Spatial View Cells in the Primate Hippocampus: Effects of Removal of View Details

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Robertson, Robert G., Edmund T. Rolls, and Pierre Georges-François. Spatial view cells in the primate hippocampus: effects of removal of view details. *J. Neurophysiol.* 79: 1145–1156, 1998. Hippocampal function was analyzed by making recordings from hippocampal formation neurons in macaques actively walking in the laboratory. ''Spatial view'' cells, which respond when the monkey looks at a part of the environment were analyzed. It is shown that many of these cells retain their spatial characteristics when the view details are obscured totally by curtains and by darkness. It is shown that many of these cells respond more when the monkey is gazing toward one location in the room than toward other locations, even though none of the view details can be seen. Such cells were found in the CA1 region, the parahippocampal gyrus, and the presubiculum. Other cells stopped responding when the monkey looked toward the normally effective location in the environment if the view details were obscured. These cells were in the CA3 region of the hippocampus. The results indicate that for CA3 cells, the visual input is necessary for the normal spatial response of the neurons, and for other cells in the primate hippocampal formation, the response still depends on the monkey gazing toward that location in space when the view details are obscured. These latter cells therefore could reflect the operation of a memory system, in which the neuronal activity can be triggered by factors that probably include not only eye position command/feedback signals, but also probably vestibular and/or proprioceptive inputs. This representation of space ''out there'' would be an appropriate part of a primate memory system involved in memories of where in an environment an object was seen and more generally in the memory of particular events or episodes for which a spatial component normally provides part of the context.

INTRODUCTION

Damage to the temporal lobe that includes the hippocampal formation or to one of its main connection pathways, the fornix, produces amnesia (see Gaffan and Gaffan 1991; Scoville and Milner 1957; Squire and Knowlton 1994). One of the memory deficits in amnesic humans is a major impairment in remembering not just what objects have been seen recently, but also where they have been seen (Smith and Milner 1981). This type of memory is used for example in remembering where one's keys have been left. In experimental studies in monkeys to define the crucial structures to which damage produces memory impairments, it was shown that hippocampal or fornix damage produces deficits in learning about where objects have been seen in object-place memory tasks (Angeli et al. 1993; Gaffan 1994; Gaffan and Saunders 1985; Parkinson et al. 1988).

To analyze how the hippocampus operates to help implement this type of memory, Rolls and colleagues have recorded from single neurons in the hippocampus while monkeys perform object-place memory tasks in which they must remember where on a video monitor a picture has been shown. They found that ~10% of hippocampal neurons responded when images were shown in some positions on the screen (Rolls et al. 1989). Moreover, they showed that the spatial representation was in allocentric (world) rather than egocentric (related to the body) coordinates, in that the spatial fields of these neurons remained in the same position on the video monitor even when the whole monitor was moved relative to the monkey's body axis (Feigenbaum and Rolls 1991).

However, in rats, the spatial representation provided by hippocampal neurons, which has been described, is of where the rat is. That is, individual hippocampal neurons in rats respond when the rat is in one place in a test environment (O'Keefe and Speakman 1987). A theory that the hippocampus is a computer for spatial navigation, computing bearings and distances to the next place, has been built on the basis of the properties of rat place cells (Burgess et al. 1994). Because it is not clear whether the primate hippocampus should be considered a spatial computer, with perhaps place cells like those of rats (Ono et al. 1993), or is instead a structure involved in storing memories including memories with a spatial component such as where an object has been seen, we recorded from single hippocampal neurons while monkeys actively locomoted in a rich spatial environment. We set up the recording situation to allow active walking by the monkey, because it is only during active locomotion that the place fields of rat hippocampal neurons become evident (Foster et al. 1989). We used a rich testing environment, as compared with a cue-controlled environment with only a few spatial cues, to maximize the possibility that many cells with spatial response properties would be found. In one previous study, without active locomotion and with a cue-controlled environment, we found a small number of hippocampal cells that responded to views of the environment not to the place where the monkey was (Rolls and O'Mara 1995). However, that study was not with active locomotion nor with a spatially rich environment. In a previous study with active locomotion in the same rich spatial environment used here, the open laboratory, we found spatial view cells that responded when the monkey looked at one part of the environment but not when he looked at another (Rolls et al. 1995, 1997). These responses occurred relatively independently of where the monkey was in the testing environment provided that he was looking toward a particular part of the environment. Eye position recordings with the monkey stationary confirmed that these neurons fired when the monkey looked at a particular part of the spatial

environment and not in relation to where he was. For these reasons, the cells were named ''spatial view'' and not ''place'' cells. Spatial view cells can be characterized as having responses when the animal looks toward a certain part of a spatial environment, independently of the place where the animal is located and of head direction. As noted in DISCUSSION, spatial view cells in primates could be part of a system involved in remembering where objects are in spatial environments as part of an associative memory system, or in representing space for spatial functions such as spatial navigation, which implies the ability to store representations of spatial environments that have been seen and to recall them.

The new investigation described here is designed to analyze how much of the detail of a spatial view must be present for these primate hippocampal spatial view cells to respond. To obtain evidence on these issues, we recorded from spatial view cells when the view was obscured by complete floor-to-ceiling curtains and in the dark.

METHODS

Single neurons were recorded with glass-insulated tungsten microelectrodes from two rhesus macaques with methods that have been described previously (O'Mara et al. 1994; Rolls et al. 1989). [All procedures were carried out in accordance with the ''Guidelines for the Use of Animals in Neuroscience Research'' of the Society for Neuroscience and were licensed under the U.K. Animals (Scientific Procedures) Act 1986.] The monkey was free to walk with his head in an upright position round an open 4×4 m laboratory in a 2.7×2.7 m area in a modified chair on four wheels. The head orientation was fixed with respect to the chair, so that the head orientation and position at all times could be monitored by tracking the chair position and orientation (see further). The chair had a removable bottom, so that testing could take place both during active locomotion by the monkey and with the monkey stationary in the environment. Three of the four cups in the corners of the room were provided with food to encourage the monkey to learn about the places of food in the spatial environment. Small pieces of food also were scattered sometimes on the floor to ensure that the monkey explored the environment fully. Eye position was measured with the search coil technique, with the field coils attached to the walker to which the head also was attached. The eye movements made by the monkey were ~35° left and right and 35° up and down with respect to head direction. The head direction and position in the room were measured using a video tracking device (Datawave, Longmont, CO) with the camera in the ceiling tracking two light-emitting diodes placed in line 25 cm apart above the head on the top of the chair. We wrote software to provide, every 67 ms, the position of the monkey's head in the room, the head direction, and the eye position (i.e., the angle horizontally and vertically of the eyes with respect to the head), and from these, the position on the wall of the room at which the monkey was looking. Every time that the cell fired, that time was recorded with an accuracy of 1 ms. The Datawave spike cutting software was used off-line to ensure that the spikes of well-isolated neurons were analyzed (see example in Fig. 2*C*). Software was written to measure the firing rate of the neuron whenever the monkey was looking at a position in space. The algorithm took a fixed length record (usually 250 ms long) whenever the eyes were still (to within typically 1°) during the record and calculated the firing rate together with where the monkey was looking during that record. The next record was taken immediately after the preceding one if there was no eye movement. (The findings described in this paper were unaffected if alternatively a new record was taken only just after a new eye movement was made.) The algorithm could lag its neuronal data collection a short latency later than the eye position data. (If the neuron started to respond 100 ms after the monkey moved his eyes to an effective location in space, this lag could be set to 100 ms. In practice, the lag was set for all neurons to a small value between 0 and 100 ms.) From all such records containing a firing rate and where the monkey was looking during the record, it was possible to plot diagrams of the firing rate of the cell when different locations were being viewed. [The records were binned typically into 64 bins horizontally (16 for each wall), and 16 vertically.] The search coil was in use for 23 of the 27 experiments that form the basis of the results described in this paper. The accuracy of the eye position data were $\pm 3°$, of the measurement of the chair orientation 5°, and of the chair position was 5 cm for 90% of the active locomotion area.

Cells were searched for while the monkey was actively locomoting. Only spatial view cells, as defined by the following properties, that could be held for long enough were used in the experiments described in this paper. The properties of the spatial view cells are that they responded differentially [as shown by an analysis of variance (ANOVA)] with respect to the place where the monkey was looking during the active locomotion, and that they did not fire in relation to the place where the monkey was located. If the cell did not respond with respect to where the monkey was looking, or was not held sufficiently long for the experiments described here to be performed, the cell was not included in the results described here. For 27 cells of 352 recorded in the experiments described here, it was possible to show that they were spatial view cells and to complete the testing described here that involved obscuring the view of the environment.

Thick black curtains hung from a matte black artificial ceiling 2.5 m above the floor. The curtains were completely open for most of the testing and were held up off the floor out of the way. After a spatial view cell had been isolated and its spatial field had been analyzed as shown in RESULTS, the curtains were drawn to hide either all of the room or part of it, and the spatial field was reanalyzed. The experiment often continued for 15 min with the curtains drawn closed before they were opened again so that the activity of the cell could be studied repeatedly with the normal view and the view obscured condition. The main experimental results described in this paper were described with this protocol. In some further experiments, described later, the room lights were extinguished with the blackout blinds and the curtain fully drawn closed, and the monkey was either allowed to explore in the darkness or his chair was moved and rotated to face in each of several directions at each of several places while the firing rate of the cell was being measured. The light level with the blinds closed was $\ll 0.1$ Lux. In this test condition, there was little to orient the experimenter, with environmental noise and residual light providing only minimal cues for orientation.

With this overall protocol, three types of experiment were performed. In the first type of experiment, the firing rate of the neuron was measured when the monkey's chair was stationary in a particular position in the environment, facing in a particular direction (with the monkey's feet touching a floor of his walker, not the lab floor, so that the monkey did not locomote). At least four such firing rate measurements each 2–3 s long were taken for each head position and direction. The firing rate measurements (the dependent variable) were taken for a number of different head positions and directions (the independent variable). The advantage of this type of experiment was that by selecting the head position and direction, the experimenter could define the spatial view that was seen by the monkey and could concentrate the data collection on a number of different head position and head direction combinations to test hypotheses such as that the firing of the neuron depended on the spatial view being seen by the monkey rather than the place where

the monkey was located. An example of data collection with this type of experiment are shown in Fig. 1.

In the second type of experiment, the monkey was positioned at one place in the environment with one head direction (with his feet touching a floor of his walker not the lab floor), and the firing rate of the cell was measured as a function of where the monkey was looking in the environment (using the search coil to show exactly where he was looking). (We show elsewhere that spatial view cells can respond when the monkey looks toward an effective view from different places, and with different head directions) (Rolls et al. 1987, 1998). The firing rate measurements were taken with the curtains drawn open to show the full details of the view. Then the recording of neuronal activity and eye position were repeated with the curtains drawn closed to obscure all details of the view. An example of this type of experiment is shown in Fig. 2. The advantage of this type of experiment is that it could demonstrate whether the spatial view fields of these neurons still are present when the part of space being processed is determined only by the position of the eyes and whether the spatial fields of these neurons remain when the view details are obscured but the monkey can still move his eyes toward a particular part of allocentric space.

In the third type of experiment, the firing rate of hippocampal cells was measured when the monkey was walking round (or was moved to different places in) the environment. The firing rate was typically measured throughout a 5- to 10-min period for each condition (curtains open or curtains drawn) during which the monkey walked round the environment, often picking up small pieces of food that had been scattered on the floor to encourage exploration of all parts of the environment. An example of this type of experiment is shown in Fig. 3. An advantage of this type of experiment is that the spatial view fields were being studied during active locomotion by the monkey.

For statistical analysis of the responses of the neurons, 4–50 values of the firing rate for each condition (e.g., direction in which the head was facing, spatial position at which the eyes were looking) were obtained. (If there were insufficient rate values for any location in space with the high resolution data collection made, then the data were resampled on a coarser spatial grid to ensure that at least 4 measurements of rate were available for every location.) A one-way ANOVA then was performed to determine whether there were significant differences between the conditions. Provided that this was significant (at the 0.05 level at least, though for the majority of the cells this was <0.001), the conditions that were significantly different from each other then were determined with post hoc Tukey test analysis. For all cells described in this paper as having spatial firing, this was verified statistically at $P < 0.01$.

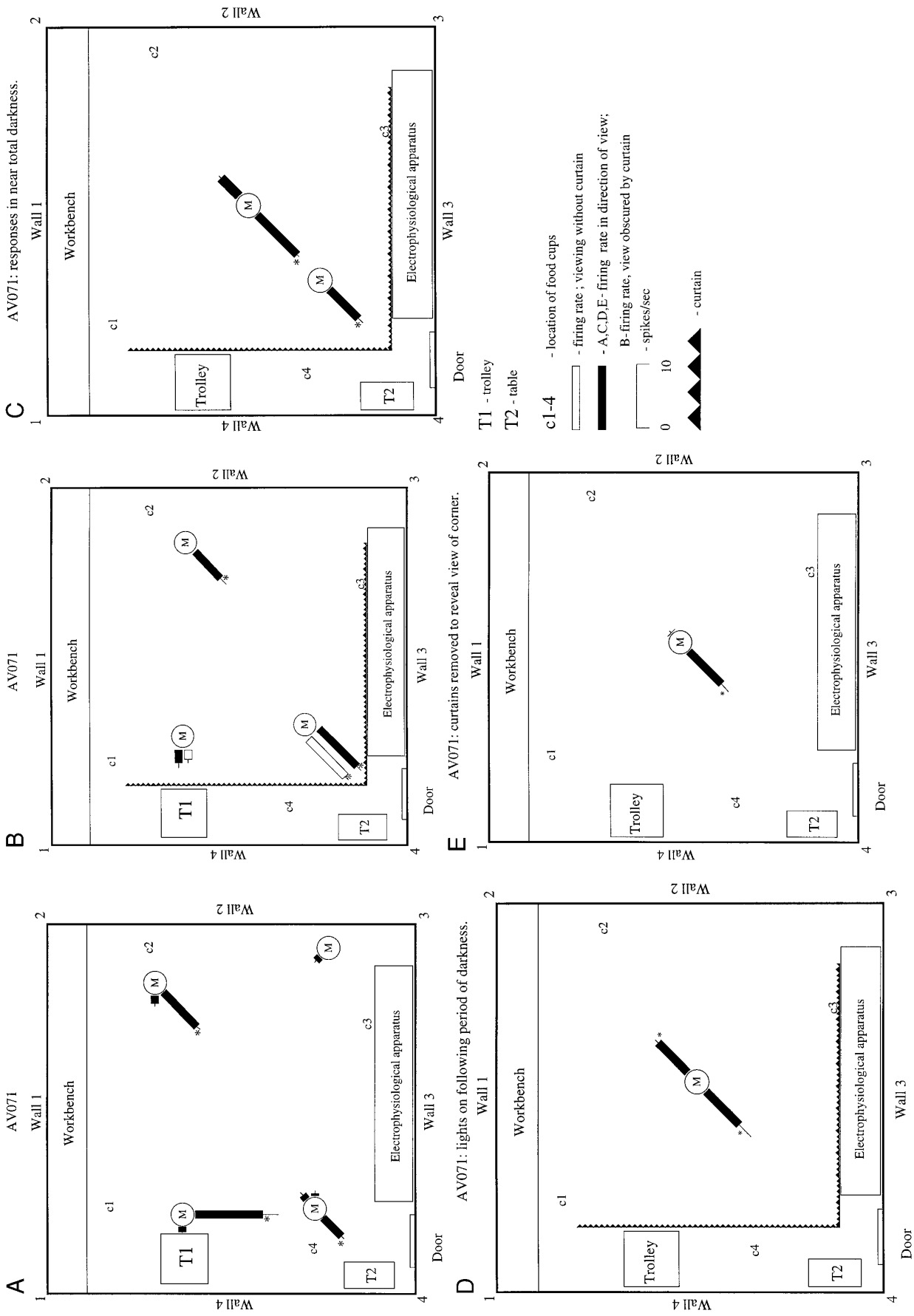
X-radiography was used to determine the position of the microelectrode after each recording track relative to permanent reference electrodes and to the anterior sphenoidal process, a bony landmark the position of which is relatively invariant with respect to deep brain structures. Microlesions (60–100 μA, 100 s) made through the tip of the recording electrode during the final tracks were used to mark the location of typical neurons. These microlesions together with the associated X-radiographs allowed the position of all cells to be reconstructed in the 50-μm brain sections with the methods described in Feigenbaum and Rolls (1991). As described previously, the spatial view cells had very low spontaneous firing rates (typically in the range 0–2 spikes/s in the locomoting monkey), low peak firing rates (typically in the range 10–20 spikes/s), and large amplitude broad spikes (Rolls et al. 1997). Other cells had faster spontaneous and peak firing rates (often in the range 20–60 spikes/s) and small amplitude short spikes. Taking into account findings in the rat (e.g., Fox and Ranck 1981), it is likely that the large slow spiking cells are pyramidal cells and that the fast firing small amplitude cells are interneurons. All the spatial view cells described here also had the large amplitude low firing rate type of activity and were recorded in regions in which there are pyramidal cells. They sometimes are referred to for brevity as pyramidal cells in this paper, but the criteria for inclusion in this category are those just given.

RESULTS

It was possible to complete the experiments described here, measuring their activity with the view details obscured as well as unobscured, in 27 spatial view neurons recorded in two macaques, as described next. The spikes recorded with the tungsten single neuron microelectrodes were from well-isolated cells, as illustrated in Fig. 2*C*.

The results for a first type of experiment we performed are illustrated for a hippocampal pyramidal cell in Fig. 1 (*cell av071*). In this type of experiment, when the monkey's chair was stationary in a particular position in the environment, facing in a particular direction, the firing rate of the neuron was measured. At least four such measurements were taken, each 2–3 s long. Figure 1*A* shows the means and SE of the firing rates with the curtains drawn open so that the monkey could see the whole environment. The cell fired significantly more when the monkey was facing *corner 4* than when he was facing toward other parts of the environment, irrespective of where he was in the environment. Figure 1*B* shows the means and SE of the firing rates with the curtains drawn closed to cover two whole walls of the test environment, including *corner 4.* It is shown that the neuron still fired when the monkey was facing *corner 4*, even though *corner 4* was obscured completely by the floor-to-ceiling curtains. The data in Fig. 1*B* also showed that under these conditions, the cell still maintained its selectivity in that it did not respond when the monkey was looking toward the completely obscured trolley (T1). In Fig. 1*C*, it is shown that, in darkness, the cell still fired when the monkey was facing in the direction of *corner 4.* Although the selectivity of the cell was rather less in the darkness, the firing was significantly less ($P < 0.001$) when the monkey was facing toward *corner 2* than when facing toward *corner 4.* This type of experiment thus provides evidence that the view details are not essential for spatial view neurons to fire. It was found that when the lights were switched on again, the cell did not regain its full selectivity when the curtains still obscured the spatial view (Fig. 1*D*) but did regain its full selectivity when the curtains were opened to show again the spatial view (Fig. 1*E*). The fact that the neuron did not regain its full selectivity immediately, that is, the neuron fired at a significant rate when the monkey was facing away from the view field, is consistent with the effectiveness of the darkness in making spatial orientation within the room difficult. (Further evidence on this from a CA3 cell is described in a following section and shown in Fig. 4.)

We could establish in a second type of experiment that the responses of such cells also depended on the direction where the monkey was looking in the spatial environment and not on the details of the visual scene immediately visible. This experiment also established that it was the particular part of space being viewed, as determined by the position of the eyes, that determined whether these hippocampal cells fired. In this type of experiment, when the monkey was positioned in one place in the environment (with his feet


A
AV071
Wall 1
Workbench
Wall 2
Wall 4
Wall 3
Door
T1
T2
Electrophysiological apparatus
Trolley
c1
c2
c3
c4
M
B
AV071
C
AV071: responses in near total darkness.
D
AV071: lights on following period of darkness.
E
AV071: curtains removed to reveal view of corner.
T1 - trolley
T2 - table
c1-4 - location of food cups
- firing rate ; viewing without curtain
- A,C,D,E - firing rate in direction of view;
B - firing rate, view obscured by curtain
- spikes/sec
0
10
- curtain

touching the floor of his walker not the lab floor), the firing rate of the cell was measured when the monkey looked at different parts of the environment (using the search coil to show where he was looking) in the light, with the curtains drawn open to show the full details of the view. Then the recording of neuronal activity and eye position were repeated with the curtains drawn closed to obscure all details of the view. An example of this type of experiment is shown in Fig. 2. The neuron's firing when the monkey was looking toward the fully visible *wall 1* is shown in Fig. 2*A*. When all the walls of the room were obscured completely by drawing the curtains, the neuron still responded whenever the monkey looked to approximately the same position in the room (Fig. 2*B*). (There was a slight drift of the view field when the curtains were closed, consistent with the hypothesis that a remembered spatial view is not as accurately located as a seen one and with the fact that the actual view of the scene was the normal determinant of the spatial response field of the cell. The slight drift of the spatial field of the cell is also consistent with the evidence from a separate study, to be presented elsewhere, that the coordinate system used by these cells is not in eye position coordinates, nor in a combination of eye position and head direction coordinates, but in allocentric, i.e., world coordinates.)

Twelve cells were tested in these ways with the monkey placed so that his head faced toward the view field when the details were obscured with curtains. (For 8 of the neurons, the experiments were of the second type, performed in the way illustrated in Fig. 2 with eye movements being recorded; and for 4 neurons, the experiments were of the first types as illustrated in Fig. 1, with eye position not being recorded.) In 8 of the 12 cases, the neuron responded when the monkey looked at a spatial view the details of which were obscured completely by drawing the curtains. The responses of these eight neurons with the curtains closed were generally 70–100% of the value when the curtains were open (mean 80%). Subsequent histological reconstruction showed that these cells were in the CA1 region, the parahippocampal gyrus, or the presubiculum (see further). In 4 of the 12 cases the response was much lower with the curtains closed. The responses of these four neurons when the curtains were closed generally were 20–40% of the value when the curtains were open (mean 27%). Subsequent histological reconstruction showed that these cells were located in the CA3 region.

Finally, in a third type of experiment, we examined the firing rate of hippocampal cells when the monkey was walking around or was moved to different places in the environment. An example of this type of experiment is shown for *cell av192* in Fig. 3. The *inner set* of four rectangular boxes show where the monkey looked on the four walls. (The top of each wall is furthest from the center.) The *outer set* of four boxes again represent the four walls, but in these, a spot indicates where the cell fired. It is clear with the curtains drawn open that the cell has a spatial view field on *wall 3* (Fig. 3*A*). The firing of the cell when the monkey moved round in the environment with the curtains closed is shown in Fig. 3*B*. It is clear that with the curtains closed, the cell responded when the monkey looked at *wall 3*, that is, the spatial selectivity of the cell was retained.

Another example of a cell recorded in this third type of experiment is shown in Fig. 4. The firing rate as a function of where horizontally the monkey was looking on the walls is shown in Fig. 4*A*, with the walls unobscured. (This form of representation allows the exact value of the firing rate to be read from the ordinate of the figure.) The monkey was locomoting round the environment during the collection of all the data shown in Fig. 4. (The data for this cell are shown with the values for all vertical positions on the walls at a given horizontal angle combined to enable the rate to be plotted on the vertical axis in spikes/s to enable the firing rates to be compared across different conditions.) In Fig. 4*B*, it is shown that the firing rate was reduced when the view was obscured by the curtains fully closed, but the spatial field was in a similar position to that when the view was not obscured by the curtains. (The cell was in the CA3 cell region.) Next the lights were extinguished, and with the room now in darkness, it was found that not only was the rate still low, but also that the field appeared to have slipped horizontally from *wall 1* to the adjacent *wall 4* (Fig. 4*C*). When the lights were switched on with the curtains still closed, the field slipped back to its normal position on *wall 1* (Fig. 4*D*), although the firing rate still was not high. Last, the lights were turned on, the curtains were drawn to reveal the walls again, and the cell's spatial view field was fully restored in its original position (Fig. 4*E*).

It was possible to repeat this third type of experiment, in which the view details were obscured by closing the curtains while the monkey was actively locomoting, on 15 cells. In 11 of the 15 cases, the neuron responded when the monkey looked at a spatial view when the details were obscured completely by drawing the curtains. The responses of these 11 neurons when the curtains were closed generally were 30 to >100% of the value when the curtains were open (mean 94%). These cells were in the CA1 region, the parahippocampal gyrus, or the presubiculum (see further). In 4 of the 15 cases, the neuron

FIG. 1. Examples of the responses of a hippocampal CA1 spatial view cell *(av071)* with and without a view of the effective part of the test environment. *A*: means and SE of the firing rates with the curtains drawn open so that the monkey could see the whole environment. *B*: means and SE of the firing rates with the curtains drawn closed to cover 2 whole walls of the test environment, including *corner 4*. *C*: in darkness, the cell still fired when the monkey was facing in the direction of *corner 4*. Although the selectivity of the cell was rather less in the darkness, the firing was significantly less ($P < 0.001$) when the monkey was facing toward *corner 2* than when facing toward *corner 4*. *D*: after the lights were turned on, but the curtains still obscured the view, the cell did not regain its full selectivity. *E*: after the lights were turned on, the cell regained its spatial selectivity as soon as the curtains were drawn open. Firing rates were measured while the monkey was stationary (M) but was facing (indicated by the direction of firing rate bar) toward different views of the environment. In this type of experiment the monkey was moved to the places indicated, faced in a particular direction, and the firing rate was acquired independently of eye movements. Means and SE of the firing rates are shown, calculated over 4–10 time trials in which the monkey was at a particular place facing in a particular direction. c1–c4, cups from which food was available. Corners of the room are numbered. Note that in *B* the open bar is the firing rate with the view unobscured, and the closed bar is the firing rate with the view obscured.

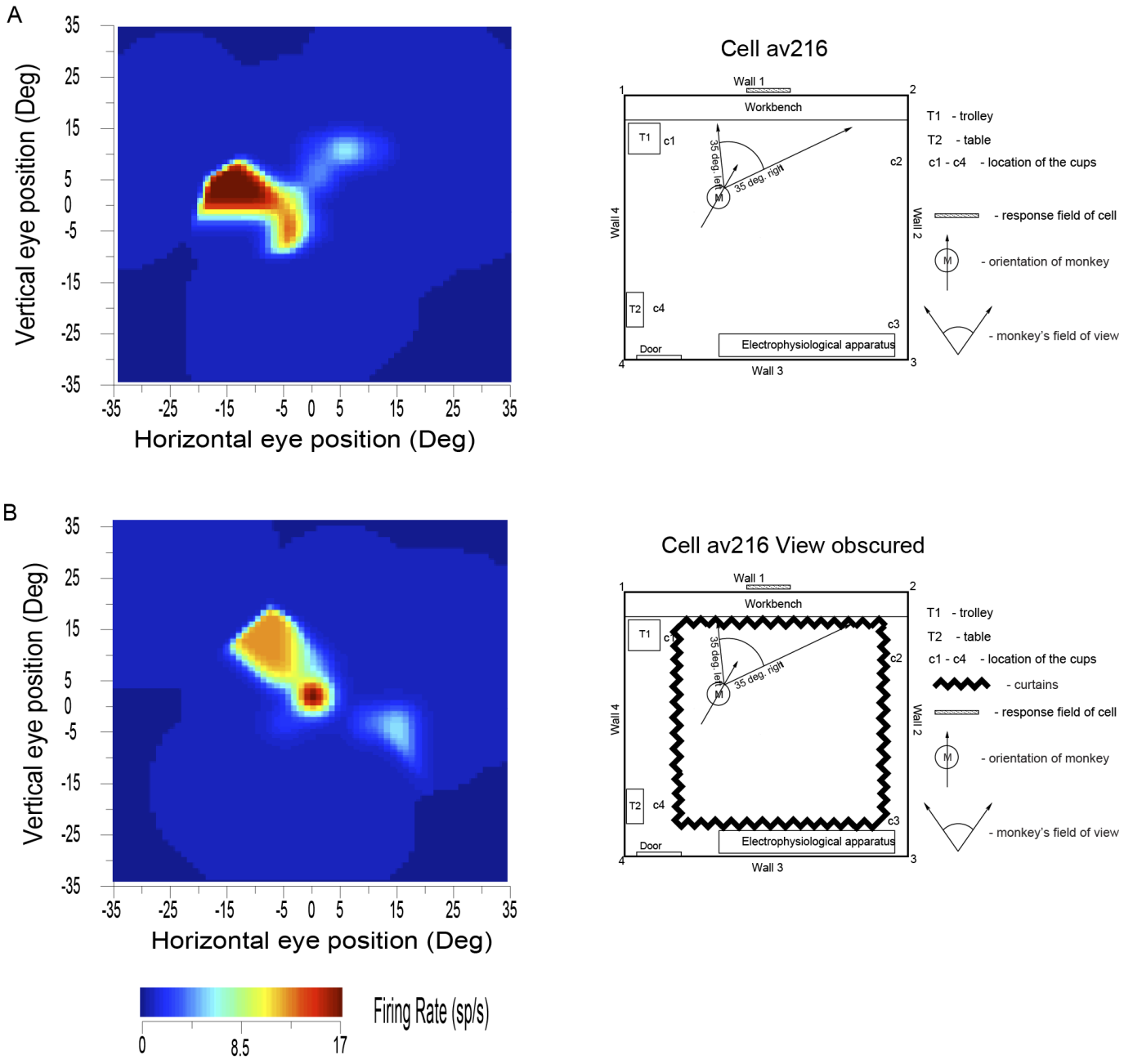


FIG. 2. Example of the firing of a hippocampal formation cell (*av216*) with the monkey stationary with his head facing in the direction indicated by the arrow when the curtains were drawn open (*A*) or were drawn closed (*B*). Firing rate of the cell in spikes/s is indicated by the blackness (*left*; calibration bar in spikes/s shown *below*) projected onto the monkey's field of view. Two-dimensional firing rate profile of the cell was smoothed for clarity using a 2-dimensional Gaussian spatial filter with a standard deviation of 0.2 of a pixel in a 14 × 14 array into which the firing rates were binned. (This degree of spatial smoothing is used to display the spatial view fields unless otherwise stated.) Space adequately sampled by the eye movements of the monkey is indicated by shading. A plan view of the room to indicate the monkey's view of the wall is shown (*right*). M, position of the monkey. *C*: raw waveform of *cell av216* is the large spike with good isolation from the spikes of a second neuron, which happened to be recorded simultaneously.

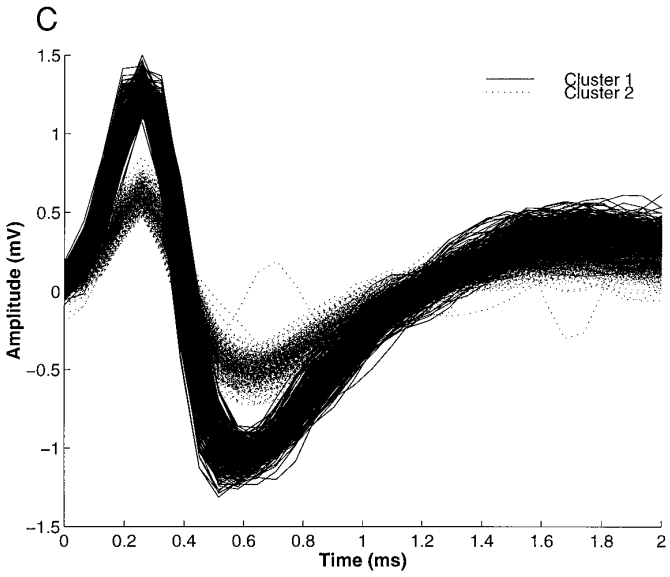


FIG. 2. (*continued*)

had only small responses with the curtains closed. The mean response with the curtains closed relative to the response with the curtains open was 19%, range 0–30%. These cells were located in the CA3 region.

In the second- and third-type experiments, some drift of the spatial view field was noted frequently when the curtains obscured the view. In addition, the fields sometimes became less sharply tuned (see examples in Figs. 2 and 4). This drift for most cells was in the range 5–15°.

The effects of obscuring the view details by closing the curtains are summarized in Fig. 5 for the whole population of 27 neurons investigated in the experiments described in this paper. Similar effects were found in the three types of experiment (as illustrated), and so Fig. 5 provides a useful summary of the data. Separate histograms are provided for non-CA3 cells and for CA3 cells. For the non-CA3 cells, that is for cells in CA1, presubiculum, and parahippocampal gyrus, the mean response with the curtains closed was 88% of that with the curtains open (range 30 to >100%). Significant differences in the reductions shown by the cells in these different subregions were not found. For the CA3 cells, the mean response with the curtains closed was 23% of that with the curtains open (range 0–40%). The percentage reduction for the CA3 cells was greater than that for the non-CA3 cells ($\chi^2 = 18.7$, df = 1, $P < 0.001$).

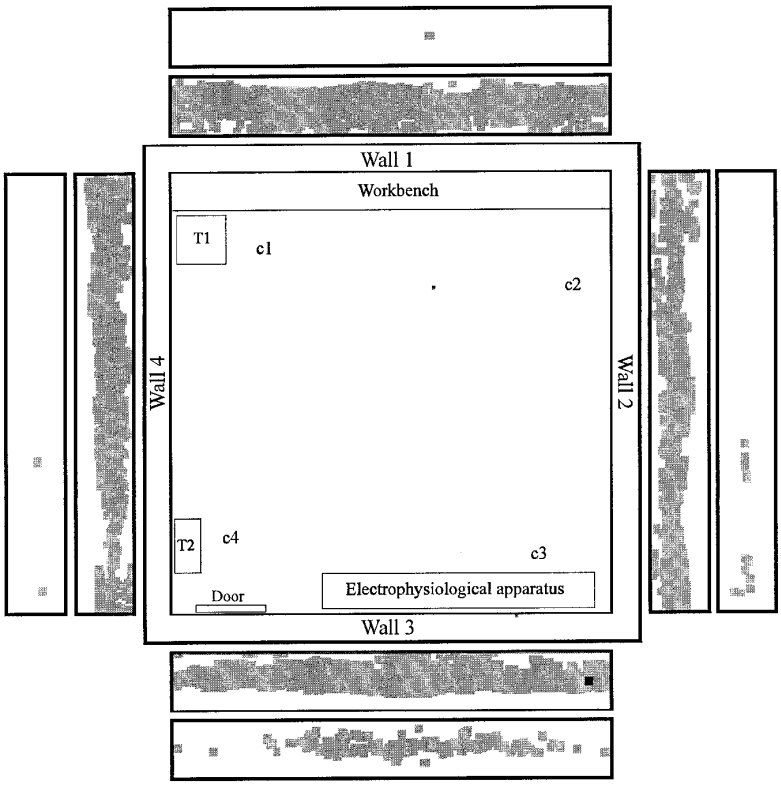
The sites at which the 27 spatial view cells analyzed in this paper were recorded are shown in Fig. 6. All the cells had low spontaneous firing rates (mean = 0.7 spikes/s, interquartile range 0.0–0.6). The peak firing rates were also relatively low, mean 10.1 spikes/s, interquartile range 6–13. These characteristics, together with the large amplitude and broad action potentials indicate that these neurons are likely to be pyramidal cells. Nineteen were in the hippocampal pyramidal cell field CA1 (7 neurons), the presubiculum (5 neurons), or the parahippocampal gyrus (7). These cells showed only minor reductions in their neural responses (to a mean of 88%) when the curtains were closed to obscure the view details. Eight were in the hippocampal CA3 cell region. These cells showed larger reductions in their neural responses (to a mean of 23%) when the curtains were closed to obscure the view details (see Fig. 5*A*). The cells recorded in the two different monkeys are shown in Fig. 6, which uses symbols V and Z to indicate that both CA3 cells and non-CA3 cells were recorded in both monkeys. As described elsewhere, the type of cell analyzed here comprises ≥10% of the cells we have isolated and analyzed in this testing situation in the primate hippocampus.

DISCUSSION

These experiments show that the responses of the majority of these spatial view cells (i.e., cells other than CA3 cells) can be produced when the details of the spatial scene are obscured (for example by using a curtain, see Fig. 3*B;* darkness is not crucial for the conclusions reached in the following discussion). What factors enable these cells to still respond when the view details are obscured? The triggering cues for the neurons to fire when the view details are obscured may include vestibular cues and proprioceptive cues. These would be activated when the monkey was rotated passively, which was sufficient if it made the monkey face toward an effective part of the environment, to make the cell fire (see e.g., in Fig. 1). The minor auditory cues in the environment also could play a role. However, these auditory cues alone were not sufficient to account for the spatial firing of these non-CA3 cells, for the firing also depended on whether the monkey was looking toward the effective part of the spatial scene (as shown in the second type of experiment, an example of which is shown in Fig. 3). Thus selection, by a combination of head and eye movements (taking into account the position where the monkey was located), of the appropriate part of the spatial scene appeared to be the condition for activation of these neurons.

For some neurons, obscuring the view details did produce a large reduction in the responses of the cells, and subsequent histological reconstruction showed that these cells were located mainly in the CA3 region (see Fig. 5*A*). This new finding provides further evidence on what activates these cells. The finding indicates that the cells are influenced by the visual input. Taken with other evidence, for example, that the neurons respond when the monkey looks at the location in space of its spatial view field independent of the place where the monkey is (Rolls et al. 1997), the new discovery thus adds to the description of these cells as spatial view cells.

These two findings lead to further consideration of what activates the non-CA3 cells. For the non-CA3 cells described here, spatial view also captures the point that the responses of these cells do depend on spatial location in that they respond when the monkey gazes to a particular spatial location and that although the neurons still can respond when the view details are obscured, the visual input is nevertheless normally important in their responses, because the spatial fields may drift or become less sharply tuned in the dark (see examples in Figs. 2 and 3). One possibility is that the neurons that did respond when the view details were obscured thus could be responding in relation to a remembered spatial view or location. The memory would be triggered by the vestibular and eye command/position signals. Neuronal responsiveness in relation to remembered events, or recall of a spatial scene from a part of it (the vestibular/eye command



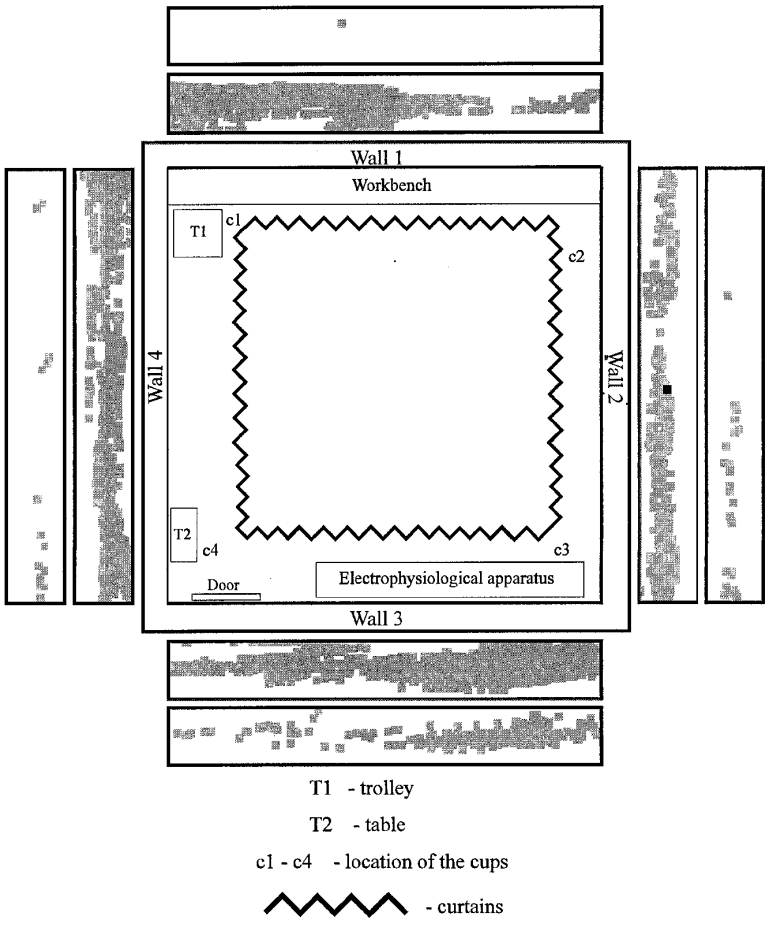


FIG. 3. Firing rate of hippocampal formation *cell av192* when the monkey was walking round in the environment. *Inner set of 4 rectangular boxes*: the monkey looked during the experiment at all 4 walls of the environment. Each time he looked at a part of a wall for ≥0.25 s, a spot was placed at the location on the wall. (Top of each wall is furthest from the center.) *Outer set of 4 boxes*: 4 walls shown, but in these a spot indicates where the cell fired. *A*: firing with the curtains drawn open so that the room was visible. *B*: firing of the cell when the monkey moved round in the environment with the curtains closed. Curtains are indicated by the zig-zag lines.

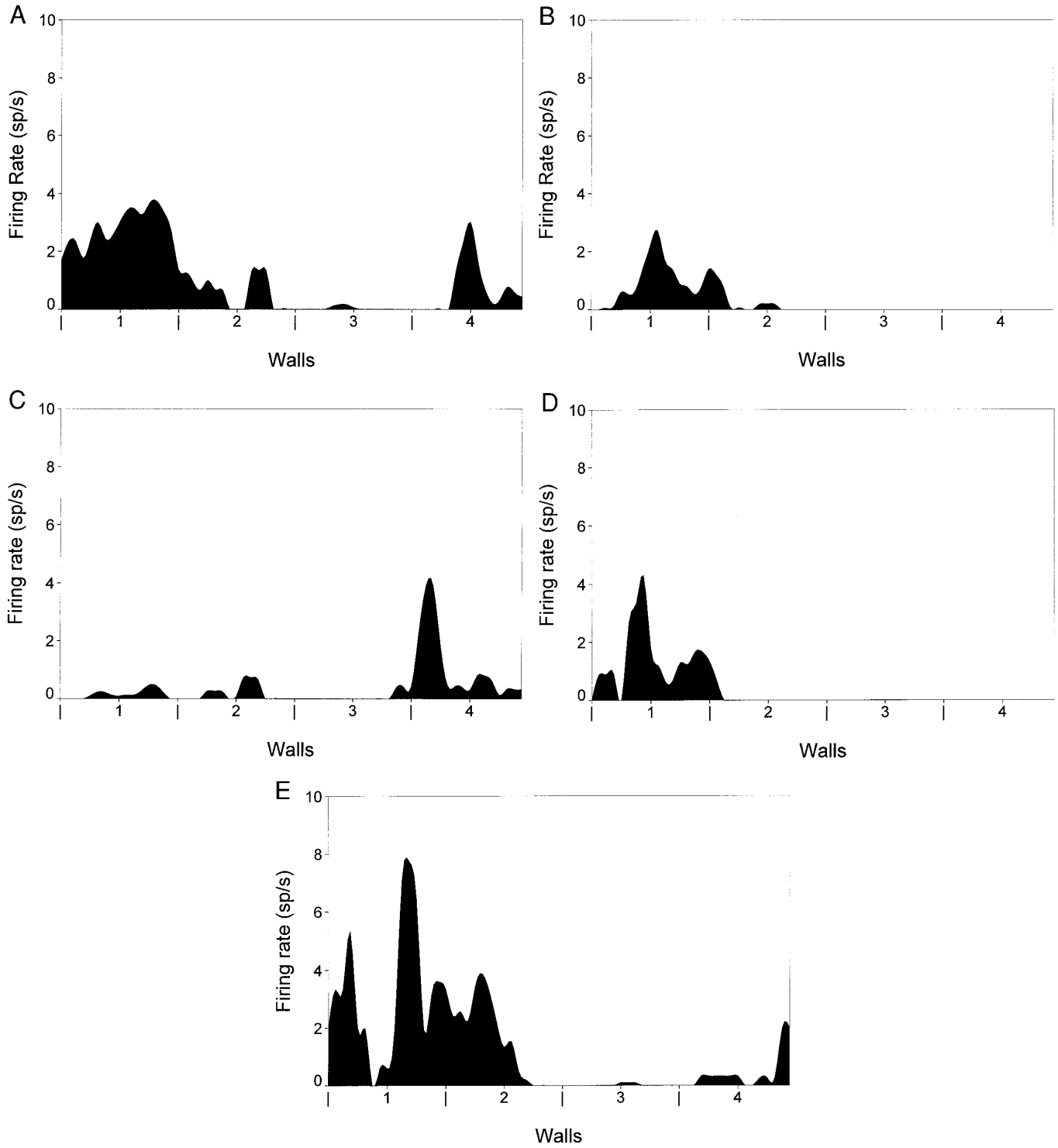


FIG. 4. Example of the firing of a hippocampal CA3 cell when the curtains were drawn open (*A*) or were drawn closed (*B*), were closed with the lights out (*C*), were closed with the lights on (*D*), and finally with the lights on and the curtains open to reveal the view again (*E*). Firing rate of the cell in spikes/s is plotted as a function of the horizontal position on the walls at which the monkey was looking. Sampling was 16 divisions horizontally for each wall, and smoothing with a 3 pixel moving average filter was applied. For a plan view of the environment, see Fig. 1.

input), seem to be very appropriate types of neuronal activity for a structure believed to be involved in the storage and retrieval from a partial cue of events, which frequently have a spatial component, at least as part of the context (Rolls 1989; Rolls and Treves 1998; Treves and Rolls 1994).

The interesting question then is raised of whether the hippocampal neurons described in this paper should be called spatial, or instead are they just responding to particular objects in the environment? Perhaps a working definition of the difference should be suggested before considering this.

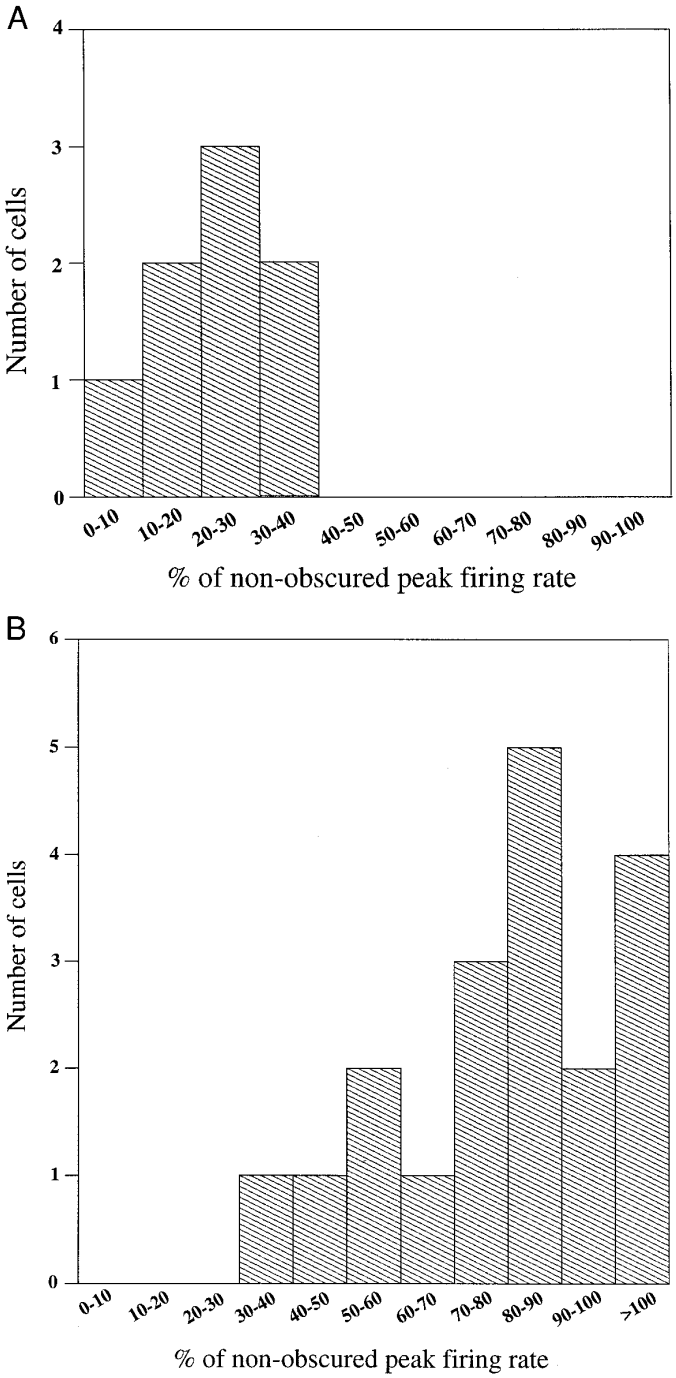


FIG. 5. *A*: histogram showing the firing rate of the 8 CA3 hippocampal neurons when the view details are obscured by curtains as a percentage of the firing rate when the view was not obscured. Firing rates used were the peaks in the smoothed firing rate 2-dimensional plots. *B*: histogram showing the firing rate of the 19 non-CA3 hippocampal formation neurons when the view details are obscured by curtains as a percentage of the firing rate when the view was not obscured.

An object could be defined as an entity that is not fixed in the environment but that normally is found moved to or moving to different parts of an environment and normally is seen with a range of different views of the object (i.e., the object can be moved to different orientations with respect to the environment). In contrast, a spatial environment normally is defined by a set of features that occur in a fixed relationship to each other in three-dimensional space. Each part of space may not need every feature normally in that part of space for it still to be classed as that part of space. Indeed, for the majority of the 27 spatial view neurons described here, their activation did still occur when most of the features defining that part of space were obscured by the curtains. (The remaining cues by which that part of space can be defined include evidence from the position of the eyes, as shown earlier). By way of additional clarification, we note that neurons that respond to objects in different parts of an environment would not be classed as spatial view cells. Indeed, there are cells in the primate hippocampal formation that respond to objects regardless of their position in space (Miyashita et al. 1989), and indeed, in the same testing conditions used here, we have found another type of cell that can be shown to respond to a particular object independently of spatial context. One of the arguments that leads to the use of ''spatial'' in the description of the spatial view neurons is that it is by virtue of the position in space that the monkey is looking toward that the representations are activated. This is shown by the fact that it is only when the monkey is turned to face the particular part occupied by spatial scene is that the presumably vestibular and eye command/position signals lead to the neuron firing in the view-obscured condition. Evidence that the visual input is important for defining and resetting the responses of these neurons was obtained for the cell illustrated in Fig. 1. The data shown in Fig. 1*D* were obtained after the monkey had been in darkness for several minutes but was currently in the light with the curtains closed. The neuron did not immediately recover its spatial selectivity. It was only immediately after the curtains were drawn open again $\sim$1 min later that the neuron then regained its spatial selectivity.

The next issue we discuss is why the CA3 cells show a larger reduction in their firing when the view is obscured than do other hippocampal or parahippocampal cells [to 23 vs. 88% of the firing rate with the view details visible. We note that although this difference is highly statistically significant, $P < 0.001$, the sample of CA3 cells analyzed in the type of experiment described here is still small (8), and so results from further cells will be helpful.] The most likely possibility is that the reduction in the firing of the CA3 cells reflects the reduction in the sensory drive or recall cue to a CA3 memory system. Even the autoassociation present in this system would be insufficient to produce full completion with the incomplete input. However, with an additional association stage of synapses implemented in the Schaffer collateral connections from the CA3 to the CA1 cells, further retrieval would occur by a pattern association effect, resulting in better firing of the CA1 than the CA3 cells. Exactly such a process has been observed when partial recall cues (which might result in experiments in which the spatial view was obscured) were used in the simulation of the hippocampus performed by Rolls (1995) and has been analyzed with an information theoretic approach by Treves (1995). The higher information content of CA1 than CA3 cells is especially evident in the simulations when the CA3 autoassociation function (of the CA3 to CA3 recurrent collaterals) is not working optimally (or, in the simulations, is switched off) (see Rolls 1995). This is the explanation we favor. An

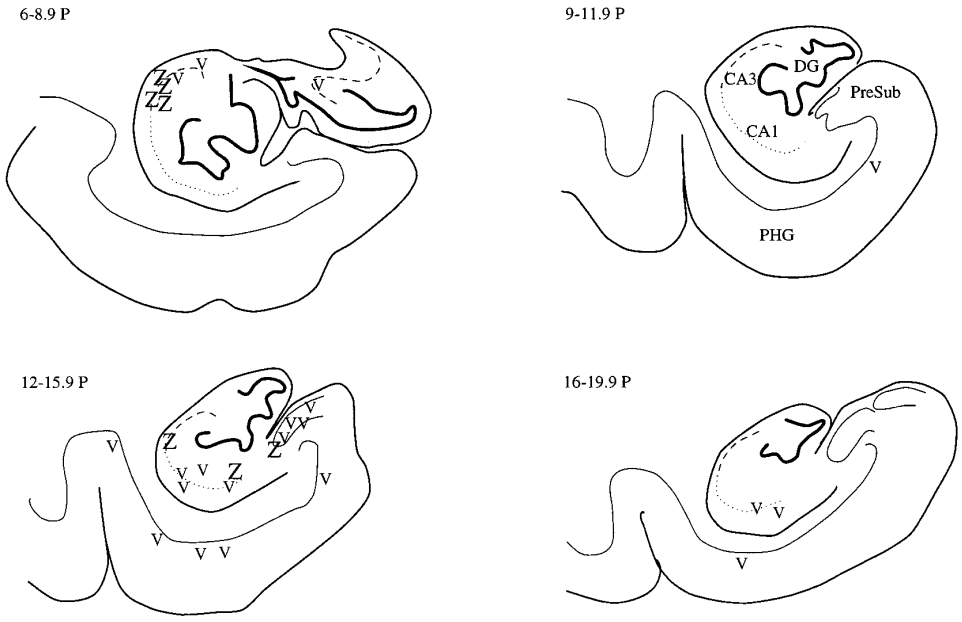


FIG. 6. Hippocampal and parahippocampal sites at which different spatial view cells were recorded. Coronal sections at different distances in mm posterior (P) to the sphenoid reference are shown. V, cells recorded in *monkey av;* Z, cells recorded in *monkey az*. ●, neurons in the CA3 cell region; CA3, CA3 hippocampal pyramidal cell field; CA1, CA1 hippocampal pyramidal cell field; DG, dentate gyrus; Pre, presubiculum; PHG, parahippocampal gyrus.

alternative possibility is that the direct perforant path input to the CA1 cells provides sufficient additional signal to the CA1 cells beyond that provided by the CA3 cell inputs to CA1 cells that the CA1 cells respond much better. The available evidence suggests that the entorhinal to CA1 inputs are weak (see Rolls 1996), but this does remain a possibility.

Figure 5 shows that most cells had *some* reduction in their firing rate when the view details were obscured. With the much smaller sample of eight view cells analyzed by Rolls and O'Mara (1995) under view-obscured conditions in non-locomoting conditions, there was, for all cells, at least some reduction in the selectivity of the spatial properties of the cells. The present study extends the previous study by quantifying the magnitude of the effects under view occluded conditions (see Fig. 5), by showing that the reduction of firing rate under view-obscured conditions is greater for CA3 than for non-CA3 cells (see Fig. 5), by performing the investigation in monkeys that could locomote, which is necessary for rat spatial cells to reveal their properties (Foster et al. 1989), and by showing that the spatial fields of many spatial view cells are activated simply when the monkey moved his eyes to look toward the spatial location of the view field with the view details obscured or in darkness.

Many view (or ''space'' or ''spatial view'') cells have been found in this series of experiments in the locomoting monkey (Rolls et al. 1995, 1997, 1998). (The current number of spatial view cells is 45.) No place cells have been found in this series of experiments that responded based on where the monkey was independently of where he was looking in the environment. (We have in addition found head direction cells in the primate, and they are very unlike spatial view cells in that the responses of spatial view cells depend on the allocentric position in the environment at which the monkey is looking, independently of the head direction required to look at that position. A report on these findings is in preparation.) These spatial view cells in the primate hippocampus are thus unlike place cells found in the rat (Muller et al. 1991; O'Keefe 1979). Primates, with their highly developed visual and eye movement control systems, can explore and remember information about what is present at places in the environment without having to visit those places. Such view cells in primates thus would be useful as part of a memory system, in that they would provide a representation of a part of space that would not depend on exactly where the monkey was and that could be associated with items that might be present in those spatial locations. An example of the utility of such a representation in monkeys might be in enabling a monkey to remember where it had seen ripe fruit. [Object-place memory tasks are impaired by hippocampal system lesions in monkeys (see Angeli et al. 1993; Gaffan 1994; Gaffan and Saunders 1985; Parkinson et al. 1988)]. An equivalent in humans might be remembering where a person had been seen or where keys had been left. The representations of space provided by hippocampal view-responsive neurons thus may be useful in forming memories useful in spatial environments.

The cells described here typically were searched for during active locomotion. If a cell had a spatial view field during active locomotion, the field also could be demonstrated with the monkey stationary. It could of course be that experience with active locomotion in the environment helped the cells to respond with the monkey stationary. The possible difference from findings in the rat (cf. Foster et al. 1989) may be due to the fact that even a stationary monkey can actively explore its environment by precise eye movements.

The representation of space in the rat hippocampus, which is of the place where the rat is, may be related to the fact that with a much less developed visual system than the primate, the rat's representation of space may be defined more by the olfactory and tactile as well as distant visual cues present and thus may tend to reflect the place where the rat is. Although the representation of space in rats therefore may be in some ways analogous to the representation of space in the primate hippocampus, the difference does have implications for theories of hippocampal function. In rats, the presence of place cells has led to theories that the rat hippo-

campus is a spatial cognitive map and can perform spatial computations to implement navigation through spatial environments (Burgess et al. 1994; O'Keefe 1991; O'Keefe and Nadel 1978). The details of such navigational theories could not apply in any direct way to what is found in the primate hippocampus. Instead, what is applicable to both the primate and rat hippocampal recordings is that hippocampal neurons contain a representation of space (for the rat, primarily where the rat is, and for the primate, primarily of positions ''out there'' in space), which is a suitable representation for an episodic memory system. In primates, this would enable one to remember, for example, where an object was seen. In rats, it might enable memories to be formed of where particular objects (e.g., defined by olfactory, tactile, and taste inputs) were found. Thus at least in primates, and possibly also in rats, the neuronal representation of space in the primate hippocampus may be appropriate for forming memories of events (which usually have a spatial component). Such memories would be useful for spatial navigation for which, according to the present hypothesis, the hippocampus would implement the memory component but not the spatial computation component.

Finally, the spatial representation found would be ideal for association within the hippocampus to a representation of an object to implement an episodic memory. We have suggested that such an episodic memory could be laid down in the hippocampus using the neuronal network process of association implemented by the recurrent collateral axons of the CA3 neurons (see Rolls 1989, 1995, 1996; Treves and Rolls 1994).

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