



Place cells, navigational accuracy, and the human hippocampus

John O'Keefe^{1,2}, Neil Burgess^{1,2}, James G. Donnett¹, Kathryn J. Jeffery¹
and Eleanor A. Maguire³

¹Department of Anatomy and Developmental Biology, and ²Institute of Cognitive Neuroscience, University College London, Gower Street, London WC1E 6BT, UK

³Wellcome Department of Cognitive Neurology, Institute of Neurology, University College London, 12 Queen Square, London WC1E 6BT, UK

The hippocampal formation in both rats and humans is involved in spatial navigation. In the rat, cells coding for places, directions, and speed of movement have been recorded from the hippocampus proper and/or the neighbouring subicular complex. Place fields of a group of the hippocampal pyramidal cells cover the surface of an environment but do not appear to do so in any systematic fashion. That is, there is no topographical relation between the anatomical location of the cells within the hippocampus and the place fields of these cells in an environment. Recent work shows that place cells are responding to the summation of two or more Gaussian curves, each of which is fixed at a given distance to two or more walls in the environment. The walls themselves are probably identified by their allocentric direction relative to the rat and this information may be provided by the head direction cells. The right human hippocampus retains its role in spatial mapping as demonstrated by its activation during accurate navigation in imagined and virtual reality environments. In addition, it may have taken on wider memory functions, perhaps by the incorporation of a linear time tag which allows for the storage of the times of visits to particular locations. This extended system would serve as the basis for a spatio-temporal event or episodic memory system.

Keywords: hippocampus; spatial navigation; rat; virtual reality; functional imaging; neural network

1. INTRODUCTION

Cells in the hippocampus of the rat signal the animal's location in an environment. Damage to this structure leads to severe spatial impairments in rats. These findings have provided support for the idea that the hippocampus in animals such as the rat operates like a cognitive map (O'Keefe & Nadel 1978). In this paper, we will discuss the way in which an environment is represented by the constellation of firing across a large number of hippocampal place cells, how the location and shape of the firing fields of the cells is controlled by environmental stimuli, how information about the animal's speed of movement through the environment is coded, and what our understanding of the rat hippocampus tells us about the functions of the human hippocampus.

2. REPRESENTATION OF AN ENVIRONMENT WITHIN THE HIPPOCAMPUS

Cells in the CA1 field of the hippocampus code for an environment using a distributed representation. Neighbouring cells are as likely to code for distant regions of an environment as they are to code for nearby regions. Figure 1 shows the place fields of 15 CA1 pyramidal cells recorded simultaneously from a single tetrode while the animal moved around a 40 cm × 40 cm box, searching for small bits of rice. There was only a small lip on the box

allowing the animal to search over the edge as well as on the floor of the box (see layout of the environment in figure 1). Each of the four individual electrodes in the tetrode has a diameter of 25 μm, approximately the size of a pyramidal cell body and can see action potentials from cells up to 100–150 μm away. If we assume that the amplitude of an action potential recorded by an extracellular electrode is a function of the distance of the spike generator from that electrode, then the tetrode allows us to get some idea of the topographical relation between the place fields of cells and their anatomical relation to each other. Cells that are anatomically closer to one electrode of the tetrode will have spikes of a larger amplitude on that tetrode. We can arrange the cells in a rough topographical ordering on the basis of the size of the potential on the different electrodes. In figure 1, cells whose amplitudes are relatively larger on electrode 1 are placed in the upper left-hand corner of the picture, those which are larger on electrode 2 are placed in the upper right-hand corner and so on. We draw two conclusions from this picture. First, the fields of the 15 cells cover a considerable area of the environment and second, there does not appear to be any obvious topographical relation between the field locations and the anatomical locations of the cells relative to each other within the hippocampus. This lack of topography contrasts with a recent claim that there is a tendency for place fields recorded on the same electrode to show similar place fields in an environment

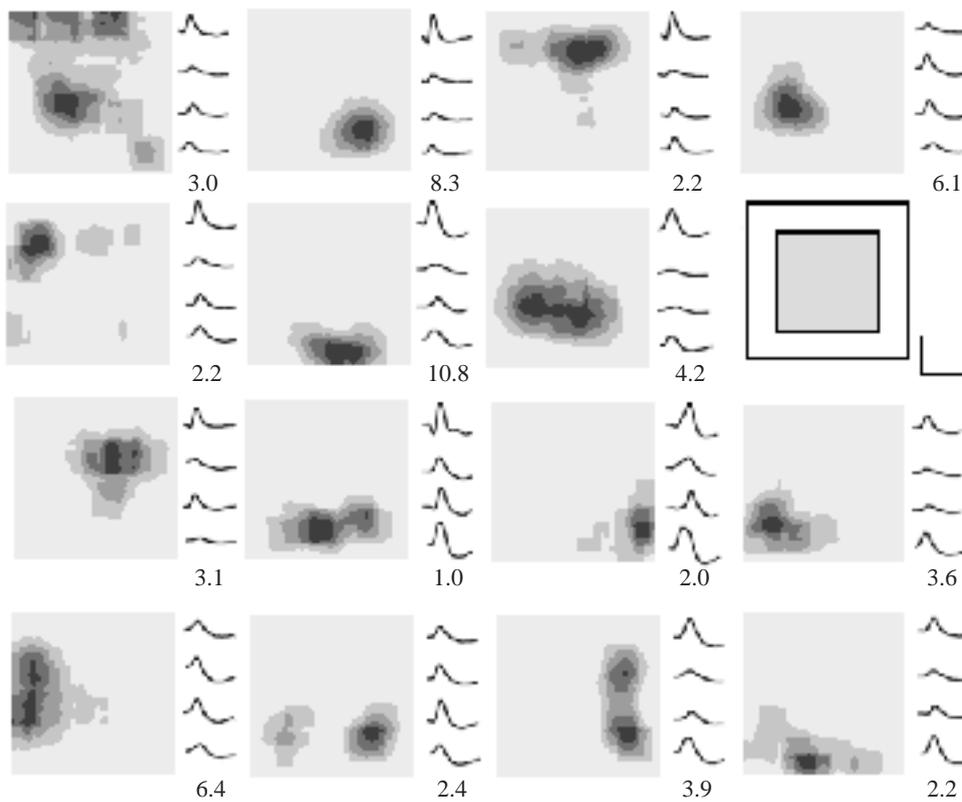


Figure 1. Place fields of 15 complex-spike cells recorded simultaneously in the CA1 field of the hippocampus of a rat searching for grains of rice on a small 40 cm \times 40 cm open platform. The surface area of the holding box relative to the overall camera view is shown in the inset. The waveform for each cell as recorded on the tetrode is shown to the right of the place field. Firing rates within the place fields are represented by four grey-scale levels, each reflecting 20% of the peak firing rate. Peak firing rate within each field is shown below the waveform. Calibrations for the spike waveform are 375 μ V, 250 μ V, 300 μ V and 300 μ V, respectively, from top to bottom and 1 ms.

(Shapiro *et al.* 1997). The conclusion that a small number of cells is adequate to represent the environment is strengthened by the inclusion of additional cells recorded on other tetrodes at the same time as those shown in figure 1. In all, 35 cells with place fields on the box were recorded at the same time and their fields are represented in figure 2. Here, the fields are represented by their relation to the environment and not to their anatomical location within the hippocampus. Cells with fields along the east side of the testing environment have been placed on the right-hand side of the figure; those with fields at the south side of the environment have been placed towards the bottom of the figure, and so on. Several aspects of the place field phenomenon can be seen from this figure. First, the 35 cells cover a large proportion of the environment. On the basis of similar recordings, Wilson & McNaughton (1993) calculated that approximately 130 place cells would be sufficient to allow the hippocampus to compute the animal's location in an environment to an accuracy of 1 cm s^{-1} and about 380 cells for an accuracy of 1 cm per 0.1 s. Second, the fields towards the edge of the environment are smaller than those towards the centre. Notice that this change in field size occurs independently in the x and y directions. For example, as one moves from left to right along the bottom row of the figure, the fields sizes get larger and then smaller in the x dimension independently of their height in the y dimension. We will discuss these properties of place fields in § 3 in the context of our model of place field formation. A second property of the place cells recorded in an open field environment is shown in figure 3. This picture shows the firing fields of four of the cells from figure 1. For each cell, the central panel shows the firing field without regard to the direction in which the animal is moving. In

the surrounding panels are shown the same firing fields when the animal's direction of movement is taken into account. It is clear that the fields in the different directions are more or less equivalent. It was this property of omnidirectionality (see O'Keefe 1976; Muller *et al.* 1987) which originally suggested that these cells were not coding for simple sensory stimuli but were instead computing the more abstract concept of place or location. In § 3 we will discuss experiments which provide information about the role that sensory information plays in the computation of the animal's location.

3. SENSORY CONTROL OVER THE LOCATION AND SHAPE OF THE HIPPOCAMPAL PLACE CELLS

Why do the hippocampal place cells fire in particular locations in an environment? The way to answer this question is to study the types of modifications of the environment that lead to changes in the location of the place fields or in the shapes of those fields. In the first set of experiments of this kind, O'Keefe & Conway (1978) recorded place cells from the hippocampus of rats that had been trained on a place discrimination on a T-maze set in a cue-controlled environment. The only spatial cues available to the animal to guide its behaviour to the goal were a set of objects and stimuli around the periphery of the environment. Rotation of the constellation of spatial stimuli resulted in a concomitant rotation of the place fields. Similar results were reported by Muller and co-workers (1987). In their experiments, cells were recorded from animals that had been trained to forage for food pellets in a cylindrical environment where the only polarizing spatial cue was a white card attached to the wall of the cylinder. Despite the fact that the animals were not

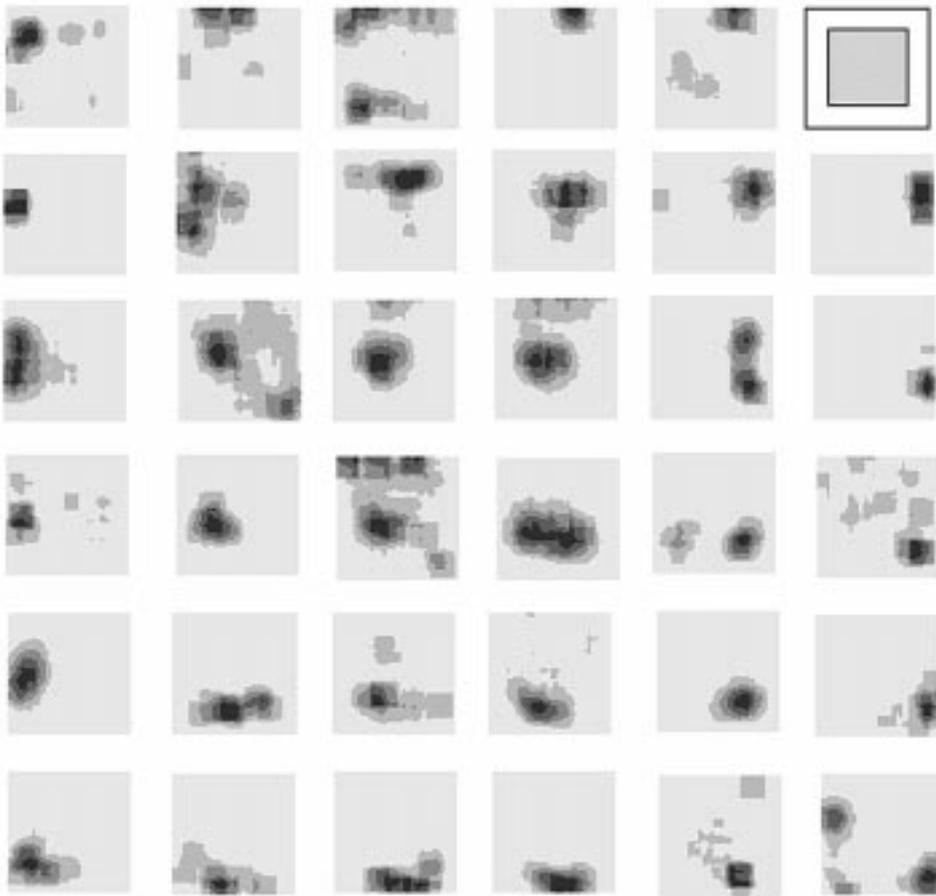


Figure 2. Place fields of 35 simultaneously recorded hippocampal complex-spike cells arranged according to field location. Fields towards the northwest of the box are shown in the upper left part of the figure, those towards the northeast in the upper right and so on. Cells with double fields are placed with respect to the stronger field. Notice that the fields collectively cover a large proportion of the environment.

trained to pay attention to the cue card to solve the behavioural task, the fields rotated with rotation of the card in a manner strictly analogous to that found in the O'Keefe & Conway (1978) study. The difference between these two studies points to an important aspect of the property of place cells: the analysis of the sensory information which determines where in the environment each cell will fire is not dependent on the animal's attention to that set of stimuli.

It would be interesting to compare the place fields of cells recorded in two different conditions, one in which the animal was using a place strategy to solve the problem and therefore presumably attending to the spatial cues, and the other in which it was reaching the goal by a non-spatial strategy.

It appears then that cues at the periphery of an environment determine the angular orientation of the place fields. In a recent and important study, Cressant *et al.* (1997) have shown that prominent objects located towards the centre of an enclosure cannot provide this polarizing information but will readily do so when the same objects are moved to the periphery of the enclosure. As we shall see shortly, it is reasonable to suppose that the function of these polarizing cues in all of these experiments is to orient the head direction system and only indirectly to control the angular location of the place cell's fields.

A second geometrical manipulation of the environment which has provided information about the sensory control of the place cells has been environmental enlargement. Muller & Kubie (1987) have shown that some place cells increase their firing field when the size of a cylindrical or

rectangular environment is doubled. Interestingly, the size of the field increase was not commensurate with the size of the increase in the environment. As we shall see in §4, this somewhat surprising result is explicable on the basis of the model we have generated for place cell construction.

The final type of environmental manipulation is one in which the size and the shape of the environment was modified. O'Keefe & Burgess (1996) recorded place cells in four rectangular boxes that varied in the length of one or both dimensions. The walls of each box were constructed from the same four planks of wood standing on edge (see figure 4*a*). These planks of wood were frequently interchanged as was the paper floor of the environment to eliminate local cues which could be used to identify position. Figure 4*b,c* shows two examples of cells recorded in this experiment. The place field of the cell in figure 4*b* signalled the animal's location in the bottom left corner of the box regardless of the shape and size of the box. In essence, the cell ignored both the top and right-hand walls. In contrast, the cell whose firing pattern is shown in figure 4*c* was influenced by both the left- and right-hand walls as well as the top wall. This is clearly shown by the firing pattern in the horizontal rectangle where the field becomes elongated along the long dimension of the box. These, and similar place field transformations, have led us to propose the model of place cell formation which is illustrated in figure 4*d,e*. The essence of the model is that each place field comprises the summation of two or more Gaussians. The location of the centre, the amplitude and the width of each Gaussian is

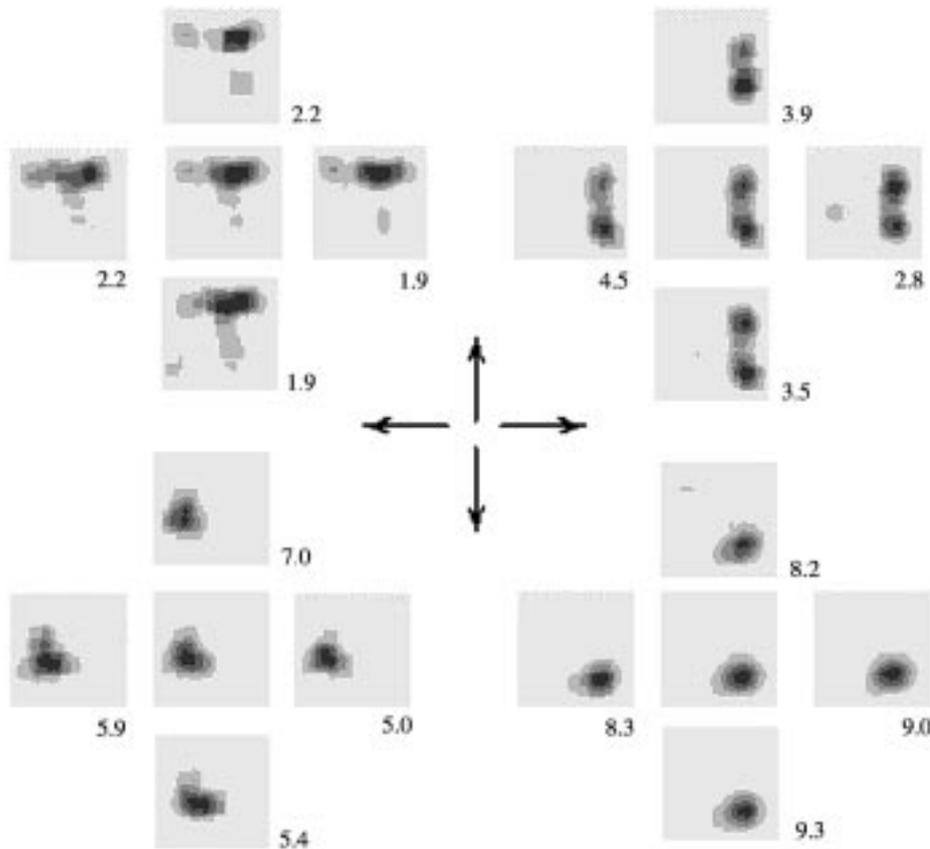


Figure 3. Omnidirectional firing pattern in four hippocampal complex-spike cells. For each cell, the central panel shows the overall firing pattern irrespective of the direction of movement of the animal through the place field. In the surrounding panels, the firing fields have been separated according to the direction of movement. Northward direction is at the top, eastward to the right, southward at the bottom, and westward to the left. Peak firing rate is shown at the bottom right of each panel. Notice that each cell fires in the appropriate location irrespective of the animal's direction of movement.

determined by its distance to a particular wall in a particular direction. Gaussians which are centred close to the wall which controls them are higher and more sharply peaked than ones centred further away. According to the model, the fields shown in figure 4*b* would be formed by the summation of one Gaussian fixed at a close distance to the left-hand wall of the box and a second Gaussian fixed to the bottom wall of the box (see figure 4*d*). The place field shown in figure 4*c* would comprise four Gaussians, each one fixed to one of the walls of the box. As one can see in figure 4*e*, stretching the box along the horizontal dimension results in a pulling apart of the Gaussian curves fixed to the left-hand and right-hand walls with the resultant flattening and stretching of their summed curve. There are two notable features of this model which we would like to discuss here. The first is that the way in which the experiment was done meant that there was no distinctive sensory input intrinsic to a wall which the animal could use to differentiate any one wall from another. This is because the same four planks of wood were regularly interchanged to form the walls of the box. It follows that the animal must have been using some other source of information to identify each wall. The model suggests that this information consists of the direction of the wall from the animal and that this information is provided by the head direction cells found in the postsubiculum and the anterior thalamus. These are cells that signal the direction in which the animal's head is pointing in its environment regardless of its location in that environment (Taube *et al.* 1990). We will discuss evidence for this suggestion in §4. The sources of direction input in the experiments under discussion were not identified but were

probably distant visual cues from the room external to the recording box and internal proprioceptive and vestibular (idiothetic) cues. The second aspect of the model which needs discussion is the means by which the animal determines its distance from the relevant wall. In our original paper, this was not specified. McNaughton (1996) has suggested that this is achieved primarily on the basis of self-motion cues. He suggests that the animal registers each contact with a wall that he bumps into and monitors the amount of movement from that wall as an indication of distance. We believe that this is too narrow a view and prefer to stick with the suggestion incorporated in the original cognitive map theory (O'Keefe & Nadel 1978) that several ways of measuring distance are available to an animal. In experimental paradigms in which there are many visual cues to distance, we believe that these are the primary source of distance information. For example, in our model of hippocampal control of navigation (Burgess & O'Keefe 1996), we suggested that the animal could calculate its distance to a wall on the basis of the vertical height, on its retina, of the line where the wall meets the floor. Under circumstances in which strong and salient visual cues are not available, the rat may use self-motion information as it moves away from identified features of the environment such as the walls of the box, but it also might use information from other modalities, for example, auditory or olfactory cues. The possibility that the animal uses self-motion cues to determine distance is strengthened by the existence of cells such as the one shown in figure 5. The firing rate of this cell was a linear function of the speed with which the animal moved through the environment. As shown in the figure, this relation between speed and firing rate was main-

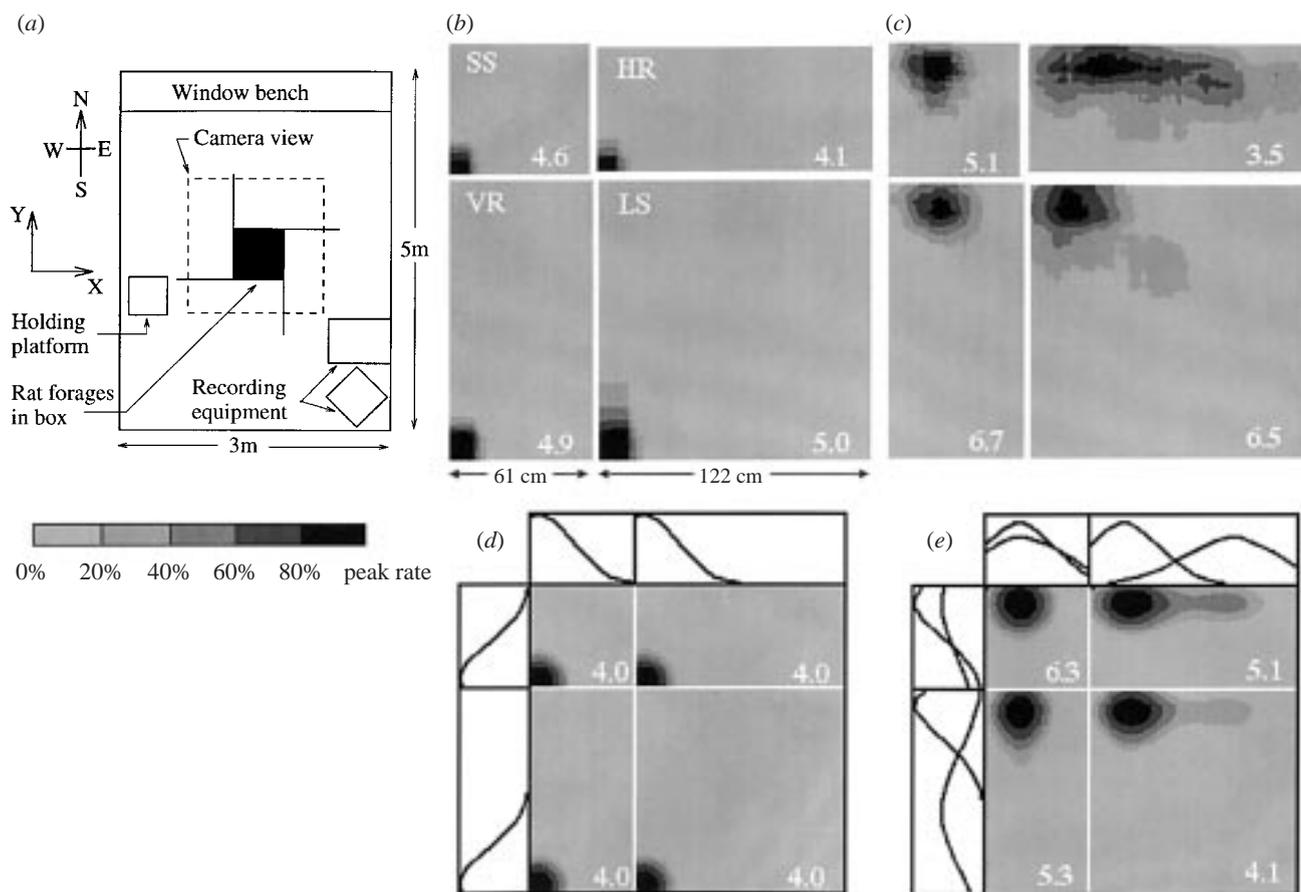


Figure 4. (a) Layout of the experimental room as seen from above. The dashed area represents the camera view and the black-filled region represents the small-square (SS) testing box. The horizontally oriented (HR), vertically oriented (VR) rectangular boxes, and the large-square (LS) testing box were all created from the same wooden planks in different configurations. (b) Firing field of a simple place field in the four rectilinear environments. The cell fired in the southwest corner of each box irrespective of the overall box shape. (c) Firing field of a more complex place cell. The field centre maintained a fixed distance from the north and west walls but was stretched towards the east wall in the horizontal rectangle (c). (d, e) Computational models of the fields shown in b and c, respectively (after O'Keefe & Burgess 1996).

tained irrespective of the direction in which the animal moved. Furthermore, requiring the animal to exert more force during the movement by pulling against a weight suspended from a pulley slowed its speed but had no effect on the speed–firing rate relation. These speed cells are only encountered rarely in the hippocampal formation and their waveform profiles suggest that they are recordings from axons. It seems likely that the cell bodies are located elsewhere, in one of the nuclei projecting to the hippocampus. As we shall see from the results of our experiments on functional imaging of the brain during human navigation (see §4), a candidate nucleus where the computation of speed through an environment might take place is the caudate nucleus.

4. HEAD DIRECTIONAL CONTROL OF THE ANGULAR ORIENTATION OF THE HIPPOCAMPAL PLACE FIELDS

As we have seen, the hippocampal place fields can be rotated by the rotation of cues at or near the periphery of the environment. Furthermore, once the place fields have been rotated into a new location they remain in that orientation following the removal of the spatial polarizing cues

at the periphery of the environment (Muller *et al.* 1987; O'Keefe & Speakman 1987). Appropriate orientation of the animal's sense of direction is maintained by both visual and self-motion cues (Sharp *et al.* 1995; Wiener *et al.* 1995). In the absence of salient visual cues, the animal's sense of direction is continually updated on the basis of self-motion information. This has been demonstrated in experiments in our laboratory in which the rat's internal direction sense was altered by slowly rotating the animal in a small enclosed box outside of the environment (Jeffery *et al.* 1997). In this experiment, we assume the animal uses self-motion cues to continually update its sense of direction. In almost every case, the place fields rotated to maintain their alignment with the rat's internal direction sense. When the visual and idiothetic cues are both present but set in opposition to each other, the visual cues usually predominate, unless they have been experienced as unreliable directional indicators (Jeffery 1998).

5. ROLE OF THE HUMAN HIPPOCAMPUS AND SPATIAL NAVIGATION

Ideas about the function of the human hippocampus have emphasized its role in memory and in particular in

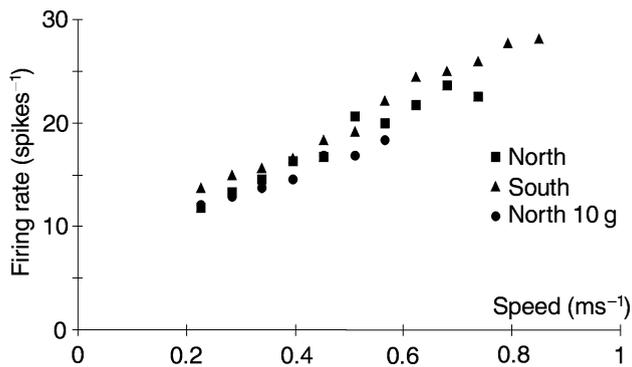


Figure 5. Relation between firing rate of speed cell and speed of running on a linear track. Relation is maintained irrespective of direction of the movement and is not affected by increasing the effort required to reach any particular speed. In condition north 10 g, the rat was required to run in a northward direction while lifting a small 10 g weight attach to it via a string and pulley arrangement (J. O'Keefe, J. G. Donnett and P. Martin, unpublished results).

declarative or episodic memory. This stems primarily from the evidence that patients with damage to the hippocampal formation are severely amnesic (Scoville & Milner 1957). Patients such as H.M. have considerable difficulty recalling events of the past. Although H.M. has damage which extends beyond the narrowly defined hippocampus, other amnesic patients such as R.B. have histologically verified damage restricted to the hippocampus (Zola-Morgan *et al.* 1986). Recent work on three patients who sustained bilateral damage limited to the hippocampus early in life (Vargha-Khadem *et al.* 1997) suggests that such damage results in memory deficits for episodes and events but not for semantic or other factual material. It is particularly noteworthy in the present context that of the two formal recognition memory tasks on which these patients were impaired, one was an object-in-location task. These results raise several questions. Is there a special role for the human hippocampus in spatial navigation analogous to that in the rat? If there is, how does this tie into the more general episodic memory deficit characteristic of amnesic patients? In this section, we will present evidence which suggests that the answer to the first question is yes and then go on to suggest how the spatial system in humans might participate in the more general function of storing information about episodes and events.

Patients with damage to the right temporal lobe which includes the hippocampus have been shown to be selectively deficient in the memory for the location of objects. This was in the context of relatively preserved memory for the identity of the objects themselves (Smith & Milner 1982, 1989; but see Cave & Squire 1991). In a direct test of human cognitive mapping, Maguire *et al.* (1996a) studied the ability of normal subjects and patients with left or right temporal lobe damage to form spatial representations on the basis of viewing film footage of two routes through a small town. They showed the film footage several times until both groups were completely successful in recognizing scenes from the film when these were shown with appropriate foils in a forced-choice recognition task. The patients required slightly more

trials than normals to reach and maintain perfect performance in scene recognition. Subsequent tests showed that the patients were particularly deficient in placing the scenes in the order in which they were encountered during the film, in estimating the distance between two scenes, and in drawing maps of the town. Of particular interest was the finding that patients with left temporal lobe damage were as impaired in many of these tasks as the right temporal patients. Maguire and her colleagues have argued that there is a role for both mesial temporal lobes in human navigation in large-scale environments.

Recent results from functional imaging experiments support a role for the medial temporal lobe in human navigation in large-scale environments. Positron emission tomography experiments in which subjects were scanned during the acquisition of spatial information provided by a film similar to that used in the Maguire *et al.* study showed activation in the right and left medial temporal lobe and in the right hippocampus (Maguire *et al.* 1996b). Furthermore, scanning of taxi drivers while they imagined driving along routes from one location to several others in London also showed activation of the right hippocampus and both parahippocampal gyri (Maguire *et al.* 1997). More recently, our group has used virtual reality techniques to allow subjects to learn about large-scale environments and to find their way from one location to another in these environments during scanning experiments. In our original experiments (Maguire *et al.* 1998a), we scanned volunteers while they were learning about two simple environments: one environment was relatively featureless while the other contained a set of distinctive objects which the subjects were asked to remember so that they could locate them subsequently. Learning the layout of the first environment did not engage temporal lobe structures while learning the second produced activation of the right parahippocampal gyrus. In our latest study (Maguire *et al.* 1998b), we have used a complex virtual environment measuring about 75 × 75 virtual metres and containing several main roads and in addition many shops and buildings which the subject could enter and navigate through. The subjects explored this environment for periods of 30–60 min until they felt they knew their way around reasonably well. At this point their brains were scanned during four conditions. In the first condition, they were instructed to go from their present location in the virtual world to a particular destination. In the second condition, they were asked to do the same except that now previously open doors were closed and a roadblock was moved across one of the main roads. These changes required the subject to take detours to reach their destinations. In a third condition, the subjects were asked to move through the environment following a trail of arrows on the floor. In this condition, therefore, they moved through the environment in a similar fashion to the first two conditions but without the requirement to use a spatial representation or a cognitive map to do so. In the fourth and final condition, subjects were asked to view static scenes from the environment and to decide whether a given scene contained a particular feature. The results enable us to map out the network of brain structures which cooperate to enable subjects to navigate

through the virtual world and, we assume, the real world as well.

The network of brain areas revealed as participating in navigation includes both left and right hippocampi, the right inferior parietal lobe, the medial parietal lobes, the right caudate nucleus, and the prefrontal cortex. All movement conditions whether guided by a spatial representation (conditions 1 and 2) or by arrows (as in condition 3) when compared with the static scene condition activated the inferior parietal and the medial parietal cortices. To show activation in the hippocampus it was necessary to take each subject's performance into account. Subjects did not always successfully reach the target destinations and these trials were identified as incorrect navigation trials. Both left and right hippocampi were active when correct navigation was compared with incorrect navigation during condition 1. We considered next only those trials in which the subjects went to the correct location. Correct navigation in conditions 1 and 2 compared with movement through the environment following arrows (condition 3) activated the right hippocampus.

To examine in more detail the relation between navigation and bloodflow in the hippocampus, we constructed a measure of the accuracy of navigation. At regular intervals along a subject's path we measured the angular deviation from the direct heading towards the goal. The average of all these angular deviations over the entire path length gives a measure of inaccuracy of navigation. We subtracted this measure of inaccuracy from 180° to give a measure of accuracy and correlated the latter with the bloodflow in the brain. The highest correlation was found in the right hippocampus ($r=0.56$) and the second highest in the right inferior parietal cortex ($r=0.43$). We interpret this finding to mean that the output of the hippocampus on the right side is a vector which continuously points to the goal location, a finding consistent with our model of the hippocampus (see Burgess & O'Keefe 1996). The lower correlation in the parietal cortex may mean that the activity here reflects other variables in addition to the simple direction to the goal.

In contrast to the accuracy results, when we surveyed the brain for areas with bloodflow selectively correlated with the speed of movement through the environment we found a significant activation in the right caudate nucleus. This pinpoints the basal ganglia as a potential source of the information about speed which we had identified in our single-unit recording in the rat hippocampus. Alternatively, the basal ganglia might be an area which receives information from the hippocampal formation and which uses it to control movement through an environment.

It is not possible on the basis of these functional imaging results to determine how the hippocampal formation and the parietal cortex interact during human navigation. We believe that one difference between the two areas is the mode of representation of the spatial information contained in each. The bulk of evidence suggests that the spatial framework coded in the parietal cortex is an egocentric one whose origin is centred on the eye, head, and trunk in contrast to the allocentric representation of an environment in the hippocampal

formation. This suggests that one mode of interaction might involve egocentric information contained in the parietal cortex being sent to parahippocampal regions and then to the hippocampus where it is transformed into an allocentric representation of the environment. Alternatively the parietal cortex might be on the output side of the circuit. Information about the heading direction from the current location to the goal location might be sent to the inferior parietal cortex. In the inferior parietal cortex this information would be used to control egocentric orientation within the local space to guide the subject's behaviour appropriately. From this point of view, the lower level of activation in the parietal cortex would reflect additional inputs such as the location of doors within egocentric body coordinates in addition to the allocentric goal from the hippocampus.

The left hippocampus was also active during successful navigation. However, unlike the right hippocampus, the left did not show a correlation with navigational accuracy. We interpret this to mean that it is involved in navigation but in a way different from the right hippocampus. Perhaps it stores representations of the goal location for use by the right hippocampus during navigation or alternatively, it provides episodic memories of trajectories which were experienced during the original exploration of the environment. These trajectories would be correct, but not necessarily optimal, ways of getting from a location to the destination.

6. RELATION BETWEEN THE NAVIGATION SYSTEM AND EPISODIC MEMORY

If we assume that the human hippocampus provides the subject with a cognitive map which is similar to that of the rat, then the question arises as to why damage to this structure should result in an episodic memory deficit in addition to a purely spatial memory deficit. One possibility, suggested by O'Keefe & Nadel (1978), is that humans possess a sense of linear time which is not available to the rat. This sense of linear time when combined with a spatial system allows events to be located in both space and time and provides the basis for an episodic memory system. Damage to this system would have a double effect. On one hand, it would directly affect the storage of spatio-temporal event memories; on the other hand, it would indirectly prevent the use of the spatio-temporal context in which items were learned from being used as a spatio-temporal retrieval cue for the recall of this information. Further exploration of the role of a spatial mapping system as the basis for a spatio-temporal event memory may close the apparent gap between the role of the hippocampus in rats and humans.

REFERENCES

- Cave, C. B. & Squire, L. R. 1991 Equivalent impairment of spatial and nonspatial memory following hippocampal damage to the human hippocampus. *Hippocampus* **1**, 329–340.
- Cressant, A., Muller, R. U. & Poucet, B. 1997 Failure of the centrally placed objects to control the firing fields of hippocampal place cells. *J. Neurosci.* **17**, 2531–2542.
- Jeffery, K. J. 1998 Learning of landmark stability and instability by hippocampal place cells. *Neuropharmacology*. (In the press.)

- Jeffery, K. J., Donnett, J. G., Burgess, N. & O'Keefe, J. 1997 Directional control of the orientation of hippocampal place fields. *Exp. Brain Res.* **117**, 131–142.
- McNaughton, B. L. 1996 Cognitive cartography. *Nature* **381**, 368–369.
- Maguire, E. A., Burke, T., Phillips, J. & Staunton, H. 1996a Topographical disorientation following unilateral temporal lobe lesions in humans. *Neuropsychologia* **34**, 993–1001.
- Maguire, E. A., Frackowiak, R. S. J. & Frith, C. D. 1996b Learning to find your way—a role for the human hippocampal region. *Proc. R. Soc. Lond. B* **263**, 1745–1750.
- Maguire, E. A., Frackowiak, R. S. J. & Frith, C. D. 1997 Recalling routes around London: activation of the right hippocampus in taxi drivers. *J. Neurosci.* **17**, 7103–7110.
- Maguire, E. A., Frith, C. D., Burgess, N., Donnett, J. G. & O'Keefe, J. 1998a Knowing where things are: parahippocampal involvement in encoding locations in virtual large-scale space. *J. Cogn. Neurosci.* **10**, 61–76.
- Maguire, E. A., Burgess, N., Donnett, J. G., Frackowiak, R. S. J., Frith, C. D. & O'Keefe, J. 1998b Knowing where, and getting there: a human navigation network. *Science* **280**, 921–924.
- Muller, R. U. & Kubie, J. L. 1987 The effects of changes in the environment on the spatial firing of hippocampal complex-spike cells in a fixed environment. *J. Neurosci.* **7**, 1951–1968.
- Muller, R. U., Kubie, J. L. & Ranck, J. B. 1987 Spatial firing patterns of hippocampal complex-spike cells in a fixed environment. *J. Neurosci.* **7**, 1935–1950.
- O'Keefe, J. 1976 Place units in the hippocampus of the freely-moving rat. *Exp. Neurol.* **51**, 78–109.
- O'Keefe, J. & Burgess, N. 1996 Geometric determinants of the place fields of hippocampal neurons. *Nature* **381**, 425–428.
- O'Keefe, J. & Conway, D. H. 1978 Hippocampal place units in the freely moving rat: why they fire where they fire. *Exp. Brain Res.* **31**, 573–590.
- O'Keefe, J. & Nadel, L. 1978 *The hippocampus as a cognitive map*. Oxford: Clarendon Press.
- O'Keefe, J. & Speakman, A. 1987 Single unit activity in the rat hippocampus during a spatial memory task. *Exp. Brain Res.* **68**, 1–27.
- Scoville, W. B. & Milner, B. 1957 Loss of recent memory after bilateral hippocampal lesions. *J. Neurol. Neurosurg. Psychiat.* **20**, 11–21.
- Shapiro, M. L., Tanila, H. & Eichenbaum, H. 1997 Cues that hippocampal place cells encode: dynamic and hierarchical representation of local and distal stimuli. *Hippocampus* **7**, 624–642.
- Sharp, P. E., Blair, H. T., Etkin, D. & Tzanetos, D. B. 1995 Influences of vestibular and visual motion information on the spatial firing pattern of the hippocampal place cells. *J. Neurosci.* **15**, 173–189.
- Smith, M. L. & Milner, B. 1982 The role of the right hippocampus and the recall of spatial location. *Neuropsychologia* **19**, 781–793.
- Smith, M. L. & Milner, B. 1989 Right hippocampal impairment in the recall of spatial location: encoding deficit or rapid forgetting? *Neuropsychologia* **27**, 71–81.
- Taube, J. S., Muller, R. U. & Ranck, J. B. 1990 Head—direction cells recorded from the postsubiculum in freely-moving rats. I. Description and quantitative analysis. *J. Neurosci.* **10**, 420–435.
- Vargha-Khadem, F., Gadian, D. G., Watkins, K. E., Connelly, A., Van Paesschen, W. & Mishkin, M. 1997 Differential effects of early hippocampal pathology on episodic and semantic memory. *Science* **277**, 376–380.
- Wiener, S. I., Korshunov, V. A., Garcia, R. & Berthoz, A. 1995 Inertial, substriatal and landmark cue control of the hippocampal CA1 place cell activity. *Euro. J. Neurosci.* **7**, 2206–2219.
- Wilson, M. A. & McNaughton, B. L. 1993 Dynamics of the hippocampal ensemble code for space. *Science* **261**, 1055–1058.
- Zola-Morgan, S., Squire, L. R. & Amaral, D. G. 1986 Human amnesia and the medial temporal region: enduring memory impairment following a bilateral lesion limited to field CA1 of the hippocampus. *J. Neurosci.* **6**, 2950–2967.