of place cells by one type of cue over another may reflect the nonlinear dynamics of an attractor circuitry within the hippocampus itself rather than a modulation of the inputs. When different sets of inputs are manipulated, the strong connections among the place cells in an assembly can cause them to be controlled as a whole by whichever set of cues is strongest at the moment without any change to the strength of the inputs themselves. Thus in a stable environment, both distal and local cues may converge on a given place cell, but the distal cues may have a stronger overall input to the network. When the distal and local cues are then put in conflict with each other in a probe test, the attractor circuitry may cause the cells to follow the stronger distal cues; this does not indicate, however, that the cells were not encoding the local cues as well in the initial stable configuration. Such a probe test can change the synaptic weights of the network, however, which may cause the system to behave differently when the probe test is repeated at a later time. For example, the probe test may cause changes in the synaptic matrix such that on the next probe test, the attractor circuitry causes the cell to follow the local cues, even though in the standard configuration the cell "encoded" both local and distal cues. Remapping may occur when the synaptic changes induced by probe tests become prevalent enough to alter the attractor basins in the network, which may explain the observations that remapping often becomes more likely after many repetitions of a given probe test (Shapiro et al. 1997; Sharp et al. 1995). Because it is easier to manipulate experimentally the representations of the inputs (by manipulating the cues themselves) than the internal dynamics of the network, it will require a combination of increasingly accurate models of hippocampal function and network architecture, together with a major increase in our currently scant understanding of the properties of the inputs into the hippocampus, to resolve these important issues underlying the nature of information processing and representations in the hippocampus.

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