



ELSEVIER

Available online at www.sciencedirect.com

SCIENCE @ DIRECT®

Neuroscience and Biobehavioral Reviews 28 (2004) 201–218

NEUROSCIENCE AND
BIOBEHAVIORAL
REVIEWS

www.elsevier.com/locate/neubiorev

A proposed architecture for the neural representation of spatial context

Kathryn J. Jeffery*, Michael I. Anderson, Robin Hayman, Subhojit Chakraborty

Department of Psychology, University College London, 26 Bedford Way, London WC1H 0AP, UK

Received 27 October 2003; revised 9 December 2003; accepted 15 December 2003

Abstract

The role of context in guiding animal behavior has attracted increasing attention in recent years, but little is known about what constitutes a context, nor how and where in the brain it is represented. Contextual stimuli can take many forms, but of particular importance are those that collectively define a particular place or situation. The representation of place has been linked to the hippocampus, because its principal neurons ('place cells') are spatially responsive; behavioral experiments also implicate this structure in the processing of contextual stimuli. Together, these findings suggest a hippocampal role in representing 'spatial context'. The present article outlines a proposed architecture for the encoding of spatial context in which spatial inputs to place cells are modulated (or 'gated') by non-spatial stimuli. We discuss recent experimental evidence that spatial context is population-coded, a property which could allow both discrimination between overlapping contexts and generalization across them, and thus provide a foundation for animals' capacity for flexible context-linked place learning. © 2003 Elsevier Ltd. All rights reserved.

Keywords: Context; Learning and memory; Spatial learning; Configural learning; Hippocampus; Place cells

1. Introduction

Since the goal of behavioral neuroscience is to understand how high-level processes like learning map to low-level processes like single neuron activity, and vice versa, studies of behavior and studies of physiology have many insights to offer each other. The present article explores recent findings regarding the processing of context, with a particular focus on physiological observations suggesting a site and possible mechanism for a particular kind of context representation, the representation of 'spatial context'.

The study of the role of context in animal learning began with Pavlov [1], who noted that during conditioning tasks, anticipatory conditioned responses could be triggered not only by discrete 'phasic' stimuli, such as the auditory stimuli used in his salivation experiments, but also with the background 'tonic' cues that constitute the laboratory environment. Thus, he found that shifting the animal to another room would cause a decrease in performance of a learned behavior, while Skinner [2] noted that instrumental behavior could be controlled not only by the discrete 'conditioned' stimuli, but also to the background. A great

deal of evidence now exists to show that contextual stimuli play an important role in animal learning, both by modulating other processes and by being learned about in their own right. The involvement of contextual stimuli in learning means that a complete understanding of learning will require an understanding of how contextual cues are processed, and how they interact with other conditioned stimuli. In this light, studies of the behavioral phenomenology of context processing interlink with studies of the neural architecture of the context representation(s).

Behavioral studies have been important and have shown, as we discuss below, that contextual stimuli have properties that distinguish them from ordinary conditioned stimuli. Studies of the neural representation of context yield insights into the 'microstructure' of the representation, and the principles by which it is modified and by which it interacts with other representations, and such studies can in turn shape the kinds of behavioral experiments that follow. This bootstrapping interplay between physiological and behavioral studies can thus allow a mapping to be found between physiological and behavioral processes.

Nadel and Willner [3] suggested that the representation of a particular kind of context, spatial context, may form an integral part of the representation of place. Context may thus be part of the so-called 'cognitive mapping system',

* Corresponding author. Tel.: +44-20-7679-5308; fax: +44-20-7436-4276.

E-mail address: k.jeffery@ucl.ac.uk (K.J. Jeffery).

thought to reside in the hippocampus and associated structures, and held by many to be responsible for instantiating an animal's knowledge about where it is. Their suggestion found support in observations that the neural representation of place, which we explore in Section 2, could be altered by manipulation of stimuli that do not carry explicitly spatial information (such as, for example, the color or odor of the environment). Thus, they suggested that the 'cognitive map' represents not space alone, but spatial context. In the present article, we outline some physiological experiments in which we recorded neurons in the hippocampus as they responded to manipulations of spatial and contextual stimuli. In doing so, we have explored how the spatial and contextual parts of Nadel and Willner's 'spatial context' interact. On the basis of our findings, described below, we suggest that this context representation occurs via a three-layer architecture in which elemental contextual cues modulate, in groups, the spatial inputs onto hippocampal cells, a finding that has analogies with behavioral studies suggesting that contextual stimuli modulate discrete stimuli.

Before turning to the physiological studies, we will briefly review some of the relevant behavioral studies of context. This is by no means a complete review of the literature, which is outside the scope of this article, but is intended to point to relevant behavioral findings that speak to the issue of how contextual stimuli interact with other kinds of stimuli.

2. Context and learning

Formal study of the role played by context in animal learning began with the finding by Rescorla [4] that despite repeated pairings of a conditioned stimulus (CS) with an unconditioned stimulus (US), learning failed to occur if the US also occurred with the same probability in the absence of the CS as in its presence. Rescorla explained these results by proposing that conditioning also occurs between the US and the background cues [5], or 'context' of the experiment, and that this conditioning attenuated conditioning to the CS. By this view, context is treated as if it is, itself, a kind of CS, with contextual and discrete stimuli thus being functionally equivalent. Even when the outcome of a task does not depend on successful processing of contextual cues (*contingent* context learning), it can be shown that animals do learn about these cues when undergoing conditioning, because a change in context reduces both conditioned responding to a CS and latent inhibition [6,7]. This *incidental* context learning is a form of latent learning.

Alternatively, it has been suggested that rather than having a functional equivalence with conditioned stimuli, contextual cues instead exist in a hierarchical relationship with them (see Ref. [8] for review). In various associative learning studies, contextual stimuli have been found to act more like 'occasion setters', which are stimuli that modulate other associations rather than directly entering into such

associations themselves. By this view, contextual stimuli serve to 'gate' the relationship between a CS and US. Evidence for this gating derives from the fact that the contextual (or occasion setting) stimuli can influence the associative status of a single CS with a US. Because the CS–US association can be altered depending on which contextual stimuli are present, there must be some influence of the context prior to the CS–US connection, either via its association with the CS (configural association, see below) or via the CS–US link. Later, we will use the same reasoning to argue that the representation of spatial context itself is also hierarchical, with some kinds of cues able to modulate others.

That contextual stimuli are functionally different from other kinds of stimuli implies that they may be processed differently in the brain, and thus require a specialized processing apparatus. This raises the interesting question of where in the brain such an apparatus might exist, and how its representation of context is constructed. Below, we examine the idea put forward by Nadel and colleagues [3,9] that context is represented by the same structure that represents space—the hippocampus—before turning to the question of how such a representation might be assembled from the incoming information stream.

3. The nature of 'contextual' stimuli

Nadel and Willner, in their elegant review of the context-learning field, first proposed a formal homology between the representation of context and the representation of place [3]. They drew attention to the so-called 'cognitive mapping system', a set of brain structures including the hippocampus which collectively have been proposed as the site of a neural representation of place [10]. Their analysis was motivated by the paradox surrounding whether, in a given situation, context cues are part of the foreground, requiring the animal's attention in order to solve a problem, or part of the background, and presumably unattended to. The difficulty with this taxonomy of stimuli is, as Nadel and Willner pointed out, that a given stimulus can be both part of the foreground and part of the context, depending on the perspective of the observer or the intentions or expectations of the animal. Foreground and background stimuli do not therefore exist in a simple mutually exclusive relationship to each other, but rather in a more hierarchical relationship in which the context 'surrounds' or 'contains' the discrete (to-be-conditioned-to) stimuli. This compound representation of context was considered by Nadel and Willner to be a function of the same system that represents 'place', and to be thus dependent on the same brain circuitry: namely, the hippocampus and associated structures.

While traditional learning theorists have assumed that the processes of learning are universal and operate on all types of information, a more recent perspective suggests that different kinds of information may be processed differently in the brain. The latter view will be adopted

here, and we will not therefore assume that all kinds of contextual stimuli are represented and processed in the same way. Instead, we will restrict our discussion to that subclass of contextual cues highlighted by Nadel and Willner as particularly important: namely, those that serve to define an environment, which collectively therefore define the ‘spatial context’. Other kinds of contextual cues, such as the background stimuli in a visual discrimination experiment, will not be considered, though some of the principles discussed here may be relevant to other domains too.

Before proceeding to an analysis of spatial context and how it might be represented, it is necessary to be clear about terminology. The terms ‘space’ and ‘spatial’ are open to confusion because they sometimes refer solely to the geometric layout of the environment, but are sometimes additionally taken to include non-geometric aspects of the environment such as its color, texture, the objects in it and so on. To avoid this confusion we will use ‘geometry’ to refer to the shape of the environment as defined by its boundaries. In contrast, non-geometric cues such as color and odor will function to impart a unique character to a particular geometric layout. The separation between geometric and non-geometric cues is not complete, however, because as we shall discuss later, some kinds of environmental features might impart both geometric and non-geometric information about an environment (an example might be the corners of a square enclosure, which provide a visual discontinuity as well as defining a space). The terms ‘space’ and ‘place’ will be used (more or less interchangeably) to mean a geometric area populated, and hence uniquely characterized, by non-geometric but physical stimuli.

As well as geometric stimuli, space can be characterized by non-geometric features such as the color and odor of the environment. In addition to such ‘featural’ information, environments can also be characterized by more intangible aspects such as what the animal is expecting to happen to it or what it plans to do. It may be, as we see below, that featural and internal cues interact in a similar way with the geometric aspects of the environment. It is for this reason, and based on recent physiological findings [11,12] to be discussed below, that we have chosen to extend the above taxonomy to include Nadel and Willner’s overarching term ‘spatial context’, which not only includes spatial and featural stimuli, but also includes non-physical aspects of the environment such as the intentions or expectations of the animal. These stimuli thus collectively define something more akin to a ‘situation’ or ‘occasion’ than simply an environment.

4. The hippocampus, space and context

Nadel and Willner’s suggestion that space and context might share a common representation in the hippocampus provided a starting point for studies of how such

a representation might be constructed. The particular role of the hippocampus and its associated structures in the processing of spatial stimuli was first highlighted by O’Keefe and colleagues, following their discovery of a class of spatially responsive neurons [13], which they labeled ‘place cells’. O’Keefe and Nadel [10] suggested on the basis of their findings that the role of the hippocampus is to construct a spatial representation, or ‘cognitive map’, which an animal can use in spatially guided behaviors such as navigation. Their proposal garnered a great deal of support from a large series of behavioral and lesion studies which confirmed that the hippocampus in many animals, ranging from birds to humans, plays a critical role in supporting spatial behavior [14]. The proposal of a specifically spatial role for the hippocampus has been the subject of considerable debate (e.g. see *Hippocampus* special issue, 9(4), 1999), which it is outside the scope of this article to review. For the present purposes, we shall acknowledge that the question of whether the hippocampus has a broader role than representation of space alone is still open to debate. However, its importance in spatial behavior is generally accepted, and the question that concerns us here is to what extent the representation of a ‘place’ incorporates more than the mere layout of an environment.

Recently, the hippocampus has been implicated in the processing not just of spatial layout alone but in spatial context. Early on, Hirsh [15] suggested that the hippocampus is involved with contextual retrieval of information, where ‘context’ was assumed to consist of cues that are associated with, but not part of, the information to be retrieved. Studies of animals with hippocampal lesions provided evidence supportive of a role in context processing. Penick and Solomon found that a change in context disrupted responding to a classically conditioned stimulus in normal rabbits but not in those with hippocampal lesions [6], while Kim and Fanselow found that electrolytic hippocampal lesions abolished recent but not more established contextual fear [16], and Phillips and Le Doux found that animals with hippocampal lesions failed to acquire a freezing response to contextual stimuli, although they conditioned normally to a single (tone) stimulus [17]. Many studies since have found supportive evidence of a role for the hippocampus in context processing (see Ref. [18], for a review).

The evidence for a hippocampal role in context learning is mixed, however, with a number of studies finding no effect of hippocampal lesions on contextual learning [19,20]. Several explanations have been offered for the disparate findings: these fall into four main categories, as follows. First, some differences in the results of lesion studies may have occurred for performance reasons: hippocampal lesions may affect the ability of an animal to express its learning rather than to actually learn per se. For example, hippocampally lesioned animals may show less of a tendency to freeze, and thus fail to show conditioned freezing in response to an aversive context [21,22]. This issue, which has been hotly debated [20,23], will not be

fully resolved until the same contextual effect has been seen with a variety of different performance measures [19].

Second, instead of entering into associative relationships directly, contextual stimuli may serve to modulate the relationships between other stimuli, thus existing in a superordinate relationship to those stimuli. For example, Winocur et al. [24] found that rats with hippocampal lesions avoided a context in which they had received electric shock, even if the shock had been signaled with a light or tone CS (something that generally attenuates contextual fear conditioning in normal animals [17]). Winocur subsequently suggested [25] that while hippocampally lesioned rats could condition to the context, they perhaps could not use contextual information to modulate the learning about CS–US relationships. Thus, while the stimuli comprising a context could be perceived and learned about, they could not enter into a modulatory relationship with other stimuli.

Third, discrepancies may have arisen in the literature because the same set of stimuli may be represented in both a hippocampal-dependent and a hippocampal-independent form. Hippocampal lesions made shortly after contextual conditioning impair retrieval of the learned fear, whereas performance is unimpaired if the lesions are made a long time afterwards [16,26], suggesting that context memory is initially stored in a hippocampal-dependent form but subsequently becomes independent of it. Contextual conditioning is also sometimes spared if the lesion is made *before* learning [27], raising the interesting possibility that animals use a hippocampally dependent context representation if they can, but some other, hippocampus-independent representation of the same stimuli if the hippocampus is damaged [20]. As we discuss later, several investigators have suggested that the hippocampal representation of these stimuli may take the form of a *configural* representation [20,28], in which the elements of the context become bound together, while outside the hippocampus the same stimuli are represented as elements, each of which can be learned about on its own.

Finally, the involvement or otherwise of the hippocampus in the processing of context may depend on whether explicit processing of the stimuli is required for the animal to solve the learning task (so-called ‘contingent processing’), or whether the contextual stimuli are irrelevant to the task at hand (‘incidental processing’). In support of this idea, Good et al. [29] have found an effect of hippocampal lesions on the incidental but not contingent processing.

Despite the above controversies, it is clear that the hippocampus is important for the processing of context, even though its exact role and the conditions for which it is essential remain to be determined. We now turn to the question of how context (or at least ‘spatial context’) might be represented, taking as our starting point the proposal by Nadel and Willner [3] that it is founded upon the representation of space.

5. Place cells

The hippocampal representation of space depends upon the place cells, a class of hippocampal neuron whose firing is tightly coupled to the location of the animal in its environment. The activity of a place cell is shown in Fig. 1. A place cell fires in a restricted region of a recording environment, the size of the region varying (in a typical laboratory) from a few centimeters to a few tens of centimeters across. The region of the environment in which it fires is called the ‘place field’, by analogy with the receptive fields of visual or other sensory cortical cells. There is, however, an important difference between visual or other primary sensory receptive fields and place fields, in that an ordinary receptive field is defined with respect to the sensory surface of the animal (the retina, in the case of vision) whereas a place field is defined with respect to the outside world. This difference captures a critical feature of the place cell representation, which is that it is *allocentric* (world-centered) rather than *egocentric* (body-centered). It was this observation that led O’Keefe and Nadel to postulate a map-like function for these cells.

The finding of spatially localized cell activity immediately suggested simple sensory correlates for the firing, such as focal odors, or other sensory features, which are uniquely

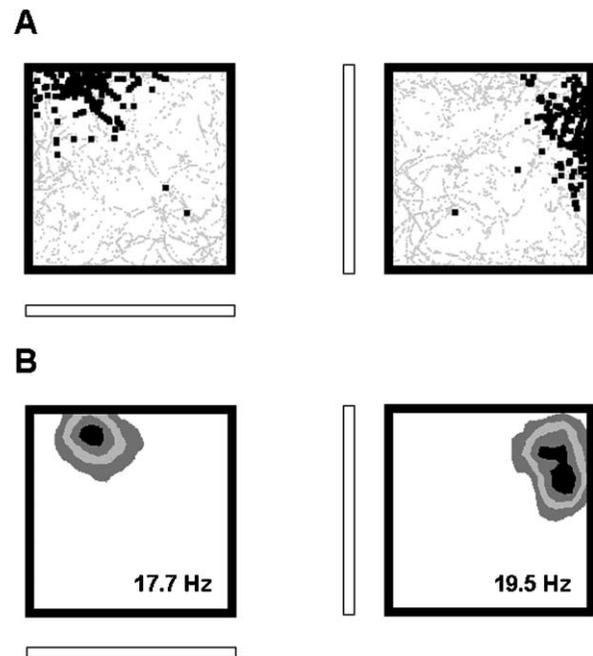


Fig. 1. The firing of a single hippocampal place cell as a rat forages for rice grains in a $60 \times 60 \text{ cm}^2$ enclosure. The enclosure was surrounded by black curtains, and a white cue card (thin rectangle) served as a polarizing cue, to disambiguate the directions. (A) The path of the rat is shown in gray, and the black squares show the action potentials fired by the cell, each one located at the place where the rat was when the cell fired. Left: when the cue card was in the South, the cell fired in the North-West corner of the box. Right: when the card was moved to the West, the cell also rotated its place field clockwise so that it now fired in the North-East. (B) The same data as in A, but shown as a firing rate contour plot, normalized to the peak firing rate and with each contour representing a step of 20% of the peak rate.

present at a given place. A number of experiments over the years, however, have shown that the stimuli that drive place cells must be more complex. For example, place cells are often unaffected by quite large sensory changes, such as turning out the lights or removing some of the objects in the environment, and yet can move their fields in response to a relatively small change like moving a cue card [30], arguing against a simple sensory basis for their activity. Similarly, place fields in an open area are omnidirectional, firing whenever the animal is in the region of the place field regardless of which way it is facing and, therefore, what stimuli are impinging on its sensory surfaces. Furthermore, stimuli that are known to collectively influence the cells can be removed without detriment to the place fields, so long as enough of the set remains to provide spatial information [31,32]. And finally, place fields in a rotationally symmetrical environment can be rotated by rotating the rat (unbeknownst to it), thus disconnecting the fields from all local sensory features [33]. Together, these experiments indicate that it is not single stimuli but rather constellations of stimuli that drive the activity of place cells. O'Keefe and Speakman [34] demonstrated this explicitly by showing that place fields rotated when a constellation of stimuli was rotated around an otherwise symmetrical recording apparatus, but persisted when some stimuli were removed provided enough remained to uniquely specify the orientation of the environment.

If place cells do not respond to simple stimuli, then what do they respond to? There are two broad schools of thought on this issue. According to one view, the constellation of cues that drive a place cell provide a unique, multimodal sensory 'snapshot', with each cell driven by its own private collection of stimuli. According to this view, inputs to the place cells are not distinguished on the basis of the type of information they convey, but all converge together on the cell and collectively drive it above its firing threshold. A snapshot-based account such as this can explain why a cell fires over an area, rather than at a single point, because it is assumed that the sensory snapshot is somewhat similar in these adjacent places (although less so as the distance increases, explaining why the firing rate falls off towards the edge of the field).

Snapshot models have some difficulty explaining the omnidirectionality of place fields, because although two snapshots should be more similar when the rat is facing the same direction in two adjacent places than when it is in the same place but facing in different directions (Fig. 2), a place cell might nevertheless fire differently in the first two conditions (if, for example, one of the places lay within a field and the adjacent place outside it) but the same way in both of the second two. This problem can be circumvented by including, among the inputs to the cell, inputs from other place cells, together with some kind of plastic process that allows the correct sets of connections to be established when the animal first enters a new environment. Thus, cells that are simultaneously activated by sets of sensory stimuli will tend to become more strongly connected, and hence able to

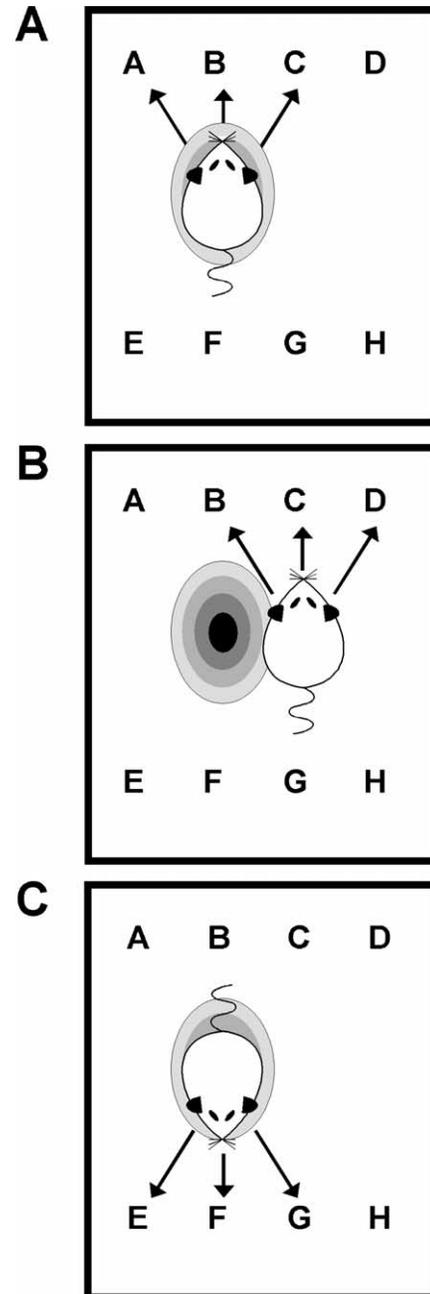


Fig. 2. A difficulty with snapshot-based models of place cell activity. The figure shows a rat in a recording apparatus in three situations. (A) The rat is located in the region of the place field (concentric circles) and facing so that it can see cues A, B and C. (B) The rat is located outside the field but facing so that it can see two of the cues (B and C) it could see from A. (C) The rat is within the place field but facing so that it sees a different set of cues (E–G). Thus, bigger differences in the cell's firing are seen for the more similar sets of cues (ABC and BCD), than for the more dissimilar sets (ABC and EFG), showing that spatial location (abstracted from the cues) is a better determinant of the cell's activity than the cues themselves.

influence each other, supporting (for example) a given place cell even when one of its sensory inputs is unavailable. Such 'attractor' models of place cell firing have been very successful in modeling much of the phenomenology of place fields [35–38], including their robustness in the face

of small changes to the environment, and the catastrophic reorganization of their activity that occurs when the change becomes sufficiently large ('remapping': see below).

The alternative view of place field generation, which is not entirely orthogonal, might be described as the 'functional differentiation' model. According to this model, sensory stimuli become highly processed on their way through the various cortical structures that precede the hippocampus proper, so that what arrives at the place cells is a more abstracted kind of information in which different kinds of stimuli play different roles. By this view, some kinds of input might provide directional information, others might convey information about the geometry of the environment, and still others might provide the non-geometric information that allow discrimination between geometrically similar spaces. To determine that place cells receive functionally differentiated inputs it would be necessary to show two things. First, either place cells or cells afferent to the hippocampus should fire in the same way in response to a particular kind of information (e.g. distance or direction) regardless of the sensory modality in which this information reached the rat. In fact, place cells do seem able to switch with ease between various sensory sources of localizing information including vision, the movements of the animal ('path integration'), touch, olfaction and so on. For example, Quirk and colleagues [39] showed that place fields that were being oriented by a visual cue nevertheless persisted when the lights were turned off, provided the rat was not removed from the environment, suggesting that the rat's tracking of its own movements could sustain the fields in the absence of vision. Similarly, blind rats have normal place fields provided they are allowed to make contact with polarizing objects (i.e. those that provide directional information) in the environment [40]. Recordings of head direction cells in structures (indirectly) afferent to the hippocampus show that they too can respond to information in different modalities [41], suggesting again that the information they represent, heading, is abstracted: i.e. mapped to a common code.

Second, if inputs to place cells are functionally differentiated then manipulation of the different functional classes of information should produce different effects on place fields. A variety of experimental findings suggest that this is true: some kinds of information produce rotation of all the place cells as an ensemble, some cause them to shift their firing fields heterogeneously by small amounts within the environment and some cause them to completely reorganize their firing patterns. These different behaviors lead us, again, to favor the functional differentiation model, and they are discussed more fully in Section 6.

6. Functional differentiation of the inputs to place cells

Hypothesizing that information arrives at place cells in abstracted and functionally differentiated forms, it becomes

of interest to ascertain exactly what forms these might be. Broadly speaking, evidence suggests that the cells receive three classes of information: geometric, directional and—we shall argue here—'contextual'. The reasons for classifying the inputs in this way are as follows.

The influence of geometry on place cells was shown most clearly by O'Keefe and Burgess [42], who recorded in a box configured as either a small or large square, or as a rectangle in one of two orthogonal orientations. They found that each place field 'followed' a subset of the box walls, acting as though its primary input came from these alone and not from other parts of the box. In general, the fields seemed most strongly influenced by the closest walls, with the result that fields close to walls were smaller with a higher peak rate, and fields closer to the center of the box were more diffuse with a lower peak rate. O'Keefe and Burgess proposed a model in which each place cell responds to the distance of the rat from a subset of walls, the exact subset varying from cell to cell, with the curious result that a change in the shape of the box could cause some fields to shift relative to others. Because of the individual variation in responsiveness to changes in the shape of the box, a complete description of this shape could only be extracted by reference to several or many place cells, suggesting a population coding of spatial layout.

Evidence for some kind of directional influence on place cells comes from various sources. The observation of eccentrically located fields in a rotationally symmetrical environment immediately suggests some kind of symmetry-breaking influence—a directional signal—on the cells. Rotation of a rat's 'sense of direction' can cause place fields to rotate in a symmetrical environment [33,43], indicating that the polarizing influence does not necessarily emanate from external sensory cues. In fact, a wealth of evidence now suggests that internal, movement-related (also called 'idiothetic') information can control the orientation of place fields [44–46]. A likely source of such information is the head direction cells mentioned earlier, which are responsive to head direction and project indirectly to the hippocampus.

The final influence on place cells is heterogeneous, and harder to characterize. It was discovered early on in the history of place cell research that placing a rat in a novel environment causes place fields to switch off or on [30], a process that was termed 'remapping' to reflect the assumption that the cells are collectively generating a new map of space. Further research found that remapping can also be elicited when the geometric properties of the environment are kept constant and only non-geometric qualities such as odor and color are changed [47,48]. More recently, it has been found that even non-physical characteristics of the environment such as factors internal to the rat—intentions, expectations and so forth—can cause remapping [11,12,49]. The kind of remapping seen following these manipulations is different from that seen following geometric or directional changes. When the geometry of

the environment is changed, place fields stretch or split (although there have been exceptions to this observation—see Refs. [50–52]—which we discuss below). When directional cues are changed then the place cells respond by rotating their fields in unison, so that the representation as a whole rotates but otherwise remains intact. The third kind of remapping is more complex than either geometric or rotational remapping: some cells switch their fields off, others switch them on and still others switch off one field and switch on another, in a different place. In cases where the environmental manipulations are quite subtle, only a subset of cells change their firing patterns (*partial remapping*). In the most extreme cases the whole spatial representation undergoes a catastrophic reorganization, which has been termed *complete remapping*. Partial and complete remapping result in a scrambling of the spatial representation, and this class of remapping has been termed *complex* [30], to distinguish it from the simpler kinds of remapping that follow geometric and directional manipulations. The non-geometric cues that can trigger this kind of remapping are varied, but many, such as the color and odor of the environment, are of the kind that have been manipulated in traditional behavioral studies of contextual conditioning. For simplicity, therefore, we refer to these cues as *contextual*. The interaction of contextual stimuli with place cells arguably provides a substrate for the neural representation of spatial context.

Before proceeding to a discussion of how contextual stimuli might modulate place cell firing, it is worth briefly discussing what kinds of cues can act in a contextual role. Obvious categories of contextual information are those that carry no spatial information at all, including color, odor, the internal state of the rat and so on. (It remains to be determined whether cues such as the weather, time of day and the animal's motivational state can also act as contextual modulators of place cells). We suggest, however, that other kinds of cues, which themselves also carry spatial information, might also act in a contextual manner. An example is the remapping to shape seen by Muller and Kubie [30], Wilson and McNaughton [51] and Lever et al. [52]. In all three studies, a change in the shape of the environment resulted in the kind of remapping that we have called *complex*—in other words, place cells switched their fields on and off. This behavior contrasts with the shifting, stretching and splitting of fields seen by O'Keefe and Burgess [42], and is hard to explain using their framework of a geometric influence of the environmental walls on place fields. However, complex remapping to shape could be accommodated if it is assumed that the shape change produced not only a change in the geometric influence of the walls on the fields, but also in the contextual modulators of these geometric inputs. In other words, perhaps the shape of the environment can itself act as a context cue. By this view, small shape changes would produce small shifts of the fields (as predicted by the two-dimensional gaussian model of O'Keefe and Burgess), but larger shape changes, particularly

if these also involved a change in the material and hence odor of the walls (as in the Muller and Kubie or Wilson and McNaughton studies), or the introduction of corners and other features where there were none previously, would also affect the contextual inputs, and cause a change in which fields were expressed by the cells.

If shape can act as a context cue then the possibility arises that the output of the hippocampus might act as one of its inputs—in other words, the processing of shape information that is (we assume) undertaken by the place cells might feed back, via the subicular/entorhinal pathway, onto the place cells themselves. It follows that lesions to the subiculum might affect the remapping of place cells to shape, while sparing other kinds of contextual remapping. A difficulty with this proposal is that recordings of subicular cells have found that they are in fact unresponsive to shape [53], raising the question of what happens to the shape information apparently encoded by the hippocampal place cells. This reflects a general puzzle regarding subicular encoding. Nevertheless, it is reasonable to assume that information represented by the hippocampus is somehow passed on to structures downstream.

Keeping in mind the theoretical suggestions discussed earlier that the hippocampus might represent spatial context (rather than simply 'space'), it becomes of interest to examine how place cells respond to manipulation of contextual stimuli, as a way of trying to determine whether they are themselves equipped to represent 'context' in any meaningful way. The remainder of this article is therefore devoted to an analysis of how contextual stimuli interact with other kinds of stimuli, drawing parallels wherever possible between the behavioral and physiological literature. As we shall see, behavioral studies have led to inferences regarding the nature of contextual modulation of behavior that closely resemble the conclusions that we have independently drawn regarding contextual modulation of place cell activity.

7. The superordinate nature of contextual stimuli

It was mentioned earlier that contextual stimuli often seem to exist in a hierarchical relationship with other conditioned stimuli, by virtue of the fact that manipulation of context can be used to switch a CS–US relationship between positive and negative. Such *bi-conditional* problems cannot be solved if the context has a separate relationship with the US, but requires that the context interact with the CSs prior to the CS–US link. These kinds of problem are known in neural network circles as 'linearly inseparable' (for reasons to do with the algebraic geometry of the problem), and require the addition of a so-called *hidden layer* of neurons, interposed between the input (stimulus) and output (response) neurons, to allow the relevant interactions to take place prior to the response elements.

Turning to the contextual modulation of place cell activity, an interesting parallel arises with the behavioral studies. Although context changes often cause place cells to switch on or off, a considerable proportion of cells shift their fields from one part of the environment to another, thus firing, for example, in place A in context *a* and place B in context *b*. Therefore, the context is able to switch the response of the place cell to the incoming stimuli between sets of stimuli, just as it can switch a CS–US relationship in a Pavlovian conditioning experiment. Again, such behavior cannot be explained by a simple connection between the context and the place cell, because in order to decide which set of spatial inputs to respond to (A or B), a place cell would need information about which context inputs (*a* or *b*) were also active. As with the learning studies discussed above, these inputs must somehow be paired before they reach the cell.

How might such pairing occur? There are two possibilities. One is that the spatial inputs to a place cell become welded to the corresponding non-spatial inputs so that the stimuli cannot be broken apart. For example, if a place cell fires in a particular place in a black box, this is perhaps because the spatial determinants of the field, the walls, are bound to the non-spatial (contextual) determinants so that the cell will only ever fire if the rat is located at the correct distance from black walls. An alternative possibility is that the spatial and contextual determinants of place fields are more loosely associated so that the cell receives spatial information (from the walls) that is paired with the contextual information, but not indissolubly so. By this view, the blackness of the box and the physical location of the wall may exert independent influences on the cells.

We have attempted to distinguish between these alternative possibilities experimentally [54]. We created contexts from 60 cm² wooden boxes with walls that were painted either black or white, with a floor composed of either black or white foamboard, so that as well as a black box or a white box, place cells could be recorded in boxes in which the wall color differed from the floor color. Place cells were recorded from the CA1 subfield as rats foraged for sweetened rice grains in these various environments. The question of interest was: would place cells always fire in the pattern dictated by the color of the walls, or not? In fact, we found that remapping of the cells was more often triggered by changes to the *floor* than the walls, and could sometimes be triggered by a small change to the floor some distance away from the field. Thus, although the cells used the boundaries of the box (determined by vision or touch) to locate their fields, the trigger to express a particular field came from a different source: in this case, the floor. Other studies have additionally found that the spatial firing of place cells can be altered by non-physical changes (e.g. to the task the rat is supposed to perform [12], or whether the rat is to turn left or right at the end of the runway it is currently on [11,49]). Thus, while spatial and contextual cues clearly interact, the fact that they can be manipulated

independently suggests that they probably are not firmly bound together. We have suggested [54] that the place cells receive context-free geometric inputs (from the walls) and that these inputs are gated by the contextual stimuli present (Fig. 3). Thus, in driving place cells, contextual stimuli modulate other inputs in the same way that they appear to modulate CS–US relationships. Again, then, contextual stimuli seem to have a different function from other kinds of stimuli.

Not only do contextual inputs apparently interact with geometric inputs upstream of the place cells, it also appears that new inputs can be added to the set of cues that collectively drive a particular cell. This conclusion derives from a recent experiment from our laboratory in which place cells were observed to acquire information in a context-dependent manner [55]. The acquisition of new information by place cells has been reported in several previous studies, and it takes the form of experience-dependent development of remapping in response to environmental manipulations. Jeffery [56] found that partial remapping could develop when place cells were recorded in geometrically identical but differently located environments (a box moved between two adjacent locations). Initially, cells expressed the same fields in both box locations, but after repeated experience in the two environments some of the cells began to remap, probably in response to information emanating from the cues outside the box. Since a given field would be expressed in both environments to begin with but only one environment after a while, the new learning must have involved both a strengthening of the inputs from outside the recording box and a reduction in the drive from the cues contained within the box itself. Because the remapping seen in this experiment was complex, involving switching on and

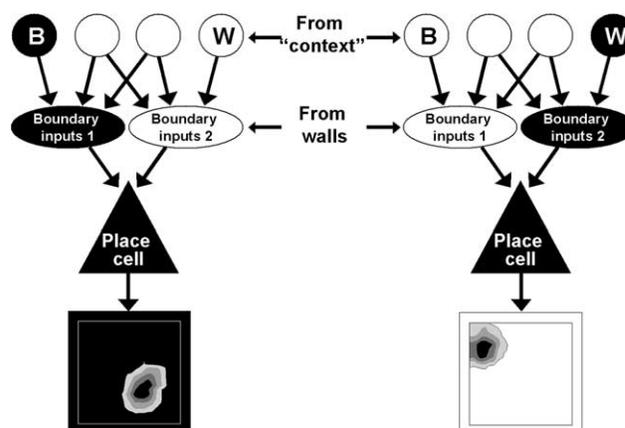


Fig. 3. A proposed model to explain contextual remapping. Elements filled in black are active. A place cell receives two sets of boundary inputs, coming from the walls of the environment and determining where a particular place field should be. Each boundary input is controlled by one or more context stimuli which, when present, activate the boundary inputs and drive the place cell. Left: in the black box, the black context inputs are active, driving boundary input set 1 and producing the field shown. Right: in the white box, the white context inputs are active and drive the cell to produce the 'white box' field. Adapted from Ref. [54].

off of fields rather than stretching or splitting, or rotation en bloc, it seems likely that the new inputs are, themselves, of a contextual type rather than a geometric or directional type.

We were interested to know whether information acquired in this way could transfer to a novel context [55]. We therefore recorded place cells and induced the above described location discrimination in one context (for example, a black box) and then recorded the cells in the same two places but in a different context (e.g. a white box). Cells acquired the location discrimination, as before, remapping between the box in one location (a northerly position in the room) and the other (a southerly position). This indicated that they had acquired information from the distal, extra-maze cues (such as, perhaps, the proximity of salient features such as the door) that enabled them to tell when the box was in one position vs. the other. The change in context also induced complete remapping of CA1 place cells, as expected. However, the information acquired by the cells in the first context did not transfer to this new context. Cells that were successfully discriminating the two adjacent locations, by switching off a field in one of them and/or switching on another field elsewhere, failed to discriminate the same locations with their new fields when the context changed (Fig. 4).

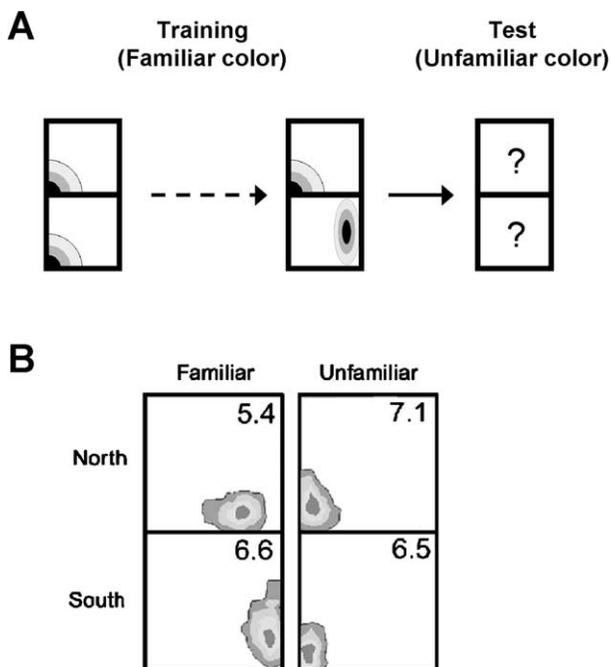


Fig. 4. (A) Schematic of the design of the experiment to test for context specificity of an acquired discrimination by place cells. The rat was exposed to two identical environments, one North and one South, and place cells were recorded until cells started to discriminate the boxes by remapping between them. The color of the box was then changed, from black to white or vice versa, and recording in the two locations continued to see whether the cells could still (with their new fields) distinguish the two locations. (B) Examples of a cell, which acquired the location discrimination in the familiar context by changing fields. The cell remapped when the context was changed but failed to express its previously learned discrimination in the new context. The contour plots show place fields in each of the boxes, and the peak firing rates (Hz) are shown. Adapted from Ref. [55].

This result is intriguing and somewhat difficult to explain. How can a place cell ‘know’ about two different box locations when it is expressing one of its fields (the black-box one, for example) but not the other? The most obvious explanation, that the rat failed to attend to the discriminative stimuli in the new context, cannot explain the results because, as discussed above, following learning the cells needed the discriminative information in order to fire at all. If the discriminative stimuli were simply not processed and passed to the place cells, the cells should fail to fire at all in the new context.

Instead, the finding that cells that had discriminated the two locations in the familiar environment failed to do so in the new environment (like the cell in Fig. 4) suggests that the interaction of the discriminative stimuli with the place cell must have taken place at the level of the inputs to the cell, rather than at the level of the cell itself. Thus, the context specificity of the cells’ location discrimination points, again, to an interaction of the incoming inputs prior to the place cell itself.

Given our assumption, outlined earlier, that the newly acquired discriminative inputs are of a contextual rather than geometric type, we have proposed [55] the following explanation for the context specificity of the acquired location discrimination (Fig. 5). We take, as an example, a place cell that remaps to location by switching off and remaps to the color change by shifting its field. We assume that the cell starts with two sets of boundary inputs, one for each field, with the context cues from the original box driving one of the boundary inputs. With experience, information from the distal cues starts to impinge on the place cell, manifest as a switching off of the field in one of the two locations. Presumably, this occurs because as new inputs develop from the distal cues (perhaps via activity-dependent Hebbian strengthening of the active inputs), the links from the original set of context cues to the boundary inputs become weaker (perhaps by some kind of normalization process that acts to keep the total synaptic drive to the cell relatively constant). Now, both sets of cues are now necessary in order to drive the boundary inputs, and hence the field. In other words, the distal cues have become part of the constellation of contextual cues that are needed to drive a particular set of boundary inputs.

Now the rat is placed in the new context. In this environment, the novel contextual stimuli activate a new set of boundary inputs, causing the cell to remap. Since this is an unfamiliar environment, activating new inputs, and no synaptic rearrangement of these inputs has yet taken place, the connections from the distal inputs onto the newly active boundary inputs are weak and the original connection, from the contextual inputs supplied by the box itself (in this case, white) are still strong. Thus, because no distal cues have yet been integrated into the constellation of contextual cues that can drive this cell (see below for a dissection of such constellations), the cell does not discriminate between locations and fires the same way in both.

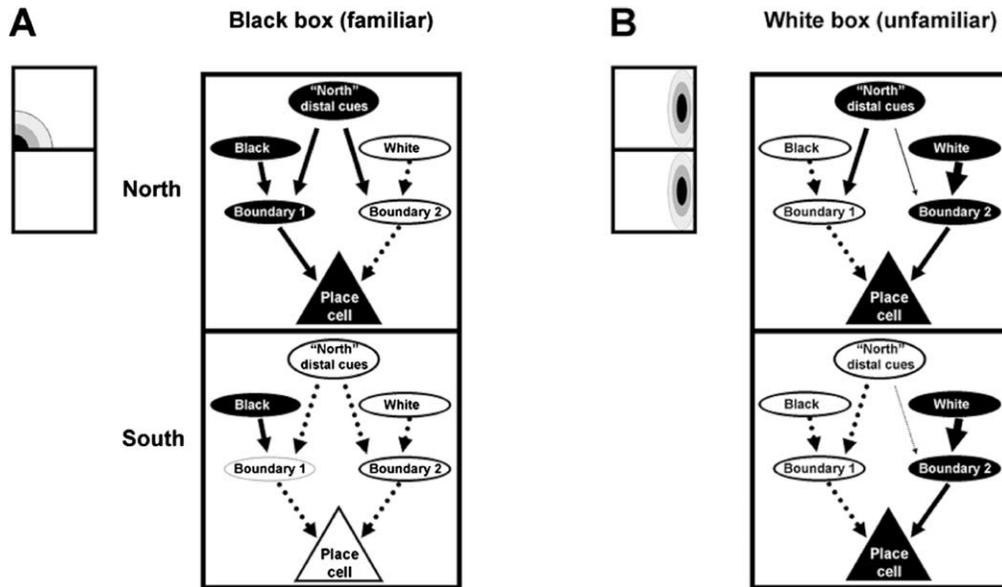


Fig. 5. Possible explanation for how repeated exposure to a recording box moved between North and South location might cause place cells to discriminate the locations in a context-dependent manner. (A) After exposure to the two environments when the box is black, the place cell becomes discriminating so that it now only fires when the box is in the North (hypothetical field as shown). It is assumed that the cell receives a number of sets of boundary inputs (in this case two sets, 'Boundary 1' and 'Boundary 2'), each set specifying a place field. One of the boundary inputs is activated by the black environment and another by the white. The cell also receives inputs from the distal, extra-maze cues, in this case from the cues present when the box is in the North that are absent when it is in the South. Because of the repeated exposure to these two environments, input strengths have rearranged so that the boundary inputs specifying that field need both the correct color (black) and the correct distal cues (North) in order to drive the cell to its firing threshold. Thus, the cell only expresses that field when the box is in the North. (B) When the box is changed in color, a new set of boundary inputs (Boundary 2) is activated by the white. Because no inputs strength changes have yet occurred in this new environment, the boundary input for that field needs only the correct color, and thus the cell will fire whether the box is in the North or the South. Adapted from Ref. [55].

The functional consequence of such context-specific input modification is that the cells are able to group their inputs so that information learned in one context is not at risk of damaging or erasing information specific to a different context. The question then arises as to what happens to information that is relevant to more than one context. We explored this issue using a different kind of place cell learning: the learning of directional landmark stability.

It was mentioned earlier that place cells use directional information to orient their fields in an environment that has rotational symmetry [33]. This directional information, which may be processed by the head direction system, is anchored to prominent distal cues in the environment but only so long as these are stable [57]. If a directional landmark is perceived by the rat as unstable, then over time, the cells will cease to use this landmark to orient their fields, and if this was the only directional cue then they will rely instead on the internal direction sense of the rat [58]. This can be tested by enclosing the rat under an opaque cover and then rotating it slowly by a certain amount, and the cue card by a different amount, and then testing the cells on the rat's release to see whether the fields are aligned with the (rotated) internal direction sense of the rat, or by the cue card.

Directional information is a class of information that one might expect to be preserved independently of context,

since the environment usually remains oriented the same way regardless of what contextual stimuli happen to be present. We explored this by inducing landmark instability learning in one context (a black box) and then testing the cells in a different context (a grey box; Chakraborty et al., in prep). After landmark instability learning has taken place, then if a conflict is now induced between the internal direction sense of the rat and the landmark, the place fields align themselves on each trial with the rat's directional sense. It is as if the cells have learned not to 'trust' the unstable landmark to be a good directional indicator, and they prefer the internal cues, even though these are normally less reliable. The question of interest is whether this learning would transfer from the context in which it was acquired to a novel context, one which induces the cells to remap their fields. We found that, unlike the extra-maze cue learning discussed above, this directional landmark learning was indeed preserved across the context change, so that even in the new context, expressing their new fields, the cells preferred the rat's internal directional cues to the landmark. This suggests that the contextual stimuli that modulate place fields do not also modulate their directional influences. That directional cue learning generalizes across contexts in this way, whereas the extra-maze cue learning (described earlier) did not, provides added support for the argument that the inputs to place cells are functionally differentiated.

8. Context configurations

Accepting our contextual modulation findings as support for Nadel and Willner's earlier-discussed contention [3] that contextual stimuli exist in a hierarchical relationship with the other stimuli that drive behavior (of either the animals as a whole or their place cells), the next question concerns the 'microstructure' of this contextual information. In other words, how is the information organized? Do contextual stimuli modulate place cell activity as a set of disparate elements, or are these stimuli combined to form a unitary, compound input, so that the place cells as a collective receive a single piece of information telling them which context they are in, and therefore which field they should each express?

We discussed earlier the concept that some kinds of behavior can only be explained if it is assumed that stimuli are bound together as packages, known as 'configurations'. When stimuli are combined in this way, the resulting configuration is able to enter into a relationship with the US independently of its elements. Some kind of configural process is needed to explain how animals can learn negative patterning tasks (of the form $A + , B + , AB -$), in which two stimuli that are rewarded by themselves become unrewarded if presented together, transverse patterning (of the form $A + B - B + C - C + A -$), in which each of three stimuli is rewarded when paired with one of the other two and unrewarded when paired with the other, and bi-conditional discrimination (of the form $AB + , CD + , AC - , BD -$), in which two pairs of stimuli are each rewarded, but when their elements are cross-paired the new pairings are both unrewarded. Again, linearly inseparable tasks like these can only be learned if the stimulus compound can form relationships with the US independently of the stimulus elements by themselves.

The hippocampus was identified as a possible site for configuration formation by Sutherland and Rudy [59], who proposed that animals with hippocampal lesions should not be able to solve configural tasks like negative and transverse patterning. However, a great deal of subsequent research has found that while rats with hippocampal formation damage are sometimes impaired in transverse [60] and negative [19] patterning, they can solve a variety of other tasks which should also require formation of configural representations [61,62]. This, as Rudy and Sutherland themselves have pointed out [63], argues strongly against an obligatory role for the hippocampus in forming stimulus configurations, but it leaves open the possibility that it might be required for the formation of *some* kinds of configuration. In particular, several investigators have suggested that it is needed for the configuration of contextual stimuli [3,15,28]. This is an interesting suggestion because, if true, it reinforces the earlier-discussed idea that the brain does not treat all kinds of stimuli equivalently (with, in this case, a particular structure being able to configure some kinds of stimuli but not others).

That contexts might be represented configurally in normal animals is suggested by a number of findings. For example, pre-exposure to the context for at least a few minutes is required for subsequent contextual fear conditioning to occur efficiently [28], in contrast with discrete stimuli, for which pre-exposure attenuates subsequent conditioning [64]. This suggests that an animal needs time to assemble a context representation before being able to learn about its predictive relationships with other stimuli. Rudy and O'Reilly found that rats underwent normal fear conditioning when pre-exposed to a context, but not if exposed to its elements individually [65], again suggesting that the elements of a context are somehow bound together prior to entering into further learning relationships. Evidence for a role for the hippocampus in this kind of representation has been, however, somewhat mixed. Animals with hippocampal lesions show impairments in contextual fear conditioning, while continuing to successfully condition to a single stimulus [16,17], again suggesting that the hippocampus treats contexts and single stimuli differently.

Despite the above findings, contextual conditioning, as discussed earlier, is sometimes spared by hippocampal lesions [19,66]. While on the face of it this argues against a configural role for the hippocampus, there are other interpretations for the mixture of results that has emerged from various studies (see Ref. [18] for review). One is that some kinds of context-learning task may be amenable to either a configural or a 'features based' (elemental) solution, with hippocampally lesioned animals sometimes able to learn using the latter solution if the former is disabled. For example, studies of anterograde vs. retrograde lesion effects find that hippocampal lesions or pharmacological disruption impair the performance of tasks based on previously learned contextual information but not of tasks requiring new context learning [67]. It has been suggested [20] that this disparity occurs because an undamaged animal will preferentially use a configural context representation to solve a contextual conditioning task, and lose the representation (and hence the solution to the task) when the lesion is made. By contrast, an already-lesioned animal, which cannot form a configural context representation at all, will focus on one of the available contextual stimuli and use that to solve the task in an elemental way (i.e. as if it were an ordinary discrete conditioned stimulus).

An alternative interpretation is that context-learning tasks differ in the requirements they make of the animal's processing machinery. As discussed earlier, while some kinds of context learning occur automatically and may or may not be necessary for a particular kind of learning to occur ('incidental' or 'background' context processing), others require the explicit formation of a context representation in order to solve a task ('contingent' or 'foreground' context processing). These two kinds of context learning have been distinguished on the basis of their susceptibility to hippocampal lesions [29,68], with incidental processing

being impaired in hippocampally lesioned animals and contingent processing being unaffected. This finding accords with the suggestion of Morris and Frey that the hippocampus is involved in automatically recording ‘attended experience’ [69], and also Tolman’s earlier suggestion [70] that spatial information, for which the hippocampus has a special role, is collected automatically (‘latent learning’) regardless of the presence of reinforcers. Putting these ideas together, the picture that is emerging is that the hippocampus automatically collects information about stimuli defining the environment and assembles these into configural representations which can enable incidental contextual learning.

9. Contextual modulation of place fields

How do these ideas pertain to contextual modulation of place fields? Using configural learning theory as a framework, we explored this issue by dissociating sets of contextual stimuli to see how place cells would respond. The idea was that if place cells treat sets of contextual stimuli as configurations, then every unique combination of stimuli should be treated as a unique configuration, eliciting a unique response. By contrast, if the cells respond to individual (or ‘elemental’) stimuli then either the cells should collectively follow only one of the stimuli, all the cells remapping in unison when this stimulus is changed, or else each cell should follow one of the stimuli but different cells should follow different stimuli. As we show below, place cells seem to receive their context information as sets of elements, supporting the idea that their role might be to synthesize a configural context representation from these elements.

We created [71] the compound contexts from two elements, a ‘color’ (actually black or white, to be called color for simplicity) and an odor (lemon or vanilla). Each context was a 60 cm² and 50 cm high recording box, with inner walls composed of scented Plexiglas and outer walls composed of black or white painted wood, enabling changing of the color of the box without affecting the odor, and vice versa. With these manipulations we thus created four contexts: black lemon, black vanilla, white lemon and white vanilla, pseudorandomly varied. Two questions were of particular interest (Fig. 6):

1. Would the changes in context induced by changing the color, odor or both, cause remapping in all cells simultaneously (complete remapping) or would only some cells remap (partial remapping)?
2. Would the patterns of remapping seen indicate that the cells received the contextual stimuli as elements, or as pre-configured compounds?

Fig. 7 shows some of the varieties of remapping that occurred in response to the hybrid contexts. As is evident

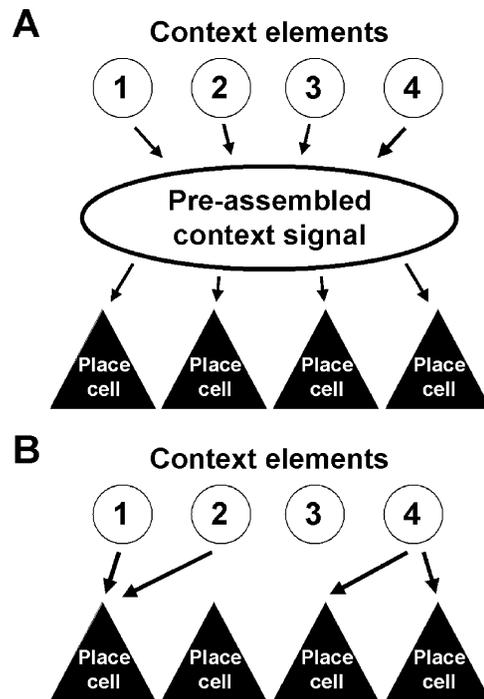


Fig. 6. Two possible ways in which contextual information could affect place cells. (A) The various elements making up a given context may be processed upstream of the hippocampus, the output being passed to the whole population of place cells as a coherent, unified representation. (B) The elements making up the context could be passed to the place cells individually, so that different place cells receive different portions of the available information about context.

from the figure, different cells responded differently, so that some remapped in response to color and not odor, some to odor and not color, and some (the great majority) to various combinations of color and odor. Thus, the answer to question 1 above is that any given change to a box caused only some of the place fields to remap. Furthermore, different subsets of the population responded to different elemental changes to the environment. Thus, the answer to question 2 is that, apparently, place cells do not all receive (or at least respond to) the same information about context.

This finding of heterogeneity of contextual modulation parallels similar findings with regard to focal (as opposed to global ‘contextual’ global) stimuli. Studies of rats performing a radial maze task found that following disjunctive rotation of local and distal cues, some cells followed the local cues and some the distal [72,73], a finding that has been replicated by Knierim [74]. Our observation that context cues are similarly dissociable adds to the growing evidence suggesting that attractor dynamics (acting to keep the place cell representation coherent) may be overridden by sensory cues under some circumstances.

It seems, then, that place cells are not in receipt of a unitary, pre-configured context signal, but instead respond to individual stimuli (at least under the conditions tested here). For an animal to use the place cells to distinguish the four contexts, it would need information from a population of the cells, since no given place cell has all the information

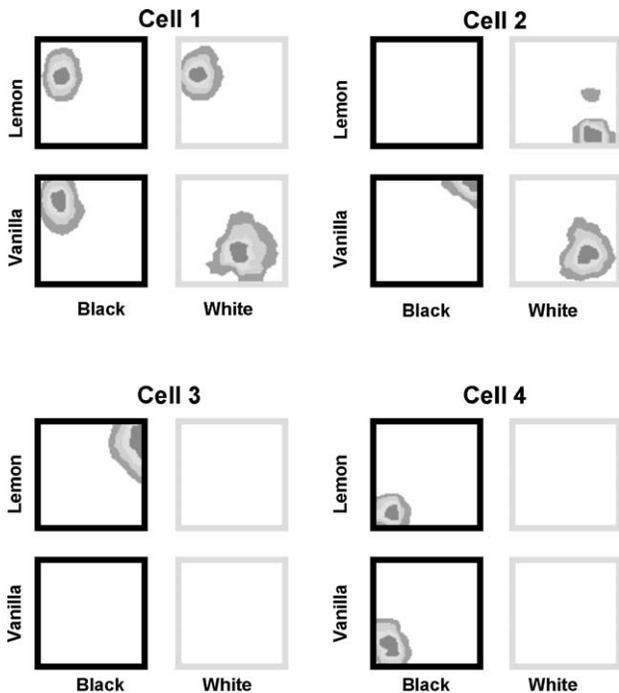


Fig. 7. Firing fields of four place cells recorded in four different contexts varying in two stimulus dimensions, color (black or white) and odor (lemon or vanilla). Different cells showed different patterns of remapping, indicating that they received different combinations of the contextual stimuli. Thus, the place cell population does not receive a single, preprocessed context signal. Adapted from Ref. [71].

that uniquely distinguishes a given context. This supports the suggestion discussed earlier that at least one function of the place cells might be to synthesize a compound context representation from a collection of elements.

Using our context-gating model of place field generation as a framework, it is possible to model the pattern of inputs that a given place cell may receive in order to produce its particular remapping pattern (Fig. 8). To explain the heterogeneity of remapping patterns we saw, it is assumed that the geometric inputs (the so-called boundary inputs) receive combinations of contextual stimuli, with different inputs receiving different combinations, weighted differentially so that some inputs are stronger than others.

Interestingly, although different fields could respond differently even though generated by the same place cell, we never saw independently remapping fields expressed in the same environment. For example, we never saw a cell with one field responding to color and one to odor that expressed both fields in the environment containing both the correct color and the correct odor. This suggests that there is some kind of competitive process that causes suppression of one of the boundary inputs in a situation where the other is active.

Also interestingly, we did not reliably (i.e. not more than expected by chance) see ‘bi-conditional’ responding, in which the same field was present in non-overlapping

contexts but not in the others—for example, in black lemon and white vanilla but not in white lemon or black vanilla. In other words, there was little evidence that the contextual stimuli arrived in pre-configured packages (such as ‘black lemon’ or ‘white vanilla’). This suggests that place cells only receive contextual inputs elementally.

How might our proposed architecture for the representation of spatial context map onto the anatomy of the hippocampal formation? At present, there is a relatively scant body of evidence to enable much more than loose speculation. Cells in the entorhinal cortex have been reported to resist changes in non-spatial context cues [50], stretching their firing fields to fit the shape of the environment, and thus might be the source of the boundary inputs. Alternatively, Sharp [53] has reported that cells in the subiculum, which is both an input to and an output from the hippocampus, respond to the shape of the environment in a context-independent manner. She has suggested [75] that the entorhinal cortex and subiculum co-operate to form a context-independent ‘universal map’ which the hippocampus uses to form the context-specific representations needed to encode episodic memories. Non-spatial contextual information such as odor might come through entorhinal cortex or might be routed through subcortical structures via the medial septum. The postulated interaction of the contextual and boundary inputs could take place anywhere upstream of CA1. CA3 remains an interesting possible site of such interaction, due to its rich recurrent architecture, and we have plans to investigate this and other possibilities further.

To summarize the experimental findings presented above, it appears that place cells have some of the properties that might be expected of a context representation, given what we know about such a representation from behavioral studies. These are as follows:

1. They are located in the hippocampus, a structure known to be important for (some kinds of) contextual learning.
2. They form their initial fields automatically and rapidly when the animal enters a new environment, a property consistent with the notion of ‘incidental’, or latent, context learning.
3. They are responsive to changes in context, in that they alter their spatial firing patterns in response to non-spatial context changes.
4. They seem to be driven by the elements of a compound context rather than by configurations of elemental stimuli. Thus, they do not (as individuals) receive a complete description of the context, but must synthesize one themselves by collectively pooling their information.

The findings summarized above lead to the possibility of an operational definition of contextual stimuli, which is ‘those stimuli that modulate the spatial firing of place cells’. By this definition, ‘spatial context’ is the collective

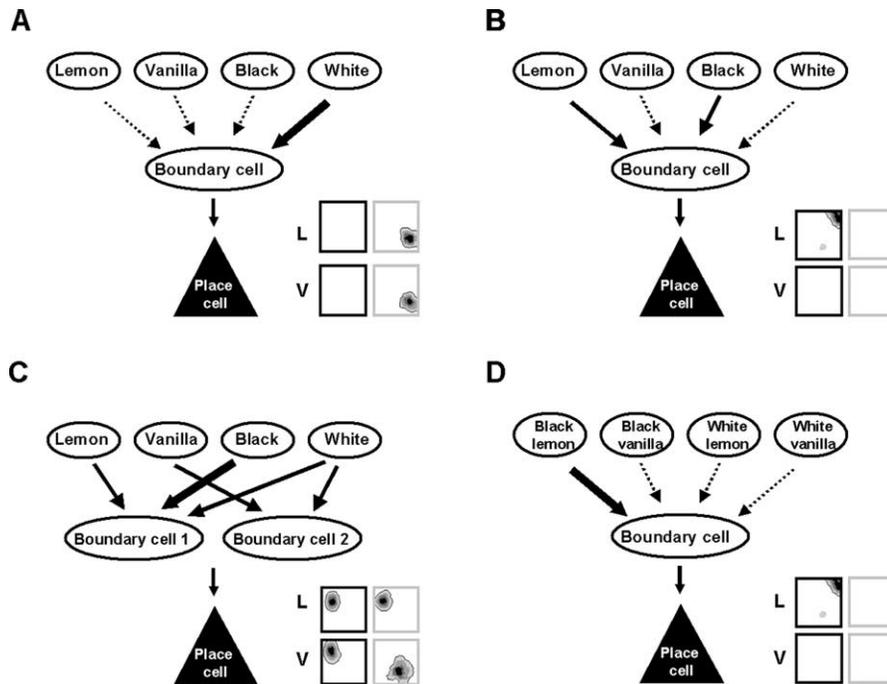


Fig. 8. Four different patterns of contextual remapping of place cells, modeled by assuming that context elements drive (in sets) the spatial inputs onto the cells. The strength of the connections is indicated by the thickness of the arrows and the box outlines indicate whether the box was black or white. (A) This field is expressed in the white box regardless of its odor, so it is assumed to have a strong connection from white and weak or non-existent connections from black or from the odors. (B) This field is only expressed in the black lemon box, and so it is assumed the boundary inputs receive weak connections from black and lemon which, when paired, can drive the cell. (C) This cell has two fields. One is present in the black box regardless of odor, and so presumably receives a strong black input. It is also present in the white box but only when the box is also lemon, so it is assumed that the same boundary input set receives weak connections from white and lemon which, when combined, are sufficient to drive the cell. The other field is only present when the box is both white and vanilla, and it is assumed that the boundary inputs determining this field are driven by weak inputs from these two elements. (D) An alternative explanation for the field also shown in (B) is that the boundary inputs receive configural inputs in which the color and odor have been paired somewhere upstream. However, we saw no evidence of configured context elements (such as bi-conditional firing: a field expressed in two non-overlapping contexts but not in the intermediate ones). Adapted from Ref. [71].

representation that results when such stimuli interact with the place cells to produce a population-coded activity. Operational definitions are by their nature circular, since the process of finding a properly matching term for a not-yet-fully-delineated phenomenon is something of a bootstrapping exercise. In the present case, having observed that changes in context cause remapping, it becomes convenient to *define* contextual stimuli as being those stimuli that cause (complex) remapping. It remains to be seen whether this continues to be a useful terminology, or whether some stimuli that cause remapping prove to be outside the bounds of what could reasonably be called 'context', in which case a new term may be required.

10. Context and behavior

What are the functional consequences of a contextually modulated representation of place? An obvious adaptive value lies in allowing an animal to express different behaviors in the same environment, according to what other (context) cues are present. An extensive literature

exists to show that rodents can use contextual cues to gate their responses to particular cues, and insects [76,77] and even nematodes [78] are capable of learning to associate different environmental cues with different behaviors. This means that an animal has added flexibility in how it behaves in particular situations.

There is a difficulty with the straightforward use of context to guide behavior, however, which is that the different contexts in which different behaviors are required may overlap in some of their elements. For example, a rat might need to know that its neighboring stream is dry in the summer but provides water in winter, unless it has frozen over, and that predators are around in the night but not the day but only in the summer, and that food can be found at night near the stream when it contains water. Therefore, if the rat is thirsty and it is winter it should go to the stream, and if it is hungry and it is summer it should go to the stream but only if it is also night, but then it must be careful of predators, and so on. Thus, its representation of context needs to contain multiple elements, of which different combinations are linked with different behaviors.

Such complex requirements of a context representation immediately suggest a function for the population coding of context seen in the place cells. Because different place cells respond to different combinations of context elements, by associating only a subset of these with a particular outcome it would be possible, in principle, to link an arbitrary set of context elements with a particular behavior, and a different (even if overlapping) set with a different behavior. By this model, the place cells act as a kind of contextual hidden layer, allowing arbitrary combinations of (spatial) contextual stimuli to be associated with different behaviors. Thus, it is possible to have a behavior that generalizes across all contexts (by being connected to everything) or discriminates between all contexts (by being connected to one thing only) or any variation in between. This endows an animal's behavioral repertoire with great flexibility.

Leaving flexibility aside for the moment, contextual remapping of place fields presents an interesting problem for the assumption that the place cells comprise a spatial map, for the following reason: if the context changes, and the place cells remap their fields, how will the animal be able to navigate to a goal that it learned in the previous context? While a context-specific representation allows

flexibility of behavior, a great deal of this advantage would be lost if, in the new context, the animal were unable to access information it had acquired in the other context (the context-specific acquisition of discriminative spatial information by place cells, which we discussed earlier, being a case in point). What happens to an animal's spatial knowledge when the context changes and the place cells remap?

We investigated this question [79] using a simple spatial task in which rats were required, on hearing a tone, to proceed to one of the four corners of a square black recording box in order to obtain a sugary reward. During the inter-trial intervals the animals foraged for rice grains so that place cells could be recorded. Hippocampal lesions prevented the acquisition of this task, consistent with the idea that it involved a spatial component and—according to cognitive map theory—should have required the place cell representation. After the task had been learned, the box was changed from black to white, provoking remapping of almost all the observed place cells (Fig. 9). Such reorganization of the place cell map should, in theory, have blocked the ability of the animals to retrieve information that had been associated with the previous map. However, despite this place map reorganization, the animals continued to navigate to

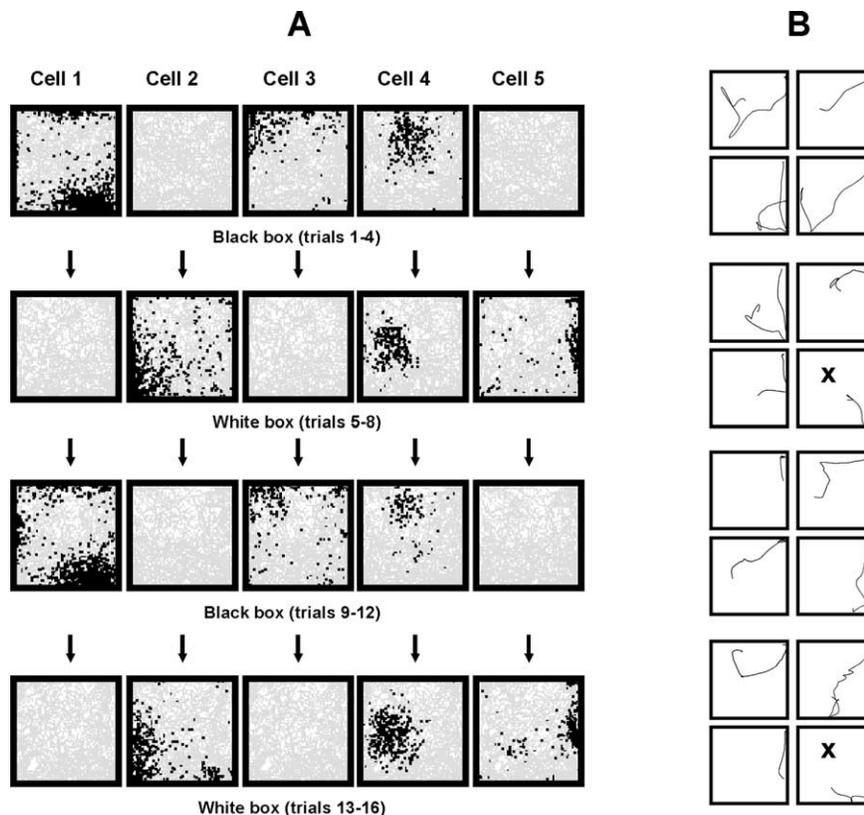


Fig. 9. Dissociation between the remapping behavior of place cells and the preserved spatial performance of rats in a task whose learning was nevertheless hippocampus-dependent. Rats were trained to proceed to one corner of a square black box to retrieve food, and then tested in a white box. (A) Plots of raw spikes, combined in sets of four two-minute trials, showing that in the inter-trial foraging periods the different colored boxes produced very different place cell firing patterns. (B) Behavioral data for the blocks of four trials shown in A. Note that despite place cell remapping when the box was changed from black to white, rats continued to choose the correct box corner on most trials. Adapted from Ref. [79].

the correct corner of the box, with only a small decrement in performance. Thus, if knowledge of the goal location was associated to the original place cell map, it nevertheless transferred successfully to the new map. The representation of the goal, in other words, was not context specific.

This finding is puzzling in light of the role that cognitive map theory assigns to place cells, but reassuring for our intuitive sense that a change in context ought not to render other information completely inaccessible. Under natural learning conditions, some kinds of information are relevant only to one context and others are relevant to several or all contexts, and it would clearly be adaptive for an animal to be able to rapidly determine which applies to which situation and to either generalize its responses or keep them context-specific, as appropriate. Thus, the preservation of spatial knowledge across a context change makes adaptive sense. But what does it imply for the hypothesis that place cell activity is the animal's spatial knowledge?

Our favored explanation for these results is that the place cells are not the sole site for the representation of spatial knowledge, and that other brain areas—which remain unaltered following context changes—can support navigation when the place cells remap. In other words, the animals could, in the face of place cell remapping, use other spatial representations (for example, those based on landmark recognition) to locate the correct goal corner. There are precedents for multiple 'maps' in other brain areas, such as primary visual, auditory and somatosensory areas, and for similar reasons it seems plausible that spatial information could be represented in multiple places, for multiple different purposes. In this light, a context-modulated representation might arguably exist for making context-specific information available for use, in tandem with the purely spatial representation that exists in parallel. In humans, such a representation might be useful in supporting episodic memory [80], which is memory for events that occurred in a unique spatio-temporal context [81]. The purely spatial computations underlying navigation may take place elsewhere, perhaps, as Sharp has suggested [75], in subiculum or entorhinal cortex. In fact, the true cognitive map, if there is such a thing, may be distributed across a number of brain areas.

11. Conclusion

In thinking about context, behavioral and theoretical work on its role in learning has identified the following questions that pertain to a given situation:

1. Is context irrelevant to executing a behavioral task and thus processed automatically (incidental, or implicit processing, apparently dependent on the hippocampus) or does the animal need to attend to it to solve a problem (contingent, or explicit processing, not dependent on the hippocampus)?
2. Is there a hierarchical or flat relationship between contextual and other stimuli?
3. Can/does an animal use just one particular contextual stimulus element to solve a problem, or must it know about how they are combined as compounds (configurations)?
4. Where and how does the brain represent context, and can study of this representation find parallels between behavioral and neural phenomena?

The hippocampal place cells form a plausible substrate for the representation of context, because they respond to both geometric and non-geometric aspects of an environment, and because lesions to the hippocampus abolish many kinds of context-dependent learning. Studies of place cells find that their properties in many ways parallel the properties of context processing that have been revealed by behavioral studies. Place cells express place fields in response to sets of (geometric and non-geometric) stimuli regardless (as far as we can tell) of whether an animal has paid explicit attention to them, and hence seem to act as agents for automatic encoding ('latent learning') of the environment, and thus for incidental context processing—something that is susceptible to hippocampal lesions. Furthermore, contextual stimuli seem to gate the geometric inputs onto place cells in a manner analogous to the way in which they modulate CS–US relationships. We have here discussed evidence that the contextual modulation of place cell firing is heterogeneous, a finding that casts some doubt on the widely accepted notion that the place cell representation is maintained in a coherent state by CA3 attractor dynamics. Rather, it seems that the place cells are more sensory-driven and less cohesive than is often supposed. This finding of input heterogeneity suggests constraints on the way in which context is processed in the hippocampus. Because a given place cell responds to only a subset of the available context elements, a particular context can only be uniquely represented by the activity of a population of place cells, since any one cell does not receive complete information about which context the animal is in. Such population coding of context allows for the possibility that different subsets of context elements can be associated with different behaviors. It means that an animal is endowed with the capacity to either discriminate between or generalize across them, depending on circumstances, and is thus equipped to behave flexibly in response to varying environmental conditions.

Acknowledgements

The work was supported by Wellcome Trust and BBSRC grants to KJ. The authors would like to thank Mark Good, Colin Lever and Robin Murphy for useful comments on the manuscript.

References

- [1] Pavlov IP. *Conditioned Reflex*. Oxford University Press, Oxford; 1927.
- [2] Skinner BF. *The behavior of organisms*. Appleton-Century-Crofts, New York; 1938.
- [3] Nadel L, Willner J. Context and conditioning: a place for space. *Physiol Psychol* 1980;8:218–28.
- [4] Rescorla RA. Probability of shock in the presence and absence of CS in fear conditioning. *J Comp Physiol Psychol* 1968;66:1–5.
- [5] Odling-Smee FJ. The role of background stimuli during Pavlovian conditioning. *Q J Exp Psychol* 1975;27:201–9.
- [6] Penick S, Solomon PR. Hippocampus, context, and conditioning. *Behav Neurosci* 1991;105:611–7.
- [7] Honey RC, Good M. Selective hippocampal lesions abolish the contextual specificity of latent inhibition and conditioning. *Behav Neurosci* 1993;107:22–33.
- [8] Pearce JM, Bouton ME. Theories of associative learning in animals. *Annu Rev Psychol* 2001;52:111–39.
- [9] Nadel L, Willner J, Kurz EM. Cognitive maps and environmental context; 1985. p. 385–406.
- [10] O'Keefe J, Nadel L. *The hippocampus as a cognitive map*. Clarendon Press, Oxford; 1978.
- [11] Wood ER, Dudchenko PA, Robitsek RJ, Eichenbaum H. Hippocampal neurons encode information about different types of memory episodes occurring in the same location. *Neuron* 2000;27:623–33.
- [12] Markus EJ, Qin YL, Leonard B, Skaggs WE, McNaughton BL, Barnes CA. Interactions between location and task affect the spatial and directional firing of hippocampal neurons. *J Neurosci* 1995;15:7079–94.
- [13] O'Keefe J, Dostrovsky J. The hippocampus as a spatial map. Preliminary evidence from unit activity in the freely-moving rat. *Brain Res* 1971;34:171–5.
- [14] Suzuki W, Clayton N. The hippocampus and memory: a comparative and ethological perspective. *Curr Opin Neurobiol* 2000;10:768–73.
- [15] Hirsh R. The hippocampus and contextual retrieval of information from memory: a theory. *Behav Biol* 1974;12:421–44.
- [16] Kim JJ, Fanselow MS. Modality-specific retrograde amnesia of fear. *Science* 1992;256:675–7.
- [17] Phillips RG, LeDoux JE. Differential contribution of amygdala and hippocampus to cued and contextual fear conditioning. *Behav Neurosci* 1992;106:274–85.
- [18] Holland PC, Bouton M. Hippocampus and context in classical conditioning. *Curr Opin Neurobiol* 1999;9:195–202.
- [19] McDonald RJ, Murphy RA, Guarraci FA, Gortler JR, White NM, Baker AG. Systematic comparison of the effects of hippocampal and fornix-fimbria lesions on acquisition of three configural discriminations. *Hippocampus* 1997;7:388.
- [20] Anagnostaras SG, Gale GD, Fanselow MS. Hippocampus and contextual fear conditioning: recent controversies and advances. *Hippocampus* 2001;11:8–17.
- [21] Good M, Honey RC. Dissociable effects of selective lesions to hippocampal subsystems on exploratory behavior, contextual learning, and spatial learning. *Behav Neurosci* 1997;111:487–93.
- [22] McNish KA, Gewirtz JC, Davis M. Evidence of contextual fear after lesions of the hippocampus: a disruption of freezing but not fear-potentiated startle. *J Neurosci* 1997;17:9353–60.
- [23] Gewirtz JC, McNish KA, Davis M. Is the hippocampus necessary for contextual fear conditioning? *Behav Brain Res* 2000;110:83–95.
- [24] Winocur G, Rawlins JN, Gray JA. The hippocampus and conditioning to contextual cues. *Behav Neurosci* 1987;101:617–25.
- [25] Winocur G. Hippocampal lesions alter conditioning to conditional and contextual stimuli. *Behav Brain Res* 1997;88:219–29.
- [26] Anagnostaras SG, Maren S, Fanselow MS. Temporally graded retrograde amnesia of contextual fear after hippocampal damage in rats: within-subjects examination. *J Neurosci* 1999;19:1106–14.
- [27] Maren S, Aharonov G, Fanselow MS. Neurotoxic lesions of the dorsal hippocampus and Pavlovian fear conditioning in rats. *Behav Brain Res* 1997;88:261–74.
- [28] Fanselow MS. Factors governing one-trial contextual conditioning. *Anim Learn Behav* 1990;18:264–70.
- [29] Good M, de-Hoz L, Morris RG. Contingent versus incidental context processing during conditioning: dissociation after excitotoxic hippocampal plus dentate gyrus lesions. *Hippocampus* 1998;8:147–59.
- [30] Muller RU, Kubie JL. The effects of changes in the environment on the spatial firing of hippocampal complex-spike cells. *J Neurosci* 1987;7:1951–68.
- [31] O'Keefe J, Black AH. Single unit and lesion experiments on the sensory inputs to the hippocampal cognitive map. *Ciba Found Symp* 1977;179–98.
- [32] O'Keefe J, Conway DH. Hippocampal place units in the freely moving rat: why they fire where they fire. *Exp Brain Res* 1978;31:573–90.
- [33] Jeffery KJ, Donnett JG, Burgess N, O'Keefe JM. Directional control of hippocampal place fields. *Exp Brain Res* 1997;117:131–42.
- [34] O'Keefe J, Speakman A. Single unit activity in the rat hippocampus during a spatial memory task. *Exp Brain Res* 1987;68:1–27.
- [35] Samsonovich A, McNaughton BL. Path integration and cognitive mapping in a continuous attractor neural network model. *J Neurosci* 1997;17:5900–20.
- [36] Redish AD, Touretzky D. The role of the hippocampus in solving the Morris water maze. *Neural Comput* 1998;10:73–111.
- [37] Tsodyks MV. Attractor neural network models of spatial maps in hippocampus. *Hippocampus* 1999;9:481–9.
- [38] Kali S, Dayan P. The involvement of recurrent connections in area CA3 in establishing the properties of place fields: a model. *J Neurosci* 2000;20:7463–77.
- [39] Quirk GJ, Muller RU, Kubie JL. The firing of hippocampal place cells in the dark depends on the rat's recent experience. *J Neurosci* 1990;10:2008–17.
- [40] Save E, Cressant A, Thinus-Blanc C, Poucet B. Spatial firing of hippocampal place cells in blind rats. *J Neurosci* 1998;18:1818–26.
- [41] Wiener SI, Berthoz A, Zugaro MB. Multisensory processing in the elaboration of place and head direction responses by limbic system neurons. *Brain Res Cogn Brain Res* 2002;14:75–90.
- [42] O'Keefe J, Burgess N. Geometric determinants of the place fields of hippocampal neurons. *Nature* 1996;381:425–8.
- [43] Jeffery KJ, O'Keefe J. Learned interaction of visual and idiothetic cues in the control of place field orientation. *Exp Brain Res* 1999;127:151–61.
- [44] Sharp PE, Kubie JL, Muller RU. Firing properties of hippocampal neurons in a visually symmetrical environment: contributions of multiple sensory cues and mnemonic processes. *J Neurosci* 1990;10:3093–105.
- [45] Sharp PE, et al. Influences of vestibular and visual motion information on the spatial firing patterns of hippocampal place cells. *J Neurosci* 1995;15:173–89.
- [46] Knierim JJ, Kudrimoti HS, McNaughton BL. Interactions between idiothetic cues and external landmarks in the control of place cells and head direction cells. *J Neurophysiol* 1998;80:425–46.
- [47] Bostock E, Muller RU, Kubie JL. Experience-dependent modifications of hippocampal place cell firing. *Hippocampus* 1991;1:193–205.
- [48] Kentros C, Hargreaves E, Hawkins RD, Kandel ER, Shapiro M, Muller RV. Abolition of long-term stability of new hippocampal place cell maps by NMDA receptor blockade. *Science* 1998;280:2121–6.
- [49] Frank LM, Brown EN, Wilson M. Trajectory encoding in the hippocampus and entorhinal cortex. *Neuron* 2000;27:169–78.
- [50] Quirk GJ, Muller RU, Kubie JL, Ranck JB Jr. The positional firing properties of medial entorhinal neurons: description and comparison with hippocampal place cells. *J Neurosci* 1992;12:1945–63.
- [51] Wilson MA, McNaughton BL. Dynamics of the hippocampal ensemble code for space. *Science* 1993;261:1055–8.

- [52] Lever C, Wills T, Cacucci F, Burgess N, O'Keefe J. Long-term plasticity in hippocampal place-cell representation of environmental geometry. *Nature* 2002;416:90–4.
- [53] Sharp PE. Subicular cells generate similar spatial firing patterns in two geometrically and visually distinctive environments: comparison with hippocampal place cells. *Behav Brain Res* 1997;85:71–92.
- [54] Jeffery KJ, Anderson MI. Dissociation of the geometric and contextual influences on place cells. *Hippocampus* 2003;13:868–72.
- [55] Hayman R, Chakraborty S, Jeffery KJ. Context-specific acquisition of location discrimination by hippocampal place cells. *Eur J Neurosci* 2003;18:2825–34.
- [56] Jeffery KJ. Plasticity of the hippocampal cellular representation of place. In: Holscher, C (Ed), *Neuronal Mechanisms of Memory Formation*. Cambridge University Press, Cambridge; 2001.
- [57] Knierim JJ, Kudrimoti HS, McNaughton BL. Place cells, head direction cells, and the learning of landmark stability. *J Neurosci* 1995;15:1648–59.
- [58] Jeffery KJ. Learning of landmark stability and instability by hippocampal place cells. *Neuropharmacology* 1998;37:677–87.
- [59] Sutherland RJ, Rudy JW. Configural association theory: the role of the hippocampal formation in learning, memory, and amnesia. *Psychobiology* 1989;17:129–44.
- [60] Alvarado MC, Rudy JW. Rats with damage to the hippocampal-formation are impaired on the transverse-patterning problem but not on elemental discriminations. *Behav Neurosci* 1995;109:204–11.
- [61] Gallagher M, Holland PC. Preserved configural learning and spatial learning impairment in rats with hippocampal damage. *Hippocampus* 1992;2:81–8.
- [62] Whishaw IQ, Tomie A. Rats with fimbria-fornix lesions can acquire and retain a visual-tactile transwitching (configural) task. *Behav Neurosci* 1995;109:607–12.
- [63] Rudy JW, Sutherland RJ. Configural association theory and the hippocampal formation: an appraisal and reconfiguration. *Hippocampus* 1995;5:375–89.
- [64] Lubow R. Latent inhibition. *Psychol Bull* 1973;79:398–407.
- [65] Rudy JW, O'Reilly RC. Contextual fear conditioning, conjunctive representations, pattern completion, and the hippocampus. *Behav Neurosci* 1999;113:867–80.
- [66] Frankland PW, et al. The dorsal hippocampus is essential for context discrimination but not for contextual conditioning. *Behav Neurosci* 1998;112:863–74.
- [67] Young S, Bohenek D, Fanselow M. NMDA processes mediate anterograde amnesia of contextual fear conditioning induced by hippocampal damage: immunization against amnesia by context preexposure. *Behav Neurosci* 1994;108:19–29.
- [68] Phillips RG, Russel G, LeDoux J. Lesions of the dorsal hippocampal formation interfere with background but not foreground contextual fear conditioning. *Learn Mem* 1994;1:34–44.
- [69] Morris RG, Frey U. Hippocampal synaptic plasticity: role in spatial learning or the automatic recording of attended experience? *Philos Trans R Soc Lond B Biol Sci* 1997;352:1489–503.
- [70] Tolman EC. Cognitive maps in rats and men. *Psychol Rev* 1948;40:40–60.
- [71] Anderson MI, Jeffery KJ. Heterogeneous modulation of place cell firing by changes in context. *J Neurosci* 2003;23:8827–35.
- [72] Tanila H, Shapiro ML, Eichenbaum H. Discordance of spatial representation in ensembles of hippocampal place cells. *Hippocampus* 1997;7:613–23.
- [73] Shapiro ML, Tanila H, Eichenbaum H. Cues that hippocampal place cells encode: dynamic and hierarchical representation of local and distal stimuli. *Hippocampus* 1997;7:624–42.
- [74] Knierim JJ. Dynamic interactions between local surface cues, distal landmarks, and intrinsic circuitry in hippocampal place cells. *J Neurosci* 2002;22:6254–64.
- [75] Sharp PE. Complimentary roles for hippocampal versus subicular/entorhinal place cells in coding place, context, and events. *Hippocampus* 1999;9:432–43.
- [76] Collett T, Fauria K, Dale K. Contextual cues and insect navigation. In: Jeffrey, K (Ed), *The Neurobiology of Spatial Behaviour*, Oxford University Press, Oxford; 2003. p. 67–82.
- [77] Weiss M, Papa D. Colour learning in two behavioural contexts: how much can a butterfly keep in mind? *Anim Behav* 2003;65:425–34.
- [78] Rankin CH. Context conditioning in habituation in the nematode *Caenorhabditis elegans*. *Behav Neurosci* 2000;114:496–505.
- [79] Jeffery KJ, Gilbert A, Burton S, Strudwick A. Preserved performance in a hippocampal dependent spatial task despite complete place cell remapping. *Hippocampus* 2003;13:133–47.
- [80] Burgess N, Maguire EA, O'Keefe J. The human hippocampus and spatial and episodic memory. *Neuron* 2002;35:625–41.
- [81] Tulving E. *Elements of episodic memory*. Clarendon Press, Oxford; 1983.