

Interactions between Location and Task Affect the Spatial and Directional Firing of Hippocampal Neurons

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When rats forage for randomly dispersed food in a high walled cylinder the firing of their hippocampal “place” cells exhibits little dependence on the direction faced by the rat. On radial arm mazes and similar tasks, place cells are strongly directionally selective within their fields. These tasks differ in several respects, including the visual environment, configuration of the traversable space, motor behavior (e.g., linear and angular velocities), and behavioral context (e.g., presence of specific, consistent goal locations within the environment). The contributions of these factors to spatial and directional tuning of hippocampal neurons was systematically examined in rats performing several tasks in either an enriched or a sparse visual environment, and on different apparatus.

Place fields were more spatially and directionally selective on a radial maze than on an open, circular platform, regardless of the visual environment. On the platform, fields were more directional when the rat searched for food at fixed locations, in a stereotypic and directed manner, than when the food was scattered randomly. Thus, it seems that place fields are more directional when the animal is planning or following a route between points of special significance. This might be related to the spatial focus of the rat’s attention (e.g., a particular reference point). Changing the behavioral task was also accompanied by a change in firing location in about one-third of the cells. Thus, hippocampal neuronal activity appears to encode a complex interaction between locations, their significance and the behaviors the rat is called upon to execute.

[Key words: place cells, place fields, spatial orientation, directionality, navigation, cognitive map]

Numerous lesion experiments in rodents have implicated the hippocampal formation in spatial learning (e.g., O’Keefe and Nadel, 1978; Sutherland et al., 1982; Barnes, 1988; Nadel, 1991; Jarrard, 1993). Perhaps the strongest evidence for a link between hippocampal function and spatial encoding, however, comes

from single unit recordings. In freely moving rats, hippocampal complex-spike (CS) cells fire selectively when the animal occupies specific locations (“place fields”; O’Keefe and Dostrovsky, 1971). These “place cells” show strong directional tuning within their place fields when recorded from while the rat traverses a radial arm maze (McNaughton et al., 1983a; O’Keefe and Recce 1993) and in other linearly organized tasks (Breese et al., 1989; Wiener et al., 1989), but little or no directionality during food foraging in a high walled cylinder (Muller et al., 1987, 1994; Leonard, 1990). Thus, in some contexts, a cell may fire robustly as an animal traverses the place field in one direction, but be virtually silent when the animal traverses the same location in the other direction. In other contexts, firing may be independent of head orientation or direction of motion. Discerning the source of the difference in place cell activity in these various experiments is important to understanding the invariants represented by hippocampal neuronal activity. One of the difficulties in understanding the sources of these differences is that apparent directional tuning can sometimes emerge spuriously because of differences in the animals’ behavior. For example, differences in running velocity in each direction could lead to apparent directionality, because running speed affects firing rate (McNaughton et al., 1983a; Leonard et al., 1987; Wiener et al., 1989). Similarly the region of the place field visited may differ when the animal passes through the field in each direction, giving the appearance of directionality if, in one direction, the rat passes through the center of the field and the cell fires robustly, whereas in the other direction, the rat passes only through the edge of the field (Muller et al., 1994). Given that directional tuning exists, it could be related to some sensory features of the environment, to the animal’s past experience (Sharp, 1991), or to the constraints imposed by the behavioral task or the structure of the different apparatus.

The task demands and the physical properties of the cylinder and radial maze differ in a number of potentially important ways. First, the visual environment in the cylinder is restricted to proximal cues on the wall, typically a single white card subtending ~90° of arc, whereas the radial maze is open and usually placed in a room with multiple distal cues. Second, in the cylinder, the rat is trained to traverse the entire floor surface in search of randomly scattered food, whereas on the radial maze the rat is trained to find food at predictable, discrete locations at the maze arm ends, and the occupancy by the rat of a particular location is typically associated with an orchestrated sequence of specific behaviors. Third, in the walled cylinder there are few physical constraints on the animal’s motion within the

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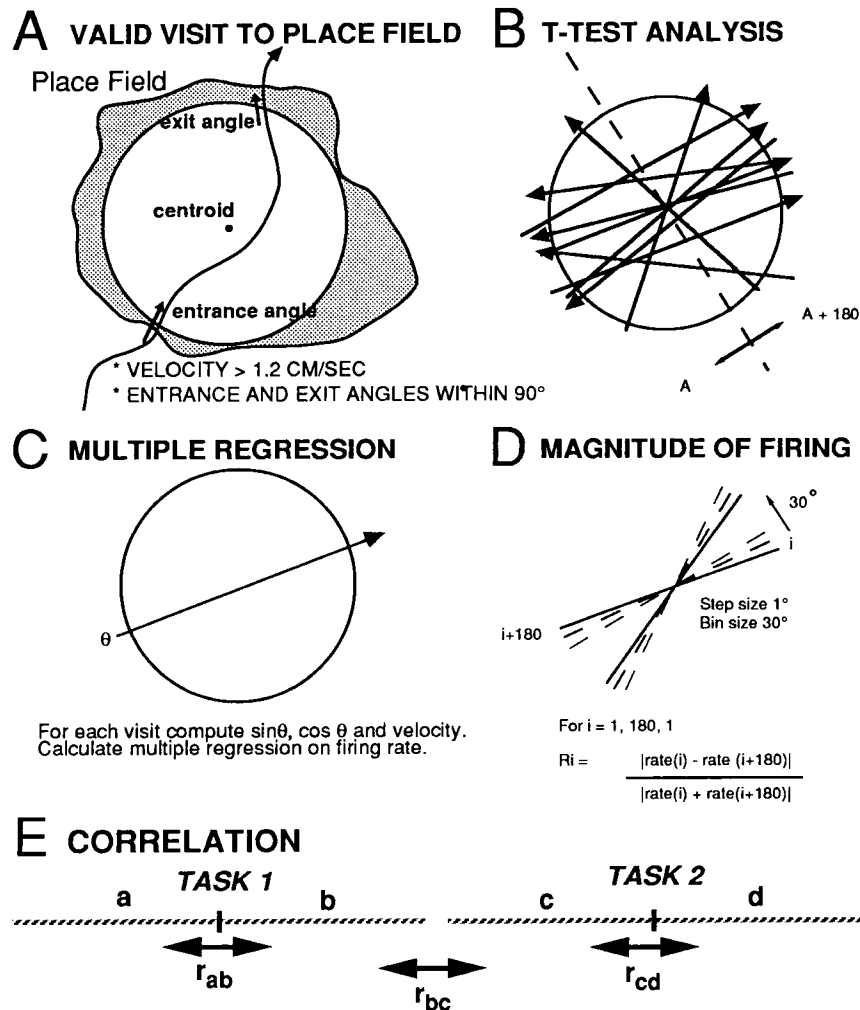


Figure 1. *A* A place field was defined as an area of adjacent locations with a firing rate greater than 2 SDs above the mean firing rate of the cell. From the centroid of the place field (hatched region), the largest circle that was entirely within the boundaries of the place field was found (white region). The region within this circle was used in all directionality calculations. A visit to the place field was defined by the rat traversing the circle with a chord greater than half the circle's radius, at a velocity greater than 1.2 cm/sec, and maintaining a trajectory within the field (entrance and exit angles) that was constant to within 90°. The vector mean of the entrance and exit angles of each visit was calculated and used to represent the direction of the visit. *B*, Place field directionality—*t* test analysis. The traverses of the rat were partitioned into two opposite 180° direction ranges, such that each had the same total number of visitations (as nearly as possible). The mean firing rates for the two directional ranges were compared using an unpaired *t* test for a significant difference in firing rates at the $p < 0.05$ two tailed level. *C*, Place field directionality—multiple regression analysis. The animal's mean velocity, and the sine and cosine of head direction were calculated for each visit to the field. These measures were entered as the independent variables in a multiple regression analysis, with firing rate the dependent variable. If the effect of sine or cosine of the traversal angle on firing rate was found to be significant ($p < 0.05$), the place field was regarded as directional. *D*, Place field directionality—magnitude of differential firing. The traversal angles of the visits through the place field were collapsed into 30° angle bins and the mean firing rate for each bin was calculated. For each bin i containing at least five visits, the ratio R_i of firing rates in direction i and $i + 180$ was computed. All possible 30° angle bin combinations that met the criterion of five visits in each direction were examined, the combination that maximized the ratio of firing rates was used. *E*, Task related changes in place field configuration. The correlation of the firing rate maps between the two halves of the first task (r_{ab}), and the two halves of the second task (r_{cd}) were compared to the correlation in firing rates between the second half of the first task and the first half of the second task (r_{bc}). This provided a measure of between-task differences relative to any within-task changes that might occur in the same time period, for example due to recording instability or other time-dependent factors.

traversable space, whereas on the radial maze, the rat is constrained to move along the narrow, raised runways surrounding a central platform.

The purpose of the present experiments was to clarify the sources of the apparent differences in directional tuning of hippocampal place fields between these situations, by manipulating visual complexity, behavioral task demands, and the characteristics of the physical apparatus.

Some of these data have been reported in abstract form (Leonard et al., 1988, 1990; Qin et al., 1993; 1994; Markus et al., 1994b).

Materials and Methods

Subjects and general procedures

Nineteen male retired breeder Fischer-344 rats (Charles River Breeding Laboratories), approximately 1 year old, served as subjects. Animals were housed individually, handled daily, and maintained on a 12 hr:12 hr light:dark cycle. Throughout the experiment, the rats were food deprived to 80% of their ad libitum weights. Animal care and surgical procedures were conducted according to NIH guidelines. The rats were trained on radial arm and platform apparatus, and to search for food in either a random or a directed manner (further details are given for each experiment).

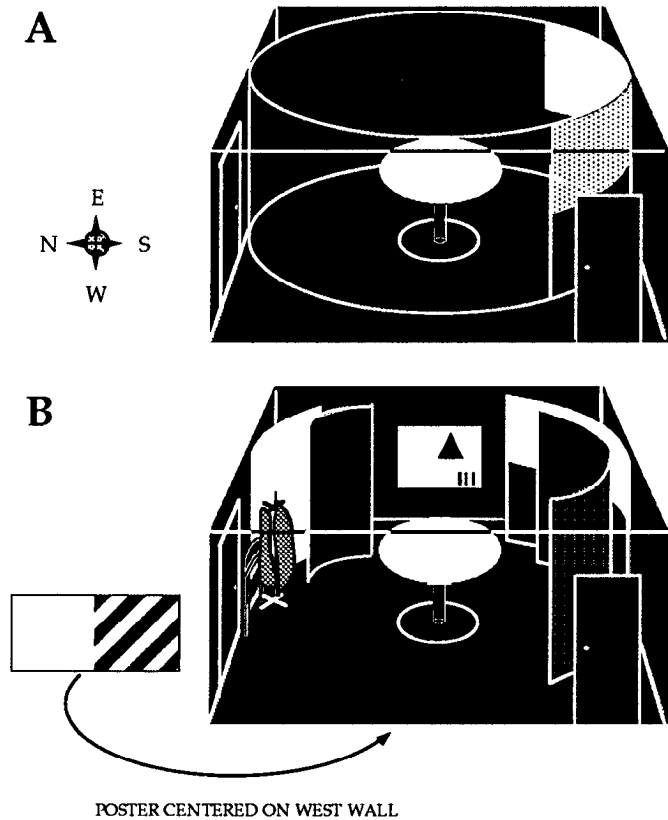


Figure 2. *A*, In the simple-cue environment, the behavioral apparatus (e.g., circular platform) was surrounded by a black curtain, with a white curtain covering a 90° arc (the curtains were 90 cm from edge of the maze/platform and extended from the ceiling to the height of the apparatus). *B*, In the multiple-cue environment the behavioral apparatus was surrounded by sections of black and white curtains, as well as posters on the walls, a coat hanger and a chair. The distance of the cues in the multiple-cue environment was equal to, or greater than, that in the simple-cue environment.

Surgery and recording

Craniotomies were made in the skull bilaterally over the dorsal hippocampus under Nembutal anesthesia (33 mg/kg). A miniature microdrive (McNaughton et al., 1989) containing two stereotrode (McNaughton et al., 1983b), or two tetrode recording probes (Recce and O'Keefe, 1991; Wilson and McNaughton, 1993), was mounted on each side of the skull with dental acrylic. Most of the recordings were obtained with tetrodes, recordings obtained with stereotrodes are indicated in Table 1. The stereotrodes had an overall diameter of approximately 50 μm and were constructed from lacquer-coated 20 μm diameter tungsten wire (California Fine Wire Co.). The tetrodes had an overall diameter of approximately 40 μm , and were constructed from four twisted polyimide-insulated nichrome wires (H.P. Reid Co., Neptune, NJ). Each recording probe was cemented into a 30 gauge guide cannula and cut with sharp scissors at right angles, so that approximately 3 mm of wire protruded from the end of the cannula. The exposed tips were then gold plated to a final impedance of about 500 K Ω at 1 kHz. The recording probes were implanted at surgery approximately 1 mm into the neocortex overlying the dorsal hippocampus, with the anterior probes placed 3.3–4.0 mm posterior and 2.2–2.4 mm lateral to Bregma, and the posterior probes between 4.6 and 5.0 mm posterior and between 3.0 and 3.9 mm lateral to bregma (Paxinos and Watson, 1982). The reference for the stereotrodes was an electrode implanted in the anterior corpus callosum; for the tetrodes, a channel from one of the other tetrodes (outside the pyramidal cell layer) was used as the reference. During recording, the animal wore a multichannel FET source-follower headstage with two arrays of infrared light emitting diodes mounted on it. One diode array was positioned above the front of the rat's head, while the second, smaller array was mounted 14 cm posterior to the first, approximately above his hindlimbs. This arrangement allowed a resolution of head

direction of about 7°. Position coordinates of both diodes were sampled at 20 Hz with an overhead video tracking system, providing data on the rat's location (taken as the position of the front diode) and head direction. Some animals had only a single diode array located above their heads (Experiment 5), and for these only position information was gathered. Neuronal signals were amplified between 5000 and 10,000 times, filtered between 600 Hz and 6 kHz and sampled concurrently with position information using an Intel 80386 based acquisition system (DataWave Systems Corp., CO).

Histology

After the last recording session, the rats were deeply anesthetized with Nembutal, perfused with a 10% formal-saline solution and the electrodes were withdrawn. The brains were removed from the skull, placed in formal-saline solution for at least 24 hr, and then in a formal-saline-30% sucrose solution until they sank. Coronal sections (40 μm) were cut and subsequently stained with cresyl violet to assist electrode track identification.

Data analysis

Multiple single unit signals recorded on a single tetrode probe were discriminated off-line using a user-interactive spike parameter cluster separation method (McNaughton et al., 1989; Mizumori et al., 1989). Typically, the relative amplitudes of unit signals across the recording channels, as well as the spike duration (measured from maximum to minimum voltage) were used for spike discrimination. For the stereotrode recordings, the unit identification method was implemented on a 80386 PC, while for the tetrode recordings, custom software on Sun Sparc workstations (Wilson and McNaughton, 1993) was used. A firing rate map was constructed for each cell by dividing the recording environment into a 64 \times 64 bin array. Each bin was a 2.4 cm by 2.4 cm square. The mean firing rate for a given bin was calculated by dividing the total number of spikes summed over all the bins within a radius of 4.8 cm from the center of the bin, by the total time spent in these bins. Place fields were defined as an area of bins sharing adjacent edges, with a firing rate per bin greater than two standard deviations above the mean firing rate of the cell in the entire apparatus. Of these, only cells with "robust" place fields were examined, that is, those having a mean firing rate of 0.1 Hz or greater, and a place field encompassing more than 15 bins. In addition, for the analysis of place field directionality, only a subregion of the place field was examined. The largest symmetrical inner circle surrounding the centroid of the place field which fell entirely within the boundaries of the place field was found (Fig. 1*A*). All subsequent directional analyses were based on the rat's occupancy sampling of this inner circle. Once a place field was found, the firing rate and head direction were calculated for each visit of the rat to this inner circle. To be considered a visit, the rat had to traverse the place field with a chord greater than half the inner circle radius, at a velocity greater than 1.2 cm/sec, and maintain a constant trajectory within this region (entrance and exit head angles within 90° of each other). The entrance and exit head orientations of each visit to the inner circle were summed vectorially and the resulting angle was used to represent the direction of the visit. In order for a cell to be included in the directionality analysis, the rat had to visit the inner circle of the place field at least 10 times.

To reduce the possibility of measurement artifacts and to ensure that the place field directionality data captured different aspects of the directional firing characteristics of the cells, the directional bias of unit firing was assessed in three different manners:

T-Test for significance of directionality

The traverses of the rat through the place field were partitioned into two opposite directional sets based on traversal angle. The directional sets chosen were those which best divided the data into equal visitations (Fig. 1*B*). This division resulted in approximately equal number of behavioral samples in each directional set without regard to the firing rate of the cell. The mean firing rates for the two directional sets were compared using a two sample *t* test for a significant difference in firing rates at the $p < 0.05$, two-tailed level.

Multiple regression analysis

The significance of head direction and velocity in predicting firing rate within the field was examined with a multiple regression analysis (Fig. 1*C*). The animal's mean velocity, and the sine and cosine of head di-

Table 1. Number of rats and place fields by electrode location and experimental condition

Experiment:	1 ^a	2		3		4		5 ^a			
Apparatus:	Cyl- inder	8-Arm maze		Circular platform		Circular platform		Plus maze		Square platform	8-Arm maze
Cues/Task:		Simple	Mul- tiple	Simple	Mul- tiple	Random	Di- rected	Random	Di- rected		
#Rats	3	3	3	6	4	8	8	7	7	3	3
CA1											
Cells	51	89	32	95	10	101	88	121	75	18	18
Total fields	54	137	49	140	14	146	102	129	84	25	12
Fields tested for directionality	44	98	32	96	13	118	60	66	69		
CA3/dentate											
Cells		3	20	7	48	46	39	60	50		
Total fields		7	32	12	65	66	44	66	52		
Fields tested for directionality		5	27	6	39	40	28	40	42		

^a Stereotrode recording.

rection were calculated for each visit to the field. These measures were entered as the independent variables, with firing rate the dependent variable in the regression procedure (SPSS Inc., Chicago).

Magnitude of differential firing

The head orientations of the visits through the place field (inner circle) were collapsed into 30° angle bins and the mean firing rate for each bin was calculated. An index of the ratio of firing rates between two opposite 30° bins was calculated as

$$\frac{|\text{rate}(A) - \text{rate}(A + 180^\circ)|}{(\text{rate}(A) + \text{rate}(A + 180^\circ))},$$

with A and $(A + 180^\circ)$ being two angle bins 180° apart (Fig. 1D). The result is constrained in value from 0 (equal firing in both directions) to 1 (firing in only one direction). All possible 30° angle bin combinations that met the criteria of five visits in each direction were examined, the combination that *maximized* the ratio of firing rates was used. This measure has an *a priori* bias against finding higher values on the directed tasks (where directionality appears to be greater) because, on the circular platform and random tasks, the animal sampled the place field from many different angles, increasing the number of reciprocal directions that could be examined. On the radial maze arms, the reciprocal comparison was restricted to a single orientation.

In addition to directionality, measures of reliability, specificity and size of the place fields were also obtained. The place field reliability was calculated by dividing the recording session into two equal parts, and measuring the correlation of firing rates between the first and second parts of the session. Specificity was calculated in terms of the amount of information (in bits) that a single spike conveys about the animal's location (i.e., how well cell firing predicts the animal's location). The spatial information content of cell discharge was calculated using the formula

$$\text{information content} = \sum P_i(R_i/R) \log_2(R_i/R),$$

where i is the bin number, P_i is the probability for occupancy of bin i , R_i is the mean firing rate for bin i , and R is the overall mean firing rate (Skaggs et al., 1993). The size of the place field was defined as the number of adjacent (shared edge) bins with a firing rate greater than 2 SDs above the mean firing rate of the cell.

Changes in place fields between two behavioral tasks in the same apparatus were measured by dividing the recording time for each task into two halves (a and b for task 1, c and d for task 2). The correlations of the firing rate maps between the two halves of the first task (r_{ab}), and the two halves of the second task (r_{cd}) were found, these were compared to the correlation in firing rates between the second half of the first task and the first half of the second task (r_{bc}). The correlations between behavioral tasks were performed only on those regions sampled in both tasks, defined by at least three visits in each epoch (Fig. 1E).

Methodological considerations regarding place field directionality

The possibility that differences in place field directionality result from a bias in the method of quantifying directionality, and that there is no relationship between constraints on the rat's behavior and place field directionality, needs to be addressed. For example, the use of number of visitations as the criterion for dividing the data (the t test analysis) had different effects on the radial mazes and circular platform. In contrast to the platform case, sampling of the arms on the radial maze was limited to two opposite ranges of directions (outward or inward). Thus, the optimal division of visitations was always perpendicular to the maze arm on the radial maze, and this could potentially inflate the directionality measure. Such an interpretation would imply that, when the rat follows a specific trajectory, the directional biases of the cells become aligned to the behavioral biases. The likelihood that this is actually what happens is addressed below. It will also be shown that both the t test analysis and the multiple regression approach lead to similar conclusions that the data indeed reflect differences in place field directionality as a function of behavioral variables.

A second possible confound could be an unequal sample size on the different apparatus or behavioral tasks. For example, if there were more visitations to place fields on the radial mazes than on the platform, then the statistical power to detect directionality in the former condition would be greater. This, however, was not the case. In fact, the situation with the best sampling of place fields was in the random task on the platform, and, as will be shown, this was the condition with the least directionality, despite the better sampling.

Procedure experiment 1: place field directionality in a high walled cylinder

The behavioral apparatus consisted of a cylindrical, flat gray walled arena 76 cm in diameter and 51 cm high (Muller et al., 1987). The floor consisted of a piece of gray construction paper, which was replaced before each recording session. Rats were trained to forage for Noyes Precision Food Pellets (45 mg, formula A; P. J. Noyes Company, Inc.), which were tossed into the arena at rate of about 3/min so that the rat would traverse all parts of the apparatus floor in a large number of directions and in a repeated, yet nonsystematic manner over a period of 30 min. The inner surface of the cylinder wall had either a single, white cue card (covering 100° of wall arc) or multiple, patterned cue cards attached to it.

Procedure experiment 2: effects of environmental complexity and apparatus type on place field directionality

Two types of visual environment were used with two different mazes.

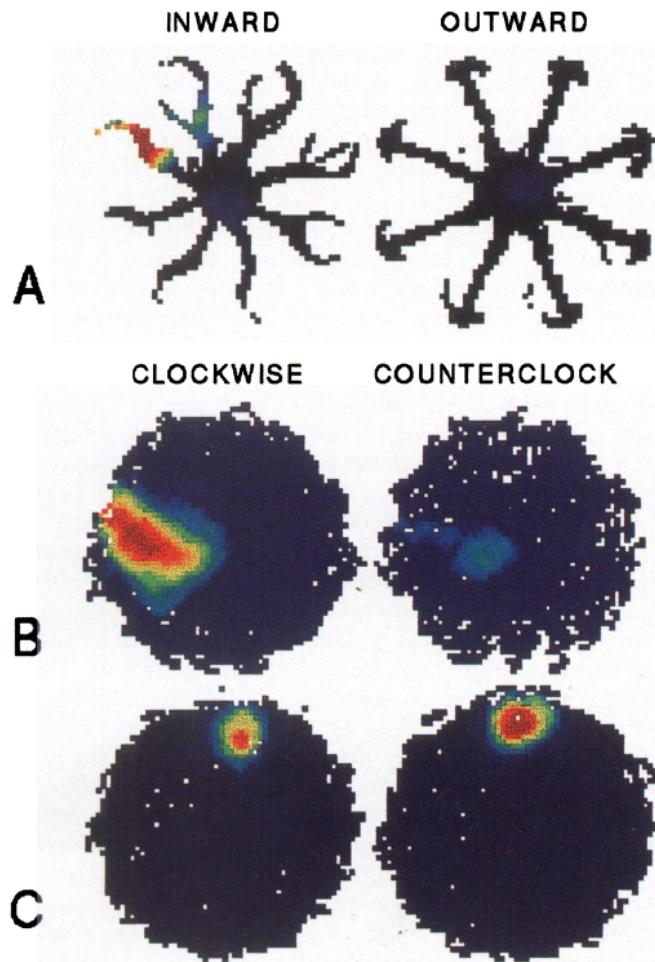


Figure 3. Examples of place fields of three different cells on the 8-arm radial maze and on the circular platform apparatus. Maximum firing rate is indicated by red, and zero rates by dark blue. White indicates regions not sampled by the rat. In order to display place field directionality, the data have been divided according to the animal's head orientation. *A*, Firing rate on the 8-arm maze separated according to whether the rat's head was facing towards the center of the maze (inward) or oriented away from the center of the maze (outward). Note that on a given maze arm the "outward" firing rate map shows the occupancies up to the end of the arm; once the animal is turning back towards the center of the maze the occupancies assigned to the "inward" firing rate map. In this case the cell fires only as the rat returns inward on the North-Western arms and not when he goes outward along the same arms (red = 50 Hz). *B*, On the platform, the data were separated into clockwise, and counterclockwise head orientations (using the center of the platform as the axis). In this case the cell fired only when the rat was in the western portion of the platform and facing North (red = 4.5 Hz). *C*, A nondirectional place field. The cell fired in a similar manner regardless of the direction that the rat passed through the field (red = 8 Hz).

Visual environment

Simple-cue environment. The behavioral apparatus, either an eight-arm maze or a circular platform (see below), was surrounded by a black curtain, with a white curtain covering a 90° arc at a distance of 90 cm from the edge of the maze/platform (Fig. 2A).

Multiple-cue environment. The behavioral apparatus (either the eight-arm maze or the circular platform) was surrounded by sections of black and white curtains, as well as posters on the walls, a coat hanger and a chair. The distance of the cues in the multiple-cue environment was equal to, or greater than, that in the simple-cue environment (Fig. 2B).

Recording apparatus and procedure

Forced choice search on an eight-arm maze. Rats were trained to perform a forced-choice task on an eight-arm radial maze (arms 58 × 5.7

cm) for a chocolate milk reward (Barnes et al., 1983). A forced-choice trial consisted of one visit, in random order, to each of the eight maze arms. Once all arms had been visited, the rat would return to a small platform at the center of the maze and rest while the maze arms were rebaited. Access to the arms was controlled by DC motor-driven drawbridges. At any given time, only the arm that the rat was currently on (obtaining its reward) and the next baited arm were accessible. A recording session consisted of at least eight visits to each maze arm.

Random search on a circular platform

Rats were trained to search continuously for small chocolate pellets distributed in a semi-random manner on the surface of a large circular platform (122 cm diameter) in a manner similar to that described in Experiment 1.

The environment (simple- or multiple-cue) was held constant across recording sessions for each rat for a given apparatus. For example, a given rat was trained and recorded from on the radial maze always within the same environmental configuration. Five rats were trained on both apparatus (radial maze and platform), in these cases the rats were first trained and recorded from on the 8-arm radial maze, then the rats were retrained and recorded from on the circular platform.

Procedure experiment 3: effects of behavioral task requirements on place field directionality and location

Place cells were continuously recorded on the circular platform as the rat performed first one behavioral task and then, without interruption, another.

Random search task

In the first part of the recording session the rats searched continuously for chocolate pellets distributed in a semi-random manner on the surface of the circular platform.

Directed search task

After approximately 30 min of random search, the platform surface was cleared of chocolate (while the rat remained on the platform). A few chocolate pellets were placed about 15 cm from the edge of the platform in one of four designated spots located at 90° intervals around the periphery. The experimenter gently tapped a finger by the baited location. Once the rat was eating at that location, the next location was baited in a sequential order. A minimum of 10 complete clockwise and counter-clockwise sequences were recorded.

Procedure experiment 4: effects of the physical characteristics of the apparatus on place field directionality and location

Place cells were continuously recorded as the rat performed first the random search task, and then the directed search task, on the surface of a plus maze consisting of four 58 cm long arms perpendicular to each other. Two arms were narrow (north and south arms, 5.7 cm wide) and two wide (east and west arms, 17.1 cm wide). In the first part of the recording session, the rats searched continuously for chocolate pellets distributed in a semirandom manner on the surface of the plus maze. Once a minimum of 10 visits to each arm were completed, the maze surface was cleared of chocolate pellets (while the rat remained on the maze). A few pellets were placed in the food cup at the end of an arm. The experimenter gently tapped a finger on the baited arm. Once the rat visited that arm, the next arm was baited in a counterclockwise order. A minimum of 10 complete counter-clockwise sequences were conducted.

Procedure experiment 5: effects of the physical characteristics of the apparatus and task on place field location

Place cells were recorded first during a direct-path task on a large open square platform, and then during the forced choice task on a radial eight-arm maze in the same room. The 1.2 m square platform was covered with flat black contact paper with a 10 cm ring of white contact paper in the center. Except for a 0.2 cm lip around its perimeter, the square platform, like the circular one, was open to the recording room. The platform was centered on the eight-arm maze also used for record-

ings. A foodcup with chocolate milk was placed at a variable location from trial to trial, and the rats were trained to take a direct path of about 0.5 m to the cup, when placed anywhere on the platform surface. After two sessions of platform adaptation (5–10 min of unreinforced exploration) the rats were trained on the direct-path task. Direct-path training consisted of gradually encouraging the rats to take increasingly longer paths through a shaping procedure. After the rat drank the reward, it was picked up and held on the experimenter's shoulder while the foodcup was moved to a new location, immediately after which the rat was placed again onto the platform. An attempt was made to sample a large number of locations and directional orientations during training and recording sessions, and a special effort was made to ensure that the rats made traverses through the relative locations of the maze arms covered by the platform. After recording on the square platform, the rat was carried out of the room, the platform was removed to expose the eight-arm maze and the rat immediately returned to the room. The task on the eight-arm maze was identical to the forced choice task described in Experiment 2.

Results

Table 1 details the number of rats and place cells recorded from in each group for all the experiments.

Effect of recording site: CA1 versus CA3-fascia dentata

Based on histology and/or physiological landmarks, cells were identified as recorded from the CA1 or CA3-fascia dentata (FD) region of the hippocampus. Because physiologically identified granule cells have spatial selectivities and firing rates similar to CA3 pyramidal cells (Jung and McNaughton, 1993), we cannot confidently distinguish these cell classes in the present experiments. Consistent with Barnes et al. (1990), CS cells recorded in CA1 fired at a higher mean rate (0.96 vs 0.55 Hz; $p < 0.01$), were more reliable ($r = 0.72$ vs 0.66; $p < 0.01$), had larger fields (69.5 vs 62.2 bins; $p < 0.01$) and conveyed less spatial information (1.23 vs 1.39 bits/spike; $p < 0.01$), than CS cells recorded in the CA3/FD region. There was no significant interaction between recording site and behavioral task. Similarly there were no differences between CA1 and CA3/FD recordings in terms of the task-related directional effects. Consequently, the data from both regions were combined in the analysis of place field directionality.

Place field directionality

Experiment 1: place field directionality in the high walled cylinder. Of 44 cells with place fields, only a small portion were directional in the high walled cylinder, 14% based on the t test method ($p < 0.05$) and 18% based on the multiple regression method ($p < 0.08$).

Experiment 2: effects of environmental complexity on place field directionality. A significant proportion of place cells were directional on both the circular platform and on the radial maze. Examples of directional and non-directional place fields are shown in Figure 3. On the circular platform 20% were directional, based on the t test analysis ($p < 0.01$), and 31% had a significant directional component based on the multiple regression analysis ($p < 0.01$). On the radial maze 64% of place fields were directional based on the t test analysis ($p < 0.01$) and 53% were directional based on the multiple regression analysis ($p < 0.01$).

More place fields showed directionality on the 8-arm radial maze than on the circular platform ($p < 0.01$; Fig. 4A), and the magnitude of directional firing was greater on the 8-arm maze ($p < 0.01$; Fig. 4B). A multiple regression analysis showed that the effect of maze type persists even when velocity was accounted for ($p < 0.01$). A similar effect was found with respect

to the quality of the place field. Place fields were smaller (40.5 vs 101.7 bins; $p < 0.01$), and conveyed more spatial information (1.11 vs 0.89 bits; $p < 0.01$), on the 8-arm radial maze than on the platform. Apart from a higher firing rate in the simple environment (0.90 vs 0.63 Hz; $p < 0.05$), there was no significant effect of visual environment on any measure of place field directionality, size, or specificity (all $p > 0.10$). The possibility that the difference in place field directionality between the 8-arm maze and circular platform was due to a difference in the behavioral task demands, was investigated in the next experiment.

Experiment 3: effects of behavioral task requirements on place field directionality. As can be seen in Figure 5 some cells with nondirectional place fields recorded during the random task had directional fields during the directed search task. In the directed search task a larger proportion of place fields were directional (t test, $p < 0.01$), although the magnitude of directionality was unaffected (Mann Whitney, $p > 0.10$; see platform data in Fig. 6A,C). This increase in directionality in the directed search task resulted largely from the emergence of new directional place fields (see below). Nevertheless, the proportion of directional place fields in the directed search task was still less than on the 8-arm radial maze. This suggested the possibility that place field directionality is also affected by physical constraints arising from the geometry of the apparatus. This was examined in Experiment 4.

Experiment 4: effects of the physical characteristics of the apparatus on place field directionality. On the plus maze, the behavioral task showed no effect on the proportion of directional place cells ($p > 0.10$); however, the magnitude of place field directionality increased in the directed search task in relation to the random search task (Mann Whitney, $p < 0.05$). In addition, the proportion of directional place fields, and the magnitude of directionality was similar on both the wide and narrow arms of the maze (all $p > 0.10$). An example of a directional place field on the plus maze is shown in Figure 6B. A two-way ANOVA comparing the results of the platform and plus maze (Fig. 6A), showed a higher proportion of directional fields on the plus maze ($p < 0.01$) and an interaction, in which there was a greater effect of behavioral task on the platform than on the plus maze ($p < 0.01$). The same was true when velocity was accounted for (multiple regression, apparatus $p < 0.01$; interaction $p < 0.05$). An increase was also found in the magnitude of directional firing, which was higher on the plus maze than on the platform, and during the directed task than on the random search task (Mann Whitney, both $p < 0.01$; Fig. 6C). Place fields were also more reliable on the plus maze than on the platform ($p < 0.01$), with no effect of behavioral task on reliability ($p > 0.10$).

Effects of behavioral task on place field location

On both radial maze and platform, the place cells were recorded continuously as the rats performed first the random and then the directed search tasks (Experiments 3 and 4). In addition to the overall changes in the quality of the place fields presented above, the location of the place field often changed with the shift in the task demands. For example, Figure 5 illustrates both a change of directionality and a change of the location of place fields with the change of task. Figure 8A illustrates that this change of place field firing can be attributed to a shift in location of the place field, the addition of a place field, or loss of a place field.

The change in place fields was quantified by comparing firing rate maps. The correlation of firing rate maps within each be-

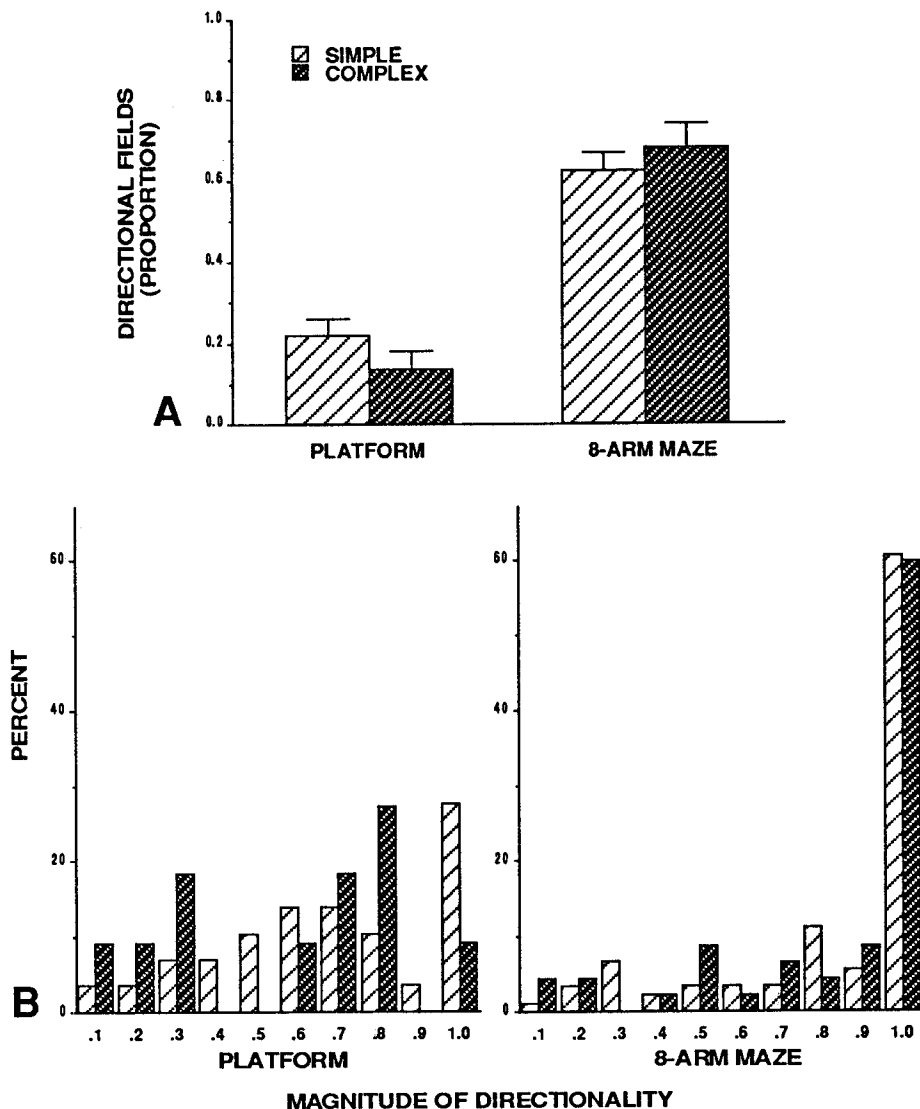


Figure 4. *A*, The proportion of place fields with a significant degree of directional selectivity (t test analysis), was greater on the 8-arm radial maze than on the circular platform ($p < 0.01$). There was no effect of environmental complexity ($p > 0.10$). *B*, The magnitude of directional firing in the directional place fields (ratio of firing rate between opposite directions) was greater on the 8-arm radial maze than on the circular platform (Mann Whitney, $p < 0.01$). There was no effect of environmental complexity (Mann Whitney, $p > 0.10$).

havioral task (r_{ab} , r_{cd}) was compared to the correlation of firing rate maps between the two behavioral tasks (r_{bc}). If the place field was unaffected by the change in task, then the correlation within a task should be equal to the correlation between tasks (i.e., it should fall on a 45° angle in a scatter plot). On the other hand, place fields that change as a result of the change in behavioral task should show a stronger correlation within a task than between tasks and thus will fall closer to the x-axis. Figure 7A–D shows this trend clearly, and Table 2 shows that the correlation of firing rate maps between tasks is significantly less than that within tasks ($p < 0.01$).

As can also be seen in Figure 7A–D, altering the behavioral task caused more change in place field locations on the circular platform than on the plus-maze. A t test comparing the relative correlation between the tasks to the correlation within each task (correlation between tasks/correlation within each task) showed a higher correlation between tasks on the plus maze than on the platform (Fig. 7E; relative to the correlation within the random task, $p < 0.05$; relative to the correlation within the directed task $p < 0.01$). Visual inspection of the place fields gave similar results with 40% of the place fields changing on the platform, and only 20% of the fields changing on the plus maze ($p < 0.01$; a change in directionality was not considered a change in

place field location; only those regions of the maze occupied in both tasks were compared). The degree of task related change in place field location was similar in CA3/FD and CA1 cells ($p > 0.10$). It should be noted that in the directed task some cells exhibited “goal approach” fields similar to those described by others (Eichenbaum et al., 1987; Wiener et al., 1989). On the circular platform this was clearly apparent, with cells firing as the animal approached a given reward site *regardless of the approach path* (see Figs. 5D, 10); however, there was no obviously disproportionate clustering of place fields around the reward sites.

The place fields were examined during the initial session in which the rats were taught the new, directed search task. It took the rats 10–30 min to learn the new task, with the rats learning more quickly on the plus maze than on the platform. As illustrated in Figure 9, the new place fields appeared abruptly during learning.

In order to confirm that the place fields were related to a specific behavioral task and not to other factors such as time or the act of changing the procedure during a recording session, two additional rats were recorded from. These rats performed tasks on the platform in the following sequences: a random, a directed, and finally a second random search for food, all within

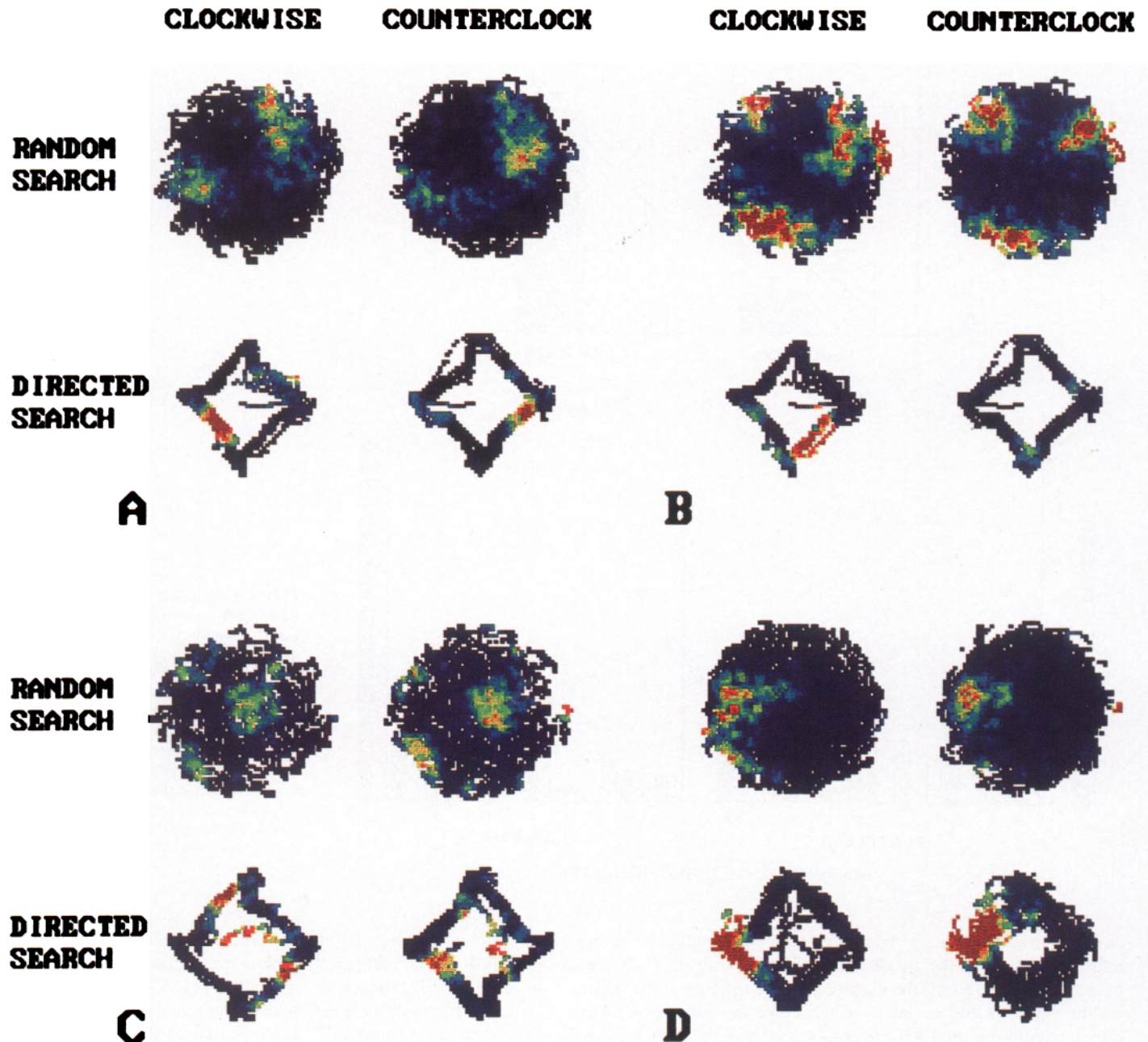


Figure 5. Examples of place fields that became directional during the directed search task. Note how the animal visits nearly all regions of the platform in his search for food during the random search, and the cells fire both during clockwise and counterclockwise head orientations. During the directed search task the animal visits only a limited region of the platform as he runs from one food location to the next (the corners of the square). The cells typically fired only during clockwise motion or only during counterclockwise motion in their place fields. Also note that the cell shown in *D* only fires as the animal approaches the eastern food location. Firing rates: *A*, red ≥ 18 Hz; *B*, red ≥ 8 Hz; *C*, red ≥ 7 Hz; and *D*, \geq red 8 Hz.

a single recording session. Of those place fields whose location was altered by the directed task, 79% (23/29) returned to their previous locations on the second random task (examples in Fig. 8*B*). For the other 21% (6/29) the field locations in the second random task were in either a new location (3/29) or in a mixture of the two locations from the random and directed task (3/29).

While the dynamics of place field change were not quantified, visual inspection revealed that the change in place field location was abrupt, and paralleled the change in the rats' behavior (Fig. 10).

Experiment 5: effects of the physical characteristics of the

apparatus on place field location. The results of Experiment 3 and 4 showed that when the room and apparatus remained constant, the location of some place fields changed in conjunction with the change in behavioral task. In this experiment only the room was identical, while both the task and the apparatus were changed. Because the rats were very familiar with the procedure, and entry and exit from the room were kept constant, presumably the rats "knew" they were in the same room. A total of 18 cells with a place field in at least one apparatus and a minimum firing rate of 0.1 Hz, were recorded from. Comparison of firing rate correlations between the apparatus to the correlation

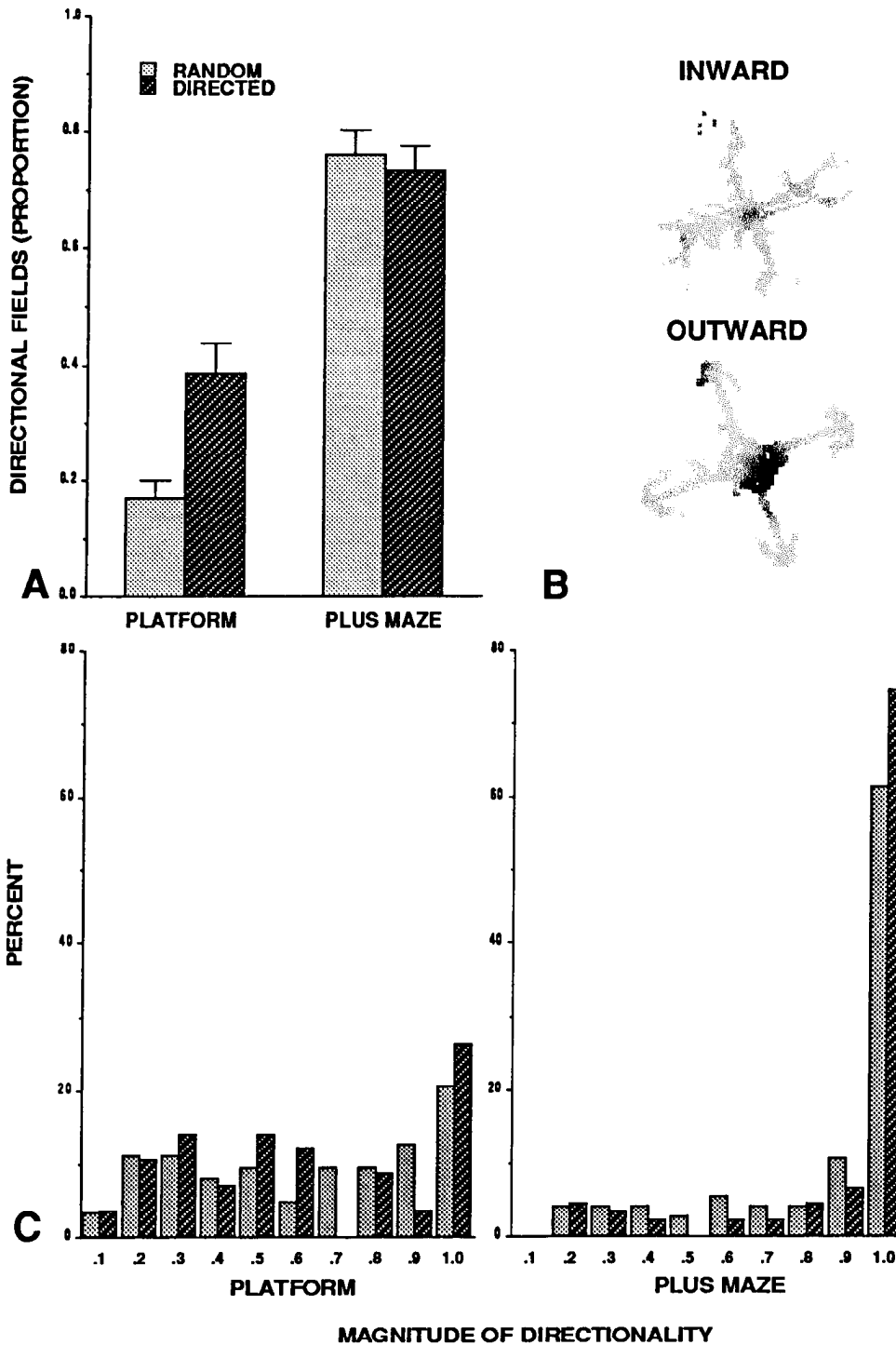


Figure 6. A, The proportion of place fields with a significant degree of directional selectivity (*t* test analysis) was greater for the directed task than for the random search task (ANOVA, $p < 0.01$). This effect was found only on the platform and not on the plus maze (interaction; $p < 0.05$). B, An example of a directional place field on the plus maze. The cell fires in the south-east region of the center of the maze, only during outward orientations of the rats head. C, The magnitude of directional firing was greater on the plus maze than on the platform task (Mann Whitney, $p < 0.01$). Magnitude of directional firing was affected only in the directed search task on the plus maze (Mann Whitney, $p < 0.05$) but not on the platform (Mann Whitney, $p > 0.10$).

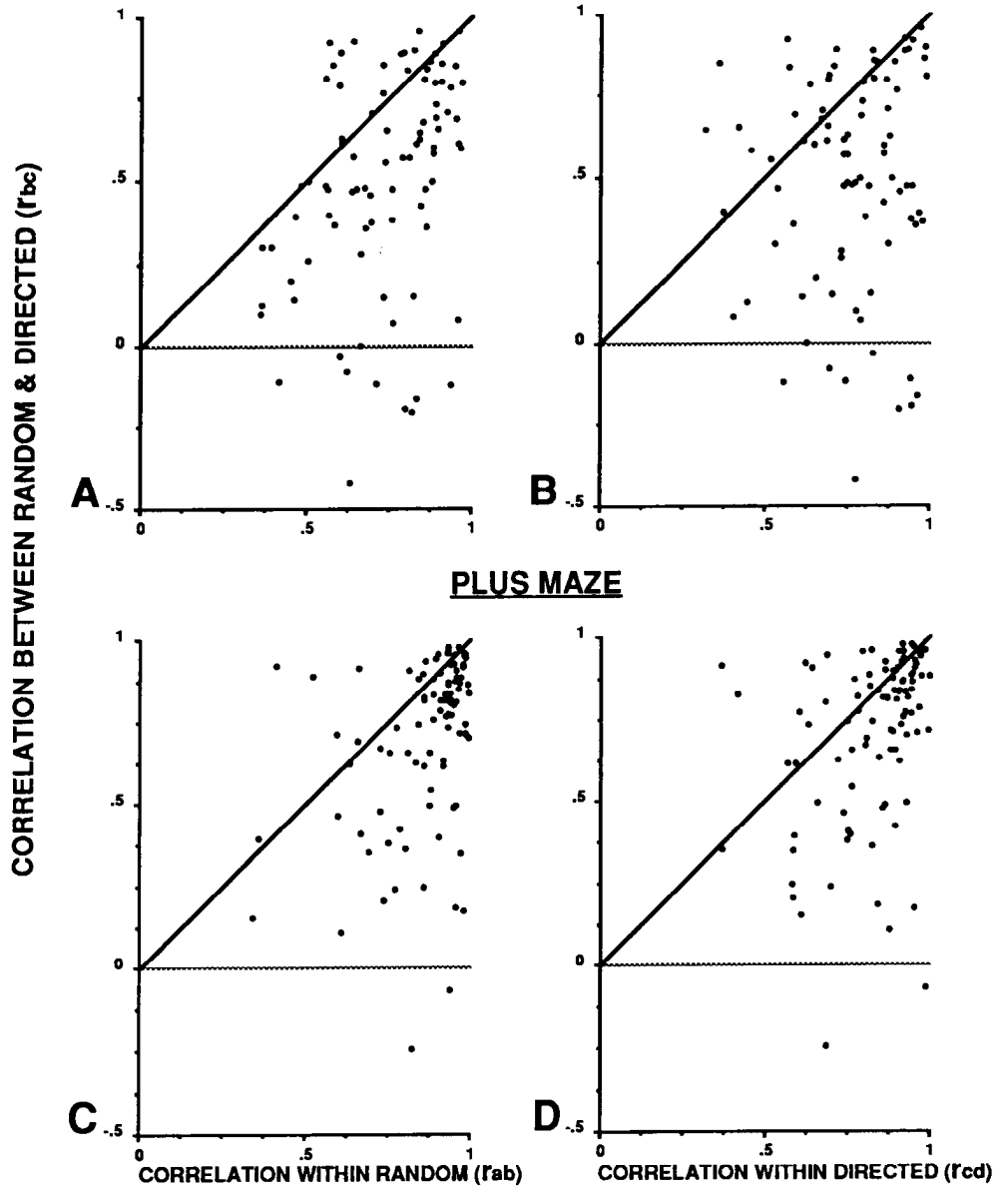
within each apparatus (correlation between tasks/correlation within each task) revealed that the firing patterns between the two recording situations were essentially independent for most cells ($r = 0.028$, see Fig. 11).

Discussion

Place field directionality was affected by the behavioral task and by the type of apparatus on which the recordings were made. Place fields showed little directionality in the small, high-walled cylinder (Experiment 1); however, on the circular platform, which was much larger than the cylinder and permitted access

to distal visual cues, place field directionality was clearly evident in some cells (Experiment 2). Although it is conceivable that these cases could have been due to subtle differences in the exact locations visited by the rats in the opposite directions (Muller et al., 1994) this is rather improbable because of the restriction of the analyses to the vicinity of the centroid of the field. Moreover, some of these directional differences were maximal in the clockwise versus counterclockwise directions, and not in the radial directions (e.g., Fig. 3), and hence could not be attributed to differential accessibility. The source of increased directionality could be attributed to either the difference in visual environment

CIRCULAR PLATFORM



PLUS MAZE

Figure 7. The correlation of spatial firing for each cell, within and between the two behavioral tasks. Correlations were calculated by dividing the total recording session into four parts. First half of the random task (*a*), second half of the random task (*b*), first half of the directed task (*c*), second half of the directed task (*d*). *A* and *B* depict the data from the circular platform, *C* and *D* depict the data from the plus maze. Only those cells with a correlation above 0.3 on both behavioral tasks were examined. *A*, Comparison of the correlation of firing on the platform within the random task (*ab*) to the correlation between the random and directed task (*bc*). Note that most cells had different firing patterns on the two tasks (points falling below the 45° angle). Some cells were unaffected by the change in behavioral task (points near the 45° angle). There were also cells with unstable fields, probably due to a drift in the recording electrode (points above the 45° angle, that is, were more similar across the end of one task and the beginning of the second task than within a task). *B*, Comparison of fields on the platform within the directed task (*cd*) to the correlation of firing across the two tasks (*bc*). Most place fields had different firing patterns on the two tasks. *C*, Comparison of fields on the plus maze within the random task to the correlation of firing across the two behavioral tasks. Note how the correlations within a behavioral task are higher on the plus maze (*C, D*) than on the platform (*A, B*). While some fields are affected by the change in behavioral task, most fields remain the same regardless of the change in task (are clustered around the 45° angle). *D*, Comparison of fields on the plus maze within the directed task to the correlation of firing across the two behavioral tasks. Most fields remain the same (are clustered around the 45° angle) regardless of the change in task. *E*, Comparison of the relative correlation between the behavioral tasks to the correlation within each task (correlation between/correlation within). There is a higher correlation between tasks on the plus maze than on the platform maze (relative to the correlation, within the random task *t* test $p < 0.05$; within the directed task, $p < 0.01$).

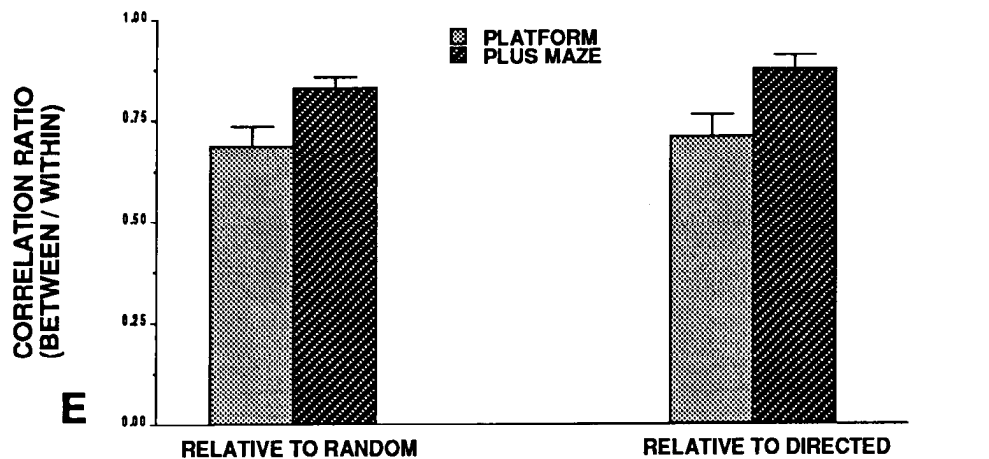


Table 2. Paired *t* test of the correlation of firing rate maps between tasks versus within tasks

	Mean difference	Degree of freedom	<i>t</i> Value	<i>p</i> Value
r_{bc} vs r_{ab}	-0.191	183	-9.211	<0.0001
r_{bc} vs r_{cd}	-0.181	183	-7.869	<0.0001
r_{ab} vs r_{cd}	0.011	184	0.732	0.4649

r_{bc} vs r_{ab} means the correlation of firing rate map between tasks versus that within random search task; r_{bc} vs r_{cd} means the correlation of firing rate map between tasks versus that within directed search task; r_{ab} vs r_{cd} means the correlation of firing rate map within random search task versus that within directed search task. The result shows that the change in place field configuration between tasks was much greater than expected on the basis of any recording instability or other time-dependent effect during a given recording session of comparable duration within a given task (see Fig. 7 caption for detailed definitions of r_{bc} , r_{ab} , and r_{cd}).

or to differences in the animals' trajectories in the larger environment.

The results of the Experiment 2 support the conclusion that directional firing is more related to the animal's behavior than to effects of different visual environments. Place fields were more directional on radial arm mazes than on a circular platform, when the distal visual environment was kept essentially constant. On the platform, place fields were more directional in rats moving between defined reward sites than in rats randomly searching for food. There was no effect of the complexity of visual environment on the directionality of place fields. Thus, even a relatively sparse visual environment is sufficient for the production of directional place fields. This result is consistent with the finding that place field directionality is retained when the visual information is temporarily obscured by darkness (McNaughton et al., 1989; Quirk et al., 1990; Markus et al., 1994a). Consequently, it seems that, at least under these experimental conditions, the visual environment per se is less important a determinant of directional tuning than constraints (behavioral and environmental) on the animal's behavior. This view is consistent with behavioral findings that, in certain situations, rats give precedence to the shape of the environment over discrete visual cues (Cheng and Gallistel, 1984), and with neurophysiological studies (Jung and McNaughton, 1993; Knierim et al., 1995) indicating that place cells are strongly affected by vestibular/path integration information, which often can override information from visible landmarks. It should also be noted that the width of the arm on the plus maze (two arms were three times wider than the other two) had no effect on the directionality of the place fields. An examination of the rats' behavior revealed that they usually proceeded to the ends of the wide arms (rather than turning around at mid-arm), in a manner similar to their behavior on the narrow arms. Thus, having the opportunity to turn around did not affect place field directionality; rather, the actual behavior seems to be the important factor.

Functional significance of place field directionality

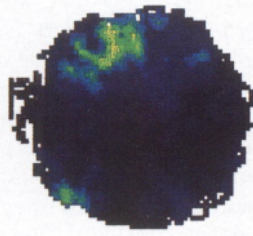
Place field directionality was related to constraints in the trajectories the animals executed, and thus to the manner in which they navigated through the environment. Directionality differences between tasks were significant even when the animal's velocity and the length of trajectory at consistent heading were accounted for. Thus, the instantaneous motor behavior is unlikely to be a major factor.

One possibility is that place fields represent the distances and bearings (i.e., vectors) to or from certain landmarks or locations in the apparatus that the animal's attention is focused on (McNaughton et al., 1994). It is reasonable to expect that, on the outward run on an arm of a radial maze, the rat's attention is focused on either the arm end, or on some landmark located in that general direction. During the inward run, however, attention might be focused reliably on the maze center or on some other landmark. Alternatively, the reference for place cells might be some special place the rat has just departed from. For example, during path integration experiments, rodents keep track of their position relative to a home nest during an outward foraging task in darkness (Mittelstaedt and Mittelstaedt, 1980). This suggests that place cells might encode the relative distance and bearing from a point of significance which the rat has recently visited, based on integration of self-motion. During random foraging experiments, there is not necessarily any set of points of particular significance and no particular reason to shift the reference for path integration. In contrast, when rats run in opposite directions between established reward locations, these locations could become reference points. This alternation of reference points would easily explain the strong directionality observed under these circumstances. A similar suggestion was made by Wan et al. (1994), and preliminary data supporting this suggestion has been reported (Gothard et al., 1995). According to this general notion, during random foraging on the circular platform, there is only one frame of reference, and thus place cells are omnidirectional. Moreover, the path integration idea would also explain why place cells are less reliable during random foraging in large open environments. Under this condition, there are fewer opportunities for correction of cumulative error of the path integrator on the basis of fixed reference points defined by local stimuli or events. This idea is also consistent with the observation that, at least under some conditions, place cells are correlated more with the animal's internal orientation system (as assessed by simultaneous monitoring of thalamic head-direction cells) than with the orientation of visible stimuli or the actual laboratory reference frame (Knierim et al., 1995).

Effects of experience on place field directionality

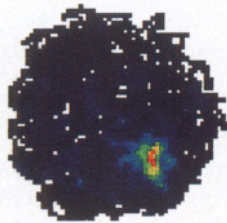
While the foregoing discussion has focused on explanations of directionality based on the shifting of attention or reference point in a fundamentally nondirectional system, an alternative view is that place fields are fundamentally directional in their origins, but become omnidirectional as a consequence of synaptic changes that depend on the experience of rotating in a particular location (Sharp, 1991). There is evidence, for example, that neurons in the primate inferotemporal cortex develop consistent responses to completely uncorrelated stimuli that are repeatedly presented in succession (Miyashita, 1988). This effect can be explained by the use of a time-dependent or sequence-dependent Hebbian learning rule (Amit et al., 1994). In the present case, this explanation is weakened by two observations. First, in addition to the linear segments, directional place fields were found also on the center platform of the plus maze (see Fig. 6B), a region where the rats often sample a wide range of directions in a given location. Second, in rats that were trained to shift repeatedly between directed and nondirected tasks, cells appeared to be able to shift rapidly between directional dependence and directional independence. These data create difficulties for any simple explanation based on the rat's having experienced multiple orientations in a given location.

CIRCULAR **PLATFORM** **PLUS MAZE**
RANDOM SEARCH **DIRECTED SEARCH** **RANDOM SEARCH** **DIRECTED SEARCH**



Shift of Place Field

Shift of Place Field



A

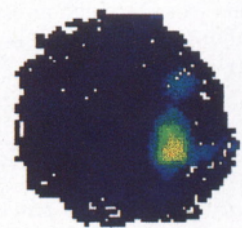
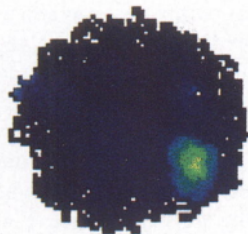
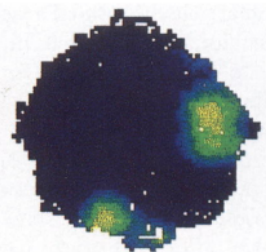
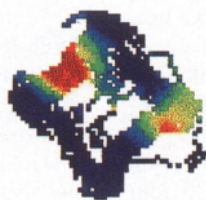
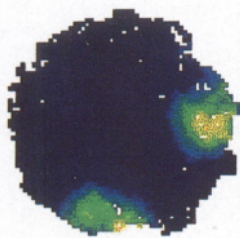
Additional Place Field

Loss of Place Field

FIRST RANDOM

DIRECTED SEARCH

SECOND RANDOM



B

Figure 8. Examples of the change in place field location with the shift in the task demand. The firing rate scale was held consistent for each cell across the different tasks. *A*, Examples of shift of place field, additional place field, and loss of place field when the tasks change from the random search to the directed search. *B*, Place fields from two additional rats that were trained on a sequence of three trials, on which the first and third were random, and the second was directed. Note that the place fields in the second random search session return to their original locations.

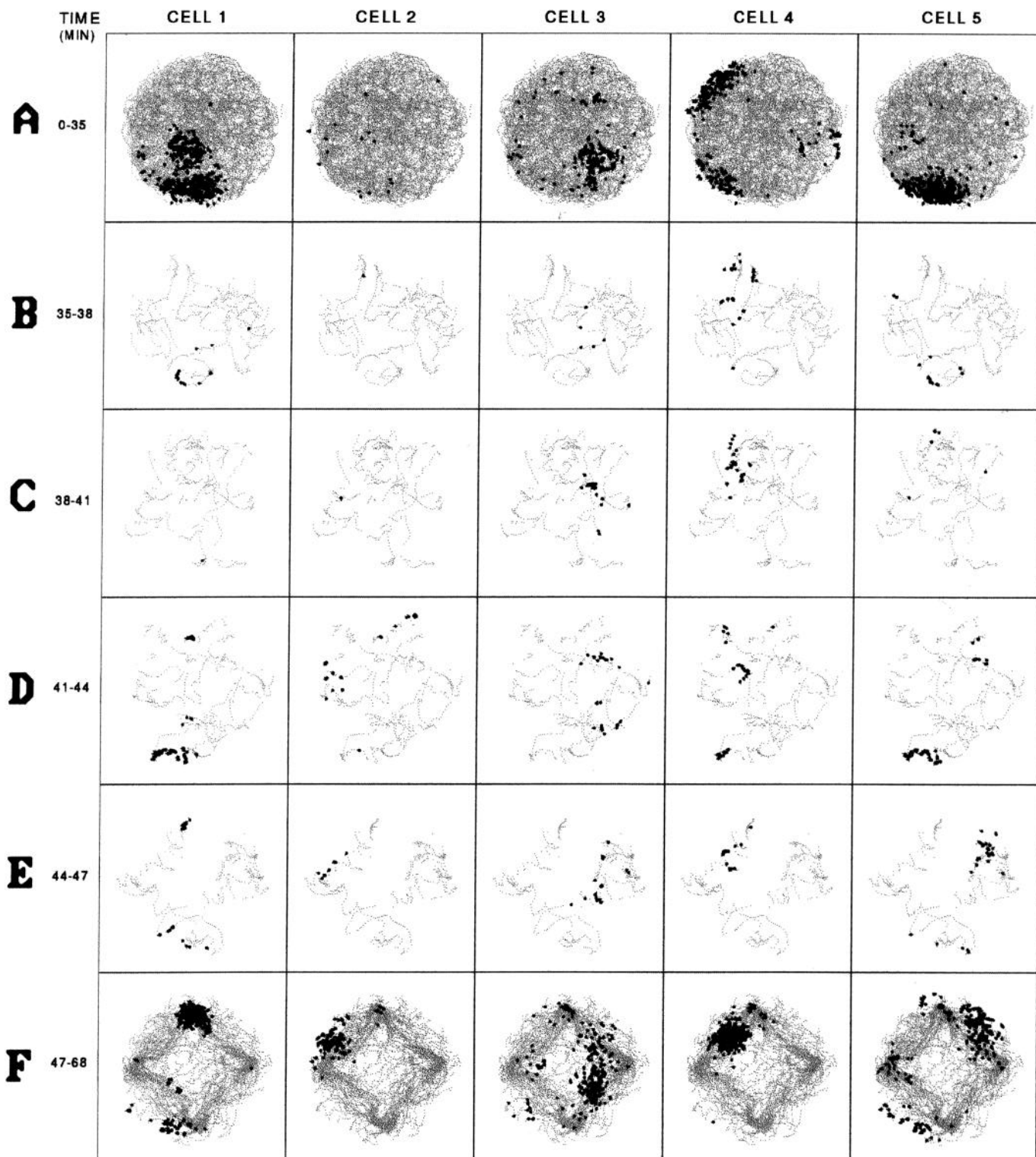


Figure 9. Examples of 5 simultaneously recorded place cells (*columns*) during the initial session in which the rat learned the directed search task. Firing of the cell is represented as a *black spot* and the animal's trajectories are depicted as *gray lines*. *A*, The first 35 min of the session, during this time the animal performed the random search task. *B–E*, Consecutive 3 min periods encompassing the time it took the animal to learn the new task. *F*, Last part of the recording session, animal is performing the directed search task. Note the change in the animal's behavior (*gray lines*) as he learns the new task. The search pattern progresses from one covering the entire surface of the platform to one restricted to a square search pattern. Also note that all changes in place fields occurred 6–9 min into the training period (*D*), and that while four of the cells seemed to be affected by the change in task, one cell was not (cell 3).

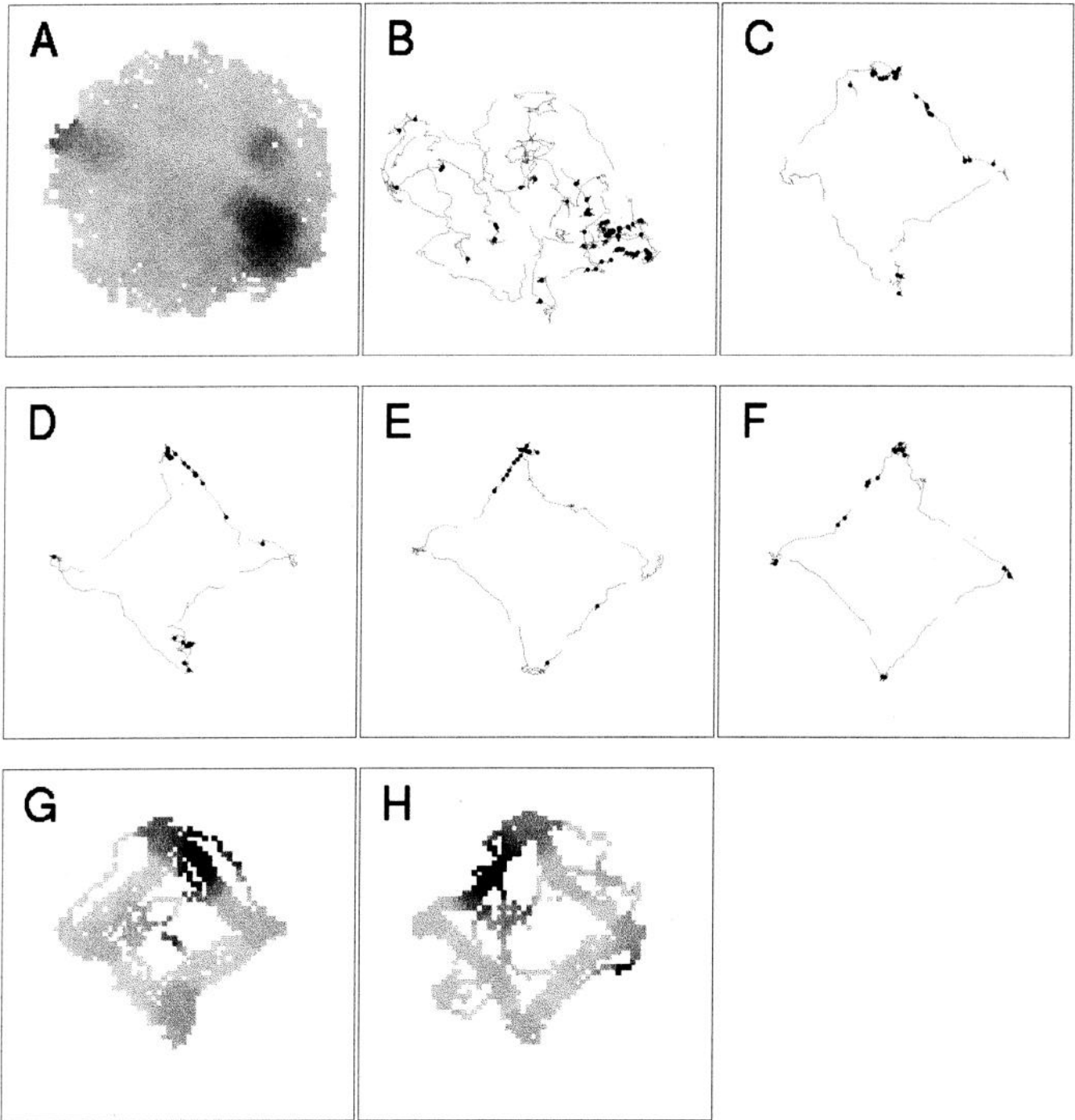


Figure 10. Time sequence of the changes in the location of a place field in conjunction with the change in behavioral task in a rat that had received prior training on both tasks. *A*, Mean firing rate of the cell during all of the random search task (*black* = 5 Hz). *B*, Firing of the cell during the last minute of the random search task. Firing of the cell is represented as a *black spot* and the animal's trajectories are depicted as *gray lines*. Note the place field in the southeast region of the platform. *C* and *D*, Firing of the cell during the first two counterclockwise directed searches. Note how robustly the cell fires in its new field (approaching northern region of platform), even immediately after the change in task (*C*). *E* and *F*, Firing of the cell during the first two clockwise directed searches. *G* and *H*, Mean firing rate of the cell during all of the directed search task, for both counterclockwise (*G*) and clockwise (*H*) motions (*black* = 5 Hz).

Place fields change with task

On both radial maze and platform, the place cells were recorded continuously as the rats performed the two behavioral tasks on the same apparatus, first the random and then the directed search for food. Changing the task resulted in about one third of the place fields changing location, and the change was rapid, par-

alleling the change in behavior. When both the task and apparatus were changed within the same room (Experiment 5), almost all place fields changed. In conjunction with previous research, these data contribute to the conclusion that hippocampal place cells are more sensitive to the behavioral context than to alterations in other parameters of the environment. Thus, when

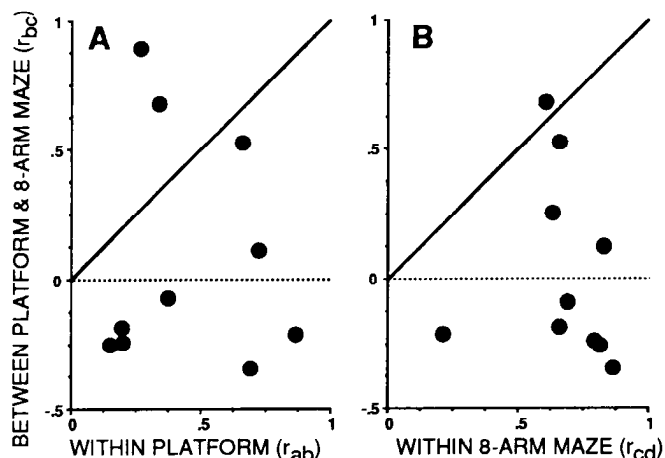


Figure 11. The correlation of spatial firing for each cell, within and between, the two apparatus. Correlations were calculated by dividing the total recording session into four parts: first half of the platform (*a*), second half of the platform (*b*), first half of the 8-arm maze (*c*), second half of the 8-arm maze (*d*). *A*, Comparison of the correlation of firing on the platform (*ab*) to the correlation between the platform and the 8-arm maze (*bc*). *B*, Comparison of the correlation of firing on the 8-arm maze (*cd*) to the correlation between the platform and the 8-arm maze (*bc*). As can be seen almost all cells had different firing patterns on the two apparatus (points falling below the 45° angle), unlike the result of changing only the behavioral task (Fig. 7) which resulted in a much smaller proportion of place fields changing their fields.

performing a constant task, place fields have been shown to be relatively stable over months (Best and Thompson, 1984), despite the removal of visual stimuli (O'Keefe and Speakman, 1987; McNaughton et al., 1989; Quirk et al., 1990; Markus et al., 1994a), and even after the inclusion of additional traversable space (Wilson and McNaughton, 1993). Conversely, the present findings and previous studies show that place field locations change when recordings are made on different apparatus in a given environment (O'Keefe and Conway, 1978; Muller and Kubie, 1987) or in conjunction with changes in the behavioral task or location of reward on the same apparatus (Breese et al., 1989; Wiener et al., 1989; Fukuda et al., 1992).

Place fields during learning

Place cells were recorded during the initial session in which the rats were first taught the new directed search task. Although the data are limited, they indicate that new place fields emerge in conjunction with the learning of the new task. The increase in directionality found on the directed search task (on the platform) was mostly due to new directional place fields emerging in the directed task, rather than a conversion of nondirectional place fields to directional place fields. This suggests the possibility that the new cells might, in fact, represent task-dependent behavioral variables such as, for example, distance from a reward site, a notion that partly overlaps the "attention" and "frame of reference" hypotheses discussed above.

In conclusion, hippocampal place fields are more directionally dependent when the animal is planning and/or following a specific route than when it is engaged in quasirandom foraging, involving erratic changes in the distance and direction of motion. This directionality may reflect the encoding by some cells of specific behavioral aspects or events of the task, or may be a secondary consequence of the manner in which the animal uses landmarks or points of reference as it navigates through the en-

vironment during different behavioral tasks. The latter hypothesis predicts that different place fields will emerge in the same location in tasks in which the animal is constrained to behave similarly in the same location, but in which its frame of reference or focus of attention is altered in that location on different trials.

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