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Place cells and place navigation

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ABSTRACT **The assumption that hippocampal place cells (PCs) form the neural substrate of cognitive maps can be experimentally tested by comparing the effect of experimental interventions on PC activity and place navigation. Conditions that interfere with place navigation (darkness, cholinergic blockade) but leave PC activity unaffected obviously disrupt spatial memory at a post-PC level. Situations creating a conflict between egocentric and allocentric orientation (place navigation in the Morris water maze filled with slowly rotating water) slow down spatial learning. PC recording in rats searching food pellets in a rotating arena makes it possible to determine which firing fields are stable relative to the room (allocentrically dependent on sighted extramaze landmarks), to the surface of the arena (dependent on egocentric path integration mechanisms and intra-arena cues), or disappear during rotation. Such comparison is made possible by the computerized tracking system simultaneously displaying a rat's locomotion and the respective firing rate maps both in the room reference and arena reference frames. More severe conflict between allocentric and egocentric inputs is produced in the field clamp situation when the rat searching food in a ring-shaped arena is always returned by rotation of the arena to the same allocentric position. Ten-minute exposure to this condition caused subsequent disintegration or remapping of 70% PCs ($n = 100$). Simultaneous examination of PC activity and navigation is possible in the place avoidance task. A rat searching food in a stationary or rotating arena learns to avoid an allocentrically or egocentrically defined location where it receives mild electric footshock. In the place preference task the rat releases pellet delivery by entering an unmarked goal area and staying in it for a criterion time. Both tasks allow direct comparison of the spatial reference frames used by the PCs and by the behaving animal.**

The invitation to write an inaugural article is a unique opportunity to combine a review of what has been done with a program statement describing how we want to continue our research, explaining the philosophy of our approach, and discussing its specific tools. We should like to stress from the outset that the article does not represent an individual but a research team, the ever changing composition of which is not a weakness but a source of strength.

History

The present Laboratory of Neurophysiology of Memory of the Institute of Physiology of the Academy of Sciences in Prague was organized in 1958 with the aim to study nonimpulse forms of neural communication. The research concentrated on the analysis of cortical spreading depression (1), which was at the time the best known example of a neurohumoral phenomenon propagating over the entire brain surface of laboratory rodents. From the very beginning this mainly electrophysiological project lead to behavioral investigations when Buresova (2) proposed to use repeated waves of spreading depression as a functional ablation procedure in studies of interhemispheric transfer, memory consolidation, and cortico–subcortical relationships (see ref. 3 for a review). The behavioral models used included active and passive avoidance, visual discrimination learning, motor skills, operant conditioning, and conditioned taste aversion (see refs. 4 and 5 for reviews). The behavioral experiments were often combined with unit activity recording in the relevant brain centers—e.g., motor cortex in case of reaching for food (6) and gustatory centers in case of conditioned taste aversion (7).

The laboratory entered spatial memory research in the early 1980s (8) when the radial maze (9) and the Morris water maze (10) were proposed as ethologically based models of declarative memory (11) amenable to behavioral and electrophysiological analysis. We were particularly impressed by the proficiency of rats at finding the direct path from anywhere in a charted environment to an unmarked goal, that in the absence of local cues could only be identified according to its relations among extramaze landmarks. A few months after reading Morris' seminal article (10) we acquired a pool and started experiments testing how place navigation is affected by functional decortication, cortical epileptic foci, hypothermia, electroconvulsive shock, and vestibular stimulation. We also used the working memory version of the water maze task to test the persistence of the spatial memory record and addressed the problem of latent learning in the water maze (see refs. 12 and 13 for reviews).

Along with the above experiments we developed a computerized tracking system that was used for interactive control of the experimental conditions in addition to recording the rat's position. This approach can be illustrated by the "on demand platform" (14) raised to the surface only after the computer has acknowledged that the rat has spent a criterion time (e.g., more than 1 s) within a criterion distance (e.g., 10 cm) from the center of the target area. This technique gives each trial some properties of the probe trial (15) but makes it at the same time possible to reward the correct solution of the task by the opportunity to escape (16).

In another experiment the computer provided a blind rat swimming in the water maze acoustically coded information about its distance from the goal (17). Using the path integration record of the immediately preceding locomotion, the rat could convert the scalar information about the changing

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Abbreviations: Coh, spatial coherence; Con, field concentration; D, field displacement; Disp, field dispersion; FF, firing field; LED, light-emitting diode; PC, place cell.

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distance from the goal into vectorial information about the direction to the goal.

Mechanisms of Place Navigation

Intensive research into the mechanism of place navigation has lead to the formulation of several concepts that form the basis of the present study of the neural representation of space (18, 19). A place is defined as a location marked by no locally perceptible cues and is therefore only recognizable relative to other perceptible landmarks or orienting gradients. Whereas animals approaching a visible or otherwise perceptible goal are using a so-called taxon strategy, finding a hidden goal requires a so-called locale strategy—i.e., place navigation. According to the cognitive map theory (20) the brain representation of a familiar environment lists the topographical relationships of prominent landmarks established in two ways. (*i*) The allocentric system records the position of an arbitrary point by its distance from several salient landmarks or by azimuths of these landmarks relative to an orienting gradient. (*ii*) The path integration system determines the current position of the animal with respect to a starting point (e.g., exit from the home cage) by integration of the path covered by locomotion from the start—i.e., by adding successive locomotion vectors (length and direction of track segments). Whereas allocentric orientation is mainly based on visual cues, path integration orientation can be called egocentric because it uses idiothetic information produced by limb muscle proprioceptors and vestibular receptors that estimate the distances traversed and the changes of direction. Typically, both orientation systems are employed by sighted animals under normal conditions (21); however, in darkness and in the absence of nonvisual allocentric cues only path integration can be used. Both systems yield identical results when used for construction of cognitive maps. This redundant representation of space increases the reliability of navigation when allocentric orientation is eliminated by darkness or when sudden danger calls for rapid return to the safe starting point (homing).

System Level Anatomy of Place Navigation

Most lesion studies have supported the assumption that cognitive maps are implemented by the hippocampus (18). Complete hippocampectomy (22), destruction (23) or inactivation of the dorsal hippocampus (24), transection of the fimbria fornix (25), or lesions of medial septum (26) cause severe impairment of place navigation in the Morris water maze. Similar impairment is induced by destruction of the retrohippocampal cortex (27) including the main hippocampal inputs (entorhinal cortex) and outputs (subicular complex). Lesions of the ventral hippocampus are less detrimental than the dorsal lesions. According to Moser *et al.* (28), normal navigation can be supported by a transverse minislab of the hippocampus at its rostral pole but not by a similar volume of the ventral hippocampus separated from the rostral pole. Navigation is impaired less consistently by lesions of the parietal, frontal, and temporal cortex (29) of thalamic nuclei (30) and basal ganglia (31), but these results can be partly due to interference with hippocampal inputs and outputs or to impaired locomotion.

Hippocampal Place Cells

The assertion that the hippocampus is the substrate of cognitive maps was prompted by the discovery (32) of hippocampal pyramidal cells that tend only to fire rapidly when a freely exploring rat enters a definite part of the environment. Such cells are called place cells (PCs) and where they fire is called the place or firing field (FF). All PCs are thought to be complex spike cells because they sometimes discharge a burst of spikes of decreasing amplitude generated at short (5–20 ms) interspike intervals (33). Outside the FF PCs are mostly silent, rarely producing complex spikes. Unlike PCs, hippocampal interneurons never fire complex spikes and they tend to be active throughout all environments. They are called theta cells because their firing rates more than double during the hippocampal electroencephalogram oscillation in the 4–10 Hz theta band and they fire in phase with the peaks of the theta oscillation (34). Their discharge cannot be described as location-specific.

In circular homogeneous environments (empty arena) PCs' FFs are usually determined by extramaze landmarks or by cue cards covering a segment of the wall rather than by cues that cannot be detected by the experimenter (e.g., scent markings on the floor). Because two PCs simultaneously recorded by the same electrode can have overlapping FFs in one arena and quite distant FFs in another arena (35–37), it is generally agreed that PCs do not form a topographically organized representation of the environment. Although visual input is indispensable for the initial determination of the FFs in a specific environment, the location and shape of already formed FFs persist after elimination of visual orientation (38). Even when the rat is brought into a circular arena in darkness, about half the PCs behave as if only the reference frame had rotated an arbitrary amount (39). Presumably the rat can use some orienting gradients or tactile cues that might be provided by the arena floor and walls (40).

Methods for Recording PCs

One focus of our current research and the topic of the present paper is the question of how PCs contribute to place navigation. After 25 years of PC research the question remains unanswered, particularly because the methods that have been used to study PCs were developed to understand the geometric determinants of FFs (see ref. 41 for a review). The probability that a particular cell will fire as a function of each position in an environment must be determined to properly characterize a FF. Thus it is necessary to record in conditions where the rat uniformly distributes its behavior over the arena surface. This is readily achieved by using the pellet chasing task (42) in which a hungry rat forages for food pellets that fall to random locations in the arena. Typically, pellet chasing is combined with recording in geometrically simple cue-controlled environments. Both conditions maximize the reproducibility of the cell's firing characteristics and thus have been very effective for understanding what environmental features determine location-specific activity. The consequence is that we can say very little about how the rat actually uses the information encoded by PCs.

The electrophysiological techniques used in our laboratory are similar to those used in standard PC studies. Briefly, under pentobarbital anesthesia, a microdrive containing a bundle of eight 25-μm nichrome electrodes is cemented on the skull so that the electrodes pass through a hole in the skull and rest 1 mm above CA1. After a week's recovery, the electrodes are lowered until single units can be isolated from the pyramidal cell layer. A standard recording session is 10 min during the pellet chasing task.

The PC-based tracking system used for interactive experimental control records the position of an infrared light-emitting diode (LED) on the rat's head at 0.4-cm spatial resolution and 100-ms temporal resolution. Extracellular signals are filtered (300 Hz to 10 kHz) and then digitized (32 kHz) and stored with a PC-based system (DataWave, Boulder, CO). Currently, we discriminate units off-line by a template matching algorithm. A waveform template is chosen for each unit of interest. The match between each digitized waveform and the templates is scored by a least-squares fit. Waveforms with

shapes sufficiently close to only one template are taken to be from a single unit.

The position and discriminated spike time series are used to calculate the session-averaged spatial firing rate distribution of each unit by dividing the total number of spikes recorded in each 5 × 5-cm pixel (or 10 × 10-cm pixel in the large arena) by the total time spent in that pixel. This is conveniently displayed as a color-coded firing rate map. In these maps white represents pixels with undefined firing rate because they were not visited by the rat. Yellow pixels were visited but the cell did not fire so the rate is exactly zero. Purple marks pixels with the highest rate representing 11% of the non-zero firing range. The other colors in the order blue, green, red, and orange reflect decreasing firing rates found in 14, 19, 25, and 31% of the firing range. For each map, legends give the median firing rates for each color category.

Whenever possible numerical methods are used to describe and compare the spatial firing of PCs. A FF is defined as an area at least four pixels large (100 cm^2) where the firing rate is at least 2 standard deviations above the over all mean firing rate. To be included in a field a pixel must share at least one side with another pixel of the field. A FF's location is defined as the firing rate-weighted average of the x and y coordinates of the pixels in the field. The linear distance between field locations in two sessions (displacement, D) was used to decide whether a FF location changed. The location was considered to be changed if the displacement was >5% of the distance from the reference location to the most remote point in the arena.

Three measures of the quality of location-specific firing were calculated. Spatial coherence (Coh) (43) measures the local smoothness of the firing rate pattern. It is the z-transform of the correlation between the list of firing rate in each pixel and the mean firing rate of the pixels with which it shares a side.

The second measure, "concentration" (Con) of the FF is used to describe how well the spatial firing was restricted to the FF. It is defined as the ratio of the number of pixels in the FF to the total number of pixels where a spike was detected. Thus a maximum concentration of 1.0 indicates that all spikes occurred within the FF.

Because concentration does not describe how the firing is distributed across the apparatus, a third measure, "dispersion" (Disp) is defined as the number of pixels in which a spike was detected divided by the apparatus area. Location specificity decreases as dispersion increases to its maximum 1.0.

PCs and Behavior

The evidence that hippocampal PCs clearly reflect the position of the animal in the charted environment and that hippocampectomized rats cannot master simple navigation tasks led to the tacit assumption that PCs play some and perhaps even a crucial role in place navigation. Although this assertion is plausible, it is obviously a logical non sequitur, a conclusion that does not follow from the premises. More data are required to test this hypothesis under conditions differentially affecting PC activity and place navigation. The assumption that PC activity is a prerequisite of efficient place navigation is supported in situations when both PC mapping and place navigation are intact or when the disappearance of PC activity or changed PC mapping is accompanied by impaired place navigation. On the other hand, the hypothesis is falsified when place navigation is impaired in spite of preserved PC activity or, more importantly, when absent or disorganized PC activity does not interfere with place navigation.

Preserved PC Activity and Impaired Place Navigation

Perhaps the best documented state eliciting severe navigation disruption is elimination of visual input by darkness. Even when some allocentric orientation based on acoustic beacons may remain possible (44, 45), the goal-directed locomotion disappears and the escape latencies in the Morris water maze increase from 5 s to more than 20 s—i.e., to the level corresponding to the learned search strategy for a randomly located goal. Efficiency of navigation in darkness remains low even under fixed start–fixed goal conditions (45, 46). The striking darkness-induced deterioration of acquisition and/or retrieval of place navigation contrasts with the almost negligible effect of sudden darkness on FFs previously established in light (39, 47–50).

The disruptive effect of darkness on place navigation is perhaps best documented in an experiment (51) requiring the animal to find the escape platform in a circular part of the pool the entering of which is always accompanied by switching off the room lights. The conditions of the experiment are schematically shown in Fig. 1. The rat was started from the periphery of the pool in the light and the light stayed on until the rat crossed into the central zero-visibility zone that contained the goal. When the animal missed the escape platform and entered the peripheral belt, the light was switched on again and the rat could make another sighted attempt to find the goal. Whereas acquisition of the standard place navigation task reaches an asymptotic escape latency of 5 s after 3 days of training (12 trials/day), navigation to the goal in the zero-visibility zone reaches escape latencies of 18 s and 12 s at days 3 and 7, respectively. Rats trained in light and then tested with

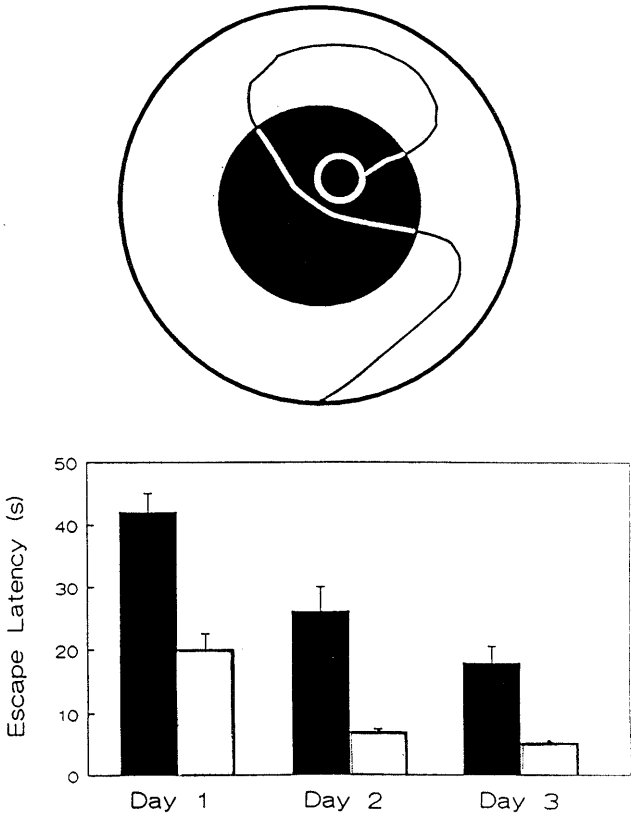

FIG. 1. Impaired navigation to the escape platform located in the zero-visibility zone. (*Upper*) The *Inset* shows the scheme of the experiment with the zero-visibility zone marked by the black circle and the escape platform by the white ring in the northeast quadrant of the pool. The rat is started from the south and the room lights are on (black track) or off (white track) when it is outside or inside the zero-visibility zone, respectively. (*Lower*) Mean (± SEM) escape latencies of naive rats learning the task in light (n = 10, white columns) and with the goal in the zero-visibility zone (n = 10, black columns) during the first 3 days of training (12 trials/day). [This figure was modified from Arolfo *et al.* (51).]

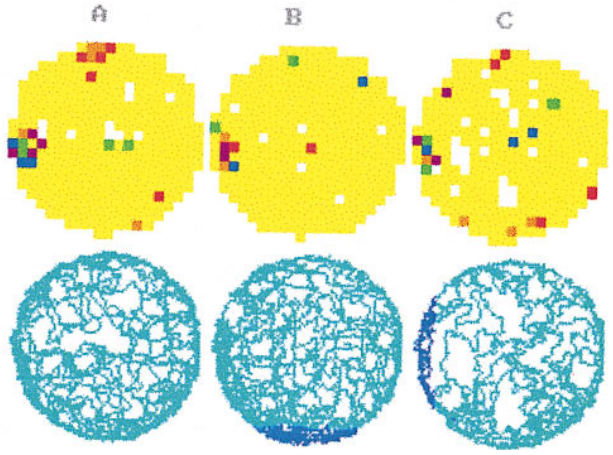

FIG. 2. Spatial firing characteristics of a hippocampal PC in a rat performing the pellet chasing task in a uniformly illuminated arena (2 m in diameter) before (*A*) and after introduction of the zero visibility are zones in the south (*B*) or west (*C*). (*Lower*) The tracks of the animal during 10-min recording sessions. The zero-visibility zones are indicated by dark tracking lines. The median firing rates from yellow to purple are 0.0, 0.2, 0.4, 1.0, 1.3, and 6.0 for *A*; 0.0, 0.1, 0.3, 0.4, 0.5, and 0.6 for *B*; and 0.0, 0.1, 0.4, 0.6, 0.8, and 2.9 for *C*. (See text for a quantitative evaluation of the maps.)

the goal in the zero-visibility zone were less markedly impaired, but their escape latencies increased from 5 s to 18 s on the first day.

To study PC activity under analogous conditions (52) rats trained in normal lighting were tested in a large (2 m diameter) circular arena where the light was only turned on when the animal was in one part of the arena. Fig. 2 shows a typical experiment. A FF characterized in the west during 10 min in the light (Fig. 2*A*; Coh = 0.54, Con = 0.43, Disp = 0.07) persisted when it was covered by a zero-visibility zone in the western segment of the arena (Fig. 2*C*; D = 0.04, Coh = 0.88, Con = 0.6, Disp = 0.03). Similarly, when the zero-visibility zone was moved to the south, remote from the field, the field persisted though it was less robust (Fig. 2*B*; D = 0.04, Coh = 0.17, Con = 0.35, Disp = 0.06). The sudden disappearance of allocentric cues does not interfere with PC mapping nor does the virtual light–dark barrier suppress PC activity like a real barrier that limits movement (53). Because PC activity appears impervious to position dependent changes of illumination, the deterioration of navigation under such conditions is probably not due to disrupted PC mapping but rather to interference occurring at some post-PC level of spatial information processing.

Comparisons of PC activity and place navigation during pharmacologically induced states compatible with spontaneous locomotion also suggest that PCs are not necessary for navigation. The best such example is systemic application of scopolamine which disrupts acquisition of place navigation in the water maze at dosages of 0.2–0.4 mg/kg and interferes with retrieval of overtrained navigation at 1 mg/kg (54). Although the peripheral effect of the drug (reduced salivation) may lower the motivation of the animal and reduce exploration, it was possible to record PC activity during 1 h after scopolamine injection. Fig. 3 shows the effect of 1 mg/kg scopolamine on PC activity during spontaneous and hand-guided free movement of the rat in a 1-m cylinder. In 15 PCs studied, under the effect of scopolamine FF locations did not change in 11 cases ($D < 5\%$) and moved to a different position or disintegrated in 4 cases ($D > 5\%$) (52). In those cases with preserved FF locations (Fig. 3 shows a typical example), the FF quality was somewhat degraded. This suggests that the scopolamine-induced impairment of place navigation is not due merely to disrupted location-specific PC activity but rather to interference with the downstream processing of this activity. Alternatively, the changed mapping of 25% to 30% of the PCs may cause substantial disorientation of the animal. The effect of cholinergic disruption on PC activity remains controversial. Mizumori *et al.* (55) found FFs of most CA1 PCs unaffected by procaine injection to the medial septum which provides an important cholinergic input to the hippocampus. On the other hand, Brazhnik *et al.* (56) reported extremely reduced PC activity after tetracaine or muscimol injection into medial septum.

Place Navigation Under Conditions Interfering with PC Activity

The question of whether PC activity is necessary for place navigation can be best answered by testing animals under conditions disrupting PC mapping—e.g., when the presumed world stability is violated by conflicting information received by egocentric and allocentric inputs. Such dissociation was achieved in the water maze by slowly rotating the water at 1 revolution per 80 s (57). In rotating water, acquisition of place navigation was slower during the first 6 days of training (8 trials/day) but reached the stable water performance level after 9 days. This learned compensation for the water movement was specific for a particular goal position and had to be updated each time the goal position changed.

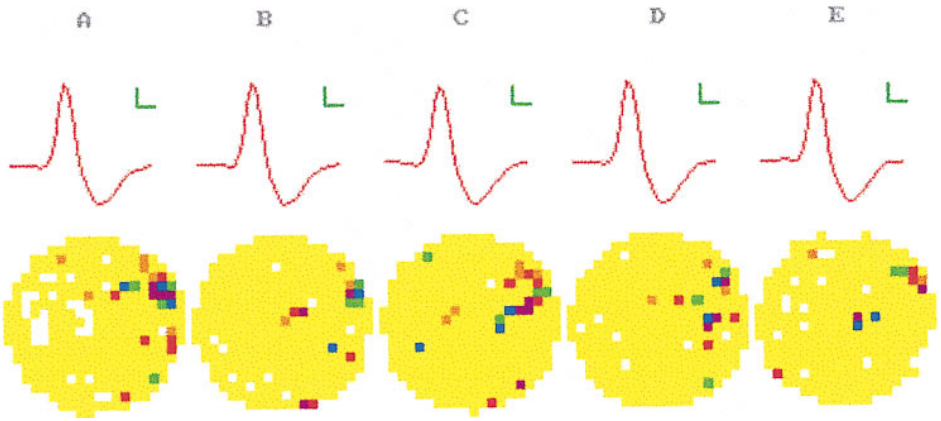

FIG. 3. Activity of a hippocampal PC during pellet chasing in the arena used in Fig. 2 before (*A*) and during four successive 10-min-long recording periods (*B–E*) after intraperitoneal injection of scopolamine (1 mg/kg). (*Upper*) The averaged shape of the selected spike (calibration 60 μV, 0.1 ms). (*Lower*) The firing rate maps. The median firing rates for the color coded pixels are 0.0, 0.2, 0.5, 1.0, 1.2, and 2.3 for *A*; 0.0, 0.3, 0.6, 0.9, 1.1, and 1.8 for *B*; 0.0, 0.1, 0.5, 0.8, 1.3, and 2.0 for *C*; 0.0, 0.3, 0.5, 1.4, 1.9, and 3.3 for *D*; 0.0, 0.1, 0.2, 0.3, 0.8, and 1.4 for *E*. (For quantitative evaluations, see text.)

Whether or not the above navigation impairment can be due to impaired PC activity was addressed by PC recording during pellet chasing first in a stationary arena and then when the same arena was rotated at 1 revolution per minute. In spite of the rotation, a PC with prevailing allocentric input (from remote extramaze landmarks) will continue to fire when the animal enters a FF defined with respect to the stable features of the room. On the other hand, a PC with prevailing egocentric input (proprioceptive and vestibular) will continue to fire in a specific area in the arena reference frame as this can be identified by the egocentric path integration system. Finally, location-specific PCs requiring the coincidence of the allocentric and egocentric inputs would either degrade, completely disappear, or change location.

To analyze the above situations the tracking system was modified to produce (*i*) tracks reflecting the combined movement of the rat and the arena with respect to the stationary (real) camera (i.e., in the room reference frame) and (*ii*) tracks reflecting the movement of the rat with respect to the arena reference frame as seen by a virtual camera fixed above and rotating with the moving arena. The arena frame analysis was made possible by tracking a second infrared LED that marked the rotation of the arena. The arena LED position was used to compute the angular correction to the rat position as seen by the real camera to that corresponding to the rat's position in the arena frame (see Fig. 4).

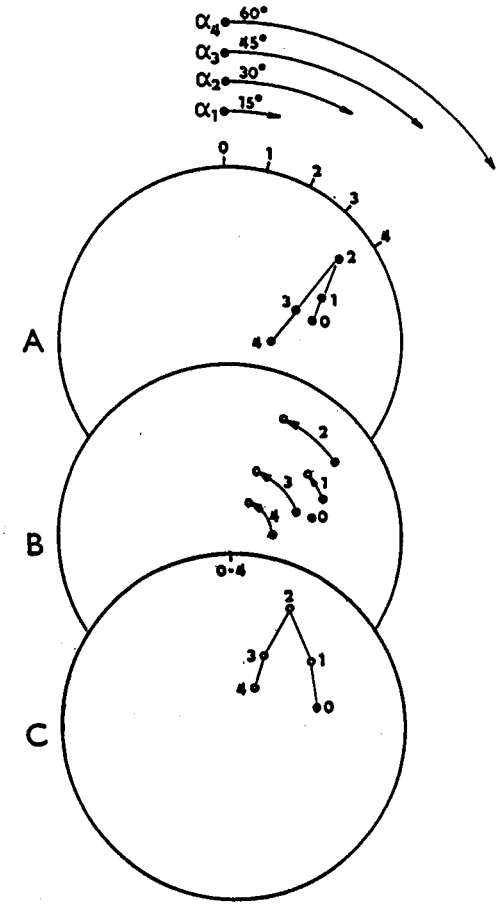

FIG. 4. Scheme of the transformation of the room frame display as seen by the real overhead camera (*A*) to the arena frame display as seen by a virtual overhead camera attached to the arena (*C*). The rat's room-related locomotion on an arena rotating at constant angular velocity (15°/s) is transformed to arena-centered coordinates. During transformation (*B*) each position of the rat seen in *A* (points 0–4) remains at the same radial distance from the center of the arena but its angular coordinate is corrected by the angle corresponding to the angular displacement of the arena indicated by the position of the simultaneously recorded LED marker at its periphery (short radial bars 0 to 4 indicating the position of the LED at time intervals 0–4 s in *A*).

Fig. 5 shows examples of FFs recorded on the stationary and rotating arenas in the room and arena reference frames. In the experiment shown in Fig. 5*A*, though pellet chasing was normal in the rotating arena, compared with the stable situation the FF was smeared in both reference frames during rotation as shown by the coherence, concentration, and dispersion values: stable (Fig. 5*A1*), Coh = 1.28, Con = 0.83, Disp = 0.39; rotation, room frame (Fig. 5*A2*), Coh = 0.81, Con = 1.0, Disp = 0.81; rotation, arena frame (Fig. 5*A3*), Coh = 0.75, Con = 0.99, Disp = 0.79. This suggests that neither the allocentric nor the egocentric orientation provided sufficiently strong input for this particular PC. During rotation, compared with the stable condition (Fig. 5*B1*, Coh = 1.25, Con = 0.78, Disp = 0.53) another unit (Fig. 5*B*) showed a somewhat displaced FF in the room (Fig. 5*B2*, D = 0.12, Coh = 1.3, Con = 0.65, Disp = 0.47) but not in the arena reference projection (Fig. 5*B3*, D = 0.35, Coh = 1.27, Con = 0.48, Disp = 0.54). A third PC (Fig. 5*C*), during rotation in the dark, compared with both the standard stable condition (Fig. 5*C1*, Coh = 1.60, Con = 0.92, Disp = 0.43) and a session in darkness on the stable arena (Fig. 5*C2*, Coh = 1.47, Con = 0.79, Disp = 0.49) displayed a FF in the arena frame (Fig. 5*C4*, D = 0.13 relative to the standard, Coh = 1.01, Con = 0.88, Disp = 0.68) but not in the room frame (Fig. 5*C3*, D = 0.35 relative to standard, Coh = 0.82, Con = 0.99, Disp = 0.77). Apparently its path integration input was sufficient to support egocentric location-specific discharge when the egocentric–allocentric conflict had been minimized by reduction of extra-arena information.

Relative to the standard condition (Fig. 5*C1*), the same unit also demonstrated displaced but spatially selective discharge in the arena frame (Fig. 5*C6*, D = 0.34, Coh = 1.26, Con = 0.85, Disp = 0.69) but not in the room frame (Fig. 5*C5*, D = 0.32, Coh = 0.75, Con = 1.0, Disp 0.81) when the rotation took place in the light with a cue card on the rotating arena wall. In spite of the conflict between remote landmark-based orientation and arena-based orientation this cell had a robust, though displaced FF.

Although we do not yet know how many PCs display such allocentric and egocentric stability, it seems that most PCs are smeared in both reference projections when the arena is rotated in light. The egocentric PC input which can reliably support FF stability in darkness (Fig. 5*C2*) is usually not strong enough to overcome the destabilizing influence of the moving surroundings in light. On the other hand, slow rotation of the arena in darkness does not deteriorate the egocentric projection which does not differ from that observed on the stationary arena (compare Fig. 5 *C1*, *C2*, and *C4*).

A modification of the rotating arena induces a stronger conflict of the allocentric and egocentric appreciation of space. In this case rotation of the arena is not continuous but is switched on and off to bring the freely moving rat into a selected region of the allocentrically defined space (58). To simplify the situation, pellet chasing is recorded in the circular alley (1 m diameter, 25 cm wide) created by putting a cone in the center of a circular arena. After a FF is characterized for a PC, a 30° sector comprising this field is defined, and whenever the rat moves out of this sector the arena is made to rotate so as to return the rat to the sector. All attempts by the rat to leave this allocentrically defined floor segment are frustrated by this "field clamp" which practically locks the animal in a definite position in the room while allowing it to explore the whole surface of the circular alley. Typical examples of PC activity recorded before, during and after application of the field clamp are shown in Fig. 6. In the stable condition this cell had its primary FF at 205° (Fig. 6*A*, Coh = 2.42, Con = 0.46, Disp = 0.18) and a secondary field at 94°

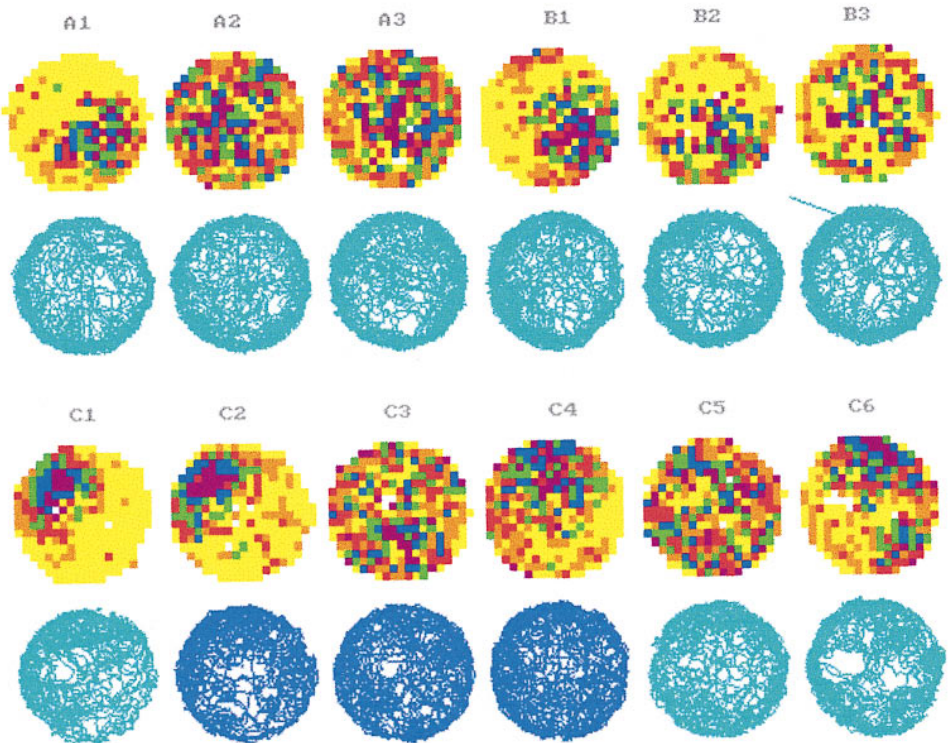

FIG. 5. Firing rate maps of hippocampal PCs in a small (1 m in diameter) stationary arena and steadily rotating (one revolution per min) arena recorded in the room reference and arena reference projections. Other description as in Fig. 2 and 3. (*A*) A FF in the southeast quadrant of the stationary arena (*A1*) disappears during rotation both in the room reference (*A2*) and arena reference (*A3*) projections, while the firing rate of the PC increase 4 times. (*B*) Another FF in the southeast quadrant of the stationary arena (*B1*) is partly preserved during rotation of the arena in the room reference (*B2*) but not in the arena reference (*B3*) projections. (*C*) Another FF in the northwest quadrant of the stationary arena (*C1*) remains preserved in darkness (*C2*). During rotation in darkness the FF disappears in the room frame (*C3*) but not in the arena frame (*C4*). Similar effect of rotation was also observed in light provided that a cue card was placed on the arena wall: the FF disappeared in the room frame (*C5*) but was preserved in the arena frame (*C6*) albeit slightly shifted clockwise. The median firing rates for the color coded pixels are 0.0, 0.5, 1.1, 2.0, 2.9, and 4.0 for *A1*; 0.0, 0.8, 1.7, 2.5, 3.7, and 6.0 for *A2*; 0.0, 0.9, 1,6, 2.5, 3.7, and 5.0 for *A3*; 0.0, 0.6, 1.3, 2.6, 3.9, and 6.2 for *B1*; 0.0, 0.3, 0.8, 1.7, 2.7, and 5.0 for *B2*; 0.0, 0.4, 0.8, 1.2, 2.2, and 4.3 for *B3*; 0.0, 0.5, 1.2, 2.7, 5.4, and 9.0 for *C1*; 0.0, 0.6, 1.1, 2.5, 5.2, and 8.0 for *C2*; 0.0, 0.6, 1.2, 1.9, 2.9, and 5.0 for *C3*; 0.0, 0.6, 1.2, 2.2, 3.1, and 6.0 for *C4*; 0.0, 0.9, 1.8, 2.5, 3.5, and 5.0 for *C5*; 0.0, 0.7, 1.7, 2.9, 4.1, and 5.9 for *C6*. (For quantitative evaluations, see the text.)

(Con = 0.14). During the 30° clamp centered at 220°, the cell continued to fire (Fig. 6*B*). However, because the rat was prevented from leaving the clamp area, it is not clear whether this is location-specific discharge. After the clamp was switched off location-specific activity reappeared at 52°, a position almost opposite to the original FF (Fig. 6*C*, D = 0.8, Coh = 2.70, Con = 0.29, Disp = 0.17). One hour later the activity resembled the standard two field pattern (Fig. 6*D*, for the main field D = 0.09, angular displacement = 10°, Coh = 1.65, Con = 0.57, Disp = 0.18).

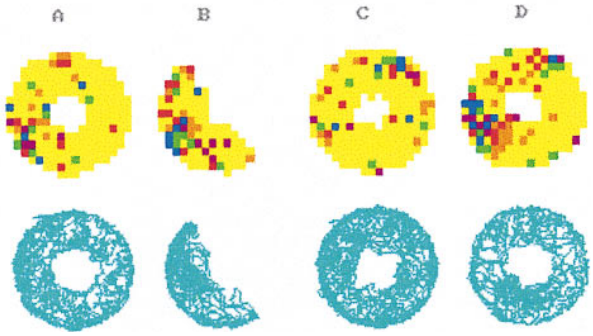

FIG. 6. Firing rate maps of a hippocampal PC recorded during pellet chasing in the ring-shaped arena before (*A*), during (*B*), immediately after (*C*) and 1 h after (*D*) exposure to the field clamp situation. In *B* rotation of the arena always returns the rat to a 30° segment between 150° and 180°. Other description as in Fig. 2. The median firing rates for the color coded pixels are 0.0, 0.2, 0.4, 0.5, 0.8, and 1.5 for *A*; 0.0, 0.2, 0.3, 0.6, 1.1, and 1.4 for *B*; 0.0, 0.2, 0.3, 0.4, 0.8, and 1.2 for *C*; 0.0, 0.2, 0.6, 1.2, 1.7, and 3.0 for *D*. (For quantitative evaluations, see the text.)

Out of 100 PCs examined with the field clamp technique only 15 continued to fire during the clamp, and after its termination, had fields in the pre-clamp location (D < 5%). Thus, in most cases, locking the rat inside or outside a place cell's FF for 5 min caused a change of the spatial firing rate pattern that could be detected when the PC activity was recorded again in the stationary alley. Some of the changes were only transient, and the original firing pattern was restored in the stationary arena after 1–24 h. Taken together, the results suggest that the clamp procedure is clearly disturbing to the PC population and that only a small percentage of PCs have an exclusively allocentric determination.

Necessity to Simultaneously Study PCs and Place Navigation

We have argued thus far, from data obtained in separate electrophysiological and behavioral studies, that the behavior of PCs can be dissociated from the cognitive spatial behavior of rats. There is, however, an inherent difficulty in applying this correlative approach to PCs and spatial cognition. As part of the rat's cognitive system PCs are strongly influenced by what an individual animal is doing and what it is asked to do. Several recent papers (59–62) show that the response properties of PCs depend on the experience of individual rats, the task they are doing, and what can only be called their perception.

The recognition that PCs respond not merely to the external world but to an individual animal's current "opinion" of the spatial environment leads to a major point of this paper and the current focus of our work with PCs. Like O'Keefe and Speakman (59), we are trying to learn how hippocampal PCs participate in spatial cognition by recording in conditions where both the cellular spatial firing patterns and the rat's spatial knowledge can be simultaneously assessed. The final section will describe some of the techniques we are developing to study the relationship of PCs and spatial cognition. In addition to novel experiments, these tasks should allow us to determine if various pharmacological and environmental manipulations known to affect PCs will cause parallel effects on spatial behavior and *vice versa*.

Place Avoidance and Place Preference Tasks for PC Studies

A place avoidance task has been developed where the rat forages for randomly dispensed food on a circular metal platform (85 cm diameter). The idea is to get a rat to distribute its behavior over the surface of the platform, thus permitting PCs to be characterized, and at the same time be able to assess the rat's ability to avoid a specific region. The computer tracking system delivers a mild footshock (<0.6 mA) whenever the rat enters the region to be avoided. The shock is delivered to the feet across the platform ground relative to a low impedance silver wire implanted under the skin at the back of the neck.

Within a single session rats learn to avoid the dangerous region and under extinction conditions this place avoidance will persist for >30 min. When the platform is made to rotate, the region to be avoided can be defined either allocentrically or egocentrically. This makes it possible to study the performance of the rat's path integration system in the dark.

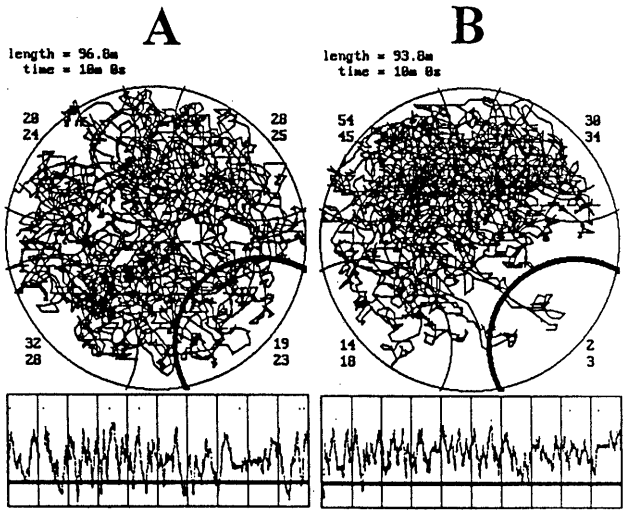

FIG. 7. Tracking of a rat searching pellets on a slowly moving (one revolution per 30 s) circular arena (1 m diameter) before (*A*) and during (*B*) acquisition of the place avoidance induced by electric foot shocks applied whenever the animal enters a southeast region of the floor (marked by the heavy semicircular line). Length, total length of the track; time, total recording time. The numbers in the corners indicate the percentage of track length and track time corresponding to four equal semicircular regions in northeast, southeast, southwest, and northwest. The lower curves show the rat's distance from the center of the shock region during the 10-min recording, with the critical radius indicated by the heavy horizontal line. The vertical lines indicate 1-min intervals. Note that all regions were equally visited before electrical stimulation in *A* and that the shock region was avoided after the two shocks received in the first and second minute of exploration in *B*.

During the rotation in light (30 s/revolution) a rat quickly learned to avoid the semicircle at the southeast where the shock was given. Fig. 7 shows the rat's track for 10 min before and 10 min after the first shock was administered. Although the rotation put path integration-supported egocentric guidance into conflict with allocentric navigation, the rat readily learned the allocentric solution. This behavioral observation also contrasts with the disturbances in PC discharge caused by rotation (Fig. 5*A*). PC recording in the stable and rotating conditions during allocentric and egocentric place avoidance will show, first, if location-specificity is disrupted and if not, second, whether the FFs are defined in the same reference frame as the behavior (63) and third, whether a virtual barrier separating the safe area from the avoided region has the same suppressing effect on PC discharge as real barriers (53).

A disadvantage of the place avoidance task is that it is based on a conflict between appetitively and aversively motivated behaviors and that the rat does not enter a part of the arena. These drawbacks are removed in the place preference task. Rats are trained to wait for 1 s at a particular location to trigger delivery of food into the recording chamber. Because the food falls to a random location, to get the food the rat must leave the start position and search the apparatus. Then, to release another pellet the animal must return to the start and wait again. This appetitively motivated task provides good coverage of the entire arena by random pellet chasing and generates at the same time a multitude of goal-directed paths allowing assessment of PC participation in planning of target-directed locomotion.

Conclusion

Over the years our group has focused on the development of experimental tools rather than on formulation of theoretical concepts. In spite of the spectacular progress of research into the neural mechanisms of spatial memory, many assumptions are mutually irreconcilable. Spotting the conflicting claims and finding tests that might resolve the controversies remains a challenging task for science. We hope that some approaches described in the present study may improve our understanding of the hippocampal system and of the role played by its PCs in spatial cognition.

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1. Leao, A. A. P. (1944) *J. Neurophysiol.* **7,** 359–390.
2. Buresova, O. (1956) *Physiol. Bohemoslov.* **5,** 350–358.
3. Bures, J., Buresova, O. & Krivanek, J. (1974) *The Mechanism and Applications of Leao's Spreading Depression of EEG Activity* (Academic, New York).
4. Bures, J., Buresova, O. & Huston, J. P. (1976) *Techniques and Basic Experiments for the Study of Brain and Behavior* (Elsevier, Amsterdam).
5. Bures, J., Buresova, O. & Krivanek, J. (1988) *Brain and Behavior: Paradigms for Research in Neural Mechanisms* (Wiley, Chichester, U.K.).
6. Dolbakyan, E., Hernandez-Mesa, N. & Bures, J. (1977) *Neuroscience* **2,** 73–80.
7. Aleksanyan, Z. A., Buresova, O. & Bures, J. (1976) *Physiol. Behav.* **17,** 173–179.
8. Buresova, O. (1980) *Acta Neurobiol. Exp.* **40,** 51–66.
9. Olton, D. S. & Samuelson, R. J. (1976) *J. Exp. Psychol. Anim. Behav. Processes* **2,** 97–116.
10. Morris, R. G. M. (1981) *Learn. Motiv.* **12,** 239–261.
11. Squire, L. R. (1987) *Memory and Brain* (Oxford Univ. Press, Oxford).

12. Brandeis, R., Brandys, Y. & Yehuda, S. (1989) *Int. J. Neurosci.* **48,** 29–69.
13. Bures, J. & Buresova, O. (1990) in *Machinery of Mind*, ed. John, E. R. (Birkhauser, Boston), pp. 291–310.
14. Buresova, O., Krekule, I., Zahalka, A. & Bures, J. (1985) *J. Neurosci. Methods* **15,** 63–72.
15. Morris, R. G. M. (1984) *J. Neurosci. Methods* **14,** 47–60.
16. Spooner, R. J. W., Thompson, A., Hall, J., Morris, R. G. M. & Salter, S. H. (1994) *Learn. Mem.* **1,** 203–211.
17. Buresova, O., Homuta, L., Krekule, I. & Bures, J. (1988) *Behav. Neural. Biol.* **49,** 240–248.
18. O'Keefe, J. & Nadel, L. (1978) *The Hippocampus as a Cognitive Map* (Oxford Univ. Press, Oxford).
19. Gallistel, C. R. (1990) *The Organization of Learning* (MIT Press, Cambridge, MA).
20. Tolman, E. C. (1948) *Psychol. Rev.* **55,** 189–208.
21. Alyan, S. & Jander, R. (1994) *Anim. Behav.* **48,** 285–298.
22. Jarrard, R. D. (1993) *Behav. Neural Biol.* **60,** 9–26.
23. Morris, R. G. M., Garrud, P., Rawlins, J. N. P. & O'Keefe, J. (1982) *Nature (London)* **297,** 681–683.
24. Fenton, A. A. & Bures, J. (1993) *Behav. Neurosci.* **107,** 552–563.
25. Whishaw, I. Q., Cassel, J.-C. & Jarrard, L. E. (1995) *J. Neurosci.* **15,** 5779–5788.
26. Kelsey, J. E. & Vargas, H. (1988) *Behav. Neurosci.* **102,** 289–293.
27. Schenk, F. & Morris, R. G. M. (1985) *Exp. Brain Res.* **58,** 11–28.
28. Moser, M.-B., Moser, E. I., Forrest, E. & Andersen, P. (1995) *Proc. Natl. Acad. Sci. USA* **92,** 9697–9701.
29. Kolb, B., Sutherland, R. J. & Whishaw, I. Q. (1983) *J. Comp. Physiol. Psychol.* **97,** 13–27.
30. Mizumori, S. J. Y., Miya, D. Y. & Ward, K. E. (1994) *Brain Res.* **644,** 168–174.
31. Whishaw, I. Q., Mittleman, G., Bunch, S. T. & Dunnett, S. B. (1987) *Behav. Brain Res.* **24,** 125–138.
32. O'Keefe, J. & Dostrovsky, J. (1971) *Brain Res.* **34,** 171–175.
33. Ranck, J. B., Jr. (1973) *Exp. Neurol.* **41,** 461–531.
34. Fox, S. E. & Ranck, J. B., Jr. (1975) *Exp. Neurol.* **49,** 299–313.
35. O'Keefe, J. & Conway, D. H. (1978) *Exp. Brain Res.* **31,** 573–590.
36. Kubie, J. L., Muller, R. U., Hawley, E. S. & Jia, C. P. (1992) *Soc. Neurosci. Abstr.* **18,** 1062.
37. Markus, E. J., Barnes, C. A., McNaughton, B. L., Gladden, V. L. & Skaggs, W. E. (1994) *Hippocampus* **4,** 410–421.
38. Knierim, J. J., Kudrimoti, H. S. & McNaughton, B. L. (1995) *J. Neurosci.* **15,** 1648–1659.
39. Quirk, G. J., Muller, R. U. & Kubie, J. L. (1990) *J. Neurosci.* **10,** 2008–2017.
40. Miniaci, M. C., Moghaddam, M. & Bures, J. (1996) *Soc. Neurosci. Abstr.* **22,** 914.
41. Muller, R. U., Stead, M. & Pach, J. (1996) *J. Gen. Physiol.* **107,** 663–694.
42. Muller R. U., Kubie J. L. & Ranck J. B., Jr (1987) *J. Neurosci.* **7,** 1935–1950.
43. Muller R. U. & Kubie J. L. (1989) *J. Neurosci.* **9,** 4101–4110.
44. Sutherland, R. J. & Dyck, R. H. (1984) *Can. J. Psychol.* **38,** 322–347.
45. Moghaddam, M. & Bures, J. (1996) *Behav. Brain Res.* **78,** 121–129.
46. Save, E. & Moghaddam, M. (1996) *Behav. Neurosci.* **110,** 74–85.
47. O'Keefe, J. (1976) *Exp. Neurol.* **51,** 78–109.
48. Hill, A. J. & Best, P. J. (1981) *Exp. Neurol.* **74,** 204–217.
49. McNaughton, B. L., Leonard, B. & Chen, L. (1989) *Psychobiology* **17,** 230–235.
50. Markus, E. J., Qin, Y.-L., Leonard, B., Skaggs, W. E., McNaughton, B. L. & Barnes, C. (1995) *J. Neurosci.* **15,** 7079–7094.
51. Arolfo, M. P., Nerad, L., Schenk, F. & Bures, J. (1994) *Behav. Neurosci.* **108,** 308–316.
52. Rashidy-Pour, A., Zinyuk, L., Kaminsky, Yu. & Bures, J. (1995) *Eur. J. Neurosci.* **S8,** 185 (abstr.).
53. Muller R. U. & Kubie J. L. (1987) *J. Neurosci.* **7,** 1951–1968.
54. Buresova, O., Bolhuis, J. J. & Bures, J. (1986) *Behav. Neurosci.* **100,** 476–482.
55. Mizumori, S. J. Y., McNaughton, B. L., Barnes, C. A. & Fox, K. B. (1989) *J. Neurosci.* **9,** 3915–3928.
56. Brazhnik, E., Muller, R. U. & Fox, S. E. (1995) *Soc. Neurosci. Abstr.* **21,** 1439.
57. Moghaddam, M. & Bures, J. (1994) *Soc. Neurosci. Abstr.* **20,** 804.
58. Zinyuk, L., Kaminsky, Yu., Kubik, S. & Bures, J. (1996) *Eur. J. Neurosci.* **S9,** 140 (abstr.).
59. O'Keefe, J. & Speakman, A. (1987) *Exp. Brain Res.* **68,** 1–27.
60. Sharp, P. E., Muller, R. U. & Kubie, J. L. (1990) *J. Neurosci.* **10,** 3093–3105.
61. Taube, J. (1995) *J. Neurosci.* **15,** 70–86.
62. Rotenberg, A., Kubie, J. L. & Muller, R. U. (1993) *Soc. Neurosci. Abstr.* **19,** 357.
63. Gothard, K. M., Skaggs, W. E., Moore, K. M. & McNaughton, B. L. (1996) *J. Neurosci.* **16,** 823–835.