



Learning of landmark stability and instability by hippocampal place cells

Kathryn J. Jeffery *

Department of Anatomy and Developmental Biology, University College London, Gower Street, London WC1E 6BT, UK

Accepted 22 March 1998

Abstract

Place cells in the rat hippocampus fire whenever the animal is in a particular location. In a symmetrical environment, their receptive fields (place fields) are oriented by visual cues, and if these are unavailable they are oriented by movement-generated (idiothetic) cues. The present study tested the hypothesis that the cells would learn not to 'trust' a visual cue if the rat experienced it to be unstable (Knierim et al., 1995. Place cells, head direction cells and the learning of landmark stability. *J. Neurosci.* 15, 1648–1659). In an otherwise symmetrical environment, a visual cue was moved with respect to the idiothetic cues, either in sight or out-of-sight of the rat. When the visual cue was moved out-of-sight of the rat, place fields were initially oriented by this cue in preference to the idiothetic cues. However, if the cue was seen by the rat to be mobile, place fields ceased following the visual cue and became oriented by the idiothetic cues instead. If the cue was not seen to be mobile until the rat had had several days of experience in the environment, then the fields continued to be oriented by the (now visibly mobile) visual cue. It thus appears that the orienting influence of a visual cue on place fields can be either strengthened or weakened relative to the idiothetic cues, depending on the experience of the rat. © 1998 Published by Elsevier Science Ltd. All rights reserved.

Keywords: Directional sense; Hippocampus; Idiothetic cues; Landmark learning; Path integration; Place cells

1. Introduction

In order to isolate and study the neural changes that accompany learning, it is necessary to understand the nature of the underlying neuronal representation, and of how it changes when new information is added. Spatial learning is an important subtype of learning because it is a fundamental competence common to all vertebrates, and understanding its physiological basis may also shed light on other types of cognitive ability. This paper explores the representational changes underlying one of the simplest sub-components of spatial learning: learning which features of an environment are stable enough to be reliable directional landmarks.

In rats (and probably also in humans), the representation of spatial location occurs mainly in the hippocampus and surrounding structures. One of the clearest indicators of this is that hippocampal pyramidal cells recorded as a rat moves around in its environ-

ment show place-specific firing: that is, a given cell (a place cell) only fires when the animal is in a particular part of its environment (the cell's place field). Understanding how place cells 'know' where to fire may also tell us how the rat knows where it is. Furthermore, understanding how new information is added to the place representation when the environment changes (or as the animal discovers new parts of it) may contribute to our understanding of more general memory processes, including those operating in humans.

Place cells use at least two types of information to be able to restrict their firing to a specific region: they use geometric information, about the distances from the rat to the boundaries of its environment (O'Keefe and Burgess, 1996), and they use directional information, which tells them which way the rat is facing and enables them to discriminate otherwise similar boundaries (such as identically coloured and shaped walls; Jeffery et al., 1997). Both types of sensory information depend in turn on both exteroceptive inputs (mainly visual and tactile information about objects and boundaries) and inputs carrying information about the rat's movements

* Tel.: +44 171 4193393; fax: +44 171 3911306; e-mail: kate@maze.ucl.ac.uk.

(probably vestibular, motor efferent and optic flow; Sharp et al., 1995; Wiener et al., 1995; Jeffery et al., 1997). There is evidence that visual directional information may be at least partly learned (Taube and Burton, 1995). This raises the question of how place cells know which environmental features to learn to 'trust' as reliable and stable indicators of direction, and which ones to ignore.

The present study explored the hypothesis that place cells would learn to trust visual features that were stable, and/or learn to distrust features that moved around (Biegler and Morris, 1993, 1996; Knierim et al., 1995; Taube and Burton, 1995). That is, a landmark that had been experienced by the rat as stable should gain control of the orientation of place fields in an environment with no other obvious orienting cues (i.e. one that is geometrically symmetrical), while a landmark that had been experienced as unstable should lose (or alternatively fail to gain) control over place field orientation. We investigated two types of stability: exteroceptive (i.e. visual) stability, and idiothetic stability (that is, stability with respect to the rat's internal motion-based direction sense).

We found the following: (1) Visual information initially predominated over idiothetic information in orienting place fields, provided the rat did not see the cue move. (2) Landmarks that were then experienced as visually stable but idiothetically unstable retained this strong control over place field orientation, even when the visual cue was subsequently made unstable. (3) By contrast, landmarks that, from the beginning, were both visually and idiothetically unstable lost control very quickly. It thus appears that the place cell representation of orientation depends partly on learned features of the visual environment. While place cells in naive rats use visual orienting information in preference, they can subsequently learn about either stability or instability of the cue and modify their responses to that cue accordingly. If they learned that it was stable, then they continued to follow the cue preferentially even when it was subsequently made unstable. If they learned it was unstable right from the beginning, then they ceased to follow it and began to follow the idiothetic cues instead.

Understanding the anatomical locus and physiology of these changes may answer some important questions about the processes underlying memory formation. In addition, these findings have implications for the mechanisms by which visual cues interact with the path integration system (the motion-based system that enables animals to navigate in the absence of external sensory cues). The features of the unstable cue that may have served to disconnect it from the place representation are discussed.

2. Methods

Place cells were recorded from four male Lister hooded rats, as follows. Single unit data were obtained with two tetrodes (O'Keefe and Recce, 1993). Each tetrode consisted of four twisted strands of 17 μ m diameter HML-coated platinum-iridium wire cut straight across. The two tetrodes were separated vertically by approximately 0.5 mm to allow one set of four wires to detect unit activity while the other acted as a reference. The tetrodes were mounted in a cannula and advanced through the brain in 25–100 μ m steps by means of a lightweight microdrive.

To implant the tetrodes each rat was anaesthetised, the skull exposed, a hole drilled over the right hippocampus and the dura peeled back from the brain surface. The tetrodes were lowered into the brain just above the CA1 hippocampal subfield (bregma: 3.8 mm AP, 2.2 mm ML) until 1.5 mm of the deeper tetrode were embedded in the neocortex. A sleeve was then pulled down over the remaining exposed wire and the whole assembly cemented to the skull. The wound was dusted with neomycin/bacitracin antibiotic powder (Cicatrin) and the rat given an intramuscular injection of buprenorphine (Temgesic, 45 μ g) for post-operative analgesia.

2.1. Unit recording

Beginning at least 1 week after surgery, each rat was connected to the recording equipment and screening begun for hippocampal place cells. The potentials recorded on each of the eight electrodes were passed through RC coupled, unity gain operational amplifiers mounted close to the rat's head, and led to recording equipment (Gignomai, UK) where the signal was amplified and filtered. The outputs of the four amplifiers were fed into a storage oscilloscope to allow visual inspection of unit activity. Each of the four wires of one tetrode was recorded differentially with respect to one of the wires of the other. As the microdrive was advanced, this enabled recording from a given cell layer by each tetrode in turn. The signal was amplified 30000 times and bandpass filtered (500 Hz–9 kHz).

Once hippocampal complex spiking cells had been identified, the animal was moved into another room, where the experiment began. Place cell activity was ascertained by recording for 4 min while the rat foraged for rice grains in a square recording box (see below). Each channel was monitored at 20 μ s intervals and 50 points per channel were sampled whenever the signal on any of the four channels exceeded a visually determined threshold (a presumptive spike). Each spike event was stamped with the time since the start of the recording and the location of the animal. The data were stored on a hard disk and later transferred to a Sun

Ultra workstation for analysis. Recording proceeded in this apparatus for as long as hippocampal cells could be isolated. If no more cells were found, the rat was brought back into the screening room and the micro-drive was advanced in a search for new cells.

2.2. Recording apparatus

The experimental set-up is shown in Fig. 1. All place cell recording was done while the rat foraged for 4 min in a square box of sides 60 cm long and 25 cm high. The centre of the floor of the box consisted of a circular platter 30 cm in diameter, which could be slowly rotated with respect to the rest of the box, in either direction, by means of a motorised turntable located underneath. The box and turntable were located in the centre of a circular arena 2 m in diameter, which was separated from the rest of the room by means of floor-length heavy black curtains and a low-set false ceiling, the latter possessing a 50 cm diameter hole to admit the recording cables, and to allow an overhead camera to view the box. Apart from minor irregularities in the curtains, ceiling and floor, the basic arena therefore possessed four-fold rotational symmetry: that is, there was no obvious way to visually distinguish the north, south, east and west walls of the box.

In order to break this symmetry, a landmark was suspended just in front of the curtains, behind one of the four walls of the box (varied from trial to trial between north, south, east and west). This consisted of a large piece of white card, 72 cm wide and 102 cm high. Four spotlights attached to the edge of the circular hole in the ceiling allowed the card to be brightly lit

when it was in any of its four positions. Because the main room lights were switched off during the whole time the rat was in the apparatus, the spotlight cue card was highly salient.

2.3. Recording protocol

The purpose of this experiment was to see what happened to place fields when the orienting information provided by the cue card conflicted with the orienting information provided by the idiothetic cues. The cue card was manipulated by rotating it from one of its four positions to another, either in view of the rat (visually unstable condition), or with the rat confined to the rotating platter by means of an opaque wraparound cover. The cover was made of cardboard, of dimensions $18 \times 23 \times 32$ cm high, and completely surrounded the rat except for a small hole in the top, approximately 6 cm in diameter, to allow the recording cable to pass through. The rat was covered for up to 4 min while the rotations took place. The rat's internal compass was manipulated on some trials by slowly rotating the central platter (at 0.13 rpm), by either 90° or 180° , while the rat was confined. Assuming the rat did not detect this rotation (which was intended to be well below the threshold for vestibular detection), its internal sense of 'north' could therefore be rotated to any of the four cardinal directions, thus dissociating it from any environmental directional cues. For ease of description hereafter, the phrase 'rotated with the rat' should be taken to mean 'rotated with the rat's internal compass'.

From the time the rat was first introduced into the recording environment, rotations of the card and/or rat took place at 15 min intervals, in order to prevent the rat from forming associations between the intramaze and extramaze environmental cues. At the start of each recording day, the rat was removed from its home cage in the animal housing facility and transported to the recording room in an opaque carrying box. Once inside the curtained arena the lid was removed, the rat lifted out, connected to the recording apparatus and placed in the recording box. This was always done in the same part of the arena each day. At this time, the cue card was always in its 'standard' position, to the east of the box. This was done so that if the rat had been able to use vestibular information to remain oriented on its way from the housing room, the cue card would appear to be in a constant location at the start of the day. At no time was any attempt made to disorient the rat by rapidly rotating it. For all types of trial, the experimenter entered and left the environment through the same entrance.

For all recording conditions, an initial baseline trial was recorded with the cue card in the standard position. When a robust place field was identified, one or more of three types of session were run.

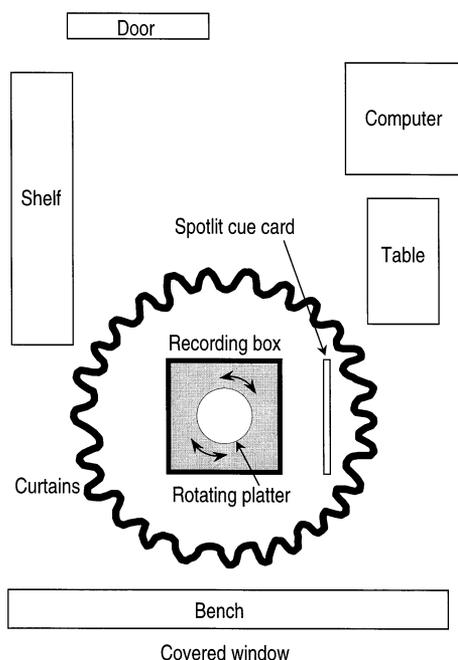


Fig. 1. The experimental set-up (see text for details).

2.3.1. Rat-only rotation sessions

In these sessions, the card was removed from the arena so that there was little if any polarising visual information, and the only light was provided by the headlight used to track the rat (which illuminated the box but little else). The rat was then confined to the central platter as described above, and rotated slowly by either 90° or 180°, in either direction. The purpose of these trials was to determine whether the rat's internal compass could control the orientation of place fields within the box, in the absence of any polarising visual information.

2.3.2. Card-only rotation sessions

In these sessions, the cue card was illuminated by one of the spotlights, so that the arena and curtains were moderately visible. The card was rotated by either 90° or 180° in either direction. This was achieved by unhooking the card from the curtain rail from which it was suspended, carrying it to one of the three other cardinal positions and hanging it up again, all in full view of the rat. Thus, the card could be seen by the rat to be unstable (that is, it moved, and also changed its position relative to other extramaze cues such as the sounds and smells of the room outside the curtains). The purpose of these trials was to see if rotating the cue card would result in a corresponding rotation of place fields.

2.3.3. Mismatch rotation sessions

In these sessions, the rat was confined to the central platter, the cue card rotated by either 90° or 180° in either direction (i.e. out of sight of the rat) and the rat also rotated by either 90° or 180° in either direction, but rotated differently from the cue card. (Occasionally, either the card or the rat remained unrotated.) Thus, when the rat was released and allowed to forage, the information provided by its internal compass would always conflict with the information provided by the cue card. The question asked was, did the place fields rotate with the card, the rat or neither?

A session consisted of a block of four mismatch trials followed or preceded (depending on the group, see below) by four rat-only rotation trials, four card-only rotation trials or nothing. Each trial was 4 min long and the interval between trials was at least 10 min. Each session contained a pseudorandom combination of rotations so that each card location, rat orientation, rotation and card/rat relationship was approximately equally experienced, evenly distributed across the experiment, and matched between animals. On a given recording day, between one and three sessions were run. If a session followed immediately from the preceding one, the last trial of the previous session was used as its baseline. If recording was suspended temporarily while the electrode position was fine-tuned, rotations

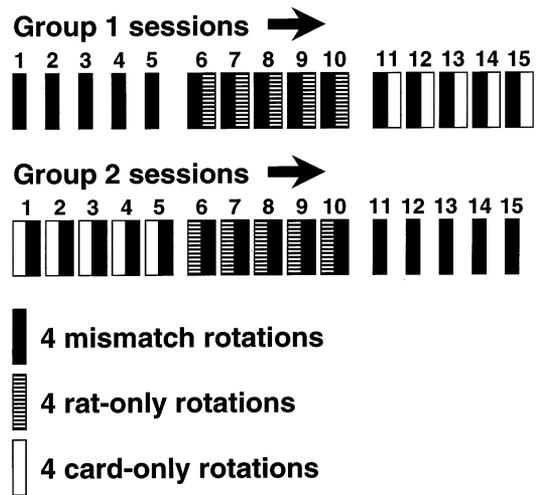


Fig. 2. The experimental protocol. Each shaded bar represents four rotations, comprising a manipulation of the cue card and/or rat (see text) followed 10 min later by 4 min of place cell recording, made while the rat foraged in the box for grains of rice. Each numbered bar or group of two bars represents a session. Between one and three sessions were run on a given day. The order of trial-blocks was reversed between Group 1 and Group 2. In all other respects recording conditions were identical between the two groups. Thus, on a given trial, only the previous experience of the rat differentiated Group 1 from Group 2.

continued at 15 min intervals so that the rat did not experience too long a time with the environment in one particular configuration—this was to minimise the influence of extramaze cues.

Four rats were studied. For two animals (Group 1), a series of five mismatch sessions was given first, followed by a second series of five mismatch sessions alternated with five rat-only sessions, and finally, a third group of five mismatch trials alternated with five card-only trials. The other two rats (Group 2) received the same series of trials but in the reverse order. These series are shown graphically in Fig. 2.

The purpose of this reversal of trial order was to see whether in rats that received the card-only (i.e. visually unstable) rotations first, place fields subsequently responded differently to the cue card from when they received them last, which would indicate a learned component to place cell responses.

2.4. Data analysis

This was performed on a Sun Ultra workstation using proprietary software (Gignomai, UK). The waveforms were separated by clustering them on the basis of the amplitude at the negative peak, the positive peak or the peak-to-peak amplitude. A place field was defined as location-specific firing (not more than two clear peaks) whose peak rate after smoothing (see below) was greater than 0.5 Hz. Although often more than one place cell was recorded, only the cell with the most

highly localised, stable and ‘well-behaved’ field was used in the following analysis. Well-behaved fields were those that appeared to rotate lawfully following a manipulation. This selection was done because (a) multiple fields recorded in the same trial tended all to behave the same way, and so could not reasonably be regarded as independent data for statistical purposes, and (b) this provided the most conservative picture of place field behaviour.

2.5. Characterisation of place fields

To determine the location and peak firing rate of each place field, a 64×64 grid was placed on the camera viewing area (about 130×130 cm) and overlapping square bins of size 20×20 cm were placed around each grid point. For each bin, the number of spikes fired by each cell and the time spent there by the rat was determined. The firing rate at each grid point was mapped as a grey-scale plot with linear interpolation between grid points. Contour plots were autoscaled so that each grey gradation represented 20% of the peak firing rate. The point at the centre of the bin containing the highest firing rate was used as a measure of the location of the peak of a place field.

The following analysis was undertaken in order to determine whether a cell’s field had rotated along with the card, the rat or neither. For each trial, the predicted position of the peak was calculated for four conditions: non-rotation, rotation with the card, rotation with the rat, or rotation to the remaining geometrically equivalent position(s) (Fig. 3). This was done by subjecting the peak position of the previous trial to the various rotations. The Euclidean distance of the actual field position from the predicted field positions was determined, and the field allocated the rotation corresponding to the smallest of these distances.

For each group of four rotations, the number of times the field followed the card, the rat or neither was

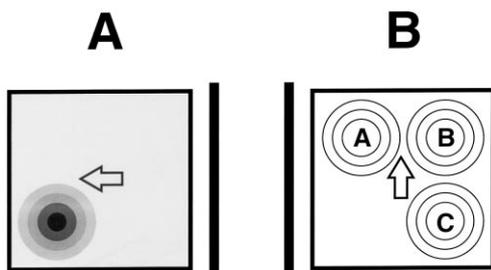


Fig. 3. How the rotations were calculated. (A) A stylized place field, located in the SW corner of the box. (B) The predicted positions of the field following a 180° rotation of the card and a 90° CW rotation of the rat. The predicted position if it had rotated with the rat is shown by A, if it rotated with the card by B, and if it had rotated to a different position, by C. The actual behaviour of the recorded field was ascertained by finding its peak and determining whether it was nearer to A or B, or to neither (unrotated, C or ceased firing).

expressed as a percentage of the total number of rotations. For a block of five sessions, the average percentage was calculated for each rat. Because it was predicted that the place fields of rats exposed to the visually unstable visual cue would cease to follow the card, comparisons between the two groups were made using a one-tailed *t*-test with a significance level of 0.05.

2.6. Histology

After completion of recording each rat was killed with an overdose of sodium pentobarbital (Lethobarb, 10 mg) and perfused transcardially with saline followed by paraformaldehyde. The brain was extracted and stored in formalin, and was later sliced coronally in frozen sections $40 \mu\text{m}$ thick, mounted and Nissl stained to allow visualisation of the electrode track. The location of each cell was estimated from the depth of the electrode at implantation plus the distance through which the microdrive had been advanced. This distance was superimposed on the electrode track obtained histologically.

3. Results

Forty-seven place cells were analysed in detail. Histology showed all of the cells recorded to be located in CA1 or CA3. The results are as follows.

3.1. Mismatch rotations

An illustration of the results of the mismatch paradigm from a single session is shown in Fig. 4. The mismatch rotations served to provide an ongoing assessment of whether place fields were controlled more by the cue card or by the rat’s internal compass.

The behaviour of the two groups over the course of the experiment is shown in Fig. 5. For Group 1 rats, in almost every mismatch trial (of which there were 60), the fields rotated with the card (Fig. 5(A)) rather than the rat (Fig. 5(B)). Thus, it appears that for these rats, when visual information was placed in conflict with idiothetic information, visual information predominated. This finding is consistent with previous studies showing that visual information tends to predominate over idiothetic information in setting the directional representation (Goodridge and Taube, 1995; Taube and Burton, 1995).

For Group 2 rats, the picture was quite different. For these rats, each of the first 10 mismatch sessions had been preceded by sessions of a different type: namely, by (visible) card-only rotations prior to the first five sessions, and by rat-only rotations prior to the second five sessions. Thus, these rats had early experience of the card as visually unstable. Fig. 5 shows that al-

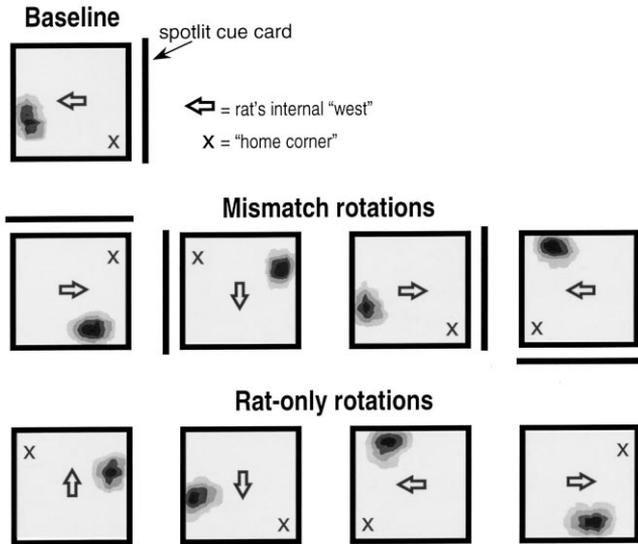


Fig. 4. Example of the results from a single session, to show how the data were obtained. In this session, a baseline recording was run (top row), followed by four mismatch rotations (middle row) and then four rat-only rotations (bottom row). In the baseline condition, with the cue card in the east, the place field lay along the southern part of the west wall. The rat's presumed internal sense of west is indicated by the arrow, and the place where the rat preferred to sit and rest during the inter-trial intervals (the 'home corner') is indicated by a cross. On the first mismatch trial, the card was rotated 90°CCW, to the north, while the rat was rotated 180°. The place field rotated 90°CCW, thus following the card rather than the rat's internal compass. Similarly, for the remaining mismatch trials, on each rotation the place field followed the card. For the rat-only rotations, the cue card was removed and the rat rotated in the absence of any polarising visual cues. Now the place field followed the rat's internal compass on every trial. For both mismatch trials and rat-only trials, the rat's home corner rotated with the place field.

though visual information tended to predominate on the first session, by the end of the fifth session the cue card had almost completely lost control, and the fields were following the idiothetic cues more often than the Group 1 rats.

To determine the relative influences of the card and the rat in controlling place fields, the following parameter was calculated using the equation below:

$$\text{card dominance} = \frac{\text{card} - \text{rat}}{\text{card} + \text{rat}}$$

where 'card' is the proportion of trials in which the field followed the card, and 'rat' is the proportion of trials in which it followed the rat. This yields a number which is +1 if the field always followed the card, -1 if it always followed the rat and zero if it followed both equally often. The data were analysed statistically by averaging the results for each block of sessions (Fig. 6) and comparing the blocks between the two groups using a one-tailed *t*-test. The difference between the groups was not quite significant for the first block ($t = 2.83$; $P = 0.053$) but was significant for the second and third blocks ($t = 39.00$ and 8.74 , respectively; $P < 0.01$).

To investigate the possible confounding effects of having run different trial sequences on the same day (that is, mismatch trials first for the Group 1 rats and last for the Group 2 rats on each mixed-trial day), a comparison was made between the results of the first five mismatch sessions for Group 1 rats and the last five mismatch sessions for Group 2 rats (Fig. 7). These sessions were run alone, with no other trial types occurring on the same day ('mismatch-only sessions'). When these data were combined into a block and compared using a *t*-test, there was a significant difference between card dominance of the fields in the two groups ($t = 14.43$; $P < 0.01$). The prior experience of the rat played thus an important part in determining whether place fields were more influenced by visual or idiothetic directional information.

One rat from Group 1 curled up and rested in a particular position in the box during the 10 min inter-

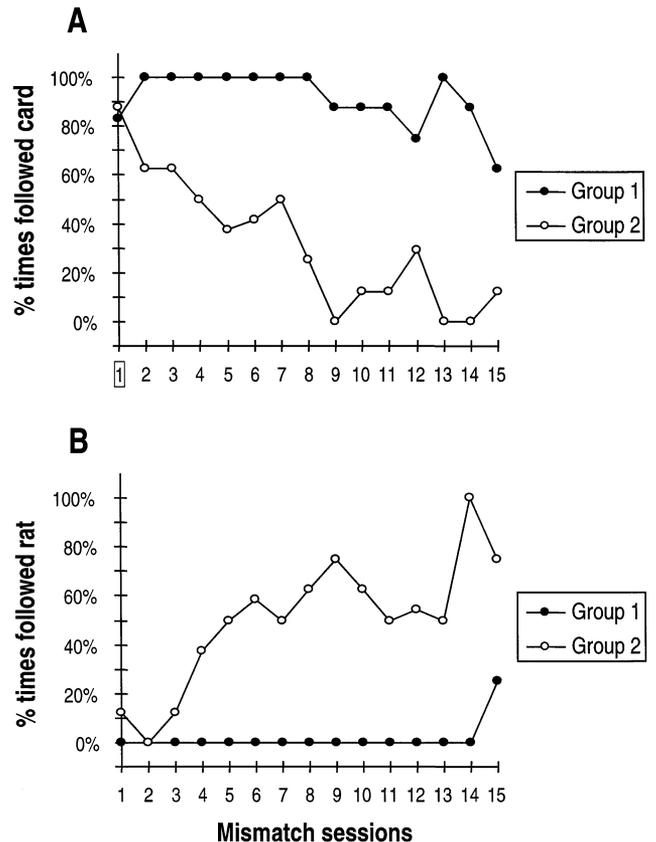


Fig. 5. Behaviour of place fields from the two groups of rats for all 60 mismatch trials (15 sessions of four trials), in which directional information conveyed by the cue card conflicted with the idiothetic cues. (A) Percentage of trials in which the fields followed the card. Fields in both groups began by following the card almost all of the time. For Group 1 rats, fields continued to follow the card predominantly, while for Group 2 rats, control of the fields by the card became weakened. (B) Percentage of trials in which the fields followed the idiothetic cues. Fields in Group 1 rats almost never followed the rat except for the last trial, whereas the idiothetic cues in the Group 2 rats developed strong control of the fields over the course of the experiment.

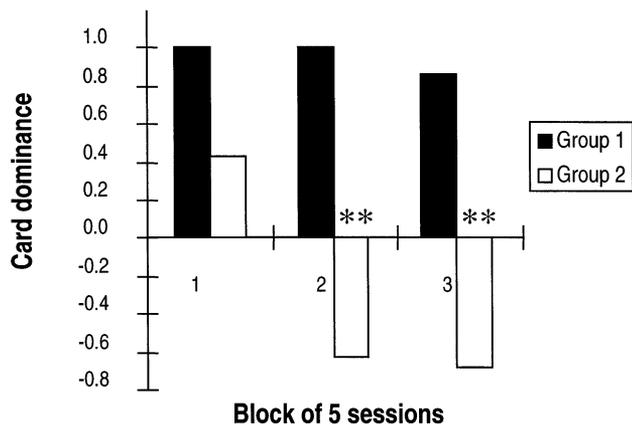


Fig. 6. The data in Fig. 5 were grouped into five-session blocks and compared. Card dominance (the degree to which the fields preferred to follow the card rather than the rat) was calculated as $(card - rat) / (card + rat)$. There was a significant difference between the groups in block 2 and 3, showing that the past experience of the rats, as well as present recording conditions, was influencing the behaviour of the fields.

trial intervals. On 90% of trials this ‘home corner’ was consistent with the position of the place field (Fig. 4). This provides some support for the hypothesis that the behaviour of place fields is coupled to the spatial behaviour of the animal.

3.2. Rat-only rotations

Fig. 8 shows that fields in both groups rotated with the rat on the rat-only rotations significantly more often than chance when the card had been removed ($t = 13.06$; $P < 0.001$). There was no difference between the groups in this regard ($t = 0.45$; NS). For the Group 1 rats, these same fields almost always rotated with the card on the mismatch rotations. Thus, it appears that the place cells received both idiothetic and cue card information about the orientation of the environment, but when the two sources of information were in conflict, the cue card was preferred.

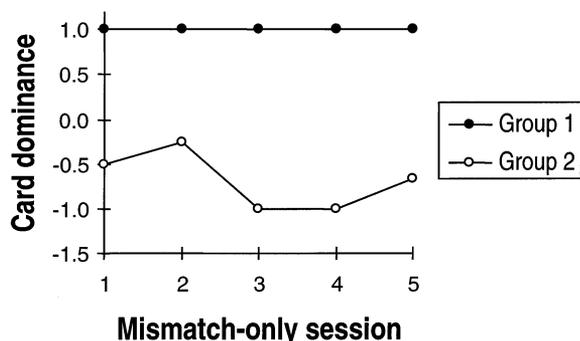


Fig. 7. A pattern similar to that in Fig. 6 was found when the five sessions of mismatch-only trials were compared (i.e. on days when there were no other trial types occurring: the first five sessions for Group 1 rats, and the last five sessions for Group 2 rats).

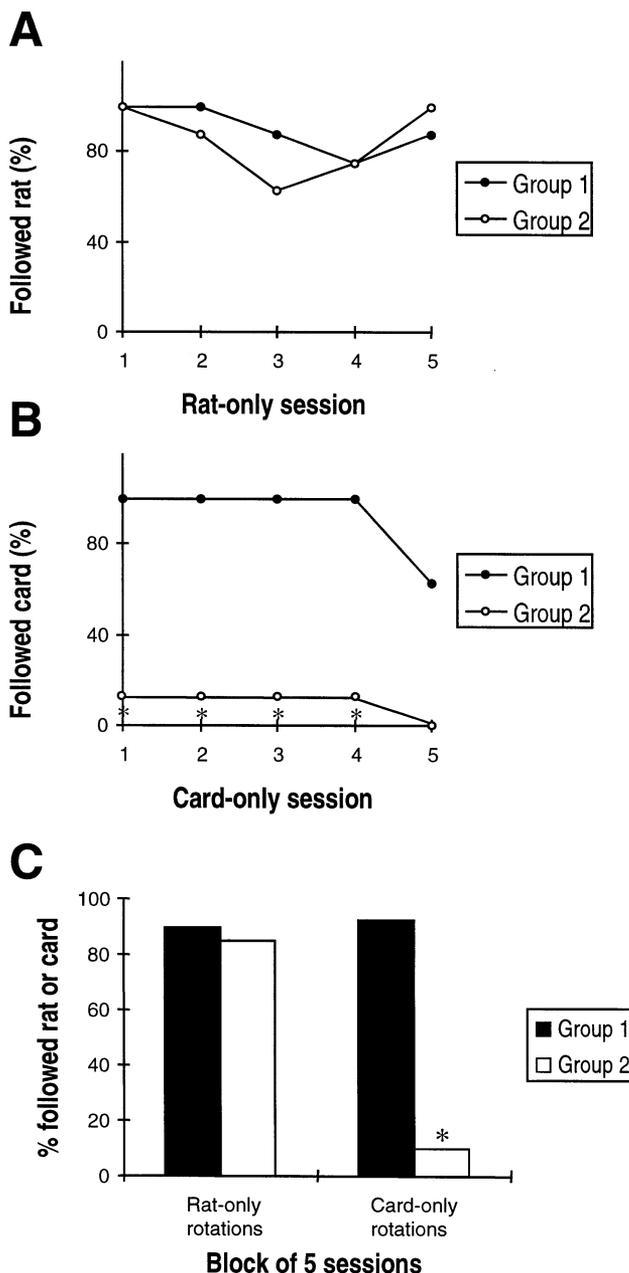


Fig. 8. Results for the rat-only and card-only rotations. (A) Rat-only rotations: fields in both groups behaved similarly, following the rat on almost all trials. This shows that in the absence of the cue card the idiothetic cues are able to exert control of place field orientation. (B) Card-only rotations: the fields followed the card in Group 1 rats but not in Group 2 rats. (C) Comparison of the two groups for the blocked data shown above: there was a significant difference in card-following in the card-only rotations, but no difference in rat-following in the rat-only rotations.

3.3. Card-only rotations

These took place at the end of the experiment for the Group 1 rats and at the beginning of the experiment for the Group 2 rats. The results of these trials are shown in Fig. 8. The effect of visibly moving the card on place fields in the Group 1 rats was somewhat surprising. In

almost every case except for the last trial of the last day, the fields continued to rotate with the cue card, even though this was moved in full view of the rat. In one trial, recording was made continuously while the cue card was being moved. Shift of the field was almost instantaneous, suggesting that the rat's internal representation of environment orientation was so strongly tied to the card that it disregarded all other sources of directional information.

For the Group 2 rats, by contrast, visible movement of the card was very rarely accompanied by rotation of the fields. The difference in card-following between the two groups for the card-only rotations was significant ($t = 6.60$; $P < 0.05$). It seems, therefore, that the prior experience of the Group 1 rats of the cue card as visually stable had 'protected' the place cells from this loss of control (although the decline evident on the last day suggests that such control may have been weakened by the five sessions of instability).

4. Discussion

There are three main results of the present study. First, in rats exposed to a symmetrical environment, visual information initially overrode motion-based (idiothetic) information in orienting place fields if the rats were isolated from the environment while the card was being moved, but not if they could see it moving. Second, if the visual cue was experienced as unstable, the balance of control became altered over time so that the idiothetic cues came to predominate instead, even in trials where the rats were unable to see the card move. This shows that place cells receive both visual and idiothetic information about orientation, and that they can learn which type of information to rely upon. Third, conversely, if the visual cue was experienced over time as being stable, this appeared to 'protect' against learning about subsequent instability. These results are discussed below, in the context of the current debate about whether visual or idiothetic cues take priority in controlling the direction sense.

4.1. Balance of visual and idiothetic cues in a novel environment

Initially, in rats that were covered while the cue card was moved, the card predominated over idiothetic information in orienting place fields. This is evident in Fig. 5, where on the first day of exposure to the recording environment, place fields in both groups of rats followed the cue card in preference to the idiothetic cues. This implies that place cells in a novel environment are predisposed to 'trust' a strong, salient visual cue unless there is a reason not to (see below). However, it was also found that early on in the trial

sequence, if the card was moved within view of the rat then very few fields followed it (Fig. 8). This observation is a replication of the finding of Rotenberg and Muller (1997) that place fields did not follow large (180°) shifts of a cue card if these were made within view of the rat.

Why did the cue card control place field orientation when it was invisibly moved, but not when it was visibly moved? There are two possibilities:

(1) The directional system is controlled by visual cues by default, but these were weakened in the rats that could see the visual cue move. The influence of the cue could be weakened if, for example, the card's movement were to activate motion detectors in the animal's visual system, signalling that the landmark moved against the visual background in a way that could not be accounted for by the rat's own movements (that is, over and above ordinary motion parallax effects).

(2) The directional system is controlled by idiothetic cues by default, and these were weakened in the rats that did not see the card move. Such weakening could occur if the internal compass relies on a constant stable visual input in order to continually correct for small drifts (Goodridge and Taube, 1995) and maintain it at full strength. In that case, a covering procedure like that employed in the present experiment, which removes all visual 'resetting' inputs, might cause the idiothetic direction sense to decay over the time during which they were covered (in this case, the 2–4 min it took to rotate the rats).

Preliminary additional results support the latter of these two explanations. In experiments in which the card was moved while the rat was covered but not rotated (and therefore isolated from visual input for only 30 s), the cue card lost control of the fields in these animals, just as it had in the uncovered animals, suggesting that it is not the covering per se but the duration of visual deprivation that is the critical factor.

A study by Knierim et al. (1995) also supports the hypothesis that idiothetic cues control the internal direction sense by default, in a new environment. In their study, head direction cells and place cells were recorded from rats exposed to a cylindrical environment containing a cue card. Half of the rats had been disoriented by vigorous rotation each day prior to being placed in the environment. During this disorientation period (lasting many days), the cue card was always in the same place. When all of the rats were subsequently disoriented and subjected to recording sessions in which the cue card was rotated from trial to trial, the cue card had poor control of the orientation of both place fields and head direction cell directional firing preference in the previously disoriented rats. By contrast, it had very good control of cell firing in the previously non-disoriented rats. Knierim et al. explained these results by suggesting that rats rely on the idiothetically based internal com-

pass until the stability of visual landmarks has been learned. According to their model, the disoriented rats entered the environment each day with a randomly oriented internal compass. Because of this, the cue card did not appear to the rats to occupy a stable directional position from day to day and so it was distrusted as a reliable visual indicator of direction (that is, the internal compass set the standard against which the stability of the visual cues was measured). By contrast, the rats that were oriented on introduction to the environment each day had the chance to learn that the visual cue was stable with respect to direction, and so these animals were subsequently able to use it to reset their direction sense on the disorientation trials.

Although the above results appear to argue in favour of idiothetic cues initially taking precedence over visual cues, the picture is complicated by additional findings of Rotenberg and Muller (1997), in the experiment discussed above, that although place fields did not follow visible shifts of the card, they did follow the card if the rotation occurred while the rat was absent from the recording chamber. At first glance, this finding seems very much like the finding of the present experiment that place fields would follow the card if the rats were covered while it was moved. In both experiments, place fields followed the cue card if the rats had not seen it move. However, if the card generally has reliable control in situations where it was not seen to move, why did the card not gain control of all the place fields in the Knierim et al. (1995) experiment? Recall that the cue card lost control over the fields in the previously disoriented rats, even though these rats had never seen the card move either. Clearly, the results of all three studies cannot be reconciled by appealing to a single explanation. Further experiments are needed in order to find out exactly what happens when rats are disoriented and/or isolated from visual inputs. It may be that methodological differences (such as degree of disorientation, or cue-card stability learning) account for the discrepancies in results.

An additional finding of Rotenberg and Muller (1997) supports the first hypothesis above, that visual cues predominate, in situations where the conflict between visual and idiothetic cues is only small. They found that although the place fields would not follow large visible shifts of the cue card, they *would* follow visible shifts if these were only 45°. This finding is in agreement with that of Goodridge and Taube (1995), who found that head direction cells would also follow a cue card in preference to the idiothetic sense provided the discrepancy was not too great. Similarly, Etienne et al. (1990) found that visual cue control over homing hamsters was weaker if it was in 180° conflict with the idiothetic cues than if it disagreed by

only 90°. Bures et al. (1997) also found that idiothetic cues did not necessarily win over visual cues in a conflict situation. They pitted these cues against each other in an ingenious experiment in which place cells were recorded from rats running around the edge of a circular arena. The arena could be rotated with respect to the outside room, so as to keep the rat stationary within the room's frame of reference even as it ran fully around the circumference of the arena. Most place fields disappeared in this situation, sometimes not returning for 1 h or more.

Putting all these studies together, the picture that seems to be emerging is that place cells receive both visual and idiothetic information, and that on initial experience of an environment, either or both can be used to orient their fields. When visual and idiothetic cues are both present but in conflict, then which influence dominates appears to depend on one of two deciding factors. The first is the relative strengths of the two competing signals. If the visual cues are weakened (by removing them, or turning down the lights, or instability learning: see below) then the balance of control shifts towards the idiothetic cues, whereas if these are weakened (for example, by visual deprivation lasting more than 1 min or so) then the visual cues assume control. The second factor is the angular distance by which the two factors disagree. Over short ranges (less than 90°) the visual cues seem to predominate, while over larger ranges (up to 180°) then the idiothetic cues take over. The functional advantages of such a system are that in the real world, small conflicts are more likely to be due to drift of the idiothetic direction sense, because of its dependence on cumulative inertial inputs, while sudden large conflicts are more likely to be due to movement of the visual cues. When the balance of power is about equal between the two sources of information, then place fields may split, break down or 're-map' (assume a new position).

4.2. Balance of visual and idiothetic cues in a familiar environment

The above discussion pertained to animals which had no prior knowledge about the reliability or otherwise of the two sources of information. However, results from the present experiment bear out previous evidence (Etienne et al., 1993; Knierim et al., 1995) that once an environment has become familiar and such reliability knowledge becomes available, the balance of control in orienting the internal compass can shift in either direction, towards either the visual or the idiothetic cues. In the present study, control shifted away from the visual cue and towards the idiothetic cues if the rat had previously experienced the cue as being visually unstable, even for trials in which the rats were then covered during rotations of

the card. This is shown by Fig. 5, where it can be seen that the superiority of the card as an orienting stimulus gradually diminished in the Group 2 rats, and was replaced by a preference for the idiothetic cues.

The loss of cue card control seen in the present experiment accords with several previous reports in the literature that have suggested a weakening of such control when the visual cues were made unreliable (but see Dudchenko et al., 1997 for a counterexample). In the Knierim et al. (1995) study discussed earlier, cue card control was poorer in the previously disoriented animals than in the never-disoriented rats, suggesting that the disorientations had caused a mismatch between the visual cue and the rats' internal compass, resulting over time in a lessening of the card's influence on place cells. Taube and Burton (1995) found that, a cue card exerted decreasing influence on head direction cells in animals that had experienced it to be in repeated conflict with their internal compass (as controlled by a second visual stimulus). Etienne et al. (1993) found that control of the behaviour of homing hamsters could shift from visual to idiothetic cues with experience. In their study, visual information was preferred over idiothetic cues as a means of guiding the foraging hamsters back to a nest box in a familiar environment. However, with repeated experience that the idiothetic cues were a better guide to the location of the nest box than the visual cues, the hamsters began to rely on those instead. In all of the above studies, including the present one, it remains to be established whether the visual cues decreased in strength, the idiothetic cues increased in strength or some combination thereof.

The present study also found the converse: that after experience of the cue card as being visually stable, place fields continued to follow the card preferentially even when it was subsequently made visually unstable. This is shown in Fig. 8(A), where it can be seen that card-following occurred significantly more often following card-only rotations in the Group 1 rats than in the Group 2 rats. During one recording session from a Group 1 rat, the card was shifted during the middle of a trial and the corresponding shift in the place field was observed to occur almost instantly. The preference of the fields for the cue card over idiothetic cues in these rats has two possible causes: either the visual cues were strengthened, or the idiothetic cues were weakened following repeated experience in which the cue card was perceived to be more reliable than the idiothetic cues. Either way, because cue card control was initially at ceiling levels in this experiment, strengthening of the relative influence of the visual cue on the place fields resulted in a masked effect that was only manifest by a decrease in the rate of subsequent instability learning.

The finding that place fields were preferentially oriented by a previously stable visual cue, even when it was then made unstable, contrasts with the findings of

a behavioural study by Biegler and Morris (1996). In their study, rats were trained to locate food in a square environment using a combination of a distal polarising stimulus (a white curtain on the wall of the arena) and asymmetric intramaze landmarks. After much training with the cues in a fixed position, subsequent rotation of the cues (including the white curtain) rotated the search pattern of the rats but only if they were disoriented before the start of that trial. If they were fully oriented, they searched instead in the place that was consistent with the combined idiothetic and extramaze cues (those outside the arena, which were uncontrolled and not visible). This contrasts with the present experiment, where rotation of a previously stable cue card invariably resulted in rotation of place fields. One possible explanation for the discrepancy in results is that in the Biegler and Morris study, unlike the present one, the (non-visual) extramaze cues were always aligned with the rats' internal compass during training. It may be that the combined idiothetic and extramaze cues could override the rotated visual stimuli, especially since the rats were being trained to pay attention to polarising cues. Another possibility, mentioned earlier, is that the experience of the rats in the present study of repeatedly having to yield the idiothetic to the visual cues resulted in a weakening over time of the effects of the idiothetic cues, so that in the trials in which the landmark was moved in full view of the rat, the idiothetic cues could no longer compete. And finally, perhaps behaviour depends on other factors than just the place field orientation (Dudchenko et al., 1997).

4.3. Interaction of visual and idiothetic cues in a novel versus familiar environment

The results of the above studies combined with those of the present experiment draw the following picture of how visual and idiothetic cues may interact in forming and sustaining a representation of the directional orientation of an environment. When a rat leaves a familiar environment and enters a new one, it carries with it an internal representation of direction (Taube and Burton, 1995) that is maintained by the firing of head direction cells, which receive their inputs from motion based cues (since the visual cues have never been seen before). Therefore, the internal directional sense is initially independent of visual cues except insofar as they are used to correct small drifts. The most salient visual cue ('salience' comprising some combination of size, luminance and distance) then becomes mapped onto this representation so that should the animal become disoriented when it re-enters the environment, this cue can be used to retrieve its orientation. However, if the cue is subsequently experienced as unstable, either because it is seen to move, because it shifts its location with respect to the constellation of other cues or because it

repeatedly conflicts with the idiothetic cues, then the connection between this cue and the direction sense will become weakened and control will pass either to another visual cue or, in the absence of a suitable candidate, to the idiothetic cues. Conversely, if it not experienced as unstable, then it will come to be preferred over the idiothetic cues as a cue with which to orient the environment. (Note that learning of the reliability of the idiothetic cues may also occur.)

The learning of stability and instability of visual landmarks in a novel environment is one of the clearest physiological demonstrations of learning by the place representation to date. As a physiological model of memory processes, it has the advantage that the place and direction representations are two of the best-understood cognitive representations in the brain. This means that associative changes in the inputs induce changes in the place representation that can be understood, and therefore dissociated from random changes in firing patterns. The technique used here of pairing or unpairing two stimuli (visual and idiothetic) opens up the possibility of devising a Hebbian model of place or head direction cell learning in a manner analogous to those of more traditional models of learning, such as classical conditioning.

Acknowledgements

The author would like to thank Steve Burton, Jim Donnett, Dave Edwards and Clive Parker for technical assistance, and John O'Keefe for useful discussion. Neil Burgess, Jim Donnett and John O'Keefe kindly reviewed the manuscript, and two anonymous referees provided invaluable comments. The work was supported by a Medical Research Council programme grant to John O'Keefe.

References

- Biegler, R., Morris, R.G.M., 1993. Landmark stability is a prerequisite for spatial but not discrimination learning. *Nature* 361, 631–633.
- Biegler, R., Morris, R.G.M., 1996. Landmark stability: further studies pointing to a role in spatial learning. *Quart. J. Exp. Psychol. B* 49, 307–345.
- Bures, J., Fenton, A.A., Kaminsky, Yu., Rossier, J., Sacchetti, B., Zinyuk, L., 1997. Dissociation of exteroceptive and idiothetic orientation cues: effect on hippocampal place cells and place navigation. *Philos. Trans. R. Soc. London B* 352, 1515–1524.
- Dudchenko, P.A., Goodridge, J.P., Taube, J.S., 1997. The effects of disorientation on visual landmark control of head direction cell orientation. *Exp. Brain Res.* 115, 375–380.
- Etienne, A.S., Teroni, E., Hurni, C., Portenier, V., 1990. The effect of a single light cue on homing behavior of the golden hamster. *Anim. Behav.* 39, 17–41.
- Etienne, A.S., Joris Lambert, S., Reverdin, B., Teroni, E., 1993. Learning to recalibrate the role of dead reckoning and visual cues in spatial navigation. *Anim. Learn. Behav.* 21, 266–280.
- Goodridge, J.P., Taube, J.S., 1995. Preferential use of the landmark navigational system by head direction cells in rats. *Behav. Neurosci.* 109, 49–61.
- 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.
- Knierim, J.J., Kudrimoti, H.S., McNaughton, B.L., 1995. Place cells, head direction cells and the learning of landmark stability. *J. Neurosci.* 15, 1648–1659.
- O'Keefe, J., Burgess, N., 1996. Geometric determinants of the place fields of hippocampal neurons. *Nature* 381, 425–428.
- O'Keefe, J., Recce, M.L., 1993. Phase relationship between hippocampal place units and the EEG theta rhythm. *Hippocampus* 3, 317–330.
- Rotenberg, A., Muller, R.U., 1997. Variable place-cell coupling to a continuously viewed stimulus: evidence that the hippocampus acts as a perceptual system. *Philos. Trans. R. Soc. London B* 352, 1505–1513.
- 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 hippocampal place cells. *J. Neurosci.* 15, 173–189.
- Taube, J.S., Burton, H.L., 1995. Head direction cell activity monitored in a novel environment and during a cue conflict situation. *J. Neurophysiol.* 74, 1953–1971.
- Wiener, S.I., Korshunov, V.A., Garcia, R., Berthoz, A., 1995. Inertial, substratal and landmark cue control of hippocampal CA1 place cell activity. *Eur. J. Neurosci.* 7, 2206–2219.