Research report

Subicular cells generate similar spatial firing patterns in two geometrically and visually distinctive environments: Comparison with hippocampal place cells

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Abstract

Cells in both the hippocampus and the subiculum show location related firing patterns, so that the momentary firing rate of a cell is related to the spatial location of a freely moving rat as it navigates in an environment. Since the subiculum receives a strong anatomical projection from the hippocampus, it seems possible that the subicular cell spatial patterns are simply driven by the spatial signals from hippocampal place cells. Data presented here, however, suggest that the two areas code space in fundamentally different ways. Here, spatial firing patterns of individual hippocampal and subicular cells were studied as rats navigated in two different environments. The two chambers were a cylinder and a square, of equal area. For some rats the two chambers were painted to have similar visual stimulus characteristics, while for others, the two were very different. The subicular cells showed very similar firing patterns in the two chambers, regardless of whether they were visually similar or different. In contrast, as predicted based on the findings of earlier studies, hippocampal place cells showed different patterns in the two (again, regardless of their visual similarity). These results suggest that the subicular cells have the ability to transfer a single, abstract spatial representation from one environment to another. This pattern is stretched to fit within the boundaries of the current environment. Thus, the subicular cells seem to provide a generic representation of the geometric relationships between different locations in an environment. It seems possible that this representation may contribute to some navigational abilities exhibited by animals, such as dead reckoning, and novel route generation in unfamiliar environments. In contrast, it appears that hippocampal place cells provide a spatial representation which is unique for each environment and which is strongly influenced by the exact details and overall context of the situation.

Keywords: Path integration; Hippocampal single cell; Cognitive map; Hippocampal formation; Spatial behavior; Navigation

1. Introduction

Cells in several different regions within the hippocampal formation show location related firing patterns (e.g., [1–7]). This means that when an animal freely navigates through a static environment, each of these cells will have one or more regions within the environment where it fires at relatively high rates, while there will be other regions where the cell fires at lower rates, or is silent. Thus, the cells seem to provide a moment-to-moment indication of the animal's current location, and cells of this type are thought to play a role in the navigational abilities of the animal (e.g. [8]).

The best studied of these cells are the hippocampal place cells (e.g. [4,9,10]). These cells are located in the hippocampus proper, and they have the property that they are silent much of the time, but may show one (or, rarely, more than one) region within any one environment in which they fire at a high rate (see Fig. 4 for examples).

The hippocampus sends a strong anatomical projection to the adjacent subiculum (e.g. [11–13]). Not surprisingly, subicular cells also show location related firing patterns [1,6]. These spatial patterns of cells in the subiculum are somewhat different from those of the hippocampal place cells, however. The subicular cell
signals tend to be more distributed, so that any one cell is likely to fire throughout much, or all, of the entire environment, but show a characteristic pattern of regions with relatively high average rates, and other regions with relatively low rates (see Figs. 2, 6 and 8).

These findings suggest the possibility that the subicular cell patterns result from convergent input from the hippocampal place cells, so that they simply provide a more distributed version of the hippocampal place cell signal. One preliminary finding, however, has suggested that it may not be as simple as this, and that, in fact, the subicular signal may be fundamentally different from the hippocampal place cell signal [6]. In that study, subicular cell activity was examined as animals navigated in a gray, cylindrical chamber which had a single, white cue card located along one portion of the wall [10]. For five of these cells, the pattern in the rectangle was remarkably similar to that in the cylinder, so that it appeared to be a 'rubber sheet' transformation of the cylinder spatial pattern. Thus, it appeared that many of the subicular cells showed nearly identical patterns in two different environments.

This finding is very different from what has been observed for hippocampal place cells (e.g. [14-17]). When place cells are recorded in more than one environment, they do not show similar place fields from one to the next. A place cell which shows a clear, robust place field in one environment may show no activity, or a completely different field in another environment, and there seems to be no way of predicting a place cell's behavior in one environment, based on its behavior in another.

Interestingly, spatial cells in the entorhinal cortex (with which the subiculum is reciprocally connected) also show similar spatial patterns when recorded in visually very similar cylindrical and square environments [5].

Thus, the Sharp and Green [6] preliminary results suggested that the subicular cells were behaving in a way which was fundamentally different from the hippocampal place cells, and, perhaps, more similar to entorhinal cells. The subicular cells appear to have an ability to transfer an overall, abstract spatial representation from one environment to the next, while the hippocampal cells appear to unpredictably generate an entirely new pattern in each environment. There were, however, some methodological aspects of the Sharp and Green [6] study which allowed for other possible interpretations. First, in that study, the animals were transferred directly from the cylinder to the rectangle for cell recording. In contrast, in the previous work on hippocampal place cells, animals were, apparently, returned to the home cage between recording sessions in each environment. Thus, it seemed possible (though not likely) that hippocampal place cells would show similar patterns in two environments if the animal were directly transferred between the two.

Second, both chambers used for subicular cells in the Sharp and Green [6] study were gray, high walled enclosures with a single white card. Thus, they were similar in many ways, so that it was possible that the cells simply could not discriminate between the two. It seemed possible that if hippocampal place cells were tested under these conditions, they might show similar generalization between the two environments (although earlier results had suggested this would not happen [5]).

This study was designed to directly compare the behavior of subicular cells and hippocampal cells, studied under identical conditions, in the same set of animals. Rats were bilaterally implanted with electrodes for chronic, single cell recording in either the subiculum or hippocampus. (Some animals were implanted with one electrode in each structure.) Cell activity was recorded, first, while animals locomoted in a cylindrical chamber, and then, while animals locomoted in an adjacent square apparatus, of equal area, (into which they were directly transferred from the cylinder). For some of the animals, the cylinder and square were painted with identical patterns, so as to appear similar, while for the remaining animals, the two chambers were painted to look very different. This enabled a test of the effects of similarity of the two environments on both the hippocampal and subicular cell populations.

In addition to recording from hippocampal place cells and subicular cells, data from hippocampal theta cells [18] were also included. These cells constitute a useful comparison population for the subicular cells, since theta cells are also tonically active, and they have been shown to evidence a modest spatial signal [9,19].

The results indicate that most subicular cells show similar firing patterns in the cylinder and the square, regardless of whether the two chambers are similar in appearance, while (as predicted based on the earlier work mentioned above) hippocampal cells did not show similar firing patterns.

2. Materials and methods

2.1. Experimental subjects

The subjects were 18 female, Long-Evans rats, weighing 200–250 gm at shipping. The animals were housed singly upon arrival, and had a 12 h on (8 : 00 a.m.–8 : 00 p.m.)/off, light/dark schedule.

2.2. Recording chambers

The recording chambers used for single cell data collection are shown in Fig. 1. Two cylindrical chambers
Recording Chamber Pairs

![Diagram of recording chamber pairs]

Fig. 1. Schematic overhead view of the four pairs of recording chambers. Each animal was assigned to one of the four pairs. The inner wall of each section of each apparatus was painted with either horizontal or vertical black and white stripes, or with a solid color (white, black, or gray), as indicated. The chambers which contain two striped walls are designated striped (S), while those with all solid colors are designated plain (P). Each square and cylinder are 4160 cm in area, with 51 cm high walls. Each of the S-S and P-P pairs were designed to provide two recording environments which were identical except for their geometry (cylinder versus square), while the S-P and P-S pairs were designed to provide two very different environments. Each recording session consisted of a 20-min period in the cylinder, followed immediately by a 20-min period in the adjacent square.

and two square chambers, each 4160 cm in area, with 51 cm high walls, were used.

One cylindrical chamber, designated striped (S), was painted with (1) a set of vertical black and white stripes (each stripe is 3.5 cm wide) which covered 90° of the inner wall, and extended from the top of the wall to the bottom; (2) an adjacent set of horizontal black and white stripes (also 3.5 cm wide) which covered 90° of the inner wall; (3) an adjacent 90° segment which was painted solid black; and (4) a solid white section. One of the square chambers (also designated S) was painted with an identical pattern, so that each of the four inner walls had a striped or solid surface which matched that of the corresponding segment of the cylinder. Thus, these two chambers were made to be as similar as possible, except for their geometry.

The other cylinder, designated plain (P) was painted with four solid, 90°-wide sections on its inner wall. One white section was located opposite to a solid black section, while two gray sections were alternated in between these. The remaining square (also designated P) was similarly painted with four solid colors, so that each wall matched the corresponding section of the P cylinder. Thus, the two P chambers were designed to be identical, except for their geometry.

During any one recording session, one cylinder and one square were placed in the curtained enclosure used for recording (see below). They were located adjacent to each other, and at the same rotational orientation (e.g., vertical stripes toward the north for both chambers) as indicated in Fig. 1. Each session consisted of an initial period of recording in the cylinder, followed immediately by a period in the square. The set of S and P chambers allowed for four unique cylinder-square pairs. The S-S and P-P pairs allowed a test of whether cells would behave similarly in two chambers which were visually similar, while the S-P and P-S pairs allowed a test of firing pattern similarity in two visually different chambers. Each animal was assigned to just one of these pairs for all recording sessions. That is, no animal was exposed to more than one pair during the course of the experiment.

The floor of each chamber consisted of a flat, gray board, which could be wiped clean after each session. The cylinder-square pair was surrounded by a circular, black curtain which formed an enclosure 175 cm high and 137 cm in diameter at its widest, and then tapered off above this to a diameter of 57 cm, and a height of 213 cm. Illumination was provided by two 75 watt overhead lights (located in an inverted position above the curtain), which spread a diffuse, uniform light over the apparatus floors. Also located above the curtain was an automatic dispenser for the remote-controlled delivery of food pellets. The pellets were released through a tube, the end of which could be positioned directly over the center of either the cylinder or the square. Pellets dispensed in this way dropped to a position near the center of each apparatus floor and scattered to random locations throughout the area of the apparatus.

The recording chambers were located in a room separate from the recording equipment. A speaker located centrally above the curtained enclosure delivered a constant white noise, designed to mask any uncontrollable auditory cues provided by the laboratory environment.

2.3. Behavioral training

Prior to training, the rats were placed on a food deprivation schedule with which they were reduced to
80% of their ad lib weight through limited daily feeding. They were then trained to search for 20-mg food pellets (BioServe, Frenchtown, NJ) that were dispensed (see above) into the recording chamber at pseudorandom locations, at approximately 15-s intervals [10]. Each animal was trained in the cylinder in which it would later receive recording sessions. Animals did not experience the square chambers during training. To begin each daily 15 min training session, each rat was placed into the cylinder at a fixed angular location, along the lower edge of the cylinder (as it is viewed in Fig. 1). A total of six training sessions were given; for the first three sessions animals chased pellets in the chamber in groups of two to three, while the last three were administered individually. During this period rats developed a pattern of nearly constant locomotion that lasted throughout the sessions and resulted in the rat covering the entire cylinder floor repeatedly throughout the session, in an apparently homogeneous fashion.

2.4. Electrode implantation

The surgical techniques have been described elsewhere [6]. Briefly, after training, two driveable microrecording electrodes (one per hemisphere), consisting of six wires each, were chronically implanted. The six separate wires, cut at an approximately 45° angle, consisted of formvar-insulated, 25-μm diameter, nichrome wire (California Fine Wire Co., Grover City, CA). Prior to surgery, animals were anesthetized with a 0.18 cc injection of 65 mg/ml pentobarbital, and supplemental doses were given during surgery, if necessary, to maintain deep surgical anesthesia. The electrodes were stereotaxically placed 1.75 mm below the brain surface, so that their tips were well above the cell layers intended for study, and could be gradually lowered through these layers after recovery. Sterile petroleum jelly was applied to the exposed brain surface, as well as the guide cannula surrounding the recording wires. The electrodes and securing screws were then cemented permanently to the skull by dental acrylic (Turotech, Wynnewood, PA). One of the securing screws was equipped with a connecting pin which protruded out from the dental acrylic, so that it could be used as a grounding wire during recording. Also cemented into the acrylic was a small connector, used for later attachment of the recording cable.

Six of the animals whose data were included in the study were implanted with one electrode aimed at the hippocampus (at 4.5 mm posterior and 3.7 mm lateral to Bregma), and the other aimed at the subiculum (6.2 mm posterior and 3.1 mm lateral to Bregma), with left versus right hemisphere counterbalanced for this variable.

The remaining 12 animals were implanted with both electrodes aimed at the subiculum. This extra number of subicular electrodes was necessary because it has proven much more difficult to isolate cells in the subiculum than in the hippocampus (see Section 2.5 for discussion).

2.5. Unit isolation and data collection

After recovery from surgery, animals were given screening/recording sessions during which the activity from the electrode wires was sampled while the rat performed the pellet-retrieving task in the cylinder. If no single cell activity was present, the electrode bundles were lowered slightly (between 0.022 and 0.044 mm) and the wires were checked again (up to four times of repeated lowering and checking per day). Upon isolation of activity from a single cell(s), a recording session (see below) was initiated. Two wires could be recorded from at the same time, and the signal from each was passed first through a field-effect transistor in source-follower configuration that was mounted on the pin attached to each electrode wire. This signal then passed through a cable (affixed to the connector on the animal’s head) to an amplifier (gain between 5000 and 20 000) and filter (300 Hz, high pass, and 10 kHz, low pass), and then to a computer, for automatic data collection. The software used for data collection and cell discrimination (Brainwave Corporation) collected an epoch of the digitized analog signal for every event from the amplifier which exceeded a user-set threshold. These events were then separated into bins, each of which captured the waveforms generated by spikes from one individual cell (see discussion below), through a cluster analysis routine which utilized information from eight different parameters extracted from each waveform. In this way, it was sometimes possible to collect data from more than one cell simultaneously. Each event, along with a timestamp, and indication of which bin it belonged to, was automatically stored.

As mentioned above, it has been our (e.g. [6]) experience that it is extremely difficult to obtain electrical isolation of single cells in the subiculum. It is not clear why this is true, although the difficulty may result from the fact that the cells in the subicular principle cell layers are somewhat close together, and many of the cells show high, tonic firing rates in the freely moving animal [6]. Thus, the electrical signal from electrodes placed in the subiculum often consists of large amplitude (100–300 μV), multiple cell activity, with no characteristic, individual waveform(s) which are clearly discriminable. In an attempt to improve this situation, we have, in the past, made numerous attempts to record from these cells using multiple wire electrodes, such as the stereotrode and tetrode [20,21]. However, these electrodes have not improved our ability to record cells in the subiculum (although, like others, we find them to be superior to single wire electrodes for work in the
hippocampus). On the contrary, using the multiple wire electrodes we are only able to attain multiple unit activity, and it is almost never the case that individual waveforms can be distinguished. It is not clear why this counterintuitive finding should be the case. One possibility is that the greater circumference of the multiple wire electrodes makes it more difficult for any one of the conductors to slide in close enough to any individual cell to allow its waveform to predominate in the signal. Whatever the explanation, we have found it impossible to obtain single cell data in the subiculum using multiple wire electrodes.

In contrast, using single wire electrodes, it is occasionally possible to obtain waveforms which are clearly distinguishable from the multiple unit background. To be acceptable for inclusion in the data set, an individual, characteristic waveform must show an amplitude which is at least twice the amplitude of the background multiple unit activity. Indeed, the waveforms are often three to five times the background level. In addition, interspike interval histograms are made for each cell, and these must show that the cell exhibited a refractory period of at least 1 to 2 ms between spikes. We reason that for the (in many cases) tonically active cells recorded here, it would not be possible for this refractory period to be exhibited by a multiple unit recording.

The animal's moment-to-moment position in the chambers was also sampled continuously throughout each session. For this, a video camera located above the chambers monitored the location of two light-emitting diodes attached to the animal's head. One of these lights was toward the front, while the other was toward the back of the animal's head. The video signal was sent to a camera tracking system (Brainwave Corporation) which extracted a digitized representation of the location of each of the two lights for transmission to the computer at a rate of 60 Hz. This information was timestamped and automatically stored. During subsequent analysis, the animal's location at each sample time was calculated as the midway point between the front and rear headlights.

2.6. Recording sessions

To begin each screening/recording session the animal was carried into the curtained enclosure (surrounding the recording chambers) in an enclosed carrying cage. The cage was then placed on the floor next to the cylinder, the top of the cage was removed, and the animal was attached to the recording cable while it was held on the experimenter's shoulder. (It should be noted that the top of the square was covered over with a black cloth during this time, so that the animal could not get an overview of the square.) The animal was then placed down into the cylinder in a fixed location along the lower edge of the wall (as it is viewed in Fig. 1). The experimenter then picked up the carrying cage, and immediately exited the curtains, and began checking the electrode wires for cell activity.

Upon isolation of single cell activity, a recording session was begun. Each session consisted of an initial 20-min-long recording phase in the cylinder (S or P, as designated for that animal), and a subsequent 20-min phase in the square (S or P, as designated for that animal), throughout both of which the animal constantly performed the pellet-chasing task described above. For the transfer between the chambers, the animal was simply lifted from the cylinder, and placed into the square, along the middle of the left wall (as it is viewed in Fig. 1). It was also necessary, at this time, to change the location of the pellet dispenser tube, so that it went from being positioned above the cylinder, to a position above the square.

Occasionally, recording phases were ended somewhat prior to the full 20 min, due to a technical problem, such as tangling of the recording cable.

To end a screening/recording session, the experimenter entered the curtained enclosure with the carrying cage and placed it on the floor, picked up the animal and detached it from the recording equipment, and replaced it into the cage for return to the colony room.

Sometimes, a third period was added to the recording session, in which the animal was transferred back into the cylinder, for another 20-min recording phase. This enabled a check for stability of the cell isolation over the session, and this was done for 10 hippocampal cells.

This return to the cylinder manipulation was also conducted for one subicular cell which was highly spatial, and was recorded over two days. On both days, the rat was returned to the cylinder after the square, but on one of these days the cylinder was first rotated counterclockwise by 90°. This enabled a test for whether the subicular cell firing pattern would rotate along with the stimuli on the walls, and, thus, tested for whether the subicular cells receive information about these stimuli.

2.7. Experimental design

Each animal was randomly assigned to one of the four recording chamber pairs shown in Fig. 1, within the constraint that approximately equal numbers of animals be assigned to each pair. Each cell encountered during screening was recorded in a session, as described above. In cases in which a cell was maintained for more than one day, repeated sessions were conducted on the same cell.

Animals were screened on an approximately daily basis, until the electrodes were eventually pushed below the layer intended for study. No animal received more than one recording session per day.
2.8. Data presentation and analysis

2.8.1. Firing rate maps

In order to visualize the spatial firing patterns, the time of occurrence for the spikes of a given cell, along with the position data, were used to construct a firing rate map for each cell [10]. For this, the cylinder was divided into 2.9 by 2.9 cm pixels, and the total amount of time spent in each pixel, along with the total number of spikes which occurred while the animal was in that pixel, were used to calculate an average rate for each. The relative rate in each was indicated in the map using a gray scale, the value of which was chosen based on the mean and standard deviation of the pixel rates for that cell (see [6]). Darker colors correspond to higher rates. A diagonal line was used to indicate pixels which the animal visited, but in which the cell did not fire. A blank pixel means that the animal did not visit that location during the session.

2.8.2. Rate

The overall rate (in Hz) for each cell was calculated by dividing the total number of spikes in the session by the total session time (in s).

2.8.3. Spatial coherence

This measure provides one way of quantifying the strength of the spatial signal for a cell, and is very similar to the spatial coherence measure developed by Kubic et al. [19]. The measure has been described elsewhere [6]; briefly, it consists of a spatial autocorrelation, in which a correlation coefficient is calculated between the rate for each pixel, and the average rate of the eight surrounding pixels. Thus, high, positive values for r result if the rate for each pixel can be better predicted by knowing the rate of the neighboring pixels. This means the r value serves as a measure of any consistent, graded, location-related variations in rate.

2.8.4. Transformation of square firing rate maps into circular firing rate maps

To facilitate visual comparison and statistical analysis (see below) of firing patterns in the cylindrical and square chambers it was necessary to transfer the data from the square onto a circular coordinate system (see right column of Figs. 2-6 and 8). For this, the head position data from each session were transformed in the following way. First, each position value from the original head position data (collected through the camera tracking system) was imagined to constitute an individual point on the perimeter of one member of a series of imagined concentrically organized squares (squares within squares) which, together, covered the square chamber floor. Then, the sine and cosine of that point (in relation to a Cartesian coordinate system centered over the chamber floor) were used to place the point on a circle of equal area to that of the square from which the point originally came. Thus, this resulted in an imaginary set of concentrically organized circles which, together made a circular region equal in area to the square chamber floor. This new series of head position values was then used to construct a circular firing rate map.

2.8.5. Correlations between firing rate maps

The main question of interest here is the extent to which the cells exhibited similar firing patterns in the cylinder and the square. To address this question quantitatively, the firing rate maps from the cylinder and square phases of each session were subjected to a cross-correlation analysis. For this, it was necessary to first transform the firing rate map from the square into a circular pattern, as described above, so that the two maps would have approximately matched sets of pixels. Then, a pixel-by-pixel correlation was conducted between the cylinder and transformed square maps. The resulting $r^2$ value served as an index of the similarity of the spatial firing patterns in the two chambers.

2.8.6. Field size

A measure of the percentage of the chamber area over which a cell fired was calculated as the percentage of total pixels (see above) in which the firing rate was greater than zero.

2.9. Histological examination and reconstruction of cell location

After recording, animals were perfused transcardially under deep anesthesia with a formyl saline solution. Prior to this a small current (30 $\mu$A × 5 s) was passed through one wire of each electrode, in order to mark the location of the electrode tips. The brains were then sectioned in the coronal plane at 40 $\mu$m intervals, mounted, and stained with both Cresyl violet and Prussian blue.

3. Results

3.1. Cell sample

Data were collected from a total of 28 hippocampal place cells in seven rats. All of these place cells sometimes showed a bursting, or complex spike [18] firing pattern, and showed one or more distinct place fields in either the cylinder or square, or both. The average firing rate (in the cylindrical chamber) for these cells was 1.06 Hz ($\pm 0.18$), the average spike width (from the initial, negative deflection from baseline to the subsequent return to baseline) was 355.88 $\mu$s ($\pm 10.6$), and the average spike amplitude (from peak to peak) was 365.00 $\mu$V ($\pm 41.67$). Note that since all the place cell
Fig. 2. Many subicular cells showed similar spatial firing patterns in the cylinder and the square. Firing rate maps (see Section 2: Materials and methods) depicting average firing rate as a function of location in the cylinder (left column) and square (middle column) for four subicular cells, each of which showed very similar spatial firing patterns in the two chambers. The right column shows the same data as in the middle column (recorded from the square), but remapped onto a circular coordinate system (see Section 2: Materials and methods). Note that one example has been chosen for each of the apparatus pairs (S-S, P-P, S-P and P-S). Many of the subicular cells showed this similarity of pattern between the two chambers, and the degree of similarity was not detectably influenced by whether the two chambers were similar (P-P or S-S) or different (S-P or P-S). The $r^2$ values for the pixel-by-pixel correlation between the cylinder (left column) and transformed square (right column) firing rate maps are, from top to bottom: 0.12, 0.25, 0.44 and 0.43. The spatial coherence values (for the cylinder rate maps) are, from top to bottom: 0.27, 0.88, 0.73 and 0.76.

Data were collected from just seven rats, this means that there were very few rats for each of the four recording chamber pairs (see Fig. 1). However, it should be noted that the two conditions in which the chambers were similar (S-S and P-P), as well as the two in which they were different (P-S and S-P) are conceptually identical, and so, can be considered together. This results in three animals in the similar (S-S and P-P) chamber condition, and four rats in the different (P-S and S-P) chamber condition.

Data were obtained from 12 cells (in four rats) which were identified as hippocampal theta cells [18], based on (1) high, tonic firing rate; (2) low spatial coherence values [19]; (3) theta-frequency modulation of firing rate; (4) correlation of high rates with locomotor behavior; and (5) short spike width. The average firing rate for these theta cells was 12.63 Hz ($\pm 1.37$), while the average spike width was 260.42 $\mu$s ($\pm 20.05$), and spike amplitude was 328.75 $\mu$V ($\pm 47.84$). Each of the four rats in which theta cells were recorded were from a
Fig. 3. Some subicular cells did not show similar patterns in the cylinder and square. Firing rate maps (see Section 2: Materials and methods) depicting average firing rate as a function of location in the cylinder (left column) and square (middle column) for four subicular cells which did not show similar spatial patterns in the two chambers. The right column shows the same data as in the middle column (recorded from the square), but remapped onto a circular coordinate system (see Section 2: Materials and methods). Note that one example has been chosen for each of the apparatus pairs (S-S, P-P, S-P and P-S). The $r^2$ values for the pixel-by-pixel correlation between the cylinder (left column) and transformed square (right column) firing rate maps are, from top to bottom: -0.03, -0.01, 0.17 and 0.11. The spatial coherence values (for the cylinder rate maps) are, from top to bottom: 0.36, 0.52, 0.54 and 0.44.

Data were collected from a total of 29 subicular cells in 12 animals. All except one of these cells fell into either the bursting, non-bursting, depolarized bursting, or theta cell categories, as described previously [6]. Unfortunately, there was only one animal for which cells were recorded in both the subiculum (one cell) and the hippocampus (two cells), and this reflects the greater difficulty of obtaining adequate waveform isolation for cells in the subiculum. (Recall that six of the animals were bilaterally implanted with one subicular, and one hippocampal electrode, while the remaining animals were bilaterally implanted with two subicular electrodes.) All remaining subicular cells came from animals which were bilaterally implanted with both electrodes in the subiculum. The average firing rate for theta cells in the subiculum was 37.19 Hz ($\pm 4.79$); the average spike width and amplitude were 209.17 $\mu$s ($\pm 10.83$) and 418.33 $\mu$V ($\pm 54.92$), respectively. The average firing rate, spike width, and amplitude for cells in the non-theta categories were 13.20 Hz ($\pm 3.72$), 349.58 $\mu$s ($\pm 22.66$) and 510.42 $\mu$V ($\pm 81.50$), respectively.
3.2. Many subicular cells showed similar spatial firing patterns in the cylinder and square

Fig. 2 shows four cells, recorded from the subiculum, which exhibited a clear similarity of the spatial firing patterns in the cylinder and the square. Note that one cell has been chosen from each of the four recording chamber pairs (see Fig. 1). Interestingly, there was no detectable effect of the similarity of the two chambers (P-P and S-S versus S-P and P-S) on this effect (see also Fig. 7 below). Note also that the spatial patterns retained approximately the same rotational orientation in the two chambers (but see exception below; Fig. 6).

Thus, for example, the cell in the third row showed a single, large region of relatively high firing, and this was located in the lower, left region of both the cylinder and square. As discussed below, this suggests that subicular cells may receive input from head direction cells [22] so that this rotational orientation is maintained as the animal travels into the square.

It should be noted that, although the cylinder and square firing patterns for each of these cells are quite similar, they are not identical. For example, the cell in the P-P condition (second row) shows tonic firing which covers most of the chamber in both the square and cylinder, as well as two separated regions of high firing.

Fig. 4. Hippocampal place cells did not show similar patterns in the cylinder and the square. Firing rate maps (see Section 2: Materials and methods) depicting average firing rate as a function of location in the cylinder (left column) and square (middle column) for four typical hippocampal place cells. The right column shows the same data as in the middle column (recorded from the square), but remapped onto a circular coordinate system (see Section 2: Materials and methods). Note that one example has been chosen for each of the apparatus pairs (S-S, P-P, S-P and P-S). The $r^2$ values for the pixel-by-pixel correlation between the cylinder (left column) and transformed square (right column) firing rate maps are, from top to bottom: 0.25, -0.20, -0.30 and -0.11. The spatial coherence values (for the cylinder rate maps) are, from top to bottom: 0.0, 0.73, 0.18 and 0.30.
Fig. 5. Hippocampal theta cells did not show similar patterns in the cylinder and the square. Firing rate maps (see Section 2: Materials and methods) depicting average firing rate as a function of location in the cylinder (left column) and square (middle column) for four typical hippocampal theta cells. The right column shows the same data as in the middle column (recorded from the square), but remapped onto a circular coordinate system (see Section 2: Materials and methods). Note that one example has been chosen for each of the apparatus pairs (S-S, P-P, S-P and P-S). Hippocampal theta cells did not show highly spatial firing patterns in general, and did not show similar patterns in the cylinder and square. The $r^2$ values for the pixel-by-pixel correlation between the cylinder (left column) and transformed square (right column) firing rate maps are, from top to bottom: 0.17, 0.04, -0.12 and -0.20. The spatial coherence values (for the cylinder rate maps) are, from top to bottom: 0.32, 0.21, 0.25 and 0.44.

along the edges of each chamber. However, these two regions are slightly closer together in the cylinder than in the square. Another example of a slight change in position can be seen for the cell in the S-S condition. In this case, the single, spotty firing pattern was slightly lower and to the right in the cylinder than it was in the square.

The right-most map for each cell shows the data from the square remapped onto a circular coordinate system (see Section 2: Materials and methods). This version of the square chamber data was used for the cross correlation analysis of the cylinder and square rate maps (see Section 2: Materials and methods).

Finally, though not examined formally, it was observed that the subicular patterns in the square were present even during the first moments of the animal's first exposure to the square. That is, for example, a cell which exhibited high rates along the north wall of the cylinder, also exhibited high rates along the north wall of the square, even on the animal's very first visit to that location.
3.3. Some subicular cells did not show a similar spatial pattern in the cylinder and square

Fig. 3 shows four cells which did not show a detectable similarity of the spatial pattern for the two chambers. In the case of the cell shown in the upper row, this resulted from the fact that the cell simply did not have a discernable spatial pattern in either apparatus. The remaining cells, however, did show some spatiality in both chambers, but the details of the pattern differed. Thus, for example, the cell in the third row showed a region of elevated firing in the lower, right region of the cylinder, and this was not present in the square.

It should be noted, however, that even though the cylinder and square firing patterns differ in detail for these cells, there is still a similarity in the global properties of the cells across the two chambers. Thus, as discussed below (see Fig. 7) each cell showed a nearly identical firing rate in the two chambers. Also, all the cells shown here were tonically active in both chambers, and all cells showed a similar spatial coherence value in both chambers (see Fig. 7).

3.4. Hippocampal cells did not show similar spatial patterns in the cylinder and square

Fig. 4 shows the data from four typical hippocampal place cells. Each cell shows firing characteristics which are clearly different in the two chambers. Each of the cells in the upper three rows showed a clear place field in only one of the two chambers, while the lower row shows a cell which had a similar field in the two chambers, but for which the location of the field was different in the two.

Fig. 5 shows the data from four typical hippocampal theta cells. As reported in previous studies [9,19] these cells did not, in general, show a strong spatial firing pattern in either apparatus. The weak spatial patterns which could be discerned, however, were different in detail in the two chambers.

3.5. One subicular cell appeared to rotate its spatial firing pattern from the cylinder to the square

Fig. 6 shows an unusual cell, located in the subiculum, which, when recorded in the square, appeared to show a rotated version of the spatial pattern exhibited in the cylinder. Thus, in both chambers the cell shows a tonic firing pattern, so that the cell is active throughout the area of the apparatus. Also, in each chamber there is a large, compact region of elevated firing along the perimeter of the apparatus, and an additional, small region of elevated firing along the edge, in a location approximately 180° away from the first region. Thus, the two patterns are remarkably similar, but rotated in relation to each other.

This was the only subicular cell which appeared to rotate its pattern. Surprisingly, this cell was from an animal in the S-S group. It might have been expected that the salient, visually similar patterns which are presumably provided by the S cylinder and S square would have stabilized the orientation of the cell, but this was not the case.

3.6. Summary and statistical analysis of effects

Fig. 7 shows a summary of several measures of the similarity of firing characteristics in the cylinder and square for all cells included in the study.

The top row of Fig. 7 shows the results of the pixel-by-pixel cross correlation analysis of the cylinder and transformed square (see Section 2: Materials and methods) firing rate maps for each cell. These $r^2$ values are displayed as a function of the spatial coherence value for the cell, when recorded in the cylinder. This method of display was chosen so that the strength of the spatial correlation between the two maps (from the cylinder and square) could be judged in relation to the baseline 'spatiality' of the cell. Thus, for example, a cell which does not have a strong spatial signal in the cylinder
Fig. 7. Summary diagram to illustrate similarity of firing characteristics in the cylinder and square for subicular, but not hippocampal cells. A different symbol is used for the data from each recording apparatus pair (see Fig. 1). , S-S; , P-P; , S-P; , P-S. Top row: $r^2$ value for the pixel-by-pixel correlation between the cylinder firing rate map and the transformed square firing rate map for each cell, plotted as a function of spatial coherence in the cylinder. Second row: spatial coherence value in the square plotted as a function of spatial coherence value in the cylinder for each cell. Third row: Average firing rate in the square plotted as a function of average firing rate in the cylinder for each cell. Last row: Field size (% of apparatus area in which the cell showed a non-zero firing rate) in the square plotted as a function of field size in the cylinder for each cell.

could not be expected to show a strong correlation of spatial signals in the cylinder and square.

The recording chamber pair (Fig. 1) for each cell is indicated in Fig. 7 by the symbol used to plot it, so that black symbols are for pairs which were similar (black squares for S-S; black circles for P-P), and the open symbols are for the dissimilar pairs (open squares for S-P; open circles for P-S).

Examination of this display for the subicular cells (upper, left panel) indicates that most subicular cells showed a cross-correlation value well above zero, and that this value tended to be higher for cells with a higher spatial coherence value. (It should be noted that one of the two apparently aberrant values, located at $r^2 = -0.18$ and spatial coherence $= 0.85$ was generated by the cell shown in Fig. 6. Thus, although this cell showed highly similar patterns in the cylinder and square, the fact that they were rotated in relation to each other resulted in an unusually low $r^2$ value. The other aberrant value, located at $r^2 = -0.22$ and spatial coherence $= 0.67$, was from an unusual subicular cell, which was highly spatial, but showed truly different spatial patterns in the cylinder and square.) The average $r^2$ value for the cross correlation for subicular cells was 0.18 ($\pm 0.04$). It can also be seen that the similarity of the recording chamber pair did not detectably influence
the $r^2$ values (as can be seen by comparing the black versus open symbols).

Examination of this same display for the hippocampal place cells (upper, middle panel) shows that the $r^2$ values for the cross-correlation analysis were centered around zero, so that the average $r^2$ value for the place cells was 0.004 ($\pm 0.018$). (It should be noted that the three hippocampal place cells which showed near zero spatial coherence values in the cylinder were from cells which had a place field only in the square.) A t-test for the difference between the $r^2$ values for the subicular cells and the hippocampal place cells was significant ($df=55$, $t=4.4$, $P<0.001$). This finding confirms the impression provided by Figs. 2 and 4, that subicular cells and hippocampal place cells differ in the degree to which their spatial firing patterns are similar in the square and cylinder. Also, there was no tendency for higher spatial coherence values to be associated with higher $r^2$ values in the hippocampal place cells.

The upper, right panel of Fig. 7 shows this same analysis for hippocampal theta cells. These cells show generally lower spatial coherence values than the hippocampal place cells, as reported by earlier studies [9,19]. Also, they generally show low $r^2$ values for the cross correlation analysis, (average $r^2= -0.058$, $\pm 0.03$) indicating that they are like hippocampal place cells in showing no detectable similarity of spatial firing patterns between the cylinder and the square.

The second row of Fig. 7 shows spatial coherence values in the square plotted as a function of spatial coherence values in the cylinder, for each of the cell categories. It can be seen that there is a linear relationship for these values for the subicular cells. A test for the strength of the correlation between the cylinder and square spatial coherence values for the subicular cells yielded $r=0.59$ ($df=28$, $P<0.005$). This suggests that the general 'spatiality' of any one cell is similar in the two environments. This is compatible with the fact that the subicular cells generally tend to show similar spatial patterns in the two environments (Fig. 2). There is no such relationship between spatial coherence in the cylinder and square for the hippocampal place cells ($df=27$, $r= -0.02$, $P>0.05$) or theta cells ($df=11$, $r=0.036$, $P>0.05$).

The third row of Fig. 7 shows average overall firing rate in the square plotted as a function of overall firing rate in the cylinder. This relationship is nearly perfectly linear for the subicular cells ($df=28$, $r=0.96$, $P<0.001$), indicating that each subicular cell had very similar overall firing rates, regardless of which recording chamber it was in. This is interesting considered in relation to the fact that many of the subicular cells show considerable variation in firing rate within any one environment (see, for example, the cell shown in Fig. 8, below, which is completely silent throughout a large portion of both chambers, but shows high rates in the lower, right portions of each). Thus, the cells are capable of showing consistent variations in rate as a function of location, but the fact that they tend to repeat the same global pattern from one environment to the next means that the overall rates from one chamber to the other are similar.

The hippocampal place cells (third row, middle panel of Fig. 7) do not show any evidence of a linear relationship between firing rates in the two recording chambers ($df=27$, $r= -0.13$, $P>0.05$), as expected based on the lack of similarity of their spatial patterns in the two chambers.

The hippocampal theta cells (third row, right panel), in contrast, do show a highly significant correlation for firing rate in the two chambers ($df=11$, $r=0.98$, $P>0.001$). Thus, each of these cells show similar, tonic, high rates, with low spatial coherence, regardless of which environment they are in.

The lower row of Fig. 7 shows field size (% of pixels showing a non-zero firing rate) in the square plotted as a function of field size in the cylinder. Many of the subicular cells (lower, left panel) are tonically active throughout both environments, so that many of the points are stacked up in the upper, right corner of the plot. The remaining subicular cells, however, clearly indicate a linear relationship between field size in the two environments. A test of the strength of the correlation of field size in the two chambers yielded $r=0.92$ ($df=28$, $P<0.001$). This relationship is expected, based on the fact that the subicular cells tend to show similar spatial patterns in the two environments.

There is not a significant relationship between field size in the cylinder and square for hippocampal place cells ($df=27$, $r=0.19$, $P>0.05$), as expected, given that they do not show similar spatial patterns in the two environments. Also, no such relationship is observable for the hippocampal theta cells (lower, right panel), all of which are tonically active throughout both chambers.

3.7. Examination of subicular cells for which repeated sessions were conducted: Correlational analysis for repeated sessions in the same chamber

Fig. 8 shows an example of a subicular cell which was recorded over three consecutive, identical sessions (on separate days). As can be seen, the firing pattern was highly similar in the cylinder and the square, both within sessions, as well as across sessions.

Repeated sessions were conducted for a total of six subicular cells. For five of these cells, two identical sessions were conducted, while, as can be seen, for the cell shown in Fig. 8, three sessions were conducted. These sessions enabled a comparison of the similarity of spatial firing patterns for different sessions in the same chamber with similarity for sessions in the cylinder versus the square. For this, a pixel-by-pixel correlation
3.8. Hippocampal place cells did not fail to show similar patterns in the cylinder and square simply because the cell discrimination was lost during transfer of the animal

As can be seen in Fig. 4, hippocampal place cells which had a robust place field in the cylinder often quit firing entirely when the animal was transferred into the square. This raises the possibility that hippocampal cells failed to repeat their cylinder place field in the square simply because the cell discrimination was lost when the animal was moved into the square. (This could result, for example, from accidental bumping of the electrode, which could result in the death of the cell under study, or in moving the electrode tip away from the cell, so that the cell can no longer be detected electrically.) To test for this possibility, for 10 of the hippocampal place cells, a third phase of the session was added, so that after recording in the square, the animal was transferred back into the cylinder, for another 20 min of recording. This enabled a test of whether the isolation for that cell was still intact. In each case, the original place field in the cylinder was reinstated during this last phase. Fig. 9 shows examples of four cells for which this manipulation was conducted. The right-most column shows the results from when the animal was returned to the cylinder from the square. As can be seen, the original place field was intact in each case, after return to the cylinder. The cross-correlation analysis was performed between the
two firing rate maps from the cylinder in each of these cases, and the average of these $r^2$ values for the entire set of cells for which this extra session was conducted was 0.50 ($\pm$ 0.05).

3.9. Subicular cells did not show similar patterns in the cylinder and the square simply because the subicular cells receive no stimulus information from these chambers.

The fact that the subicular cells tend to show similar patterns in the cylinder and square suggests the possibility that the subicular cells are simply showing stimulus generalization. That is, it could be that environmental information that reaches the subiculum is not sufficiently detailed to allow discrimination between the two chambers.

One way to test whether the subicular cells receive information from the cylinder walls is to test how the cells respond when the chamber is rotated. Thus, for example, hippocampal place cells are known to rotate their place fields in response to a rotation of familiar, salient environmental cues, so that the place field always has the same spatial relationship to these environmental cues. If subicular cells receive information from the environmental cues presented here (e.g., the vertical stripes, white wall, etc.), then it might be expected that...
they, too, would rotate their spatial firing patterns along with these cues.

To test this, one highly spatial subicular cell, which showed a similar pattern in the cylinder and the square, was subjected to two sessions (on consecutive days), as shown in Fig. 10. For both sessions, the animal was returned to the cylinder after the usual cylinder-square recording sequence. For the first of these sessions, the cylinder was rotated 90° counterclockwise, prior to returning the animal. As a control, the cylinder was not rotated prior to the animal's return in the second session.

As can be seen in Fig. 10, the spatial pattern upon return to the cylinder for Session 1 appeared to be a rotated version of the pattern observed in the initial cylinder recording phase of that session. In contrast, the spatial patterns in the cylinder phases of Session 2 were similar, both in overall spatial pattern and spatial orientation.

To test these conclusions quantitatively, the two cylinder recording phases in each session were subjected to a cross correlation analysis. This yielded a low value ($r^2 = -0.06$) for the two cylinder maps in Session 1, but a high value ($r^2 = 0.63$) for the cylinder maps in Session 2. This is compatible with the idea that the cylinder spatial pattern in the last phase of Session 1 had rotated out of alignment with the initial cylinder pattern for that session. To further test this idea, each of the initial cylinder maps from Sessions 1 and 2 were rotated 90° counterclockwise, and the crosscorrelations were again conducted. Note that this rotation of the initial cylinder map for Session 1 would be expected to bring it into rotational alignment with the map from the final, rotated cylinder phase. As expected, this rotational analysis revealed a high ($r^2 = 0.58$) value for the two cylinder maps of Session 1. In contrast, rotation of the initial cylinder map for Session 2 placed it out of rotational alignment with the final cylinder phase, yielding a low value ($r^2 = -0.07$) for the crosscorrelation of the cylinder maps of Session 2.

### 3.10. Similarity of cylinder and square firing patterns for different cell types in the subiculum

In an earlier report on the spatial firing properties of cells in the subiculum ([6]), examination of the temporal firing patterns of the cell sample revealed that most of the cells could be categorized into different types, based on their overall rate and temporal patterns. These types corresponded to those which had been identified in vitro, intracellular studies of subicular cells ([23,24]). Briefly, these categories were (1) bursting cells, which tend to fire in bursts, with an approximately 2 ms
interspike interval; (2) non-bursting cells, which lack this pattern; (3) putative depolarized bursting cells, which oscillate between a bursting and non-bursting pattern; and (4) theta cells, which show an overall high firing rate which is modulated at theta frequency. These latter cells also have a short spike duration, compared to the other cell categories, and this supports the idea that, in many ways, the subicular theta cells are analogous to hippocampal theta cells [18].

Sharp and Green [6] found that there were few obvious differences in the spatial firing patterns of the different cell types, except that the depolarized bursters had somewhat higher average spatial coherence values. Also, the theta cells and depolarized bursters showed larger average field sizes.

It was of interest here to see whether the different cell types would differ in their tendency to show similarity in their spatial patterns in the cylinder and square. Fig. 11 shows a plot of $r^2$ values for the correlation analysis of the cylinder and transformed square maps for each cell, plotted as a function of spatial coherence in the cylinder (as in the upper, left panel of Fig. 7). Here, the cell type is designated by the symbol type used to display it (as indicated). It can be seen that there were no obvious differences between the different cell types on this measure. The theta cells show generally lower $r^2$ values, but this is predictable, based on their lower average spatial coherence values.

Fig. 11. The similarity of the cylinder and square spatial patterns was predictable, based on spatial coherence values, for all subicular cell types. $r^2$ value for the pixel-by-pixel correlation between the cylinder firing rate map and the transformed square firing rate map for each subicular cell, plotted as a function of spatial coherence in the cylinder. These data are replotted from the upper, left panel of Fig. 7, but, in this case, the symbol used for each point indicates the cell type (see Section 3: Results). There were no differences in the $r^2$ values between the different cell types which could not be predicted based on the spatial coherence values.

4. Discussion

4.1. Subicular cells represent different environments using similar spatial firing patterns

These results show that many individual subicular cells show similar spatial firing patterns in two geometrically different environments. Within the range of the conditions tested here, the extent to which the two environments were visually similar did not have an influence on the similarity of spatial firing patterns in the two chambers. Even two environments which were painted to be quite different, resulted in very similar patterns for subicular cells. (It should be noted, however, that each of the recording chambers used here were actually similar in many ways, including total area, general lighting, odor, and sound conditions, and in the fact that they were both enclosed, high-walled containers.) This suggests the possibility that the subicular cell population has a generic, abstract spatial firing pattern which is instantly transferred, and `stretched' to fit in each new environment, regardless of any of the particular sensory or geometric aspects of that environment.

There were some subicular cells which did not show an obviously similar spatial pattern in the two environments (see Fig. 3). However, this was most often observed in cells which were not strongly spatial in the first place, so that they could not be expected to show any spatial correlations. In general, the strength of the correlation between the firing patterns in the cylinder and square was linearly related to the strength of the cells' spatial signal (the spatial coherence value) in the cylinder (see Fig. 7; upper left).

It should be noted that no attempt was made here to classify the subicular cells as being spatial or non-spatial prior to recording/analysis. Rather, all cells which were electrically isolated on each electrode wire were included for study, and for the statistical analyses. This approach seemed appropriate since, as reported earlier ([6]; and see Fig. 7, upper left) the cells do not seem to fall into clear categories along the spatiality dimension. Rather, they fall along a continuum from highly spatial, to not noticeably spatial. From Fig. 7 (upper left) it seems clear that the estimates of similarity of the cylinder and square spatial firing patterns would have been higher, if only highly spatial cells had been included for analysis.

In addition to the similarity in the details of the spatial firing pattern observed for many cells, there were universally exhibited similarities in more general aspects of cell firing. Thus, all subicular cells were similar in the two environments in their spatial coherence (that is, how generally 'spatial' they are, regardless of the specific spatial field characteristics), firing rate, and field size. This could be, in part, because at least some of the cells are signalling non-spatial aspects of the situation which are common to both recording chambers (odors, white
noise, locomotor behavior, etc.). Alternatively, it could be that all cells are generating a signal which is related mainly to spatial variables (although only weakly so, for some cells), and that, as already suggested, this spatial signal is similar in the two environments. If this latter statement is true, then it would also have to be the case that each cell would show similar spatial coherence, firing rate and field size in the two environments.

4.2. The rotational orientation of subicular spatial firing patterns is controlled by both path integration and learned relationships to environmental stimuli

It is of interest that, in addition to the general similarity of overall firing pattern, the spatial patterns in the two environments usually also had the same rotational orientation (but see Fig. 6, for an exception). That is, if a cell had a region of high firing located along the north edge of the cylinder, then that region was also located along the north wall of the square. In the cases in which the two environments were similar (the P-P and S-S groups) this constant orientation could possibly be explained by the fact that the two environments were also rotationally aligned (see Fig. 1). However, in the cases in which the two environments were different (the S-P and P-S groups), this kind of environmental influence was not present. (Note that even these ‘different’ pairs shared similar components, in that each had one solid black, and one solid white wall; however neither of these were in rotational alignment across the two environments; see Fig. 1.)

This suggests that some form of path integration is used to enable the subicular cell firing patterns to retain the same rotational orientation as the animal is transferred from the cylinder to the square. One possibility is that the subiculum may receive information (indirectly) from head direction cells located in the nearby postsubiculum [22] and elsewhere [25-28]. These head direction cells provide an ongoing representation of momentary directional heading, and this directional firing is thought to be based, in part, on path integration processes. These cells could serve to somehow maintain the rotational orientation of the subicular cell patterns as the animal moves from a familiar environment (the cylinder) to a novel one (as the square was on the first recording session). For example, if a particular subicular cell tends to fire at high rates along the north edge of the cylinder, then the head direction cell signal could help to inform the subicular cell system which wall is the north wall in the square. Compatible with this suggestion, it has been observed that head direction cells can maintain a constant directional setting even when the animal moves from one environment into another, novel environment [29]. Alternatively, it could be that directional information was provided by extra-apparatus cues, such as equipment noise.

The data presented in Fig. 10 (see also [6]) suggest that, in addition to this possible path integration mechanism, the rotational orientation of the subicular cells may also be controlled by learned relationships to the environmental stimuli (once these are familiar). For the session shown in the upper row of Fig. 10, the animal was returned to the cylinder after the usual square recording phase, but before this return, the cylinder was rotated by 90°. In this case, the subicular cell firing pattern also rotated by 90° in the same direction. This suggests that the subicular cells receive information about the details of the environmental stimuli, and that they develop a tendency to retain a constant rotational relationship to these cues, once they have had some experience in an environment. As discussed below, one possible source of this environmental information could be the hippocampal place cells, which are also known to rotate along with salient environmental cues.

In review, it seems that as an animal moves from one environment to another, subicular cells establish the same spatial firing pattern in each, regardless of the details of the environmental stimuli. Only information about the environment size and shape are used to fit the generic spatial firing pattern into each new environment. When the animal moves into a novel environment, the rotational orientation of the generic pattern will be the same as that established in the previous environment, perhaps as a result of a path integration process. In a familiar environment, however, the rotational orientation is set by the orientation of the familiar environmental landmarks.

4.3. Hippocampal cells represent different environments using different spatial patterns

As anticipated based on earlier work [14–17] the hippocampal place cells did not show similar firing characteristics in the cylinder and the square. Often, place cells which showed a robust place field in the cylinder were completely silent when recorded in the square (Fig. 4). Conversely, some cells did not appear during the initial session in the cylinder, but became evident in the square, by showing a clear place field (like the cell shown in the top row of Fig. 4). Even in the S-S and P-P conditions, there was no case in which a place cell appeared to have a similar field in the two chambers.

Indeed, other work has shown that even within a single environment, place cells can sometimes show completely different spatial signals at different times, depending on the behavioral [30], or recent historical (e.g. [31,32]) context of the situation. This is generally consistent with findings which show that hippocampal cells are influenced by a wide variety of sensory and
behavioral variables, both spatial and non-spatial (see, e.g. [33]). Thus, it appears that the hippocampal place cells provide place information which is highly specific to (conditional on) particular sensory, behavioral, temporal, and other contextual aspects of the situation.

As expected, hippocampal theta cells also did not show similar spatial firing patterns in the cylinder and square, although all theta cells were tonically active throughout both chambers, and individual theta cells showed similar rates in the two chambers. Interestingly, the theta cells showed lower pixel-by-pixel correlation values for the cylinder and square firing rate map correlation analysis, than that shown by the subset of subicular cells which were similarly low in spatial coherence values (Fig. 7; top row). This provides some support for the suggestion that even the subicular cells with low spatial coherence values were, in fact carrying a 'weak' spatial signal which was replicated from the cylinder to the square.

4.4. Different parts of the hippocampal formation provide fundamentally different forms of spatial location information

As mentioned above, cells in several regions throughout the hippocampal formation have been shown to contain cells which exhibit location related firing patterns. Thus, location related firing has been observed for cells in the entorhinal cortex [5], the dentate gyrus [2] and the parasubiculum [7], in addition to the hippocampus and subiculum. Like the cells described here, cells in each of these areas fire in a way which is related to the momentary spatial location of a freely moving animal, although the spatial patterns in each area are phenomenologically somewhat different, in that some are highly distributed, so that any one cell fires throughout much of the environment (subiculum and entorhinal cortex) while others are quite sparsely coded, so that each cell fires only in a small portion of the environment (hippocampus, dentate gyrus, and parasubiculum). The fact that these areas are all closely interconnected anatomically suggests the possibility that the same, basic locational signal is sent around the hippocampal 'loop', becoming only more or less distributed at different points.

The data presented here, however, suggest that this is not the case for the hippocampal and subicular cell populations. Thus, although it seems likely that the hippocampal place cells do, in fact, have some influence on the subicular cells, it cannot be the case that the subicular signal is generated solely on the basis of these inputs. That is, it does not seem possible that the similar patterns in the cylinder and square exhibited by subicular cells could be created simply by convergent input from the hippocampal place cells, since the latter cells show entirely different patterns in these two environments. Rather, it appears that these two regions provide two very different, possibly complimentary spatial representations of each environment (see below).

Interestingly, cells in the entorhinal cortex are, apparently, similar to subicular cells, in that they also show similar firing characteristics when recorded in a cylindrical and square environment [5]. In that study, entorhinal cells were recorded in separate sessions in a cylindrical and a square chamber, both of which were painted with gray walls, and had a single, white card on the wall. The two chambers were located in the same spot (over different sessions) in the curtained recording room, and the angular position of the card was the same for both chambers. The results from the Quirk [5] study showed that the entorhinal cells, like the subicular cells studied here, tended to show similar levels of spatial coherence, firing rate, and field size in the two environments. Also, for cells which showed a location-related signal, this pattern tended to be similar in the two chambers. In that report, the similar firing patterns were interpreted as being due to the similar sensory properties of the two chambers, and it was suggested that the entorhinal cells were more sensory bound than hippocampal cells. It is not clear, however, whether the entorhinal signals would also be similar when recorded in two visually distinctive environments. Thus, it is not yet clear how similar the fundamental aspects of the spatial signal in the entorhinal and subicular cortices are.

Finally, cells in the parasubiculum and dentate gyrus have not yet received enough study to determine whether these regions may provide yet other, fundamentally different types of representation.

4.5. The hippocampus and subiculum /entorhinal cortex may share their complementary information to help generate their respective representations

In keeping with the data presented here, earlier work on hippocampal place cells has shown that the location of the cells' place fields is influenced by salient environmental stimuli (e.g. [15,16,34]). This has led to the suggestion that place cell fields could, in fact, be generated simply as a response to environmental inputs present in the cell's field [34–37]. Other information, however, suggests that this cannot provide the complete explanation. Specifically, once established, place cell activity can be maintained even after all orienting stimuli are removed, or the room lights are extinguished [4,31,38–40]. This has led to the suggestion that the place cells must also receive some kind of information about the animal's own movements through space, since, in the absence of orienting stimuli, the only ongoing indicator of current location would have to be based on an integration of the animal's own translational movements [4,35]. A recent study has provided further support for this idea, by showing that the location of a
place field can, in fact, be changed ('updated') by direct, experimenter-induced activation of vestibular and/or visual motion cues suggesting movement through space [32].

A model for how the place cell system could accomplish this integration of movement signals has been suggested by McNaughton [35]; see also [41,42]. According to this idea, hippocampal place cell activity indicating the current location is projected onto another cell population, which also receives information about the animal's movements and directional heading. This other area, thus, has cells which fire in relation to particular combinations of place and movement. The output from this region is postulated to then project back onto the hippocampus itself, so that part of the information received by hippocampal place cells during navigation is a signal specific to recent location/movement combinations. This information is assumed to converge onto the hippocampal place cells, along with environmental sensory information about orienting cues. During initial exploration in a novel environment, place cells are driven to fire by combinations of these two inputs, and, eventually, the connections between the place/movement cells and the hippocampal place cells becomes strong enough so that they are sufficient, alone, to drive appropriate place cell activity. Thus, after learning, place cell activity can remain stable, even if the environmental cues are removed.

There is, as identified by McNaughton [35], however, one problem with this model. To see this, imagine that an animal is exploring a new environment, and starts out at some location, A. Sensory inputs at A drive activity in a particular subset of hippocampal cells, so that these cells now represent location A. The animal then begins to walk, so that it arrives at an adjacent location, B. Somewhat different sensory inputs available at B combine with cells coding place/movement information, so that a new place cell activity pattern is generated at B, and that activity pattern should become the permanent representation of location B. Next, the animal continues on a long, winding trajectory through the environment, and eventually arrives back at B, but this time it has approached the location (B) from a different direction (not from location A). This presents a problem for the model because, at this point, the original B location activity pattern should be reinstated in the hippocampal place cells. However, since the pattern in the place/movement cells can be expected to be different from what it was the last time the animal entered B (from location A), and also, the sensory inputs at B might be somewhat different from that approach (there is a slightly different view of B when facing this direction), it is not clear that the original B pattern can be reinstated. To deal with this problem, McNaughton [35] suggested that there might be a region of the brain which contains information about all possible motor pattern equivalencies, so that the entire set of trajectories which could lead to location B will be coded similarly.

The data presented here suggests that the subiculum (and, possibly, also the entorhinal cortex [5], and see above) may, in fact, be that postulated region. Thus, regardless of the details of an environment (and even in a novel environment), the subiculum appears to have a generalizable set of information about the consequences of different movement trajectories, so that any given location, B, is always represented by the same firing pattern, regardless of how the animal arrived there, or what the local view is like from the direction of arrival. Thus, it could be that during initial exploration of a new environment, the subiculum provides the hippocampus with information which helps the hippocampal place cell population to establish a coherent spatial representation for that environment.

Thus, the subicular information could contribute to two of the major features of the hippocampal place cell representation of an environment. One of these features is that, in many environments (but not all [9,43]) the pattern of place cell activity is identical and repeatable within a given location, regardless of the direction the animal faces within it, or the direction from which the location was approached. Since the subicular firing patterns are similarly, largely non-directional [6], and can, apparently, be transferred, with fidelity, to new environments, the subicular signal could help the hippocampal place cells to identify arrival at a previously visited location within an environment. Thus, they could assist the hippocampal population in showing the dual properties of being very sensitive to particular details of a situation (presumably due to different sensory inputs offered in each environment), yet have an invariant representation of a given location within each environment.

Another major feature of the hippocampal place cell representation is that any two regions within an environment are almost always represented by different hippocampal place cell patterns. This is true even in a visually symmetrical environment, which is designed to have sets of two or more regions which are visually identical [32,44]. Any two such regions are likely to be differentially represented by the hippocampal place cells, even though control manipulations demonstrate that the hippocampal population cannot distinguish between the identical locations based on sensory cues alone. It seems possible that the hippocampus is assisted with this differentiation by the subicular representation, which is, presumably, insensitive to these sensory similarities.

Thus, according to this view, the subiculum may serve as a path integrator, which provides information to the hippocampal place cell representation, as has been suggested elsewhere [45].
Conversely, it seems possible that the hippocampal place cell representations may contribute to some of the properties of the subicular spatial patterns. For example, the hippocampal place cells could help to stabilize the rotational orientation for the subicular representation over repeated episodes in the same environment. Data presented here, as well as by Sharp and Green [6] revealed that the subicular cells rotated their spatial representation in response to a rotation of the cylinder. This is surprising, given the fact that the subicular cells seem otherwise insensitive to specific sensory inputs. It could be, however, that in a familiar environment, the hippocampal place cells have ‘learned’ to recognize each location within the environment based on the sensory inputs available there. It could, then, upon arrival into a familiar environment, use experience-dependent connections with the subiculum, to inform the subicular cell population about which part if its generic representation corresponds to each particular location in a specific environment. Thus, upon entry into the environment, the subicular pattern could be ‘rotated’ into the proper orientation.

The scheme proposed here for hippocampal interaction with the subicular/entorhinal system is similar to ideas proposed by Touretzky and Redish [45], and to the Naive Path Integrator version of a set of models recently proposed by Samsonovich and McNaughton [42].

4.6. The subicular spatial firing patterns could possibly play a role in certain navigational abilities demonstrated by rats

As might be expected, examination of the effects of selective subicular lesions on spatial behavior has revealed navigational deficits after subicular damage ([46]; see [47], for review). Since there have been few studies involving selective subicular lesions, however, it is difficult to speculate what, if any, unique role the subiculum may have in orchestrating navigational behavior.

However, it seems possible that this structure could be uniquely involved in some kinds of ‘short cut’ behavior which has been demonstrated (e.g. [48–50]). Thus, it seems possible that the generic spatial representation provided by the subiculum may enable generation of ‘novel’ routes in relatively unfamiliar environments. From the viewpoint of the subicular cell representation, it may be that neither the environment nor the route are novel.

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References


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