HIPPOCAMPUS 9:206–219 (1999)

RESEARCH ARTICLES

Head Direction Cells in the Primate Pre-Subiculum

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ABSTRACT: The function of the primate hippocampus and related structures was analysed by making recordings from the hippocampus, subiculum, presubiculum, and parahippocampal gyrus in monkeys actively walking in the laboratory. Head direction cells were found in the presubiculum. The firing rate of these cells was a function of the head direction of the monkey, with a response that was typically 10–100 times larger to the best as compared to the opposite direction. The mean half-amplitude width of the tuning of the cells was 76°. The response of head direction cells in the presubiculum was not influenced by the place where the monkey was, there being the same tuning to head direction at different places in a room, and even outside the room. The response of these cells was also independent of the "spatial view" observed by the monkey, and also the position of the eyes in the head. The average information about head direction was 0.64 bits, about place was 0.10 bits, about spatial view was 0.27 bits, and about eye position was 0.04 bits. The cells maintained their tuning for periods of at least several minutes when the view details were obscured or the room was darkened. This representation of head direction could be useful together with the hippocampal spatial view cells and whole body motion cells found in primates in such spatial and memory functions as path integration. *Hippocampus 1999; 9:206–219.* © 1999 Wiley-Liss, Inc.

KEY WORDS: hippocampus; space; view; place; memory; monkey; subiculum

Damage to the temporal lobe, which includes the hippocampal formation, or to one of its main connection pathways, the fornix, produces amnesia (see Scoville and Milner, 1957; Squire and Knowlton, 1994; Gaffan, 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). In experimental studies in monkeys to define the crucial structures to which damage produces memory impairments, it has been shown that hippocampal or fornix damage produces deficits in learning about where objects have been seen, in object-place memory tasks (Parkinson et al., 1988; Angeli et al., 1993; Gaffan, 1994). To analyze how the hippocampus operates to help implement this type of memory, recordings have been made 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. It was found that approximately 10% of hippocampal neurons responded when images were shown in some positions on the screen (Rolls et al., 1989). Moreover, the 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 that has been described is of the place where the rat is (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 were moved to different places in a cue-controlled spatial environment. We found "spatial view" cells that responded to the position in space a monkey could see, rather than the place where the monkey was (Rolls and O'Mara, 1995). However, because it is only during active locomotion that the place fields of rat hippocampal neurons become evident (Foster et al., 1989), we set up a recording situation to allow active walking by the monkey, in a rich spatial environment. We again 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., 1997a). The majority of these cells (in, e.g., CA1) can respond when the view details are obscured, so that they encode an abstract representation of space (Robertson et al., 1998). The use of information theoretic techniques has shown that the information available from an ensemble of these cells increases approximately

Grant sponsor: Medical Research Council; Grant number: PG8513579; Grant sponsor: Human Frontier Science Program.
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Accepted for publication 5 January 1998

linearly with the number of cells in the ensemble, so that an ensemble of these cells provides rich information about spatial view (Rolls et al., 1998). It has also been shown that the encoding used by these cells is in allocentric coordinates, in that their responses do not depend on eye position, the place where the monkey is, or head direction (Georges-François et al., 1999). Evidence that these findings in macaques are very relevant to understanding human hippocampal function is that Epstein and Kanwisher (1998) have reported in an fMRI study that views of space are very effective stimuli for activation of the human hippocampus.

In addition to these spatial view cells, another class of hippocampal cell in primates responds to whole body motion, such as linear translation or axial rotation (O'Mara et al., 1994). At least some of these cells appear to be influenced by vestibular inputs, in that they can respond when the view details are obscured.

While making the recordings of spatial view cells in the actively locomoting monkey, we discovered a new population of cells, which we describe here. We call these cells head direction cells because they have many similarities to head direction cells in rats. Rat head direction cells have a firing rate which is a simple function of head direction in the horizontal plane (see Taube et al., 1996; Muller et al., 1996). The firing does not depend on the place where the rat is located. The cells in the rat are found in the dorsal presubiculum (also referred to as the postsubiculum), and also in some other brain structures including the anterior thalamic nuclei (Taube et al., 1996). The rat head direction cells appear to be able to be influenced by vestibular input, in that they maintain their tuning even when the rat is in darkness. The cells can be reset by visual landmarks. The discovery of these cells in primates is of interest, because it provides useful evidence with which to develop hypotheses of primate hippocampal function in the context of what is encoded in the primate hippocampus in terms of spatial view.

METHODS

To perform the experiments, we arranged for the monkey to see positions in space with different head directions, with different eye positions, and when the monkey was located at different positions in the laboratory. The recordings were made both during active locomotion, and when the monkey was still for a few seconds visually exploring the environment by eye movements. The neuronal activity for a cell was sorted according to each hypothesis to be tested (head direction, allocentric view, place, and eye position), and an ANOVA was performed to determine whether the cell had significantly different firing rates when sorted according to each of the hypotheses. In addition, the quantitative measure of the information that was available in the firing rate of the cell about the different hypotheses, was calculated. We were able to show for example that these cells convey much more information about head direction than about spatial view, the place where the monkey is, or about eye position. We were also able to test the cells when the view details in the room were completely obscured with curtains.

Recordings

Single neurons were recorded with glass-insulated tungsten microelectrodes from two rhesus macaques with methods that have been described previously (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 UK Animals (Scientific Procedures) Act 1986.) The monkey was free to walk on all fours with his head in an upright position round an open 4 x 4 m laboratory in a 2.7 x 2.7 m area in a modified chair on four wheels, using methods described more fully elsewhere (Rolls et al., 1997a, 1998; Robertson et al., 1998; Georges-François et al., 1999). 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 below). 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 wells were provided with food to encourage the monkey to learn about the places of food in the spatial environment. Small pieces of food were also sometimes scattered 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 was also attached. The eye movements made by the monkey were approximately 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, Tucson, AZ) 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, 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 the cell fired, that time was recorded with an accuracy of 1 ms. The Datawave spike cutting software was used offline to ensure that the spikes of well-isolated neurons were analyzed. The firing rate could then be analyzed as a function of head direction, eye position, and place where the monkey was. Software was also 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 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 the records containing a firing rate and the place of the monkey, the head direction, and the eye position, it was possible to plot diagrams and perform statistical and information theoretic analyses of the firing rate of the cell when different locations in the room were being viewed, and also in relation to eye position, place, and head direction. For allocentric position, the records were binned typically into 64 bins horizontally (16 for each wall), and 16 vertically. The accuracy of the eye position data was ± 3°, of the measurement of the chair orientation 5°, and of the chair position was 5 cm for 90% of the active locomotion area.

Procedure

Cells were searched for while the monkey was actively locomoting. Cells that responded differently with respect to different head directions were analyzed for this paper. Polar firing rate response plots were made when the monkey was actively locomoting, and when he was stationary, in the following two types of experiment.

In the first 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 5–10-min period for each condition during which the monkey walked round the environment, often picking up small pieces of food scattered on the floor to encourage exploration of all parts of the environment. An advantage of this type of experiment is that the responses of cells were being studied during active locomotion by the monkey.

In the second 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). The eye position as well as the firing rate and the head direction and place were recorded for several minutes. Then the procedure was repeated for a number of different head positions and directions. The advantage of this type of experiment was that the experimenter could define by selecting the head position and direction 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 head direction independently of the spatial view being seen by the monkey, or the place where the monkey was located, or of eye position.

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, eye position, place, and spatial position at which the eyes were looking) were obtained. A one-way analysis of variance was then performed, to determine whether there were significant differences between the conditions. In some cases, as shown in Figures 1 and 2, tests of a hypothesis required comparison of certain conditions. For example, to test whether a cell responded differently to different head directions, a good comparison was to compare the rates statistically for two different head directions for each of which (because of different eye positions or places of the monkey) the monkey could see the location in the environment that made the cell respond. The use of these different comparisons is made clear in the Results section when actual data are described. In addition to performing one-way ANOVAs to test for significant differences of neuronal firing rate for the different conditions, the information the neuron conveyed about each parameter (head direction, eye position, etc.) was also calculated as follows. The usefulness of information measures of neuronal responses, and an introduction to the application of information theory to neuronal activity, is provided by Rolls and Treves (1998, appendix 2).

Information Available in the Responses of Single Neurons

The rigorous quantitative way to analyse the degree to which the neuronal responses enable stimuli or events to be discriminated is to use an information theoretic measure. This will reflect both the differences of the firing rates to the different stimuli, and how significant those differences are taking into account the variability of the neuronal responses (see Optican and Richmond, 1987; Tovée et al., 1993; Rolls and Treves, 1998). The transmitted information carried by neuronal firing rates about the stimuli was computed with the use of techniques that have been described fully previously (e.g., Rolls et al., 1997b; Rolls and Treves, 1998). In brief, the procedure was as follows. The response r of a neuron to a particular stimulus s from a set S of stimuli was computed by measuring the firing rate of the neuron in a time window, which in this case was 3 s long. The measured firing rate responses take discrete rather than continuous values, which consist of the number of spikes in the time window on a particular trial, and span a discrete set of responses R across all stimuli and trials. To prevent undersampling, and resulting incorrectly high values of calculated information, the number of firing rate bins that can be used should be smaller than (or equal to) the number of trials available for each stimulus (Panzeri and Treves, 1996). We, therefore, quantized the measured firing rates into a smaller number of bins d, chosen according to the following: d was the number of trials per stimulus (or the number of different rates that actually occurred if this was lower). This procedure is very effective, when used with the appropriate correction for the limited number of trials, in minimizing information loss due to over-regularization of responses, as shown by Panzeri and Treves (1996). After this response quantization, the experimental joint stimulus-response probability table $P(s, r)$ was computed from the data (where $P(r)$ and $P(s)$ are the experimental probability of occurrence of responses and of stimuli, respectively), and the information $I(S, R)$ transmitted by the neurons averaged across the stimuli was calculated by using the Shannon formula (Shannon, 1948; Cover and Thomas, 1991):

$$I(S, R) = \sum_{s,r} P(s, r) \log_2 \frac{P(s, r)}{P(s)P(r)} \quad (1)$$

and then subtracting the correction for the limited number of trials of Panzeri and Treves (1996). This procedure leads to the

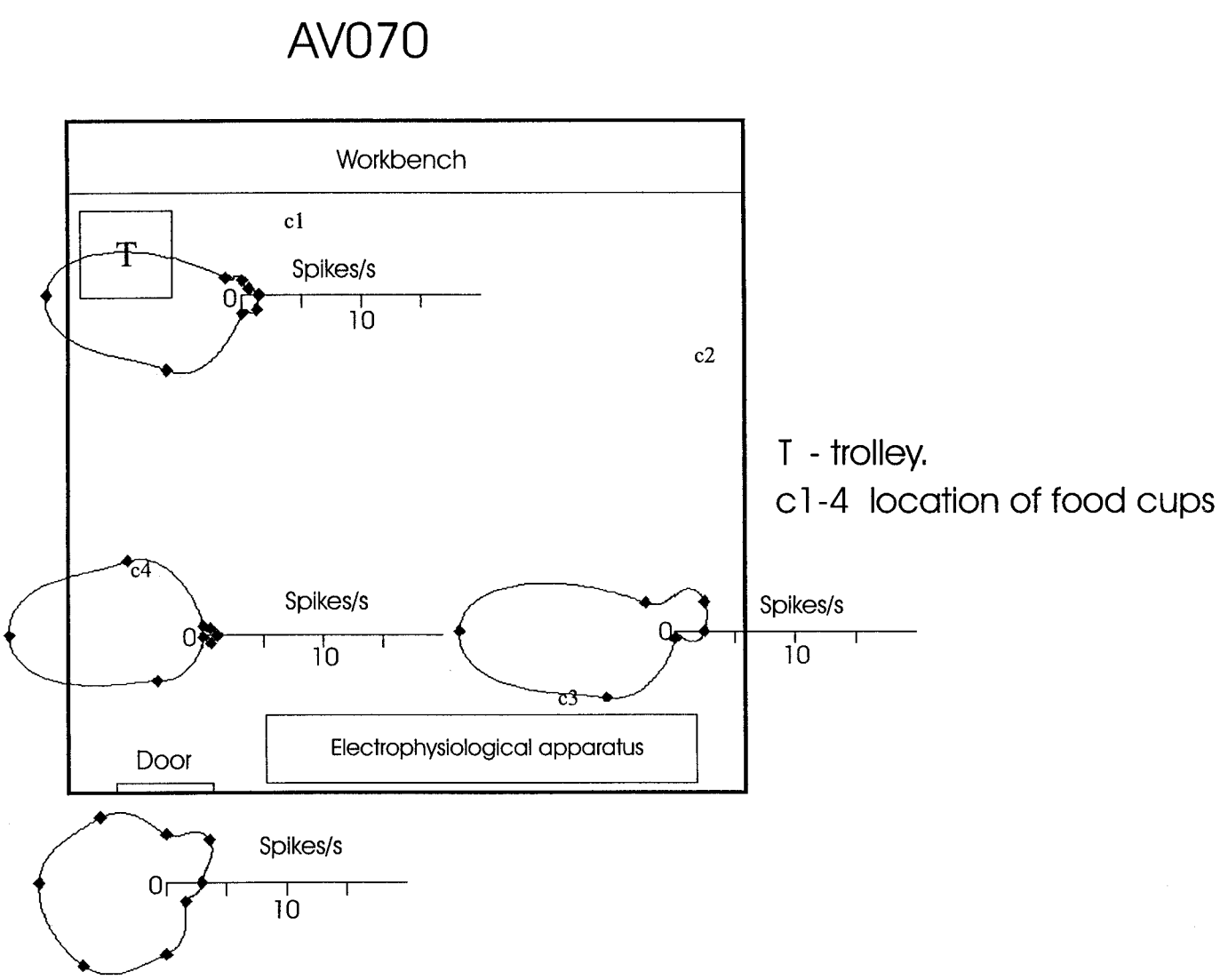

FIGURE 1. The responses of a head direction cell. Polar response plots of the firing rate (in spikes/s) when the monkey was stationary at different positions (shown at the 0 on the firing rate scale) in (and one outside) the room are shown. The monkey was rotated to face in each direction . The mean response of the cell from at least 4 different firing rate measurements in each head direction in pseudorandom sequence are shown. c1–c3: cups to which the monkey could walk to obtain food.

information available in the firing rates about the stimulus. The information about individual stimuli is obtained using the same procedure (for full details see Rolls et al., 1997b).

We used this procedure to calculate the information available in the firing rates about head direction, about allocentric spatial view (i.e., the position in the environment being looked at by the monkey), about the place where the monkey was in the environment, and about eye position. We had sufficient trials and different stimuli to enable the data to be discretized into typically 4–15 different classes.

Information Available in the Responses of a Population of Neurons

The first step in estimating the information carried by the responses of several cells is the construction of a vector **r** for each trial that describes the firing rates of each cell on that trial (**r** is a vector with one component for each of the C cells considered). The dataset then consists of a set **R** of such response vectors, which now contains the responses of all cells on all trials to all stimuli. (If the cells are not recorded simultaneously, as here, then pseudosimultaneous response vectors **r,** are simply constructed from the data available. Of course in this case, it is not possible to address the issue of whether there is any information in the relative time of firing of the cells.) Then from the probability table P(*s*,**r**), embodying a relationship between stimuli *s* and cell population responses **r**, one could compute directly the information in the population responses by using Eq. 1 with the population response vector **r** instead of the single cell response. The practical problem with this approach is that the minimum number of trials needed to sample efficiently the response space, and prevent biases due to

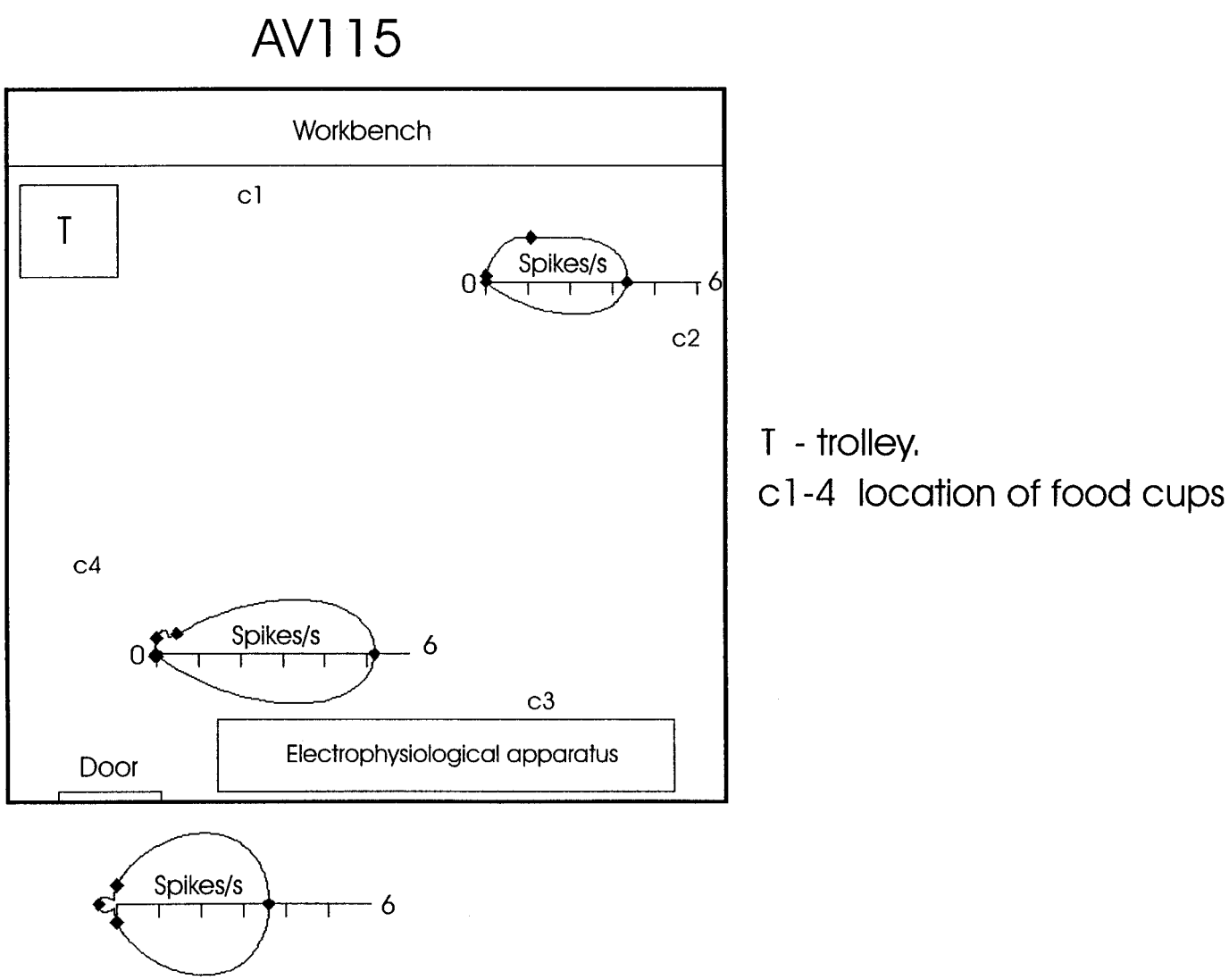

FIGURE 2. The responses of a different head direction cell, recorded at two positions in and one outside the room.

undersampling, grows exponentially with the population size. This rules out, in the case of limited datasets, any attempt to evaluate directly the information in the population for more than one or two cells (see Rolls and Treves, 1998). An effective solution is to use a decoding procedure to estimate for every trial which stimulus was shown. (This is interesting also because decoding might give insights into how the brain uses the information available in neuronal responses.) The decoding is performed by taking a single "test" trial of the data, and predicting from the average response and its distribution to each stimulus which was the stimulus on the test trial. When performing this, the population response probability distributions to each stimulus are calculated without the data in the test trial, as this provides the most effective cross-validation procedure (Rolls et al., 1997b; Rolls and Treves, 1998). We call s^P the stimulus predicted, on each trial, from the observation of the responses. The percentage of correct predictions canbe obtained directly for different numbers of cells. The information about the true stimulus s that was shown can then be measured from the predictions s^P , as follows

$$I = \sum_{s,s^P} P(s)\, Q(s^P|s) \log_2 Q(s^P|s)/Q(s^P) \qquad (2)$$

$Q(s^P|s)$ is the fraction of times an actual stimulus s elicited a test response that led to a predicted stimulus s^P. This procedure and the relevant correction for finite sampling that must be applied to Eq. 2 are described in detail in Rolls et al. (1998). The prediction of the stimulus, (or "decoding"), involves an algorithm that takes the current test response **r** and measures how close it is to the response probability distributions for each stimulus. We used the following five different stimulus prediction procedures (as comparing them sheds very interesting light on how information may be encoded by neuronal activity):

TABLE 1.

Head Direction Cells†

	Head direction					Allocentric view				Eye position				Place			
			Anova				Anova				Anova				Anova		
Cell	Information (bits)	I_{max} (bits)	F	(df)	*P*	Information (bits)	I_{max} (bits)	F	(df)	*P*	Information (bits)	I_{max} (bits)	F	(df)	*P*	Information (bits)	I_{max} (bits)	F	(df)	*P*
av070	0.58	2.26	51.1	(7)	$<10^{-4}$	0.08	0.08	0.776	(1)	0.391		n.a.				0.16	0.49	1.78	(3)	0.153
av115	0.62	2.59	23.5	(7)	$<10^{-4}$	0.09	0.10	2.91	(1)	0.103		n.a.				0.03	0.05	1.08	(2)	0.342
av195	1.11	1.67	59.21	(23)	3×10^{-16}	0.55	1.74	49.31	(14)	0.0001	0.03	0.08	3.56	(7)	0.001	0.16	0.19	26.12	(2)	0.0001
az080	0.41	1.14	19.26	(23)	3×10^{-13}	0.32	0.54	40.78	(7)	0.0001	0.01	0.21	2.17	(12)	0.011	0.05	0.12	10.36	(4)	0.0001
av192	0.38	0.99	13.98	(7)	$<10^{-4}$	0.28	0.29	0.077	(1)	0.784	0.03	0.89	1.88	(14)	0.024*	0.12	0.15	8.01	(2)	0.001
AVG	0.64	1.71				0.27	0.55				0.02	0.39				0.10	0.20			

†The average information, and the maximum information about any one condition (Imax) with the data cast according to head direction, allocentric view, eye position, and place.
n.a., not available.

1. Probability Estimator (PE). The predicted stimulus is the one which has the maximal probability of being observed, conditional to response **r.** For the calculation of the maximally likely stimulus, a Gaussian model of probability distribution of responses (truncated at zero) to different stimuli was used. This method makes use of the complete shape of the response probabilities, not just of the preferred directions.
2. Euclidean Distance (ED). The predicted stimulus *s* is the one whose corresponding mean response population vector $\mathbf{r}_s$ has the minimal Euclidean Distance $d = (\mathbf{r}_s - \mathbf{r})$ from the test vector **r.**
3. Dot Product (DP). The predicted stimulus is the one whose corresponding mean responses population vector has the maximal scalar (dot) product with the test vector **r.** The predicted stimulus is thus the one whose mean response is most aligned with the current vector. The interest in the ED and DP algorithm arise form the fact that they can potentially be performed by downstream neurons using biophysically plausible operations. They both might be performed by a cell that received the test vector as a set of input firings, and produced an output that depends on its synaptic weight vector, which represents the average response vector to a stimulus (see Rolls and Treves, 1998). The slight additional factor introduced with the ED algorithm is that it is not just the direction of the neuronal response vector that is used, but also the lengths of the vectors, which reflect the actual firing rates of the neurons. We refer to Rolls et al. (1997c, 1998) for a complete description of the PE, ED, and DP algorithms.
4. Vector Reconstruction (VR). This method (Georgopoulos et al., 1986), unlike the first three, can be applied only to neurons tuned to vectorial quantities, like the direction of the head, and cannot be used with stimuli that are not vectors in space (e.g., scalar quantities, or separate stimuli such as different objects). Instead of decoding the stimuli on the basis of the properties of response profiles in the abstract vector space of population responses, the VR algorithm supposes that each neuron codes for the preferred direction (in this case of the head). The contribution of each neuron *c* to the estimation of the true head direction vector $\mathbf{S}^p$ is along the neurons's preferred direction $\mathbf{V}_c$, and proportional to the neuronal response (i.e., the difference between the actual neuronal firing rate r_c and the spontaneous activity b_c). (In the case of head direction cells, the spontaneous firing rate is taken to be the firing rate in the direction opposite to the preferred direction of the cell.)

$$\mathbf{S}^p = \sum_c (r_c - b_c)\mathbf{V}_c \tag{3}$$

5. Optimal Linear Estimator (OLE). This method is similar to VR, except that the contribution of each neuron to the estimation of the true head direction is not along the neuron's preferred direction, but along a possibly different direction vector, which is calculated in order to correct for problems arising from non-symmetric tuning curves and inhomogeneous distributions of preferred directions (see Salinas and Abbott, 1994). This algorithm is the estimator linear in the neuronal firing rates which minimizes the mean square reconstruction error. The Equation is similar to that of Eq 3 except that the vector associated with each cell is not $\mathbf{V}_c$, but is computed according to the algorithm described by Salinas and Abbott (1994).

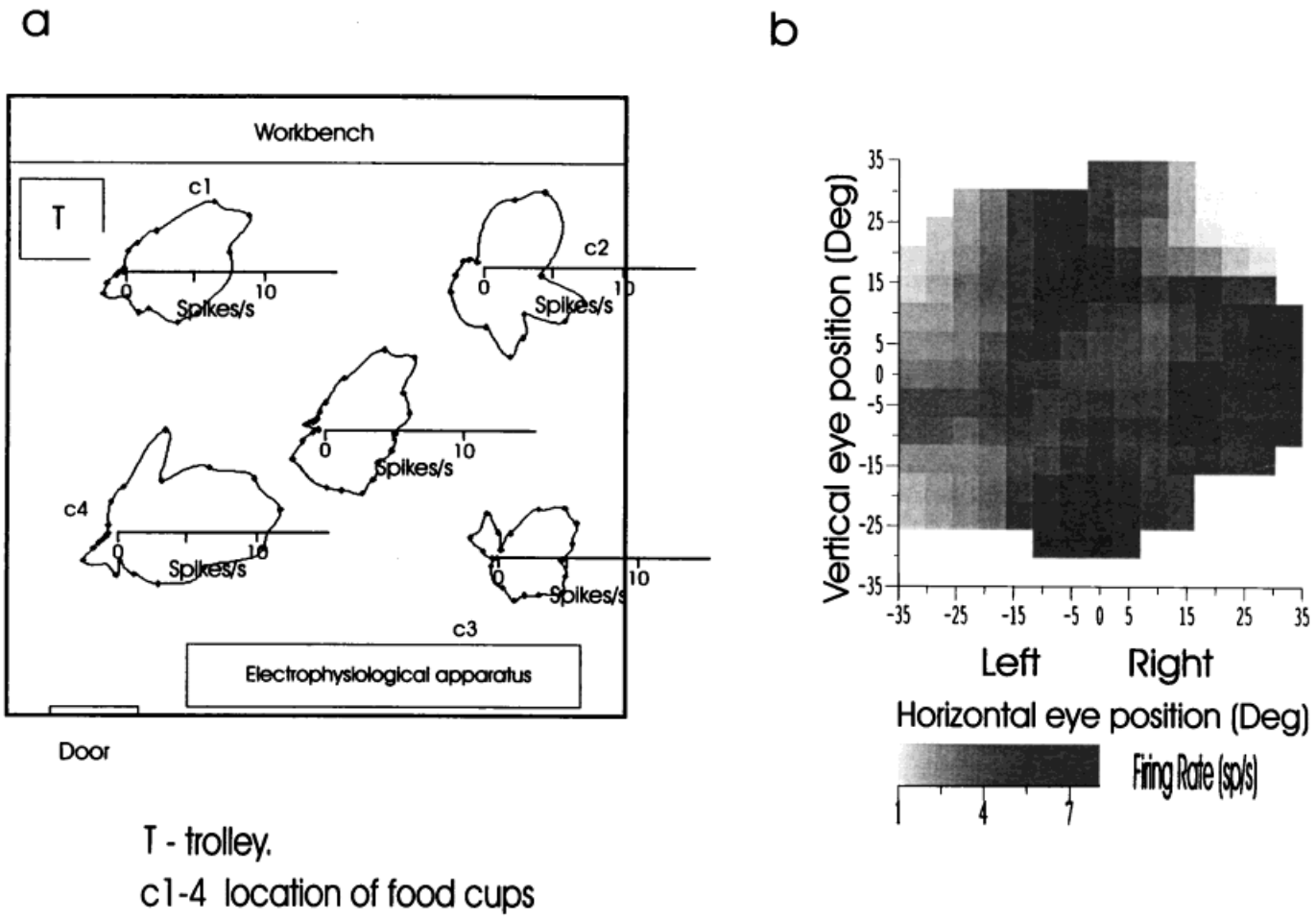

FIGURE 3. a: The response plots are shown for different places in the environment, and recorded during active locomotion, of cell az080. The cell responded optimally to a head direction of northeast. b: The firing rate as a function of eye position. The darkness of each square represents the firing rate of the cell in spikes/s.

It is important to note that the decoded information, Eq. 2, cannot be bigger than the information encoded in the neuronal responses **r,** which is Eq. 1 computed with the population response vector **r**. This is because the decoding step cannot add new information on its own to what is contained in the responses. Therefore, the information encoded in the neuronal responses is the maximum amount of information inherent in the neuronal responses that can be extracted for any stimulus prediction, and sets the natural scale for a comparison of efficiency of different decoding schemes. A comparison of the efficiency of vectorial vs. probabilistic methods for decoding spike trains has already been performed in a number of studies (Salinas and Abbott, 1994; Zhang et al., 1998, Brown et al., 1998). What is entirely new in our analysis is the use of Shannon information for assessing the performance of the reconstruction, and the application to head direction cells.

Recording Sites

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 whose position 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).

RESULTS

An example of a head direction cell recorded in a macaque is shown in Figure 1 (av070c2). The data for this diagram were obtained with the monkey stationary in the positions shown at the 0 on the firing rate scale. The mean response of the cell from at least 4 different firing rate measurements in each head direction are shown. The polar firing rate response plot shows that the cell has its maximum firing rate when the monkey was facing "West."

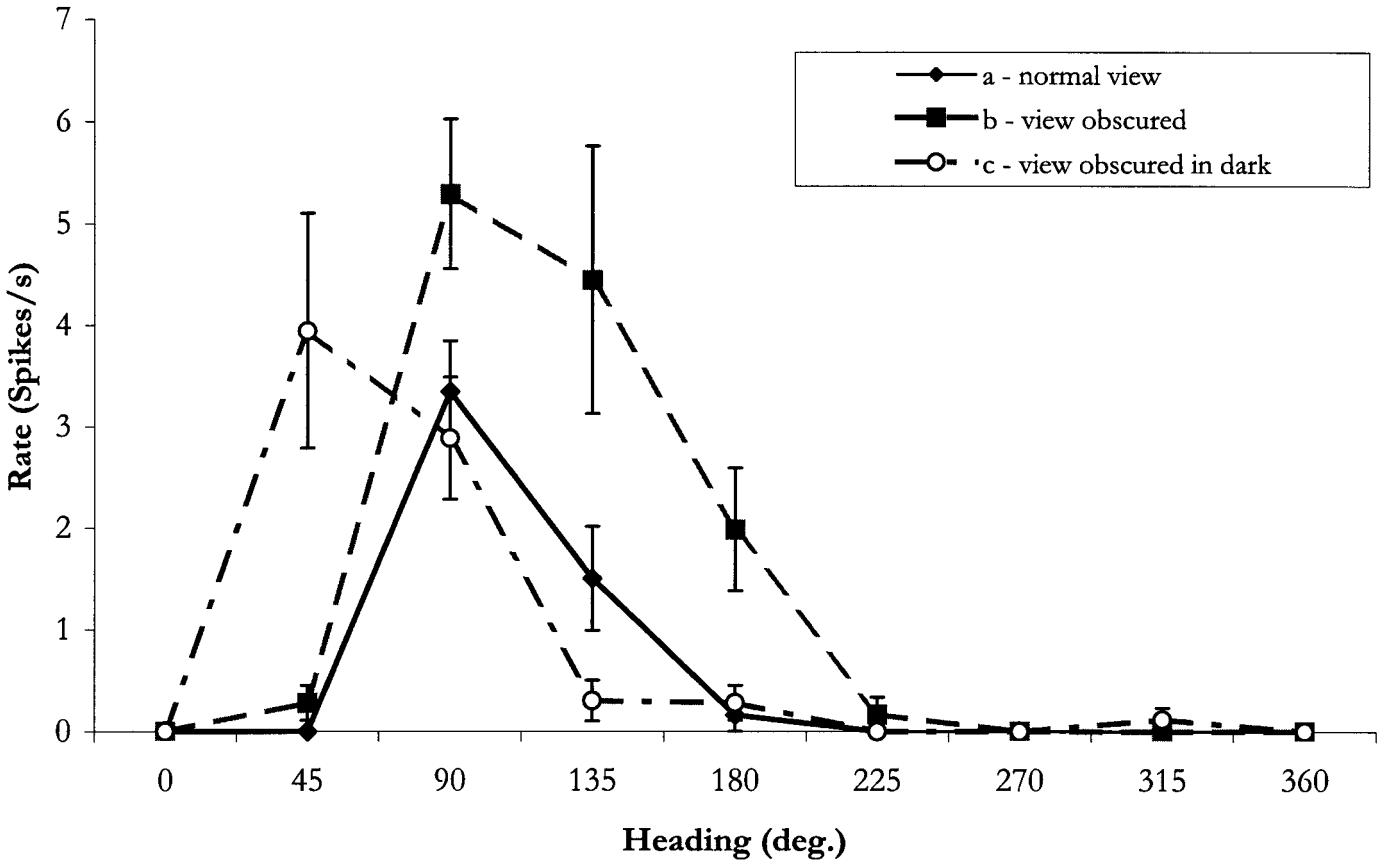

FIGURE 4. a: The firing of a head direction cell recorded with the normal view of the room. b: The firing rate when the room was completely obscured by ceiling-to-floor curtains. c: The responses of the same cell recorded not only with the blackout curtain, but also with the lights off. The mean and standard error of the mean response is shown.

The polar response plots were remarkably similar for three different positions in the room. A one-way ANOVA for the different head directions showed highly significantly different firing for the different head directions ($F(1, 7) = 51.1$, $P < 0.0001$) (see Table 1). The average information over the eight head directions was 0.58 bits, and the maximal information about any one head direction was 2.26 bits (see Table 1). The cell showed the same head direction tuning outside the laboratory in the corridor (see Fig. 1), a place where the monkey had never been previously walking at floor level. (Being in this novel environment did excite the monkey, and perhaps related to this the spontaneous firing rate of the neuron did increase a little to several spikes/s.) When the data for the cell were cast to show how much information the cell firing provided about the place where the monkey was located, the information was low (0.16 bits), and the ANOVA across different places was not significant (see Table 1). The neuron conveyed little information about spatial view (0.08 bits), in that the firing rate of the cell was very similar inside and outside the room even though the spatial views were completely different. This is a complete contrast to spatial view cells. The cell was located in the presubiculum (see Fig. 7).

Another example of a head direction cell is shown in Figure 2 (av115c3). The cell had its maximal firing to "East," and the firing was very similar in the three different places, including a location outside the room in the corridor where the monkey was not normally tested. The results of the ANOVAs and information analyses for the cell are shown in Table 1. It is clear that the neuron conveyed information about head direction, but very little about where the monkey was located, or about spatial view (see Table 1). The cell was located in the presubiculum (see Fig. 7).

Eye position did not have a marked effect on the firing rates of these head direction cells. An example is shown in Figure 3. The head-direction polar response plots are shown for different places in the environment, and recorded during active locomotion, in Figure 3a (cell az080). The cell responded optimally to a head direction of northeast. The firing rate as a function of eye position is shown in Figure 3b. The cell clearly did not respond markedly differently for different eye positions, and this is borne out by the low information about eye position (0.01 bits) contained in the responses of the neuron (see Table 1). It was possible to repeat this type of experiment on three head direction cells. In all cases, as shown in Table 1, the cells' firing was little affected by eye position.

The results of an experiment in which the firing of a head direction cell was recorded for many minutes while the room was completely obscured by ceiling-to-floor curtains is shown in Figure 4 , curve b (av115c3). The head direction tuning was very similar when the curtains were drawn closed (compare to Fig. 4,

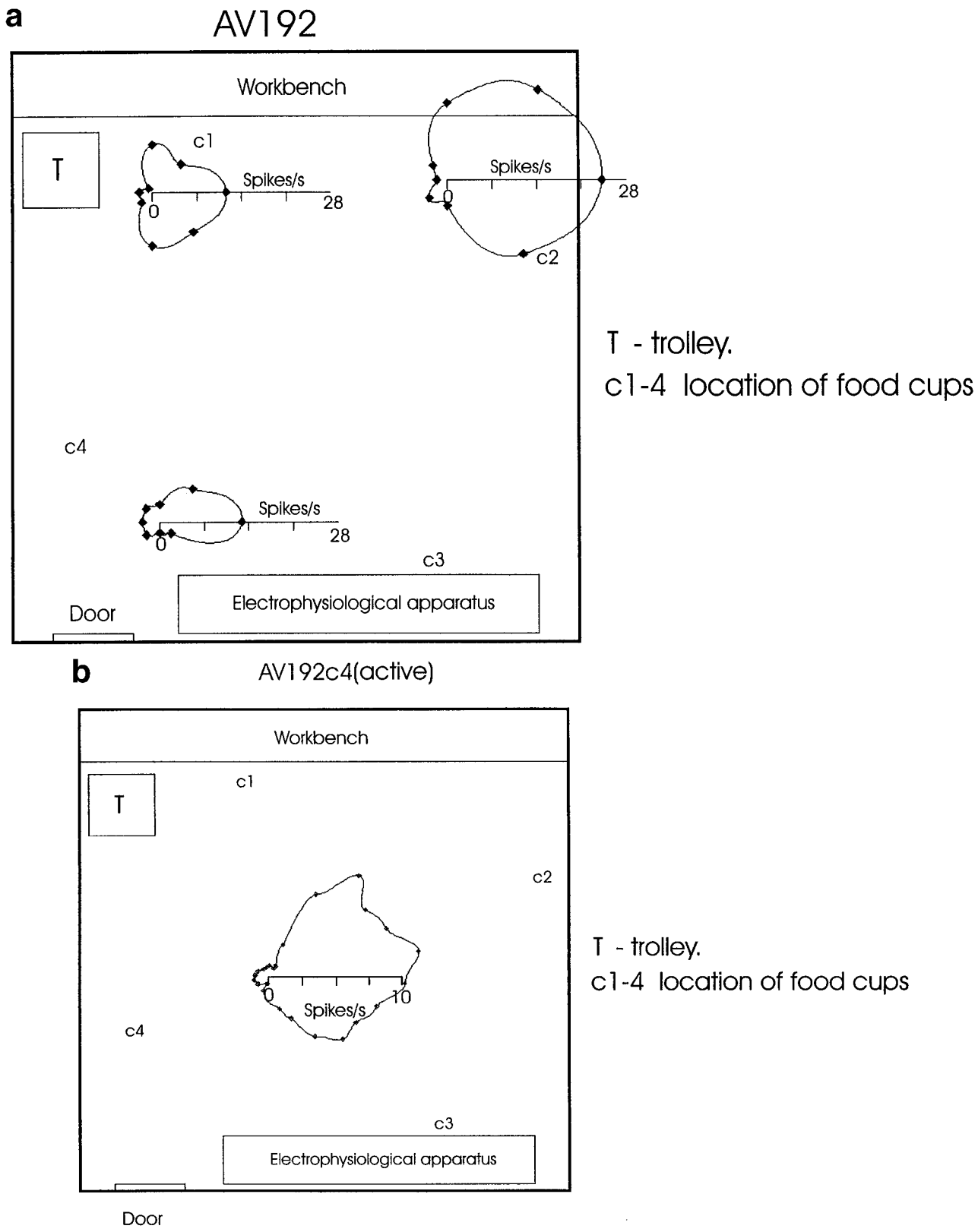

FIGURE 5. a: A cell with some of the characteristics of a head direction cell recorded in the parahippocampal gyrus. Conventions as in Figure 1, with the head direction tuning measured with the monkey stationary. b: The head direction tuning for the same cell during active locomotion throughout the laboratory.

TABLE 2.

Head Direction Cells: Firing Rates

Location	Cell number	Peak rate (spikes/s)	½ amplitude width (deg.)	Null rate (spikes/s)
Presubiculum	(1) AV070c2	17.2	72	0.8
Presubiculum	(2) AV115c3	4.3	54	0.0
Presubiculum	(3) AV195	29.1	89	0.9
Presubiculum	(4) AZ080	2.3	90	0.0
	Mean	13.2	76.3	0.4
Parahippo-campal gyrus	(5) AV192c4	15.7	139	2.2

curve a with the curtains open). When the room lights were subsequently extinguished, a head direction tuning curve was still present, though with no visual anchor, and the peak of the tuning did drift a little during several minutes in darkness, as shown in Figure 4, curve c.

A cell with some of the characteristics of a head direction cell but recorded in the parahippocampal gyrus is shown in Figure 5a (av192). The cell had similar head direction tuning in the three places shown, but was different from other head direction cells in having a somewhat higher firing rate when in the Northeast corner of the room. The head direction tuning for this cell during active locomotion throughout the laboratory is shown in Figure 5b. The tuning is generally similar to that found when the monkey was stationary as in Figure 5a.

The results over all head direction cells fully tested are shown in Table 1, and in Table 2, which summarizes the half-amplitude tuning widths of the cells, and the peak firing rates. For cells av070 and av115, data were not available (n.a.) for eye position. The first four cells in Table 1 were recorded in the presubiculum, and were among a set of 12 different cells analyzed in the presubiculum. The individual head direction cells shown in Table 1 had very highly significant head direction tuning, as shown. The probability of this set of significance values arising by chance calculated using the Fisher generalized significance test was $P \ll 0.001$ (Chi-square = 167, df = 24; critical value for $P < 0.001$ = 51.18). This test shows that the head direction tuning of these cells is most unlikely to have arisen by chance.

The results of the multiple cell decoding and information analysis are shown in Figure 6. For homogeneity, only the four cells from the same animal (av) were considered. Both the percentage of correct decodings and the information in the population are plotted for different supopulation sizes. The Probability Estimator (PE) and Euclidean Distance (ED) algorithm perform very well. The information encoded in the neuronal responses, Eq 1, can be calculated directly for the single cell case, and compared to the decoded information. Both the PE and ED decodings lead to information values that come close to the directly calculated value (within 5%); thus PE and ED decode, at least for single cells, essentially all the information that can be decoded by any algorithm. In contrast, the vector reconstruction methods perform poorly, especially when information, not the percent correct, is considered. The Dot Product (DP) decoding performs for these data considerably less well than the PE and ED estimator, probably because some of the cells in this small sample were tuned to similar head directions, and because the DP algorithm does not make effective use of the absolute firing rates of the neurons.

The sites in the brain where the cells were located are shown in Figure 7. All the cells had low spontaneous firing rates (mean = 0.8 spikes/s, interquartile range 0– 1.0). The peak firing rates were also relatively low, mean 10.0 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. Four cells were in the presubiculum, and 1 in the parahippocampal gyrus.

DISCUSSION

These findings show that there are head direction cells in primates. They are found in the presubiculum, and some cells with similar properties are found in the parahippocampal gyrus. We have not so far found head direction cells in the hippocampus itself (CA3, and CA1), nor in the dentate gyrus. Although because of the technical difficulties of recording from cells in the presubiculum of the freely locomoting macaque we have not been able to increase the number of cells recorded in the presubiculum beyond 12, we note that the individual head direction cells shown in Table 1 had very highly significant head direction tuning, as shown. Further, the probability of this set of significance values arising by chance calculated using the Fisher generalized significance test was $P \ll 0.001$. For these reasons, the actual finding of head direction cells reported for the first time in primates in this paper can be taken as a firm result.

The head direction cells are very different from the spatial view cells, which are found in the primate hippocampus and parahippocampal gyrus. For example, for a given head direction, if the monkey is moved to different places in the environment where the spatial view is different, spatial view cells give different responses. In contrast, the response of head direction cells remains constant for a given head direction, even when the spatial view is very different, as the data shown in Figures 1–4 and Tables 1 and 2 show. To provide a simple concept to emphasize the difference, one can think of head direction cells as responding like a compass attached to the top of the head, which will signal head direction even when the compass is in different locations, including in a totally different, and even novel, spatial environment, as illustrated in Figures 1 and 2. Each head direction cell is tuned to different directions, and indeed more information about head direction is present from an ensemble of such cells than from a single cell, which would not be the case if they were all tuned to

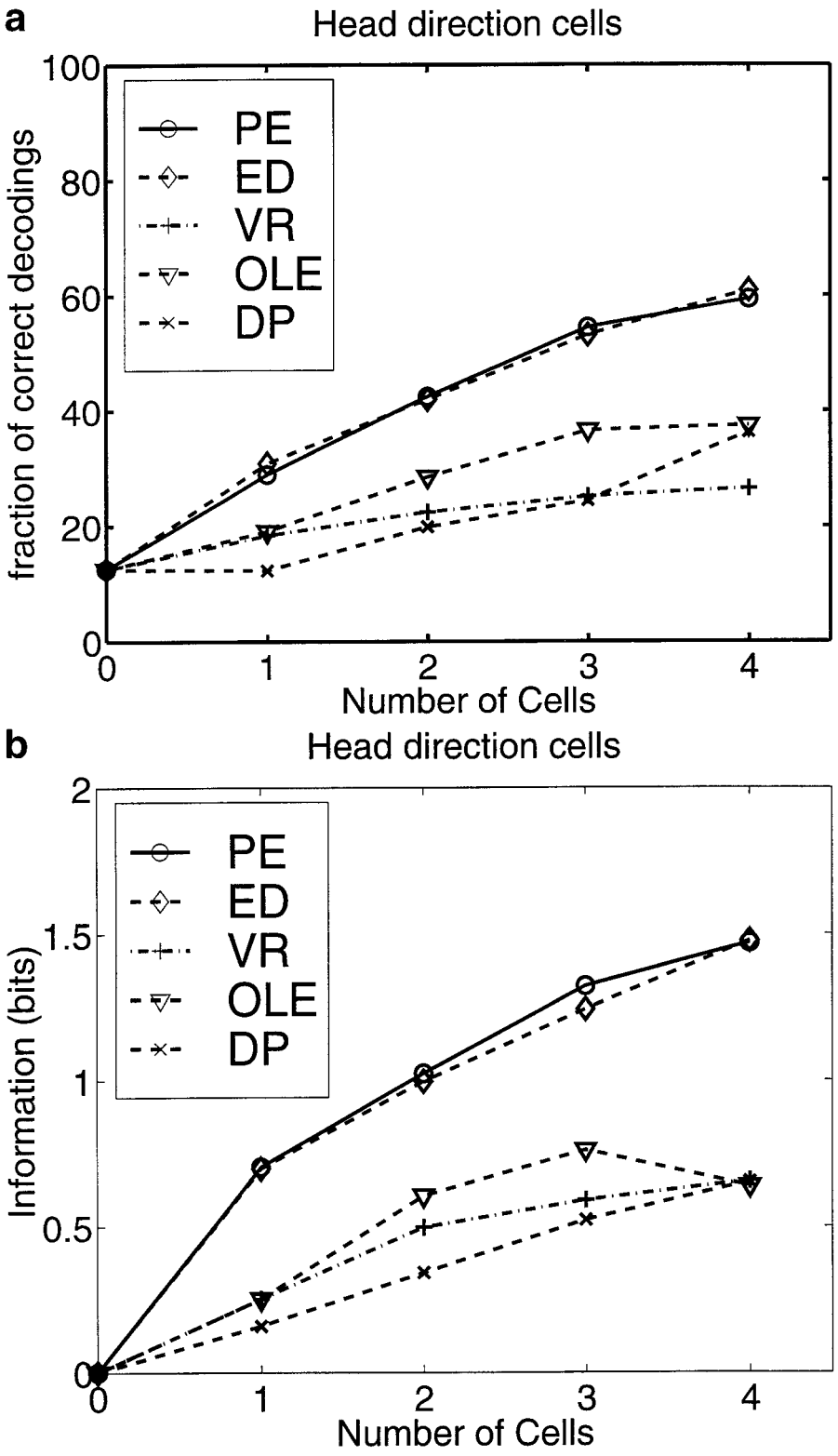

FIGURE 6. a: The percentage of correct decodings for a set of four cells recorded from animal av as a function of the population size. Notations as in the main text. b: The same as in a, but the mutual information is plotted on the ordinate axis.

the same compass direction (apart from some noise reduction increasing as the square root of the number of cells).

The head direction cells continued to signal head direction even when the view details were obscured by curtains and the monkey was in darkness (see Fig. 4). This type of experiment involved rotating the monkey to different head directions during darkness. The experiment indicates that signals that are probably of vestibular origin provide inputs to head direction cells. However, in darkness the firing of head direction cells may drift a little, consistent with the hypothesis that visual cues can reset the cells, and prevent them from drifting over

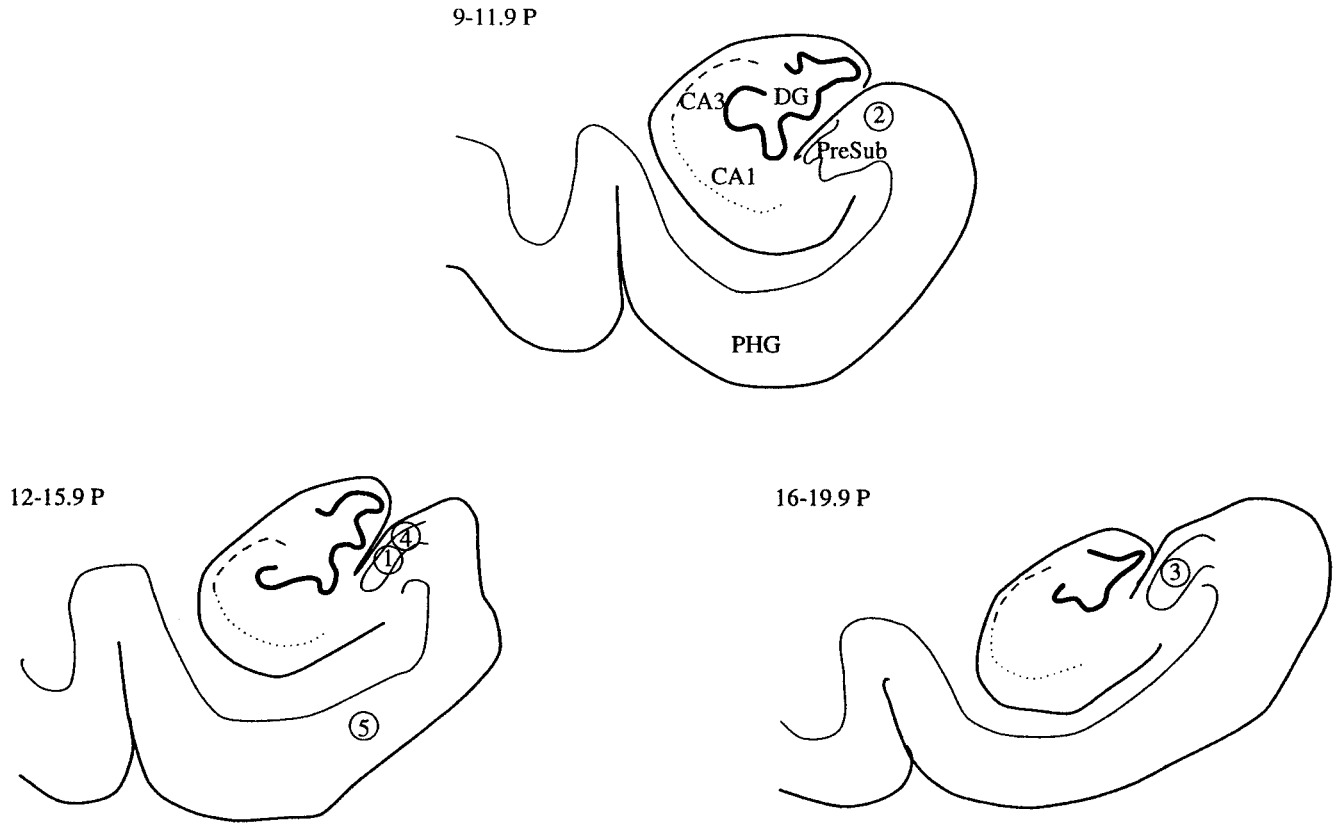

FIGURE 7. The hippocampal and parahippocampal sites at which different spatial view cells were recorded. Coronal sections at different distances in mm posterior (P) to the sphenoid reference are shown. The number inside each circle corresponds to the cell number shown in Table 1. CA3, CA3 hippocampal pyramidal cell field; CA1, CA1 hippocampal pyramidal cell field; DG, dentate gyrus; PHG, parahippocampal gyrus; PreSub, presubiculum.

long periods. This is similar to the hypothesis for head direction cells in rats (see Taube et al., 1996; Muller et al., 1996).

A hypothesis that can be tested in primates is whether eye position affects the responses of head direction cells. They might respond to compass-related head direction, or to compass-related eye-gaze (i.e., the direction of the eye taking into account head direction and eye position in the head). The evidence we have so far indicates that their firing rate for a given head direction does not depend on eye position (see Fig. 3b and Table 1). Moreover, they carried little information about eye position (Table 1). Thus, the evidence so far available suggests that the cells signal head direction rather than (allocentric or compass-related) eye gaze angle. However, because the tuning of the head direction cells is relatively broad, the range of possible eye positions might not move the firing to a part of the head direction tuning where the effect of differences in eye position (in the head) would make a significant difference to the (allocentric) eye gaze angle. It will be of interest in future research to explore this further when the head direction is set to the steepest part of the head direction tuning of a cell.

Taken in the context of evidence on the neurophysiology and functions of the primate (including human) hippocampal system, head direction cells could perform a number of functions. One would be as part of a memory system. By remembering the compass bearing (head direction) and distance travelled, it is possible to find one's way back to the origin, even with a number of sectors of travel, and over a number of minutes. This is referred to as path integration, and can occur even without a view of the environment. Head direction cells provide part of the information to be remembered for such spatial memory functions. Complementary information also required for this is available in the whole body motion cells that we have described in the primate hippocampus (O'Mara et al., 1994). These cells provide information about linear translation, for example, or axial whole body rotation. Part of the way in which head direction cell firing could be produced is by taking into account axial movements, which is what are signalled by some of these whole body motion cells (O'Mara et al., 1994), and it is an interesting hypothesis that this function is performed by some of the structures related to the hippocampal system such as the presubiculum. Spatial memory and navigation can also benefit from visual information about places being looked at, which can be used as landmarks, and spatial view cells added to the head direction cells and whole body motion cells would provide the basis for a good memory system useful in navigation. Another possibility is that primate head direction cells are part of a system for computing during navigation which direction to head in next. For this, not only would a memory system of the type just described and elaborated elsewhere be needed (Rolls, 1989, 1996; Treves and Rolls, 1994;

Rolls and Treves, 1998), which can store spatial information of the type found in the hippocampus, but also an ability to use this information in spatial computation of the appropriate next bearing would be needed. Such a system might be implemented using a hippocampal memory system that associated together spatial views, whole body motion, and head direction information. The system would be different from that in the rat (Burgess et al., 1994; McNaughton et al., 1996), in that spatial view is represented in the primate hippocampus.

The results of the multiple cell decoding and information analysis show that decodings that use the response probability distributions (like PE and ED), and operate in the abstract vector space of neuronal population responses, actually do decode most of the information available in the firing rates. This means that these methods, which utilize the full shape of the neuronal response probabilities, not only the preferred head direction, would be good ones for the brain to use when other neurons "interpret" (i.e., receive information about) the responses of a population of neurons. Further, the ED algorithm can be easily implemented by a set of receiving neurons, and therefore can be easily implemented in the brain to achieve accurate head direction reconstruction. The decodings based on reconstruction from the physical direction vectors of each neuron, perform much more poorly (see Fig. 6). This is not due to the fact that the preferred head direction of our limited sample of cells might not arise from a uniform distribution, nor it is due to possible non-symmetricity of tuning curves (see Fig. 4). These facts, which might produce problems for the VR algorithm, are in fact corrected for by the OLE, which also performs poorly on this set of data. The implication is that methods in general that are based on reconstruction from physical vectors estimated for different cells are much less powerful that reading the output of neuronal populations more directly, using, for example, a Euclidean Distance measure. Such a measure is also very biologically plausible. Moreover, the finding shows that direction-tuned cells, including head direction cells, convey much more information about head direction than can be captured just by specifying the direction to which the neuron has its optimal response, and weighting the contribution of that physical direction vector by the intensity of the neuronal response.

ACKNOWLEDGMENTS

This research was supported by the Medical Research Council, PG8513579, and by the Human Frontier Science Program. P.G.-F. and S.P. are European Community Research Fellows.

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